Biological Report 85(1.1)
March 1985

Contaminant Hazard Reviews
Report No. 1

MIREX HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Mirex (dodecachlorooctahydro - 1,3,4 - metheno - 2H - cyclobuta (c, d) pentalene) has been used extensively in pesticidal formulations to control the imported fire ant (*Solenopsis invicta*), and as a flame retardant in electronic components, plastics, and fabrics. One environmental consequence of mirex was the severe damage recorded to fish and wildlife in nine Southeastern States and the Great Lakes, especially Lake Ontario. In 1978, the U.S. Environmental Protection Agency banned all further use of mirex, partly because of the hazards it imposed on nontarget biota. These included delayed mortality and numerous birth defects in aquatic and terrestrial fauna; tumor formation; histopathology; wildlife population alterations; adverse effects on reproduction, early growth, and development; high biomagnification and persistence; degradation into toxic metabolites; movement through aquatic and terrestrial environmental compartments; disrupted mammalian energy metabolism; and detection of residues in human milk and adipose tissues.

Among susceptible species of aquatic organisms, significant damage effects were recorded when concentrations of mirex in water ranged from 2 to 3 ppb. Evidence suggested that sensitive species of wildlife are adversely affected at 0.1 ppm of dietary mirex. For comparison, current tolerance limits for mirex in food for human consumption range from 0.01 ppm for raw agricultural commodities to 0.1 ppm for eggs, milk, and animal fat to 0.4 ppm for various seafood products. Additional research is needed on the fate of mirex degradation products and their effects on natural resources. Further, it is strongly recommended that environmental use of all mirex replacement compounds be preceded by intensive ecological and toxicological evaluation. (Eisler, R. 1985. Mirex hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.1), Contaminant Hazard Reviews Report No. 1. 42 pp.)

Table of Contents

TABLES

INTRODUCTION

Fish and wildlife resources associated with approximately 51 million ha (125 million acres) in the Southeastern United States, and with the Great Lakes, especially Lake Ontario, have been negatively affected by intensive or widespread use of mirex, a chlorinated hydrocarbon compound (Waters et al. 1977; Bell et al. 1978; Kaiser 1978; NAS 1978; Lowe 1982). Contamination of the Southeast and of Lake Ontario by mirex probably occurred between 1959 and 1978. During that period, mirex was used as a pesticide to control the imported fire ant (*Solenopsis invicta*), which infested large portions of Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, and Texas. Under the trade name of Dechlorane, mirex was used as a fire retardant in electronic components, fabrics, and plastics; effluents from manufacturing processes resulted in the pollution of Lake Ontario.

Regulatory agencies, environmentalists, and the general public became concerned as evidence accumulated demonstrating that mirex was associated with high death rates, numerous birth defects, and tumors, and that it disrupted metabolism in laboratory mammals, birds, and aquatic biota. Mirex also tends to bioaccumulate and to biomagnify at all trophic levels of food chains. Field studies corroborated the laboratory

findings and showed that mirex appeared to be one of the most stable and persistent organochlorine compounds known, being resistant to chemical, photolytic, microbial, metabolic, and thermal degradation processes. Upon degradation, a series of potentially hazardous metabolites are formed, although it is generally acknowledged that the fate and effects of the degradation products are not fully understood. Mirex was also detected in human milk and adipose tissues at low concentrations, the levels related to the degree of environmental contamination.

In 1978, the U.S. Environmental Protection Agency banned all uses of mirex. It is probable, however, that mirex and its metabolites will continue to remain available to living organisms in this country for at least 12 years, although some estimates range as high as 600 years. In this account, I briefly review the evidence leading to the ban of mirex, with emphasis on afflicted natural resources, and provide current recommendations for the protection of fish and wildlife resources. It is part of a continuing series of synoptic reviews prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service.

CHEMICAL PROPERTIES

Mirex is a white, odorless, free-flowing, crystalline, nonflammable, polycyclic compound composed entirely of carbon and chlorine; the empirical formula is $C_{10}Cl_{12}$, and the molecular weight 545.54 (Hyde 1972; Waters et al. 1977; Bell et al. 1978; NAS 1978; Menzie 1978; Kaiser 1978). In the United States, the common chemical name is dodecachlorooctahydro-1,3,4 - metheno - 2H - cyclobuta(c,d)pentalene; the systematic name is dodecachloropentacyclo $5.3.0.0^{2,6}.0^{3,9}.0^{4,8}$decane. Mirex was first prepared in 1946, patented in 1955 by Allied Chemical Company, and introduced in 1959 as GC 1283 for use in pesticidal formulations against hymenopterous insects, especially ants. It was also marketed under the trade name of Dechlorane for use in flame retardant coatings for various materials. Mirex is also known as ENT 25719 (Tucker and Crabtree 1970), CAS 2385-85-5 (Schafer et al. 1983), Dechlorane 510, and Dechlorane 4070 (Kaiser 1978). Technical grade preparations of mirex consists of 95.19% mirex and less than 2.58×10^{-7} % contaminants, mostly kepone $C_{10}Cl_{10}0$ (NAS 1978).

Mirex is comparatively soluble in various organic solvents, such as benzene, carbon tetrachloride and xylene, with solubilities ranging from about 4,000 to 303,000 ppm (mg/L). However, mirex has a very low solubility in water, not exceeding 1.0 ppb (µg/L) in freshwater or 0.2 ppb in seawater (Bell et al. 1978). In biological systems, mirex lipophilicity would account for the high concentrations observed in fatty tissues and reserves.

Mirex, which is composed of 22% carbon and 78% chlorine, is highly resistant to chemical, thermal, and biochemical degradation. It is reportedly unaffected by strong acids, bases, and oxidizing agents, and is resistant to photolysis in hydrocarbon solvents, but less so in aliphatic amines. Thermal decomposition begins at about 550°C and is rapid at 700°C; degradation products include hexachlorobenzene, hexachlorocyclopentadiene, and kepone. Several additional degradation products of mirex have been isolated, but not all have been identified (Holloman et al. 1975; Menzie 1978). At least one photodegradation product, the 8-monohydro analog, sometimes accumulates in sediments and animals, but the fate and effects of these photoproducts is unclear (Cripe and Livingston 1977).

Mirex is rapidly adsorbed onto various organic particles in the water column, including algae, and eventually is removed to the sediments. Not surprisingly, mirex has a long half-life in terrestrial and aquatic sediments; large fractional residues were detected at different locations 12 and 5 years after initial application (Bell et al. 1978). Some degradation of mirex to the 10-monohydro analog was reported in anaerobic sewage sludge after 2 months in darkness at 30°C (Menzie 1978). Other studies with mirex-contaminated anaerobic soils, anaerobic lake sediments, and soil microorganisms showed virtually no bacterial degradation over time (Jones and Hodges 1974). In Lake Ontario, mirex from contaminated sediments remained available to lake organisms for many years and, as judged by present sedimentation rates, mirex may continue to be bioavailable for 200 to 600 years in that system (Scrudato and DelPrete 1982). Disappearance of mirex from baits over a 12-month period was about 41% for those exposed on the ground, 56% from those exposed in soil, and 84% from those exposed in pond water (de la Cruz and Lue 1978b). Mirex disappearance was probably related to uptake by biological organisms, as has been demonstrated in marine ecosystems contaminated with mirex (Waters et al.

1977), and not to degradation.

Mirex is a highly stable chlorinated hydrocarbon with lipophilic properties, and its accumulation and persistence in a wide variety of nontarget biological species has been well documented. The biological half-life of mirex reportedly ranges from 30 days in quail to 130 days in fish and to more than 10 months in the fat of female rats (Menzie 1978); this subject area is further developed later. At this juncture, it is sufficient to state that most authorities agree on two points: there is little evidence of significant mirex metabolism; and mirex ranks among the more biochemically stable organic pesticides known.

TOXICITY

AQUATIC ORGANISMS

Aquatic organisms are comparatively resistant to mirex in short term toxicity tests. Among various species of freshwater biota, LC-50 (96 h) values were not obtained at the highest nominal concentrations tested of 1,000 ppb for insects, daphnids, and amphipods (Johnson and Finley 1980; Sanders et al. 1981) and 100,000 ppb for five species of fish (Johnson and Finley 1980). Similar results were reported for other species of freshwater invertebrates (Muncy and Oliver 1963; Lue and de la Cruz 1978) and fishes (Van Valin et al. 1968), although waterborne mirex at concentrations of 1,000 ppb was lethal to postlarval freshwater prawns (*Macrobrachium rosenbergerii*) in 24 h (Eversole 1980). It is probable that bioavailable concentrations from the water in each test did not exceed 1.0 ppb. However, delayed mortality frequently occurs for extended periods after exposure, and the potential for adverse effects at the population level remains high (NAS 1978). Latent biocidal properties of mirex were documented for fish (Van Valin et al. 1968; Koenig 1977) and crustaceans (Ludke et al. 1971; Hyde 1972; Cripe and Livingston 1977). Crustaceans were the most sensitive group examined. For example, the crayfish (*Procambarus blandingi*) immersed in nominal concentrations of 0.1 to 5.0 ppb mirex for periods of 6 to 144 h died 5 to 10 days after initial exposure (Ludke et al. 1971). Immature crayfish were more sensitive than adults, and mortality patterns were similar when mirex was administered in the water or in baits (Ludke et al. 1971).

BIRDS AND MAMMALS

Acute oral toxicity of mirex to warm blooded organisms was low, except for rats and mice, which died 60 to 90 days after treatment with 6 to 10 mg mirex/kg body weight (Table 1). Birds were comparatively resistant. The red-winged blackbird (*Agelaius phoeniceus*) was unaffected at 100 mg mirex/kg body weight, even though it was considered the most sensitive of 68 species of birds tested with 998 chemicals for acute oral toxicity, repellency, and hazard potential (Schafer et al. 1983).

Mortality due to dietary mirex is variable among species, although high death rates were usually associated with high dietary concentrations and long exposure periods (Table 2). One significant effect of mirex fed to breeding adult chickens, voles, and rats was a decrease in survival of the young (Naber and Ware 1965; Shannon 1976; Waters et al. 1977; Chu et al. 1981). Prairie voles (*Micropterus ochrogaster*) fed diets containing 15 ppm of mirex bred normally, but all pups died by day 21 (Shannon 1976). Survival of the pups of prairie voles decreased in the first litter when the diet of the parents contained 10 ppm mirex, in the second litter when it contained 5 ppm, and in the third litter when it contained 0.1, 0.5, 0.7, or 1.0 ppm (Shannon 1976).

Table 1. Acute oral toxicity of mirex to birds and mammals.

Organism	Dose, in mg/kg body weight	Mortality	Reference
Mice, *Mus* sp.	5	None, 60 days posttreatment	Gaines and Kimbrough 1969
Rat, female, *Rattus* sp.	6	50%, 90 days posttreatment	Gaines and Kimbrough 1969
Mice	10	100%, 60 days posttreatment	Gaines and Kimbrough 1969
Red-winged blackbird	100	None	Schafer et al. 1983
Mice	100-132	50% in 10 days	Fujimori et al. 1983
Common quail, *Coturnix coturnix*	300	12-30%	Stickel 1963
Rat, male	306	Some	Hyde 1972
Mice	330	50%	Waters et al. 1977

Rat, female	365	50%, 14 days posttreatment	Gaines and Kimbrough 1969
Rat, male	400	Lowest fatal dose	NAS 1978
Rat, female	500	Lowest fatal dose	NAS 1978
European starling, *Sturnus vulgaris*	562	None	Schafer et al. 1983
Rat, female	600	Some	Hyde 1972
Rabbit, *Lepus* sp.	800[a]	50%	Waters et al. 1977
Dogs, *Canis* sp.	1000	None	Larson et al. 1979
Ring-necked pheasant, *Phasianus colchicus*	1400-1600	50%	Waters et al. 1977
Mallard, *Anas platyrhynchos*	2400	None	Tucker and Crabtree 1970
Japanese quail, *Coturnix coturnix japonica*	10,000	50%	Waters et al. 1977

[a] Dermal

Table 2. Dietary toxicity of mirex to vertebrate organisms.

Organism	Mirex dietary concentration, in ppm	Exposure interval	Percent mortality	Reference
Mallard	1.0	25 weeks	6.2	Hyde 1972
Old-field mouse, *Peromyscus polionotus*	1.8	60 weeks	20.0	Wolfe et al. 1979
Mice	5.0	30 days	Some	Chernoff et al. 1979
Prairie vole	5.0-15	90 days	Some	Shannon 1976
Old-field mouse	17.8	60 weeks	91.7	Wolfe et al. 1979
Beagle dog	20	13 weeks	None	Larson et al. 1979
Pinfish, Lagodon *rhomboides*	20	20 weeks	None	Lowe 1982
Prairie vole	25	90 days	100	Shannon 1976
Rat	25	30 days	Some	Chernoff et al. 1979
Rat	50	14 days	None	NAS 1978
Mice	50	14 days	100	NAS 1978
Coho salmon	50	12 weeks	None	Leatherland et al. 1979
Beagle dog	100	13 weeks	Some	Larson et al. 1979
Mallard	100	25 weeks	27.4	Hyde 1972
Channel catfish	400	4 weeks	None	McCorkle et al. 1979
Ring-necked pheasant	1540	5 days	50.0	Heath et al. 1972
Common bobwhite, *Colinus virginianus*	2511	5 days	50.0	Heath et al. 1972
Japanese quail	5000	5 days	20.0	Heath et al. 1972
Mallard ducklings	5000	5 days	None	Heath et al. 1972

SUBLETHAL EFFECTS

AQUATIC ORGANISMS

The maximum acceptable toxicant concentration (MATC) values calculated for mirex and various freshwater species were <2.4 ppb for amphipods (*Gammarus* sp.), based on growth inhibition at higher concentrations (Sanders et al. 1981); 2 to 3 ppb for fathead minnows (*Pimephalas promelas*), as judged by disruption of swim bladder hydroxyproline content, vitamin C metabolism, and bone collagen (Mehrle et al. 1981); 34 ppb for fathead minnows, based on impaired reproduction (Buckler et al. 1981); and >34 ppb for daphnids (*Daphnia* sp.) and midges (*Chaoborus* sp.), predicated on daphnid reproduction and midge emergence (Sanders et al. 1981). Other mirex-induced sublethal effects included reduced photosynthesis in freshwater algae (Hollister et al.

1975), gill and kidney histopathology in the goldfish *Carassius auratus* (Van Valin et al 1968), reduced growth in the bluegill *Lepomis macrochirus* (Van Valin et al. 1968), cessation of reproduction in *Hydra* sp. (Lue and de la Cruz 1978), and disrupted behavior in the blue crab *Callinectes sapidus* (Shannon 1976) and the marine annelid *Arenicola cristata* (Schoor and Newman 1976). McCorkle et al. (1979) showed that channel catfish (*Ictalurus punctatus*) are particularly resistant to high dietary concentrations of mirex; juveniles fed 400 ppm mirex for 4 weeks showed no significant changes in enzyme-specific activities of brain, gill, liver, or muscle. However, yearling coho salmon (*Oncorhynchus kisutch*) fed 50 ppm mirex for 3 months showed significant reduction in liver weight and whole body lipid content (Leatherland et al. 1979). Additional studies with coho salmon and rainbow trout (*Salmo gairdneri*) fed 50 ppm mirex for 10 weeks demonstrated a significant depression in serum calcium, and significant elevation of skeletal magnesium in salmon; trout showed no measurable changes in calcium and magnesium levels in serum, muscle, or skeleton, although growth was reduced, muscle water content was elevated, and muscle lipid content was reduced (Leatherland and Sonstegard 1981). Interaction effects of mirex with other anthropogenic contaminants are not well studied, despite the observations of Koenig (1977) that mixtures of DDT and mirex produced more than additive deleterious effects on fish survival and reproduction.

BIRDS

Among captive American kestrels (*Falco sparverius)* fed 8 ppm mirex for 69 days by Bird et al. (1983), there was a marked decline in sperm concentration and a slight compensatory increase in semen volume, but an overall net decrease of 70% in sperm number. These investigators believed that migratory raptors feeding on mirex-contaminated food organisms could ingest sufficient toxicant to lower semen quality in the breeding season which, coupled with altered courtship, could reduce the fertility of eggs and the reproductive fitness of the individual. Altered courtship in ring-necked doves (*Streptopelia capicola*) fed dietary organochlorine compounds was reported by McArthur et al. (1983).

Most investigators, however, agree that comparatively high dietary concentrations of mirex had little effect on growth, survival, reproduction, and behavior of nonraptors, including chickens (*Gallus* sp.), mallards, several species of quail, and red-winged blackbirds. For domestic chickens, levels up to 200 ppm dietary mirex were tolerated without adverse effects on various reproductive variables (Waters et al. 1977), but 300 ppm mirex for 16 weeks was associated with reduced chick survival, and 600 ppm for 16 weeks reduced hatching by 83% and chick survival by 75% (Naber and Ware 1965). Mallard ducklings experienced temporary mild ataxia and regurgitation when given a single dose of 2,400 mg/kg body weight but not when given 1,200 mg/kg or less (Tucker and Crabtree 1970). Mallards fed up to 100 ppm mirex for prolonged periods showed no significant differences from controls in egg production, shell thickness, shell weight, embryonation, hatchability, or duckling survival (Hyde 1972). However, in other studies with mallards fed 100 ppm dietary mirex, eggshells were thinned and duckling survival was reduced (Waters et al. 1977), suggesting that 100 ppm dietary mirex may not be innocuous to mallards. No adverse effects on reproduction were noted in the common bobwhite at 40 ppm dietary mirex (Kendall et al. 1978), or in two species of quail fed 80 ppm mirex for 12 weeks (Waters et al. 1977). Red-winged blackbirds were not repelled by foods contaminated with mirex, but consumed normal rations (Schafer et al. 1983); a similar observation was recorded for bobwhites (Baker 1964).

MAMMALS

Mirex has considerable potential for chronic toxicity since it is only partly metabolized, is eliminated very slowly, and is accumulated in the fat, liver, and brain. The most common effects observed in small laboratory mammals fed mirex included weight loss, enlarged livers, altered liver enzyme metabolism, and reproductive failure. Mirex reportedly crossed placental membranes and accumulated in fetal tissues. Among the progeny of mirex-treated mammals, developmental abnormalities included cataracts, heart defects, scoliosis, and cleft palates (NAS 1978).

Mirex has caused liver tumors in mice and rats and must be considered a potential human carcinogen (Waters et al. 1977; NAS 1978). Long-term feeding of 50 and 100 ppm of mirex to rats of both sexes was associated with liver lesions that included neoplastic nodules and hepatocellular carcinomas; neither sign was found in controls (Ulland et al. 1977).

Adults of selected mammalian species showed a variety of damage effects of mirex: enlarged livers in rats at 25 ppm dietary mirex (Gaines and Kimbrough 1969) or at a single dose of 100 mg/kg body weight (Ervin

1982); liver hepatomas in mice at 10 mg mirex/kg body weight daily (Innes et al. 1969); decreased incidence of females showing sperm in vaginal smears, decreased litter size, and thyroid histopathology in rats fed 5 ppm dietary mirex since weaning (Chu et al. 1981); elevated blood and serum enzyme levels in rats fed 0.5 ppm mirex for 28 days (Yarbrough et al. 1981); and diarrhea, reduced food and water consumption, body weight loss, decreased blood glucose levels, and disrupted hepatic microsomal mixed function oxidases in mice receiving 10 mg/kg daily (Fujimori et al. 1983). In studies of field mice, decreased litter size was observed at 1.8 ppm dietary mirex, and complete reproductive impairment at 17.6 ppm after 6 months (Wolfe et al. 1979). At comparatively high sublethal concentrations of mirex, various deleterious effects were observed: thyroid histopathology and decreased spermatogenesis in rats fed 75 ppm mirex for 28 days (Yarbrough et al. 1981); abnormal blood chemistry, enlarged livers, reduced spleen size, and loss in body weight of beagles fed 100 ppm for 13 weeks (Larson et al. 1979); and decreased hemoglobin, elevated white blood cell counts, reduced growth, liver histopathology, and enlarged livers in rats fed 320 ppm for 13 weeks (Larson et al. 1979).

Cataract formation, resulting in blindness, in fetuses and pups from maternal rats fed comparatively low concentrations of dietary mirex is one of the more insidious effects documented. Mirex fed to maternal rats at 6 mg/kg body weight daily on days 8-15 of gestation, or at 10 mg/kg daily on days 1-4 postpartum, caused cataracts in 50% of fetuses on day 20 of gestation, and in 58% of pups on day 14 postpartum (Rogers 1982). Plasma glucose levels were depressed in fetuses with cataracts, and plasma proteins were depressed in neonates; both hypoproteineia and hypoglycemia are physiological conditions known to be associated with cataracts (Rogers 1982). Mirex-associated cataractogenicity has been reported in female pups from rats fed 5 ppm dietary mirex since weaning (Chu et al. 1981), in rat pups from females consuming 7 ppm dietary mirex on days 7-16 of gestation or 25 ppm in diets for 30 days prior to breeding (Chernoff et al. 1979), and in mice fed 12 ppm dietary mirex (Chernoff et al. 1979). Offspring born to mirex-treated mothers, but nursed by nontreated mothers showed fewer cataracts (Waters et al. 1977). Other fetotoxic effects in rats associated with dietary mirex included: edema and undescended testes (Chernoff et al. 1979); lowered blood plasma proteins, and heart disorders, including tachycardia and blockages (Grabowski 1981); and, as noted by Kavlock et al (1982), hydrocephaly; decreases in weight of brain, lung, liver, and kidney; decreases in liver glycogen, kidney proteins and alkaline phosphatase; and disrupted brain DNA and protein metabolism.

In prairie voles exposed continuously to dietary mirex of 0.5, 0.7, 1.0, 5.0, or 10.0 ppm, the numbers of litters produced decreased (Shannon 1976). Maximum number of litters per year were four at 1.0 ppm dietary mirex; three at 5.0 ppm; and two at 10.0 ppm. Furthermore, the number of offspring per litter also decreased progressively. Concentrations as low as 0.1 ppm in the diet of adults were associated with delayed maturation of pups and with an increase in number of days required to attain various behavioral plateaus such as bar-holding ability, hind-limb placing, and negative geotaxis (Shannon 1976). On the basis of residue data from field studies, as is shown later, these results strongly suggest that mirex was harmful to the reproductive performance and behavioral development of prairie voles at environmental levels approaching 4.2 g mirex/ha, a level used to control fire ants before mirex was banned.

BIOACCUMULATION

AQUATIC ORGANISMS

All aquatic species tested accumulated mirex from the medium and concentrated it over ambient water levels by factors ranging up to several orders of magnitude; uptake was positively correlated with nominal dose in the water column (Table 3). Other investigators have reported bioconcentration factors from water of 8,025X in daphnids (Sanders et al. 1981), 12,200 in bluegills (Skaar et al. 1981), 56,000 in fathead minnows (Huckins et al. 1982), and 126,600 in the digestive gland of crayfish (Ludke et al. 1971). Rapid uptake of mirex by marine crabs, shrimps, oysters, killifishes, and algae was reported after the application of mirex baits to coastal marshes (Waters et al. 1977; Cripe and Livingston 1977). Mirex was also accumulated from the diet (Table 3; Ludke et al. 1971; Zitko 1980) but not as readily as from the medium. Mirex may also be accumulated from contaminated sediments by marine teleosts (Kobylinski and Livingston 1975), but such accumulation has not been established conclusively. Although terrestrial plants, such as peas and beans, accumulate mirex at field application levels, mangrove seedlings require environmentally high levels of 11.2 kg mirex/ha before accumulation occurs (Shannon 1976).

There is general agreement that aquatic biota subjected to mirex-contaminated environments continue to accumulate mirex, and that equilibrium is rarely attained before death of the organism from mirex poisoning or

from other causes. There is also general agreement that mirex resists metabolic and microbial degradation, exhibits considerable movement through food chains, and is potentially dangerous to consumers at the higher tropic level (Hollister et al. 1975; NAS 1978; Mehrle et al. 1981). Marine algae, for example, showed a significant linear correlation between amounts accumulated and mirex concentrations in the medium. If a similar situation existed in nature, marine unicellular algae would accumulate mirex and, when grazed upon, act as passive transporters to higher trophic food chain compartments (Hollister et al. 1975). The evidence for elimination rates of mirex from aquatic biota on transfer to mirex-free media is not as clear. Biological half-times of mirex have been reported as 12 h for daphnids (Sanders et al. 1981), more than 28 days for fathead minnows (Huckins et al. 1982), about 70 days in Atlantic salmon (*Salmo salar*) (Zitko 1980), 130 days for mosquitofish (*Gambusia affinis)*, and 250 days for pinfish (as quoted in Skea et al. 1981). However, Skea et al. (1981) averred that biological half-times may be much longer if organism growth is incorporated into rate elimination models. For example, brook trout *(Salvelinus fontinalis*) fed 29 ppm mirex for 104 days contained 6.3 mg/kg body weight or a total of 1.1 mg of mirex in whole fish. At day 385 postexposure, after the trout had tripled in body weight, these values were 2.1 mg/kg body weight, an apparent loss of 67%; however, on a whole fish basis, trout contained 1.2 mg, thus showing essentially no elimination on a total organism basis (Skea et al. 1981).

No mirex degradation products were detected in whole fathead minnow or in hydrosoils under aerobic or anaerobic conditions (Huckins et al. 1982). In contrast, three metabolites were detected in coastal marshes after mirex bait application, one of which, photomirex, was accumulated by fish and oysters (Cripe and Livingston 1977). The fate and effects of mirex photoproducts in the environment is unclear and merits additional research.

The significance of mirex residues in various tissues is unresolved, as is the exact mode of action of mirex and its metabolites. Minchew et al. (1980) and others indicated that mirex is a neurotoxic agent, with a mode of action similar to that of other chlorinated hydrocarbon insecticides, such as DDT. In studies with crayfish and radiolabeled mirex, mirex toxicosis was associated with neurotoxic effects that included hyperactivity, uncoordinated movements, loss of equilibrium, and paralysis (Minchew et al. 1980). Before death, the most significant differences in mirex distributions in crayfish were the increases in concentrations in neural tissues, such as brain and nerve cord, by factors up to 14X (or 0.4 ppm) in low-dose groups held in solutions containing 7.4 ppb mirex, and up to 300X (or 6.2 ppm) in high-dose groups held in solutions with 74.0 ppb. With continued exposure, levels in the green gland and neural tissues approached the levels in the hepatopancreas and intestine (Table 3). Schoor (1979) also demonstrated that mirex accumulates in the crustacean hepatopancreas, but suggested that other tissues, such as muscle and exoskeleton, have specific binding sites that, once filled, shunt excess mirex to hepatopancreas storage sites.

Table 3. Bioaccumulation of mirex from ambient medium or diet by selected species.

Habitat, organism, and tissue	Mirex concentration in ppb in medium (M), or in ppm in diet (D)	Exposure period	Bioconcentration factor	Reference[a]
FRESHWATER				
Fish				
Fathead minnow				
Whole	2.0 (M)	120 days	28,000	Buckler
"	7.0 (M)	120 days	18,400	et al. 1981
"	3.0 (M)	120 days	12,000	
"	34.0 (M)	120 days	13,800	
"	2.0 (M)	120 + 56 days	12,000	
"	7.0 (M)	120 + 56 days	6,860	
"	13.0 (M)	120 + 56 days	5,460	
"	34.0 (M)	120 + 56 days	7,880	
Bluegill				

Whole	1.3 (M)	60 days	1,540	Van Valin
"	1,000.0 (M)	90 days	150	et al. 1968
Goldfish				
Skin	100.0 (M)	224 days	1,220	
Muscle	100.0 (M)	224 days	460	
Liver	100.0 (M)	224 days	370	
Gut	100.0 (M)	224 days	1,520	
Atlantic salmon				
Whole	0.6 (D)	15 days	0.06	Zitko 1980
"	0.6 (D)	42 days	0.13	
Brook trout				
Whole	29.0 (D)	17 days	0.04	Skea
"	29.0 (D)	104 days	0.22	et al. 1981
"	29.0 (D)	104 + 385 days	0.07	
Crustaceans				
Crayfish				
Muscle	7.4 (M)	10-21 days	81	Minchew
Brain	7.4 (M)	(interval	54	et al. 1980
Nerve cord	7.4 (M)	represents	54	
Green gland	7.4 (M)	appearance of	243	
Gill	7.4 (M)	late symptoms	108	
Digestive gland	7.4 (M)	of mirex	622	
Intestine	7.4 (M)	toxicity)	257	
Muscle	74.0 (M)	7-14 days	8	
Brain	74.0 (M)	(see above)	80	
Nerve cord	74.0 (M)	(see above)	84	
Green gland	74.0 (M)	(see above)	76	
Gill	74.0 (M)	(see above)	23	
Digestive gland	74.0 (M)	(see above)	105	
Intestine	74.0 (M)	(see above)	43	
MARINE				
Fish				
Diamond killifish, Adinia xenica				
(Exposed adults)				
Embryo	1.5 (D)	9 days	1.7	Koenig 1977
"	6.0 (D)	9 days	1.3	
"	24.0 (D)	9 days	1.2	
"	96.0 (D)	9 days	0.9	
Hogchoker, Trinectes maculatus				
Muscle	56.0-5,000.0 (M)	4 weeks	3,800-10,400	Kobylinski and Livingston 1975
Striped mullet, Mugil cephalus				
Whole	10.0 (M)	4 days	17-38	Lee et al. 1975

Crustaceans				
Shrimp, Palaemonetes vulgaris				
Hepatopancreas	0.04 (M)	4 days	9,250	Schoor 1979
"	0.04 (M)	13 days	16,250	
Muscle	0.04 (M)	4 days	2,250	
"	0.04 (M)	13 days	2,000	
Whole	0.04 (M)	4 days	4,000	
"	0.04 (M)	13 days	3,250	
Algae				
Whole	0.04 (M)	13 days	375	Schoor 1979
Whole, 4 spp.	0.01 (M)	7 days	3,200-7,500	Hollister et al. 1975.
TERRESTRIAL				
Birds				
Chickens				
Fat	1.06 (D)	39 weeks	24	Waters et al. 1977
Kidney	1.06 (D)	39 weeks	3	
Liver	1.06 (D)	39 weeks	2	
Muscle	1.06 (D)	39 weeks	0.3	
Skin (chick)	1.0 (D)	2 weeks	37	Ahrens et al. 1980
Fat (chick)	1.0 (D)	2 weeks	586	
Mallards (exposed adults)				
Eggs	1 (D)	18 weeks	2.4	Hyde 1972
Eggs	100 (D)	18 weeks	28	
Fat	100 (D)	18 weeks	29	
American kestrels, yearling males				
Muscle lipids	8.0 (D)	69 days	7	Bird et al. 1983
Testes lipids	8.0 (D)	69 days	6	
Liver lipids	8.0 (D)	69 days	3	
Common bobwhite				
Fat	1.0 (D)	36 weeks	20	Kendall et al. 1978
"	20.0 (D)	36 weeks	10	
"	40.0 (D)	36 weeks	9.5	
Breast muscle	1.0 (D)	36 weeks	0.7	
" "	20.0 (D)	36 weeks	0.6	
" "	40.0 (D)	36 weeks	0.3	
Mammals				
Rat				
Adipose fat	3.0 (D)	6 days	16	NAS 1978
" "	12.5 (D)	6 days	23	
" "	5.0 (D)	16 weeks	62	Chu et al. 1981
" "	10.0 (D)	16 weeks	42	
" "	20.0 (D)	16 weeks	43	
" "	40.0 (D)	16 weeks	18	

Liver	5.0 (D)	16 weeks	1	
"	10.0 (D)	16 weeks	1.4	
"	20.0 (D)	16 weeks	1.6	
"	40.0 (D)	16 weeks	3	
Old-field mouse				
Liver	1.8 (D)	24 weeks	3.3	Wolfe et al. 1979
"	17.8 (D)	24 weeks	3.6	
Rhesus monkey, Macaca mulatta				
Fat	1.0 (D)	single dose	1.7-5.8	NAS 1978

[a]Reference cited applies to data in that row and to data in other rows immediately following.

BIRDS AND MAMMALS

Like aquatic organisms, birds and mammals accumulated mirex in tissue lipids, and the greater accumulations were associated with the longer exposure intervals and higher dosages (Table 3). Sexual condition of the organism may modify bioconcentration potential. For example, in adipose fat of the bobwhite, males contained 10X dietary levels and females only 5X dietary levels; the difference was attributed to mirex loss through egg laying (Kendall et al. 1978).

Data on excretion kinetics of mirex are incomplete. Prairie voles fed mirex for 90 days contained detectable whole body levels 4 months after being placed on a mirex-free diet (Shannon 1976). Levels of mirex in voles after 4 months on uncontaminated feed were still far above levels in their mirex diets. Humans living in areas where mirex has been used for ant control contained 0.16 to 5.94 ppm in adipose fat; 60% of the mirex was excreted and most of the rest was stored in body tissues, especially fat (28%), and in lesser amounts of 0.2 to 3% in muscle, liver, kidney, and intestines (Waters et al. 1977). Almost all excretion of mirex takes place through feces; less than 1% is excreted in urine and milk. The loss rate pattern is biphasic; the fast phase was estimated at 38 h and the slow phase at up to 100 days. Mirex binds firmly to soluble liver proteins and appears to be retained in fatty tissues, a property that may contribute to its long biological half-life. Chickens given single doses of mirex at 30 mg/kg intravenously or 300 mg/kg orally demonstrated a biphasic decline in blood concentrations (Ahrens et al. 1980). The fast component, constituting about 25% of the total, was lost during the first 24 h; the loss of the slow component was estimated to be at a constant rate of about 0.03% daily, suggesting a half-life of about 3 years. Growing chicks fed 1 or 10 ppm dietary mirex for 1 week lost the compound rather rapidly; disappearance half-times were 25 days for skin and 32 days for fat (Ahrens et al. 1980). It is clear that much additional research is warranted on loss rate kinetics of this persistent compound and its metabolites.

MIREX IN THE SOUTHEASTERN UNITED STATES

Between 1961 and 1975, about 400,000 kg of mirex were used in pesticidal formulations, of which approximately 250,000 kg were sold in the Southeastern U.S. for control of native and imported fire ants (*Solenopsis* spp.); most of the rest was exported to Brazil for use in fire ant control in that country (NAS 1978). Mirex was also used to control big-headed ant populations in Hawaiian pineapple fields (Bell et al. 1978), Australian termites (Paton and Miller 1980), South American leaf cutter ants, South African harvester termites, and, in the U.S., western harvester ants and yellow jackets (Shannon 1976). Chemical control measures for imported fire ants began in the Southeastern United States during the 1950s with the use of heptachlor, chlordane, and dieldrin. The large mounds built by ants in cultivated fields were believed to interfere with mowing and harvesting operations, the “vicious sting” of the insects presented a hazard to workers harvesting the crops, and the species was considered to be a pest in school playgrounds and homes (Lowe 1982). In 1965, the use of organochlorine insecticides to control fire ants was discontinued, due partly to their high acute toxicity to nontarget biota and their persistence. Previously used compounds were replaced by mirex 4X bait formulations, consisting of 0.3% mirex by weight, dissolved in 14.7% soybean oil, and soaked into corncob grits

(85%). Initially, the 4X baits were broadcast from low flying airplanes at a total yearly rate of 1.4 kg bait/ha (1.25 lbs total bait/acre) or 4.2 g mirex/ha. Usually, three applications were made yearly. More than 50 million ha in nine Southeastern States were treated over a 10-year period. Later, dosages were modified downward, and mirex was applied to mounds directly. Ecologically sensitive areas, such as estuaries, prime wildlife habitats, heavily forested areas, and State and Federal parks, were avoided. In 1977, for example, the formulation was changed to 0.1% mirex and the application rate lowered to 1.12 g/ha; about 8,200 kg of the lower concentration bait were manufactured in 1977 (Bell et al. 1978). Under ideal aerial application conditions, about 140 particles of mirex-impregnated bait were distributed/m^2. When an infested area is treated, the bait is rapidly scavenged by the oil-loving fire ant workers, placed in the mound, and distributed throughout the colony, including queen and brood, before any toxic effects become evident; death occurs in several days to weeks. The exact mode of action is unknown, but is believed to be similar to that of other neurotoxic agents, such as DDT (Waters et al. 1977; NAS 1978).

Widespread use of mirex may lead to altered population structure in terrestrial systems, with resurgence or escalation of nontarget pests due to selective mirex-induced mortality of predators (NAS 1978). For example, populations of immature horn flies and rove beetles, two species of arthropods normally preyed upon by fire ants, were higher in mirex-treated areas than in control areas (Howard and Oliver 1978). Conversely, other species, such as crickets, ground beetles, and various species of oil-loving ants, were directly affected and populations were still depressed or eliminated 14 months posttreatment (NAS 1978), whereas fire ants recovered to higher than pretreatment levels, as judged by mound numbers and mound size (Summerlin et al. 1977).

Field results from aquatic and terrestrial ecosystems receiving mirex bait formulations indicated, with minor exceptions, that mirex accumulates sequentially in food complexes and concentrates in animals at the higher trophic levels. In both ecosystems, omnivores and top carnivores contained the highest residues (Hyde 1972; Shannon 1976; Waters et al. 1977; de la Cruz and Lue 1978a; Hunter et al. 1980). In South Carolina, where the 4X formulation was used to control fire ants from 1969 to 1971, mirex was translocated from treated lands to nearby marshes and estuarine biota, including crustaceans, marsh birds, and raccoons (Lowe 1982). Juvenile marine crustaceans showed delayed toxic effects after ingesting mirex baits, or after being exposed to low concentrations in seawater. About 18 months posttreatment, mirex residues of 1.3 to 17.0 ppm were detected in shrimp, mammals, and birds (Table 4); however, 24 months after the last mirex treatment, less than 10% of all samples collected contained detectable residues (Lowe 1982). A similar study was conducted in pasturelands of bahia grass (*Paspalum notatum*) (Markin 1981). Within a month after application, the target fire ant colonies were dead. Of the 4.2 g mirex/ha applied to the 164 ha block, 100% was accounted for on day 1, 63% at 1 month, and 3% at 1 year (Table 5). Unaccounted mirex residues could include loss through biodegradation; through movement out of the study area by migratory insects, birds, other fauna, and ground water; and through photodecomposition and volatilization (Markin 1981).

Mirex residues in bobwhites from South Carolina game management area were documented after treatment with 4.2 g mirex/ha (Kendall et al. 1977). Pretreatment residues in bobwhites ranged from nondetectable to 0.17 ppm mirex in breast muscle on a dry weight basis, and 0.25 to 2.8 ppm in adipose tissues on a lipid weight basis. Mirex residues in adipose tissue increased up to 5X within 1 month posttreatment and declined thereafter; however, another residue peak was noted in the spring after mirex treatment and corresponded with insect emergence (Kendall et al. 1977).

Heavily treated watershed areas in Mississippi were investigated by Wolfe and Norment (1973) and Holcombe and Parker (1979). After treatment, mirex residues were elevated in crayfish and stream fish; among mammals, residues were highest in carnivores and insectivores, lower in omnivores, and lowest in herbivores (Wolfe and Norment 1973). Mirex residues in liver and eggs were substantially higher in the box turtle *(Terrapene carolina)* an omnivorous feeder, than in the herbivorous slider turtle (*Chrysemys scripta*); mirex did not accumulate for protracted periods in tissues of these comparatively long-lived reptiles (Holcombe and Parker 1979). Among migratory reptiles, mirex was detected in only 11% of the eggs of the loggerhead turtle (*Caretta caretta*) and not at all in eggs of the green turtle (*Chelonia mydas*) corrected during summer 1976 in Florida (Clark and Krynitsky 1980). However, DDT or its isomers were present in all eggs of both species, and PCB's were detected in all loggerhead turtle eggs. The low levels of mirex and other organochlorine contaminants suggest that these turtles, when not nesting, live and feed in areas remote from Florida lands treated with mirex

and other insecticides (Clark and Krynitsky 1980).

Table 4. Mirex residues in water, sediments, and fauna in a South Carolina coastal marsh 18 months after application of 4.2 g/ha (after Lowe 1982).

Sample	Maximum mirex residues, in ppm	Percent samples with mirex residues
Water	<0.01	0
Sediments	0.7	1
Crabs	0.6	31
Fishes	0.8	15
Shrimp	1.3	10
Mammals	4.4	54
Birds	17.0	78

Table 5. Temporal persistence of residues for 1 year after applications of mirex 4X formulation to bahia grass pastures. Values represent rounded percentages recovered of the original 4.2 g/ha applied (after Markin 1981).

	Time, postapplication						
Sample	1 d	2 wk	1 mo	3 mo	6 mo	9 mo	12 mo
Imported fire ants	44	8	0	0	0	0	0
Grit from bait	40	35	a	-	-	-	-
Soil from mound	0.3	2	4	3	2	b	-
Pasture soil	18	18	52	26	24	5	3
Bahia grass	0.3	0.9	0.4	0.7	0.3	0.6	0.0
Invertebrates	0.3	0.2	0.3	0.2	0.0	0.1	0.1
Vertebrates	-	0.1	0.2	0.2	0.1	0.1	0.1
Not accounted for	0	35	43	69	74	94	97

[a]Grit now included with pasture soil.

[b]Mounds badly weathered, not possible to identify.

A 10-5 bait formulation containing 0.1% mirex was designed to make more of the toxicant available to the fire ant and less to nontarget biota. In one study, the 10-5 formulation was applied to a previously untreated 8,000-ha area near Jacksonville, Florida, infested with fire ants (Wheeler et al. 1977). The bait was applied by airplane at 1.12 kg/ha, or 1.12 g mirex/ha. Insects accumulated mirex to the greatest extent during the first 6 months after application, and most of the mirex was lost by 12 months (Table 6); other invertebrates accumulated only low levels during the first 9 months, and no residues were detected after 12 months. Fish also showed low concentrations for 9 months and no detectable residues afterward; amphibians contained detectable residues after 12 months, but not at 24; reptiles contained measurable, but low, residues for the entire 24-month study period. Mammals had higher residue levels than reptiles, particularly in fat, whereas birds contained low to moderate residues (Table 6). After 24 months, mirex was found infrequently and only at low concentrations in birds, mammals, reptiles, and insects. It was concluded that 10-5 mirex formulations were as effective in controlling fire ants as the 4X formulation and that residues in nontarget species were reduced from that following 4X treatment, or were lacking (Wheeler et al. 1977).

Eggs of the American crocodile (*Crocodylus acutus*) from the Florida Everglades contained up to 2.9 ppm fresh weight of DDE and 0.86 ppm of PCB'S, but less than 0.02 ppm mirex (Hall et al. 1979). Livers of the deep sea fish (*Antimora rostrata*) collected in 1971-74 from a depth of 2,500 m off the U.S. east coast, contained measurable concentrations of DDT and its degradation products, and dieldrin, but no mirex (Barber and Warlen 1979).

MIREX IN THE GREAT LAKES

Between 1959 and 1975, 1.5 million kg of mirex were sold, of which 74% or more than 1.1 million kg were predominantly Dechlorane, a compound used in flame-resistant polymer formulations of electronic components and fabrics (Bell et al., 1978; NAS 1978). The total amounts are only approximate because almost half the mirex sold from 1962 to 1973 could not be accounted for (NAS 1978). Kaiser (1978) reported that all fish species in Lake Ontario were contaminated with mirex, and that concentrations in half the species exceeded the Food and Drug Administration guideline of 0.1 ppm; other aquatic species had mirex residues near this level. Reproduction of the herring gull (*Larus argentatus*) on Lake Ontario was poor; mirex levels were an order of magnitude higher in gull eggs from Lake Ontario than in eggs from other Great Lakes locations (Kaiser 1978). It was concluded that the probable source of contamination was a chemical manufacturer that used mirex (Dechlorane) as a flame retardant, and that only Lake Ontario was contaminated (Kaiser 1978; NAS 1978).

Gilman et al. (1977, 1978) observed poor reproductive success and declines in colony size of the herring gull at Lake Ontario at a time when dramatic increases of this species were reported along the Atlantic seaboard. In 1975, herring gull reproduction in Lake Ontario colonies was about one-tenth that of colonies on the other four Great Lakes. In addition, in Lake Ontario colonies, there were reductions in nest site defense, in number of eggs per clutch, in hatchability of eggs, and in chick survival. Hatching success of Lake Ontario gull eggs was 23 to 26%, compared with 53 to 79% for eggs from other areas. Analysis of herring gull eggs from all colonies for organochlorine compounds and mercury demonstrated that eggs from Lake Ontario colonies had mean mirex levels of 5.06 ppm fresh weight (range, 2.0-18.6), or about 10X more mirex than any other colony. Mean PCB and mercury levels were up to 2.8X and 2.3X higher, respectively, in gull eggs from Lake Ontario than in those from other colonies, but only mirex levels could account for the colony declines (Gilman et al. 1977, 1978). As judged by log-linear regression models, the half-life for mirex in herring gull eggs was 1.9 to 2.1 years, or essentially none was lost during egg incubation (Weseloh et al. 1979). Reproductive success of the Lake Ontario herring gull colonies improved after the early 1970s, an improvement that was directly paralleled by a decline in mirex, other organochlorine pesticides, and PCB's (Weseloh et al. 1979).

Table 6. Mirex residues in fauna near Jacksonville, Florida, at various intervals posttreatment following single application of 1.12 g mirex/ha (after Wheeler et al. 1977).

Taxonomic group and time (in months posttreatment)	Maximum residue, in ppm wet weight whole organism
Insects	
1	4.1
3	19.8
6	7.8
12	1.1
24	0.8
Amphibians	
1	0.78
24	ND[a]
Reptiles	
1-9	1.2
24	0.06
Fish	
1	0.08
3-9	0.25
>>9	ND
Birds	
1-12	10.0 (fat)
9-24	b
Mammals	
1-6	3.4 (fat)
12-18	0.7 (fat)
24	0.09 (fat)

[a]ND = not detectable.

[b]Pretreatment levels.

Table 7. Mirex and its degradation products in herring gull eggs collected from the Great Lakes in 1977 (after Norstrom et al. 1980).

Compound	Mirex concentration, in ppm fresh weight	Percent of samples containing compound
Mirex	2.58	66.7
8-monohydro mirex (photomirex)	0.95	24.5
10-monohydro mirex	0.199	5.1
$C_{10}C1_{11}H$(III), possibly 9-monohydro mirex	0.077	2.0
$C_{10}Cl_{12}$(II)	0.039	1.0
2,8-dihydromirex	0.016	0.4
$C_{10}Cl_{10}H_2$(II), possibly 3,8-dihydromirex	0.011	0.3
Total	3.872	100

The fate of mirex in the environment and the associated transfer mechanisms have not been well defined (NAS 1978). One of the more significant works on this subject area was that by Norstrom et al. (1978), who documented levels of mirex and its degradation products in herring gull eggs collected from Lake Ontario in 1977 (Table 7). They concluded that photodegradation was the only feasible mechanism for production of the degradation compounds, although mirex and its photoproducts rapidly become sequestered in the ecosystem and protected from further degradation. Norstrom et al. (1980) found mirex degradation products in herring gull eggs from all of the Great Lakes, and suggested that a high proportion of mirex and related compounds in herring gull eggs from Lakes Erie and Huron originated from Lake Ontario fish, whereas lower levels in eggs from Lakes Superior and Michigan originated from other sources. Mirex in sediments was considered an unlikely source because it was not being recycled into the ecosystem at an appreciable rate.

Biomagnification of mirex through food chains was investigated by Norstrom et al. (1978). Their basic assumption was that both herring gulls and coho salmon ate alewives (*Alosa pseudoharengus)* and rainbow smelt (*Osmerus mordax*). Mirex residues in these organisms, in parts per million fresh weight, were 4.4 in gull eggs, 0.23 in salmon muscle, 0.10 in salmon liver, and 0.09 in whole alewives and smelt retrieved from stomachs of salmon. Bioconcentration factors (BCF) from prey to predator ranged up to 50, and those from water to gull egg were estimated to be near 25 million (Table 8). Norstrom et al. (1978) indicated that salmon muscle and gull eggs are complementary indicators of organochlorine contamination in the Great Lakes.

Among Great Lakes fishes, the highest mirex value recorded was 1.39 ppm in whole eels (*Anguilla* sp.) collected from Lake Ontario (NAS 1978). This was substantially in excess of the tolerated limit of 0.3 ppm for human consumption (NAS 1978). High mirex values were also reported in chinook salmon *(Oncorhynchus tshawytscha)* and coho salmon from South Sandy Creek, a tributary of Lake Ontario, during autumn 1976; as a consequence, possession of all fish from that area was prohibited by the State of New York (Farr and Blake 1979). The significance of mirex residues in salmonid fishes is unclear. Skea et al. (1981), in laboratory studies with brook trout, showed that whole body residues of 6.3 ppm fish weight were not associated with adverse effects on growth or survival and speculated that long-lived species, such as the lake trout (*Salvelinus namaycush*), would probably continue to accumulate mirex in Lake Ontario as long as they were exposed, and may continue to contain residues for most of their lives, even after the source has been eliminated.

There was no widespread mirex contamination of urban environments near Lake Ontario as a result of Dechlorane use, although local contamination of the Lake Ontario area was high when compared with other Great Lake areas (NAS 1978). Among humans living in the Great Lakes area, there was great concern that mother's milk might be contaminated, owing to the high lipophilicity of mirex. Bush (1983) found mirex concentrations in mother's milk from residents of New York State to be 0.07 ppb in Albany, 0.12 in Oswego, and 0.16 in Rochester, confirming that mirex was present in human milk but that concentrations were sufficiently low to be of little toxicological significance. It is noteworthy that none of the mothers had eaten Lake Ontario fish or any freshwater fish, and only a few had eaten marine fishes (Bush 1983). For a 5-kg infant consuming 500 g of milk daily, this amount would approximate a dietary intake of 0.01 µg mirex/kg body weight daily (Bush 1983) or about 1/10,000 of the lowest recorded dietary value causing delayed maturation in prairie voles (Shannon 1976). It is not known if a safety factor of 10,000 is sufficient to protect human health against delayed toxic effects of mirex, but it now appears reasonable to believe that it is.

Table 8. Biomagnification of mirex in Great Lakes food chains (after Norstrom et al. 1978).

From	To	Bioconcentration factor
Water	Whole rainbow smelt or whole alewife	500,000
Water	Muscle of coho salmon	1,500,000
Water	Egg of herring gull	25,000,000
Alewife and smelt	Salmon muscle	2.6
Alewife and smelt	Gull egg	50.0

MIREX IN OTHER GEOGRAPHIC AREAS

Mirex residues were determined in birds collected Nationwide or from large geographic areas of the United States; however, aside from the Southeast and the Great Lakes, concentrations were low, considered nonhazardous, and occurred in a relatively small proportion of the samples collected (Cain and Bunck 1983).

Among wings of mallards and American black ducks (*Anas rubripes)* collected from the four major flyways during 1976-77, mirex concentrations were highest and percent occurrence greatest in samples from the Atlantic Flyway: mallards, 50% occurrence, 0.14 ppm fresh weight; black ducks, 19% and 0.04 ppm (White 1979). Data for mallards collected from other flyways follow: Mississippi, 29% and 0.03 ppm; Central, 14% and 0.06 ppm; and Pacific 4% and 0.03 ppm (White 1979). Carcasses of several species of herons found dead or moribund Nationwide from 1966 to 1980 were analyzed for a variety of common organochlorine pesticides by Ohlendorf et al. (1981); they detected mirex in less than 15% of the carcasses, a comparatively low frequency, and only in nonhazardous concentrations. However, about 20% of all herons found dead or moribund had lethal or hazardous concentrations of dieldrin or DDT. In bald eagles *(Haliaeetus leucocephalus)* found dead Nationwide, elevated mirex levels were recorded in carcass lipids (24.0 ppm) and in fresh brain tissues (0.22 ppm) (Barbehenn and Reichel 1981). Among endangered species such as the bald eagle, it was determined that the most reliable indicator for assessing risk of organochlorine compounds was the ratio of carcass to brain residues on a lipid weight basis (Barbehenn and Reichel 1981). Wings from American woodcocks (*Philohela minor*) collected from 11 States in 1970-71 and 14 States in 1971-72 were analyzed for mirex and other compounds by McClane et al. (1978). Mirex residues in the 1971-72 wings showed the same geographical pattern of recovery as those observed in 1970-71: residues were highest in the Southern States and New Jersey, and lowest in the Northern and Midwestern States. Mirex residues were significantly lower in 1971-72 than in 1970-71. As judged by the analysis of wings of immature woodcocks in Louisiana, mirex residues were significantly lower in immatures than in adults: 2.48 ppm lipid weight vs. 6.20 ppm (McLane et al. 1978).

Mirex and other organochlorine compounds in eggs of anhingas (*Anhinga anhinga*) and 17 species of waders (including herons, egrets, bitterns, ibises, and storks) were measured in various locations throughout the Eastern United States during 1972 and 1973 (Ohlendorf et al. 1979). The highest mean concentration of 0.74 ppm mirex, range 0.19 to 2.5, was found in eggs of the green heron (*Butorides striatus*) from the Savannah National Wildlife Refuge in South Carolina; a single egg of the cattle egret (*Bubulcus ibis*) analyzed from there contained 2.9 ppm mirex. However, the overall frequency of mirex occurrence was higher in eggs collected from the Great Lakes region (24%) than in those from the South Atlantic Coast (15.6%), inland areas (10.7%), Gulf Coast (4.4%), or North Atlantic region (3.2%).

Measurable mirex residues were detected in migratory birds collected from a variety of locations, including areas far from known sources or applications of mirex. For example, 22% of all eggs from 19 species of Alaskan seabirds collected in 1973-76 contained mirex. The highest concentration was 0.044 ppm in eggs of a fork-tailed storm petrel (*Oceanodroma furcata*) from the Barren Islands. Mirex residues were low compared with those of other organochlorine compounds (Ohlendorf et al. 1982). Eggs from the clapper rail (*Rallus longirostris*) collected in New Jersey from 1972—74 contained 0.16 to 0.45 ppm mirex (Klaas et al. 1980). Eggs from the greater black-backed gull (*Larus marinus)* collected from Appledore Island, Maine, in 1977 contained up to 0.26

ppm, but no mirex was detected in eggs of common eider (*Somateria mollissima)* or herring gull from the same area (Szaro et al. 1977). The greater black-backed gull is an active carnivore; 36-52% of its diet consists of small birds and mammals, whereas these items compose less than 1% in eider and herring gull diets. The higher mirex levels in black-backed gulls is attributed to its predatory feeding habits (Szaro et al. 1979). In New England, eggs of the black-crowned night-heron (*Nycticorax nycticorax)* contained between 0.28 and 0.66 ppm mirex wet weight in 1973; in 1979, this range was 0.11-0.37 ppm (Custer et al. 1983). Falcon eggs contained detectable mirex; levels were highest in the pigeon hawk (*Falco columbarius*) (0.25 ppm) and in the peregrine falcon (*Falco peregrinus*) (0.43 ppm), two species that feed on migratory birds or migrate to mirex-impacted areas (Kaiser 1978). Active mirex was also found in eggs of a cormorant (*Phalacrocorax* sp.) from the Bay of Fundy on the Atlantic coast; the suspected source of contamination was the southern wintering range (Kaiser 1978).

Mirex residues in 20 great horned owls *(Bubo virginianus)* found dead or dying in New York State in 1980-82 contained concentrations of mirex and PCB's higher than those reported for great horned owls elsewhere (Stone and Okoniewski 1983). Owls in “poor flesh” contained higher residues than those in “good flesh”; these values were 6.3 vs. 0.07 for brain, and 5.56 vs. 0.12 ppm for liver (Stone and Okoniewski 1983).

CURRENT RECOMMENDATIONS

Before the banning of mirex for all uses in 1978, the tolerance limits in food for human consumption were 0.1 ppm for eggs, milk, and fat of meat from cattle, goats, hogs, horses, poultry, and sheep, and 0.01 ppm for all other raw agricultural commodities (Waters et al. 1977; Buckler et al. 1981). Higher limits of 0.3 ppm mirex in fish and shellfish and 0.4 ppm in crabs were tolerated (NAS 1978). However, mirex concentrations as low as 0.1 ppm in diets of adult prairie voles were associated with delayed maturation of pups, and with significant delays in the attainment of various early development behaviors such as bar-holding ability, hind-limb placing, and negative geotaxis (Shannon 1976). It is not known whether or not prairie voles can serve as a model for protection of health of humans or various wildlife species. In the absence of supporting data, however, it seems prudent now to establish a dietary threshold of mirex at some level lower than 0.1 ppm. A maximum concentration of 0.01 ppm total dietary mirex, which is the current recommended level for most raw agricultural commodities, appears reasonable and conservative for the protection of fish, wildlife, and human health. This value could be modified as new data become available.

Although mirex is extremely persistent in the environment, recent data indicate that some degradation occurs and that some of the degradation products, such as photomirex, are biologically active. Accordingly, additional research is warranted on the fate and effects of mirex degradation products, with special emphasis on biomagnification through aquatic and terrestrial food chains.

Alternate means of controlling imported fire ants are under consideration. One approach has been to reduce the concentrations of active mirex in bait formulations from the current 0.3% to some lower, but effective, level. Paton and Miller (1980) demonstrated that mirex baits containing 0.07% mirex were effective in controlling Australian termites, reporting a 90% kill in 9 days; baits containing as little as 0.01% mirex were also reported effective, although termite mortality was delayed considerably. Waters et al. (1977) indicated that alternate chemical control agents, such as chloropyrifos, diazinon, dimethoate, or methyl bromide may be suitable and that nonbiocidal chemicals, such as various pheromones and hormones, which are capable of disrupting reproductive behavior of fire ants, are also under active consideration. Another proposal was to modify mirex chemically to a more water soluble and rapidly degradable product (Waters et al. 1977). The formulation Ferriamicide, which consisted of 0.05% mirex, ferrous chloride, and a small amount of long-chain alkyl amines, was formulated in baits during 1978-79 for ant control (Lowe 1982). Ferriamicide degraded within a few days after initial application; however, approval was revoked in 1980 when it was learned that the toxicity of various degradation products to mammals, especially that of photomirex, exceeded that of 4X bait formulations (Lowe 1982). In 1980, the use of Amdro (tetrahydro-5,5-dimethyl-2 (lH)-pyrimidine) was conditionally approved by the U.S. Environmental Protection Agency (Lowe 1982). Amdro reportedly has good ant control properties, degrades rapidly in sunlight, has a biological half life of less than 24 h, is nonmutagenic, and is relatively nontoxic to other than targeted species, except fish. Amdro was more acutely toxic than mirex to fish.

Mirex replacements should not manifest the properties that led to the discontinuance of mirex for all uses; namely, delayed mortality in aquatic and terrestrial fauna; numerous birth defects; tumor formation; histopathology; adverse effects on reproduction, early growth, and development; high biomagnification and persistence; disrupted energy metabolism; degradation into toxic metabolites; population alterations; and movement through aquatic and terrestrial environmental compartments. It is emphasized that mirex replacement compounds must be thoroughly tested before widespread application in the environment; if testing is incomplete, it is almost certain that the Nation's fish and wildlife resources will be adversely affected.

ACKNOWLEDGMENTS

I thank L. Garrett, M. Shawe, and B. Graff for library services; V. Lumsden, and I. Moore for secretarial help; K. A. King, J. B. Hunn, H. M. Ohlendorf, and V. Adomaitis for reviewing the manuscript; and P. H. Eschmeyer, and C. I. Short for editorial services.

LITERATURE CITED

Ahrens, F. A., D. C. Dyer, and W. E. Lloyd. 1980. Mirex kinetics in chickens. J. Toxicol. Environ. Health 6:835-842.

Baker, M. F. 1964. Studies on possible effects of mirex bait on the bobwhite quail and birds. Proc. Annu. Conf. Southeast. Assoc. Fish Game Comm. 18:153-159.

Barbehenn, K. R., and W. L. Reichel. 1981. Organochlorine concentrations in bald eagles: brain/body lipid relations and hazard evaluation. J. Toxicol. Environ. Health 8:325-330.

Barber, R. T., and S. M. Warlen. 1979. Organochlorine insecticide residues in deep sea fish from 2500 m in the Atlantic Ocean. Environ. Sci. Technol. 13:1146-1148.

Bell, M. A., R. A. Ewing, and G. A. Lutz. 1978. Reviews of the environmental effects of pollutants: I mirex and kepone. U.S. Environ. Protection Agency Rep. 600/1-78-013. 235 pp.

Bird, D. M., P. H. Tucker, G. A. Fox, and P. C. Lague. 1983. Synergistic effects of Aroclor^{R} 1254 and mirex on the semen characteristics of American kestrels. Arch. Environ. Contam. Toxicol. 12:633-640.

Buckler, D. R., A. Witt, Jr., F. L. Mayer, and J. N. Huckins. 1981. Acute and chronic effects of kepone and mirex on the fathead minnow. Trans. Am. Fish. Soc. 110:270-280.

Bush, B., J. Snow, S. Connor, L. Rueckeit, Y. Han, P. Dymerski, and D. Hilker. 1983. Mirex in human milk in upstate New York. Arch. Environ. Contam. Toxicol. 12:739-746.

Cain, B. W., and C. M. Bunck. 1983. Residues of organochlorine compounds in starlings *(Sturnus vulgaris)*, 1979. Environ. Monitor. Assess. 3:161-172.

Chernoff, N., R. E. Linder, T. M. Scotti, E. H. Rogers, B. D. Carver, and R. Kavlock. 1979. Fetotoxicity and cataractogenicity of mirex in rats and mice with notes on kepone. Environ. Res. 18:257-269.

Chu, I., D. C. Villaneuve, V. E. Secours, V. E. Valli, and G. C. Becking. 1981. Effects of photomirex and mirex on reproduction in the rat. Toxicol. Appl. Pharmacol. 60:549-556.

Clark, D. R., Jr., and A. J. Krynitsky. 1980. Organochlorine residues in eggs of loggerhead and green sea turtles nesting at Merritt Island, Florida—July and August 1976. Pestic. Monitor. J. 14:7-10.

Cripe, C. R., and R. J. Livingston. 1977. Dynamics of mirex and its principal photoproducts in a simulated marsh system. Arch. Environ. Contam. Toxicol. 5:295-303.

Custer, T. W., C. M. Bunck, and T. E. Kaiser. 1983. Organochlorine residues in Atlantic coast black-crowned night-heron eggs, 1979. Colonial Waterbirds 6:160-167.

de la Cruz, A. A., and K. Y. Lue. 1978a. Mirex incorporation in estuarine animals, sediment, and water, Mississippi Gulf Coast—1972-74. Pestic. Monitor. J. 12:40-42.

de la Cruz, A. A., and K. Y. Lue. 1978b. Mirex incorporation in the environment: *in situ* decomposition of fire ant bait and its effects on two soil macroarthropods. Arch. Environ. Contam. Toxicol. 7:47-61.

Ervin, M. G. 1982. The role of the pituitary-adrenal cortical-liver axis in mirex-induced adaptive liver hypertrophy. Ph.D. Thesis, Mississippi State Univ., Mississippi State. 84 pp.

Eversole, A. G. 1980. Effects of water-borne mirex on the survival and production of *Macrobrachium rosenbergii* (de Man). Water Resour. Res. Inst., Clemson Univ., Clemson SC, OWRT Proj. B-115-SC. 44 pp.

Farr, D. H., and L. M. Blake. 1979. A creel census of the salmonid fishery in South Sandy Creek, New York. N.Y. Fish Game J. 26:1-10.

Fujimori, K., I. K. Ho, H. M. Mehendale, and D. C. Villeneuve. 1983. Comparative toxicology of mirex, photomirex and chlordecone after oral administration to the mouse. Environ. Toxicol. Chem. 2:49-60.

Gaines, T. B., and R. D. Kimbrough. 1969. The oral toxicity of mirex in adult and suckling rats. Toxicol. Appl. Pharmacol. 14:631-632.

Gilman, A. P., G. A. Fox, D. B. Peakall, S. M. Teeple, T. R. Carroll, and G. T. Haymes. 1977. Reproductive parameters and egg contaminant levels of Great Lakes herring gulls. J. Wildl. Manage. 41:458-468.

Gilman, A. P., D. J. Hallett, G. A. Fox, L. J. Allan, W. J. Learning, and D. B. Peakall. 1978. Effects of injected organochlorines on naturally incubated herring gull eggs. J. Wildl. Manage. 42:484-493.

Grabowski, C. T. 1981. Plasma proteins and colloid osmotic pressure of blood of rat fetuses prenatally exposed to mirex. J. Toxicol. Environ. Health 7:705-714.

Hall, R. J., T. E. Kaiser, W. B. Robertson, Jr., and P. C. Patty. 1979. Organochlorine residues in eggs of the endangered American crocodile *(Crocodylus acutus)*. Bull. Environ. Contam. Toxicol. 23:87-90.

Heath, R. G., J. W. Spann, E. F. Hill, and J. F. Kreitzer. 1972. Comparative dietary toxicities of pesticides to birds. U.S. Fish Wildl. Serv. Spec. Sci. Rep.—Wildl. 152. 57 pp.

Holcombe, C. M., and W. S. Parker. 1979. Mirex residues in eggs and livers of two long-lived reptiles (*Chrysemys scripta* and *Terrapene carolina*). Bull. Environ. Contam. Toxicol. 23:369-371.

Hollister, T. A., G. E. Walsh, and J. Forester. 1975. Mirex and marine unicellular algae: accumulation, population growth and oxygen evaluation. Bull. Environ. Contam. Toxicol. 14:753-759.

Holloman, M. E., B. R. Layton, M. V. Kennedy, and C. R. Swanson. 1975. Identification of the major thermal degradation products of the insecticide mirex. J. Agric. Food Chem. 23:1011-1012.

Howard, F. W., and A. D. Oliver. 1978. Arthropod populations in permanent pastures treated and untreated with mirex for red imported fire ant control. Environ. Entomol. 7:901-903.

Huckins, J. N., D. L. Stalling, J. D. Petty, D. R. Buckler, and B. T. Johnson. 1982. Fate of kepone and mirex in the aquatic environment. J. Agric. Food Chem. 30:1020-1027.

Hunter, R. G., J. H. Carroll, and J. C. Randolph. 1980. Organochlorine residues in fish of Lake Texoma, October 1979. Pestic. Monitor. J. 14:102-107.

Hyde, K. M. 1972. Studies of the responses of selected wildlife species to mirex bait exposure. Ph.D. Thesis, Louisiana State University, Baton Rouge. 170 pp.

Innes, J. R. M., B. M. Ulland, M. G. Valerio, L. Petrucelli, L. Fishbein, E. R. Hart, A. J. Pallotta, P. R. Bates, H. L. Falk, J. J. Gart, M. Klein, I. Mitchell, and J. Peters. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: a preliminary report. J. Nat. Cancer Inst. 42:1101-1114.

Johnson, W. W., and M. T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. Summaries of toxicity tests conducted at Columbia National Fisheries Research Laboratory, 1965-78. U.S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Jones, A. S., and C. S. Hodges. 1974. Persistence of mirex and its effects on soil microorganisms. J. Agric. Food Chem. 22:435-439.

Kaiser, K. L. E. 1978. The rise and fall of mirex. Environ. Sci. Technol. 12:520-528.

Kavlock, R. J., N. Chernoff, E. Rogers, D. Whitehouse, B. Carver, J. Gray, and K. Robinson. 1982. An analysis of fetotoxicity using biochemical endpoints of organ differentiation. Teratology 26:183-194.

Kendall, R. J., R. Noblet, J. D. Hair, and H. B. Jackson. 1977. Mirex residues in bobwhite quail after aerial application of bait for fire ant control, South Carolina—1975-76. Pestic. Monitor. J. 11:64-68.

Kendall, R. J., R. Noblet, L. H. Senn, and J. R. Holman. 1978. Toxicological studies with mirex in bobwhite quail. Poult. Sci. 57:1539-1545.

Klaas, E. E., H. M. Ohlendorf, and E. Cromartie. 1980. Organochlorine residues and shell thicknesses in eggs of the clapper rail, common gallinule, purple gallinule, and limpkin (Class Aves), Eastern and Southern United States, 1972-74. Pestic. Monitor. J. 14:90-94.

Kobylinski, G. J., and R. J. Livingston. 1975. Movement of mirex from sediment and uptake by the hogchoker, *Trinectes maculatus*. Bull. Environ. Contam. Toxicol. 14:692-698.

Koenig, C. C. 1977. The effects of DDT and mirex alone and in combination on the reproduction of a salt marsh cyprinodont fish, *Adinia xenica*. Pages 357-376 *in* F. J. Vernberg, A. Calabrese, F. P. Thurberg, and W. B. Vernberg (eds.). Physiological responses of marine biota to pollutants. Academic Press, New York.

Larson, P. S., J. L. Egle, Jr., G. R. Hennigar, and J. F. Borzelleca. 1979. Acute and subchronic toxicity of mirex in the rat, dog, and rabbit. Toxicol. Appl. Pharmacol. 49:271-277.

Leatherland, J. F., and R. A. Sonstegard. 1981. Effect of dietary mirex and PCB's on calcium and magnesium metabolism in rainbow trout, *Salmo qairdneri* and coho salmon, *Oncorhynchus kisutch*; a comparison with Great Lakes coho salmon. Comp. Biochem. Physiol. 69C:345-351.

Leatherland, J. F., R. A. Sonstegard, and M. V. Holdrient. 1979. Effect of dietary mirex and PCB's on hepatosomatic index, liver lipid, carcass lipid and PCB and mirex bioaccumulation in yearling coho salmon, *Oncorhynchus kisutch*. Comp. Biochem. Physiol. 63C:243-246.

Lee, J. H., C. E. Nash, and J. R. Sylvester. 1975. Effects of mirex and methoxychlor on striped mullet, *Muqil cephalus* L. U.S. Environ. Protection Agency Rep. EPA-660/3-75-015. 18 pp.

Lowe, J. I. 1982. Mirex, fire ants, and estuaries. Pages 63-70 in Proceedings of the workshop on agrichemicals and estuarine productivity. Duke Univ. Mar. Lab., Beaufort, NC. Sept. 18-19, 1980. U.S. Dep. Comm. NOAA/OMPA.

Ludke, J. L., M. T. Finley, and C. Lusk. 1971. Toxicity of mirex to crayfish, *Procambarus blandingi*. Bull. Environ. Contam. Toxicol. 6:89-96.

Lue, K. Y., and A. de la Cruz. 1978. Mirex incorporation in the environment: toxicity in *Hydra*. Bull. Environ. Contam. Toxicol. 19:412-416.

Markin, G. P. 1981. Translocation and fate of the insecticide mirex within a bahia grass pasture ecosystem. Environ. Pollut. 26A:227-241.

McArthur, M. L. B., G. A. Fox, D. B. Peakall, and B. J. R. Philogene. 1983. Ecological significance of behavioral and hormonal abnormalities in breeding ring doves fed an organochlorine mixture. Arch. Environ. Contam. Toxicol. 12:343-353.

McCorkle, F. M., J. E. Chambers, and J. D. Yarbrough. 1979. Tissue enzyme activities following exposure to dietary mirex in the channel catfish, *Ictalurus punctatus*. Environ. Pollut. 19:195-199.

McLane, M. A. R., E. H. Dustman, E. R. Clark, and D. L. Hughes. 1978. Organochlorine insecticide and polychlorinated biphenyl residues in woodcock wings, 1971-72. Pestic. Monitor. J. 12:22-25.

Mehrle, P. M., F. L. Mayer, and D. R. Buckler. 1981. Kepone and mirex: effects on bone development and swim bladder composition in fathead minnows. Trans. Am. Fish. Soc. 110:638-643.

Menzie, C. M. 1978. Metabolism of pesticides. Update II. U.S. Fish Wildl. Serv. Spec. Sci. Rep.—Wildl. 212. 381 pp.

Minchew, C. D., R. N. Hunsinger, and R. C. Giles. 1980. Tissue distribution of mirex in adult crayfish (*Procambarus clarki*). Bull. Environ. Contam. Toxicol. 24:522-526.

Muncy, R. J., and A. D. Oliver. 1963. Toxicity of ten insecticides to the red crawfish, *Procambarus clarki* (Girard). Trans. Am. Fish. Soc. 92: 428-431.

Naber, E. C., and G. W. Ware. 1965. Effects of kepone and mirex on reproductive performance in the laying hen. Poult. Sci. 44:875-880.

NAS. 1978. Scientific and technical assessments of environmental pollutants. Kepone/mirex/hexachlorocyclopentadiene: an environmental assessment. Nat. Acad. Sci., Washington, DC. 73 pp.

Norstrom, R. J., D. J. Hallett, and R. A. Sonstegard. 1978. Coho salmon (*Oncorhynchus kisutch*) and herring gulls *(Larus argentatus)* as indicators of organochlorine contamination in Lake Ontario. J. Fish. Res. Board Canada 35:1401-1409.

Norstrom, R. J., D. J. Hallett, F. I. Onuska, and M. E. Comba. 1980. Mirex and its degradation products in Great Lakes herring gulls. Environ. Sci. Technol. 14:860-866.

Ohlendorf, H. M., E. E. Klaas, and T. E. Kaiser. 1979, Environmental pollutants and eggshell thickness: anhingas and wading birds in the Eastern United States. U.S. Fish Wildl. Serv. Spec. Sci. Rep.—Wildl. 216. 94 pp.

Ohlendorf, H. M., D. M. Swineford, and L. N. Locke. 1981. Organochlorine residues and mortality of herons. Pestic. Monitor. J. 14:125-135.

Ohlendorf, H. M., J. C. Bartonek, G. J. Divoky, E. E. Klaas, and A. J. Krynitsky. 1982. Organochlorine residues in eggs of Alaskan seabirds. U.S. Fish Wildl. Serv. Spec. Sci. Rep.—Wildl. 245. 1-41.

Paton, R., and L. R. Miller. 1980. Control of *Mastotermes darwiniensis* Froggatt (Isoptera: Mastotermitidae) with mirex baits. Aust. For. Res. 10:249-258.

Rogers, J. M. 1982. The perinatal cataractogenicity of the pesticide mirex: lens changes and related systemic effects. Ph.D. Thesis, Univ. Miami, Coral Gables. 100 pp.

Sanders, H. O., J. Huckins, B. T. Johnson, and D. Skaar. 1981. Biological effects of kepone and mirex in freshwater invertebrates. Arch. Environ. Contam. Toxicol. 10:531-539.

Schafer, E. W., Jr., W. A. Bowles, Jr., and J. Hurlbert. 1983. The acute oral toxicity, repellency, and hazard potential of 998 chemicals to one or more species of wild and domestic birds. Arch. Environ. Contam. Toxicol. 12:355-382.

Schoor, W. P. 1979. Distribution of mirex in an experimental estuarine ecosystem. Bull. Environ. Contam. Toxicol. 21:315-321.

Schoor, W. P., and S. M. Newman. 1976. The effect of mirex on the burrowing activity of the lugworm (*Arenicola cristata*). Trans. Am. Fish. Soc. 105:700-703.

Scrudato, R. J., and A. DelPrete. 1982. Lake Ontario sediment—mirex relationships. J. Great Lakes Res. 8:695-699.

Shannon, V. C. 1976. The effects of mirex on the reproductive performance and behavioral development of the prairie vole *Micropterus ochrogaster*. Ph.D. Thesis, Iowa State Univ., Ames. 318 pp.

Skaar, D. R., B. T. Johnson, J. R. Jones, and J. N. Huckins. 1981. Fate of kepone and mirex in a model aquatic environment: sediment, fish, and diet. Can. J. Fish. Aquat. Sci. 38:931-938.

Skea, J. C., H. J. Simonin, S. Jackling, and J. Symula. 1981. Accumulation and retention of mirex by brook trout fed a contaminated diet. Bull. Environ. Contam. Toxicol. 27:79-83.

Stickel, L. F. 1963. Wildlife studies, Patuxent Wildlife Research Center. Pages 77-115 *in* Pesticide-wildlife studies, 1963. A review of fish and wildlife investigations during the calendar year. U.S. Fish Wildl. Serv. Circ. 199.

Stone, W. B., and J. C. Okoniewski. 1983. Organochlorine toxicants in great horned owls from New York, 1981-82. Northeast. Environ. Sci. 2:1-7.

Summerlin, J. W., A. C. F. Hung, and S. B. Vinson. 1977. Residues in nontarget ants, species simplification and recovery of populations following aerial applications of mirex. Environ. Entomol. 6:193-197.

Szaro, R. C., N. C. Coon, and E. Kolbe. 1979. Pesticide and PCB of common eider, herring gull and great black-backed gull eggs. Bull. Environ. Contam. Toxicol. 22:394-399.

Tucker, R. K., and D. G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 84. 131 pp.

Ulland, B. M., N. P. Page, R. A. Squire, E. K. Weisburger, and R. L. Cypher. 1977. A carcinogenicity assay of mirex in Charles River CD rats. J. Natl. Cancer Inst. 58:133-140.

Van Valin, C. E., A. K. Andrews, and L. L. Eller. 1968. Some effects of mirex on two warm-water fishes. Trans. Am. Fish. Soc. 97:185-196.

Waters, E. M., J. E. Huff, and H. B. Gerstner. 1977. Mirex. An overview. Environ. Res. 14:212-222.

Weseloh, D. V., P. Mineau, and D. J. Hallett. 1979. Organochlorine contaminants and trends in reproduction in Great Lakes herring gulls, 1974-1978. Trans. N. Am. Wildl. Nat. Resour. Conf. 44:543-557.

Wheeler, W. B., D. P. Jouvenay, D. P. Wojcik, W. A. Banks, C. H. Van Middelem, C. S. Lofgren, S. Nesbitt, L. Williams, and R. Brown. 1977. Mirex residues in nontarget organisms after application of 10-5 bait for fire ant control, Northeast Florida—1972-74. Pestic. Monitor. J. 11:146-156.

White, D. H. 1979. Nationwide residues of organochlorine compounds in wings of adult mallards and black ducks, 1976-77. Pestic. Monitor. J. 13:12-16.

Wolfe, J. L., and B. R. Norment. 1973. Accumulation of mirex residues in selected organisms after an aerial treatment, Mississippi, 1971-1972. Pestic. Monitor. J. 7:112-114.

Wolfe, J. L., R. J. Esher, K. M. Robinson, and J. D. Yarbrough. 1979. Lethal and reproductive effects of dietary mirex and DDT on old-field mice, *Peromyscus polionotus*. Bull. Environ. Contam. Toxicol. 21:397-402.

Yarbrough, J. D., J. E. Chambers, J. M. Grimley, E. G. Alley, M. M. Fang, J. T. Morrow, B. C. Ward, and J. D. Conroy. 1981. Comparative study of 8-monohydromirex and mirex toxicity in male rats. Toxicol. Appl. Pharmacol. 58:105-117.

Zitko, V. 1980. The uptake and excretion of mirex and dechloranes by juvenile Atlantic salmon. Chemosphere 9:73-78.

Biological Report 85(1.2)
July 1985

Contaminant Hazard Reviews
Report No. 2

CADMIUM HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

By
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Cadmium contamination of the environment is especially severe in the vicinity of smelters and urban industrialized areas. There is no evidence that cadmium, a relatively rare heavy metal, is biologically essential or beneficial; on the contrary, cadmium is a known teratogen and carcinogen, a probable mutagen, and has been implicated as the cause of severe deleterious effects on fish and wildlife. The freshwater biota is the most sensitive group; concentrations of 0.8 to 9.9 ug Cd/L (ppb) in water were lethal to several species of aquatic insects, crustaceans, and teleosts, and concentrations of 0.7 to 570 ppb were associated with sublethal effects such as decreased growth, inhibited reproduction, and population alterations. These effects were most pronounced in waters of comparatively low alkalinity. Marine organisms were more resistant than freshwater biota. Decapod crustaceans, the most sensitive saltwater group, died at concentrations of cadmium in seawater ranging from 14.8 to 420 ppb. Sublethal effects to marine animals recorded at Cd concentrations of 0.5 to 10 ppb included decreased growth, respiratory disruption, altered enzyme levels, and abnormal muscular contractions; effects were usually most obvious at relatively low salinities and high temperatures. Freshwater and marine aquatic organisms accumulated measurable amounts of cadmium from water containing Cd concentrations not previously considered hazardous to public health or to many species of aquatic life; i.e., 0.02 to 10 ppb.

Mammals and birds are comparatively resistant to the biocidal properties of cadmium. The lowest oral doses producing death in rats and guinea pigs ranged from 150 to 250 mg Cd/kg body weight (ppm). Although mallards and chickens tolerated 200 ppm of cadmium in diets for protracted periods, kidney cadmium exceeded 130 ppm fresh weight under this regimen, a concentration considered life-threatening to some organisms. Sublethal effects of cadmium in birds, which were similar to those in other animals, included growth retardation, anemia, and testicular damage; however, these effects were observed at higher concentrations than in aquatic biota. Although the evidence is incomplete, wildlife populations, especially migratory birds that feed on crops growing on fields fertilized with municipal sewage sludges, may be exposed to considerable risk of harmful effects from cadmium.

It is now conservatively estimated that adverse effects on fish or wildlife are either pronounced or probable when cadmium concentrations exceed 3 ppb in fresh water, 4.5 ppb in saltwater, 100 ppb in the diet, or 100 g Cd/m^3 in air. Cadmium residues in vertebrate kidney or liver that exceed 10 ppm fresh weight or 2 ppm whole body fresh weight should be viewed as evidence of probable Cd contamination; residues of 200 ppm fresh weight kidney, or more than 5 ppm whole animal fresh weight, are probably life-threatening to the organism. (Eisler, R. 1985. Cadmium hazards to fish, wildlife , and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.2), Contaminant Hazard Reviews Report No. 2. 46 pp.)

Table of Contents

TABLES

INTRODUCTION

There is no evidence that cadmium (Cd) is biologically essential or beneficial; on the contrary, it has been implicated as the cause of numerous human deaths and various deleterious effects in fish and wildlife. In sufficient concentration, it is toxic to all forms of life, including microorganisms, higher plants, animals, and man. It is a relatively rare metal, usually present in small amounts in zinc ores, and is commercially obtained as an industrial by-product of the production of zinc, copper, and lead. Major uses of cadmium are in electroplating, in pigment production, and in the manufacture of plastic stabilizers and batteries. Anthropogenic sources of cadmium include smelter fumes and dusts, the products of incineration of Cd-bearing materials and fossil fuels, fertilizers, and municipal wastewater and sludge discharges; concentrations are most likely highest in the localized regions of smelters or in urban industrialized areas (Hammons et al. 1978; Hutton 1983b). Industrial consumption of cadmium in the United States, estimated at 6,000 metric tons in 1968, is increasing; projected use in the year 2000 is about 14,000 tons, primarily for electroplating of motor parts and in the manufacture of batteries. The cadmium load in soils and terrestrial biota in other industrialized countries also appears to be increasing; it is currently of great concern in Scandinavia (Tjell et al. 1983), Germany (Markard 1983), and the United Kingdom (Hutton 1983a).

This account summarizes ecological and toxicological aspects of cadmium in the environment, with special reference to game fish and migratory waterfowl and their predators and prey. It also provides recommendations for the protection of sensitive species of wildlife and aquatic biota. It is part of a continuing series of synoptic reviews prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service.

ENVIRONMENTAL CHEMISTRY AND BACKGROUND RESIDUES

Cadmium is a silver-white, blue-tinged, lustrous metal that melts at 321°C and boils at 765°C. This divalent element has an atomic weight of 112.4 and an atomic number of 48. It is insoluble in water, although its chloride and sulphate salts are freely soluble (Windholz et al. 1976). The availability of Cd to living organisms from their immediate physical and chemical environs depends on numerous factors, including adsorption and desorption rates of cadmium from terrigenous materials, pH, Eh, chemical speciation, and many other modifiers. The few selected examples that follow demonstrate the complex behavior of Cd in freshwater systems.

Adsorption and desorption processes are likely to be major factors in controlling the concentration of cadmium in natural waters and tend to counteract changes in the concentration of cadmium ions in solution (Gardiner 1974). Adsorption and desorption rates of cadmium are rapid on mud solids and particles of clay, silica, humic material, and other naturally occurring solids. Concentration factors for river muds varied between 5,000 and 500,000 and depended mainly on the type of solid, the particle size, the concentration of cadmium present, the duration of contact, and the concentration of complexing ligands; humic material appeared to be the main component of river mud responsible for adsorption (Gardiner 1974). Changes in physicochemical conditions, especially pH and redox potential, that occur during dredging and disposal of Cd-polluted sediments may increase chemical mobility and, hence, bioavailability of sediment-bound Cd (Khalid et al. 1981). For example, cadmium in Mississippi River sediments spiked with radiocadmium was transformed from potentially available organic forms to more mobile and readily available dissolved and exchangeable forms (i.e., increased bioavailability) under regimens of comparatively acidic pH and high oxidation (Khalid et al. 1981). The role of dissolved oxygen and aquatic plants on Cd cycling was studied in Palestine lake, a 92-ha eutrophic lake in Kosciusko County, Indiana, a long-term recipient of cadmium and other waste metals from an electroplating plant. The maximum recorded concentration of dissolved Cd in the water column was 17.3 ppb; for suspended particulates, it was 30.3 ppb (Shephard et al. 1980). During anaerobic conditions in the lake's hypolimnion, a marked decrease in the dissolved fraction and a corresponding increase in the suspended fraction were noted. The dominant form of cadmium was free, readily bioavailable, cadmium ion, Cd^{2+}; however, organic complexes of Cd, which are comparatively nonbioavailable, made up a significant portion of the total dissolved Cd. Cadmium levels in sediments of Palestine Lake ranged from 1.5 ppm in an uncontaminated area of the lake to 805 ppm near the outlet of a metal-bearing ditch that entered the lake (McIntosh et al. 1978). The dominant form of Cd in sediments was a carbonate. Levels of Cd in water varied over time and between sites, but usually ranged from 0.5 to 2.5 ppb. It is possible that significant amounts of cadmium are transferred from the sediments into rooted aquatic macrophytes and later released into the water after macrophyte death (natural or herbicide-induced), particularly in heavily contaminated systems. In Palestine Lake, Cd levels in pondweed

(*Potomogeton crispus*), a rooted aquatic macrophyte, were about 90 ppm dry weight; a maximum burden of 1.5 kg was retained by the population of *P*. *crispus* in the lake (McIntosh et al. 1978). Release of the total amount could raise water concentrations by a maximum of 1 ppb. This amount was considered negligible in terms of the overall lake Cd budgets; however, it might have limited local effects. As judged by these and other complexities regarding Cd bioavailability, it appears that the organism remains the ultimate arbiter of its environment, regardless of the source of cadmium and its geophysical surroundings.

Background levels of cadmium in uncontaminated, nonbiological compartments extended over several orders of magnitude (Korte 1983). Concentrations (ppb) of cadmium reported ranged from 0.05 to 0.2 in freshwater, up to 0.05 in coastal seawater, from 0.01 to 0.1 in open ocean seawater, up to 5,000 in riverine and lake sediments, 30 to 1,000 in marine sediments, 10 to 1,000 in soils of nonvolcanic origin, up to 4,500 in soils of volcanic origin, 1 to 600 in igneous rock, up to 100,000 in phosphatic rock, and 0.001 to 0.005 $\mu g/m^3$ in air (Korte 1983). Where Cd is comparatively bioavailable, these values are very near those that have been shown to produce harmful effects in sensitive biological species, as will be discussed later.

Cadmium, unlike synthetic compounds, is a naturally occurring element, and its presence has been detected in more than 1,000 species of aquatic and terrestrial flora and fauna. Concentrations of cadmium in a few selected species of biota are shown in Table 1; more extensive documentation was presented by Hammons et al. (1978), NRCC (1979), Jenkins (1980), and Eisler (1981). At least six trends are evident from Table 1. First, marine biota generally contained significantly higher cadmium residues than their freshwater or terrestrial counterparts, probably because total cadmium levels are higher in seawater. Second, cadmium tends to concentrate in the viscera of vertebrates, especially the liver and kidneys. Third, concentrations of Cd are higher in older organisms than in younger stages; this relationship is especially pronounced in carnivores and marine vertebrates (Eisler 1984). Fourth, higher concentrations reported for individuals of a single species collected at several locations are almost always associated with proximity to industrial and urbanized areas or to point source discharges of Cd-containing wastes. Fifth, background levels of cadmium in crops and other plants are usually <1.0 mg/kg (ppm). Little is known about the Cd concentrations required to reduce plant yields; however, plants growing in cadmium-contaminated soils contain abnormally high residues that may be detrimental to plant growth and to animal and human consumers. And finally, it is apparent from Table 1 that species analyzed, season of collection, ambient Cd levels, and sex of organism all probably modify Cd concentrations.

The relationship between reported tissue cadmium concentrations of “unstressed” populations and hazard to the organism or its consumer is not well documented. For example, cadmium in eggs of successful nests of Cooper's hawks collected in Arizona and New Mexico ranged from 0.015 to 0.24 ppm fresh weight (FW); concentrations were higher in eggs from unsuccessful nests (Snyder et al. 1973). Cadmium concentrations in livers of breeding birds were higher in two declining colonies of puffins in St. Kilda and Clo Mor (12.9-22.3 ppm, dry weight) than in colonies of puffins from other areas, or in livers of other seabirds examined (Parslow et al. 1972); however, the link to cadmium requires elucidation. Among marine teleosts, whole body levels exceeding 5 ppm FW or 86 ppm ash weight (AW) in laboratory-stressed fish suggested that death would follow within 4 weeks (Eisler 1971). Marine bivalve molluscs occasionally contain more than 13 ppm of Cd in soft parts FW (Table 1), a level considered acutely toxic to human consumers (Zaroogian and Cheer 1976). The significance of cadmium residues to organism health is further developed later.

Table 1. Cadmium concentrations in field collections of selected species of flora and fauna. Values shown are in mg Cd/kg fresh weight (FW), dry weight (DW), or ash weight (AW).

Ecosystem, taxonomic group, organism, tissue, location, and other variables	Concentration (mg/kg or ppm)	Reference[a]
Marine		
Algae and Macrophytes		
Brown alga, *Ascophyllum nodosum*		
Whole		
Norway locations:		
Sorfjorden	6.0-15.0 DW	Melhuus et al. 1978
Eikhamrane	3.5-7.7 DW	Myklestad et al. 1978
Flak	<1.0 DW	
Transferred from Eikhamrane to Flak, 120 days	<1.0-4.0 DW	
Lofoten	<0.7 DW	Haug et al. 1974
Trondheimsfjord	<0.7-1.0 DW	
Hardangerfjord	0.7-16.0 DW	
United Kingdom locations		
Menai Straits	1.8 DW	Foster 1976
Dulas Bay	1.5 DW	
Bladder wrack, *Fucus vesiculosus*		
Whole		
Sorfjorden, Norway	8.6-10.6 DW	Melhuus et al. 1978
Tamar estuary, UK	1.8-9.0 DW	Bryan and Uysal 1978
Menai Straits, UK	2.1 DW	Foster 1976
Dulas Bay, UK	1.8 DW	
Irish Sea	1.4 DW	Preston et al. 1972
Severn estuary, UK	220.0 DW	Butterworth et al. 1972
Molluscs		
Sydney rock oyster, *Crassostrea commercialis*		
Soft parts	0.4-18.6 FW	Ratkowsky et al. 1974
Soft parts	0.1-1.0 FW	Mackay et al. 1975
Pacific oyster, *Crassostrea gigas*		
Soft parts	0.2-2.1 FW	Pringle et al. 1968
Soft parts	0.0-30.7 FW	Ratkowsky et al. 1974
Soft parts	1.1 FW	Kopfler and Mayer 1967
Soft parts	3.7-9.0 DW	Watling and Watling 1976
Red abalone, *Haliotis rufescens*		
Gill	4.0-10.0 DW	Anderlini 1974
Mantle	2.8-12.8 DW	
Digestive gland	183.0-1163.0 DW	
Foot	0.2-0.5 DW	
Periwinkle, *Littorina littorea*		
Soft parts	0.9-1.5 DW	Leatherland & Burton 1974
Soft parts	0.0-0.5 FW	Topping 1973
Soft parts	210.0 DW	Butterworth et al. 1972
Squid, *Ommastrephes bartrami*		
Liver	80.6-782.0 DW	Martin and Flegal 1975; Hamanaka et al. 1977
Muscle	0.7 DW	
Gonad	0.4 DW	

Common mussel, *Mytilus edulis*		
Soft parts		
U.S. West Coast	2.3-10.5 DW	Goldberg et al. 1978
U.S. East Coast	0.6-6.2 DW	
Port Phillip Bay, Australia	0.2-1.3 FW	Phillips 1976
Western Port Bay, Australia	up to 18.2 FW	
Scottish waters	0.1-2.0 FW	Topping 1973
Looe estuary, U.K.	0.8-2.6 DW	Bryan and Hummerstone 1977
Tasmania	5.5 FW	Eustace 1974
Corio Bay, Australia	2.0-63.0 DW	Talbot et al. 1976
Mussel, *Mytilus edulis planulatus*		
Soft parts		
Mean dry weight		
0.09 g	0.6 DW	Harris et al. 1979
0.39 g	0.8 DW	
0.48 g	1.1 DW	
0.69 g	1.3 DW	
Scallop, *Pecten maximum*		
Soft parts	13.0 DW	Segar et al. 1971
Muscle	1.9 DW	
Gut and digestive gland	96.0 DW	
Mantle and gills	3.2-17.0 DW	
Gonad	2.5 DW	
Shell	0.0 DW	
Soft parts	32.5 DW	Bryan 1973
Kidney	79.0 DW	
Kidney	54.0 DW	George et al. 1980
Kidney concretion	546.6 DW	Carmichael et al. 1979
Digestive gland	321.0 DW	Bryan 1973
Edible tissues	5.1-23.0 FW	Topping 1973
Giant scallop, *Placopecten magellanicus*		
Muscle		
March	up to 8.8 DW	Reynolds 1979
Rest of year	<3.7 DW	
Viscera		
March	104.1 DW max.	
August	121.2 DW max.	
February	161.8 DW max.	
June	105.3 DW max.	
Gonad	0.5-3.2 FW	Greig et al. 1978
Visceral mass	3.7-27.0 FW	
Clam, *Scrobicula plana*		
Digestive gland		
Gannel estuary, U.K.	39.8 DW	Bryan and Hummerstone 1978
Camel estuary, U.K.	1.7 DW	
Transferred from Camel to l		
Ganne estuary for 352 days	5.6 DW	
Transferred from Gannel to		
Camel estuary for 352 days	21.0 DW	
Whelk, *Thais lapillus*		
Soft parts	425.0 DW	Butterworth et al. 1972
Crustaceans		
Rock crab, *Cancer irroratus*		
Flesh	0.1-1.0 FW	Greig et al. 1977

Digestive gland	1.1-4.8 FW	
Gills	0.7-2.7 FW	
Brown shrimp, *Penaeus* sp.		
Flesh	0.2 DW	Horowitz and Presley 1977
Exoskeleton	0.5 DW	
Viscera	2.6 DW	
Whole	<0.4 DW	Sims and Presley 1976
American lobster, *Homarus americanus*		
Whole	0.5 FW; 5.3 AW	Eisler et al. 1972
Meats	0.2 FW; 10.0 AW	
Exoskeleton	0.6 FW; 4.1 AW	
Gill	0.5 FW; 17.2 AW	
Viscera	1.2 FW; 33.8 AW	
Prawn, *Pandalus montagui*		
Tail	0.0 DW	Ray et al. 1980
Egg	0.1 DW	
Carcass	0.3 DW	
Hepatopancreas	6.4 DW	
Whole	0.5 DW	
Spiny lobster, *Panulirus interruptus*		
Muscle	0.3 FW	Vattuone et al. 1976
Hepatopancreas	5.6-29.3 FW	
Grass shrimp, *Palaemonetes pugio*		
Whole	1.4-6.2 DW	Pesch and Stewart 1980
Annelids		
Marine worm, *Nephtys hombergi*		
Whole		
March	9.0 FW	Rosenberg 1977
October	89.0 FW	
Sandworm, *Nereis diversicolor*		
Whole	0.1-3.6 DW	Bryan and Hummerstone 1973, 1977
Echinoderms		
Asteroid, *Echinus esculentus*		
Intestines	8.9 DW	Riley and Segar 1970
Remaining tissues	<0.7 DW	
Fish		
Flounder, *Platichthys flesus*		
Whole		
Barnstaple Bay, U.K.		
Age II	1.1 DW	Hardisty et al. 1974
Age III	1.4 DW	
Age IV	1.6 DW	
Age V	1.7 DW	
Oldbury on Severn, U.K. (metals-contaminated area)		
Age II	4.0 DW	
Age III	4.5 DW	
Age IV	5.1 DW	
Age V	5.2 DW	
Yellowtail flounder, *Limanda limanda*		
Liver	0.4 DW	Westernhagen et al. 1980
Skin	0.2 DW	
Otoliths	0.2 DW	
Gills	0.2 DW	
Fin	0.2 DW	

Muscle	0.1 DW	
Backbone	0.05 DW	
Blue marlin, *Makaira indica*		
Muscle	0.1-0.4 FW	Mackay et al. 1976
Liver	0.2-83.0 FW	
Striped bass, *Morone saxatilis*		
Muscle	0.03 FW	Heit 1979
Liver	0.3 FW	
Atlantic cod, *Gadus morrhus*		
Roe	0.0-0.5 DW	Julshamn & Braekkan 1978
Muscle	0.02 DW	Julshamn & Braekkan 1975
Gonad	0.0-0.07 DW	
Liver	0.09 DW	
Bluefish, *Pomatomus saltatrix*		
Muscle	up to 0.08 FW	Bebbington et al. 1977
Shorthorn sculpin, *Myoxocephalus scorpius*		
Muscle	1.4 DW	Bohn and Fallis 1978
Liver	4.1 DW	
Birds		
Adelie penguin, *Pygoscelis adeliae*		
Liver	90.0 DW	Robertson et al. 1972
Lesser scaup, *Aythya affinis*		
Liver	0.6 FW	White et al. 1979
Kidney	2.3 FW	
New Zealand estuaries, 5 spp.		
Liver	0.1-1.5 FW	Turner et al. 1978
Kidney	0.1-14.8 FW	
Corpus Christi, Texas, 7 spp.		
Kidney	0.4-22.7 FW	White et al. 1980
Puffins, 2 spp.		
St. Kilda, Scotland		
Males		
Liver	14.6-29.4 DW	Bull et al. 1977
Kidney	67.0-133.0 DW	
Females		
Liver	14.1-39.9 DW	
Kidney	75.1-231.0 DW	
Sea gull, *Larus atricilla*		
Downy young		
Kidney	0.5 FW	Hulse et al. 1980
Other tissues	<0.05 FW	
Adults		
Muscle	0.1 FW	
Heart	0.1 FW	
Brain	0.5 FW	
Bone	0.4 FW	
Liver	0.6 FW	
Kidney	5.0 FW	
Common eider, *Somateria mollissima*		
Egg	1.0 DW	
Lande 1977		
Muscle	2.0 DW	
Liver	13.0 DW	
Kidney	25.0 DW	

Brown pelican, *Pelecanus occidentalis*		
Florida		
Liver	1.3-2.4 FW	Jenkins 1980
Muscle	0.2-0.3 FW	
California		
Liver	0.6-13.6 FW	
Muscle	0.2-0.4 FW	
Common tern, *Sterna hirundo*		
Liver	3.8 FW	
Kidney	21.3 FW	
Mammals		
Northern fur seal, *Callorhinus ursinus*		
Kidney	0.1-15.6 FW	Anas 1974
Liver	0.5-4.6 FW	
Pilot whale, *Globicephala macrorhynchus*		
Blubber	0.4-0.8 FW	Stoneburner 1978
Liver	11.3-19.0 FW	
Kidney	27.1-41.8 FW	
California sea lion, *Zalophus californianus*		
Liver	2.0-2.6 FW	Buhler et al. 1975
Kidney	10.2 FW	
Cerebellum	0.6 FW	
Other tissues	<0.2 FW	
Sea otter, *Enhydra lutris*		
Kidney	89.0-300.0 DW	Jenkins 1980
Walrus, *Odobenus rosmarus*		
Kidney	51.6 FW	
Liver	7.7 FW	
Muscle	0.3-0.7 FW	
Freshwater		
Macrophytes		
Water lily, *Nuphar luteum*		
Whole	0.5-1.8 DW	Jenkins 1980
Pondweed, *Potamogeton richardsoni*		
Leaf and stem	0.6-4.9 DW	
Root	1.3-6.7 DW	
Molluscs		
Clams, Illinois River		
Soft parts, 3 spp.	0.2-1.4 FW	Hammons et al. 1978
Annelids		
Whole, Illinois River	0.5-3.2 FW	
Fish		
United States, Nationwide, 1976-1977		
Whole	0.07 FW (0.01-1.04)	May and McKinney 1981
Upper Clark Fork River, western Montana		
Muscle, 3 spp.	0.2-0.6 FW	Hammons et al. 1978
Liver, 7 spp.	0.3-0.8 FW	
Great Lakes		
Whole, 3 spp.	0.0-0.14 FW	
Liver, 10 spp.	0.1-1.4 FW	
Illinois River		
Whole, 10 spp.	<0.08 FW	
New York State, various locations		
Whole		
Adirondacks region	0.02-0.05 FW	Lovett et al. 1972
Hudson River	up to 0.14 FW	

47 other areas	<0.02 FW	
Rainbow trout, *Salmo gairdneri*		
Alaska		
Whole	<0.07 FW	Jenkins 1980
Arizona		
Whole	<0.05 FW	
White crappie, *Pomoxis annularis*		
Whole	0.0-0.3 FW	
Sauger, *Stizostedion canadense*		
Whole	<0.05 FW	
Walleye, *Stizostedion vitreum vitreum*		
Liver	0.2 FW	
Whole	up to 0.16 FW	
Terrestrial		
Plants		
Lettuce, *Lactuca sativa,* whole		
Cd in soil, mg/kg		
<2.5	2.8 DW	Jenkins 1980
2.5	11.5 DW	
10.0	27.1 DW	
Soybean, *Glycine max*, plant top		
Cd in soil, mg/kg		
10	13.0 DW	
50	24.0 DW	
100	26.0 DW	
Tobacco, *Nicotiana tobacum*	2.0 DW	
Wheat, *Triticum aestivum*, grain		
Tons sewage sludge/hectare		
6.5	119.0 DW	
58.0	257.0 DW	
Control	<0.15 DW	
Annelids		
Earthworms, whole, 4 spp.		
distance from highway, meters		
3	12.6 DW	Gish and Christensen 1973
6.1	8.8 DW	
12.2	8.3 DW	
24.4	6.9 DW	
48.8	7.1 DW	
Control	3.0 DW	
Birds		
Ring-necked pheasant, *Phasianus colchicus*		
Liver	0.9 FW	Jenkins 1980
Kidney	7.4 FW	
American robin, *Turdus migratorius*		
Kidney	2.0 FW	
Liver	0.6 FW	
European starling, *Sturnus vulgaris*		
Whole, various U.S. locations		
Bakersfield, CA	0.24 FW	Martin and Nickerson 1973
Lansing, MI	0.12 FW	
Elkins, WV	0.12 FW	
Farmington, NM	0.12 FW	
Phoenix, AZ	0.11 FW	
Other U.S. areas	<0.05 FW	

Cooper's hawk, *Accipiter cooperii*		
Egg	0.12 (0.015-0.24 FW)	Snyder et al. 1973
Mammals		
Short-tailed shrew, *Blarina brevicauda*		
Liver	1.3 FW	Jenkins 1980
Whole	0.4 FW	
Cow, *Bos bovis*		
Distance from smelter		
Liver		
0.8 km	0.9 FW	
72.4 km	0.3 FW	
Kidney		
0.8 km	3.7 FW	
72.4 km	1.4 FW	
Coyote, *Canis latrans*		
Kidney	0.4 FW	
Elk, *Cervus* sp.		
Liver	1.5 DW	
Kidney	8.1 DW	
Muscle	0.6 DW	
Porcupine, *Erethizon dorsatum*		
Heart	0.4 FW	
Meadow vole, *Microtus pennsylvanicus*		
Collected from fields near Oxford, Ohio, receiving sewage sludge for 4 years at yearly rate of 8960 kg sludge/ha.		
Liver		
Adult males	0.8 FW	Maly and Barrett 1984
Adult females	3.1 FW	
Subadult males	1.2 FW	
Subadult females	1.1 FW	
Kidney		
Adult males	6.3 FW	
Adult females	19.1 FW	
Subadult males	3.5 FW	
Subadult females	6.2 FW	
From control fields		
Liver		
Adult males	0.7 FW	
Adult females	0.1 FW	
Subadult males	0.1 FW	
Subadult females	0.1 FW	
Kidney		
Adult males	0.3 FW	
Adult females	1.1 FW	
Subadult males	0.3 FW	
Subadult females	0.3 FW	
White-tailed deer, *Odocoileus virginianis*		
Kidney	0.7-11.7 FW	Jenkins 1980
Muscle	0.0-0.3 FW	
Liver	0.0-0.7 FW	
Gray squirrel, *Sciurus carolinensis*		
Kidney		
2 years old		
Urban area	15.9 FW	

Rural	2.0-4.6 FW
Red squirrel, *Sciurus hudsonicus*	
Kidney	7.8-17.4 FW
Liver	0.7-2.0 FW
Eastern cottontail, *Sylvilagus floridanus*	
Liver	up to 2.1 FW
Kidney	up to 13.5 FW
Muscle	up to 0.5 FW

[a]Each reference applies to the values in the same row and in the rows that follow for which no other reference is indicated.

ACUTE TOXICITY

A substantial toxicological data base for cadmium and freshwater biota demonstrates that ambient cadmium water concentrations exceeding 10 ppb are associated with high mortality, reduced growth, inhibited reproduction, and other adverse effects. Inasmuch as the current recommended drinking water criterion for human health protection is 10 ppb cadmium (EPA 1980), it is noteworthy that several species of freshwater aquatic insects, crustaceans, and teleosts exhibited significant mortality at cadmium concentrations of 0.8 to 9.9 ppb during exposures of 4 to 33 days; mortality generally increased as exposure time increased, water hardness decreased, and organism age decreased (Table 2).

Resistance to cadmium is higher in marine than in freshwater organisms; survival usually is higher at the lower temperatures and higher salinities for any given level of cadmium in the medium. Decapod crustaceans are the most sensitive marine group in short-term tests; LC-50 (96 h) values ranged from 320 to 420 ppb for the grass shrimp (*Palaemonetes vulgaris*), the hermit crab (*Pagurus longicarpus*), and the sand shrimp (*Crangon crangon*) (Eisler 1971). Studies of longer duration demonstrated that survival of shrimp groups was low at >250 ppb during 6 weeks of exposure and that hermit crab deaths were recorded at 60 ppb after 6 weeks, although some survivors remained at 10 weeks when the studies ended (Pesch and Stewart 1980). In another study, an LC-50 range of 14.8 to 19.5 ppb Cd was reported for two species of mysid shrimp subjected to “lifetime” (i.e., 23 to 27 days) exposure to cadmium salts (Gentile et al. 1982).

Birds are comparatively resistant to the biocidal properties of cadmium. Adult drake mallards (*Anas platyrhynchos*) fed up to 200 ppm cadmium in the diet for 90 days all survived with no loss of body weight (White and Finley 1978). Laying hens fed 200 ppm dietary Cd also survived; egg production was suppressed at that concentration but not at lower concentrations tested (White and Finley 1978). Marine and terrestrial animals, including ducks, have been shown to be particularly abundant in a wildlife community associated with a marine sewer outfall (Brown et al. 1977); these animals were contaminated with high levels of cadmium, as well as zinc and copper, but were apparently protected from the deleterious effects of high metal body burdens by metallothioneins. Amounts of these metal-binding proteinaceous metallothioneins and heavy metal loading appear to depend primarily on the degree of pollution and secondarily on the species of animal and its position in the food web. Ducks contained the highest levels of metallothioneins of all groups examined (Brown et al. 1977). Mammals are also comparatively resistant to cadmium. The lowest oral dose, in mg/kg body weight of cadmium (as fluroborate) producing death, was 250 in rats and 150 (as cadmium fluoride) in guinea pigs (EPA 1980).

Table 2. Lethal concentrations (LC) of cadmium to freshwater biota during various exposure intervals. Concentrations shown are in µg Cd/L (ppb) of medium fatal to 10% or 50% of test organisms.

Group, taxon, or life state	Water hardness, in mg $CaCO_3$/L	LC values, in ppb	Exposure interval	Reference[a]
Insects				
Ephemerella sp.	44-48	LC-50, <3.0	28 days	Spehar et al. 1978
Tanytarsus dissimilis	47	LC-50, 3.8	10 days	Anderson et al. 1980
Cladocerans				
Daphnia magna	51	LC-50, 9.9	96 h	EPA 1980
Daphnia magna	51	LC-50, 5.0	21 days	Biesinger and Christian 1972
Daphnia magna	"soft"	LC-50, 0.7	20 days	Canton and Slooff 1982
Simocephalus serrulatus	11	LC-50, 3.5-8.6	96 h	Giesy et al. 1977
Fish				
Threespine stickleback, *Gasterosteus aculeatus*	--	LC-50, 0.8	33 days	Pascoe and Mattey 1977
Striped bass, *Morone saxatilis*				
Larvae	70	LC-50, 1.0	96 h	Hughes 1973
Fingerlings	70	LC-50, 2.0	96 h	
Chinook salmon, *Oncorhynchus tshawytscha*				
Swimup	23	LC-10, 1.2	200 h	Chapman 1978
Swimup	23	LC-50, 1.8	96 h	
Parr	23	LC10, 1.3	200 h	
Parr	23	LC-50, 3.5	96 h	
Smolt	23	LC-10, 1.5	200 h	
Juveniles	--	LC-50, 0.6-1.6	96 h	Finlayson and Verrue
Coho salmon, *Oncorhynchus kisutch*				
Juveniles	22	LC-50, 2.0	217 h	Chapman and Stevens 1978
Adults	22	LC-50, 3.7	215 h	
Rainbow trout, *Salmo gairdneri*				
Swimup	23	LC-10, 1.0	200 h	Chapman 1978
Swimup	23	LC-50, 1.3	96 h	
Parr	23	LC-10, 0.7	200 h	
Parr	23	LC-50, 1.0	96 h	
Smolt	23	LC-10, 0.8	200 h	
Age 2-months	82-132	LC-50, 6.6	96 h	Hale 1977
Age 2-months	31	LC-50, 1.8	96 h	Davies 1976
Age 2-months	--	LC-50, 6.0-7.0	96 h	Kumada et al. 1973, 1980
Adult	54	LC-50, 5.2	17 days	Chapman

				and Stevens 1978
		LC-50, 5.0-7.0	10 days	Kumada et al. 1973
Brook trout, *Salvelinus fontinalis*				
	330-350	LC-50, 3.8-4.4	96 h	Carroll et al. 1979
	44	LC-50, 2.4	96 h	

[a]Each reference applies to the values in the same row and in the rows that follow for which no other reference is indicated.

SUBLETHAL EFFECTS

Studies of 30 to 60 days duration with three comparatively sensitive species of freshwater fishes demonstrated that concentrations of >1 and <3 ppb cadmium in water of low alkalinity caused reductions in growth, survival, and fecundity of brook trout, the most sensitive species tested (Table 3). Under conditions of increasing alkalinity, the maximum allowable cadmium concentration range for brook trout increased to >7 and <12 ppb; a similar case was made for the walleye (Table 3).

Among all species of freshwater biota examined, cadmium concentrations of 0.47 to 5.0 ppb were associated with decreases in standing crop, decreases in growth, inhibition of reproduction, immobilization, and population alterations (Table 4). There is an abundant technical literature documenting numerous sublethal effects at higher Cd concentrations; however, these were excluded from the present account if the effects were observed at >10.0 ppb, the currently recommended criterion for drinking water.

For marine organisms, ambient Cd levels between 0.5 and 10.0 ppb resulted in decreases in growth, respiratory disruption, molt inhibition, shortened life span of F1 generation crustaceans, altered enzyme levels, and abnormal muscular contractions. Effects, in general, were more pronounced at the lower salinities and higher temperatures tested (Table 4).

Table 3. Maximum allowable toxicant concentrations (MATC) of cadmium to sensitive species of freshwater teleosts (after Brungs et al. 1978).

Organism and exposure period (days)	Water alkalinity, in mg $CaCO_3$/L	MATC, in µg Cd/L or ppb medium
Brook trout, *Salvelinus fontinalis*		
60	30	>1-<3
60	177	>7-<12
Channel catfish, *Ictalurus punctatus*		
60	34	>11-<17
60	172	>12-<17
Walleye, *Stizostedion vitreum vitreum*		
30	33	>9-<25
30	172	>86.7

Sublethal effects in birds are similar to those in other species and include growth retardation, anemia, and testicular damage (Hammons et al. 1978). However, harmful damage effects were observed at higher concentrations when compared to aquatic biota. For example, Japanese quail fed 75 ppm Cd in diet developed bone marrow hypoplasia, anemia, and hypertrophy of both heart ventricles at 6 weeks (Richardson et al. 1974). In zinc-deficient diets, effects were especially pronounced and included all of the signs mentioned plus testicular

hypoplasia; a similar pattern was evident in cadmium-stressed quail on an iron-deficient diet. In all tests, 1% ascorbic acid in the diet prevented Cd-induced effects in Japanese quail (Richardson et al. 1974). Adult male white leghorn chickens given 2 ppm $CdSO_4$ daily by intraperitoneal injection for 15 to 22 days, or a total dose of 60 mg Cd per chicken, developed anemia, an enlarged heart, myocardial infarction, and other abnormalities (Sturkie 1973). Testicular damage was observed in ringdoves 20 days after intramuscular injection of 6.6 ppm Cd body weight (Richardson et al. 1974); in domestic pigeons, however, testicular damage was observed after a single subcutaneous injection of only 0.5 ppm (Sarker and Mondal 1973), and cardiovascular disease developed after exposure to 600.0 ppb in drinking water (Revis et al. 1981). In mallard ducklings fed 20 ppm dietary cadmium for 12 weeks, blood chemistry was altered, and mild to severe kidney lesions developed (Cain et al. 1983). Altered avoidance behavior in the form of hyperresponsiveness was observed in young American black ducks (*Anas rubripes*) produced from parents fed 4 ppm dietary cadmium for about 4 months before egg laying; this behavioral effect was observed only at comparatively low dietary cadmium levels and is considered harmful to wild birds (Heinz and Haseltine 1983). Cadmium readily reacts with sulfhydral groups and may compete, especially with zinc, for binding sites on proteins and, thus, may inhibit a variety of enzymatic reactions. The addition of zinc, iron, ascorbic acid, calcium, or selenium to diets ameliorated Cd damage effects, whereas the addition of lead or mercury exacerbated them (Hammons et al. 1978).

Among small laboratory mammals it appears that physiologically bound cadmium is more effective than $CdCl_2$ in producing metabolic iron irregularities. For example, in young mice fed oysters containing 1.8 ppm of Cd for 28 days, hematocrit and hemoglobin values were depressed and other blood chemistry factors were altered (Siewicki et al. 1983). Diets containing intrinsic oyster Cd at 1.8 ppm were more effective in producing hematopoietic alterations than were diets containing $CdCl_2$ at 3.6 ppm Cd (Siewicki et al. 1983).

Table 4. Sublethal effects of cadmium to selected species of aquatic biota

Type of medium, taxonomic group, organism, and other variables	Ambient Cd concentration, in ppb	Exposure period	Effect	Reference[a]
Freshwater				
Algae				
Asterionella formosa	2.0	--	Decreased growth rate	Conway 1978
Arthropoda				
Daphnia pulex	1.0	20 weeks	Reduced reproduction	Bertram and Hart 1979
Daphnia galeata mendotae	4.0	22 weeks	Reduced biomass	Marshall 1978
Eucyclops agilis	5.0	52 weeks	Population reduction	Giesy et al. 1979
Cambarus latimanus	5.0	22 weeks	Increased mortality	Thorp et al. 1979
Daphnia magna	2.6	21 days	Immobilization threshold	Biesinger and Christian 1972
Daphnia magna	0.7	21 days	Decreased reproduction (50%)	
Daphnia magna	0.17	21 days	No effect	
Daphnia magna	0.37	20 days	No effect	Canton and Slooff 1982
Daphnia magna	4.7	20 days	Decreased reproduction (50%)	
Annelida				

Pristina sp.	5.0	52 weeks	Population reduction	Giesy et al. 1979
Miscellaneous				
Mixed macroinvertebrates	5.0	52 weeks	Reduction in biomass and number of taxa	
Fish				
Brook trout, *Salvelinus fontinalis*	2.0	8 weeks	Disrupted lactic dehydrogenase activity and blood glucose levels	Christensen et al. 1977
Atlantic salmon, *Salmo salar*	0.47	12 weeks	Alevin growth reduction	Rombough and Garside 1982
Salmo salar	2.0	60 days	Cranial pathology, reduced growth, death	Peterson et al. 1983
Salmo salar	0.2	60 days	Normal growth and development	
Medaka, *Oryzias latipes*	6.0	96 h	No effect	Canton and Slooff 1982
Marine				
Algae				
Phaeodactylum tricornutum	10.0-25.0	--	Decreased growth	Cossa 1976
Skeletonema costatum	10.0-25.0	--	Decreased growth	Berland et al. 1977
Arthropoda				
Crab, Pontoporeia	6.5	265 days	Reduced F1 life span	Sundelin 1983
Fiddler crab, *Uca pugilator*	1.0	--	Reduced respiration	Vernberg et al. 1974
Mysid shrimp, *Mysidopsis* spp.	10.0	23-27 days	Molt inhibition	Gentile et al. 1982
Mysidopsis spp.	5.1	23-27 days	No effect	
Coelenterata				
Laomedea loveni				
Salinity 10 ppt	3.0	7 days	EC-50, irreversible polyp retraction	Theede et al. 1979
Salinity 15 ppt	5.6	7 days	" "	
Temperature 15° C	9.0	7 days	" "	
Temperature 17.5° C	5.6	7 days	" "	
Fish				
Striped bass, *Morone saxatilis*				
Juveniles	5.0	90 days	Enzyme disruption	Dawson et al. 1977
Juveniles	0.5-5.0	30 days	Decreased oxygen consumption	
Winter flounder,				

Pseudopleuronectes 5*americanus*	5.0	60 days	Increased gill tissue respiration	Calabrese et al. 1975

[a]Each reference applies to the values in the same row and in the rows that follow for which no other reference is indicated.

A study by Beyer et al. (1985) of metal contamination in wildlife from the vicinity of two zinc smelters in Palmerton, Pennsylvania, demonstrated the difficulties in interpretation of cadmium residues from biota in the presence of other potentially hazardous metal contaminants (Table 5). The soil litter horizon at Palmerton was heavily contaminated with lead (2,700 ppm), zinc (24,000 ppm), copper (440 ppm), and cadmium (710 ppm). Invertebrates that fed on soil litter or soil organic matter, such as earthworms, slugs, and millipedes, were rare or absent in the vicinity of the smelters but not at more distant sampling sites (Table 5). Concentrations of all metals tended to be higher in these invertebrates than in other invertebrate groups collected. Amphibians and reptiles were also rare or absent at the Palmerton site, but not at more distant stations. Mean concentrations, in ppm dry weight, of cadmium were highest in carrion insects (25), followed by fungi (9.8), leaves (8.1), shrews (7.3), moths (4.9), mice (2.6), songbirds (2.5), and berries (1.2). By contrast, average concentrations of lead, in ppm dry weight, were highest in shrews (110), followed by songbirds (56), leaves (21), mice (17), carrion insects (14), moths (4.3), berries (4), and fungi (3.7). Evidence for lead poisoning in shrews included high residues in kidney (280 ppm wet weight) and reduced blood enzyme levels. In addition, livers from two cuckoos from Palmerton had lead concentrations of 18 and 25 ppm wet weight; however, the cuckoos and other songbirds appeared to be healthy. Concentrations of zinc and copper tended to be highest in the same organisms that contained the highest concentrations of cadmium, emphasizing the importance of documenting organism body burdens of all suspected contaminants before significance is attributed to any single component. Beyer et al. (1985) demonstrated that only a small portion of all metals measured in the soil became incorporated into plant foliage and suggested that most of the metal contamination detected in biota came from aerial deposition.

In human tissues, there was a significant increase in cadmium burdens in the years 1897-1939 vs. 1980. cadmium content in the renal cortex portion of the kidney increased by a factor of 47 during this interval, and whole body burden increased by a factor near 5 (Drasch 1983). The significance of this increase is not fully clear; however, recent work has suggested that cadmium and lead are associated with increased risk of heart-related death, even in the light of known conventional causes of such fatalities (Voors et al. 1982). Similar data for wildlife are lacking, and this clearly indicates an area for additional research.

Table 5. Cadmium residues, in mg/kg dry weight (ppm), in soil, flora, and fauna collected near two zinc smelters in Palmerton, Pennsylvania (from Beyer et al. 1985).

Soil and category of plants and animals	Direction and distance of areas from smelter emissions	
	Downwind about 2.1 km	Upwind 9.7 km
Soil		
Upper litter layers	250-710	6-13
Upper mineral layers	3-35	1-3
Foliage	8.1	2.3
Acorns and berries	1.2	0.6
Fungi	9.8	2.2
Moths, 8 spp.	0.8-11.0	0.4-1.7
Caterpillars	3.3	0.8
Earthworms, 2 spp.	NF[a]	62-140
Slugs	NF	20
Millipedes	NF	2.1-4.5
Beetles	1.3	0.8
Flies, 2 spp.	29-44	NF
Hornets	NF	2.3
Centipedes	28	NF
Birds		
Carcasses, 9 spp.	--	1.2
Carcasses, 10 spp.	2.5	--
White-footed mouse, carcass	2.6	1.2
Short-tailed shrew, carcass	NF	4.8
Amphibians, 5 spp.	NF	1.4

[a]NF = organism not found.

BIOACCUMULATION

Biological half times of cadmium in humans is lengthy. Based on body burden and excretion data, Cd may remain in the human body 13 to 47 years. Although Cd is excreted primarily in urine and feces, cadmium tends to increase in concentration with age of the organism and eventually acts as a cumulative poison (Hammons et al. 1978). These phenomena have not been documented adequately in wildlife species.

Freshwater and marine aquatic organisms accumulate cadmium from water containing Cd concentrations not previously considered hazardous to public health or to many species of aquatic life (Table 6). In American oysters, held for 40 weeks in flowing seawater containing 5.0 ppb of Cd, edible meats contained 13.6 ppm Cd fresh weight, a level considered to be an emetic threshold for human consumers (Zaroogian and Cheer 1976). These oysters retained virtually all accumulated cadmium (12.5 ppm) during a 16-week posttreatment immersion in clean seawater (Zaroogian 1979). Emetic thresholds for Cd in oysters were surpassed in 5 weeks at 25 ppb and in only 2 weeks at 100 ppb (Shuster and Pringle 1969). There is considerable variation in the ability of teleost tissues to accumulate cadmium from the ambient medium. Among rainbow trout, for example, exposed for 2 weeks to 9 ppb Cd, bioconcentration factors (BCF) were 260 for gill, 17 for liver, 26 for kidney, and zero for spleen and heart tissues (Roberts et al. 1979). At slightly higher ambient Cd levels of 10 ppb and exposure for 3 months, BCF values were substantially higher: 1,740 for gill, 4,900 for liver, 740 for kidney, 160 for spleen, and 100 for heart tissues (Roberts et al. 1979). The evidence for cadmium transfer through various trophic levels suggests that only the lower trophic levels exhibit biomagnification. In the freshwater food chain extending from the alga *Chlorella vulgaris*, to the cladoceran *Daphnia magna*, to the teleost *Leucospius delineatus*, it was demonstrated that algae held 10 days in water containing 10 ppb of cadmium contained 30 ppm dry weight, up from 4.5 ppm at the start (Ferard et al. 1983). Cladocerans feeding on cadmium-loaded algae for 20 days contained 32 ppm Cd dry weight, up from 1.4 ppm at the start. However, fish fed Cd-contaminated cladocerans for 4 days showed no change in body burdens.

Table 6. Bioconcentration of cadmium from ambient medium by selected species of aquatic biota.

Type of medium, taxonomic group, and organism	Ambient concentration of Cd, in ppb	Exposure period, in weeks	Bioconcentration factor, whole organism	Reference[a]
Freshwater				
Insects				
Ephemerella sp.	5.0	52	1,630	Giesy et al. 1979
Pantala hymenea	5.0	52	736	
Ischnura sp.	5.0	52	1,500	
Fam. Pytiscidae	5.0	52	164	
Fam. Chironomidae	5.0	52	2,200	
Fam. Ceratopogonidae	5.0	52	936	
Fish				
Salmo gairdneri	4.0	10	33	Kumada et al. 1980
Gambusia affinis	0.02	8	4,100	Williams and Giesy 1978
Gambusia affinis	5.0	26	7,440	Giesy et al. 1977
Algae				
Chlorella vulgaris	10.0	1.4	2,550	Ferard et al. 1983
Marine				
Molluscs				
Aquipecten irradians	10.0	3	131	Eisler et al. 1972
Crassostrea virginica	10.0	3	116	
Crassostrea virginica	5.0	40	2,720	Zaroogian and Cheer 1976
Fish				
Fundulus heteroclitus	10.0	3	15	Eisler et al. 1972
Crustaceans				
Homarus americanus	10.0	3	21	
Pontoporeia affinis	6.5	66	3,500	Sundelin 1983

[a]Each reference applies to the values in the same row and in the rows that follow for which no other reference is indicated.

In laboratory studies with chipping sparrows fed radiocadmium-109 in their diets for 3 weeks, it was demonstrated that cadmium became localized in the liver and kidneys (Anderson and Van Hook 1973). During posttreatment on a radiocadmium-free diet, there was an initial rapid drop in radioactivity, and the remaining radiocadmium had an estimated biological half-life of 99 days (Anderson and Van Hook 1973). Marine killifish containing radiocadmium-115m lost 90% of the accumulated radiocadmium during a 6-month posttreatment observation period; the liver usually contained 75 to 80% of the total body dose at any time (*Fundulus heteroclitus* (L.) (Eisler 1974). Mallards fed 200 ppm Cd in the diet for about 13 weeks all survived but levels in liver and kidney were elevated at 110 and 134 ppm fresh weight, respectively (White and Finley 1978). Mallard ducklings fed only 20 ppm dietary cadmium for 12 weeks contained 42 ppm Cd in the liver (Cain et al. 1983).

The exact mechanism of acute cadmium poisoning is unknown, but, among teleosts, it depends in part on exposure period, concentration of Cd in the medium, and water temperature and salinity. Under conditions of high Cd concentration and short exposure, the gill seems to be the primary site of damage and accumulation; under conditions of prolonged exposure and low Cd levels, the intestine, kidney, and possibly other tissues were measurably affected. Retention of cadmium by teleosts depends on tissue biomagnification potential, length of postexposure recovery period, and other factors. The significance of comparatively low concentrations of cadmium in tissues of fish, other aquatic organisms, and wildlife, and the implications for organism health, is not fully understood. Although numerous physical, chemical, and biological factors demonstrably modify uptake and

retention of cadmium by fish and wildlife (Hammons et al. 1978; EPA 1980; Eisler 1981, 1984), the significance of relatively high cadmium residues to animal and plant health is difficult to interpret. There is some evidence, however, that life-threatening concentrations are 200 ppm Cd fresh weight in the renal cortex portion of the mammalian kidney (Hammons et al. 1978) and 5.0 ppm fresh weight whole body of estuarine teleosts (Eisler 1974).

TERATOGENESIS, MUTAGENESIS, CARCINOGENESIS

Teratogenic effect on animals appears to be greater for cadmium than for other metals, including lead, mercury, copper, indium, and arsenic (Ferm and Layton 1981). Among amphibians, frog embryos reared in 5,000 to 7,500 ppb Cd showed nonclosure of the neural tube (Ferm and Layton 1981). In embryos of fathead minnows from adults reared in water containing 37 to 57 ppb Cd, and from eggs transferred directly to such media, percent hatching was reduced, deformities were increased, and various blood clots developed (Pickering and Gast 1972). Embryos of the bluegill (*Lepomis macrochirus*) held in water at 80 ppb Cd or more showed edema, microcephalia, and malformed caudal fins (Eaton 1974). Eggs of a marine killifish (*Fundulus heteroclitus*) were little affected at up to 10,000 ppb of cadmium (Weis and Weis 1977). Caudal and hindlimb abnormalities were observed in chickens following injection of eggs with 0.1 to 1.0 ppm of cadmium chloride; excess zinc appeared to have a protective effect (Ferm and Layton 1981). Rats subjected to >6 mg Cd per kg body weight daily during pregnancy produced fetuses with jaw defects, cleft palates, club feet, and pulmonary hyperplasia (Ferm and Layton 1981). Among hamsters, cadmium administration was associated with embryonic tail defects; effects were synergized by salts of lead or mercury and antagonized by selenium (Ferm and Layton 1981). No conclusive evidence of Cd teratogenesis in humans is available.

From a variety of studies in which mice and bacteria were used as models, it appears likely that cadmium has mutagenic effects. Mice injected with 3 or 6 mg $CdCl_2$/kg body weight showed changes in chromosome number 12 h later; similar changes were observed in hamsters at 1.5 to 3.0 mg/kg (Ferm and Layton 1981). Very high dosages (>100 mg/kg) produced chromosomal abnormalities in plant seeds. Also, $CdCl_2$ had a mutagenic effect on indicator strains of *Salmonella* bacteria. However, the evidence for these effects is still diffuse and often contradictory (Ferm and Layton 1981).

Laboratory studies with mice and rats have conclusively demonstrated that the injection of cadmium metal or salts causes malignancies (sarcoma) at the site of injection and testicular tumors; however, the simultaneous administration of zinc is protective against sarcoma and interstitial cell tumor development (EPA 1980). Among humans, the available epidemiological evidence is not sufficient to conclude that cadmium is definitely implicated as a carcinogen (EPA 1980; Nomiyama 1982).

CURRENT RECOMMENDATIONS

Proposed limits for cadmium in water, food, and air for protection of human health and aquatic life are shown in Table 7. It is noteworthy that the current upper limit of 10.0 ppb of cadmium in drinking water for human health protection is not sufficient to protect many species of freshwater biota against the biocidal properties of cadmium or against sublethal effects, such as reduced growth and inhibited reproduction. Ambient water quality criteria formulated for protection of freshwater aquatic life state that, for total recoverable cadmium, the criterion, in µg/L, is the numerical value given by e to the power (1.05 (ln (hardness))-8.53) as a 24-h average and the concentration, in ppb, should never exceed the numerical value given by e to the power (1.05 (ln (hardness)) -3.73). Thus, at water hardnesses of 50, 100, and 200 mg/L as $CaCO_3$, the criteria are 0.012, 0.025, and 0.051 ppb, respectively, and the concentration of total recoverable cadmium should never exceed 1.5, 3.0, and 6.3 ppb, respectively. Unfortunately, data are accumulating that demonstrate that even these comparatively rigorous criteria are not sufficient to protect the most sensitive species of freshwater insects, plants, crustaceans, and teleosts. It now appears that levels in excess of 3.0 ppb of cadmium in freshwater are potentially hazardous to aquatic biota and that levels near 1.0 ppb are cause for concern in waters of low alkalinity. Not listed in Table 7, but still recognized as proposed criteria (EPA 1973), are the comparatively high levels of 10.0 ppb allowed for agricultural use on all soils (except neutral and alkaline soils, which may be irrigated with water having levels as high as 50.0 ppb) and public water supplies for livestock purposes, which may not exceed 50.0 ppb of cadmium.

The saltwater aquatic life protection criterion of 4.5 ppb seems adequate to prevent death, but will not prevent potentially deleterious physiological effects, including disrupted respiration in crustaceans and teleost. Incidentally, at 5.0 ppb of cadmium, the lowest concentration critically examined, oysters biomagnify ambient levels to concentrations hazardous to human consumers and possibly other animal consumers. The maximum allowable saltwater concentration (MAC) during a 24-h period was recommended as 59.0 ppb (Table 7). However, death of various species of marine crustaceans was reported at 60.0 ppb after exposure for 6 weeks and at 14.8 to 19.5 ppb after 23 to 27 days. Furthermore, a MAC of 59 ppb may be met with daily discharges of 59 ppb for 2 h and no discharge of cadmium for the rest of the day. The effects of exposure of marine life to 59 ppb of cadmium salts for 2 h daily for protracted periods have not yet been investigated. Accordingly, seawater concentrations in excess of 4.5 ppb of total cadmium at any time should be considered as potentially hazardous to marine life, until additional data prove otherwise.

Food is recognized as the major source of cadmium in humans, except in comparatively rare cases of occupational air exposure. The recommended upper limit for cadmium in food is 75 µg/day (Table 7). On the basis of an absorption factor of 0.1 (EPA 1980), a total of 7.5 µg Cd will be retained daily. A 70-kg adult ingests an estimated 0.75 kg of food daily, which suggests that human diets should not exceed 100 µg/kg. Ducks, geese, and other species of wildlife, unlike adult humans, may consume 6 to 7% of their total body weight daily and may graze extensively on crops directly affected by sewage and other wastes containing high Cd residues. Feeding studies with mallards indicated that diets containing 200 mg Cd/kg produced no obvious deleterious effects after 13 weeks. At the end of that study, however, kidney cadmium levels under those conditions were about 134 ppm fresh weight, a level near the 200 ppm fresh weight designated a “critical threshold” (and presumably life-threatening) for the renal cortex portion of the human kidney. Field observations on ducks and laboratory studies are not strictly comparable. Under field conditions, birds and other wildlife may consume food containing high Cd levels, but it is almost certain that these diets also contain other potentially harmful contaminants, as well as metals or compounds that may ameliorate cadmium toxicity. The significance of foods containing complex mixtures of contaminants and their resultant toxicological interactions are imperfectly understood. Until other data become available, wildlife dietary levels exceeding 100 µg Cd/kg diet fresh weight on a sustained basis should be viewed with caution.

Current recommendations for cadmium in air and human health protection under the worst scenario (Table 7) assume that total daily air intake is 27.14 m^3 for an adult human who spends about 6.3 h in occupational exposure to air containing 100 µg Cd/m^3 (EPA 1980). Under these conditions, a 70-kg adult would retain about 361 µg Cd/day, based on an absorption factor of 0.5 (EPA 1980), and most of this Cd would probably be translocated to the kidney; a critical threshold level of 200 mg Cd/kg in the kidney would be reached in about 1.52 years. It is not now known whether respiration rates of wildlife, particularly birds, are comparable to those of humans, or whether cadmium absorption energetics are similar, or whether wildlife species that frequent point sources of air contaminated by high Cd levels for protracted periods are at greater risk than humans. Evidence given by Beyer et al. (1985) demonstrated that flora and fauna in the vicinity of industrial smelters were affected by Cd and its associated heavy metals. This strongly suggest that current recommendations for cadmium levels under occupational air exposure should be revised downward for wildlife protection.

Finally, the issue of the significance of cadmium residues in various body parts requires resolution. At this time, it appears that cadmium residues in the vertebrate kidney or liver that exceed 10.0 mg/kg fresh weight or 2.0 mg/kg in whole body fresh weight should be viewed as evidence of probable cadmium contamination. Elevated levels of 13.0 to 15.0 ppm Cd tissue fresh weight probably represent a significant hazard to animals of the higher trophic levels, and residues of 200 ppm fresh weight kidney or more than 5.0 ppm whole animal fresh weight should be considered life-threatening.

Table 7. Current recommendations for cadmium in water, food, and air (adapted from EPA 1980).

Ecosystem, environmental compartment, and other variables		Cadmium concentration[a]
Water		µg/1
Freshwater aquatic life protection		
at water hardness, in mg $CaCO_3$/1, of		
50		1.5
100		3.0
200		6.3
Saltwater aquatic life protection		
24-h average		4.5
Maximum allowable concentration		59.0
Human health protection		
Best case		0.5
Average case		1.3
Worst case		10.0
Food	µg/day	µg/kg diet/day
Human health protection[b]		
Best case	12	16
Average case	30	40
Worst case	75	100
Air		$\mu g/m^3$
Human health protection		
Best case, ambient exposure		0.001
Average case, ambient exposure		0.03
Worst case		
Occupational exposure		100.0
Ambient exposure		0.4

[a]Units of concentration shown apply to the ecosystem concerned (water, food, air).

[b]Assumes consumption of 0.75 kg food per day by 70 kg adult.

ACKNOWLEDGMENTS

I thank L. Garrett, M. Shawe, and B. Graff for literature retrieval; J. Cyphers and I. Moore for secretarial services; G. H. Heinz, O. H. Pattee, J. Jacknow, and S. Hamilton for reviewing the manuscript; and P. H. Eschmeyer and C. I. Short for editorial services.

LITERATURE CITED

Anas, R. E. 1974. Heavy metals in northern fur seals, *Callorhinus ursinus*, and harbor seals, *Phoca vitulina richardi*. U.S. Dep. Comm. Fish. Bull. 72:133-137.

Anderlini, V. 1974. The distribution of heavy metals in the red abalone, *Haliotis rufescens*, on the California coast. Arch. Environ. Contam. Toxicol. 2:253-265.

Anderson, R. L., C. T. Walbridge, and J. T. Fiandt. 1980. Survival and growth of *Tanytarsus dissimilis* (Chironomidae) exposed to copper, cadmium, zinc and lead. Arch. Environ. Contam. Toxicol. 9:329-335.

Anderson, S. H., and R. I. Van Hook, Jr. 1973. Uptake and biological turnover of Cd in chipping sparrows, *Spizella passerina*. Environ. Physiol. Biochem. 3:243-247.

Bebbington, G. N., N. J. Mackay, R. Chvojka, R. J. Williams, A. Dunn, and E. H. Auty. 1977. Heavy metals, selenium and arsenic in nine species of Australian commercial fish. Aust. J. Mar. Freshwater Res. 28:277-286.

Berland, B. R., D. J. Bonin, O. J. Guerin-Ancey, V. I. Kapkov, and D. P. Arlhac. 1977. Action de metaux lourds a des doses subletales sur les caracteristiques de la croissance chez la diatomee *Skeletonema costatum*. Mar. Biol. 42:17-30.

Bertram, P. E., and B. A. Hart. 1979. Longevity and reproduction of *Daphnia pulex* (de Geer) exposed to cadmium-contaminated food or water. Environ. Pollut. 19:295-305.

Beyer, W. N., O. H. Pattee, L. Sileo, D. J. Hoffman, and B. M. Mulhern. 1985. Metal contamination in wildlife living near two zinc smelters. Environ. Pollut. 38 A:63-86.

Biesinger, K. E., and G. M. Christensen. 1972. Effects of various metals on survival, growth, reproduction, and metabolism of *Daphnia magna*. J. Fish. Res. Board Canada 29:1691-1700.

Bohn, A., and B. W. Fallis. 1978. Metal concentrations (As, Cd, Cu, Pb and Zn) in shorthorn sculpins, *Myoxocephalus scorpius* (Linnaeus), and Arctic char, *Salvelinus alpinus* (Linnaeus), from the vicinity of Strathcona Sound, Northwest Territories. Water Res. 12:659-663.

Brown, D. A., C. A. Bawden, K. W. Chatel, and T. R. Parsons. 1977. The wildlife community of Iona Island jetty, Vancouver, B.C., and heavy-metal pollution effects. Environ. Conserv. 4:213-216.

Brungs, W. A., R. A. Carlson, W. B. Horning II, J. H. McCormick, R. L. Spehar, and J. D. Young. 1978. Effects of pollution on freshwater fish. J. Water Pollut. Control Fed. 50:1582-1637.

Bryan, G. W. 1973. The occurrence and seasonal variation of trace metals in the scallops *Pecten maximum* (L.) and *Chlamys opercularis* (L.). J. Mar. Biol. Assoc. U.K. 53:145-166.

Bryan, G. W., and L. G. Hummerstone. 1973. Adaptation of the polychaete *Nereis diversicolor* to estuarine sediments containing high concentrations of zinc and cadmium. J. Mar. Biol. Assoc. U.K. 53:839-857.

Bryan, G. W., and L. G. Hummerstone. 1978. Heavy metals in the burrowing bivalve *Scrobicularia plana* from contaminated and uncontaminated estuaries. J. Mar. Biol. Assoc. U.K. 58:401-419.

Bryan, G. W., and H. Uysal. 1978. Heavy metals in the burrowing bivalve *Scrobicularia plana* from the Tamar estuary in relation to environmental levels. J. Mar. Biol. Assoc. U.K. 58:89-108.

Buhler, D. R., R. R. Claeys, and B. R. Mate. 1975. Heavy metal and chlorinated hydrocarbon residues in California sea lions (*Zalophus californianus californianus*). J. Fish. Res. Board Canada 32:2391-2397.

Bull, K. R., R. K. Murton, D. Osborn, P. Ward, and L. Cheng. 1977. High levels of cadmium in Atlantic seabirds and sea-skaters. Nature 269:507-509.

Butterworth, J., P. Lester, and G. Nickless. 1972. Distribution of heavy metals in the Severn Estuary. Mar. Pollut. Bull. 3:72-74.

Cain, B. W., L. Sileo, J. C. Franson, and J. Moore. 1983. Effects of dietary cadmium on mallard ducklings. Environ. Res. 32:286-297.

Calabrese, A., F. P. Thurberg, M. A. Dawson, and D. R. Wenzloff. 1975. Sublethal physiological stress induced by cadmium and mercury in winter flounder, *Pseudopleuronectes americanus*. Pages 15-21 *in* J. H. Koeman and J. J. T. W. A. Strik (eds.). Sublethal effects of toxic chemicals on aquatic animals, Elsevier Sci. Publ. Co., Amsterdam.

Canton, J. H., and W. Slooff. 1982. Toxicity and accumulation studies of cadmium (Cd^{2+}) with freshwater organisms of different trophic levels. Ecotoxicol. Environ. Safety 6:113-128.

Carmichael, N. G., K. S. Squibb, and B. A. Fowler. 1979. Metals in the molluscan kidney: a comparison of two closely related bivalve species (*Argopecten*), using X-ray microanalysis and atomic absorption spectroscopy. J. Fish. Res. Board Canada 36:1149-1155.

Carroll, J. J., S. J. Ellis, and W. S. Oliver. 1979. Influences of hardness constituents on the acute toxicity of cadmium to brook trout (*Salvelinus fontinalis*). Bull. Environ. Contam. Toxicol. 22:575-581.

Chapman, G. A. 1978. Toxicities of cadmium, copper, and zinc to four juvenile stages of chinook salmon and steelhead. Trans. Am. Fish. Soc. 107:841-847.

Chapman, G. A., and D. G. Stevens. 1978. Acutely lethal levels of cadmium, copper and zinc to adult male coho salmon and steelhead. *Tran. Am. Fish. Soc. 107:837-840.*

Christensen, G., E. Hunt, and J. Fiant. 1977. The effect of methylmercuric chloride, cadmium chloride and lead nitrate on six biochemical factors of the brook trout (*Salvelinus fontinalis*). Toxicol. Appl. Pharmacol. 42:523-530.

Conway, H. L. 1978. Sorption of arsenic and cadmium and their effects on growth, micronutrient utilization, and photosynthetic pigment composition of *Asterionella formosa*. J. Fish. Res. Board Canada 35:286-294.

Cossa, D. 1976. Sorption du cadmium par une population de la diatomee *Phaeodactylum tricornutum* en culture. Mar. Biol. 34:163-167.

Davies, P. H. 1976. Use of dialysis tubing in defining the toxic fractions of heavy metals in natural waters. Pages 110-117 *in* R. W. Andrew, P. V. Hodson, and D. E. Konasewich (eds.). Toxicity to biota of metal forms in natural water. Proc. Workshop, Duluth, MN, October 7-8, 1975, Great Lakes Res. Advis. Bd., Int. Joint Comm.

Dawson, M. A., E. Gould, F. P. Thurberg, and A. J. Calabrese. 1977. Physiological response of juvenile striped bass, *Morone saxatilis*, to low levels of cadmium and mercury. Chesapeake Sci. 18:353-359.

Drasch, G. A. 1983. An increase of cadmium body burden for this century: an investigation on human tissues. Sci. Total Environ. 26:111-120.

Eaton, J. G. 1974. Chronic cadmium toxicity to the bluegill (*Lepomis macrochirus* Rafinesque). Trans. Am. Fish. Soc. 103:729-735.

Eisler, R. 1971. Cadmium poisoning in *Fundulus heteroclitus* (Pisces: Cyprinodontidae) and other marine organisms. J. Fish. Res. Board Canada 28:1225-1234.

Eisler, R. 1974. Radiocadmium exchange with seawater by *Fundulus heteroclitus* (L.) (Pisces; Cyprinodontidae). J. Fish Biol. 6:601-612.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. Biol. Trace Element Res. 6:165-180.

Eisler, R., G. E. Zaroogian, and R. J. Hennekey. 1972. Cadmium uptake by marine organisms. J. Fish. Res. Board Canada 29:1367-1369.

EPA. 1973. Water Quality Criteria 1972. U.S. Environ. Protection Agency Rep. R3-73-033. 594 pp.

EPA. 1980. Ambient water quality criteria for cadmium. U.S. Environ. Protection Agency Rep. 440/5-80-025. 183 pp.

Eustace, I. J. 1974. Zinc, cadmium, copper, and manganese in species of finfish and shellfish caught in the Derwent Estuary, Tasmania. Aust. J. Mar. Freshwater Res. 25:209-220.

Ferard, J. F., J. M. Jouany, R. Truhaut, and P. Vasseur. 1983. Accumulation of cadmium in a freshwater food chain experimental model. Ecotoxicol. Environ. Safety 7:43-52.

Ferm, V. H., and W. M. Layton, Jr. 1981. Teratogenic and mutagenic effects of cadmium. Pages 743-756 *in* J. O. Nriagu (ed.). Cadmium in the environment. Part 2, Health effects. John Wiley, New York.

Finlayson, B. J., and K. M. Verrue. 1982. Toxicities of copper, zinc, and cadmium mixtures to juvenile chinook salmon. Trans. Am. Fish. Soc. 111:645-650.

Foster, P. 1976. Concentrations and concentration factors of heavy metals in brown algae. Environ. Pollut. 10:45-53.

Gardiner, J. 1974. The chemistry of cadmium in natural water-II. The adsorption of cadmium on river muds and naturally occurring solids. Water Res. 8:157-164.

Gentile, S. M., J. H. Gentile, J. Walker, and J. F. Heltshe. 1982. Chronic effects of cadmium on 2 species of mysid shrimp *Mysidopsis bahia* and *Mysidopsis bigelowi*. Hydrobiologia 93:195-204.

George, S. G., B. J. S. Pirie, and T. L. Coombs. 1980. Isolation and elemental analysis of metal-rich granules from kidney of the scallop. *Pecten maximum* (L.). J. Exp. Mar. Biol. Ecol. 42:143-156.

Giesy, J. P., Jr., H. J. Kania, J. W. Bowling, R. L. Knight, S. Mashburn, and S. Clarkin. 1979. Fate and biological effects of cadmium introduced into channel microcosms. U.S. Environ. Protection Agency Rep. 600/3-79-039. 157 pp.

Giesy, J. P., Jr., G. J. Leversee, and D. R. Williams. 1977. Effects of naturally occurring aquatic organic fractions on cadmium toxicity to *Simocephalus serrulatus* (Daphnidae) and *Gambusia affinis* (Poeciliidae). Water Res. 11:1013-1020.

Gish, C. D., and R. E. Christensen. 1973. Cadmium, nickel, lead and zinc in earthworms from roadside soil. Environ. Sci. Technol. 7:1060-1072.

Goldberg, E. D., V. T. Bowen, J. W. Farrington, G. Harvey, J. H. Martin, P. L. Parker, R. W. Risebrough, W. Robertson, E. Schneider, and E. Gamble. 1978. The mussel watch. Environ. Conserv. 5:101-125.

Greig, R. A., D. R. Wenzloff, A. Adams, B. Nelson, and C. Shelpuk. 1977. Trace metals in organisms from ocean disposal sites of the middle eastern United States. Arch. Environ. Contam. Toxicol. 6:395-409.

Greig, R. A., D. R. Wenzloff, C. L. MacKenzie, Jr., A. S. Merrill, and V. S. Zdanowicz. 1978. Trace metals in sea scallops *Placopecten magellanicus*, from eastern United States. Bull. Environ. Contam. Toxicol. 19:326-334.

Hale, J. G. 1977. Toxicity of metal mining wastes. Bull. Environ. Contam. Toxicol. 17:66-73.

Hamanaka, T., H. Kato, and T. Tsujita. 1977. Cadmium and zinc in ribbon seal, *Histriophoca fasciata*, in the Okhotsk Sea. Pages 547-561 *in* Special Volume, Res. Inst. N. Pac. Fish. Hokkaido Univ.

Hammons, A. S., J. E. Huff, H. M. Braunstein, J. S. Drury, C. R. Shriner, E. B. Lewis, B. L. Whitfield, and L. E. Towill. 1978. Reviews of the environmental effects of pollutants: IV cadmium. U.S. Environ. Protection Agency Rep. 600/1-78-026. 251 pp.

Hardisty, M. W., S. Kartar, and M. Sainsbury. 1974. Dietary habits and heavy metal concentrations in fish from the Severn Estuary and Bristol Channel. Mar. Pollut. Bull. 5:61-63.

Harris, J. E., G. J. Fabris, P. J. Statham, and F. Tawfik. 1979. Biogeochemistry of selected heavy metals in Western Port, Victoria, and use of invertebrates as indicators with emphasis on *Mytilus edulis planulatus*. Aust. J. Mar. Freshwater Res. 30:159-178.

Haug, A., S. Melson, and S. Omang. 1974. Estimation of heavy metal pollution in two Norwegian fjord areas by analysis of the brown alga *Ascophyllum nodosum*. Environ. Pollut. 7:179-192.

Heinz, G. H., and S. D. Haseltine. 1983. Altered avoidance behavior of young black ducks fed cadmium. Environ. Toxicol. Chem. 2:419-421.

Heit, M. 1979. Variability of the concentrations of seventeen trace elements in the muscle and liver of a single striped bass, *Morone saxatilis*. Bull. Environ. Contam. Toxicol. 23:1-5.

Horowitz, A., and B. J. Presley. 1977. Trace metal concentrations and partitioning in zooplankton, neuston, and benthos from the south Texas Outer Continental Shelf. Arch. Environ. Contam. Toxicol. 5:241-255.

Hughes, J. S. 1973. Acute toxicity of thirty chemicals to striped bass (*Morone saxatilis*). Proc. Western Assoc. State Game Fish Comm. 53:399-413.

Hulse, M., J. S. Mahoney, G. D. Schroder, C. S. Hacker, and S. M. Pier. 1980. Environmentally acquired lead, cadmium, and manganese in the cattle egret, *Bubulcus ibis*, and the laughing gull, *Larus atricilla*. Arch. Environ. Contam. Toxicol. 9:65-78.

Hutton, M. 1983a. A prospective atmospheric emission inventory for cadmium: the European community as a study area. Sci. Total Environ. 29:29-48.

Hutton, M. 1983b. Sources of cadmium in the environment. Ecotoxicol. Environ. Safety 7:9-24.

Jenkins, D. W. 1980. Biological monitoring of toxic trace metals. Volume 2. Toxic trace metals in plants and animals of the world. Part 1. U.S. Environ. Protection Agency Rep. 600/3-80-090. 503 pp.

Julshamn, K., and O. R. Braekkan. 1975. Determination of trace elements in fish tissues by the standard addition method. Atom. Absorp. Newsl. 14:49-52.

Julshamn, K., and O. R. Braekkan. 1978. The relation between the concentration of some main elements and the stages of maturation of ovaries in cod (*Gadus morrhua*). Fiskeridir. Skr. Ser. Ernaering 1:1-15.

Khalid, R. A., R. P. Gambrell, and W. H. Patrick, Jr. 1981. Chemical availability of cadmium in Mississippi River sediment. J. Environ. Qual. 10:523-528.

Kopfler, F. C., and J. Mayer. 1967. Studies of trace metals in shellfish. Pages 67-80 *in* Proc. Gulf South Atlantic States Shellfish Sanit. Res. Conf.

Korte, F. 1983. Ecotoxicology of cadmium: general review. Ecotoxicol. Environ. Safety 7:3-8.

Kumada, H., S. Kimura, and M. Yokote. 1980. Accumulation and biological effects of cadmium in rainbow trout. Bull. Jpn. Soc. Sci. Fish. 46:97-103.

Kumada, H., S. Kimura, and M. Yokote, and Y. Matida. 1973. Acute and chronic toxicity, uptake and retention of cadmium in freshwater organisms. Bull. Freshwater Fish. Res. Lab. (Tokyo) 22:157-165.

Lande, E. 1977. Heavy metal pollution in Trondheimsfjorden, Norway, and the recorded effects on the fauna and flora. Environ. Pollut. 12:187-198.

Leatherland, T. M., and J. D. Burton. 1974. The occurrence of some trace metals in coastal organisms with particular reference to the Solent region. J. Mar. Biol. Assoc. U.K. 54:457-468.

Lovett, R. J., W. H. Gutenmann, I. S. Pakkala, W. D. Youngs, D. J. Lisk, G. E. Burdick, and E. J. Harris. 1972. A survey of total cadmium content of 406 fish from 49 New York State freshwaters. J. Fish Res. Board Canada 29:1283-1290.

Mackay, N. J., M. N. Kazacos, R. J. Williams, and M. I. Leedow. 1975. Selenium and heavy metals in black marlin. Mar. Pollut. Bull. 6:57-60.

Markard, C. 1983. Impact of cadmium in the environment of the Federal Republic of Germany. Ecotoxicol. Environ. Safety 7:111-116.

Maly, M. S., and G. W. Barrett. 1984. Effects of two types of nutrient enrichment on the structure and function of contrasting old-field communities. Am. Midl. Nat. 111:342-357.

Marshall, J. S. 1978. Population dynamics of *Daphnia galeata mendotae* as modified by chronic cadmium stress. J. Fish. Res. Board Canada 35:461-469.

Martin, J. H., and A. R. Flegal. 1975. High copper concentrations in squid livers in association with elevated levels of silver, cadmium, and zinc. Mar. Biol. 30:51-55.

Martin, W. E., and P. R. Nickerson. 1973. Mercury, lead, cadmium, and arsenic residues in starlings—1971. Pestic. Monit. J. 7:67-72.

May, T. W., and G. L. McKinney. 1981. cadmium, lead, mercury, arsenic, and selenium concentrations in freshwater fish, 1976-77—National Pesticide Monitoring Program. Pestic. Monit. J. 15:14-38.

McIntosh, A. W., B. K. Shephard, R. A. Mayes, G. J. Atchison, and D. W. Nelson. 1978. Some aspects of sediment distribution and macrophyte cycling of heavy metals in a contaminated lake. J. Environ. Qual. 7:301-305.

Melhuus, A., K. L. Seip, H. M. Seip, and S. Myklestad. 1978. A preliminary study of the use of benthic algae as biological indicators of heavy metal pollution in Sorfjorden, Norway. Environ. Pollut. 15:101-107.

Myklestad, S., I. Eide, and S. Melson. 1978. Exchange of heavy metals in *Ascophyllum nodosum* (L.) Le Jod. *in situ* by means of transplanting experiments. Environ. Pollut. 16:277-284.

Nomiyama, K. 1982. Carcinogenicity of cadmium. Jpn. J. Indust. Health 24:13-23.

NRCC. 1979. Effects of cadmium in the Canadian environment. Nat. Res. Coun. Canada, NRCC No. 16743. 148 pp.

Parslow, J. L. F., D. J. Jefferies, and M. C. French. 1972. Ingested pollutants in puffins and their eggs. Bird Study 19:18-33.

Pascoe, D., and D. L. Mattey. 1977. Studies on the toxicity of cadmium to the three-spined stickleback, *Gasterosteus aculeatus* L. J. Fish Biol. 11:207-215.

Pesch, G. G., and N. E. Stewart. 1980. Cadmium toxicity to three species of invertebrates. Mar. Environ. Res. 3:145-156.

Peterson, R. H., J. L. Metcalfe, and S. Ray. 1983. Effects of cadmium on yolk utilization, growth, and survival of Atlantic salmon alevins and newly feeding fry. Arch. Environ. Contam. Toxicol. 12:37-44.

Phillips, J. H. 1976. The common mussel *Mytilus edulis* as an indicator of pollution by zinc, cadmium, lead and copper. II. Relationship of metals in the mussel to those discharged by industry. Mar. Biol. 38:71-80.

Pickering, Q. H., and M. Gast. 1972. Acute and chronic toxicity of cadmium to the fathead minnow (*Pimephales promelas*). J. Fish. Res. Board Canada 29:1099-1106.

Preston, A., D. F. Jeffries, J. W. R. Dutton, B. R. Harvey, and A. K. Steele. 1972. British isles coastal waters: the concentrations of selected heavy metals in sea water, suspended matter and biological indicators—a pilot survey. Environ. Pollut. 3:69-82.

Pringle, B. H., D. E. Hissong, E. L. Katz, and S. T. Mulawka. 1968. Trace metal accumulation by estuarine mollusks. J. Sanit. Engin. Div. 94 SA3:455-475.

Ratkowsky, D. A., S. J. Thrower, I. J. Eustace, and J. Olley. 1974. A numerical study of the concentration of some heavy metals in Tasmanian oysters. J. Fish. Res. Board Canada 31:1165-1171.

Ray, S., D. McLeese, and D. Pezzack. 1980. Accumulation of cadmium by *Nereis virens*. Arch. Environ. Contam. Toxicol. 9:1-8.

Revis, N. W., A. R. Zinsmeister, and R. Bull. 1981. Athero sclerosis and hypertension induction by lead and cadmium ions: an effect prevented by calcium ion. Proc. Nat. Acad. Sci. 78:6494-6498.

Reynolds, B. H. 1979. Trace metals monitoring at two ocean disposal sites. U.S. Environ. Protection Agency Rep. 600/3-79-037. 64 pp. (Avail. from Nat. Tech. Inf. Serv., U.S. Dep. Comm., Springfield, VA 22161).Avail. from Nat. Tech. Inf. Serv., U.S. Dep. Comm., Springfield, VA 22161).

Richardson, M. E., M. R. S. Fox, and B. E. Fry, Jr. 1974. Pathological changes produced in Japanese quail by ingestion of cadmium. J. Nutr. 104:323-338.

Riley, J. P., and D. A. Segar. 1970. The distribution of the major and some minor elements in marine animals. I. Echinoderms and coelenterates. J. Mar. Biol. Assoc. U.K. 50:721-730.

Roberts, K. S., A. Cryer, J. Kay, J. F. de L. G. Solbe, J. R. Wharfe, and W. R. Simpson. 1979. The effects of exposure to sub-lethal concentrations of cadmium on enzyme activities and accumulation of the metal in tissues and organs of rainbow and brown trout (*Salmo gairdneri*, Richardson and *Salmo trutta fario* L.). Comp. Biochem. Physiol. 62C:135-140.

Robertson, D. E., L. A. Rancitelli, J. C. Langford, and R. W. Perkins. 1972. Battelle-Northwest contribution to the IDOE base-line study. Battelle Pac. Northwest Lab., Richland, Wash.:1-46.

Rombough, P. J., and E. T. Garside. 1982. Cadmium toxicity and accumulation in eggs and alevins of Atlantic salmon, *Salmo salar*. Can. J. Zool. 60:2006-2014.

Rosenberg, R. 1977. Effects of dredging operations on estuarine benthic macrofauna. Mar. Pollut. Bull. 8:102-104.

Sarkar, A. K., and R. Mondal. 1973. Injurious effect of cadmium on testis of domestic pigeon and its prevention by zinc. Indian J. Exp. Biol. 11:108-109.

Segar, D. A., J. D. Collins, and J. P. Riley. 1971. The distribution of the major and some minor elements in marine animals. Part II. Molluscs. J. Mar. Biol. Assoc. U.K. 51:131-136.

Shephard, B. K., A. W. McIntosh, G. J. Atchison, and D. W. Nelson. 1980. Aspects of the aquatic chemistry of cadmium and zinc in a heavy metal contaminated lake. Water Res. 14:1061-1066.

Shuster, C. N., Jr., and B. H. Pringle. 1969. Trace metal accumulation by the American Oyster, *Crassostrea virginica*. 1968 Proc. Nat. Shellfish. Assoc. 59:91-103.

Siewicki, T. C., J. E. Balthrop, and J. S. Sydlowski. 1983. Iron metabolism of mice fed low levels of physiologically bound cadmium in oyster or cadmium chloride. J. Nutr. 113:1140-1149.

Sims, R. R., Jr., and B. J. Presley. 1976. Heavy metal concentrations in organisms from an actively dredged Texas bay. Bull. Environ. Contam. Toxicol. 16:520-527.

Snyder, N. F. R., H. A. Snyder, J. L. Lincer, and R. T. Reynolds. 1973. Organochlorines, heavy metals, and the biology of North American accipiters. BioScience 23:300-305.

Spehar, R. L., R. L. Anderson, and J. T. Fiandt. 1978. Toxicity and bioaccumulation of cadmium and lead in aquatic invertebrates. Environ. Pollut. 15:195-208.

Stoneburner, D. L. 1978. Heavy metals in tissues of stranded short-finned pilot whales. Sci. Total Environ. 9:293-297.

Sturkie, P. D. 1973. Effects of cadmium on electrocardiogram, blood pressure, and hematocrit of chickens. Avian Dis. 17:106-110.

Sundelin, B. 1983. Effects of cadmium on *Pontoporeia affinis* (Crustacea: Amphipoda) in laboratory soft bottom microcosms. Mar. Biol. 74:203-212.

Talbot, V. W., R. J. Magee, and M. Hussain. 1976. Cadmium in Port Phillip Bay mussels. Mar. Pollut. Bull. 7:84-86.

Theede, H., N. Scholz, and H. Fisher. 1979. Temperature and salinity effects on the acute toxicity of cadmium to *Laomedea loveni* (Hydrozoa). Mar. Ecol. Prog. Ser. 1:13-19.

Thorp, J. H., J. P. Giesy, and S. A. Wineriter. 1979. Effects of chronic cadmium exposure on crayfish survival, growth, and tolerance to elevated temperatures. Arch. Environ. Contam. Toxicol. 8:449-456.

Tjell, J. C., T. H. Christensen, and F. Bro-Rasmussen. 1983. Cadmium in soil and terrestrial biota with emphasis on the Danish situation. Ecotoxicol. Environ. Safety 7:122-140.

Topping, G. 1973. Heavy metals in shellfish from Scottish waters. Aquaculture 1:379-384.

Turner, J. C., S. R. B. Solly, J. C. M. Mol-Krijnen, and V. Shanks. 1978. Organochlorine, fluorine, and heavy metal levels in some birds from New Zealand estuaries. N. Z. J. Sci. 21:99-102.

Vattuone, G. M., K. S. Griggs, D. R. McIntyre, J. L. Littlepage, and F. L. Harrison. 1976. Cadmium concentrations in rock scallops in comparison with some other species. U.S. Energy Res. Dev. Admin. UCRL 52022: 1-11. (Avail. from Nat. Tech. Inf. Serv., U.S. Dep. Comm., Springfield, VA 22151.)

Vernberg, W. B., P. J. DeCoursey, and J. O'Hara. 1974. Multiple environmental factor effects on physiology and behavior of the fiddler crab, *Uca pugilator*. Pages 381-425 *in* F. J. Vernberg, and W. B. Vernberg (eds.). Pollution and physiology of marine organisms. Academic Press, New York.

Voors, A. W., M. S. Shuman, and W. D. Johnson. 1982. Additive statistical effects of cadmium and lead on heart related disease in a North Carolina USA autopsy series. Arch. Environ. Health 37:98-102.

Watling, H. R., and R. J. Watling. 1976. Trace metals in oysters from Knysna Estuary. Mar. Pollut. Bull. 7:45-48.

Weis, J. S., and P. Weis. 1977. Effects of heavy metals on development of the killifish, *Fundulus heteroclitus*. J. Fish Biol. 11:49-54.

Westernhagen, H. V., V. Dethlefsen, and H. Rosenthal. 1980. Correlation between cadmium concentrations in the water and tissue residue levels in dab, *Limanda limanda* L., and plaice, *Pleuronectes platessa* L. J. Mar. Biol. Assoc. U.K. 60:45-58.

White, D. H., and M. T. Finley. 1978. Uptake and retention of dietary cadmium in mallard ducks. Environ. Res. 17:53-59.

White, D. H., R. C. Stendell, and B. M. Mulhern. 1979. Relations of wintering canvasbacks to environmental pollutants—Chesapeake Bay, Maryland. Wildon Bull. 91:279-287.

White, D. H., K. A. King, and R. M. Prouty. 1980. Significance of organochlorine and heavy metal residues in wintering shorebirds at Corpus Christi, Texas, 1976-77. Pestc. Monit. J. 14:58-63.

Williams, D. R., and J. P. Giesy, Jr. 1978. Relative importance of food and water sources to cadmium uptake by *Gambusia affinis* (Poeciliidae). Environ. Res. 16:326-332.

Windholz, M., S. Budavari, L. Y. Stroumtsos, and M. N. Fertig (eds.). 1976. The Merck Indes, ninth edition. Merck and Co., Rahway, New Jersey.

Zaroogian, G. E. 1979. Studies on the depuration of cadmium and copper by the American oyster *Crassostrea virginica*. Bull. Environ. Contam. Toxicol. 23:117-122.

Zaroogian, G. E., and S. Cheer. 1976. Cadmium accumulation by the American oyster, *Crassostrea virginica*. Nature 261:408-410.

Biological Report 85(1.3)
August 1985

Contaminant Hazard Reviews
Report No. 3

CARBOFURAN HAZARDS TO FISH WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Carbofuran (2, 3-dihydro-2, 2-dimethyl-7-benzofuranyl methyl carbamate) and other carbamate compounds, together with organophosphorus compounds, have virtually replaced the more persistent and hazardous organochlorine systemic pesticides used in agriculture. In general, carbofuran effectively controls insects through an anticholinesterase mode of action. Compared with chlorinated hydrocarbon insecticides, it has a relatively short residual life in the environment, degrades rapidly, and is almost completely excreted by nontarget organisms. Carbofuran degradation is complex and demonstrably modified by numerous biological and physicochemical factors; little is known of the biological properties of the degradation products, especially nitrosated metabolites, in relation to chronic toxicity, teratogenicity, mutagenicity, or carcinogenicity.

At currently recommended application rates and in present formulations, carbofuran has caused sporadic, and sometimes extensive, field kills of fish, wildlife, and invertebrates. In short-term laboratory tests, significant death rates were observed at concentrations of about 200 ppb carbofuran (in water) for sensitive species of aquatic biota, 238 ppb (acute oral, µg/kg body weight) and 190,000 ppb (dietary, µg/kg diet) for birds, and 2000 ppb (acute oral) and 100,000 ppb (dietary) for mammals. Among representative indicator species, harmful and sometimes life-threatening effects of carbofuran have been recorded for fish at nominal water concentrations of >15 ppb and for aquatic invertebrates at >2.5 ppb. For birds and mammals, harmful effects were observed at 10 to 50 ppb in the diet and 1000 ppb in drinking water. For comparison, the "safe" level of carbofuran in meat products for human consumption is 50 ppb. Current maximum permissible aerosol levels of 0.05 ppb (50.0 $\mu g/m^3$) carbofuran appear sufficient to protect wildlife; however, evidence suggests that aerosol concentrations should never exceed 2 ppb. Plants are significantly more resistant to carbofuran than are invertebrates and higher organisms. Carbofuran hazards to migratory waterfowl may be reduced by prohibiting granular formulations containing more than 3% active ingredients. In rice culture, carbofuran should be applied before the fields are flooded and after the peak of bird migration. Since annual domestic use of carbofuran exceeds 3.2 million kg (7 million pounds), it appears that additional research is merited on the biotic effects of various formulations of carbofuran, especially flowable formulations, and on applications to crops other than rice, such as corn, alfalfa, and hay.

This report should be cited as:

Eisler, R. 1985. Carbofuran hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.3). 36 pp.

TABLES

ACKNOWLEDGMENTS

I thank V. Adomaitis, L.R. DeWeese, C.J. Henny, and J.B. Hunn for reviewing the manuscript; P.H. Eschmeyer and C.I. Short for editorial services; L. Garrett, M. Shawe, and B. Graff for library services; and J. Cyphers and I. Moore for secretarial help.

INTRODUCTION

Carbofuran is a broad spectrum systemic insecticide that is currently registered for use on agricultural crops such as alfalfa (*Medicago sativa*), peanuts (*Arachis hypogaea*), rice (*Oryza sativa*), sugar cane (*Saccharum officinarum*), and especially corn (*Zea mays*) Anon. 1971; Dorough 1973; Palmer and Schlinke 1973; EPA 1976; Finlayson et al. 1979; Flickinger et al. 1980). Carbofuran, together with other carbamate compounds, organophosphorus insecticides, and pyrethroids, are the major substitutes for the more persistent pesticides such as DDT, chlordane, and heptachlor. In 1974, domestic carbofuran use was slightly over 3.2 million kg (7 million pounds) active ingredients, most of which was applied to control corn pests (EPA 1976). As a group, the carbamates, including carbofuran, have controlled insects effectively: their residual life in the environment is relatively short; excretion from the animal body is comparatively rapid and almost quantitative; and the terminal residues produced are polar and formed by chemical processes normally considered as steps in metabolic detoxication.

However, at recommended application rates, which range from 0.28 to 10.9 kg active ingredients/ha (0.25 to 9.7 lb/acre), and in a variety of formulations, carbofuran has been held responsible for sporadic kills of fish, wildlife, beneficial insects, and terrestrial and aquatic invertebrates. For example, among birds that only occasionally consume domestic crops, carbofuran applied to vegetables reportedly killed about 1400 ducks, largely green-winged teal (*Anas carolinensis*), pintail (*A. acuta*), and American wigeon (*A. americana*) in British Columbia between 1973 and 1975 (Flickinger et al. 1980). Carbofuran applied to alfalfa killed 2450 American wigeons at one California location in 1974 (Stickel 1975), 500 Canada geese (*Branta canadensis*) in southern Oklahoma in 1976, 1000 wigeons in Kansas in 1976, and more than 1063 wigeons in California in 1976-1977 (Flickinger et al. 1980). Secondary poisoning of red-shouldered hawks (*Buteo lineatus*) was reported after the application of carbofuran to Maryland cornfields (Balcomb 1983). Aerial application to flooded rice fields in various portions of Texas between 1970 and 1975 at the rate of 0.56 kg/ha resulted in deaths of three species of sandpipers (*Erolia* spp.) and red-winged blackbirds (*Agelaius phoeniceus*), as well as frogs, crayfish, leeches, earthworms, and four species of fish; however, no carbofuran residues were detectable among survivors 2 to 11 days postexposure (Flickinger et al. 1980).

In this account, I summarize the technical literature documenting environmental hazards associated with carbofuran, with special emphasis on game fish and migratory birds, and provide recommendations for protection of sensitive species of fish and wildlife. It is part of a continuing series of synoptic reviews prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service.

CHEMICAL PROPERTIES AND PERSISTENCE

Carbofuran (2, 3-dihydro-2, 2-dimethyl-7-benzofuranyl methyl carbamate) is also known as Furadan, Bay 70142, CAS 1563-66-2, Curaterr, D-1221, ENT-27164, and FMC 10242 (Johnson and Finley 1980) and Niagara NIA-10242 (Leuck et al. 1968). Carbofuran has a molecular weight of 221.25 and a melting point of 150-152°C; it is comparatively stable under neutral or acidic conditions, but degrades rapidly in alkaline media (Anon. 1971). This white, crystalline, solid of empirical formula $C_{12}H_{l5}NO_3$ is soluble at concentrations up to 700 ppm (mg/l) in water, but at < 30 ppm in various organic solvents. It degrades at >130° and supports combustion if ignited (FMC 1979). The compound is available as a wettable powder, a granular formulation, and in solution as a flowable formulation (Anon. 1971; EPA 1976).

Pharmacologically, carbofuran inhibits cholinesterase, resulting in stimulation of the central, parasympathetic, and somatic motor systems. Acute toxic clinical effects resulting from carbofuran exposure in animals and humans appear to be completely reversible and have been successfully treated with atropine sulfate. However, treatment should occur as soon as possible after exposure because acute carbofuran toxicosis can be fatal; younger age groups of various species are more susceptible than adults (Finlayson et al. 1979). Carbofuran labels indicate that application is forbidden to streams, lakes, or ponds. In addition, manufacturers have stated that carbofuran is poisonous if swallowed, inhaled, or absorbed through the skin; users are cautioned not to breathe carbofuran dust, fumes, or spray mist; and treated areas should be avoided for at least 2 days (Anon. 1971). Three points are emphasized at this juncture. First, some carbofuran degradation products have not been identified. Second, toxicologic, mutagenic, carcinogenic, and teratogenic properties of most carbofuran degradation products have not been satisfactorily evaluated. And third, numerous physical, chemical, and biological vectors modify carbofuran degradation processes, as well as biological uptake, retention, and translocation. Each of these points is developed in greater detail later.

Carbofuran is metabolized by hydroxylation and hydrolysis in plants, insects, and mammals (Metcalf et al. 1968). The primary transformation product in most plants appears to be 3-hydroxycarbofuran. However, levels of 3-hydroxycarbofuran and other degradation products in plants are influenced by numerous factors, including plant age, soil type, pesticide formulation, application method and rate, and weather conditions, as is shown later. Oxidation of unconjugated 3-hydroxycarbofuran yields 3-ketocarbofuran, which is, in turn, rapidly hydrolyzed to the much less toxic 3-ketocarbofuran phenol. Accordingly, 3-ketocarbofuran is not likely to be detected as a terminal residue in plants above trace levels. Residue analyses indicated that carbofuran and 3-hydroxycarbofuran are the compounds that occur most often in plant tissues after treatment (Finlayson et al. 1979). In measurement of carbofuran and its degradation products in corn at 117 and 149 days after carbofuran application (Table 1), the decrease of 62% in the total carbamate residues detected between silage and harvest was attributed to cessation of root uptake, volatilization from drying plant surfaces, and further degradation to phenolic compounds. No losses of carbofuran or 3-hydroxycarbofuran were detected in fortified corn silage after storage at minus 18°C for 1 year (Finlayson et al. 1979).

Variation in content of carbofuran and its degradation products was evident among crop species (Finlayson et al. 1979). Strawberries (*Fragaria vesca*), for example, contained higher residues of phenol than of' either carbamate or hydroxy products. Carbofuran can persist in Mugho pine needles for at least 2 years at insecticidally-active concentrations. This unequal distribution of carbofuran in different parts of a plant has also been observed for tobacco (*Nicotiana tabacum*), in which more of the compound was in large leaves than in the tops of plants, suggesting that carbofuran moved in the plant fluids to the point of greatest transpiration in the leaves.

Carbofuran in animals may also be hydrolyzed to produce carbofuran-7-phenol; hydrolysis of the 3-hydroxyderivitive leads to formation of 3-hydrocarbofuran-7-phenol. Other degradation products include N-hydroxymethyl carbofuran and, as in plants, 3-hydroxy and 3-ketoderivitives. All of these compounds may become conjugated and excreted by animals in urine and, presumably, bile (Metcalf et al. 1968; Finlayson et al. 1979). At least 10 metabolites of carbofuran are known at present; their interrelations are shown in detail by Menzie (1978).

In water, the carbofuran degradation rate is strongly influenced by pH (Chapman and Cole 1982). The time to 50% degradation of carbofuran in water was 3.2 years at pH 4.5, 13.3 years at pH 5.0 and 6.0, 1.9 months at pH 7.0, and only 1 week at pH 8.0. The rate of carbofuran loss is also influenced by sunlight, trace impurities, and temperature, but not as dramatically as by pH (Seiber et al. 1978).

Persistence of carbofuran in soils is a function of many factors, including pesticide formulation, rate and method of application, soil type, pH, rainfall, temperature, moisture content, and microbial populations (Ahmad et al. 1979; Deuel et al. 1979; Finlayson et al. 1979; Fuhremann and Lichtenstein 1980; Gorder et al. 1982). Results of several studies indicate that loss from soil samples also takes place at low temperatures when air drying is used; this loss may present a problem to chemists who are unable to conduct analyses immediately after samples are collected (Finlayson et al. 1979). Soil pH is one of the more extensively documented variables affecting degradation; it may become increasingly important as acidic precipitation (acid rain) increases. Carbofuran decomposes rapidly at pH levels >7.0, but becomes increasingly stable as pH decreases. The hydrolysis half-life is about 16 years at a soil pH of 5.5; the half-lives are about 35, 6, and 0.25 days at pH levels of 7.0, 8.0, and 9.0, respectively (Finlayson et al. 1979). Similar results were reported by Getzin (1973), Caro et al. (1976), Seiber et al. (1978), and, in Table 2, by Chapman and Cole (1982). Temperature and moisture content of soils were both positively related to degradation of carbofuran to 3-hydroxycarbofuran, 3-ketocarbofuran, carbofuran phenol, and 3-ketocarbofuran phenol. In general, an increase in temperature from 15° to 27°C had a greater influence on degradation than did an increase from 27° to 35°C, although 27° to 35° was the range in which maximum degradation rates were observed (Ou et al. 1982). Similar results were recorded by Caro et al. (1976), Seiber et al. (1978), and Gorder et al. (1982).

The role of soil bacteria in carbofuran degradation is unclear. Most investigators agree that carbofuran is hydrolyzed to its phenol, which is immediately bound to soil constituents and then metabolized by microorganisms, either slowly (Getzin 1973; Siddaramappa et al. 1978) or rapidly, especially when associated with a *Pseudomonas* sp. isolate (Felsot et al. 1981). Others believe that carbofuran is degraded primarily by chemical hydrolysis, in which bacterial processes assume a negligible role (Venkateswarlu and Sethunathan 1978; Finlayson et al. 1979). Evidence exists demonstrating that soil microbial populations increased by up to 3

times following application of carbofuran (Mathur et al. 1976, 1980); that prior treatment with carbofuran produced rapid degradation attributed to acclimatized soil bacteria (Felsot et al. 1981); that estuarine bacteria are comparatively resistant to carbofuran (Brown et al. 1975); that sterilized soils did not show evidence of carbofuran degradation (Felsot et al. 1981); and that degradation to carbofuran phenol was most rapid under anaerobic conditions (Venkateswarlu and Sethunathan 1978). It appears that additional research is required on bacterial degradation of carbofuran, with special emphasis on acid-resistant strains.

LETHAL EFFECTS

GENERAL

In acute toxicity tests with aquatic organisms, LC-50 (96h) values, with only one exception, exceeded 130 ppb. The exception was the larva of a marine crab with an LC-50 (96h) value of 2.5 ppb. In tests of longer duration with fish, safe concentrations were estimated to range between 15 and 23 ppb. Among the most sensitive species of birds tested, the acute oral LD-50 was 238 ppb (µg/kg body weight), the dietary carbofuran LD-50 value was 190 ppm, dermal LD-50's exceeded 100 ppm, and the LC-100 value in drinking water was 2 ppm. Mammals were comparatively resistant, having LD-50 acute oral toxicities >2 ppm, a dietary LD-38 of 100 ppm after 8 months, and dermal LD-50's >120 ppm. However, only 2 ppb as an aerosol killed 50% of rhesus monkeys in 6 hours, and 40 ppb killed all pheasants within 5 minutes. Bees and earthworms were relatively sensitive to carbofuran, but test conditions were sufficiently different to preclude a strict comparison with vertebrate species. Among photosynthetic species, concentrations of 200 ppm carbofuran partly inhibited germination of rice seeds, but not other species tested, after exposure for 24 hours. Effects of carbofuran on plants are considered negligible when contrasted to faunal damage effects.

AQUATIC ORGANISMS

Among freshwater organisms, LC-50 values for carbofuran ranged from 130 to 14,000 ppb in tests of 72 to 96 hours; fish were the most sensitive and worms the most resistant (Table 3). A relatively narrow toxic range for carbofuran in the climbing perch (*Anabas testudineus*) was indicated by the LC-0 (120 hour) value of 560 ppb and the LC-100 (24 hour) value of 1560 ppb (Bakthavasalam and Reddy 1981). It is noteworthy that carbofuran was not as toxic to aquatic biota as were various cyclodiene chlorinated hydrocarbon insecticides, almost all of which were subsequently withdrawn from commercial use and replaced by carbofuran and other carbamates, and organophosphorus and other compounds.

In flow-through toxicity tests with the marine sheepshead minnow (*Cyprinodon variegatus*), LC-50 values had stabilized by day 60 of exposure with no significant mortality afterwards; however, the LC-50 value was 386 ppb at 96 hours, or 7.8 times greater than that (49 ppb) at 131 days (Table 3). At concentrations up to 49 ppb, carbofuran did not significantly affect the growth of parent fish nor the number of eggs produced. But mortality of fry from fish exposed to 23 and 49 ppb was measurably greater than that of controls (Parrish et al. 1977). On the basis of these and other observations that indicate that growth of surviving fry in all concentrations was not affected and that carbofuran was degraded rapidly in seawater and in sheepshead minnows, it was concluded that the MATC (maximum allowable toxicant concentration) for carbofuran and sheepshead minnow lies between 15 and 23 ppb (Parrish et al. 1977). This observation is similar to that of Caldwell (1977), who demonstrated that adult Dungeness crabs (*Cancer magister*) showed no deleterious effects on growth, survival, or reproduction during exposure to 25 ppb of carbofuran for 69 days. Larvae of Dungeness crabs were substantially more sensitive than adults in 96-hour tests (Table 3). In addition, Caldwell (1977) indicated that 1.5 ppb of carbofuran inhabited swimming ability in zoeal stages of Dungeness crabs and 1.0 ppb inhibited molting and prevented metamorphosis to more advanced larval stages. These observations require verification because mortality in control groups was high, a typical problem in bioassays with larvae of marine invertebrates.

BIRDS AND MAMMALS

Acute oral toxicities of carbofuran to birds ranged from 238 ppb (µg/kg body weight) for fulvous whistling-ducks (*Dendrocygna bicolor*) to 38,900 ppb for domestic chickens (Table 4). The fulvous whistling-duck has been listed as endangered since 1972 by the Texas Organization for Endangered Species (Flickinger et al. 1980). Concentrations of 1 ppm of carbofuran in drinking water of the ducks caused symptoms of intoxication in 7 days, and 2 ppm was lethal in the same period (Tucker and Crabtree 1970). Acute symptoms of carbofuran poisoning in birds, which may persist for up to 7 days, include a loss in muscular coordination, wings crossed high over the back, head nodding, vocal sounds, salivation, tears, diarrhea, immobility with wings spread,

labored breathing, eye pupil constriction, arching of back, and arching of neck over back; death may occur within 5 minutes after ingestion (Tucker and Crabtree 1970). Among mallards (*Anas platyrhynchos*), sensitivity to carbofuran was greater in ducklings than in older birds (Table 4); this relation appears to hold true for other birds for which data are available. Acute oral toxicities of carbofuran to various species of mammals ranged from 2000 ppb in mice to 34,500 ppb in rats (Table 4). Mammals were generally more resistant than birds to acute biocidal properties of carbofuran.

Carbofuran administered to birds in the diet for 5 days, plus 3 days postexposure on an untreated diet, produced 50% kill values of 140 to 1459 ppm dietary carbofuran; younger birds were more sensitive than older ones (Table 5). Food consumption in groups of Japanese quail (*Coturnix japonica*) with high carbofuran-induced mortality was markedly depressed during the first 3 days of treatment (Hill and Camardese 1982). Red-winged blackbirds, the most sensitive bird species tested in food repellency tests, consumed a normal ration of food contaminated with carbofuran (Schafer et al. 1983). As a result, carbofuran has a high potential for causing acute poisoning episodes in birds (Schafer et al. 1983). Field application of carbofuran granules to corn, at planting, in Maryland during 1980 was presumed to be responsible for deaths of songbirds (order Passeriformes) and white-footed mice (*Peromyscus leucopus*); all organisms contained high levels of carbofuran in the gastrointestinal tract and liver, suggesting extensive feeding in treated fields (Balcomb et al. 1984a). A similar situation occurred in Perry, Florida, after treatment of pine seed orchards (Overgaard et al. 1983). Laboratory studies with house sparrows (*Passer domesticus*) and red-winged blackbirds demonstrated that ingestion of a single carbofuran granule is fatal to either species (Balcomb et al. 1984a,b). In groups of old-field mice (*Peromyscus polionotus*) fed 100 ppm dietary carbofuran for 8 months, mortality was 38%; however, growth, development and behavior was normal among survivors from this group and their offspring (Wolfe and Esher 1980). In a preliminary study with rats and old-field mice fed 100 ppm of dietary carbofuran, parents lost weight (but none died), and the survival of young was reduced (Wolfe and Esher 1980).

Aerosol toxicity of carbofuran to warm-blooded animals ranged from about 2 ppb for rhesus monkeys to 110 ppb for rats (Table 6). These values substantially exceed the established Threshold Limit Value (TLV) of 0.05 ppb (50.0 ug/m^3) for protection of human health (Draper et al. 1981). The TLV is a time-weighted concentration for a 40-hour work week that nearly all workers can withstand without adverse effects, including eye and skin irritations and other minor irritations. Inhalation doses to humans were estimated during and immediately after aerial spraying of Furadan 4-Flowable at the rate of 446 g active ingredients carbofuran/ha, a concentration that generally controls most pests. During aerial sprayings of this level, the concentration of carbofuran in ambient air did not exceed 0.0033 ppb at any location (Draper et al. 1981), suggesting that most birds and wildlife are afforded a high degree of protection during aerial spraying at current recommended dosages. Studies with rats subjected to 1.2 ppb carbofuran aerosols for 50-70 minutes showed a substantial (55%) decrease in red blood cell cholinesterase 10 minutes posttreatment and a return to normal levels in 2 hours (Ferguson et al. 1982). After 8 hours, a maximum of 55% of the carbofuran was excreted by respiration (38%) or in the urine (12%) or feces (5%); the remainder was located primarily in the liver and gastrointestinal tract. Plasma half-lives in rats for carbofuran (36 minutes) and 3-hydroxycarbofuran (62 minutes) were similar to those previously determined after oral and intravenous exposures (Ferguson et al. 1982).

Dermal toxicity of carbofuran to birds and mammals is comparatively low. The LD-50 dermal values ranged from about 1000 ppm in cattle (Palmer et al. 1981) down to 100 ppm in birds; i.e., house sparrows and queleas (Schafer et al. 1983); rats and rabbits were intermediate in sensitivity at 120 and 885 ppm, respectively (Draper et al. 1981). Birds contaminated by carbofuran spray could possibly ingest significant amounts while preening (Finlayson et al. 1979), but such ingestion has not been demonstrated. For humans, the maximum potential dermal exposure based on exposed face, hands, forearms, back and front of the neck, and "V" of the chest is 3.1 mg (Draper et al. 1981) or 0.04 ppm for a person weighing 70 kg. This relationship suggests that human populations would be at greater risk than wildlife populations under current carbofuran spray application protocols.

Secondary poisoning of avian raptors with carbofuran is a recent and disturbing event (Balcomb 1983). Consider the case of a female red-shouldered hawk in adult plumage weighing 683 g, found in a cornfield near Beltsville, Maryland, in May, 1981. The field had been treated the previous day with Furadan 10 granules (10% carbofuran), applied at 1.12 kg/ha active ingredients. The bird was entirely paralyzed except for some head and neck movement, salivating a brown fluid, and respiring in rapid pants. These signs are consistent with those

observed in birds dosed in the laboratory with carbofuran. Stomach contents contained remains of a northern short-tailed shrew (*Blarina brevicauda*) and a common grackle (*Quiscalus quiscula*). A total of 96.6 ug of carbofuran was extracted from the gastrointestinal tract and stomach contents and tissues. Judging by the body weight of the hawk, and an LD-50 range of 0.26 to 5.6 mg/kg in various nondomesticated birds (Table 4), this amount of carbofuran would constitute between 2.5 and 59% of the known LD-50 values; however, carbofuran in birds is readily absorbed from the gut and widely transported in the body. Accordingly, the amount of toxicant extracted from the digestive tract was probably only a portion of that ingested by the hawk. In the same cornfield, at the same time, a smaller adult red-shouldered hawk (possibly the female's mate) was found that showed similar, but less severe, signs. Within 24 hours, it appeared to have recovered completely and was released. As judged by carbofuran residues in small mammals and birds at this site, the residues present in the digestive tract of the female hawk, and the nature of the toxic symptoms observed, the two red-shouldered hawks were probably poisoned by carbofuran acquired from small vertebrate prey or scavenged from the treated areas (Balcomb 1983).

TERRESTRIAL INVERTEBRATES

At recommended field application rates of granular carbofuran formulations, some losses of earthworms, springtails, and other soil-inhabiting organisms should be expected; spray and dust formulations adversely affect honeybees and other airborne crop pollinators (Finlayson et al. 1979). Bees are extremely susceptible to carbofuran. In one study with honeybees (*Apis* spp.), subjected to high levels of carbofuran, some young adults in the contaminated hive were unable to emerge from their cells, and those that did emerge remained weak and unfed. Eventually, the hive became vulnerable to invasion by the greater wax moth (*Galleria melonella*), an insect that subsequently destroyed the entire hive (Keener and Pless 1974). The LD-50 dose for honeybees was estimated at 0.16 ug/bee. If 1.12 kg carbofuran/ha were uniformly distributed at a height of 10 m, flying bees could encounter a lethal dose in only 2 seconds (Atkins et al. 1976).

Studies with susceptible and selectively bred carbofuran-resistant houseflies (*Musca domestica*) indicated that LD-50 values for susceptible and resistant strains were 0.1 and 1.3 ug/insect, respectively (Dorough 1973). Resistant flies contained up to 34% more cholinesterase than susceptible strains and could excrete carbofuran almost twice as fast (Dorough 1973). Carbofuran resistance among pestiferous insects is not yet widely known or adequately documented.

Among earthworms, the characteristic symptoms of carbofuran poisoning were rigidity, immobility, lesions, and segmental swelling, as well as cholinesterase inhibition (Stenerson et al. 1973). Worms maintained in soils to which commercial applications of carbofuran had been applied developed two types of lesions within 72 hours: multisegmental swelling that often ulcerated, causing death of the worm, and a discrete nodular mass protruding from the surface of the worm (Sileo and Gilman 1975). The LC-50 values were 0.5 ppm at 5 hours for *Lumbricus herculeus* (Lebrun et al. 1981), but 2.4 and 13.0 ppm at 5 days for *Lumbricus terrestris* and *Eisenia foetida*, respectively; the differences in sensitivity were attributed to a greater excretion rate of carbofuran by Eisenia (Gilman and Vardanis 1974). When applications of carbofuran to soils was 9.1 kg/ha, 50% of the *Lumbricus* died in 72 hours (Ruppel and Laughlin. 1977). At lower application rates of 2 kg/ha, populations of two species of Australian earthworms were reduced; juvenile stages were most severely affected (Martin 1980). The loss of earthworms could result in reduced food for many wildlife species.

Finlayson et al. (1979) indicated that some species of birds might absorb a lethal dose of carbofuran through foraging on poisoned invertebrates. For example, the woodcock (*Philohela minor*) which preys intensively on earthworms, may consume up to 50% of its body weight (about 125 g of food) per day. If each worm contained 1.3 ppm carbofuran, a woodcock would then ingest 0.16 mg of carbofuran or the equivalent of 0.65 mg/kg body weight (Finlayson et al. 1979), an oral dose lethal to many bird species. To date, secondary poisoning of woodcocks has not been verified under controlled conditions.

PLANTS

Carbofuran was more toxic to blue-green alga (*Nostoc muscorum*) at pH 5 to 6 than at pH 7.5 to 10; toxicity was lessened under conditions of reduced illumination and low population density (Kar and Singh 1978). All effects were observed at comparatively high carbofuran concentrations of 25 to 100 PPM.

Seeds of okra (*Abelmoschus esculentus*) treated with carbofuran, at 1, 3, or 5% active ingredient carbofuran by weight of seed, germinated normally after 90 days of storage (Gaikwad and Pawar 1979). After 6 months of storage, however, germination was measurably reduced at all carbofuran treatments. Okra plants developed normally except for a reduction in plumule length, but this effect was also observed among okra seeds tested with a wide variety of agricultural chemicals.

The effect of carbofuran on the germination of seeds of cotton (*Gossypium hirsutum*), rice, and groundnut (*Arachis hypogea*) were investigated by Arunachalam and Lakshmanan (1982), in rice seeds exposed for 24 hours to 100 or 200 ppm carbofuran, germination decreased 8 and 23%, respectively; seeds of the other two species were not affected at these exposure rates. Treated rice seedlings that germinated grew two to three times faster than controls, especially in the roots and leaves; no reasons were offered to account for these differences in rice plants. Carbofuran residues in seeds of the three test species exposed for 24 hours to 100 ppm carbofuran ranged from 17.5 to 28.1 ppm; at 200 ppm carbofuran these values ranged from 24.0 to 30.4 ppm. At 72 hours posttreatment, residues had declined markedly to 0.1 to 4.7 ppm in the groups treated with 100 ppm carbofuran and 2.3 to 3.8 ppm in the groups treated with 200 ppm. Observed growth promotion effects in certain plants by carbofuran and some of its metabolites may be due to effects on plant oxidase systems, rather than on insecticidal or nematocidal properties of the compound; however, the source of the effects has not been demonstrated conclusively (Finlayson et al. 1979).

SUBLETHAL EFFECTS

GENERAL

Most investigators agree that carbofuran degrades or is biotransformed rapidly, with negligible accumulations in biota. Numerous studies have demonstrated that carbofuran, at high sublethal concentrations, was capable of disrupting enzyme and lipid metabolism, but that effects were reversible with no observable permanent damage. Three major data gaps appear still to exist. First, latent biochemical and physiological effects that appear at substantial intervals posttreatment have not been explained. Second, interaction of carbofuran with other environmental compounds, especially other agricultural chemicals, are largely unknown, and the effects may cause more than additive damage. Third, and most important, data are scarce or lacking on chronic toxicity, teratogenicity, mutagenicity, and carcinogenicity of the degradation products of carbofuran, especially degradation products that may also form nitroso compounds; nitrosated carbofuran metabolites, for example, are demonstrably mutagenic.

AQUATIC ORGANISMS

Carbofuran reportedly disrupts enzyme and lipid metabolism in fishes and may not degrade as rapidly under field conditions as suggested by laboratory studies. However, most investigators argue that carbofuran, under current application rates, does not accumulate to a significant extent in aquatic systems and rapidly degrades under field and model microcosm study conditions.

In studies with the African catfish (*Mystus vittatus*) exposed to 31 or 62 ppb of carbofuran for 30 days, serum transaminases were significantly elevated (Verma et al. 1981a). In comparison with catfish exposed to concentrations of 21 ppb or less during the same period, there were also significant depressions in alkaline phosphatase activity in the liver; acid phosphatase activity in the liver, kidneys, and gills; and gulucose-6-phosphatase in the liver and kidneys (Verma et al. 1981b). In climbing perch, mean lipid levels in muscle and liver were elevated after exposure to an LC-0 (120 hour) dose of 560 ppb carbofuran for 120 hours; a similar pattern was observed following exposure to an LC-100 (24 hour) concentration of 1560 ppb for 6 hours (Bakthavasalam and Reddy 1981). Carbofuran-induced alterations have also been documented in serum chemistry of the African catfish during immersion in 21 ppb for 30 days (Verma et al. 1982b); in brain acetylcholinesterase activity of climbing perch and milkfish (*Channa punctatus*) 30 days after exposure to high sublethal levels for 48 hours (Jash and Bhattacharya 1983); and in blood and tissue enzyme and ammonia levels in the air-breathing catfish (*Clarias batrachus*) 1 month after exposure for 30 days to 500 ppb carbofuran (Mukhopadhyay et al. 1982). In field studies with *Trichogaster pectoralis*, a fish extensively cultured in flooded Malaysian rice paddies, (Gill (1980) found that the degradation of carbofuran in the liver was slower than that reported for laboratory animals and suggested that caution be exercised in the extrapolation of rates of carbofuran oxidative hydroxylation activity from laboratory organisms to fishes cultured in rice fields.

On the other hand, negligible accumulations of carbofuran were observed in egg masses of the caddisfly (*Triaenodus tardus*) during immersion for 120 hours in water containing 8 ppb of carbofuran . ; the low uptake was apparently related to the low partition coefficient of carbofuran (Bellick and Fels 1981). Rapid equilibrium and low accumulation was also reported for the sheepshead minnow (*Cyprinodon variegatus*); in a 28-day flow-through study, maximum tissue concentrations were measured between days 3 to 10 when upper concentration factors of 5 to 20X were recorded (Parrish et al. 1977). Field applications of carbofuran in farm ponds in Arkansas and Kansas were associated with low. mortality in fish (Davey et al. 1976) or negligible effects on fish and plankton (Klaassen and Kadoum 1979). Kansas farm ponds subjected to 25 ppb of carbofuran contained 10.6 ppb in surface waters 1 day later, but nondetectable residues thereafter; residues were <0.4 ppb at 1 day in mud, zooplankton, and fish (Klaassen and Kadoum 1979). Farm ponds treated with 50 ppb of carbofuran after 3 days contained 15 ppb carbofuran in surface water and 26 to 46 ppb in mud, but nondetectable residues in biota; no measurable residues were found in any sample after 25 days (Klaassen and Kadoum 1979). When atrazine at 300 ppb was applied in combination with 50 ppb carbofuran, carbofuran was detectable in surface water at 23 days posttreatment at 1.5 ppb, but not in the soil, biota, or any other compartment (Klaassen and Kadoum 1979).

Koeppe and Lichtenstein (1982), in a well-designed agromicrocosm study, evaluated the influence of percolating water on soils containing 3.6 ppm of radiolabeled (C-14) carbofuran. After 3 weeks, 49% of the carbofuran had been removed with percolating water from soils, and 37% was later recovered from soils and corn. In nonpercolated soils, 80% of the carbofuran was still associated with soils and corn. The aquatic components, including water, lake mud, plants (*Elodea*), and fish (the guppy *Poecilia*), contained 25% of the soil-applied carbofuran, although 49% had been- initially added to the aquariums by way of percolated water. This loss of 24% was attributed partly to the degradation of carbofuran to $C0_2$. About 75% of all the radiocarbon was in lake mud, most of it unextractable. Carbofuran was the major compound recovered from control and percolated soils, accounting for 39 and 15%, respectively; 3-ketocarbofuran and 3-hydroxycarbofuran were identified as the major metabolites. The addition of captafol, a fungicide, to carbofuran-treated soils resulted in a more rapid disappearance of the insecticide from terrestrial soils and reduced uptake by corn. The addition of EPTC, a herbicide, had no measurable effect on terrestrial components, but EPTC and captafol both caused increased recoveries of C-14 labeled carbofuran residues from lake bottom mud. In another study, radiolabeled carbofuran was applied at 1.12 kg/ha to a model ecosystem containing seedling sorghum plants (*Sorghum halopense*) saltmarsh caterpillar larvae (*Estigmene acrea*), the alga *Oedogonium cardiacum*, freshwater clams (*Corbicula manilensis*), crabs (*Uca minax*), a cladoceran (*Daphnia* sp.), mosquito larvae, unidentified species of frogs and snails, and the freshwater macrophyte *Elodea canadensis* (Yu et al. 1979). Carbofuran was rapidly, but not completely, degraded in water to carbofuranphenol, 3-ketocarbofuran, 3-hydroxycarbofuranphenol, N - hydroxy - methyl carbofuran, 3-hydroxycarbofuran, and several unknown compounds. Carbofuran was highly toxic to crabs, clams, and *Daphnia* immediately after application to the model ecosystem, but all animals, except one crab, survived restocking 20 days later.

The freshwater bivalve molluscs *Glebula rotundata* and *Rangia cuneata* absorbed waterborne carbofuran but did not appear to concentrate it (Zakour 1980). Both species of clams were very tolerant, even though symptoms of poisoning, such as shell gaping, foot extension, and incoordination, were evident when carbofuran exposures were high (75 ppm). *Glebula* converted injected radiolabeled carbofuran to a variety of free metabolites, primarily hydrolysis products, and also polar carbofuran metabolites that were not degraded by conditions known to hydrolyze glycosidic conjugates. These polar metabolites may contain some type of amino acid moiety. The rate of carbofuran metabolism by *Glebula* was slower than that reported for most other animals, but was more rapid than that of plants and microorganisms (Table 7). Bacterial metabolism of carbofuran was negligible in both *in vivo* and *in vitro* studies with bivalve molluscs (Zakour 1980).

BIRDS

Birds may encounter carbofuran through respiratory, dermal, and oral routes. Depending on the dietary requirements of particular species, ingestion of contaminated vegetables and poisoned invertebrates may be important exposure routes (Finlayson et al. 1979). Carbofuran may prove harmful alone or in combination with other substances. For example, male Japanese quail fed 0.5 ppm dietary carbofuran for 18 weeks exhibited a 79% inhibition of plasma cholinesterase activity (Dieter and Ludke 1978). The reduction was slightly greater (84%) when carbofuran was fed in combination with 0.05 ppm dietary morsodren, a methyl mercury compound, although morsodren had no measurable effect on cholinesterase activity when fed alone at that dosage. Since

many species of fish-eating birds frequently contain 0.05 ppm of mercury in various tissues, interaction effects of mercury with carbofuran and other cholinesterase-inhibiting compounds may produce synergistic, deleterious effects (Dieter and Ludke 1978).

Low oral dosages or high dietary levels of carbofuran produced no permanent damage effects in northern bobwhites. A single oral dose of 2 mg carbofuran/kg body weight did not affect brain cholinesterase levels at 48 hours, or growth, metabolic efficiency, or metabolized energy at 8 days (Solomon and Robel 1980). The activities of bobwhites fed 131 ppm dietary carbofuran for 14 days was reduced, but this effect was temporary and recovery was complete within 14 days on a carbofuran-free diet. The temporarily reduced activity was attributed to the rapid metabolic breakdown of carbofuran (Robel et al. 1983).

Among laying white leghorn hens, 80% of a single oral dose of 2.7 mg carbofuran/kg body weight was eliminated in feces within 10 days (Hicks et al. 1970). All eggs contained detectable carbofuran; the highest concentration of 0.13 ppm developed on day 4. Residues in liver and kidney were about 2.6 ppm at 6 hours but declined to 0.2 ppm in 24 hours. Muscle and fat contained about 0.3 ppm at 6 hours and <0.l ppm at 24 hours. Hicks et al. (1970) indicated that hydroxylation of carbofuran and hydrolysis of the carbamate ester were the predominant pathways in the metabolism of carbofuran by laying hens; similar results were obtained at single oral doses of 2.7 or 0.3 mg carbofuran/kg body weight.

MAMMALS

Among larger mammals, carbofuran is associated with a variety of stress symptoms, including increased salivation, muscle tremors, prostration, labored breathing, loss of appetite and (in rare cases) death. These symptoms were observed in 1- to 2-week old calves given single doses of carbofuran at 0.25-5.0 mg/kg body weight orally or 0.05-0.1% dermally, in cattle yearlings at 1.0-5.0 mg/kg orally or 0.1% dermally, and in sheep at 2.5-5.0 mg/kg orally (Palmer and Schlinke 1973). All survivors had completely recovered at 5 days posttreatment. Lactating cows fed corn silage containing 1.4-3.9 ppm carbofuran for 8 weeks, or about 74 mg carbofuran daily, showed no decrease in blood cholinesterase; furthermore, no carbofuran residues were detected in the milk (Leuck et al. 1968). Other studies with lactating cows dosed orally with carbofuran (Dorough and Ivie 1968; Ivie and Dorough 1968) showed almost complete excretion in 10 days, mostly through urine (94%), feces (0.7%) and milk (0.2%). Carbofuran metabolites in urine, feces, and excreted milk included the 3-hydroxy-, 3-keto-, and 3-hydroxy-N-hydroxymethyl derivatives, both conjugated and free, and unknown constituents, perhaps carbon dioxide formed by carbofuran hydrolysis.

In investigations of the effects of carbofuran or its metabolites on mice and rats, pregnant mice receiving 0.01 or 0.5 mg dietary carbofuran/kg daily throughout gestation gave birth to viable, overtly normal offspring at term (Barnett et al. 1980). Significant elevation of serum immunoglobins was measured in 101-day old male offspring of female parents receiving 0.5 mg/kg dietary carbofuran. This effect was not observed at day 400 or 800. In female offspring from the group receiving 0.01 mg/kg carbofuran, serum immunoglobins were significantly depressed at day 101, but not thereafter (Barnett et al. 1980). Disturbances in immunoglobulin contents may decrease immunocompetence and, thus, indirectly contribute to morbidity and premature mortality. In rats fed comparatively high dietary levels of 30 ppm carbofuran for 90 days, with mean daily intake of 1.97 mg carbofuran/kg body weight, growth was significantly reduced and ventral prostate gland metabolism of RNA, DNA, and protein was altered (Shain et al. 1977). Prenatal exposure of mice to 0.01 mg carbofuran/kg body weight daily, administered orally during gestation, resulted in persistent postnatal endocrine dysfunction in adults; specifically, the impairment of hepatic metabolism and elevation of plasma corticosterone (Crammer et al. 1978). Unexpectedly, however, at a higher dose of 0.05 mg/kg, there were no significant differences from controls, and the endocrine function of tested mice was normal. In female rats given a single dose of 0.05 mg carbofuran per kg body weight orally on the 18th day of gestation, acetylcholinesterase (AchE) activity decreased significantly in maternal and fetal blood and in the maternal liver within 1 hour (Cambon et al. 1979). At higher dosages of 0.25 and 2.5 mg/kg, AchE was also depressed in the fetal liver and in the maternal and fetal brains; the effects were not measurable 24 hours postadministration.

Carbamate pesticides can easily be converted to N-nitroso derivatives in the presence of sodium nitrite under acidic conditions. The N-nitroso form of carbofuran could possibly be formed in the human stomach (Nelson et al. 1981). Since carbofuran is used routinely on a variety of crops and nitrite is a common component of the human diet and is present in human saliva, nitrosation of carbamates under conditions simulating those in the human stomach is possible. Lijinsky and Schmal (1978) tested nitrosocarbofuran and

five other nitrosated carbamate pesticides for carcinogenicity in rats. Nitrosocarbofuran, at 16.5 mg/kg body weight administered orally once weekly for 23 weeks, was the most toxic compound tested and caused the death of several animals by liver damage early in the experiment. Among survivors, nitrosocarbofuran was the most carcinogenic, as judged by the numbers of carcinomas and tumors that developed. Nitrosation rates of carbofuran in the environment are not now adequately documented, but conceivably could represent an environmental risk to wildlife. Surprisingly, nitrosocarbofuran was among the least mutagenic compounds tested in rats; no obvious explanation is available of the differences in carcinogenic and mutagenic properties (Lijinsky and Schmal 1978). It is noteworthy that data on chronic toxicity, teratogenicity, mutagenicity, and carcinogenicity of degradation products of carbofuran, especially carbofuran-7-phenol, and 3-hydroxycarbofuran-7-phenol are either scarce or lacking (Finlayson et al. 1979); a similar case is made for nitrosocarbofuran and other degradation products of carbofuran which may also form nitroso compounds. More recent work (Nelson et al. 1981) indicated that nitrosated 3-hydroxycarbofuran and 3-ketocarbofuran produced mutagenic responses in bacterial strains of *Salmonella typhimurium* and chromosome aberrations in ovary cells of Chinese hamsters. Nitrosocarbofuran and 3-hydroxynitrosocarbofuran also induced large numbers of sister chromatid exchanges in the same cells. Furthermore, nitroso derivatives of carbofuran were considerably more active than nitroso forms of other carbamate pesticides in producing mutagenicity in *Salmonella* (Nelson et al. 1981). On the other hand, technical formulations of the parent carbofuran were neither genotoxic nor mutagenic to bacteria, yeast, or corn (Gentile et al. 1982).

TERRESTRIAL INVERTEBRATES

In decomposing the dead organic matter in a deciduous forest ecosystem, the detritus food chain may account for more than half the energy flowing through the ecosystem. Carbofuran can significantly disturb decomposition rates of litter communities, with profound consequences for nutrient recycling and incorporation of organic matter into the soils. For example, application of 0.29 kg/ha of carbofuran to a red maple (*Acer rubrum*) litter community near Ottawa, Canada, reduced daily decomposition rates by about 40%; all of the groups of macrodecomposers present, including Collembola, Acarina, Lepidoptera, Coleoptera, Diplopoda, and Annelida, have been shown to be susceptible to carbofuran and may have been affected by the treatment (Weary and Merriam 1978).

CURRENT RECOMMENDATIONS

In Canada, for regulatory purposes, the tolerance level for carbofuran in animal tissues or food, feed, and fiber crops is based on the total carbamate content of the sample, as indicated by total carbofuran, 3-hydroxycarbofuran, 3-ketocarbofuran, and their conjugates (Finlayson et al. 1979), presumably carbofuran phenol, 3-ketocarbofuran phenol , and 3-hydroxycarbofuran phenol. In the United States, the tolerance level is based on carbofuran and four metabolites: 3-hydroxycarbofuran; carbofuran phenol; 3-hydroxycarbofuran phenol; and 3-ketocarbofuran phenol (EPA 1976). Carbofuran levels considered safe range from 0.05 ppm (including 0.02 ppm carbofuran metabolites) in meat, fat, and meat by-products to 40.0 ppm (including 20.0 ppm carbofuran metabolites) in alfalfa hay; intermediate values are 0.1 ppm in milk, 0.2 ppm in corn grain, and 25.0 ppm in corn fodder and forage (EPA 1976). No recommended carbofuran level is currently being promulgated by any regulatory agency for the protection of sensitive species of aquatic biota and wildlife.

On the basis of evidence presented herein, I conservatively estimate that, in terms of total carbofuran in water, damage is possible to aquatic invertebrates at >2.5 ppb and to teleosts at >15 ppb. These levels could he attained during a heavy rainfall shortly after carbofuran treatment of adjacent fields. Among sensitive species of warm-blooded animals, dietary concentrations as low as 10 ppb have demonstrable effects, which were measurable only after extended periods postingestion; for comparison, this level is about 1/5 that allowed in meat by-products for human consumption. Current maximum permissible aerosol levels of 0.05 ppb (50 ug/m^3) appear sufficient to protect wildlife with the proviso that concentrations not exceed 2.0 ppb at any time.

Sporadic kills of migratory birds were associated with carbofuran formulations containing 3% active ingredients (a.i.). For example, migratory sandpipers died after eating Furadan 3 G granules (3% a.i.) applied to rice crops in Texas (Flickinger et al. 1980). The granules probably were ingested while the sandpipers were probing and skimming the surface of wet soil for insects and crustaceans. Other species of migratory waterfowl may have mistaken the small size and density of Furadan granules for seed, particularly in areas where concentrations of granules were abundant after misuse and careless applications. It appears that granular carbofuran formulations need to be developed that contain less than 3% a.i. in order to protect waterfowl, yet

still maintain their effectiveness against target organisms. In rice field pest control, carbofuran should be applied before the fields are flooded and delayed to avoid peak bird migration. Research also appears warranted on the effects on fish and wildlife of the numerous carbofuran formulations used, especially liquid spray formulations (flowables), and on applications to crops other than rice, such as corn, alfalfa, and hay.

Additional long-term research is urgently needed on potential impacts of degradation products of carbofuran on sensitive species of aquatic organisms and wildlife, with special attention to nitrosated carbofuran metabolites. Such data are now scarce or lacking. Research is also needed on chemical and biological interactions of carbofuran with other agricultural chemicals applied to the same locations, which are imperfectly understood. Finally, researchers must elucidate the significance of metabolic upset recorded in various species of laboratory mammals at considerable periods after carbofuran insult.

LITERATURE CITED

Ahmad, N., D.D. Walgenbach, and G.R. Sutter. 1979. Degradation rates of technical carbofuran and a granular formulation in four soils with known insecticide use history. Bull. Environ. Contam. Toxicol. 23:572-574.

Anon. 1971. Furadan. Insecticide-acaricide-nematicide. Chemagro Corp. Kansas City, MO. 4 pp.

Arunachalam, K., and M. Lakshmanan. 1982. Translocation, accumulation and persistence of carbofuran in paddy, ground nut, and cotton. Bull. Environ. Contam. Toxicol. 28:230-238.

Atkins, E.L. Jr., L.D. Anderson, D. Kellum, and K.W. Newman. 1976. Protecting honeybees from pesticides. Univ. California, Div. Agric. Sci., Leafl. 2883. 14 pp.

Bakthavasalam, R., and Y.S. Reddy. 1981. Lipid kinetics in relation to the toxicity of three pesticides in the climbing perch, *Anabas testudineus* (Bloch). Proc. Indian Nat. Sci. Acad. B 47:670-676.

Balcomb, R. 1983. Secondary poisoning of red-shouldered hawks with carbofuran. J. Wildl. Manage. 47:1129-1132.

Balcomb, R., C.A. Bowen II, D. Wright, and M. Law. 1984a. Effects on wildlife of at-planting corn applications of granular carbofuran. J. Wildl. Manage. 48:1353-1359.

Balcomb, R., R. Stevens, and C. Bowen II. 1984b. Toxicity of 16 granular insecticides to wild-caught songbirds. Bull. Environ. Contam. Toxicol. 33:302-307.

Barnett, J.B., J.M. Spyker-Cranmer, D.L. Avery, and A.M. Hoberman. 1980. Immunocompetence over the lifespan of mice exposed in utero to carbofuran or diazinon: I. Changes in serum immunoglobin concentrations. J. Environ. Pathol. Toxicol. 4:53-63.

Belluck, D., and A. Felsot. 1981. Bioconcentration of pesticides by egg masses of the caddisfly, *Triaenodes tardus* Milne. Bull. Environ. Contam. Toxicol. 26:299-306.

Brown, K.W., D.C. Anderson, S.G. Jones, L.E. Deuel, and J.D. Price. 1979. The relative toxicity of four pesticides in tap water and water from flooded rice paddies. Int. J. Environ. Stud. 14:49-54.

Brown, L.R., E.G. Alley, and D.W. Cook. 1975. The effects of mirex and carbofuran on estuarine microorganisms. U.S. Environ. Protection Agency Rep. 660/3-75-024. 47 pp.

Brungs, W.A., R.A. Carlson, W.B. Horning II, J.H. McCormick, R.L. Spehar, and J.D. Yount. 1978. Effects of pollution on freshwater fish. J. Water Pollut. Control Fed. 50:1582-1637.

Caldwell, R.S. 1977. Biological effects of pesticides on the dungeness crab. U.S. Environ. Protection Agency Rep. 600/3-77-131. 125 pp.

Cambon, C., C. Declume, and R. Derache. 1979. Effect of the insecticidal carbamate derivatives (Carbofuran, Pirimicarb and Aldicarb) on the activity of acetylcholinesterase in tissues from pregnant rats and fetuses. Toxicol. Appl. Pharmacol. 49:203-208.

Caro, J.H., A.W. Taylor, and H.P. Freeman. 1976. Comparative behavior of dieldrin and carbofuran in the field. Arch. Environ. Contam. Toxicol. 3:437-447.

Chapman, R.A., and C.M. Cole. 1982. Observations on the influence of water and soil pH on the persistence of pesticides. J. Environ. Sci. Health B 17:487-504.

Cheah, M-L., J.W. Avault, Jr., and J.B. Graves. 1980. Acute toxicity of selected rice pesticides to crayfish *Procambarus clarkii*. Prog. Fish-Cult. 42:169-172.

Crammer, J.S., D.L. Avery, R.R. Grady, and J.I. Kitoy. 1978. Postnatal endocrine dysfunction resulting from prenatal exposure to carbofuran, diazinon or chlordane. J. Environ. Pathol. Toxicol. 2:357-369.

Dad, N.K., S.A. Qureshi, and V.K. Pandya. 1982. Acute toxicity of two insecticides to tubificid worms, *Tubifex tubifex* and *Limnodrilus hoffmeisteri*. Environ. Int. 7:361-363.

Davey, R.B., M.V. Meisch, and F.L. Carter. 1976. Toxicity of five ricefield pesticides to the mosquitofish, *Gambusia affinis*, and green sunfish, *Lepomis cyanellus*, under laboratory and field conditions. Environ. Entomol. 5:1053-1056.

Deuel, L.E., Jr., J.D. Price, F.T. Turner, and K.W. Brown. 1979. Persistence of carbofuran and its metabolites, 3-keto and 3-hydroxy carbofuran, under flooded rice culture. J. Environ. Qual. 8:23-26.

Dieter, M.P., and J.L. Ludke. 1978. Studies on combined effects of organophosphates or carbamates and morsodren in birds. II. Plasma and cholinesterase in quail fed morsodren and orally dosed with parathion or carbofuran. Bull. Environ. Contam. Toxicol. 19:389-395.

Dorough, H.W. 1973. Metabolism of carbamate insecticides. U.S. Environ. Protection Agency Rep. 650/1-74-002. 244 pp.

Dorough, H.W., and G.W. Ivie. 1968. Carbon-14 milk constituents fed carbamate labelled with carbon-14 on the carbonyl. Science 159(3816):732-733.

Draper, W.M., R.D. Gibson, and J.C. Street. 1981. Drift from and transport subsequent to a commercial aerial application of carbofuran: an estimation of potential human exposure. Bull. Environ. Contam. Toxicol..26:537-543.

EPA. 1976. Substitute chemical program. Initial scientific and minieconomic review of carbofuran. U.S. Environ. Protection Agency Rep. 540/1-76-009. 187 pp.

Felsot, A., J.V. Maddox, and W. Bruce. 1981. Enhanced microbial degradation of carbofuran in soils with histories of Furadan use. gull. Environ. Contam. Toxicol. 26:781-788.

Ferguson,, P.W., S.A. Jewell, R.I. Krieger, and O.G. Raake. 1982. Carbofuran disposition in the rat after aerosol inhalation. Environ. Toxicol. Chem. 1:245-258.

Finlayson, D.G., J.R. Graham, R. Greenhalgh, J.R. Roberts, E.A.H. Smith, P. Whitehead, R.F. Willes, and I. Williams. 1979. Carbofuran: criteria for interpreting the effects of its use on environmental quality. Nat. Res. Coun. Canada, Publ. NRCC 16740. 191 pp.

Flickinger, E.L., K.A. King, W.F. Stout, and M.M. Mohn. 1980. Wildlife hazards from Furadan 3 G applications to rice in Texas. J. Wildl. Manage. 44:190-197.

FMC. 1979. Technical Bulletin, Furadan. FMC Corp., Middleport, NY. 4 pp.

Fuhremann, T.W., and E.P. Lichtenstein. 1980. A comparative study of the persistence, movement, and metabolism of six carbon-14 insecticides in soils and plants. J. Agric. Food Chem. 28:446-452.

Gaikwad, S.K., and V.M. Pawar. 1979. Effect of systemic insecticides on the germination and seedling development of okra (*Abelmoschus esculentus* (L) Moench). Seed Res. 7:28-33.

Gentile, J.M., G.J. Gentile, J. Bultman, R. Sechriest, E.D. Wagner, and M.J. Plewa. 1982. An evaluation of the genotoxic properties of insecticides following plant and animal activation. Mutation Res. 101:19-29.

Getzin, L.W. 1973. Persistence and degradation of carbofuran in soil. Environ. Entomol. 2:461-467.

Gill, S.J. 1980. In vitro metabolism of carbofuran by liver microsomes of the padifield fish *Trichogaster pectoralis*. Bull. Environ. Contam. Toxicol. 25:697-701.

Gilman, A.P., and A. Vardanis. 1974. Carbofuran. Comparative toxicity and metabolism in the worms *Lumbricus terrestris* L. and *Eisenia foetida* S. J. Agric. Food Chem. 22:625-628.

Gorder, G.W., P.A. Dahm, and J.J. Tollefson. 1982. Carbofuran persistence in cornfield soils. J. Econ. Entomol. 75:637-642.

Hicks, B.W., H.W. Dorough, and R.B. Davis. 1970. Fate of carbofuran in laying hens. J. Econ. Entomol. 63:1108-1111.

Hill, E.F., R.G. Heath, J.W. Spann, and J.S. Williams. 1975. Lethal dietary toxicities of environmental pollutants to birds. U.S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 191. 61 pp.

Hill, E.F., and M.B. Camardese. 1982. Subacute toxicity testing with young birds: response in relation to age and interest variability of LC-50 estimates. Pages 41-65 in D.W. Lamb, and E.E. Kenaga (eds.). Avian and mammalian wildlife toxicology: second conference. Am. Soc. Testing Mater. ASTM STP 757.

Hudson, R.H., R.K. Tucker, and M.A. Haegele. 1972. Effect of age on sensitivity: acute oral toxicity of 14 pesticides to mallard ducks of several ages. Toxicol. Appl. Pharmacol. 22:556-561.

Ivie, G.W., and H.W. Dorough. 1968. Furadan-C metabolism in a lactating cow. J. Agric. Food Chem. 6:849-855.

Jash, N.B., and S. Bhattacharya. 1983. Delayed toxicity of carbofuran in freshwater teleosts, *Channa punctatas* (Bloch) and *Anabas testudineus* (Bloch). Water Air Soil Pollut: 19:209-213.

Johnson, W.W., and M.T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. Summaries of toxicity tests conducted at Columbia National Fisheries Research Laboratory, 1965-78. U.S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Kar, S., and P. K. Singh. 1978. Effect of pH, light intensity and population on the toxicity of the pesticide carbofuran to the blue-green alga *Nostoc muscorum*. Microbios 21:177-184.

Keener, J.A., and C.D. Pless. 1974. Effects of direct application of selected pesticides on honeybee colonies. Tenn. Farm Home Sci. 89:5-8.

Klaassen, H.E., and A.M. Kadoum. 1979. Distribution and retention of atrazine and carbofuran in farm pond ecosystems. Arch. Environ. Contam. Toxicol. 8:345-353.

Koeppe, M.K., and E.P. Lichtenstein. 1982. Effects of percolating water, captafol, and EPTC on the movement and metabolism of soil-applied (14C) carbofuran in an agromicrocosm. J. Agric. Food Chem. 30:116-121.

Lebrun, P., A. de Medts, and G. Wauthy. 1981. Eco-toxicologie comparee et bioactivite de trois insecticides carbamates sur une population experimentale de vers de terre, *Lumbricus herculeus*. Pedobiologia 21:225-235.

Leuck, D.B., M.C. Bowman, J.-C. Johnson, Jr., E.W. Beck, and R.S. Lowery. 1968. Niagara NIA-10242 insecticide residues: their persistence in coastal bermudagrass, corn, and silages, and their effect, fed in silage, on lactating cows. J. Econ. Entomol. 61:1349-1352.

Lijinsky, W., and D. Schmal. 1978. Carcinogenesis by nitroso derivatives of methylcarbamate insecticides and other nitrosoamides in rats and mice. Pages 495-501 in E.A. Walker, M. Castenegro, L. Griciute, and R.E. Lyle (eds.). Environmental aspects of N-nitroso compounds. World Health Org., Int. Agency Res. Cancer, IARC Sci. Publ. 19.

Martin, N.A. 1980. Earthworm (Oligochaeta: Lumbricidae) populations and late summer pasture renovation. N. Z. J. Agric. Res. 23:417-419.

Mathur, S.P., H.A. Hamilton, R. Greenhalgh, K.A. Macmillan, and S.U. Khan. 1976. Effect on microorganisms and persistence of field-applied carbofuran and dyfonate in a humic mesisol. Canad. J. Soil Sci. 56:89-96.

Mathur, S.P., H.A. Hamilton, and T.C. Vrain. 1980. Influence of some field.-applied nematicides on microflora and mineral nutrients in an organic soil. J. Environ. Sci. Health B 15:61-76.

Menzie, C.M. 1978. Metabolism of pesticides. Update II. U.S. Fish Wild. Serv. Spec. Sci. Rep.-Wildl. 212. 381 pp.

Metcalf, R.L., T.R. Fukuto, C. Collins, K. Borck, S.A. El-Aziz, R. Munoz, and C.C. Cassil. 1968. Metabolism of 2,2-dimethyl-2,3- dihydrobenzofuranyl-7 N-methylcarbamate (Furadan) in plants, insects, and mammals. J. Agric. Food Chem. 16:300-311.

Mukhopadhyay, P.K., A.P. Mukherji, and P.V. Dehadrai. 1982. Certain biochemical responses in the air-breathing catfish *Clarias batrachus* exposed to sublethal carbofuran. Toxicology 23:337-345.

Nelson, J., E.A. MacKinnon, H.F. Mower, and L. Wong. 1981. Mutagenicity of N -nitroso derivatives of carbofuran and its toxic metabolites. J. Toxicol. Environ. Health 7:519-531.

Ou, L-T., D.H. Gancarz, W.B. Wheeler, P.S.C. Rao, and J.M. Davidson. 1982. Influence of soil temperature and soil moisture on degradation and metabolism of carbofuran in soils. J. Environ. Qual. 11:293-298.

Overgaard, N.A., L.R. Barber, D.F. Walsh, R.E. Mapor, G.D. Hestel, and J.E. Gates. 1983. Evaluation of modified Powr-Till seeder for soil incorporation of carbofuran to provide insect control and minimize bird mortality in pine seed orchards. U.S. Dep. Agric., Forest Serv., South. Reg., Tech. Publ. R8-TP3. 35 pp.

Palmer, J.S., and J.C. Schlinke. 1973. Toxic effects of carbofuran in cattle and sheep. J. Am. Vet. Med. Assoc. 162:561-563.

Parrish, P.R., E.E. Dyar, M.A. Lindberg, C.M. Shanika, and J.M. Enos. 1977. Chronic toxicity of methoxychlor, malathion, and carbofuran to sheepshead minnows (*Cyprinodon variegatus*). U.S. Environ. Protection Agency Rep. 36 pp.

Robel, R.J., R. W. Felthousen, and A.D. Dayton. 1983. Effects of dietary carbofurans on bobwhite activity patterns. Bull. Environ. Contam. Toxicol. 30:105-109.

Ruppel, R.F., and C.W. Laughlin. 1977. Toxicity of some soil pesticides to earthworms. J. Kansas Entomol. Soc. 50:113-118.

Schafer, E.W., Jr., R.B. Brunton, N.F. Lockyer, and J.W. DeGrazio. 1973. Comparative toxicity of seventeen pesticides to the quelea, house sparrow, and red-winged blackbird. Toxicol. Appl. Pharmacol. 26:154-157.

Schafer, E.W., Jr., W.A. Bowles, Jr., and J. Hurlbert. 1983. The acute oral toxicity, repellency, and hazard potential of 998 chemicals to one or more species of wild and domestic birds. Arch. Environ. Contam. Toxicol. 12:355-382.

Seiber, J.N., M.P. Catahan, and C.R. Barril. 1978. Loss of carbofuran from rice paddy water: chemical and physical factors. J. Environ. Sci. Health B 13:131-148.

Shain, S.A., J.C. Shaeffer, and R.W. Boesel. 1977. The effect of chronic ingestion of selected pesticides upon rat ventral prostate homeostasis. Toxicol. Appl. Pharmacol. 40:115-130.

Sherman, M., and E. Ross. 1969. Acute and subacute toxicity of Japanese quail of the carbamate insecticides, carbofuran, and SD 8530. Poult. Sci. 48:2013-2018.

Siddaramappa, R., A.C. Tirol, J.N. Seiber, E.A. Heinrichs, and I. Watanabe. 1978. The degradation of carbofuran in paddy water and flooded soil of untreated and retreated rice fields. J. Environ. Sci. Health B 13:369-380.

Sileo, L., and A. Gilman. 1975. Carbofuran-induced muscle necrosis in the earthworm. J. Invert. Pathol. 25:145-148.

Solomon, K.E., and R.J. Robel. 1980. Effects of carbaryl and carbofuran on bobwhite energetics. J. Wildl. Manage. 44:682-686.

Stenersen, J., A. Gilman, and A. Vardanis. 1973. Carbofuran: its toxicity to and metabolism by earthworm (*Lumbricus terrestris*). J. Agric. Food Chem. 21:166-171.

Stickel, W.H. 1975. Some effects of pollutants in terrestrial ecosystems. Pages 25-74 in A.D. McIntyre and C.F. Mills (eds.). Ecological toxicology research. Plenum Press, New York.

Tucker, R.K., and D.G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 84. 131 pp.

Turner, B.C., and J.H. Caro. 1973. Uptake and distribution of carbofuran and its metabolites in field-grown corn plants. J. Environ. Qual. 2:245-247.

Venkateswarlu, K., and N. Sethunathan. 1978. Degradation of carbofuran in rice soils as influenced by repeated applications and exposure to aerobic conditions following anaerobiosis. J. Agric. Food Chem. 26:1148-1151.

Verma, S.R., S. Rani, S.K. Bansal, and R.C. Dalela. 1980. Effects of the pesticides thiotox, dichlorvos and carbofuran on the test fish *Mystus vittatus*. Water Air Soil Pollut. 13:229-234.

Verma, S.R., S.R. Rani, and R.C. Dalela. 1981a. Isolated and combined effects of pesticides on serum transaminases in *Mystus vittatus* (African catfish). Toxicol. Lett. 8:67-71.

Verma, S.R., S. Rani, and R.C. Dalela. 1981b. Pesticide-induced physiological alterations in certain tissues of a fish, *Mystus vittatus*. Toxicol. Lett. 9:327-332.

Verma, S.R., S.K. Bansal, A.K. Gupta, N. Pal, A.K. Tyagi, M.C. Bhatnagar, V. Kumar, and R.C. Dalela. 1982a. Bioassay trials with twenty-three pesticides to a fresh water teleost, *Saccobranchus fossilis* Water Res. 16:525-529.

Verma, S.R., S. Rani, and R.C. Dalela. 1982b. Indicators of stress induced by pesticides in *Mystus vittatus*: haematological parameters. Indian J. Environ. Health 24: 58-65.

Weary, G.C., and H.G. Merriam. 1978. Litter decomposition in a red maple wood lot under natural conditions and under insecticide treatment. Ecology 59:180-184.

Wolfe, J.L., and R.J. Esher. 1980. Toxicity of carbofuran and lindane to the old-field mouse (*Peromyscus polionotus*) and the cotton mouse (*P. gossypinus*). Bull. Environ. Contam. Toxicol. 24:894-902.

Yu, C-C., G.M. Booth, D.J. Hansen, and J.R. Larsen. 1974. Fate of carbofuran in a model ecosystem. J. Agric. Food Chem. 22:431-434.

Zakour, H.R. 1980. Toxicity, uptake and metabolism of the N-methylcarbamate pesticide carbofuran by the freshwater bivalve mollusc *Glebula rotundata* (Lamarck). Ph. D. Thesis, Rice University, Houston. 148 pp.

Table 1. Carbofuran and its degradation products, in parts per million dry weight, in corn (*Zea mays*) at silage stage (117 days) and at harvest (149 days) following application of carbofuran (10%) granules at 5.41 kg/ha (after Turner and Caro 1973).

	Carbamates			
Plant stage and part	Carbofuran	3-ketocarbofuran	3-hydroxy-carbofuran	Total carbamates
Silage				
Leaves	0.43	0.40	4.67	5.50
Stalks	0.24	0.00	0.04	0.28
Cobs	0.04	<0.02	<0.02	0.05
Kernels	0.00	<0.01	0.00	<0.01
Harvest				
Leaves	0.21	0.34	1.51	2.06
Stalks	0.03	0.00	0.05	0.08
Cobs	0.06	0.00	0.00	0.06
Kernels	<0.01	<0.01	0.00	<0.01

Table 2. Effect of pH, soil type, and application rate on carbofuran degradation in soils (from Chapman and Cole 1982).

Soil type	pH	Initial application rate of carbofuran (ppm)	Carbofuran remaining after 3 weeks (%)
Alumina soils			
Acid	5.4-6.1	1	76
Acid	5.4-6.1	20	82
Neutral	6.9-7.1	1	85
Neutral	6.9-7.1	20	79
Basic	8.3-8.5	1	55
Basic	8.3-8.5	20	72
Natural soils			
Mineral	8.0	1	95
Mineral	8.0	20	92
Mineral	6.8	1	100
Mineral	6.8	20	100
Organic	6.1	1	58
Organic	6.1	20	73
Organic	5.2	1	47
Organic	5.2	20	73
Sandy	6.6	1	8[a]
Sandy	8.0	1	28[a]

[a]Carbofuran remaining after 8 weeks (rather than 3 weeks as indicated in boxheading).

Table 3. Acute toxicities of carbofuran to aquatic organisms. Concentrations shown are in micrograms of carbofuran per liter of medium (ppb) fatal to 50% of test organisms in the designated time period.

Type of water and species tested	Time (h)	LC-50 (ppb)	Reference[a]
Freshwater			
Yellow perch, *Perca flavescens*	96	147	1
Green sunfish, *Lepomis cyanellus*	72	160	2
Lake trout, *Salvelinus namaycush*	96	164	1
Bluegill, *Lepomis macrochirus*	96	240	1
Channel catfish, *Ictalurus punctatus*	96	248	1
Static test, tapwater	96	1,420	3
Partial media replacement	96	510	3
Rice paddy water[b]			
With history	96	130	3
With no prior history	96	370	3
African catfish, *Mystus vittatus*	96	310	4
Rainbow trout, *Salmo gairdneri*	96	380	1
Crayfish, *Procambarus acutus acutus*	96	500	5
Mosquitofish, *Gambusia affinis*	72	520	6
Coho salmon, *Oncorhynchus kisutch*	96	530	1
Indian carp, *Saccobranchus fossilis*	96	547	7
Brown trout, *Salmo trutta*	96	560	1
Fathead minnow, *Pimephales promelas*	96	872	1
Annelid worm, *Limnodrilus hoffmeisteri*	96	11,000	8
Annelid worm, *Tubifex tubifex*	96	14,000	8
Marine			
Dungeness crab, *Cancer magister*			
Larva	96	2.5	9
Adult	96	190	9
Sheepshead minnow			
Cyprinodon variegatus	96	386	10
C. variegatus	3,144	49	10
Bivalve molluscs			
Cockle, *Clinocardium nuttali*	96	3,750	11
Clam, *Macoma nasuta*	96	17,000	11
Mussel, *Mytilus edulis*	96	22,000	11
Clam, *Rangia cuneata*	96	125,000	11

[a]References: 1, Johnson and Finley 1980; 2, Brungs et al. 1978; 3, Brown et al. 1979; 4, Verma et al. 1980; 5, Cheah et al. 1980; 6, Davey et al. 1976; 7, Verma et al. 1982a; 8, Dad et al. 1982; 9, Caldwell 1977; 10, Parrish et al. 1977; 11, Zakour 1980.

[b]Rice paddy water from rice paddies with and without a history of pesticide application, as shown.

Table 4. Acute oral toxicities of carbofuran to birds and mammals. Concentrations shown are in micrograms carbofuran administered per kilogram body weight (ppb) in a single dose fatal to 50% within 14 days.

Taxonomic groupand species tested	LD-50 (ppb)	Reference[a.]
Birds		
Fulvous whistling-duck,		
Dendrocygna bicolor	238	1
Mallard, *Anas platyrhynchos*		
Age 36 h	280-480	2
Age 7 days	530-740	2
Age 30 days	410-640	2
Age 3-4 months	320-500	1
Age 6 months	330-520	2
Red-winged blackbirds,		
Agelaius phoeniceus	422	3
Quelea, *Quelea quelea*	422-562	3
House finch,		
Carpodacus mexicanus	750	3
Japanese quail,		
Coturnix japonica	1,300-2,100	4
House sparrow,		
Passer domesticus	1,330	3
Common grackle,		
Quiscalus quiscula	1,300-3,160	3
Rock dove,		
Columba livia	1,330	3
Brown-headed cowbird,		
Molothrus ater	1,330	3
Ring-necked pheasant,		
Phasianus colchicus	2,380-7,220	1
Northern bobwhite,		
Colinus virginianus	3,640-6,990	1
European starling,		
Sturnus vulgaris	5,620	3
Domestic chicken,		
Gallus gallus	25,00-38,900	5
Mammals		
Mouse, *Mus musculus*	2,000	4
Cat, *Felis domesticus*	2,500-3,500	5
Rat, *Rattus* sp.	3,800-34,500	5

Old-field mouse,		
Peromyscus polionotus	4,000	6
Beagle dog,		
Canis familiaris	7,500-18,900	5
Sheep, *Ovis aries*	8,000	7
Guinea pig,		
Cavia cobaya	9,200	5

[a]References: 1, Tucker and Crabtree 1970; 2, Hudson et al. 1972; 3, Schafer et al. 1983; 4, Sherman and Ross 1969; 5, Finlayson et al. 1979; 6, Wolfe and Esher 1980; 7, Palmer et al. 1973.

Table 5. Toxicity of dietary carbofuran to birds and mammals.

Organism	Concentration[a]	Exposure interval (days)		Mortality (%)	Reference[b]
		Exposure	Postexposure		
Mallard					
Anas platyrhynchos	190	5	3	50	1
Ring-necked pheasant,					
Phasianus colchicus	573	5	3	50	1
Japanese quail,					
Coturnix japonica					
Age 1 day	140-471	5	3	50	2
Age 7 days	436-1,103	5	3	50	2
Age 14 days	586-1,004	5	3	50	2
Age 21 days	779-1,459	5	3	50	2
Old-field mouse,					
Peromyscus polionotus	500	4		100	3
Old-field mouse	250	4		20	3
Old-field mouse	100	240		38	3

[a]Concentration of carbofuran in diet, in mg/kg (ppm) fresh weight.

[b]References: 1, Hill et al. 1975; 2, Hill and Camardese 1983; 3, Wolfe and Esher 1980.

Table 6. Acute aerosol inhalation toxicity of carbofuran to warm-blooded animals.

Organism	Exposure time (min)	Concentration (ppb)	Effect	Reference[a]
Rhesus mondey, *Macaca* sp.	360	2	LC-50	1
Guinea pig, *Cavia* sp.	240	10-70	LC-50	1
Rat, *Rattus* sp.	50-70	26	LC-50	2
Pheasant, *Phasianus* sp.	5[b]	40	LC-100	1
Guinea pig	—	43-53	LC-50	3
Dog, *Canis* sp.	60	50	LC-50	1
Pheasant	5[c]	80	LC-10	1
Rat	60	90-100	LC-50	1
Human	2,400[d]	0.05	[d]	4

[a]References: 1, Finlayson et al. 1979; 2, Ferguson et al. 1982; 3, Anon. 1971; 4, Draper et al. 1981.
[b]Air delivery rate of 8 1/min.
[c]Air delivery rate of 10 1/min.
[d]Exposure = 40 h work week; threshold limit value.

Table 7. Rates of carbofuran metabolism by various organisms (from Zakour 1980).

Organism	Parent carbofuran converted (%)	Time (d = day; h = hour)
Rat, *Rattus* sp.	100	24 h
Chicken, *Gallus* sp.	100	24 h
Saltmarsh caterpillar, *Estigmene* sp.	100	7 h
Intact cotton plant, *Gossypium* sp.	100	5 d
Alfalfa, roots, *Medicago* sp.	95	30 d
Land snail, *Helix aspersa*	90	1 h
Bean plants, *Phaseolus* sp.	68	3 d
House fly, *Musca* sp.	58	1 h
Bivalve, *Glebula rotundata*	54-62	24-48 h
Tobacco, leaves, *Nicotiana* sp.	50	4 d
Microorganisms, unidentified	40-70	7-56 d
Cotton, leaves	20	2 d
Mugho pine, needles, *Pinus* sp.	17	14 d

Biological Report 85(1.4)
August 1985

Contaminant Hazard Reviews
Report No. 4

TOXAPHENE HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

By

Ronald Eisler
Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

And

Joel Jacknow
Division of Resource Contaminant Assessment
U.S. Fish and Wildlife Service
Washington, DC 20240

SUMMARY

Toxaphene (chlorinated camphene, 67-69% chlorine) is a broad-spectrum insecticide which, until recently, was one of the most heavily-used agricultural chemicals on a global scale, especially against pests of cotton. It is extremely persistent in soil and water, with documented half-times of 9 to 11 years; however, in air and in warm-blooded organisms, toxaphene degradation is rapid with half-times of 15 and 3 days, respectively. Toxaphene is especially hazardous to nontarget marine and freshwater organisms, with death recorded at ambient water concentrations substantially below 10 ug/l, and adverse effects observed on growth, reproduction, and metabolism at water concentrations between 0.05 and 0.3 ug/l. Aquatic organisms readily accumulate toxaphene from the ambient medium and diet, sometimes spectacularly, retain it for lengthy periods, and biomagnify the chemical through food chains. These phenomena could account for the numerous fish kills recorded after toxaphene application, as well as the high residues measured in fish from the Rio Grande Valley in southern Texas and other locations of high agricultural use of toxaphene. Atmospheric vectors, including prevailing winds and rainfall, may transport toxaphene hundreds of kilometers from known point sources of application. This, in part, would explain the levels of 5 to 10 mg/kg whole body wet weight recorded in various species of fish from the Great Lakes.

Based on estimated environmental exposure levels, toxaphene does not appear to constitute a major threat to warm-blooded animals, including migratory birds and other wildlife, domestic poultry and livestock, small laboratory mammals, and humans. Wildlife typically contain low or nondetectable levels of toxaphene, except for some species of fish-eating raptors, and the frequency of occurrence is low when compared with that of other organochlorine agricultural compounds. However, toxaphene has been implicated as a human carcinogen and mutagen at relatively high test dosages and was associated with some bird kills following aerial applications.

In water, the concentration of toxaphene considered safe for protection of freshwater life is conservatively estimated to lie between 0.008 and 0.013 ug/l; for marine life, it is 0.07 ug/l. This is in sharp contrast to the current recommended drinking water criterion for human health protection of 5.0 to 8.8 ug/l. Similarly, residues in fish tissue in excess of 0.4 to 0.6 mg/kg wet weight may be hazardous to fish health and should be considered as presumptive evidence of significant environmental contamination, although fish may contain up to 5.0 mg/kg before they are considered hazardous to human consumers. At present, other existing criteria for human health protection, which range in various foods from 0.1 mg/kg for sunflower seeds to 7.0 mg/kg in meat, fats, and citrus fruits, also appear adequate to safeguard sensitive species of wildlife.

In 1982, the U.S. Environmental Protection Agency cancelled the registrations of toxaphene for most uses. However, current stocks of toxaphene may be used, with restrictions, through 1986. Furthermore, considerable, but unknown, quantities of toxaphene previously discharged into the environment over the past several decades may remain undegraded and potentially available to living resources. Accordingly, we recommend, to all natural resources managers, that toxaphene application is contraindicated if there is a history of extensive prior treatment with toxaphene in their jurisdictional areas, if alternative control methods are available, or if there is no clear threat to crop production or to the health of livestock and humans.

This report should be cited as:

Eisler, R. and J. Jacknow. 1985. Toxaphene hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85(1.4).

TABLES

ACKNOWLEDGMENTS

We thank L. Garrett and M.E. Shawe for literature retrieval, M. Oesby and I. Moore for secretarial help, C. Schmitt for reviewing the manuscript, and C.H. Halvorson and C.I. Short for editorial services.

INTRODUCTION

Environmental hazards and increasing public concerns associated with toxaphene (chlorinated camphene, 67-69% chlorine) are documented in a series of useful review articles (Pollock and Kilgore 1978; EPA 1980a; Cohen et al. 1982; Rice and Evans 1984). Although toxaphene was introduced in the mid-1940's as a new insecticide, only a few years elapsed before it was being used commercially on a large scale to effectively control a variety of pests. In the mid-1950's, toxaphene was first used in ponds, lakes, and streams as a piscicide. By 1966, toxaphene was the chemical of choice in fish eradication programs in Canada and second in the United States after rotenone (Lennon et al. 1970). Its use for this purpose was discontinued in the 1960's due to its lengthy persistence in water, high acute toxicity to aquatic biota, and significant bioaccumulation and biomagnification in various environmental compartments. By 1974, cumulative world use of toxaphene, mainly against insect pests of cotton, was estimated at 450,000 metric tons. Production of toxaphene declined from 1973 to 1980; however, annual consumption in 1980 was estimated at 105,000 tons, thus qualifying toxaphene as one of the most heavily-utilized agricultural chemicals worldwide. Until recently, toxaphene was extensively applied in California to control fruitworms on tomatoes, bollworm on cotton, and a wide range of pestiferous insects that infested alfalfa, broccoli, celery, beans, clover, lettuce, cauliflower, and pears. In time, toxaphene-resistant strains of cotton pests, including bollworm and lygus bug, appeared in California, Texas, Egypt, and India. In November, 1982, most registered uses of toxaphene were cancelled by the U.S. Environmental Protection Agency (EPA), although existing available stocks may be used through 1986 (EPA 1982). Prior to the EPA action, similar actions that banned or restricted toxaphene use had been implemented in a number of countries, including Canada, England, Sweden, Finland, Denmark, France, Switzerland, Hungary, Italy, Egypt, and Algeria (Cohen et al. 1982).

In this account, we briefly summarize available information on the environmental fate and effects of toxaphene, with special emphasis on gamefish, migratory birds, and their predators and prey. The recommendations on current and proposed safe limits for toxaphene residues in air, water, and biota are reviewed. This effort is part of a continuing series of synoptic reviews on contaminant hazards to natural resources and was prepared in response to informational requests from environmental specialists of the U.S. Fish and Wildlife Service.

ENVIRONMENTAL CHEMISTRY

The commercial production of toxaphene involves the reaction of camphene, chlorine activated by ultraviolet radiation, and certain catalysts to yield chlorinated camphene with a chlorine content of 67 to 69% by weight. This product is a relatively stable material composed of a mixture of structurally similar compounds and isomers. Of the 177 components, 26 have been isolated but only 10 have been identified; these 26 components comprise 40% of the toxaphene. Information on chemical properties and the fate and effects of the remaining components is missing or incomplete (Cohen et al. 1982). Several components that have been tested are more toxic to houseflies than the technical mixture, especially di-, tri-, and tetrachlorobornane compounds (Pollock and Kilgore 1978). Technical toxaphene is a yellow, waxy solid of empirical formula $C_{10}H_{10}Cl_8$ and an average molecular weight of 414. Toxaphene is soluble in water to 3 mg/l and is readily soluble in fats and organic solvents, based on its high partition coefficient of 10 to the power 3.3-6.4. Toxaphene has a tendency to adsorb on sediments and to bioaccumulate in aquatic organisms.

Because toxaphene consists of numerous compounds, it seems inappropriate and misleading to continue using the name toxaphene to describe this insecticide. We now know that chemical properties, such as solubility, toxicity, volatility, and other properties, are the sum of the individual contribution of many different compounds in differing relative amounts. A 50-fold difference between toxicities of toxaphene components can occur, and, with a wide range in the polarity of different fractions, there probably are also significant solubility differences. In addition, the composition of toxaphene changes with time, and residues in fat are not of the same composition as parent toxaphene (Pollock and Kilgore 1978). The metabolism of toxaphene has been an area of limited research activity, owing to the analytical difficulties involved in detecting a multicomponent substance (Pollock and Kilgore 1978). However, toxaphene has been reported more often in biological samples in recent years. This increased recognition is probably due to better analytical methods for toxaphene analysis (Ribick et al. 1982), greater awareness by analysts, and the continuing widespread use of toxaphene while use of potentially interfering organochlorine insecticides has slowly decreased.

Toxaphene was available as an emulsifiable concentrate, wettable power, or dust. The commercial product is relatively stable but may decay upon prolonged exposure to sunlight, alkalis, or temperatures above 120°C. Toxaphene is also known as chlorinated camphene, Synthetic 3956, Octachlorocamphene, Alltox, Geniphene, Toxakil (Negherbon 1959), polychlorocamphene, camphechlor, Clor Chem T-590, Cristoxo, Moto, Phenacide, Phenatox, Strobane-T, Toxon 63, and Vapotone (Johnson and Finley 1980). Chemically, it is known as a mixture of various chlorinated camphenes (Tucker and Crabtree 1970).

Toxaphene residues have been detected in various environmental compartments hundreds of kilometers distant from known applications of this insecticide. Prevailing winds, rainfall, and sediment runoff probably account for substantial portions of this transport. Rainfall, for example, has been implicated as a significant toxaphene vector in South Carolina estuaries (Harder et al. 1980). During and immediately after the summer use season, toxaphene levels in rain exceeded, by several times, the concentrations reported to produce bone damage in fish under controlled laboratory conditions. Toxaphene becomes sorbed to soils when it is used in agriculture; therefore, a major mode of toxaphene transport in areas planted continuously in cotton is through sediment loss in runoff (McDowell et al. 1981). Measurements indicated a linear relation between toxaphene yield and sediment yield in runoff water. Atmospheric transport of toxaphene is well documented. Air samples from the western North Atlantic contained measurable levels of toxaphene at distances up to 1,200 km from the nearest point source of application on land (Bidleman and Olney 1975). Similarly, Nationwide monitoring of toxaphene in fish showed increases during 1970-74 (Schmitt et al. 1981), especially in areas where the insecticide was not used, suggesting that atmospheric transport is essential to widespread distribution. Airborne toxaphene is resistant to photodecomposition; however, selective volatilization of toxaphene components is a major cause of degradation resulting in an estimated half-time of 15 days while in the atmosphere (Cohen et al. 1982).

Toxaphene degrades more rapidly in most environmental compartments than other chlorinated pesticides, such as DDT and dieldrin (Matsumura 1978). Toxaphene persistence and degradation in soil, water, and biota is modified by numerous and disparate biological and abiotic factors. In lakes, toxaphene persistence was significantly related to lake depth, stratification, and turnover, but not related to surface area, pH, temperature, sunlight, and oxygen (Cohen et al. 1982). Data from studies where toxaphene was used to control nongame fish in lakes suggest that it may persist in water from several months to more than 9 years. For example, two mountain lakes in Oregon that were treated with toxaphene in fish eradication programs remained toxic for 1 to 6 years (Terrierre et al. 1966). Davis Lake, a shallow lake rich in aquatic life, which was treated with 88 ug/l toxaphene, could be restocked with rainbow trout (*Salmo gairdneri*) within 1 year when water toxaphene levels were 0.63 ug/l. Trout grew rapidly, although whole body burdens up to 24 mg/kg were recorded. Miller Lake, a deep, biologically sparse lake, was treated with 40 ug/l toxaphene; trout could not be restocked for 6 years until water levels had dropped to 0.8 ug/l toxaphene. Toxaphene at 50 ug/l was used to eradicate fish from Clayton Lake, New Mexico (Kallman et al. 1962). Water concentrations of 1.0 ug/l were measured 250 days post-treatment, but the lake remained toxic for 9 months, with restocking possible only after 12 months. Residues in fish surviving treatment were 3.5 mg/kg whole body wet weight shortly after exposure and 0.3 mg/kg about 5 months postapplication. Some lakes treated with toxaphene to kill fish have remained toxic for 3 to 4 years (Webb 1980). In another study (Johnson et al. 1966), lake water that contained 1.0 ug/l toxaphene (9 years after toxaphene treatment) supported healthy fish populations. In this lake, particulate matter contained 70 ug of toxaphene/kg, and plankton contained 15,000 ug/kg. However, there were changes in gas chromatographic profiles of toxaphene residues taken from the lakes, suggesting that the parent toxaphene had been altered or degraded into compounds with lower environmental hazards to biota. Clearly, this subject area merits additional research effort.

In soils, toxaphene can persist for lengthy periods, with microbial degradation occuring under aerobic and anaerobic conditions (Cohen et al. 1982). Pimentel (1971) reported that toxaphene, applied at 140 mg/kg of soil persisted for more than 6 years; when applied at 50 mg/kg, half the toxaphene was measurable after 11 years. Further, in sandy loam soils, 45% of the toxaphene remained 14 years after initial application of 100 mg/kg. Some investigators suggest that toxaphene degradation is more rapid under anaerobic conditions (Pollock and Kilgore 1978). Thus, toxaphene in anaerobic salt marsh sediments generally degraded within a few days to shorter-lived components (Williams and Bidleman 1978). Toxaphene accumulated only slightly in anaerobic marsh soils not flooded daily by tides (Gallagher et al. 1979), and the highest pesticide concentrations were associated with roots of dead plants.

Degradation of toxaphene in plant, air, and soil samples was evident following toxaphene application of 9

kg/ha to a San Joaquin Valley, California, cotton field (Seiber et al. 1979). Cotton leaves contained 661 mg toxaphene/kg immediately after application and 135 mg toxaphene/kg after 58 days, with the greatest loss attributed to components of highest volatility. Air samples were essentially the same at 2 and 14 days postapplication (1.8-1.9 ug/m^3); this was attributed to a corresponding enrichment of volatile components. Top soil samples immediately after application and 58 days later contained 13.1 and 6.4 mg/kg, respectively; loss was primarily via vaporization, but at least one component was significantly degraded. One year later, soil cores and irrigation ditch samples showed extensive toxaphene degradation resulting in a selective decline of some components; anaerobic reduction occurred in these environmental compartments.

In rats, the half-time of toxaphene (time to 50% excretion) was 1 to 3 days. If the trend persisted, virtually all toxaphene would be eliminated in five half-lives. Elevated blood toxaphene levels in a human subject who had eaten catfish fillets containing 52 mg of toxaphene/kg dropped 67% in 11 days. By 14 days after the initial measurement, toxaphene blood levels were below analytical detection limits (EPA 1980a).

RESIDUES IN FIELD POPULATIONS

National contaminant monitoring surveys, conducted in the period 1974-76, show that toxaphene was detected in about 6% of all fish sampled; this is a higher percentage than recorded in fruits, vegetables, poultry, and meat (Ludke and Schmitt 1980). Fish collected Nationwide at 109 stations between 1976 and 1979 had measurable toxaphene residues at about 60% of all stations sampled; concentrations in fish from the Great Lakes stations exceeded those in fish from most of the rest of the United States, including locations within the cotton-growing areas (Schmitt et al. 1983). Lake trout (*Salvelinus namaycush*) from Lake Michigan typically contained 5 to 10 mg of toxaphene/kg whole body on a wet weight basis; lake trout from Lake Huron contained 9 mg/kg. These residues are considered harmful to various sensitive species of freshwater teleosts (Schmitt et al. 1983). Since relatively little toxaphene has been used in the Great Lakes region when compared to cotton-growing areas in the mid-South, Northeast, and Southeast, it is postulated that atmospheric transport from areas to the south and southwest are the sources of toxaphene contamination in the Great Lakes (Schmitt et al. 1983).

Freshwater fishes of the Arroyo Colorado, a major waterway traversing the lower Rio Grande Valley in Southern Texas, were highly contaminated with toxaphene and DDE residues when compared to fish collected elsewhere in the Valley; toxaphene concentrations ranged up to 31.5 mg/kg wet weight in whole fish composite samples (Table 1). These values were within or above the range producing adverse effects in sensitive species of fish. In addition, toxaphene residues in carcasses of fish-eating birds contained up to 3 mg/kg toxaphene (Table 1). Unlike fishes, avian species readily metabolize and excrete toxaphene, so that little accumulation occurs in tissues; in any event, these levels of toxaphene in carcasses of piscivorous birds are probably biologically insignificant (White et al. 1983). In the Arroyo Colorado area, toxaphene was being used, to some extent, on crops such as cotton, not only as an insecticide, but as a carrier for more effective chemicals. Another possible source of contamination is a former pesticide plant at Mission, Texas, near the headwaters of the Arroyo Colorado. Soil at this site contained high concentrations of various pesticides, including toxaphene. Contaminant laden runoff from this site could eventually reach the Arroyo from storm sewers and other water diversion facilities. The contaminated Arroyo Colorado, in turn, empties into the Laguna Madre, one of the more important breeding and nursery grounds for fish and wildlife in the United States. The Texas Department of Health, in an advisory to consumers, has stated that consumption of fishes from the Arroyo Colorado, especially blue catfish *(Ictalurus furcatus*) and gizzard shad (*Dorosoma cepedianum*), is not advised (White et al. 1983)

Birds, unlike fish, generally contained low or nondetectable levels of toxaphene, and the frequency of occurrence was relatively low when compared with that of other organochlorine pesticides. This generalization held for eggs of the osprey (*Pandion haliaetus*) collected in southern New Jersey in 1974 (Wiemeyer et al. 1978); carcasses of 103 skinned shorebirds from Corpus Christi, Texas, during winter 1976-77 (White et al. 1980); eggs of the brown pelican (*Pelecanus occidentalis*) from 1971-76 in Louisiana (Blus (et al. 1979); and eggs of clapper rail (*Rallus longirostris*), purple gallinules (*Porphyrula martinica*), and limpkins (*Aramus guarauna*) from the Southeast in 1972-74 (Klass et al. 1980). Among 105 herons found dead Nationwide since 1976, only nine contained measurable quantities of toxaphene; for DDE, PCB'S, dieldrin, and DDD, these frequencies were 96, 90, 37 and 35, respectively (Ohlendorf et al. 1981). Levels of toxaphene and other organochlorines in canvasbacks (*Aythya valisineria*) from Chesapeake Bay, Maryland, during 1973-76 were below the levels known to cause problems in other species (White et al. 1979). However, adipose tissues from 55 male wild turkeys (*Meleagris gallopavo*) killed during the 1974 hunting season in southern Illinois contained 0.2 to 0.9 mg/kg of toxaphene (Bridges and Andrews 1977), suggesting that certain species of birds may

selectively accumulate low concentrations of toxaphene.

Two bird kills reported in California have been attributed to toxaphene poisoning (Pollock and Kilgore 1978). In one case, the apparent route of exposure was from contaminated fish, with bird poisoning the result of toxaphene biomagnification in the food chain. In that case, algae contained 0.1 to 0.3 mg toxaphene/kg wet weight, snails and daphnids 0.2, fish 3 to 8, and fish-eating birds 39 mg/kg. The latter value is substantially in excess of 3 mg/kg, a concentration considered biologically insignificant to fish-eating birds (White et al. 1983). The second incident involved some birds that were apparently killed by toxaphene when it was used to control grasshoppers on a shortgrass range. At 2 to 3 weeks postspray, bird carcasses contained 0.1 to 9.6 mg toxaphene/kg.

Biomagnification of toxaphene through food webs was clearly demonstrated in 16 species of organisms collected from oxbow lakes in northeastern Louisiana during 1980 (Neithammer et al. 1984). Without exception, residues were highest (3.6 mg/kg whole body wet weight, range 1.7 to 5.5) in tertiary consumers, such as green-backed heron (*Butorides striatus*), various species of snakes, spotted gar (*Lepisosteus oculatus*), and largemouth bass (*Micropterus salmoides*). Secondary consumers, such as bluegill (*Lepomis macrochirus*) blacktail shiner (*Notropis venustus*), and yellow-crowned night-heron (*Nycticorax violaceus*), contained lower residues (0.9 mg/kg wet weight, range 0.7 to 1.2). Primary consumers, including crayfish (*Procambarus* spp.) and threadfin shad (*Dorosoma petenense*), contained the lowest levels (0.8 mg/kg wet weight, range 0.6 to 1.0) of all consumer groups. Toxaphene levels were not detectable in water and sediments from these oxbow lakes.

LETHAL EFFECTS

Toxaphene is extremely toxic to freshwater and marine biota. In laboratory tests of 96 hours duration, 50% mortality was recorded for the most sensitive species of freshwater and marine teleosts, marine crustaceans, and freshwater insects at nominal water concentrations of less than 10 ug/l of toxaphene, and, in several cases, less than 1 ug/l (Table 2). Bioassays of longer duration, based on exposure of aquatic organisms for the entire or most of the life cycle, produced significant adverse effects on growth, survival, and reproduction at toxaphene concentrations between 0.025 and 1.0 ug/l (Table 3). Based on its high toxicity and extensive use, it is not suprising that toxaphene was considered a major cause of Nationwide fish kills in 1977 (EPA 1980b).

Warm-blooded organisms are relatively resistant to toxaphene, as determined from results of short-term tests involving oral, dermal, and dietary routes of administration. In acute oral toxicity tests with birds and mammals, LD-50 values ranged between 10 and 160 mg/kg body weight (Table 4). The acute oral toxicities of toxaphene to rats, mice, dogs, guinea pigs, cats, rabbits, cattle, goats, and sheep extended from 25 to 270 mg/kg body weight (Pollock and Kilgore 1978; EPA 1980a); these values are in good agreement with those shown in Table 4. Dermal toxicities of toxaphene ranged from 250 mg/kg body weight for rabbits and 930 mg/kg for rats to 25,000 mg/kg for cattle (Pollock and Kilgore 1978). As was true for acute oral and dermal toxicity data, comparatively high levels of dietary toxaphene were required, i.e., 538 to 828 mg/kg diet, to produce significant death rates in various species of birds (Heath et al. 1972). In their study on four species of gamebirds, each aged 2 weeks, Heath et al. (1972) fed them diets containing graded concentrations of toxaphene for 5 days, followed by 3 days of untreated food. LD-50 values at the end of day 8 were 828 mg toxaphene/kg diet for northern bobwhite, 686 for Japanese quail (*Coturnix coturnix japonica*), 542 for ring-necked pheasant (*Phasianus colchicus*), and 538 for mallard (*Anas platyrhynchos*). It appears that toxaphene is not a major hazard to bird survival at previously recommended field application rates (Hoffman and Albers 1984). However, at toxaphene levels not considered life-threatening to birds and mammals, fetotoxic effects have been recorded. For example, ring-necked pheasants fed 100 mg/kg dietary toxaphene produced eggs with significantly reduced hatch over controls; similarly, toxaphene administered orally to pregnant rats and mice during organogenesis caused fetal toxicity at 15 mg/kg body weight (Pollock and Kilgore 1978).

Some human deaths, especially those of children, have been reported following the ingestion of toxaphene-contaminated foods (EPA 1980a). Known toxaphene residues in food items of victims ranged from 9.7 to 47 mg/kg; a total dose of 2 to 7 g of toxaphene is considered acutely toxic to a 70 kg adult. For comparison purposes, a 4.5 kg bird would probably die after consumption of 45 to 450 mg of toxaphene.

SUBLETHAL EFFECTS

Among sensitive species of marine and freshwater fish and invertebrates, water concentrations of 0.054 to 0.299 ug/l of toxaphene were associated with growth inhibition, reduced reproduction, backbone abnormalities, or histopathology (Table 5). Aquatic biota are capable of spectacular accumulations of toxaphene from the medium; factors ranged between 1,270 and 52,000X those of water under laboratory conditions (Table 6). A similar pattern was observed in Big Bear Lake, California, where toxaphene was applied at 200 ug/l to eradicate goldfish (Pimentel 1971). Biomagnification factors of 365 were calculated for plankton, 1,000 for goldfish, and 8,500 in pelican fat, representing residues of 73 mg/kg toxaphene in phytoplankton, 200 in goldfish, and 1,700 in pelican fat. Accumulation of toxaphene by various species of fish food organisms is dependent on exposure time and concentration. For example, insect nymphs subjected to 20 ug/l of toxaphene for <24 hours did not accumulate doses lethal to fish; however, algae, diatoms, and protozoan ciliates held for 24 hours in 20 ug/l toxaphene solutions, and *Daphnia magna* held 120 hours in 10 ug/l, were lethal when fed to fish (Schoettger and Olive 1961).

Fish accumulated part-per-million toxaphene concentrations in various tissues within a few days when placed in toxaphene-treated lakes that contained less than 1.0 ug/l (Cohen et al. 1982). Freshwater teleosts experienced acute and chronic effects when whole body levels were in excess of 0.4 mg/kg but less than 5 mg/kg (this latter value being the Food and Drug Administration "action level" for human consumption; Cohen et al. 1982). Thus, groups of brook trout eggs containing 900 ug toxaphene/kg had drastically reduced survival when compared to controls (Cohen et al. 1982), and brook trout tissue residues exceeding 400 ug toxaphene/kg were associated with reductions in growth, abnormal bone development, and reduced fecundity (Mayer and Mehrle 1977). Fathead minnows containing more than 400 ug toxaphene/kg grew more slowly than controls (Mayer and Mehrle 1977); similar results were reported in channel catfish fry containing 600 to 3,400 ug toxaphene/kg (Mayer and Mehrle 1977). Toxaphene retention by aquatic organisms is relatively lengthy when compared to mammals. In one case, eastern oysters (*Crassostrea virginica*) held for 24 weeks in 10 ug/l toxaphene solutions contained 32.4 mg/kg in soft tissues; after 16 weeks in noncontaminated seawater, oysters still contained 3.0 mg/kg (Pollock and Kilgore 1978).

Sublethal effects of toxaphene observed in mammals, small laboratory animals, and birds were similar to those recorded for aquatic organisms; however, there was general agreement that effects were induced at much higher concentrations. In domestic white leghorn chickens, for example, toxaphene at 100 mg/kg in the diet for 30 weeks did not significantly alter egg production, hatchability, or fertility, although some bone deformation and kidney lesions were recorded (Bush et al. 1977). The highest dietary dose of toxaphene fed to chickens in life-time exposure studies, which produced no effect on any parameter measured, ranged between 3.8 and 5 mg/kg (Bush et al. 1977). Several studies with the American black duck (*Anas rubripes*) produced effects similar to those recorded in chickens. In one study, ducklings that were fed diets containing 10 or 50 mg of toxaphene/kg for 90 days had reduced growth and impaired backbone development (Mehrle et al. 1979). Collagen, the organic matrix of bone, was significantly decreased in cervical vertebrae of ducklings fed the 50 ppm toxaphene diet. Calcium concentrations increased in vertebrae of ducklings fed either 10 or 50 mg/kg dietary toxaphene; effects were observed only in female ducklings. In a long-term feeding study lasting 19 months, which included two breeding seasons, American black ducks, fed 10 or 50 mg toxaphene/kg in a dry mash diet, showed no significant differences when compared to control birds in survival, egg production, fertility, hatchability, eggshell thickness, or growth and survival of young (Haseltine et al. 1980). The only negative effects recorded included weight loss among treated males during summer and a slight delay in the number of days required to complete a clutch. Carcass toxaphene residues, which seldom exceeded 0.5 mg/kg, were found in only one duck fed the 50 mg/kg diet (Haseltine et al. 1980), suggesting low body accumulations in American black duck. However, toxaphene residues were present in the liver of all birds fed toxaphene. At dietary concentrations of 10 or 50 mg/kg, there was no change in avoidance behavior of young American black ducks (Heinz and Finley 1978), which, if interrupted, is considered life-threatening.

Ring-necked pheasants (*Phasianus colchicus*) fed diets containing 300 mg toxaphene/kg showed decreases in egg deposition, egg hatch, food intake, and weight gain; at 100 mg/kg, all of these parameters, except reduced hatch, were the same as controls (Pollock and Kilgore 1978). In a field study, aerial applications of a DDT-toxaphene mixture in southwestern Idaho during 1970, at recommended concentrations to control pests, had no major impact on penned or feral ring-necked pheasants (Messick et al. 1974), suggesting that conformance with recommended application rates should be endorsed whenever possible. However, we emphasize that recommended toxaphene application rates, until recently, varied widely and depended, in part,

on the pest species to be controlled, the number and type of other pesticides applied jointly, and climatic conditions. Laboratory studies with mallard eggs suggest that recommended toxaphene application rates in excess of 1.12 kg/ha, which is generally exceeded in most cases, may produce severe embryotoxic effects, including dislocated joints and poor growth (Hoffman and Eastin 1982).

Northern bobwhite fed 5 mg/kg dietary toxaphene for 4 months showed thyroid hypertrophy (Pollock and Kilgore 1978) and interference with the ability of bobwhites to discriminate patterns (Kreitzer 1980). In the latter investigation, Kreitzer fed 10 or 50 mg/kg dietary toxaphene to 3-day old bobwhites for 20 weeks and found that toxaphene-treated birds made 50% more errors than controls on initial testing. These effects appeared as early as 30 days after toxaphene exposure. In a second test, there was no difference between experimentals and controls, indicating that the ability to learn these tasks was not permanently impaired.

Rats, mice, dogs, deer, sheep, and cattle are all relatively resistant to toxaphene. No-effect levels of 20 to 25 mg/kg dietary toxaphene were documented during multigeneration exposure of rats and during 2-year feeding studies with mice and dogs (EPA 1980a). No effects were observed in monkeys over a 2-year period during which they were fed diets containing 0.7 ppm toxaphene (Pollock and Kilgore 1978). However, carcinogenic responses have been induced in mice and rats by toxaphene when residues in the diet exceeded 50 mg/kg during lifetime exposure (EPA 1980a). "These results, together with the positive mutagenic response (to *Salmonella* bacteria) constitute substantial evidence that toxaphene is likely to be a human carcinogen" (EPA 1980a). Penned and wild deer fed toxaphene at 1,000 mg/kg appeared normal but showed a decreased digestion rate, which was attributed to a decrease in rumen bacteria (Schwartz and Nagy 1974). Steers fed alfalfa hay containing 306 mg toxaphene/kg for 19 weeks stored 772 mg/kg in abdominal fat and 27 mg/kg in lean meat without apparent ill effects, demonstrating the lipophilicity of toxaphene and the relatively low accumulation rates. For sheep under an identical regimen, these values were 317 mg/kg in fat and 36 mg/kg in meat (Pollock and Kilgore 1978).

RECOMMENDATIONS

In November, 1982 the U.S. Environmental Protection Agency cancelled the registration of toxaphene for most uses and, thus, joined a growing number of Nations in Western Europe, Scandinavia, North America, and North Africa that previously initiated similar actions. With some restrictions, toxaphene presently may be used domestically for treatment of scabies in cattle and sheep; controlling sporadic infestations of armyworms, cutworms, and grasshoppers on cotton, corn, and small grains; and, in Puerto Rico and the Virgin Islands, to control mealy bugs, pineapple gummosis moths, and banana weevils. Existing stocks of toxaphene may be used through 1986 for control of sicklepod in soybeans and peanuts, for insects in corn cultivated without tillage, and for pests of dry and southern peas (EPA 1982).

Although toxaphene is not markedly hazardous to most wildlife species for which data were available, the decision to withdraw or curtail agricultural uses of toxaphene was popular with most natural resource managers. Their concerns, apparently shared by others, were based, in part, on the following observations. First, toxaphene causes death and deleterious effects to nontarget aquatic biota at extremely low concentrations, i.e., <1.0 ug/l. Second, toxaphene is persistent in soils, water, and other environmental compartments, with residence times measured in years. Third, toxaphene accumulates in aquatic organisms and biomagnifies through food chains. Fourth, toxaphene is widely-distributed, even when the initial application point is hundreds of kilometers distant; transport is presumably by atmospheric and other vectors. Fifth, technical difficulties continue to exist in the chemical analysis of toxaphene, a 177-isomer compound. Sixth, there is an imperfect understanding of the fate and effects of individual toxaphene components. Seventh, there is inadequate knowledge of interaction effects of toxaphene with other agricultural chemicals (especially when mixtures are applied simultaneously) and with other persistent compounds in aquatic ecosystems, such as PCB'S, DDT and its isomers, and petroleum. Finally, there is the perception that suitable alternative pesticidal chemicals are available, including some carbamates, organophosphorus compounds, and synthetic pyrethroids.

At present, available stocks of toxaphene may be used throughout 1986. However, large but unknown quantities of toxaphene that were discharged into the environment over the past several decades remain undegraded and potentially bioavailable. Also, knowledge of toxaphene ecotoxicology is incomplete or inadequate. Accordingly, we recommend to fish and wildlife managers that they review all current and proposed uses of this compound in their jurisdictional areas. Specifically, we recommend that toxaphene use should not be permitted if there is a history of extensive prior treatment with toxaphene, if alternative control methods are available, or if there is no clear threat to crop existence or to health of livestock and humans. Current limits for

toxaphene residues in air, water, biota, and other environmental compartments for the protection of fish, livestock, and human health are summarized in Table 7. The concentration of toxaphene in seawater considered safe for marine life protection is 0.07 ug/l; for sensitive freshwater species this lies between 0.008 and 0.013 ug/l. This contrasts sharply with the current recommended drinking water criterion for human health protection of 5.0 to 8.8 ug/l. Other existing criteria for human health protection, which range in various foods from 0.1 to 7.0 mg/kg, appear adequate at this time to protect sensitive species of wildlife. We emphasize that these values, and others shown in Table 7, are considered criteria and not administratively-legislated standards.

LITERATURE CITED

Bidleman, T.F., and C.E. Olney. 1975. Long range transport of toxaphene insecticide in the atmosphere of the Western North Atlantic. Nature (London) 257(5526):475-477.

Blus, L.E., E. Cromartie, L. McNease, and T. Joanen. 1979. Brown pelican: population status, reproductive success, and organochlorine residues in Louisiana, 1971-1976. Bull. Environ. Contam. Toxicol. 22:128-135.

Bridges, J.M., and R.D. Andrews. 1979. Agricultural pesticides in wild turkeys in Southern Illinois. Trans. Illinois State Acad. Sci. 69:473-484.

Bush, P.B., J.T. Kiker, R.K. Page, N.H. Booth, and O.J. Fletcher. 1977. Effects of graded levels of toxaphene on poultry residue accumulation, egg production, shell quality and hatchability in white leghorns. J. Agric. Food Chem. 25:928-932.

Bush, P.B., M.Tanner, and J. Kiker. 1978. Tissue residue studies on toxaphene in broiler chickens. J. Agric. Food Chem. 26:26-30.

Cohen, D.B., G.W. Bowes, and S.M. Ali. 1982. Toxaphene. California State Water Res. Control Bd., Toxic Substances Control Prog., Spec. Proj. Rep. 82-4SP. 126 pp.

EPA. 1980a. Ambient water quality criteria for toxaphene. U.S. Environ. Protection Agency Rep. 440/5-80-076. 113 pp.

EPA. 1980b. Fish kills caused by pollution in 1977: Eighteenth report. U.S. Environ. Protection Agency Rep. 440/4-80-004. 73 pp.

EPA. 1982. Toxaphene, intent to cancel or restrict registrations of pesticide products containing toxaphene; denial of applications for registration of pesticide products containing toxaphene; determination containing the rebuttable presumption against registration; availability of decision document. Federal Register 47 (229):53784-53793.

Gallagher, J.L., S.E. Robinson, W.J. Pfeiffer, and D.M. Seliskar. 1979. Distribution and movement of toxaphene in anaerobic marsh soils. Hydrobiologia 63:1-9.

Hall, R.J., and D. Swineford. 1980. Toxic effects of endrin and toxaphene on the southern leopard frog *Rana sphenocephala*. Environ. Pollut. 23A:53-65.

Harder, H.W., E.C. Christensen, J.R. Matthews, and T.F., Bidleman. 1980. Rainfall input of toxaphene to a South Carolina estuary. Estuaries 3:142-147.

Haseltine, S.D., M.T. Finley, and E. Cromartie. 1980. Reproduction and residue accumulation in black ducks fed toxaphene. Arch. Environ. Contam. Toxicol. 9:461-471.

Heath, R.G., J.W. Spann, E.F. Hill, and J.F. Kreitzer. 1972. Comparative dietary toxicities of pesticides to birds. U.S. Fish Wildl. Serv., Spec. Sci. Rep. - Wildl. 152. 57 pp.

Heinz, G.H, and M.T. Finley. 1978. Toxaphene does not effect avoidance behavior of young black ducks. J. Wildl. Manage. 42:408-409.

Hoffman, D.J., and W.C. Eastin, Jr. 1982. Effects of lindane, paraquat, toxaphene, and 2,4,5-trichlorophenoxyacetic acid on mallard embryo development. Arch. Environ. Contam. Toxicol. 11:79-86.

Hoffman, D.J., and P.H. Albers. 1984. Evaluation of potential embryotoxicity and teratogenicity of 42 herbicides, insecticides, and petroleum contaminants to mallard eggs. Arch. Environ. Contam. Toxicol. 13:15-27.

Hudson, R.H., R.K. Tucker, and M.A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp.

Isensee, A.R., G.E. Jones, J.A. McCann, and F.G. Pitcher. 1979. Toxicity and fate of nine toxaphene fractions in an aquatic model ecosystem. J. Agric. Food Chem. 27:1041-1046.

Johnson, W.D., G.F. Lee, and D. Spyridakis. 1966. Persistence of toxaphene in treated lakes. Air Water Pollut. Int. J. 10:555-560.

Johnson, W.W., and M.T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Kallman, B.J., O.B. Cope, and R-.J. Navarre. 1962. Distribution and detoxication of toxaphene in Clayton Lake, New Mexico. Trans. Am. Fish. Soc. 91:14-22.

Klass, E.E., H.M. Ohlendorf, and E. Cromartie. 1980. Organochlorine residues and shell thickness in eggs of clapper rail, common gallinule, purple gallinule, and limpkin (Class Aves), Eastern and Southern United States, 1972-74. Pestic. Monitor. J. 14:90-94.

Kreitzer, J.F. 1980. Effects of toxaphene and endrin at very low dietary concentrations on discrimination acquisition and reversal in bobwhite quail, *Colinus virginianus*. Environ. Pollut. 23A:217-230.

Lennon, R.E., J.B. Hunn, R.A. Schnick, and R.M. Burress. 1970. Reclamation of ponds, lakes, and streams, with fish toxicants; a review. FAO Fisheries Tech. Paper 100, Food Agric. Org. U.N., Rome. 99 pp. Reprinted by U.S. Fish Wildl. Serv., 1971.

Ludke, J.L., and C.J. Schmitt. 1980. Monitoring contaminant residues in freshwater fishes in the United States: The National Pesticide Monitoring Program. Pages 97-110 in W. R. Swain and V. R. Shannon (eds). Proc. 3rd US-USSR Symp. Effects of Pollutants upon Aquatic Ecosystems. U.S. Environ. Protection Agency Rep. 600/9-80-034.

Matsumura, F. 1978. Mechanisms of pesticide degradation. U.S. sEnviron. Protection Agency Rep. 600/1-78-065. 43 pp.

Mayer, F.L., Jr., P.M. Mehrle, Jr., and W.P. Dwyer. 1975. Toxaphene effects on reproduction, growth, and mortality of brook trout. U.S. Environ. Protection Agency Rep. 600/3-75-013. 43 pp.

Mayer, F.L., Jr., and P.M. Mehrle. 1977. Toxicological aspects of toxaphene in fish: a summary. Trans. N. Am. Wildl. Mat. Res. Conf. 42:365-373.

Mayer, F.L., Jr., P.M. Mehrle, Jr., and W.P. Dywer. 1977. Toxaphene: chronic toxicity to fathead minnows and channel catfish. U.S. Environ. Protection Agency Rep. 600/3-77-069. 39 pp.

McDowell, L.L., G.H. Willis, C.E. Murphree, L.M. Southwick, and S. Smith. 1981. Toxaphene and sediment yields in runoff from a Mississippi Delta watershed. J. Environ. Qual. 10:168-173.

Mehrle, P.M., M.T. Finley, J.L. Ludke, F.L. Mayer, and T.E. Kaiser. 1979. Bone development in black ducks as affected by dietary toxaphene. Pestic. Biochem. Physiol. 10:168-173.

Messick, J.P., E.C. Bizeau, W.W. Benson, and W.H. Mullins. 1974. Aerial pesticide applications and ring-necked pheasants. J. Wildl. Manage. 38:679-685.

Negherbon, W.O. (ed.). 1959. Handbook of toxicology. Vol. III. Insecticides, a compendium. WADC Tech. Rep. 55-16. 854 pp. Available from Armed Services Technical Information Agency, Arlington Hall Station, Arlington, VA.

Neithammer, K.R., D.M. Swineford, and L.N. Locke. 1981. Organochlorine residues and mortality of herons. Pestic. Monitor. J. 14:125-135.

Pimentel, D., 1971. Ecological effects of pesticides on non-target species. Exec. Off. President, Off. Science Technol. 220 pp. Available from U.S. Govt. Printing Office, Washington DC, 20402, as Stock Number 4106-0029.

Ribick, M.A., G.R. Dubay, J.D. Petty, D.L. Stalling, and C.J. Schmitt. 1982. Toxaphene residues in fish: identification, quantification and confirmation at part per billion levels. Environ. Sci. Technol. 16:310-318.

Pollock, G.A., and W.W. Kilgore. 1978. Toxaphene. Residue Rev. 69:87-140.

Rice, C.P., and M.S. Evans. 1984. Toxaphene in the Great Lakes. Pages 163-194 in J.O. Nriagu and M.S. Simmons (eds.). Toxic contaminants in the Great Lakes. John Wiley, New York.

Sanders, H.O. 1980. Sublethal effects of toxaphene on daphnids, scuds, and midges. U.S. Environ. Protection Agency Rep. 600/3-80-006. 17 pp.

Schmitt, C.J., J.L. Ludke, and D.F. Walsh. 1981. Organochlorine residues in fish, National Pesticide Monitoring Program. Pestic. Monitor. J. 14:136-206.

Schmitt, C.J., M.A. Ribick, J.L. Ludke, and T.W. May. 1983. National Pesticide Monitoring Program: organochlorine residues in freshwater fish, 1976-79. U.S. Fish Wildl. Serv. Resour. Publ. 152. 62 pp.

Schoettger, R.A., and J.R. Olive. 1961. Accumulation of toxaphene by fish-food organisms. Limnol. Ocean. 6:216-219.

Schwartz, C.C., and G.J. Nagy. 1974. Pesticide effects on in vitro dry matter digestion in deer. J. Wildl. Manage. 38:531-534.

Seiber, N.J., S.C. Madden, M.M. McChesney, and W.L. Winterlin. 1979. Toxaphene dissipation from treated cotton field environments: component residual behavior on leaves, and in air, soil and sediments determined by capillary gas chromatography. J. Agric. Food Chem. 27:284-290.

Terrierre, L.C., U. Kiigemaki, A.R. Gerlach, and R.L. Borovicka. 1966. The persistence of toxaphene in lake water and its uptake in aquatic plants and animals. J. Agric. Food Chem. 14:66-69.

Tucker, R.K., and D.G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 84. 131 pp.

Webb, D.W. 1980. The effects of toxaphene pesticide on benthic macro invertebrates. J. Kansas Entomol. Soc. 53:731-744.

White, D.W., R.C., Stendell, and B.M. Mulhern. 1979. Relation of wintering canvasbacks Aythya valisineria to environmental pollutants, Chesapeake Bay, Maryland, USA. Wilson Bull. 91:279-287.

White, D.H., K.A. King, and R.M. Prouty. 1980. Significance of organochlorine and heavy metal residues in wintering shorebirds at Corpus Christi, Texas, 1976-77. Pestic. Monitor. J. 14:58-63.

White, D.H., C.A. Mitchell, H.D. Kennedy, A.J. Krynitsky, and M.A. Ribick. 1983. Elevated DDE and toxaphene residues in fishes and birds reflect local contamination in the lower Rio Grande Valley, Texas. Southwest. Natur. 28:325-333.

Wiemeyer, S.N., D.M. Swineford, and P.R. Spitzer. 1978. Organochlorine residues in New Jersey osprey eggs. Bull. Environ. Contam. Toxicol. 19:56-63.

Williams, R.R., and T.R. Bidleman. 1978. Toxaphene degradation in estuarine sediments. J. Agric. Food Chem. 26:260-262.

Table 1. Toxaphene residues in whole composite samples of freshwater fish and fish-eating birds collected from the Arroyo Colorado, Texas, in 1978 and 1979 (White et al. 1983).

Taxonomic group, year of collection, species	Residue, in ppm wet weight
Fish	
1978	
Blue catfish, *Ictalurus furcatus*	9.7-31.5
Gizzard shad, *Dorosoma cepedianum*	11.2-29.6
Sea catfish, *Arius felis*	ND[a]-0.4
Spotted seatrout, *Cynoscion nebulosus*	ND
1979	
Blue catfish	19.5-24.8
Gizzard shad	5.4
Channel catfish, *Ictalurus punctatus*	0.8-19.5
Striped mullet, *Mugil cephalus*	4.4
Birds	
1978	
Laughing gull, *Larus atricilla*	ND-3.0
Ringed-billed gull, *L. delawarensis*	ND-3.0
Franklin's gull, *L. pipixcan*	ND-2.0
Herring gull, *L. argentatus*	ND
Pied-billed grebe, *Podilymbus podiceps*	ND
Forster's tern, *Sterna forsteri*	1.7
Great-tailed grackle, *Quiscalus mexicanus*	ND
Red-winged blackbird, *Agelaius phoeniceus*	ND
1979	
Laughing gull	ND-0.4

[a]ND = not detectable.

Table 2. Acute toxicity of toxaphene to aquatic organisms. Concentrations shown are in micrograms of toxaphene per liter (ppb) of medium fatal to 50% of the test organisms in 96 hours.

Type of water, taxonomic group, species	LC-50 (96 h)	Reference[a]
Freshwater		
Insects		
Stonefly, *Claassenia* sp.	1.3	1
Stonefly, *Pteronarcys* sp.	2.3	1
Cranefly, *Tipula* sp.	18.0	1
Midge, *Chironomus* sp.	30.0[b]	1
Snipefly, *Atherix* sp.	40.0	1
Amphibians		
Leopard Frog, *Rana sphenocephala*	32.0-54.0	2
Crustaceans		
Daphnid, *Daphnia magna*	10.0[b]	1
Daphnid, *Daphnia pulex*	14.2[b]	1
Daphnid, *Simocephalus* sp.	19.0[b]	1
Amphipod, *Gammarus fasciatus*	26.0	1
Glass shrimp, *Palaemonetes kadiakensis*	28.0	3
Fish		
Largemouth bass, *Micropterus salmoides*	2.0	1
Bluegill, *Lepomis macrochirus*	2.4-29.0	1,3,4
Brown trout, *Salmo trutta*	3.1	1
Common carp, *Cyprinus carpio*	3.7	1
Channel catfish, *Ictalurus punctatus*	4.2-13.1	1,3
Black bullhead, *Ictalurus melas*	5.8	1
Coho salmon, *Oncorhynchus kisutch*	8.0	1
Rainbow trout, *Salmo gairdneri*	10.6	1
Yellow perch, *Perca flavescens*	12.0	1
Green sunfish, *Lepomis cyanellus*	13.0	1
Redear sunfish, *Lepomis microlophus*	13.0	3
Goldfish, *Carassius auratus*	14.0	1
Fathead minnow, *Pimephales promelas*	18.0	1
Guppy, *Poecilia reticulata*	20.0	3
Saltwater		
Molluscs		
Eastern oyster, *Crassostrea virginica*	16.0	3
Quahaug clam, embryo, *Mercenaria mercenaria*	1,120.0	3
Crustaceans		
Drift-line crab, *Sesarma cinereum*	0.05-8.8	3
Copepod, *Acartia tonsa*	0.11	3
Pink shrimp, *Penaeus duorarum*	1.4-2.2	3
Grass shrimp, *Palaemonetes pugio*	4.4	3
Mysid shrimp, *Mysidopsis bahia*	4.5	3
Korean shrimp, *Palaemon macrodactylus*	21.0	3
Mud crab, larva, *Rithropanopeus harrisii*	43.8	3
Blue crab, *Callinectes sapidus*	824.0	3
Fish		
Pinfish, *Lagodon rhomboides*	0.5	3
Sheepshead minnow, *Cyprinodon variegatus*	1.1	3
Striped bass, *Morone saxatilis*	4.4	3
Threespine stickleback, *Gasterosteus aculeatus*	8.2	3

[a]References: 1, Johnson and Finley 1980; 2, Hall and Swineford 1980; 3, EPA 1980a; 4, Isensee et al. 1979.
[b]48-hour value.

Table 3. Maximum acceptable toxicant concentration values (MATC) for toxaphene and aquatic organisms, based on exposure for the entire or most of the life cycle. Concentrations are in micrograms of toxaphene per liter (ppb).

Type of water, organism	MATC (µg/1)	Reference[a]
Freshwater		
Arthropods		
Daphnid, *Daphnia magna*	0.07-0.12	1
Amphipod, *Gammarus pseudolimnaeus*	0.13-0.25	1
Midge, larva, *Chironomus plumosus*	1.0-3.2	1
Fish		
Fathead minnow, *Pimephales promelas*	0.025-0.054	2
Channel catfish, *Ictalurus punctatus*	0.049-0.072	2
Saltwater		
Fish		
Sheepshead minnow, *Cyprinodon variegatus*		
Early life stage	1.1-2.5	3

[a]References: 1, Sanders 1980; 2, Mayer et al. 1977; 3, EPA 1980a.

Table 4. Acute oral toxicity of toxaphene to birds and mammals (Tucker and Crabtree 1970; Hudson et al. 1984). Concentrations shown are in milligrams of toxaphene ingested per kilogram body weight fatal to 50% of test animals. A single dose was administered orally and survival data gathered over a 14-day posttreatment observation period.

Organism	LD-50 (ppm)
Birds	
California quail, *Callipepla californica*	11.9-47.4
Sharp-tailed grouse, *Tympanuchus phasianellus*	14.1-28.2
Gray partridge, *Perdix perdix*	20.0-28.3
Ring-necked pheasant, *Phasianus colchicus*	20.0-80.0
Mallard, *Anas platyrhynchos*	
Duckling	23.3-40.6
Adult	37.6-133.0
Fulvous whistling-duck, *Dendrocygna bicolor*	37.2-264.0
Northern bobwhite, *Colinus virginianus*	59.3-123.0
Lesser sandhill crane, *Grus canadensis canadensis*	100.0-316.0
Horned lark, *Eremophila alpestris*	425.0-794.0
Mammals	
Mule deer, *Odocoileus hemionus hemionus*	139.0-240.0
Domestic goat, *Capra hircus*	>160.0

Table 5. Sublethal effects of toxaphene to aquatic biota.

Type of medium, organism	Toxaphene concentration in medium, in µg/1 (ppb)	Exposure duration, in days	Effect	Reference[a]
Freshwater				
Daphnid, *Daphnia magna*	0.12	14	Reduced reproduction	1
Midge, *Chironomus plumosus*	3.2	20	Delayed emergence	1
Goldfish *Carassius auratus*	0.44-1.8	4	Behavioral disruption	2
Brook trout, *Salvelinus fontinalis*	0.068	161	Reduced reproduction	3
Brook trout	0.288	161	Growth inhibition	4
Fathead minnow, *Pimephales promelas*				
Adult	0.097	30	"	4
Fry	0.054	30	"	4
Channel catfish, *Ictalurus punctatus*				
Adult	0.299	30	"	4
Fry	0.072	15	Backbone abnormalities	4
Largemouth bass, *Micropterus salmoides*				
Larvae	0.2	14	Histopathology of kidney and GI tract	2
Saltwater				
Eastern oyster, *Crassostrea virginica*	100.0	1	Growth inhibition	5
Mysid shrimp, *Mysidopsis bahia*	0.14	28	Reduced reproduction	5
Spot, (teleost) *Leiostomus xanthurus*	0.1	long-term	Histopathology	2

[a]References: 1, Sanders 1980; 2, Pollock and Kilgore 1978; 3, Mayer et al. 1975; 4, Mayer et al. 1977; 5, EPA 1980a.

Table 6. Bioconcentration factors (BCF) for toxaphene and selected species of aquatic biota (modified from EPA 1980a).

Medium, tissue, species, developmental stage	BCF	Exposure duration in days
Freshwater		
Whole body		
Brook trout	10,000	140
Fathead minnow	52,000	98
Channel catfish		
Adults	22,000	100
Fry	40,000	90
Muscle		
Brook trout	3,400	161
Channel catfish	7,800	137
Saltwater		
Whole body		
Eastern oyster	32,800	168
Sheepshead minnow	9,800	28
Longnose killifish, *Fundulus similis*		
Fry	27,900	28
Juvenile	29,400	28
Adult	5,400	32
Egg		
Longnose killifish	1,270	14
Longnose killifish	3,700	52

Table 7. Current recommendations on toxaphene concentrations (EPA 1980a).

Environmental or other factor	Allowable concentration
Freshwater life protection[a]	0.013 µg/1 (24-hour average); 1.6 µg/1 maximum at any time
Saltwater life protection	0.07 µg/1 maximum at any time
Fish tissues	5.0 mg/kg maximum, wet weight basis; 0.4 to 0.6 µg/kg maximum, wet weight basis (Mayer and Mehrle 1977)
Fat of meat from livestock	7.0 mg/kg
Milk and milk products, fat weight basis	0.5 mg/kg
Sunflower seeds	0.1 mg/kg wet weight basis
Citrus fruits	5.0-7.0 mg/kg wet weight basis (Canada); 0.4 mg/kg wet weight (W. Germany, Netherlands)
Drinking water	5.0-8.75 µg/1
Safe daily dose: human	3.4 µg/kg body weight
Acceptable daily intake: human	1.25 µg/kg body weight
Daily intake from air: human	0.00018 µg/kg body weight

[a]The International Joint Commission of the United States and Canada recommended a water standard of 0.008 µg/1 for protection of freshwater aquatic life. This standard is based on the study by Mayer et al. (1975), who found that toxaphene at 0.039 µg/1 in water, caused a significant increase in mortality and a significant decrease in growth of surviving brook trout fry over a 90-day period. The standard of 0.008 µg/1 is obtained by applying an application factor of 5.

Biological Report 85(1.5)
October 1985

Contaminant Hazard Reviews
Report No. 5

SELENIUM HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

By

Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Ecological and toxicological aspects of selenium (Se) in the environment are reviewed, including its chemistry, background residues in biological and other materials, and toxic, sublethal, and latent effects (including the effects of Se deficiency). Recommendations are presented, including proposed Se criteria for protection of sensitive species of fish and wildlife.

Most authorities agree on five points. First, Se deficiency is not as well documented as Se poisoning, but may be equally significant. Second, Se released as a result of anthropogenic activities (including fossil fuel combustion and metal smelting), as well as that in naturally seleniferous areas, poses the greatest threat of poisoning to fish and wildlife. Third, additional research is required on chemical and biological transformations among valence states, allotropic forms, and isomers of Se. Fourth, Se metabolism and degradation are both significantly modified by interaction with various heavy metals, agricultural chemicals, microorganisms, and numerous physicochemical factors, and until these interactions are resolved it will be difficult to meaningfully interpret Se residues in various tissues. And fifth, documented biological responses to Se deficiency or to selenosis vary widely, even among closely related taxonomic groups.

It is generally agreed that Se deficiency may be prevented in fish, small laboratory mammals, and livestock by feeding diets containing 50 to 100 ppb of Se. The concentration range of total inorganic selenite currently recommended for aquatic life protection--35 ppb in freshwater to 54 ppb in marine waters--is below the range of 60 to 600 ppb that is fatal to sensitive aquatic species. In freshwater, it is also below the range of 47 to 53 ppb associated with growth inhibition of freshwater algae, anemia and reduced hatching in trout, and shifts in species composition of freshwater algae communities. Accordingly, current recommendations for Se with respect to aquatic life appear to afford an adequate measure of protection. However, some studies have shown that Se water concentrations of 9 to 12 ppb are associated with inhibited reproduction of certain freshwater teleosts, suggesting that the current Se criterion for protection of freshwater life should be revised downward. Also, high bioconcentration and accumulation of Se from water by numerous species of algae, fish, and invertebrates is well documented at levels of 0.015 to 3.3 ppb, which are substantially below the recommended range of 35 to 54 ppb. The significance of Se residues in aquatic biota is still unclear, and more research appears to be needed on Se pharmacokinetics in aquatic environments.

Aerosol concentrations exceeding 4.0 ug Se/m^3 are considered potentially harmful to human health; however, no comparable data base for birds and other wildlife species is available at this time.

Selenium in natural foods is less toxic than are purified forms of Se. The consensus is that Se toxicity is prevented in livestock if dietary Se concentrations do not exceed 5,000 ppb in natural forage, or 2,000 ppb in feeds supplemented with purified Se. Minimum toxic concentrations of Se in the rat (a sensitive species), fed diets containing natural Se were 1,400 ppb of Se as judged by evidence of liver changes, and 3,000 ppb as estimated from longevity and histopathology; these values were only 350 and 750 ppb, respectively, when diets low in natural Se were fortified with purified Se. The evidence is incomplete for migratory waterfowl and other birds, but diets containing more than 5,000 ppb of Se are demonstrably harmful.

This report should be cited as:

Eisler R. 1985. Selenium hazards to fish, wildlife and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.5).

TABLES

ACKNOWLEDGMENTS

I thank L. Garrett, M. Shawe and B. Graff for library services; I. Moore for secretarial help; J. Jacknow, D.J. Hoffman, H.M. Ohlendorf, and T.P. Lowe for reviewing the manuscript; and P.H. Eschmeyer and J.R. Zuboy for editorial services.

INTRODUCTION

Selenium (Se) was first identified as an element in 1817 by the Swedish chemist Berzelius. It is now firmly established that Se is beneficial or essential in amounts from trace to part-per-billion concentrations for humans and some plants and animals, but toxic at some concentrations present in the environment. Selenium deficiency was recently reported among cattle grazing in the Florida Everglades, which showed evidence of anemia, slow growth, and reduced fertility (Morris et al. 1984). Conversely, calves of Indian buffaloes died of Se poisoning after eating rice husks grown in naturally seleniferous soils (Prasad et al. 1982); severe reproductive and developmental abnormalities were observed in aquatic birds nesting at Se-contaminated irrigation drainwater ponds in the San Joaquin Valley, California (Ohlendorf et al. 1986); and fish contained high body burdens of Se and failed to reproduce in a lake receiving dissolved Se by way of a power plant fly ash sluice water return (Cumbie and Van Horn 1978). Selenium poisoning is an ancient and well-documented disease (Rosenfeld and Beath 1964). Signs of it were reported among domestic livestock by Marco Polo in western China near the borders of Turkestan and Tibet in about the year 1295; among livestock, chickens, and children in Columbia, South America, by Father Pedro Simon in 1560; among human adults in Irapuato, Mexico, in about 1764; and among horses of the U.S. Cavalry in South Dakota in 1857 and again in 1893 (Rosenfeld and Beath 1964). In 1907-08, more than 15,000 sheep died in a region north of Medicine Bow, Wyoming, after grazing on seleniferous plants. The incidents have continued, and the recent technical literature abounds with isolated examples of selenosis among domestic animals.

Selenium has been the subject of many reviews (Rosenfeld and Beath 1964; Frost 1972; Sandholm 1973; Zingaro and Cooper 1974; Frost and Ingvoldstad 1975; Anon. 1975; NAS 1976; Harr 1978; EPA 1980; Lo and Sandi 1980; Shamberger 1981; Wilber 1980, 1983; Fishbein 1977, 1983; NRC 1983; Reddy and Massaro 1983). These authorities agree that Se is widely distributed in nature, being especially abundant with sulfide minerals of various metals, such as iron, lead, and copper. The major source of environmental Se is the weathering of natural rock. The amount of Se entering the atmosphere as a result of anthropogenic activities is estimated to be 3,500 metric tons annually, of which most is attributed to combustion of coal; however, aside from highly localized contamination, the contribution of Se by man's activities is small in comparison with that attributable to natural sources. Collectively, all authorities agree that Se may favorably or adversely affect growth, survival, and reproduction of algae and higher plants, bacteria and yeasts, crustaceans, molluscs, insects, fish, birds, and mammals (including humans). Most acknowledge that sensitivity to Se and its compounds is extremely variable in all classes of organisms and, except for some instances of Se deficiency or of selenosis, metabolic pathways and modes of action are imperfectly understood. For example, selenium “indicator” plants can accumulate Se to concentrations of thousands of parts per million without ill effects; in these plants Se promotes growth, whereas in crop plants accumulations as low as 25 to 50 ppm may be toxic. Thus, plants and waters high in Se are considered potentially hazardous to livestock and to aquatic life and other natural resources in seleniferous zones.

In this account I briefly review the technical literature on ecological and toxicological aspects of selenium (with emphasis on fish and wildlife and their predators and prey), and provide current recommendations for the protection of sensitive species of concern to the U.S. Fish and Wildlife Service. This is part of a continuing series of synoptic reviews prepared in response to informational requests from environmental specialists of the Service.

ENVIRONMENTAL CHEMISTRY

Selenium is characterized by an atomic weight of 78.96, an atomic number of 34, a melting point of 271°C, a boiling point of 685°C, and a density of 4.26-4.79. Chemical properties, uses, and environmental persistence of selenium were documented by a number of researchers whose works constitute the major source material for this section: Rosenfeld and Beath (1964); Bowen (1966); Lakin (1973); Stadtman (1974, 1977); Frost and Ingvoldstad (1975); Chau et al. (1976); Harr (1978); Wilber (1980, 1983); Zieve and Peterson (1981); Robberecht and Von Grieken (1982); Cappon and Smith (1982); and Nriagu and Wong (1983).

There was general agreement on four points. First, that selenium chemistry is complex, and that additional research is warranted on chemical and biochemical transformations among valence states, allotropic forms, and isomers of selenium. Second, that selenium metabolism and degradation is significantly modified by interaction with heavy metals, agricultural chemicals, microorganisms, and a variety of physicochemical factors. Third, that anthropogenic activities (including fossil fuel combustion and metal smelting) and naturally seleniferous areas pose the greatest hazards to fish and wildlife. And fourth, that selenium deficiency is not as well documented as

Se poisoning, but may be equally significant. These points are developed here in greater detail.

Selenium chemistry is complex (Rosenfeld and Beath 1964; Harr 1978; Wilber 1983). In nature, selenium exists: as six stable isotopes (Se-74,-76,-77,-78,-80, and -82), of which Se-80 and -78 are the most common, accounting for 50 and 23.5%, respectively; in three allotropic forms; and in five valence states. Changes in the valence state of Se from -2 (hydrogen selenide) through 0 (elemental Se), +2 (selenium dioxide), +4 (selenite), and +6 (selenate) are associated with its geologic distribution, redistribution, and use. Soluble selenates occur in alkaline soils, are slowly reduced to selenites, and are then readily taken up by plants. In drinking water, selenates represent the dominant chemical species. Selenites are less soluble than the corresponding selenates and are easily reduced to elemental Se. In seawater, selenites are the dominant chemical species under some conditions (Cappon and Smith 1981). Selenium dioxide is formed by combustion of elemental Se present in fossil fuels or rubbish. Selenium is the most strongly enriched element in coal, being present as an organoselenium compound, a chelated species, or as an adsorbed element. On combustion of fossil fuels, the sulfur dioxide formed reduces the selenium to elemental Se.

Elemental Se is insoluble and largely unavailable to the biosphere, although it is still capable of satisfying metabolic nutritional requirements. Hydrogen selenide is highly toxic (at 1-4 ppb in air), unstable, acidic, and irritative. Selenides of mercury, silver, copper, and cadmium are very insoluble, although their insolubility may be the basis for the reported detoxification of methylmercury by dietary selenite, and for the decreased heavy metal toxicity associated with selenite. Metallic selenides are thus biologically important in sequestering both Se and heavy metals in a largely unavailable form.

In areas of acid or neutral soils, the amount of biologically available Se should steadily decline. The decline may be accelerated by active agricultural or industrial practices. In dry areas, with alkaline soils and oxidizing conditions, elemental Se and selenides in rocks and volcanic soils may oxidize sufficiently to maintain the availability of biologically active selenium. Concentrations of selenium in water are a function of selenium levels in the drainage system and of water pH. In Colorado, for example, streams with pH 6.1-6.9 usually contain <1 ppb of Se, but those with pH 7.8-8.2 may contain 270 to 400 ppb (Lakin 1973).

Selenium volatilizes from soils at rates that are modified by temperature, moisture, time, season of year, concentration of water-soluble selenium, and microbiological activity. Conversion of inorganic and organic selenium compounds to volatile selenium compounds (such as dimethyl selenide, dimethyl diselenide, and an unknown compound) by microorganisms has been observed in lake sediments of the Sudbury area of Ontario. This conversion may have been effected by pure cultures of *Aeromonas*, *Flavobacterium*, *Pseudomonas*, or an unidentified fungus, all of which are found in methylated lake sediments. Production of volatile selenium is temperature dependent. Compared with the amount of $(CH_3)_2$ Se produced at an incubation temperature of 20°C, 25% less was produced at 10°C and 90% less at 4°C. Details of Se reduction and oxidation by microorganisms are not clear. One suggested mechanism for selenite reduction in certain microorganisms involves attachment to a carrier protein and transformation from selenite to elemental Se, which in turn may be oxidized to selenite by the action of *Bacillus* spp., as one example. It is apparent that much additional research on this problem is warranted.

Selenium is an essential nutrient for some plants and animals; it constitutes an integral part of the enzyme glutathione peroxidase and may have a role in other biologically active compounds, especially vitamin E and the enzyme formic dehydrogenase. Some animals require Se-containing amino acids (viz. selenocysteine, selenocystine, selenomethionine, selenocystathionine, Se-methylselenocysteine, and Se-methylselenomethionine), but reportedly are incapable of producing them. Selenium also forms part of certain proteins, including cytochrome C, hemoglobin, myoglobin, myosin, and various ribonucleoproteins. It now appears that selenates and selenites are absorbed by plants, reduced, and then incorporated in amino acids synthesis. The biological availability of Se is higher in plant foods than in foods of animal origin (Lo and Sandi 1980). The net effect of soil, plant, and animal metabolism is to convert Se to inert and insoluble forms such as elemental Se, metallic selenides, and complexes of selenite with ferric oxides.

Selenium was used in the early 1900's as a pesticide to control plant pests, and is still used sparingly to control pests of greenhouse chrysanthemums and carnations (Rosenfeld and Beath 1964). It has been used to control cotton pests (in Trinidad), mites and spiders that attack citrus, and mites that damage apples. Although no insect-resistant strains have developed, the use of selenium pesticides has been discontinued, owing to their stability in soils and resultant contamination of food crops, their high price, and their proven toxicity to mammals

and birds. Selenium shampoos, which contain about 1% selenium sulfide, are still used to control dandruff in humans and dermatitis and mange in dogs. Selenium is used extensively in the manufacture and production of glass, pigments, rubber, metal alloys, textiles, petroleum, medical therapeutic agents, and photographic emulsions.

Air and surface waters generally contain nonhazardous concentrations of Se. Significant increases of Se in specific areas are attributed exclusively to industrial sources, and to leaching of groundwater from seleniferous soils. In the United States, about 4.6 million kg of selenium are released annually into the environment: 33% from combustion of fossil fuels, 59% from industrial losses, and 8% from municipal wastes. Of the total, about 25% is in the form of atmospheric emissions, and the rest in ash. Mining and smelting of copper-nickel ores at Sudbury, Ontario, Canada, alone releases about 2 metric tons of Se to the environment daily, and probably represents the greatest point source of Se release in the world. In 1977, 680,000 kg of Se was produced at Sudbury, but only about 10% was recovered, suggesting that about 90% was lost to the environment. Of the amount lost, perhaps 50 metric tons was dispensed into the atmosphere, probably as selenium dioxide (airborne Se levels 1-3 km from Sudbury were as high as 6.0 $\mu g/m^3$). The rest was probably associated with mine tailings, wastewater, and scoria, and is a local source of Se contamination, most notably in lakes. The present annual rates of Se accumulation in lake sediments in the Sudbury area range from 0.3 to 12.0 mg/m^2; these deposition rates exceed those of pre-colonial times by factors of 3 to 18, and are among the highest recorded in North America (Nriagu and Wong 1983).

Selenium is a serious hazard to livestock and probably to people in a wide semiarid belt that extends from inside Canada southward across the United States into Mexico (NRC 1983). Selenium tends to be present in large amounts in areas where the soils have been derived from Cretaceous rocks. Total Se in such soils averages about 5 ppm, but is sometimes as high as 80 ppm. Lack of rainfall has prevented the solution of the Se minerals and the removal of their salts in drainage waters. In some areas, modern fertilization practices and the buildup of sulfates in the soil due to acid precipitation partly lessen the availability of Se to plants and forage crops. In the United States, highly seleniferous natural areas (200-300 ppb in forage) are most abundant in the Rocky Mountain and High Central Plains areas; areas with lower concentrations (20-30 ppb) in forage are typical in the Pacific Northwest and the Southeast. However, huge variations are not uncommon from one specific location to another. Among plants, primary and secondary selenium accumulators are almost always implicated in cases of acute or chronic selenium poisoning of livestock. Primary Se accumulator plants, such as various species of *Astragalus*, *Oonopsis*, *Stanelya*, *Zylorhiza*, and *Machaeranthera*, may require 1 to 50 ppm Se in either soil or water for growth, and may contain 100 to 10,000 ppm Se as a glutamyl dipeptide or selanocystanthionine. Secondary accumulator plants (representative genera: *Astor*, *Gutierrezia*, *Atriplex*, *Grindelia*, *Castilleja*, and *Comandra*) grow in either seleniferous or nonseleniferous soils and may contain 25-100 ppm Se. Nonaccumulator plants growing on seleniferous soils contain 1-25 ppm fresh weight of Se. Meat and eggs of domestic animals may contain 8-9 ppm of Se in seleniferous areas, compared with 0.01-1.0 ppm in nonseleniferous areas. Tissues from animals maintained on high-Se feeds generally contain 3-5 ppm Se fresh weight vs. up to 20 ppm in animals dying of Se poisoning (Harr 1978).

Selenium is nutritionally important as an essential trace element, but is harmful at slightly higher concentrations. Although normal Se dietary levels required to ensure human health range from 0.04 to 0.1 ppm, toxicity may occur if food contains as little as 4.0 ppm. Minimum Se concentrations required are usually higher in livestock than in humans. In areas with highly seleniferous soils, excess Se is adsorbed onto a variety of plants and grains and can be fatal to grazing livestock. There is general agreement, however, that selenium inadequacy can be of greater concern to health than is selenium toxicity. Studies in humans and small animals indicated that Se deficiency (in part) underlies various chronic diseases, increasing susceptibility to cancer, arthritis, hypertension, heart disease, and possibly periodontal disease and cataracts. Selenium reportedly protects mammals and some birds against the toxic effects of mercury, cadmium, arsenic, thallium, and the herbicide paraquat (Hill 1975; Wilber 1983). There is no doubt that high dietary levels of these compounds, as well as of salts of copper, zinc, and silver, contribute to selenium deficiency effects. However, too little is known of the chemical mechanisms to enable scientists to account for these phenomena. Selenium has a comparatively short effectual biological life in various species of organisms for which data are available. Studies with radioselenium-75 indicated that its biological half-life is 10 to 64 days: 10 in pheasants, 13 in guppies and voles, 15 in ants, 27 in eels, 28 in leeches, and 64 in earthworms (Wilber 1983). Many investigators concluded that the greatest current and direct use of selenium is in the transportation of grains grown in seleniferous areas to Se-deficient areas as animal and human food.

Table 1. Selenium concentrations in nonbiological materials.

Sample, and unit of concentration	Concentration	Reference[a]
TERRESTRIAL (ppm)		
Earth's crust	0.05	Frost and Ingvoldstad 1975
Soils	0.2	Ebens and Shacklette 1982
Limestones	0.08	
Sandstones	up to 0.05	
Shales	0.6	
Chondrites	8.0	
Ocean sediments	0.34-4.8	de Goeij et al. 1974
Coal	3.36(0.46-10.65)	NAS 1976; Kuhn et. al. 1980
Fossil fuels	1-10	Harr 1978
Lake sediments		
NY, Lake George	0.22	Heit et al. 1980
Great Lakes	0.35-0.75	Adams and Johnson 1977
Freshwater lakes, Canada	0.2-14.5	Speyer 1980
AQUATIC (ppb)		
Drinking water		
Worldwide	0.12-0.44	Robberecht and
Groundwater		Von Grieken 1982
Nebraska, USA	<1-480	
Argentina	48-67	
Australia	0.008-0.33	
France	<5-75	
Israel	0.9-27	
Italy	<0.002-1.9	
Sewage waters		
USA		
Raw sewage	280	NAS 1976
Primary effluent	45	
Secondary effluent	50	
Worldwide		
Japan	480-700	Ebens and Shacklette 1982
USA	10-280	
USSR	1.8-2.7	
Germany	1.5	
River waters		
Japan	0.03-0.09	Nriagu and Wong 1983
Germany	0.015	Ebens and Shacklette 1982
Amazon River, South America	0.021	
USA		

Ohio River	<0.01	Robberecht and
Mississippi River	0.14	Von Grieken 1982
Michigan	0.8-10	
Nebraska	<1-20	
Colorado River	30	
Lake waters		
Sweden	0.04-0.21	Nriagu and Wong 1983
USA	0.04-1.4	NAS 1976
Great Lakes	0.001-0.036	Adams and Johnson 1977
Sea water		
Worldwide	0.009-0.045	Frost and Ingvoldstad 1975; Ebens and Shacklette 1982
Worldwide	0.09-0.45	Whittle et al. 1977
Worldwide	0.09-<6.0	NAS 1976
Israel, Dead Sea	0.8	Robberecht and Von Grieken 1982
Japan	0.04-0.08	
AIR (µg/m^3)		
Near Se industrial plant	0.7	NAS 1976
Control area	0.001	
Near Sudbury (Canada) smelter	up to 6.0	Nriagu and Wong 1983
INTEGRATED STUDIES (ppb)		
California		
Rainwater	0.05	Robberecht and
Lake water	0.018	Von Grieken 1982
Sea water	0.058-0.08	
Irrigation drain water		
Subsurface	300-1,400	Ohlendorf et al. 1986
Surface	300	
Vicinity of nickel-copper smelter, Sudbury, Ontario		
Lake waters	0.1-0.4	Nriagu and Wong 1983
Lake sediments	2,000-6,000	
Lake sediments 240 km south of Sudbury	1,000-3,000	
Cu-Ni ores	20,000-80,000	
Fly ash ponds		
Sediment	14,000	Furr et al. 1979
Water	350	

[a]Each reference applies to the values in the same row, and in the rows that follow for which no other reference is indicated.

BACKGROUND CONCENTRATIONS

Selenium concentrations in nonbiological materials extend over several orders of magnitude (Table 1). In terrestrial materials, concentrations in excess of 5 ppm Se are routinely recorded in meteorites, copper-nickel ores, coal and other fossil fuels, lake sediments in the vicinity of a nickel-copper smeltery, and in sediments of fly ash settling ponds. Water concentrations exceeding 50 ppb Se have been documented in groundwater, especially in areas with seleniferous soils, in sewage wastes, in irrigation drain water, and in water of fly ash settling ponds. Selenium concentrations in air samples were >0.5 $\mu g/m^3$ in the vicinity of Se production plants, and these were at least 500 times higher than in a control area. As a result of natural and anthropogenic processes, comparatively high concentrations of selenium in nonbiological materials may pose significant risks to fish and wildlife (this point is discussed later).

Selenium concentrations in representative species of freshwater, marine, and terrestrial flora and fauna are listed in Table 2. Additional information on body and tissue burdens of selenium was given by Birkner (1978), Jenkins (1980), Lo and Sandi (1980), Eisler (1981), and Wilber (1983). It is emphasized that, for all organisms, Se concentrations tended to be significantly higher when collected from locales having certain characteristics: highly seleniferous soils or sediments (*in* Comparative studies of food and environmental contamination. Int. Atomic Energy Agency, Vienna.de Goeij et al. 1974; Birkner 1978; Speyer 1980; Wilber 1983); high human population densities (Beal 1974); heavy accumulations of Se-laden wastes, such as effluents from systems used to collect fly ash scrubber sludge or bottom ash (Cumbie and Van Horn 1978; Sorensen et al. 1982, 1984); and Se-contaminated subsurface irrigation drainwater (Ohlendorf et al. 1986). There is evidence that Se concentrations are positively correlated with mercury residues in piscivorous mammals (Reijnders 1980; Wren 1984) and teleosts (Ganther et al. 1972; Leonzio et al. 1982), although the evidence for teleosts is conflicting (Tamura et al. 1975; Speyer 1980; Maher 1983), and that Se varies seasonally in crustaceans (Zafiropoulos and Grimanis 1977). In general, concentrations of Se in various tissues are usually higher in older than in younger organisms; among marine vertebrates, Se increases were especially pronounced among the older specimens of predatory, long-lived species (Eisler 1984).

All reported Se levels in tissues of marine invertebrates and plants have been less than 2 ppm Se on a wet weight basis, or 12 ppm dry weight. Higher levels are routinely recorded in liver and kidney tissues of marine and coastal vertebrates, including teleosts, birds, and mammals. Livers from adult seals were comparatively rich in selenium (Table 2); however, high concentrations in liver of maternal California sea lions were not reflected in liver of newborn pups (Martin et al. 1976). Mean concentrations of Se in kidneys of seven species of coastal birds collected from the highly industrialized Corpus Christi, Texas, area usually varied between 1.7 and 5.6 ppm Se fresh weight, but were 10.2 ppm in one bird. According to White et al. (1980), Se concentrations of this magnitude may be sufficient to impair reproduction in shorebirds.

Selenium levels in freshwater biota are relatively low, compared with those in their marine counterparts. In freshwater organisms, about 36% of the total Se was present as selenate, and the rest as selenite and selenide. In marine samples, only 24% of the total Se was present as selenate (Cappon and Smith 1982). The implications of this difference are not now understood, but have great relevance in the ability of Se to complex and detoxify various potentially toxic heavy metals, such as mercury and cadmium. In the most recent Nationwide monitoring of selenium and other contaminants in freshwater fishes, Se ranged from 0.05 to 2.9 ppm (fresh weight, whole fish) and averaged about 0.6 ppm; stations where concentrations in fish exceeded 0.82 ppm (>85th percentile) were in three areas: Atlantic coastal streams; Mississippi River system; and California (May and McKinney 1981). Among fish from Atlantic coastal streams, those from the Delaware River near Camden, New Jersey, had elevated whole body concentrations (i.e., >1.0 and <3.0 ppm Se), which were attributed to the industrialized character of the river. In the Big Horn and Yellowstone Rivers, high Se concentrations in fish may result from geologic sources of the element, including coal, phosphate, and sedimentary rock. Fish from the South Platte River near Denver, Colorado, may receive Se from industrial effluents, or from natural and anthropogenic activities associated with the removal of deposits of coal, barite, and sulfur. In California, where Se was elevated in fish from the San Jouquin River, it was speculated that Selocide, an Se-containing pesticide registered for use on citrus fruits in the 1960's, may have been a source, although contaminated irrigation drain water was considered a more likely possibility (Ohlendorf et al. 1986).

Among terrestrial plants, selenium accumulations in species of *Aster*, *Astragalus*, and several other genera are sometimes spectacularly high (Table 2). *Astragalus* is the most widely distributed. About 24 of its more than 200 species are Se accumulators that require Se to grow well . The highest reported Se concentration in plants

was 15,000 ppm dry weight, in loco weed, *Astragalus racemosus* (Wilber 1983). Consumption of these and other Se-accumulating forage plants by livestock has induced illness and death from selenium poisoning. Even at much lower concentrations, Se may harm animals that eat considerable amounts of the forage. Plants that accumulate Se tend to be deeper rooted than the grasses and survive more severe aridity, thus remaining (unfortunately) as the principal forage for grazing in time of drought (Wilber 1983).

Table 2. Selenium concentrations in field populations of selected species of flora and fauna. Values shown are in total Se (mg/kg, or ppm) fresh weight (FW), dry weight (DW), or ash weight (AW). Hyphenated numbers show range and single numbers the mean; where both appear, the range is in parentheses.

Ecosystem, taxonomic group, organism, tissue, location, and other variables	Concentration (ppm)	Reference[a]
MARINE		
Algae and macrophytes		
Whole	0.04-0.24 DW	Chau and Riley 1970; Lunde 1970; Tijoe et al. 1979
Edible seaweeds, whole	0.16-0.39 DW; 0.047 FW	Noda et al. 1979
Molluscs		
American oyster, *Crassostrea virginica*		
Redwood Creek, San Francisco, CA		
Mantle	4.8 DW	Okazaki and Panietz 1981
Digestive gland	8.8 DW	
Kidney	4.7 DW	
Tomales Bay, CA		
Mantle	2.2 DW	
Digestive gland	6.4 DW	
Kidney	2.5 DW	
Transferred from Redwood Creek to Tomales Bay for 56 days		
Mantle	3.5 DW	
Digestive gland	6.5 DW	
Kidney	3.8 DW	
Bivalve molluscs		
Shell	0.03-0.06 DW	Bertine and Goldberg 1972
Soft parts	0.1-0.9 FW; 1.3-9.9 DW	Lunde 1970; Bertine and Goldberg 1972; Karbe et al. 1977; Hall et al. 1978;

		Fukai et al. 1978;
		Luten et al. 1980
Muscle	1.1-2.3 DW	Maher 1983
Viscera	1.6-2.5 DW	
Edible fresh, 3 spp.		
Total Se	0.22(0.16-0.31) FW	Cappon and Smith 1982
As selenate	0.05 FW	
As selenite and selenide	0.17 FW	
Mussel, *Mytilus edulis*		
Gills	2.0-16.0 DW	Stump et al. 1979
Viscera	up to 5.0 DW	
Mussel, *Mytilus galloprovincialis*		
Gills	7.0 DW	Fowler and
Soft parts	6.0 DW	Benayoun 1976c
Mantle	5.2 DW	
Viscera	3.2 DW	
Muscle	1.9 DW	
Shell	<0.05 DW	
Echinoderms		
Whole, 7 spp.	0.8-4.4 DW	Papadopoulu et al.1976
Crustaceans		
Digestive system, 3 spp.	3.0-3.5 DW	Maher 1983
Edible tissues sold for human consumption		
17 spp.	0.2-2.0 FW	Hall et al. 1978;
		Noda et al. 1979;
		Luten et al. 1980
Edible tissues, 2 spp.		
Total Se	0.21 FW	Cappon and Smith 1982
As selenate	0.05 FW	
As selenite and selenide	0.16 FW	
Muscle, 5 spp.	2.4-4.4 DW	Maher 1983
Soft tissues, 2 spp.	2.0-2.8 DW	
Copepods, whole	1.8-3.4 DW	Zafiropoulos and
		Grimanis 1977;
		Tijoe et al. 1977
Euphausid, *Meganyctiphanes norvegica*		
Viscera	11.7 DW	Fowler and Benayoun
Eyes	7.8 DW	1976a
Muscle	1.8 DW	
Exoskeleton	0.8 DW	
Shrimp, *Lysmata seticaudata*		
Viscera	7.0 DW	Fowler and Benayoun 1976c
Eyes	4.8 DW	
Whole	2.6 DW	

Muscle	1.9 DW	
Exoskeleton	1.5 DW	
Molts	0.3 DW	
Sharks		
Muscle	0.2-0.8 FW	Glover 1979
Fish		
Digestive system, 4 spp.	1.0-2.4 DW	Maher 1983
Liver		
2 spp.	2.6-6.6 DW	Grimanis et al. 1978
74 spp.	0.6-5.0 FW	de Goeij et al. 1974; Hall et al. 1978; Luten et al. 1980
13 spp.	5.0-30.0 FW	Hall et al. 1978
Meals, 3 spp.	1.0-4.0 DW	Kifer and Payne 1968
Muscle		
4 spp.	0.5-1.5 DW	Maher 1983
182 spp.	0.1-2.0 FW	Bebbington et al. 1977; Grimanis et al. 1978; Kari and Kauranen 1978; Hall et al. 1978; Noda et al. 1979; Luten et al.1980
5 spp. Total Se	0.4(0.2-0.6) FW	Cappon and Smith 1982
As selenate	0.1 FW	
As selenite and selenide	0.3 FW	
Whole, 21 spp.	0.3-2.0 FW	Kari and Kauranen 1978; Hall et al. 1978; United Nations 1979
Japanese tunas, 4 spp.		
Liver	10.0-15.0 FW	Tamura et al. 1975
White muscle	0.5-1.3 FW	
Red muscle	3.5-9.1 FW	
Black marlin, *Makaira indica*		
Muscle	0.4-4.3 FW	MacKay et al. 1975
Liver	1.4-13.5 FW	
Blue marlin, *Makaira nigricans*		
Kidney	23.0 FW	Schultz and Ito 1979
Blood	1.0 FW	
Gill	1.0 FW	
Muscle		
Total Se	3.3(2.5-4.1) FW	Cappon and Smith 1982
As selenate	0.2(0.09-0.3) FW	
As selenite and selenide	3.1(2.4-3.8) FW	

Striped bass, *Morone saxatilis*		
Muscle	0.3 FW	Heit 1979
Liver	0.6 FW	
Tuna, canned	1.9-2.9 FW	Ganther et al. 1982
Swordfish, *Xiphias gladius*		
Muscle	0.3-1.3 FW	Freeman et al. 1978
Birds		
Kidney, 12 spp.	1.2-5.6 FW	Turner et al. 1978; White et al. 1980
White-faced ibis, *Plegadis chihi*		
Egg	0.3-1.1 FW	King et al. 1980
Royal tern, *Sterna maxima*		
Egg	0.4-2.1 FW	King et al. 1983
Sooty tern, *Sterna fuscata*		
Egg	1.1-1.4 FW	Ohlendorf and Harrison 1986
Brown pelican, *Pelecanus occidentalis*		
Egg	0.19-0.38 FW	Blus et al. 1977
Liver	1.0-4.2 FW	
Wedge-tailed shearwater, *Puffinus pacificus*		
Egg	1.1-1.3 FW	Ohlendorf and Harrison 1986
Red-footed booby, *Sula sula*		
Egg	0.8-0.9 FW	
Oystercatcher, *Haematopus ostralegus*		
Kidney	12.7(2.3-17.5) DW	Hutton 1981
Liver	12.8(5.0-20.5) DW	
Herring gull, *Larus argentatus*		
Kidney	14.1(8.6-19.4) DW	
Liver	7.9(6.9-9.3) DW	
Great Skua, *Catharacta skua*		
Kidney	32.8(13.3-89.1) DW	
Liver	19.7(6.7-34.6) DW	
Mammals		
Pilot whale, *Globicephala macrorhynchus*		
Blubber	0.8-1.4 FW	Stoneburner 1978
Liver	22.8-61.6 FW	
Kidney	3.0-10.0 FW	

Ringed seal,		
Phoca hispida saimensis		
Muscle	0.2-2.8 FW	Kari and Kauranen 1978
Liver	29.0-170.0 FW	
Kidney	0.3-3.0 FW	
Blubber	0.06-0.11 FW	
Harbor seal, *Phoca vitulina*		
Juveniles		
Kidney	0.6(0.0-1.3) FW	Reijnders 1980
Liver	2.8(2.6-6.5) FW	
Brain	1.1(0.0-7.4 FW	
Adults		
Kidney	3.5(1.9-7.3) FW	
Liver	109.0(409.0 Max.) FW	
Brain	3.7(1.5-8.2) FW	
Seals		
Liver, 4 spp.	6.1-170.0 FW	Kari and Kauranen 1978; Smith and Armstrong 1978; van de Ven et al. 1979
California sea lion,		
Zalophus californianus		
Mothers with normal pups		
Liver	260.0 DW	Martin et al. 1976
Kidney	22.0 DW	
Normal pups		
Liver	4.1 DW	
Kidney	6.1 DW	
Mothers with premature pups		
Liver	79.0 DW	
Kidney	12.0 DW	
Pups born prematurely		
Liver	2.9 DW	
Kidney	3.7 DW	
FRESHWATER		
Algae and higher plants		
Algae, whole	<2.0 DW	Jenkins 1980
Higher plants	0.1 DW	Rossi et al. 1976
Aquatic mosses	0.8 DW	
Filamentous algae		
Se-contaminated area	35.2(12-68) DW	Ohlendorf et al. 1986

Control area	<0.5 DW	
Rooted plants		
Se-contaminated area	52.1(18-79) DW	
Control area	0.4 DW	
Molluscs		
Mussels, 3 spp., NY State		
Soft parts	2.0-4.0 DW	Heit et al. 1980
Asiatic clam, *Corbicula fluminea*		
Whole, Florida	0.7 FW	Winger et al. 1984
Arthropoda		
Zooplankton	0.8-3.9 DW	Adams and Johnson 1977
Plankton		
Se-contaminated area	85(58-124) DW	Ohlendorf et al. 1986
Control Site	2(1.4-2.9) DW	
Insects		
Se-contaminated area	20-218 DW	
Control site	1.1-3.0 DW	
Mayfly, *Hexagenia* sp.	0.3-0.5 FW	Winger et al. 1984
Amphibians		
Liver	0.7-4.7 FW	Jenkins 1980
Reptiles		
Water snake, *Natrix* sp.		
Whole, Florida	0.3-0.5 FW	Winger et al. 1984
Fish		
Common carp, *Cyprinus carpio*		
Whole	1.0(0.7-1.4) DW	Wiener et al. 1984
Liver	3.6(2.2-5.2) DW	
Bluegill, *Lepomis macrochirus*		
From water containing <5 ppb Se		
White muscle	0.04 FW	Lemly 1982b
Liver	0.7 FW	
Spleen	1.6 FW	
Erythrocytes	0.04 FW	
Heart	1.0 FW	
From water containing 22.6 ppb Se		
White muscle	3.1 FW	
Liver	11.2 FW	
Spleen	17.7 FW	
Erythrocytes	7.2 FW	
Heart	12.8 FW	
Upper Mississippi River		
Whole	1.2(0.7-1.4) DW	Wiener et al. 1984
Largemouth bass, *Micropterus salmoides*		

From water containing <5 ppb Se		
White muscle	0.05 FW	Lemly 1982b
Liver	0.8 FW	
Spleen	1.8 FW	
Erythrocytes	0.07 FW	
Heart	1.2 FW	
From water containing 22.6 ppb Se		
White muscle	1.7 FW	
Liver	10.2 FW	
Spleen	16.6 FW	
Erythrocytes	8.0 FW	
Heart	12.0 FW	
Apalachicola River, Florida		
Whole		
Females	0.3-0.4 FW	Winger et al. 1984
Males	0.3-0.5 FW	
Juveniles	0.3-0.5 FW	
Eggs	0.7-1.0 FW	
Channel catfish, *Ictalurus punctatus*		
Apalachicola River, Florida		
Whole		
Females	1.1-0.3 FW	
Males	0.2-0.3 FW	
Juveniles	0.4-0.6 FW	
Eggs	0.8-2.1 FW	
Threadfin shad, *Dorosoma petenense*		
Whole	0.3-0.5 FW	
Green sunfish, *Lepomis cyanellus*		
From water containing 13 ppb Se		
Liver	7.0-21.4 FW	Sorensen et al. 1984
Muscle	2.3-12.9 FW	
From control site		
Liver	1.3 FW	
Muscle	1.3 FW	
Trout, 2 spp., Wyoming		
From water containing 12.3-13.3 ppb Se		
Liver	50.0-70.0 FW	Kaiser et al. 1979
Muscle	<2.0 FW	
Skin		Max. 4.8 FW
Mosquitofish, *Gambusia affinis*, whole		
From Se-contaminated irrigation		

drainwater pond	170(115-283) DW	Ohlendorf et al. 1986
Control site	1.3(1.2-1.4) DW	
Coho salmon, *Oncorhynchus kisutch*		
Muscle	0.7-1.0 DW	Rancitelli et al. 1968
Liver	3.8 DW	
Chinook salmon, *Oncorhynchus tshawytscha*		
Muscle	1.6 DW	
Fish		
Muscle		
25 spp.	0.0-0.5	Uthe and Bligh 1971; Willford 1971; Tonget al. 1971; Pakkala et al. 1972; Rossi et al. 1976; Luten et al. 1980
18 spp.	0.5-1.0 FW	Willford 1971; Tong etal.1972; Pakkala et al. 1972
3 spp.	1.0-2.0 FW	Schroeder et al. 1970; Pakkala et al. 1972
3 spp.		
Total Se	0.25 FW(0.15-0.34)	Cappon and Smith 1982
As selenate	0.09 FW	
As selenate and selenide	0.16 FW	
10 spp.		
Western Lake Erie	0.4-1.5 FW; 1.8-8.1 DW	Adams and Johnson 1977
Liver		
17 spp.	0.0-0.5 FW	Lucas et al. 1970
7 spp.	0.5-1.0 FW	
4 spp.	0.6-5.0 FW	Luten et al. 1980
Whole		
Nationwide, USA		
1972	0.60(0.57-0.64) FW	May and McKinney 1981
1973	0.46(0.42-0.49) FW	
1976-77	0.58(0.53-0.62) FW	
5 spp.	0.5-1.9 FW	Pratt et al. 1972
4 spp.	0.2-0.3 DW	Rossi et al. 1976
6 spp.	0.0-0.5 FW	Walsh et al. 1977
12 spp.	0.5-1.0 FW	
6 spp.	1.0-2.0 FW	

6 spp.	2.1-6.0 FW	
Birds		
Common loon, *Gavia immer*		
Egg	0.4(0.3-0.7) FW	Haseltine et al. 1983
Red-breasted merganser, *Mergus serrator*		
Egg	0.47-1.0 FW	Haseltine et al. 1981
Mallard, *Anas platyrhynchos*		
Egg	0.28-0.81 FW	
From Kesterson National Wildlife Refuge, California, nesting on Se-contaminated irrigation drainwater ponds - 1983		
American coot, *Fulica americana*		
Liver	37.2(21-63) DW	Ohlendorf et al. 1986
Egg	54.0(34-110) DW	
Ducks, *Anas* spp.		
Liver	28.6(19-43) DW	
Egg	9.9(2.2-46) DW	
Black-necked stilt, *Himantopus mexicanus*		
Egg	32.7(12-74) DW	
American avocet, *Recurvirostra americana*		
Egg	9.1 DW	
Eared grebe, *Podiceps nigricollis*		
Liver	130.0 DW	
Egg	81.4(72-110) DW	
From Volta Wildlife Area, California, Control Site -1983		
American coot		
Liver	5.0(4.4-5.6) DW	
Ducks, 2 spp.		
Liver	4.1(3.9-4.4) DW	
Black-necked stilt		
Liver	6.1 DW	
From Apalachicola River, Florida		
Little green heron, *Butorides virescens*		
Whole	0.1-0.5 FW	Winger et al. 1984
TERRESTRIAL		
Fungi	<2.0 DW	Jenkins 1980
Macrophytes		
Western wheat grass, *Agropyron smithii*		

South Dakota, plant top	11.5(0.0-8.4) DW
Little bluestem, *Andropogon scoparius*	
Plant top	0.0-6.0 DW
Asparagus, *Asparagus officinale*	
Western U.S.	2.7-11.0 DW
Aster, whole	
Aster caerulescens	560.0 DW
A. commutatus	Max. 590.0 DW
A. multiflora	Max. 320.0 DW
A. occidentalis	284.0 DW
Milk vetch,	
Astragalus argillosus	
Top	385.0 DW
Root	27.0 DW
A. beathii	
Top	1,963.0 DW
Root	66.0 DW
A. bisulcatus	
Top	Max. 10,239.0 DW
Seed	305.1 DW
A. confertiflorus	
Top	1,372.0 DW
A. crotulariae	
Top	2,000.0 DW
Root	45.0 DW
Locoweed,	
Astragalus spp.	Max. 46,000.0 AW; Max. 6,000.0 DW
Saltbush,	
Atriplex spp.	300.0-1,734.0 DW
Oats, *Avena sativa*	2.0-15. DW
Buffalo grass,	
Bouteloua dactyloides	2.7(0.0-12.0) DW
Indian paint brush,	
Castilleja spp.	0.0-1,812.0 DW
Gumweed, *Grindelia*	
squarrosa	38.0(0.0-2,160.0) DW
Broomweeds,	
Gutierrezia spp.	up to 723.0 DW
Haplopappus spp.	up to 4,800.0 DW
Tobacco, *Nicotiana tabacum*	
Leaf	5.8 DW
Stem	44.2 DW
Rice, *Oryza sativa*	

Grain	0.09-0.11 FW	
Pear, *Pyrus communis*		
Fruit	0.02 FW	
Rye, *Secale cereale*	0.9-25.0 DW	
Potato, *Solanum tuberosum*		
Tuber	0.2-0.9 DW	
Wheat, *Triticum aestivum*		
Grain	1.1-35.0 DW	
Stem and leaf	17.0 DW	
Root	36.0 DW	
Corn, *Zea mays*		
Grain	1.0-20.0 DW	
Grape, *Vitis* sp.		
Raisin	<0.001 FW	
Annelids		
Earthworms, whole		
From normal soil	2.2 FW	Birkner 1978
From selenite-enriched soil	7.5 FW	
From soil amended with sewage sludge		
Whole	15.0-22.4 DW	Helmke et al. 1979
Casts	0.6-0.7 DW	
From control field		
Whole	22.1 DW	
Casts	0.6 DW	
Arthropods		
Sow bug, *Porcellio* sp.	0.9 FW	Jenkins 1980
Crane fly, larva, *Tipula* sp.	0.9 FW	
“Fly larvae,” whole, from *Astragalus* plant with 1800 ppm Se	20.0 FW	
Birds		
Blackbird, *Turdus merula*		
Whole	2.1 DW	Nielsen and Gissel-Nielsen1975
House sparrow, *Passer domesticus*		
Whole	0.6 DW	
Pheasant, *Phasianus colchicus*		
Whole	0.6 DW	
Mammals		
Beaver, *Castor canadensis*		
Liver	0.2 FW	Wren 1984
Kidney	0.9 FW	

Intestine	0.04 FW	
Muscle	0.09 FW	
Otter, *Lutra canadensis*		
Liver	2.1 FW	
Kidney	1.9 FW	
Intestine	1.1 FW	
Muscle	0.2 FW	
Woodchuck, *Marmota monax*		
From fly ash landfill vicinity		
Adults		
Liver	2.2-10.7 DW	Fleming et al. 1979
Lung	1.4-4.4 DW	
Juveniles		
Liver	3.9-6.4 DW	
Lung	2.1-2.8 DW	
From control area		
Adults		
Liver	0.4 DW	
Lung	0.4 DW	
Juveniles		
Liver	0.2-0.4 DW	
Lung	0.2 DW	
Field mole, *Microtus agrestis*		
Whole	0.5 DW	Nielsen and Gissel-Nielsen1975
White-tailed deer, *Odocoileus virginianus*		
Muscle	0.16(0.05-0.49) DW	Ullrey et al. 1981
Raccoon, *Procyon lotor*		
Liver	1.8 FW	Wren 1984
Kidney	1.9 FW	
Muscle	0.2 FW	
Rat, *Rattus norvegicus*		
Whole	0.4 DW	Nielsen and Gissel-Nielsen1975
Rock squirrel, *Spermophilus variegatus*		
Kidney	8.9-53.0 (Max. 90.0) DW	Sharma and Shupe 1977
Mole, *Talpa europaea*		
Whole	2.6 DW	Nielsen and Gissel-Nielsen1975

[a] Each reference applies to the values in the same row, and in the rows that follow for which no other reference is indicated.

DEFICIENCY AND PROTECTIVE EFFECTS

Selenium is a critical nutrient and a key component of several enzymes. There is a general consensus that Se deficiency in livestock is increasing in many countries, resulting in a need for added Se in the food. Selenium deficiency is considered by some researchers to constitute a greater threat to health than selenium poisoning. Studies with animals and humans have suggested that Se deficiency, in part, underlies susceptibility to cancer, arthritis, hypertension, heart disease, and possibly periodontal disease and cataracts (Frost and Ingvoldstad 1975; Shamberger 1981; Robberecht and Von Grieken 1982). These linkages have not yet been demonstrated conclusively; for example, eye lens cataract was induced in 10-day-old male rats by selenate, selenite, selenomethionine, and selenocystine, presumably through interference with glutathione metabolism (Ostadalova and Babicky 1980). On the other hand, adverse effects of Se inadequacy have been clearly documented for a wide variety of organisms, including bacteria, protozoans, Atlantic salmon, rainbow trout, Japanese quail, ducks, poultry, rats, dogs, horses, sheep, swine, cattle, antelopes, gazelles, deer, monkeys, and humans (Jensen 1968; Frost and Ingvoldstad 1975; *Methanococcus vanniellii*: culture and effects of selenium and tungsten on growth. J. Bacteriol. 130:1404-1406.

Jones and Stadtman 1975; Fishbein 1977; Harr 1978; Kaiser et al. 1979; Hilton et al. 1980; Shamberger 1981; Bovee and O'Brien 1982; Robberecht and Von Grieken 1982; NRC 1983; Levander 1983, 1984; Morris et al. 1984). Selenium deficiency, whether induced experimentally by use of low Se feeds supplemented with alpha tocopherol or by chronic ingestion of low Se diets, has caused a number of maladies: high embryonic mortality in cattle and sheep; anemia in cattle; poor growth and reproduction in sheep and rats; reduced viability of newly hatched quail; nutritional myopathy (white muscle disease) in sheep, swine, and cattle; hepatic necrosis and lameness in dogs, horses, and breeding bulls; hair loss and sterility in rat offspring; and spermatozoan abnormalities in rats. Deficiencies were usually prevented or reversed by supplements with sodium selenate or selenite at 100 ppb Se in the diet, or 20 µg Se/kg body weight administered parenterally.

The availability of Se to plants may be lessened by modern agricultural practices, eventually contributing to Se deficiency in animal consumers. For example, fertilizers containing nitrogen, sulfur, and phosphorus all influence Se uptake by plants through different modes of action, the net effect being a reduction in Se uptake (Frost and Ingvoldstad 1975). The buildup of sulfur (as sulfates) in the soil, due to acid rain, fertilizers, and other sources, interferes with Se accumulation by crops (Frost and Ingvoldstad 1975). In addition, high dietary levels of various heavy metals (including copper, zinc, silver, and mercury) contribute to Se deficiency in animals (Frost and Ingvoldstad 1975; Harr 1978), presumably as a result of Se binding with the metal into biologically unavailable forms (Harr 1978; Kaiser et al. 1979).

The protective action of selenium against the adverse or lethal effects induced by various metals and metalloids is well documented for a wide variety of plant and animal species. Among marine organisms, for example, selenium protects against toxic levels of mercury in algae (Gotsis 1982), shrimp (Lucu and Skreblin 1982), crabs and oysters (Glickstein 1978), fish (Sheline and Schmidt-Nielsen 1977), and mammals (Koeman et al. 1975). Similar observations have been recorded for copper and marine algae (Gotsis 1982); cadmium and freshwater snails (Wilber 1983), marine crabs (Bjerragaard 1982), earthworms (Helmke et al. 1979; Beyer et al. 1982), and rats (Harr 1978); mercury or methylmercury and rats (Cappon and Smith 1982), eggs of lake trout (Klaverkamp et al. 1983b), freshwater teleosts (Kim et al. 1975, 1977) and (temporarily) Japanese quail (El-Bergearmi et al. 1977, 1982; Beijer and Jernelov 1978); and arsenic and freshwater and marine teleosts (Luten et al. 1980; Orvini et al. 1980). Not all tests were conclusive. Studies with some species of freshwater teleosts demonstrated negligible antagonism of Se against mercury (Klaverkamp et al. 1983a) or cadmium (Duncan and Klaverkamp 1983). Selenium reportedly protects mammals and poikilotherms against poisoning by thallium, the herbicide paraquat, cadmium, mercury, lead, arsenic, and copper (Wilber 1983).

Reasons, to account for the antagonism of Se and heavy metals (here mercury is used as an example) include dietary source and chemical form of Se, influence of sulfur, biological translocation of Se or mercury to less critical body parts, and chemical linkage of Se to mercury on a linear basis. The exact mode of interaction is probably complex and has not yet been resolved. In regard to diet, Se of animal origin and in the form of selenate is less effective than Se from plant and inorganic sources in preventing methylmercury neurotoxicity in experimental animals (Cappon and Smith 1982). Disruption of sulfur metabolism by Se, the sulfur being replaced by seleno-amino acids and other cell constituents containing Se in living organisms, is one probable cause of Se poisoning. It is conceivable that Se-Hg compounds formed within the organism would be sufficiently

nonreactive biologically to interfere with sulfur kinetics, presumably -SH groups (Koeman et al. 1975; Beijer and Jernelov 1978; Cappon and Smith 1982; Gotsis 1982). Differential redistribution of Se or Hg to less critical body parts may partly account for observed antagonisms. Pretreatment of marine minnows with Se protects against Hg poisoning and causes a marked redistribution of Hg among organs, presumably to non-critical body parts, and this transfer may partly account for the observed Se-Hg antagonisms in that species (Sheline and Schmidt-Nielsen 1977). Some investigators have reported that Se results in increased Hg accumulations. Increased retention of Hg and other metals may lead to a higher level of biomagnification in the food chain and higher body burden in the individual, which might counteract the positive effect of decreased intoxication (Beijer and Jernelov 1978). Extensive research is under way on the chemical linkage of Se and Hg. In marine mammals and humans, Se and Hg concentrations are closely related, almost linearly in a 1:1 molar ratio, but this relation blurs in teleosts in which Se is in abundance, and fails in birds (Koeman et al. 1975; Beijer and Jernelov 1978; Orvini et al. 1980; Cappon and Smith 1982).

TOXICITY

MAMMALS AND BIRDS

“The element selenium can be traced in an orderly sequence from its origin in the earth's crust to specific geological formation, to distribution of specific genera and groups of plants which require the element for their growth, to the accumulation in vegetation, and to its subsequent toxicity to birds or mammals that consume the seleniferous foods” (Rosenfeld and Beath 1964). Selenium poisoning in livestock, discussed here, was largely extracted from reviews by Rosenfeld and Beath (1964), Frost (1972), Fishbein (1977), Harr (1978), Shamberger (1981), NRC (1983), and Wilber (1983).

In livestock, there are three basic types of selenium poisoning: acute, resulting from consumption (usually in a single feeding) of a sufficient quantity of highly seleniferous weeds; “blind staggers,” from consumption of moderately toxic amounts of seleniferous weeds over an extended period of time; and "alkali disease," caused by the consumption of moderately seleniferous grains and forage grasses over a period of several weeks to months.

Acute poisoning is associated with plant materials containing 400 to 800 ppm Se: sheep died when fed amounts of plant material ranging from 8 to 16 g/kg body weight, or about 3.2 to 12.8 mg Se/kg body weight. The minimum lethal dose of Se administered orally as selenite (mg Se per kg body weight) ranged from 3.3 for horses and mules to 11 for cattle and 15 for swine. Other modes of administration were more toxic, e.g., 2 and 1.2 mg Se/ kg body weight given subcutaneously killed swine in 4 hours and 5 days, respectively; and 1.5-6.0 mg Se/kg body weight given intravenously or intraperitoneally to rats and rabbits were fatal. Accidental toxicosis of sheep and cattle from overtreatment with commercial mixtures of Se salts and vitamin E are also documented for Australia and New Zealand. Acute Se poisoning in domestic livestock is characterized by abnormal movements, lowered head, drooped ears, diarrhea, elevated temperature, rapid pulse, labored breathing, bloating with abdominal pain, increased urination, and dilated pupils. Before death, which is due to respiratory failure, there is complete prostration and lethargy. Duration of illness extends from a few hours to several days, depending on the toxicity of plant material ingested. In these cases, Se is distributed by the circulatory system to all body organs, the concentrations being highest in liver, blood, kidney, spleen and brain, and lowest in muscle, skin, hair and bone. Elimination is primarily in the urine; smaller quantities are excreted with the feces, breath, perspiration, and bile. Postmortem examinations indicate many pathological changes in the heart, lungs, rumen, liver, kidney, and other organs. No effective treatment is known for counteracting toxic effects of large amounts of ingested selenium.

Chronic selenosis may be induced by dietary exposure to natural selenite, selenate, or seleniferous feedstuffs at dietary concentrations between 1 ppm (rat) and 44 ppm (horse), or from water containing 0.5 to 2.0 ppm of Se. Cattle fed 0.5 mg Se/kg body weight 3 times weekly lost their appetite; sheep fed up to 75 mg selenite daily developed myocardial degeneration and fibrosis, pulmonary congestion, and edema. The minimum toxic concentration of Se in lifetime exposure of rats (a comparatively sensitive species) fed Se-deficient diets fortified with Se was 0.35 mg Se/kg diet, as judged by changes in liver chemistry; and 0.75 mg Se/kg diet, as judged by longevity, and histological changes in heart, kidney, and spleen. These concentrations are 10 times the nutritional threshold for Se, and about 25% of the minimum lifetime exposure to Se in natural feedstuffs that produces similar effects under the same experimental conditions. Signs of chronic selenosis include skin lesions, lymph channel inflammation, loss of hair and nails, anemia, enlarged organs (spleen, pancreas, liver), fatigue, lassitude, and dizziness. “Blind staggers” is characterized by anorexia, emaciation, and sudden collapse, followed by death. Typically, the upper intestinal tract is ulcerated. In “alkali disease,” in cattle,

hogs, and horses that had eaten seleniferous grains, the signs were deformation and sloughing of the hooves, hair loss, lassitude, erosion of the articular cartilages, reduced conception, increased reabsorption of fetuses, and degeneration of heart, kidney, and liver. It is likely that Se displaces sulfur in keratin, resulting in structural changes in hair, nails, and hooves (Fishbein 1977).

Among birds, it appears that domestic chickens are extremely sensitive to Se; reduced hatching of eggs was recorded at 7 to 9 ppm Se in feed (Ort and Latshaw 1978). Similar results were observed by El-Bergearmi et al. (1977) in Japanese quail at 6 and 12 ppm dietary selenite. Studies in progress at the Patuxent Wildlife Research Center with adult mallards indicated that 100 ppm dietary selenium (as sodium selenite) was fatal within one month, but that survival was high at 25 ppm after 3 months. Poor egg hatchability was recorded in the 25 ppm selenite group, but not in the 10 ppm selenite group; however, hatching percent was reduced in eggs of adults fed 10 ppm of Se as selenomethionine (Dr. G. Heinz, pers. comm.). It appears obvious that additional research is needed on the toxicology of organoselenium compounds.

Selenosis in warm blooded organisms is modified by numerous factors, including method of administration, chemical form of Se, dietary composition, and age and needs of the organism. For example, Se administered in natural feedstuffs is only about one-fourth as toxic as are similar exposures in water or purified feeds (Harr 1978). Concurrent ingestion of minerals and rough or high protein feeds reduces Se toxicity, and exposure by diet is less toxic than exposure parenterally or by inhalation.

Many compounds are known to prevent or reduce toxic effects of subacute and chronic selenosis in pigs, beef cattle, and other warmblooded organisms. A partial list includes arsenic, strychnine sulfate, tungsten, germanium, antimony, beet pectin, high-fat diets, ACTH injections, sulfate, increased dietary proteins, lactalbumin, ovalbumin, wheat protein, dried brewer's yeast, desiccated liver, linseed oil meal, glucosamine, hemocysteine, creatine, methionine, and choline. Not all of these compounds afforded equal protection against various Se formulations; the reasons for the difference are not clear, but it appears that the subject of selenoprotective agents warrants additional research effort.

AQUATIC ORGANISMS

Among sensitive species of aquatic organisms, death was observed at water concentrations between 60 and 600 ppb Se; early life history stages that were subjected to comparatively lengthy exposures accounted for most of these data (Table 3). Latent mortality after exposure to comparatively high Se concentrations has been documented, but not extensively. For example, all embryos of the zebrafish (*Brachydanio rerio*) survived exposure to 3,000 ppb of Se during development, but more than 90% of the resultant larvae died soon after hatching; at 1,000 ppb, survival was similar to that in controls (Niimi and LaHam 1975). It has been suggested (EPA 1980) that selenite is more toxic than selenate and is preferentially concentrated over selenate by mussels, *Mytilus galloprovincialis* (Measures and Burton 1980). Selenite is generally more toxic to early life history stages and effects are most pronounced at elevated temperatures (Klaverkamp et al. 1983a). Also, Se salts may be converted to methylated forms by microorganisms, and these are readily accumulated by aquatic vertebrates (Klaverkamp et al. 1983a). Among freshwater algae species, it has been demonstrated that selenite, selenate, selenomethionine, and selenopurine are all toxic, but that sulphur, as sulphate, has a significant protective role against Se toxicity (Kumar and Prakash 1971). Numerous additional chemical compounds and mixtures probably protect against Se toxicity, much as Se protects against toxic effects of mercury salts and other chemicals, but data are sparse on Se protective agents.

Almost 50 years ago, Ellis et al. (1937) recorded a long list of signs of selenium poisoning in teleosts: loss of equilibrium, lethargy, contraction of dermal chromatophores, loss of coordination, muscle spasms, protruding eyes, swollen abdomen, liver degeneration, reduction in blood hemoglobin and erythrocyte number, and increase in white blood cells. Sorensen et al. (1984), observed most of these signs in Se-poisoned green sunfish together with elevated liver Se concentrations, reduced blood hematocrit, enlarged liver, histopathology of kidney and heart, swollen gill lamellae with extensive cellular vacuolization, and necrotic and degenerating ovarian follicles.

Table 3. Toxicity of selenium salts to aquatic biota. Values shown are in µg/l (ppb) in medium fatal to 50% of the organisms during exposure for various intervals.

Medium, taxonomic group, and species	Exposure interval in hours (h), days (d), or life cycle (LC)	LC-50 (ppb)	Reference[a]
FRESHWATER			
Algae			
Anabaena variabilis	96 h	15,000-17,000	Kumar and Prakash 1971
Anacystis nidulans	96 h	30,000-40,000	
Oedogonium cardiacum	48 h	<100	Nassos et al. 1980
Molluscs			
Snail, *Physa* sp.	96 h	24,000	Reading 1979
Snail, *Physa* sp.	48 h	>10,000	Nassos et al. 1980
Insects			
Mosquito larvae, *Culex fatigans*	48 h	<3,100	
Midge, *Tanytarsus dissimilis*	96 h	42,400	EPA 1980
Crustaceans			
Cladoceran, *Daphnia magna*	48 h	<250	Nassos et al. 1980
"	96 h	710	Halter et al. 1980
"	14 d	430	
"	28 d	240	EPA 1980
"	LC	70-120	
Scud,	96 h	760	Adams 1976
Hyallela azteca	96 h	340	Murphy 1981
"	14 d	70	Halter et al. 1980
Cladoceran, *Daphnia pulex*	96 h	3,870	Reading 1979
	LC	600-800	EPA 1980
Amphibians			
Frog, *Xenopus laevis*			
Embryo	27 h	20,000	Browne and Dumont 1979
"	61 h	10,000	
"	96 h	4,000	
"	113 h	2,000	
Tadpole	3 d	8,000	
"	5 d	2,600	
"	7 d	1,500	
Fish			
Goldfish, *Carassius auratus*	96 h	26,100	Cardwell et al. 1976
"	14 d	6,300	
White sucker, *Catostomus*	48 h	48,600	Duncan and Klaverkamp
commersoni	96 h	31,400	1983

Common carp,	24 h	72,000	Sato et al. 1980
Cyprinus carpio	96 h	35,000	Spehar et al. 1982
Northern pike, *Esox lucius*	75 h	11,100	Klaverkamp et al. 1983a
Mosquitofish,	48 h	>>6,000	Nassos et al. 1980
Gambusia affinis	96 h	12,600	Reading 1979
Channel catfish, *Ictalurus punctatus*	96 h	13,600	Cardwell et al. 1976
Flagfish, *Jordanella floridae*	96 h	6,500	
Bluegill, *Lepomis macrochirus*	96 h	28,500	
"	14 d	12,500	
"	48 d	400-2,000	Adams 1976
Coho salmon, *Oncorhynchus kisutch*			
Fry	43 d	160	
Yellow perch,			
Perca flavescens	10 d	4,800	Klaverkamp et al. 1983a
Fathead minnow, *Pimephales promelas*			
Fry	96 h	2,100	Cardwell et al. 1976
Juvenile	96 h	5,200	
Adult	96 h	2,200-12,500	Adams 1976
"	96 h	620-970	EPA 1980
"	96 h	1,000	Halter et al. 1980
"	9 d	2,100	Cardwell et al. 1976
"	48 d	1,100	Adams 1976
	LC	83-153	EPA 1980
Rainbow trout, *Salmo gairdneri*	96 h	8,100	Spehar et al. 1982
"	96 h	4,200-4,500	Adams 1976
"	96 h	12,500	EPA 1980
"	96 h	7,200-8,800	Hodson et al. 1980
"	9 d	5,400-7,000	
"	21 d	460	Adams 1976
"	96 d	290	
"	LC	60-130	EPA 1980
Brook trout, *Salvelinus fontinalis*	96 h	10,200	Cardwell et al. 1976
MARINE			
Molluscs			
Pacific oyster, *Crassostrea gigas*			
Larvae	48 h	>10,000	Glickstein 1978
Crustaceans			
Copepod, *Acartia clausi*	96 h	1,740	EPA 1980
Copepod, *A. tonsa*	96 h	800	
Blue crab, *Callinectes sapidus*	96 h	4,600 (2,700-7,800)	Ward et al. 1981
Dungeness crab, *Cancer magister*			
Larvae	96 h	1,040	Glickstein 1978
Mysid shrimp, *Mysidopsis bahia*			

Adult	96 h	1,500 (1,100-2,100)	Ward et al. 1981
Juvenile	96 h	600	EPA 1980
Egg	LC	127-143	
Brown shrimp, *Penaeus aztecus*	96 h	1,200 (800-1,800)	Ward et al. 1981
Fish			
Fourspine stickleback, *Apeltes quadracus*	96 h	17,350	EPA 1980
Sheepshead minnow, *Cyprinodon variegatus*			
Adult	96 h	7,400-67,100	
Egg through juvenile	LC	470-970	Ward et al. 1981
Pinfish, *Lagodon rhomboides*	96 h	4,400 (2,900-6,700)	
Haddock, *Melanogrammus aeglifinus*			
Larvae	96 h	600	EPA 1980
Atlantic silverside, *Menidia menidia*	96 h	9,725	
Summer flounder, *Paralichthys dentatus*			
Larvae	96 h	3,500	
Winter flounder, *Pseudopleuronectes americanus*			
Larvae	96 h	14,250-15,100	

[a]Each reference applies to the values in the same row, and in the rows that follow for which no other reference is indicated.

SUBLETHAL AND LATENT EFFECTS

Results of laboratory studies and field investigations with fish, mammals, and birds have led to general agreement that elevated concentrations of selenium in diet or water were associated with reproductive abnormalities including congenital malformations, selective bioaccumulation by the organism, and growth retardation. Not as extensively documented, but nevertheless important, are reports of selenium-induced chromosomal aberrations, intestinal lesions, shifts in species composition of freshwater algal communities, swimming impairment of protozoans, and behavioral modifications.

AQUATIC ORGANISMS

In green sunfish from a lake in North Carolina receiving selenium (as fly ash wastes from a coal-fired power station), reproduction failed and the population declined markedly. In these fish, Se levels were elevated in liver (up to 21.4 ppm fresh weight) and other tissues; kidney, heart, liver, and gill showed histopathology; and blood chemistry was altered. Ovaries of fish had numerous necrotic and ruptured egg follicles that may have contributed to the population extinction (Sorensen et al. 1984). It is probable that Se uptake by plankton (containing 41-97 ppm dry weight) from lake water (9-12 ppb) introduced Se to the food chain where it ultimately reached elevated levels in fish through biomagnification (Cumbie and Van Horn 1978). In laboratory tests, however, eggs of common carp hatched normally when incubated in media containing 5,000 ppb of Se (Huckabee and Griffith 1974), as did eggs of lake trout (*Salvelinus namaycush)* at 10,000 ppb of Se (Klaverkamp et al. 1983b). In frogs (*Xenopus laevis*), cranial and vertebral deformities and lowered survival were documented during development in water with Se concentrations of 2,000 ppb or higher (Browne and Dumont 1979).

At water concentrations of 47 to 53 ppb, Se was associated with anemia and reduced hatch of rainbow trout (Hodson et al. 1980), growth retardation of freshwater green algae (Hutchinson and Stokes 1975; Klaverkamp et al. 1983a), and shifts in species composition of freshwater algal communities (Patrick 1978). At 250 ppb Se, growth was reduced in rainbow trout fry after exposure for 21 d (Adams 1976), and goldfish demonstrated an avoidance response after 48 h (Weir and Hine 1970). At Se water concentrations of 7,930-11,000 ppb, growth

was inhibited in freshwater and marine algae (Patrick 1978; EPA 1980), and swimming rate was reduced in the protozoan *Tetrahymena pyriformis* (Bovee and O'Brien 1982). Eggs of channel catfish exposed to certain metals (including cadmium, mercury, and copper) produced an increased percentage of albino fry; however, eggs exposed to 250 ppb Se produced fry with normal pigmentation (Westernman and Birge 1978).

A significant number of chromosomal aberrations was induced in the edible goby, *Boleophthalmus dussumieri*, by Se after intramuscular and water exposures (Krishnaja and Rege 1982). Intramuscular injections of Se as low as 0.1 mg/kg body weight, or 3,200 ppb in the water column, were associated with a marked enhancement of polyploid cells 76-96 h postadministration; some deaths were recorded at higher test concentrations. Selenite was more effective than selenate in inducing chromosomal aberrations. The authors concluded that a relatively narrow range of Se concentrations lead to a mutagenic rather than a lethal effect.

Accumulation of Se by aquatic organisms is highly variable. In short-term (48 h) laboratory tests at Se water concentrations of 0.015 to 3.3 ppb, Nassos et al. (1980) reported biological concentration factors (BCF) of 460 for mosquitofish to 32,000 for a freshwater gastropod; values were intermediate for daphnids (2,100), plankton (2,600), and *Fundulus kansae* (3,300), the freshwater killifish. High BCF's (>680) were recorded for freshwater diatoms subjected to maximum concentrations of 40 ppb Se (Patrick 1978). Livers from rainbow trout and brown trout may contain from 50 to 70 ppm Se fresh weight during lifetime exposure in seleniferous (12.3-13.3 ppb) water, and have BCF values of 3,759 to 5,691 (Kaiser et al. 1979); BCF values were 361 to 390 for skin, and about 180 for muscle (Kaiser et al. 1979). In short-term exposures, most of the Se was probably adsorbed to the body surface (Fowler and Benayoun 1976c), and was then rapidly lost on transfer to Se-free media (Browne and Dumont 1979). In longer exposures, the BCF values in aquatic organisms were lower after immersion in high ambient Se concentrations over extended periods. Thus, marine crabs exposed to a water concentration of 250 ppb of Se for 29 days accumulated Se over water concentration level by a factor of 25 for carapace, and 3.8 for gill; accumulations in muscle and hepatopancreas were negligible. Cadmium in solution enhanced Se uptake (Bjerragaard 1982). Exposure of common carp to 1,000 ppb Se for 85 days resulted in a whole body BCF of 6; additional studies of 7 weeks exposure plus 7 weeks postexposure at Se concentrations between 500 and 5,000 ppb (Sato et al. 1980) yielded a BCF range of 0.6 (5,000 ppb) to 1.8 (500 ppb). Highest BCF's in carp were 50 for kidney and 80 for liver after exposure of the fish to 100 ppb Se for 7 weeks plus 7 weeks in Se-free media. For carp, Se tended to accumulate in kidney, liver, gill, gall bladder, heart, bone, and muscle, in that general order (Sato et al. 1980). Studies with freshwater organisms collected from a farm pond contaminated by fly ash with high Se levels (Furr et al. 1979), and with marine bivalves and nereid worms held for 4 months in seawater flowing through coal fly ash containing 6,200 ppb Se (Ryther et al. 1979), showed that accumulation was slight. Contrasted to this are the observations of Cherry et al. (1976) and Ohlendorf et al. (1986). Cherry and his coworkers collected mosquitofish from a drainage system that received high coal fly ash concentrations at one end and thermal discharges at the other; mosquitofish contained up to 9.0 ppm Se whole body fresh weight. Of 40 elements examined, only Se, zinc, and calcium were accumulated in excess of the levels measured in the water. Ohlendorf et al. found mean residues of 172 ppm dry weight (range 110-280 ppm) in whole mosquitofish from irrigation drainwater ponds contaminated by about 300 ppb of Se; based on a wet/dry factor of 4, the BCF for whole mosquitofish was >91.

Selenium accumulation is modified by water temperature, age of the organism, organ or tissue specificity, mode of administration, and other factors. In the marine mussel, *Mytilus galloprovincialis*, an increase in water temperature from 13 to 29°C doubled the BCF in 13 days (Fowler and Benayoun 1976b). Mussels preferentially accumulated selenite over selenate (Fowler and Benayoun 1976b); however, mussels did not reach a steady state in 63 days (Fowler and Benayoun 1976c), indicating that Se kinetics in some species are difficult to elucidate in short-term studies. Accumulation rates were higher in small than in large mussels (Fowler and Benayoun 1976b), as they were in freshwater teleosts (Furr et al. 1979). However, the reverse was documented for marine mammals and teleosts (Eisler 1984). When Se was available from both the diet and the medium, concentrations were highest in liver, kidney, and gills of teleosts (Sorensen et al. 1982; Furr et al. 1979; Kaiser et al. 1979), exoskeleton of crustaceans (Fowler and Benayoun 1976c; Bjerragaard 1982), and visceral mass and gills of molluscs (Fowler and Benayoun 1976c). When Se was administered in food to marine shrimps, concentrations were highest in viscera and exoskeleton, suggesting that ingested Se is readily translocated from internal to external tissues (Fowler and Benayoun 1976c). Concentrations of Se in crustaceans usually were higher in fecal pellets than in the diet; fecal pellets may represent a possible biological mechanism for downward vertical transport of Se in the sea (Fowler and Benayoun 1976a), as well as in freshwater environments.

The time for 50% excretion of accumulated Se has ranged from 13 to 181 days in various species of marine and freshwater fauna. Biological half-life of Se accumulated from the medium has been estimated at 28 days for carp (Sato et al. 1980), 37 days for the marine euphausid crustacean *Meganyctiphanes norvegica* (Fowler and Benayoun 1976a), 63 to 81 days for the marine mussel *Mytilus galloprovincialis* (Fowler and Benayoun 1976b), 58 to 60 days for the marine shrimp *Lysmata caudata* (Fowler and Benayoun 1976b), and, as reviewed by Stadtman (1974, 1977), 13 days for guppies, 27 days for eels, and 28 days for leeches. Studies by Lemly (1982a) with bluegills and largemouth bass showed elevated tissue levels after exposure to 10 ppb of Se for 120 days. Time for 50% excretion in 30-day elimination trials was about 15 days from gill and erythrocytes; however, there was essentially no elimination from spleen, liver, kidney, or muscle. It appears that research is needed on preferential tissue retention of Se and its implications for biochemical and metabolic transport mechanisms.

TERRESTRIAL INVERTEBRATES

Concentrations of Se decreased in whole earthworms from 22.4 to 15.0 ppm (dry weight) as the rate of sludge application increased from 15 to 60 metric tons/ha. Concentrations of Se in soil and sludge were 0.3 and 0.5 ppm dry weight, respectively (Helmke et al. 1979). Other studies indicated that some metals, notably cadmium, decreased in worms living in soils amended with sewage sludge but that Se concentrations were not affected (Beyer et al. 1982). The biological half life of Se in earthworms is estimated to be 64 days, a period consistent with values of 10 to 81 days documented for ants, birds, mammals, and aquatic biota (Stadtman 1974, 1977).

BIRDS

Embryos of the domestic chicken (*Gallus domesticus)* are extremely sensitive to Se. The hatchability of eggs is reduced by concentrations of Se in feeds(6 to 9 ppm) that were too low to produce poisoning in other avian species. Dietary Se excess was associated with decreased egg weight, decreased egg production and hatchability, anemia, elevated kidney Se residues in chicks, and a high incidence of grossly deformed embryos with missing or distorted eyes, beaks, wings and feet (Ort and Latshaw 1978; Harr 1979). Selenomethionine was more effective than sodium selenite in raising the Se content of tissues and eggs (Moksnes 1983). Until recently, there was little credible evidence that selenium adversely affected wild birds. However, Ohlendorf et al. (1986) reported severe reproductive effects in ducks (*Anas* spp.), American coot (*Fulica americana*), and other species of aquatic birds nesting at irrigation drainwater ponds in the San Joaquin Valley, California. Water in these ponds contained abnormally high concentrations of about 300 ppb of Se, but low or non-detectable levels of silver, chromium, arsenic, cadmium, mercury, lead, and zinc. Of 347 nests examined from this site, about 40% had at least one dead embryo and about 20% had at least one embryo or chick with obvious external anomalies, including missing or abnormal beaks, eyes, wings, legs, or feet. In addition, brain, heart, liver, and skeletal anomalies were recorded. Concentrations of selenium (ppm, dry weight) were 2-110 in eggs and 19-130 in livers of birds, 12-79 in plants, 23-200 in invertebrates, and 110-280 in fish from the ponds, or 7 to 130 times those found at a nearby control area. It was concluded that Se was the probable cause of poor reproduction and developmental abnormalities in the aquatic nesting birds, due to interference with their reproductive processes. The concentrations of Se in breast muscle of coots were sufficiently high (up to 11.0 ppm fresh weight) to induce State agencies to post the area, advising against the consumption of more than one meal per week of this species, or of any coots by children or pregnant women (Ohlendorf et al. 1986).

In studies at the Patuxent Wildlife Research Center, Dr. G. Heinz (pers. comm.) is evaluating effects of dietary Se on mallard reproduction. Ducks given diets containing 100 ppm of inorganic selenite usually died within a month; for some time before death they exhibited reduced food intakes (bordering on repellence) and significant weight loss. In birds receiving 25 ppm, survival was high after 3 months, but growth and reproduction were dramatically reduced. Teratogenic effects were evident at 3 months in ducklings of mallards receiving 10 ppm, and preliminary evidence suggested that selenomethionine at 10 ppm dietary Se was more effective than inorganic selenite in producing developmental abnormalities. Ducks and their progeny appeared normal after 3 months of exposure to 5 ppm and less of dietary selenite.

MAMMALS

Harr (1978) and NRC (1983) summarized nonlethal effects of selenium on mammals, including reproductive anomalies. Selenosis caused congenital malformations in rats, mice, swine, and cattle. In general, young born to females with selenosis were emaciated and unable to nurse. Mice given Se in drinking water reproduced normally for three generations, but litters were fewer and smaller when compared to controls, pups were runts with high mortality before weaning, and most survivors were infertile.

In rats, selenium did not induce cirrhosis or neoplasia; however, intestinal lesions were observed among those fed diets containing 0.8 to 1.0 ppm Se during lifetime exposure. The threshold requirement for optimal rat nutrition under similar conditions is about 0.08 ppm, again demonstrating the relatively narrow range separating selenium deficiency from selenium poisoning. Absorption of oral radioselenite by rats was as high as 95 to 100%. A single dose of radioselenite concentrated in the pancreas, intestine, erythrocytes, liver, kidney and testes, in that general order; tissue distributions from chronic exposure were similar. As expected, levels of Se in poisoned rats were highest in liver and kidney. Rats, and probably other mammals, can regulate dietary Se accumulations. Dietary concentrations in excess of 54-84 ppb were usually excreted in urine; however, when Se intake exceeded 1,000 ppb, pulmonary excretion was active. Excretion of Se in feces, bile, saliva, and hair appears to be relatively constant regardless of the amount of exposure. Yonemoto et al. (1983) demonstrated that some selenotoxic effects in mice, including abortion and maternal death, were prevented by prior treatment with vitamin E, but exacerbated by reduced glutathione; the mechanisms for these interactions are unknown, and merit additional research.

Table 4. Proposed selenium criteria for prevention of Se deficiency and for protection against selenosis.

Criterion	Selenium concentration	Reference
PREVENTION OF		
SE DEFICIENCY		
Rainbow troup, *Salmo gairdneri*		
(water levels of 0.4 ppb Se)	70 ppb in diet	Hilton et al. 1980
Poultry	30-50 ppb in diet	Fishbein 1977
Rats	54-84 ppb in diet	Harr 1978
Cattle	20 ppb in diet	Fishbein 1977
Grazing sheep and cattle	100 ppb in diet	Shamberger 1981
Humans	40-100 ppb in diet	Wilber 1983
"	50-200 ppb in diet	Harr 1978
"	60 µg daily (range 22-220)	Robberecht and Von Greichen 1982
"	100-200 µg daily	Shamberger 1981
"	20 ppb in drinking water (if water sole Se source, 2 liters/day)	Robberecht and Von Greichen 1982
PROTECTION AGAINST		
SELENOSIS		
Aquatic life protection		
Freshwater		
As inorganic selenite	Up to 35 ppb in water (24 hr average), not to exceed 260 ppb at any time	EPA 1980
As inorganic selenate	<760 ppb	EPA 1980
Great Lakes	10 ppb in water	Wong et al. 1978
Saltwater, as inorganic selenite	Up to 54 ppb in water (24 hr average), not to exceed 410 ppb at any time	EPA 1980
Livestock protection		
Drinking water	<50 ppb	NAS 1974; Wilber 1983
Diet (total)	<2,000 ppb (dry wt.)	NRC 1983

Diet (natural)	<4,000 ppb	Wilber 1983
Feeds (natural	<2,000 ppb	Frost 1972
Forage (natural)	<5,000 ppb	Frost 1972
Crop protection		
Irrigation water	<50 ppb	Birkner 1978; Wilber 1983
Human health protection		
Seafood	Not to exceed 2,000 ppb fresh wt.	Bebbington et al. 1977
Drinking water	<500 ppb (as sole Se source)	Robberecht and Von Greichen 1982
Food (natural)	<5,000 ppb	Wilber 1983
Milk or water	<500 ppb	Wilber 1983
Daily intake (all sources)		
Adults		
Safe	200 µg	Shamberger 1981
Normal	60-250 µg	Lo and Sandi 1980
Maximum tolerable level	<500 µg	Levander 1984
Infants	4-35 µg	Lo and Sandi 1980
Children		
Age 1-3	20-80 µg	Levander 1984
Age 4-6	30-120 µg	Levander 1984
Age 7-11 +	50-200 µg	Levander 1984
Air		
Japan	<100 µg/m^3	NAS 1976
USSR	<100 µg/m^3	NAS 1976
USA	<200 µg/m^3	NAS 1976
-	1 to 4 µg/m^3	Harr 1978

CURRENT RECOMMENDATIONS

All investigators appear to agree on four points. First, that insufficient selenium in the diet may have harmful and sometimes fatal consequences. Second, that exposure to grossly elevated levels of Se in the diet or water, is inevitably fatal over time to terrestrial and aquatic organisms. Third, that there is a comparatively narrow concentration range separating effects of selenium deficiency from those of selenosis. And fourth, that additional fundamental and basic research is required on selenium metabolism, physiology, recycling, interactions with other compounds or formulations, and chemical speciation in order to elucidate its nutritive role as well as its toxic effects. Accordingly, the proposed selenium criteria shown in Table 4 for prevention of Se deficiency and for protection of aquatic life, livestock, crops, and human health, should be viewed as guidelines, pending acquisition of additional, more definitive, data.

Regarding Se deficiency, it appears that diets containing 50 to 100 ppb Se provide adequate protection to humans and to various species of fish, small laboratory mammals, and livestock (Table 4). Factors contributing to Se deficiency in crops include increasing use of agricultural fertilizers and increasing atmospheric fallout of sulfur; furthermore, foliar applications of selenate, although efficient in raising Se levels in plants, have only

short-term value (Frost and Ingvoldstad 1975). There is a general consensus that Se deficiency in livestock in many countries is increasing, resulting in a need for added Se in the food chain.

Current recommendations for protection of freshwater aquatic life are that inorganic selenite concentrations in the water should not exceed 35 ppb on a daily average, or 260 ppb at any time (Table 4). These values are higher for saltwater life: 54 ppb daily average, 410 ppb at any time. The concentration range of 35 to 54 ppb recommended for protection of aquatic life is below the range of 60 to 600 ppb that is fatal to various sensitive species of marine and freshwater fauna, and in this respect affords an adequate measure of protection. It is very near the range (47 to 53 ppb) that has been associated with growth inhibition of freshwater algae, anemia and reduced hatch in rainbow trout, and shifts in species composition of freshwater algal communities. But studies by Cumbie and Van Horn (1978) and Sorensen et al. (1984) showed that water concentrations of 9 to 12 ppb of Se were associated with reduced reproduction of freshwater fishes, and their results strongly indicated that some downward modification of the Se freshwater aquatic life protection criterion may be appropriate. Furthermore, high bioconcentration and accumulation of Se from the water column by numerous species of algae, fish, and invertebrates is well documented at levels between 0.015 and 3.3 ppb, which is substantially below the recommended range of 35 to 54 ppb. The significance of Se residues in aquatic biota in terms of bioavailability and Se receptor sites is imperfectly understood, and it appears that much additional research is warranted on Se pharmacokinetics in aquatic environments.

Livestock appear to be protected against selenosis provided that their diets contain less than 4,000 ppb of natural (i.e., nonsupplemented) selenium (Table 4). This concentration is somewhat higher than levels reported for rats (Wilber 1983). Minimum toxic concentrations of Se in lifetime exposure of rats given diets containing natural Se were 1,400 ppb dietary Se, as judged by evidence of liver changes, and 3,000 ppb as estimated from longevity and histological changes in heart, kidney, and spleen. These values were only 350 and 750 ppb, respectively, when rat diets contained purified, rather than natural, Se. This relationship emphasizes that accidental poisoning of livestock, and presumably fish and wildlife, may occur when soils are deliberately supplemented with purified Se, or when soils or aquifers are contaminated as a result of faulty waste disposal practices. Although the concentration of <50 ppb for livestock drinking water and irrigation water for crop protection is inconsistent with that of < 35 ppb for aquatic life protection, neither livestock nor crops appear threatened at the higher level. Since many waterways that abut agricultural lands or areas of high anthropogenic loadings of Se contain valuable and desirable aquatic species, it would appear that some downward modification of the current livestock drinking water concentration of Se is necessary.

Recent field studies demonstrated that migratory waterfowl were heavily and adversely affected while nesting at Se-contaminated irrigation drainwater ponds in California, where food chain organisms contained between 12,000 and 280,000 ppb of Se. The source and fate of Se in irrigation drainwater ponds are largely unknown; they must be determined so that alternate technologies for Se control can be implemented to protect waterfowl in that geographical region.

Aerosol concentrations in excess of 4.0 µg Se/m^3 are potentially harmful to human health (Harr 1978); concentrations in excess of this value (6.0 µg Se/m^3) were regularly encountered in the vicinity of the smeltery at Sudbury, Canada (Nriagu and Wong 1983). It is not now known whether respiration rates of wildlife, particularly birds, are comparable to those of humans, or whether Se absorption energetics are similar, or whether wildlife species that frequent point sources of air contaminated by high Se levels for protracted periods are at greater risk than humans. Until additional and more conclusive data become available, aerosol concentrations of less than 4.0 µg Se/m^3 are recommended for the protection of sensitive species of wildlife.

Acute lethal doses for livestock species ranged from 3,300 µg/kg body weight of Se for horses and mules to 15,000 µg/kg for swine; appetite loss in cattle was noted at 500 µg/kg. For humans, the maximum tolerance level is usually set at 500 µg of Se daily (Lo and Sandi 1980), and the “safe” level at 200 µg/day (Shamberger 1981). Selenium dietary levels for man should not exceed 5,000 ppb; however, recommended maximum dietary levels in other mammals ranged from 1,000 ppb for rats to 4,000 ppb for horses. For all species, including man, there is a tendency to list Se dosage levels in terms of “natural” and “supplemented” levels, with the tacit understanding that “natural” levels are about one-fourth as toxic as “supplemented” values. Given the complexities of Se metabolism and speciation, it appears that greater precision and clarity are necessary in formulating Se criteria if these criteria are to become administratively enforced standards through passage of appropriate legislation.

LITERATURE CITED

Adams, W. J. 1976. The toxicity and residue dynamics of selenium in fish and aquatic invertebrates. Ph.D. Thesis, Michigan State Univ., East Lansing. 109 pp.

Adams, W. J., and H. E. Johnson. 1977. Survey of the selenium content in the aquatic biota of western Lake Erie. J. Great Lakes Res. 3:10-14.

Anon. 1975. Preliminary investigation of effects on the environment of boron, indium, nickel, selenium, tin, vanadium and their compounds. Vol. IV. Selenium. U.S. Environ. Protection Agency Rep. 560/2-75-005d. Available as PB - 245 987 from Nat. Tech. Inform. Serv., U.S. Dep. Commer., Springfield, VA. 92 pp.

Beal, A. R. 1974. A study of selenium levels in freshwater fishes of Canada's Central Region. Canada Dep. Environ. Fish. Mar. Serv., Tech. Rep. Ser. CEN/T-74-6:14 pp.

Bebbington, G. N., N. J. Mackay, R. Chvojka, R. J. Williams, A. Dunn, and E. H. Auty. 1977. Heavy metals, selenium and arsenic in nine species of Australian commercial fish. Aust. J. Mar. Freshwater Res. 28:277-286.

Beijer, K., and A. Jernelov. 1978. Ecological aspects of mercury-selenium interactions in the marine environment. Environ. Health Perspec. 25:43-45.

Bertine, K. K., and E. D. Goldberg. 1972. Trace elements in clams, mussels, and shrimp. Limnol. Ocean. 17:877-884.

Beyer, W. N., R. L. Chaney, and B. M. Mulhern. 1982. Heavy metal concentrations in earthworms from soil amended with sewage sludge. J. Environ. Qual. 11:381-385.

Birkner, J. H. 1978. Selenium in aquatic organisms from seleniferous habitats. Ph.D. Thesis, Colorado State Univ., Fort Collins. 121 pp.

Bjerragaard, P. 1982. Accumulation of cadmium and selenium and their mutual interaction in the shore crab Carcinus maenus (L.). Aquat. Toxicol. 2:113-125.

Blus, L. J., B. S. Neely, Jr., T. G. Lamont, and B. Mulhern. 1977. Residues of organochlorines and heavy metals in tissues and eggs of brown pelicans, 1969-73. Pestic. Monitor. J. 11:40-53.

Bovee, E. C., and T. L. O'Brien. 1982. Some effects of selenium, vanadium and zirconium, on the swimming rate of *Tetrahymena pyriformis*: a bioassay study. Univ. Kans. Sci. Bull. 52 (4):39-44.

Bowen, H. J. M. 1966. Trace elements in biochemistry. Academic Press, New York. 241 pp.

Browne, C. L., and J. N. Dumont. 1979. Toxicity of selenium to developing *Xenopus laevis* embryos. J. Toxicol. Environ. Health 5:699-709.

Cappon, C. J., and J. C. Smith. 1981. Mercury and selenium content and chemical form in fish muscle. Arch. Environ. Contam. Toxicol. 10:305-319.

Cappon, C. J., and J. C. Smith. 1982. Chemical form and distribution of selenium in edible seafood. J. Anal. Toxicol. 6:10-21.

Cardwell, R. D., D. G. Foreman, T. R. Payne, and D. J. Wilbur. 1976. Acute toxicity of selenium dioxide to freshwater fishes. Arch. Environ. Contam. Toxicol. 4:129-144.

Chau, Y. K., and J. P. Riley. 1965. The determination of selenium in sea water, silicates and marine organisms. Anal. Chim. Acta 33:36-49.

Chau, Y. K., P. T. S. Wong, B. A. Silverberg, P. L. Luxon, and G. A. Bengert. 1976. Methylation of selenium in the aquatic environment. Science 192:1130-1131.

Cherry, D. S., R. K. Guthrie, J. H. Rodgers, Jr., J. Cairns, Jr., and K. L. Dickson. 1976. Responses of mosquitofish (*Gambusia affinos)* to ash effluent and thermal stress. Trans. Am. Fish. Soc. 105:686-694.

Cumbie, P. M., and S. L. Van Horn. 1978. Selenium accumulation associated with fish mortality and reproductive failure. Proc. Annu. Conf. Southeast Assoc. Fish Wildl. Agencies 32:612-624.

de Goeij, J. J. M., V. P. Guinn, D. R. Young, and A. J. Mearns. 1974. Neutron activation analysis trace-element, studies of dover sole liver and marine sediments. Pages 189-200 *in* Comparative studies of food and environmental contamination. Int. Atomic Energy Agency, Vienna.

Duncan, D. A., and J. F. Klaverkamp. 1983. Tolerance and resistance to cadmium in white suckers *Catostomus commersoni* previously exposed to cadmium, mercury, zinc, or selenium. Can.-J. Fish. Aquat. Sci. 40:128-138.

Ebens, R. J., and H. T. Shacklette. 1982. Geochemistry of some rocks, mine spoils, stream sediments, soils, plants, and waters in the western energy region of the conterminous United States. U.S. Geol. Surv. Prof. Paper 1237. U.S. Govt. Printing Off., Washington DC. 173 pp.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. Biol. Trace Element Res. 6:165-180.

El-Begearmi, M. M., M. L. Sunde, and H. E- Ganther. 1977. A mutual protective effect of mercury and selenium in Japanese quail. Poult. Sci. 56:313-322.

El-Begearmi, M. M., H. E. Ganther, and M. L. Sunde. 1982. Dietary interaction between methylmercury, selenium, arsenic, and sulfur amino acids in Japanese quail. Poult. Sci. 61:272-279.

Ellis, M. M., H. L. Motley, M. D. Ellis, and R. O. Jones. 1937. Selenium poisoning in fishes. Proc. Soc. Exp. Biol. Med. 36:519-522.

EPA. 1980. Ambient water quality criteria for selenium. U.S. Environ. Protection Agency Rep. 440/5-80-070. 123 pp.

Fishbein, L. 1977. Toxicology of selenium and tellurium. Pages 191-240 *in* R. A. Goyer and M. A. Mehlman (eds.). Advances in modern toxicology, Vol. 2, Toxicology of trace elements. Hemisphere Publ. Corp., Washington DC.

Fishbein, L. 1983. Environmental selenium and its significance. Fundam. Appl. Toxicol. 3:411-419.

Fleming, W. J., W. H. Gutenmann, and D. J. Lisk. 1979. Selenium in tissues of woodchucks inhabiting fly ash landfills. Bull. Environ. Contam. Toxicol. 21:1-3.

Fowler, S. W., and G. Benayoun. 1976a. Selenium kinetics in marine zooplankton. Mar. Sci. Comm. 2:43-67.

Fowler, S. W., and G. Benayoun. 1976b. Influence of environmental factors on selenium flux in two marine invertebrates. Mar. Biol. 37:59-68.

Fowler, S. W., and G. Benayoun. 1976c. Accumulation and distribution of selenium in mussel and shrimp tissues. Bull. Environ. Contam. Toxicol. 16:339-346.

Freeman, H. C., G. Shum, and J. F. lithe. 1978. The selenium content in swordfish (*Xiphias gladius*) in relation to total mercury content. J. Environ. Sci. Health A13(3):235-240.

Frost, D. V. 1972. The two faces of selenium. Can selenophobia be cured? CRC Crit. Rev. Toxicol. 1:467-514.

Frost, D. V., and D. Ingvoldstad. 1975. Ecological aspects of selenium and tellurium in human and animal health. Chem. Scr. 8A:96-107.

Fukai, R., B. Oregioni, and D. Vas. 1978. Interlaboratory comparability of measurements of trace elements in marine organisms: results of intercalibration exercise on oyster homogenate. Oceanol. Acta 1:391-396.

Furr, A. K., T. F. Parkinson, W. D. Youngs, C. O. Berg, W. H. Gutenmann, I. S. Pakkala, and D. J. Lisk. 1979. Elemental content of aquatic organisms inhabiting a pond contaminated with coal fly ash. N.Y. Fish Game J. 26:154-161.

Ganther, H. E., C. Goudie, M. L. Sunde, M. J. Kopecky, P. Wagner, S. H. Oh, and W. G. Hoekstra. 1972. Selenium: relation to decreased toxicity of methylmercury added to diets containing tuna. Science 175:1122-1124.

Glickstein, N. 1978. Acute toxicity of mercury and selenium to *Crassostrea gigas* embryos and *Cancer magister* larvae. Mar. Biol. 49:113-117.

Glover, J. W. 1979. Concentrations of arsenic, selenium and ten heavy metals in school shark, *Galeorhinus australis* (Macleay), and gummy shark, *Mustelus antarcticus* Gunt south-eastern Australian waters. Aust. J. Mar. Freshwater Res. 30:505-510.

Gotsis, O. 1982. Combined effects of selenium/mercury and selenium/copper on the cell population of the alga *Dunaliella minuta*. Mar. Biol. 71:217-222.

Grimanis, A. P., D. Zafiropoulos, and M. Vassilaki-Grimani. 1978. Trace elements in the flesh and liver of two fish species from polluted and unpolluted areas of the Aegean Sea. Environ. Sci. Technol. 12:723-726.

Hall, R. A., E. G. Zook, and G. M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resource. U.S. Dep. Commer. NOAA Tech. Rep. NMFS SSRF-721. 313 pp.

Halter, M. T., W. J. Adams, and H. E. Johnson. 1980. Selenium toxicity to *Daphnia magna*, *Hyallela azteca*, and the fathead minnow in hard water. Bull. Environ. Contam. Toxicol. 24:102-107.

Harr, J. R. 1978. Biological effects of selenium. Pages 393-426 *in* F. W. Oehme (ed.). Toxicity of heavy metals in the environment, Part l. Marcel Dekker, New York.

Haseltine, S. D., G. H. Heinz, W. L. Reichel, and J. F. Moore. 1981. Organochlorine and metal residues in eggs of waterfowl nesting on islands in Lake Michigan off Door County, Wisconsin, 1977-78. Pestic. Monitor. J. 15:90-97.

Haseltine, S. D., J. S. Fair, S. A. Sutcliffe, and D. M. Swineford. 1983. Trends in organochlorine and mercury residues in common loon (*Gavia immer*) eggs from New Hampshire. Pages 131-141 in R. H. Yahner (ed.), Transactions of the Northeast section, The Wildlife Society, 40th Northeast Fish and Wildlife Conference, May 15-18, 1983, West Dover, VT.

Heit, M. 1979. Variability of the concentrations of seventeen trace elements in the muscle and liver of a single striped bass, *Morone saxatilis*. Bull. Environ. Contam. Toxicol. 23:1-5.

Heit, M., C. S. Klusek, and K. M. Miller. 1980. Trace element, radionuclide, and polynuclear aromatic hydrocarbon concentrations in Unionidae mussels from northern Lake George. Environ. Sci. Technol. 14:465-468.

Helmke, P. A., W. P. Robarge, R. L. Korotev, and P. J. Schomberg. 1979. Effects of soil-applied sewage sludge on concentrations of elements in earthworms. J. Environ. Qual. 8:322-327.

Hill, C. H. 1975. Interrelationships of selenium with other trace elements. Fed. Proc. 34:2096-2100.

Hilton, J. W., P. V. Hodson, and S. J. Slinger. 1980. The requirement and toxicity of selenium in rainbow trout (*Salmo gairdneri*). J. Nutr. 110:2527-2535.

Hodson, P. V., D. J. Spry, and B. R. Blunt. 1980. Effects on rainbow trout (*Salmo gairdneri*) of a chronic exposure to waterborne selenium. Can. J. Fish. Aquat. Sci. 37:233-240.

Huckabee, J. W., and N. A. Griffith. 1974. Toxicity of mercury and selenium to the eggs of carp (*Cyprinus carpio)*. Trans. Am. Fish. Soc. 103:822-825.

Hutchinson, T. C., and P. M. Stokes. 1975. Heavy metal toxicity and algal bioassays. Pages 320-343 in S. Barabas (ed.). Water quality parameters. ASTM Spec. Tech. Publ. 573. American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA.

Hutton, M. 1981. Accumulation of heavy metals and selenium in three seabird species from the United Kingdom. Environ. Pollut. 26A:129-145.

Jenkins, D. W. 1980. Biological monitoring of toxic trace metals. Vol. 2. Toxic trace metals in plants and animals of the world. Part III. U.S. Environ. Protection Agency Rep. 600/3-80-0921:1090-1129.

Jensen, L. S. 1968. Selenium deficiency and impaired reproduction in Japanese quail. Proc. Soc. Exp. Biol. Med. 128:970-972.

Jones, J. B., and T. C. Stadtman. 1977. *Methanococcus vanniellii*: culture and effects of selenium and tungsten on growth. J. Bacteriol. 130:1404-1406.

Kaiser, I. I., P. A. Young, and J. D. Johnson. 1979. Chronic exposure of trout to waters with naturally high selenium levels: effects on transfer RNA methylation. J. Fish. Res. Board Canada 36:689-694.

Karbe, L., Ch. Schnier, and H. O. Slewers. 1977. Trace elements in mussels (*Mytilus edulis*) from coastal areas of the North Sea and the Baltic. Multielement analyses using instrumental neutron activation analysis. J. Radioanal. Chem. 37:927-943.

Kari, T., and P. Kauranen. 1978. Mercury and selenium contents of seals from fresh and brackish water in Finland. Bull. Environ. Contam. Toxicol. 19:273-280.

Kifer, R. R., and W. L. Payne. 1968. Selenium content of fish meal. Feedstuffs 31 (Aug 68):32.

Kim, J. H., E. Birks, and J. F. Heisinger. 1977. Protective action of selenium against mercury in northern creek chubs. Bull. Environ. Contam. Toxicol. 17:132-136.

King, K. A., D. L. Meeker, and D. M. Swineford. 1980. White-faced ibis populations and pollutants in Texas, 1969-1976. Southwest. Nat. 25:225-240.

King, K. A., C. A. Lefever, and B. M. Mulhern. 1983. Organochlorine and metal residues in royal terns nesting on the central Texas coast. J. Field Ornithol. 54:295-303.

Klaverkamp, J. F., D. A. Hodgkins, and A. Lutz. 1983a. Selenite toxicity and mercury-selenium interactions in juvenile fish. Arch. Environ. Contam. Toxicol. 12:405-413.

Klaverkamp, J. F., W. A. Macdonald, W. R. Lillie, and A. Lutz. 1983b. Joint toxicity of mercury and selenium in salmonid eggs. Arch. Environ. Contam. Toxicol. 12:415-419.

Koeman, J. H., W. S. M. van de Ven, J. J. M. de Goeij, and P. S. Tijoe. 1975. Mercury and selenium in marine mammals and birds. Sci. Total Environ. 3:279-287.

Krishnaja, A. P., and M. S. Rege. 1982. Induction of chromosomal aberrations in fish *Boleophthalmus dussumieri* after exposure in vivo to mitomycin C and heavy metals mercury, selenium and chromium. Mutation Res. 102:71-82.

Kuhn, J. K., F. L. Fiene, R. A. Cahill, H. J. Gluskoter, and N. F. Shimp. 1980. Abundance of trace and minor elements in organic and mineral fractions of coal. Environ. Geol. Notes 88. Illinois State Geol. Surv. Div., Urbana, IL. 67 pp.

Kumar, H. D., and G. Prakash. 1971. Toxicity of selenium to the blue-green algae, *Anacystis nidulans* and *Anabaena variabilis*. Ann. Bot. 35:697-705.

Lakin, H. W. 1973. Selenium in our environment. Pages 96-111 *in* E. L. Kothny (ed.). Trace elements in the environment. Adv. Chemistry Ser., Am. Chem. Soc., Washington, D.C.

Lemly, A. D. 1982a. Response of juvenile centrarchids to sublethal concentrations of waterborne selenium. I. Uptake, tissue distribution, and retention. Aquat. Toxicol. 2:235-282.

Lemly, A. D. 1982b. Determination of selenium, in fish tissues with differential pulse polarography. Environ. Technol. Lett. 3:497-502.

Leonzio, C., S. Focardi, and E. Bacci. 1982. Complementary accumulation of selenium and mercury in fish muscle. Sci. Total Environ. 24:249-254.

Levander, O. A. 1983. Recent developments in selenium nutrition. Pages 147-162 *in* J. Weininger and C. Briggs (eds.). Nutrition update, Vol. 1. John Wiley, New York.

Levander, O. A. 1984. The importance of selenium in total parenteral nutrition. Bull. N.Y. Acad. Med. 60:144-155.

Lo, M. T., and E. Sandi. 1980. Selenium: occurrence in foods and its toxicological significance. A review. J. Environ. Pathol. Toxicol. 4:193-218.

Lucas, H. F., D. N. Edgington, and P. J. Colby. 1970. Concentrations of trace elements in Great Lakes fishes. J. Fish. Res. Board Canada 27:677-684.

Lucu, C., and M. Skreblin. 1981. Evidence of the interaction of mercury and selenium in the shrimp *Palaemon elegans*. Mar. Environ. Res. 5:265-274.

Lunde, G. 1970. Analysis of arsenic and selenium in marine raw materials. J. Sci. Food Agric. 21:242-247.

Luten, J. B., A. Ruiter, T. M. Ritskes, A. B. Rauchbaar, and G. Riekwel-Booy. 1980. Mercury and selenium in marine and freshwater fish. J. Food Sci. 45:416-419.

Mackay, N. J., M. N. Kazacos, R. J. Williams, and M. I. Leedow. 1975. Selenium and heavy metals in black marlin. Mar. Pollut. Bull. 6:57-60.

Maher, W. A. 1983. Selenium in marine organisms from St. Vincent's Gulf, South Australia. Mar. Pollut. Bull. 14:35-36.

Martin, J. H., P. D. Elliot, V. C. Anderlini, D. Girvin, S. A. Jacobs, R. W. Risebrough, R. L. Delong, and W. G. Gilmartin. 1976. Mercury-seleniumbromine imbalance in premature parturient California sea lions. Mar. Biol. 35:91-104.

May, T. W., and G. L. McKinney. 1981. Cadmium, lead, mercury, arsenic, and selenium concentrations in freshwater fish, 1976-77 - National Pesticide Monitoring Program. Pestic. Monitor. J. 15:14-38.

Measures, C. I., and J. D. Burton. 1980. The vertical distribution and oxidation states of dissolved selenium in the northeast Atlantic ocean and their relationship to biological processes. Earth Plan. Sci. Lett. 46:385-396.

Moksnes, K. 1983. Selenium deposition in tissues and eggs of laying hens given surplus of selenium as selenomethionine- Acta Vet. Scand. 24:34-44.

Morris, J. G., W. S. Cripe, H. L. Chapman, Jr. , D. F. Walker, J. B. Armstrong, J. D. Alexander, Jr., R. Miranda, A. Sanchez, Jr., B. Sanchez, J. R. Blair-West, and D. A. Denton. 1984. Selenium deficiency in cattle associated with Heinz bodies and anemia. Science 223:491-493.

Murphy, C. P. 1981. Bioaccumulation and toxicity of heavy metals and related trace elements. J. Water Pollut. Control Fed. 53:993-999.

NAS. 1973. Water quality criteria 1972. U.S. Environ. Protection Agency Rep. R3-73-033. 594 pp.

NAS. 1976. Selenium. Comm. Med. Biol. Eff. Environ. Poll., Div. Med. Sci., Natl. Res. Counc., Nat. Acad. Sci., Washington, DC. 203 pp.

Nassos, P. A., J. R. Coats, R. L. Metcalf, D. D. Brown, and L. G. Hansen. 1980. Model ecosystem, toxicity, and uptake evaluation of 75Se-selenite. Bull. Environ. Contam. Toxicol. 24:752-758.

Nielsen, M. G., and G. Gissel-Nielsen. 1975. Selenium in soil-animal relationships. Pedobiologia 15:65-67.

Niimi, A. J., and Q. N. LaHam. 1975. Selenium toxicity on the early life stages of zebrafish (*Brachydanio rerio*). J. Fish. Res. Board Canada 32:803-806.

Noda, K., S. Hirai, K. Sunayashiki, and H. Danbara. 1979. Neutron activation analyses of selenium and mercury in marine products from along the coast of Shikoku Island. Agric. Biol. Chem. 47:1381-1386.

NRC. 1983. Selenium in nutrition. Subcomm. on selenium, Comm. animal nutrition, Board on Agricul., Natl. Res. Counc., National Academy Press, Washington, DC. 174 pp.

Nriagu, J. O., and H. K. Wong. 1983. Selenium pollution of lakes near the smelters at Sudbury, Ontario. Nature 301:55-57.

Ohlendorf, H. M., and C. S. Harrison. 1986. Mercury, selenium, cadmium, and organochlorines in eggs of three Hawaiian seabird species. Environ. Pollut. 11B:169-191.

Ohlendorf, H. M., D. J. Hoffman, M. K. Saiki, and T. W. Aldrich. 1986. Embryonic mortality and abnormalities of aquatic birds: apparent impacts of selenium from irrigation drainwater. Sci. Total Environ. 52:49-63.

Okazaki, R. K., and M. H. Panietz. 1981. Depuration of twelve trace metals in tissues of the oysters *Crassostrea gigas* and *C. virginica.* Mar. Biol. 63:113-120.

Ort, J. F., and J. D. Latshaw. 1978. The toxic level of sodium selenite in the diet of laying chickens. J. Nutr. 108:1114-1120.

Orvini, E., V. Caramella-Crespi, and N. Genova. 1980. Activation analysis of As, Hg and Se in some marine organism. Pages 441-448 *in* J. Albaiges (ed.). Analytical techniques in environmental chemistry. Pergamon Press, New York.

Ostadalova, I., and A. Babicky. 1980. Toxic effect of various selenium compounds on the rat in the early postnatal period. Arch. Toxicol. 45:207-211.

Pakkala, I. S., W. H. Gutenmann, D. J. Lisk, G. E. Burdick, and E. J. Harris. 1972. A survey of the selenium content of fish from 49 New York State waters. Pestic. Monitor. J. 6:107-114.

Papadopoulu, C., G. D. Kanias, and E. M. Kassimati. 1976. Stable elements of radioecological importance in certain echinoderm species. Mar. Pollut. Bull. 7:143-144.

Patrick, R. 1978. Effects of trace metals in the aquatic ecosystem. Am. Sci. 66:185-191.

Prasad, T., S. P. Arora, and R. C. Chopra. 1982. Selenium toxicity as induced by feeding rice husk to buffalo calves: a clinical case report. Indian Vet. J. 59:235-237.

Pratt, D. R., J. S. Bradshaw, and B. West. 1972. Arsenic and selenium analyses in fish. Utah Acad. Arts Sci. Proc., Part 1, 49:23-26.

Rancitelli, L. A., W. A. Haller, and J. A. Cooper. 1968. Trace element variations in silver salmon and king salmon muscle tissue. Rapp. Americain BNWL - 715, Part 2: 42-47.

Reading, J. T. 1979. Acute and chronic effects of selenium on *Daphnia pulex*. Thesis. Virginia Polytechnic Institute, Blacksburg. 91 pp.

Reddy, C. C., and E. J. Massaro. 1983. Biochemistry of selenium: a brief overview. Fundam. Appl. Toxicol. 3:431-436.

Reijnders, P. J. H. 1980. organochlorine and heavy metal residues in harbour seals from the Wadden Sea and their possible effects on reproduction. Neth. J. Sea Res. 14:30-65.

Robberecht, H., and R. Von Grieken. 1982. Selenium in environmental waters: determination, speciation and concentration levels. Talanta 29:823-844.

Rosenfeld, I., and O. A. Beath. 1964. Selenium. Geobotany, biochemistry, toxicity, and nutrition. Academic Press, New York. 411 pp.

Rossi, L. C., G. F. Clemente, and G. Santaroni. 1976. Mercury and selenium distribution in a defined area and in its population. Arch. Environ. Health 31:160-165.

Ryther, J., T. M. Losordo, A. K. Furr, T. F. Parkinson, W. H. Gutenmann, I. S. Pakkala, and D. J. Lisk. 1979. Concentration of elements in marine organisms cultured in seawater flowing through coal-fly ash. Bull. Environ. Contam. Toxicol. 23:207-210.

Sandholm, M. 1973. Biological aspects of selenium: uptake of selenium by SH- groups and different organic materials in the ecosystem. Thesis, Dept. Medicine, Coll. Veterinary Medicine, Helsinki, Finland. 35 pp.

Sato, T., Y. Ose, and T. Sakai. 1980. Toxicological effect of selenium on fish. Environ. Pollut. 21A:217-224.

Schroeder, H. A., D. V. Frost, and J. J. Balassa. 1970. Essential trace metals in man: selenium. J. Chron. Dis. 23:227-243.

Schultz, C. D., and B. M. Ito. 1979. Mercury and selenium in blue marlin, *Makaira nigricans*, from the Hawaiian Islands. U.S. Natl. Mar. Fish. Serv., Fish Bull. 76:872-879.

Shamberger, R. J. 1981. Selenium in the environment. Sci. Total Environ. 17:59-74.

Sharma, R. P., and J. L. Shupe. 1977. Trace metals in ecosystems: relationships of residues of copper, molybdenum, selenium, and zinc in animal tissues to those in vegetation and soil in the surrounding environment. Pages 595-608 *in* H. Drucker and R. E. Wildung (eds.). Biological implications of metals in the environment. Avail. as CONF 750929 from Nat. Tech. Infor. Serv., U.S. Dep. Commer., Springfield VA.

Sheline, J., and B. Schmidt-Nielsen. 1977. Methylmercury-selenium interaction in the killifish, *Fundulus heteroclitus*. Pages 119-130 *in* F. J. Vernberg, A. Calabrese, F. P. Thur berg and W. B. Vernberg (eds.). Physiological responses of marine biota to pollutants. Academic Press, New York.

Smith, T. G., and F. A. J. Armstrong. 1978. Mercury and selenium in ringed and bearded seal tissues from Arctic Canada. Arctic 31:75-84.

Sorensen, E. B., T. L. Bauer, J. S. Bell, and C. W. Harlan. 1982. Selenium accumulation and cytotoxicity in teleosts following chronic, environmental exposure. Bull. Environ. Toxicol. Contam. 29:688-696.

Sorensen, E. M. B., P. M. Cumbie, T. L. Bauer, J. S. Bell, and C. W. Harlan. 1984. Histopathological, hematological, condition-factor, and organ weight changes associated with selenium accumulation in fish from Belews Lake, North Carolina. Arch. Environ. Contam. Toxicol. 13:153-162.

Spehar, R. L., G. M. Christensen, C. Curtis, A. E. Lemke, T. J. Norberg, and Q. H. Pickering. 1982. Effects of pollution on freshwater fish. J. Water Pollut. Control Fed. 54:877-922.

Speyer, M. R. 1980. Mercury and selenium concentrations in fish, sediments, and water of two northwestern Quebec lakes. Bull. Environ. Contam. Toxicol. 24:427-432.

Stadtman, T. C. 1974. Selenium biochemistry. Science 183:915-921.

Stadtman, T. C. 1977. Biological function of selenium. Nutr. Rev. 35:161-166.

Stoneburner, D. L. 1978. Heavy metals in tissues of stranded short-finned pilot whales. Sci. Total Environ. 9:293-297.

Stump, I. G., J. Kearney, J. M. D'Auria, and J. D. Popham. 1979. Monitoring trace elements in the mussel, *Mytilus edulis* using X-ray energy spectroscopy. Mar. Pollut. Bull. 10:270-274.

Tamura, Y., T. Maki, H. Yamada, Y. Shimamura, S. Ochiai, S. Nishigaki, and Y. Kimura. 1975. Studies on the behavior of accumulation of trace elements in fishes. III. Accumulation of selenium and mercury in various tissues of tuna. Tokyo Toritsu Eisei Kenkyusho Nenpo 26:200-204. (In Japanese. translation available from multilingual Serv., Dep. Secr. State Canada, Fish. Mar. Serv. No. 3994, 1977:11 pp.)

Tijoe, P. S., J. J. M. de Goeij, and M. de Bruin. 1977. Determination of trace elements in dried sea-plant homogenate (SP-M-1) and in dried copepod homogenate (MA-A-1) by means of neutron activation analysis. Interuniv. Reactor Inst. Rept. 133-77-05, Delft, Nederlands:14 pp.

Tong, S. S. C., W. H. Gutenmann, D. J. Lisk, G. E. Burdick, and E. J. Harris. 1972. Trace metals in New York State fish. N.Y. Fish Game J. 19:123-131.

Turner, J. S., S. R. B. Solly, J. C. M. Mol-Krijnen, and V. Shanks. 1978. Organochlorine, fluorine, and heavy-metal levels in some birds from N. Z. estuaries. N. Z. J. Sci. 21:99-102.

Ullrey, D. E., W. G. Youatt, and P. A. Whetter. 1981. Muscle selenium concentrations in Michigan deer. J. Wildl. Manage. 45:534-536.

United Nations. 1979. Review of harmful substances. Reports and studies. No. 2. Jnt. Group Experts Sci. Aspect. Mar. Pollut. GESAMP-76-98245. N.Y.:79 pp.

Uthe, J. F., and E. G. Bligh. 1971. Preliminary survey of heavy metal contamination of Canadian freshwater fish. J. Fish. Res. Board Canada 28:786-788.

van de Ven, W. S. M., J. H. Koeman and A. Svenson. 1979. Mercury and selenium in wild and experimental seals. Chemosphere 8:539-555.

Walsh, D. F., B. L. Berger, and J. R. Bean. 1977. Mercury, arsenic, lead, cadmium and selenium residues in fish, 1971-73. National Pesticide Monitoring Program. Pestic. Monitor. J. 11:5-34.

Ward, G. S., T. A. Hollister, P. T. Heitmuller, and P. R. Parrish. 1981. Acute and chronic toxicity of selenium to estuarine organisms. Northeast Gulf Sci. 4:73-78.

Westernman, A. G., and W. J. Birge. 1978. Accelerated rate of albinism in channel catfish exposed to metals. Prog. Fish-Cult. 40:143-146.

White, D. H., K. A. King, and R. M. Prouty. 1980. Significance of organochlorine and heavy metal residues in wintering shorebirds at Corpus Christi, Texas, 1976-77. Pestic. Monitor. J. 14:58-63.

Whittle, K. J., R. Hardy, A. V. Holden, R. Johnston, and R. J. Pentreath. 1977. Occurrence and fate of organic and inorganic contaminants in marine animals. Ann. N.Y. Acad. Sci. 298:47-79.

Wiener, J. G , G. A. Jackson, T. W. May, and B. P. Cole. 1984. Longitudinal distribution of trace elements (As, Cd, Cr, Hg, Pb, and Se) in fishes and sediments in the upper Mississippi River. Pages 139-170 *in* J. G. Weiner, R. V. Anderson, and D. R. McConville (eds.). Contaminants in the upper Mississippi River. Butterworth Publ., Stoneham, MA.

Wilber, C. G. 1980. Toxicology of selenium: A review. Clin. Toxicol. 17:171-230.

Wilber, C. G. 1983. Selenium. A potential environmental poison and a necessary food constituent. Charles C. Thomas, Springfield IL. 126 pp.

Willford, W. A. 1971. Heavy metals research in the Great Lakes, 1970-1971. Pages 53-65 *in* Prevalence and effects of toxic metals in the aquatic environment. Proc. Univ. North Carolina, Rep. 57.

Winger, P. V., C. Sieckman, T. W. May, and W. W. Johnson. 1984. Residues of organochlorine insecticides, polychlorinated biphenyls, and heavy metals in biota from Apalachicola River, Florida, 1978. J. Assoc. Off. Anal. Chem. 67:325-333.

Wong, P. T. S., Y. K. Chau, and P. L. Luxon. 1978. Toxicity of a mixture of metals on freshwater algae. J. Fish. Res. Board Canada 35:479-481.

Wren, C. D. 1984 Distribution of metals in tissues of beaver, raccoon and otter from Ontario, Canada. Sci. Total Environ. 34:177-184.

Wrench, J. J., and N. C. Campbell. 1981. Protein bound selenium in some marine organisms. Chemosphere 10:1155-1161.

Yonemoto, J., H. Satoh, S. Himeno, and T. Suzuki. 1983. Toxic effects of sodium selenite on pregnant mice and modification of the effects by Vitamin E or reduced glutathione. Teratology 28:333-340.

Zafiropoulos, D., and A. P. Grimanis. 1977. Trace elements in *Acartia clausi* from Elefsis Bay of the upper Saronikos Gulf, Greece. Ma . Pollut. Bull. 8:79-81.

Zieve, R. and P. J. Peterson. 1981. Factors influencing the volatilization of selenium from soil. Sci. Total Environ. 19:277-284.

Zingaro, R. A., and W. C. Cooper (eds.). 1974. Selenium. Van Nostrand Reinhold Co., New York. 835 pp.

Biological Report 85(1.6)
January 1986

Contaminant Hazard Reviews
Report No. 6

CHROMIUM HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Ecological and toxicological aspects of chromium (Cr) in the environment are reviewed, including its chemistry, background residues in biological and abiotic materials, beneficial and protective properties, and toxic and sublethal effects. Recommendations are presented, including proposed criteria for protection of sensitive species of wildlife and aquatic organisms.

Most authorities agree on eight points: (1) chromium levels are elevated in soil, air, water, and biota in the vicinity of electroplating and metal finishing industries, publicly owned municipal treatment plants, tanneries, oil drilling operations, and cooling towers; (2) hexavalent chromium (Cr+6) is the most biologically active Cr chemical species, although little is known about the properties of organochromium compounds, water soluble species, or their interactions in complex mixtures; (3) chromium chemistry is imperfectly understood, and existing analytical methodologies are inadequate for quantification of Cr species and ionic states; (4) chromium is an essential trace element in humans and some species of laboratory animals, but the data base is incomplete for other groups of organisms; (5) at high environmental concentrations, Cr is a mutagen, teratogen, and carcinogen; (6) no biomagnification of Cr has been observed in food chains, and concentrations are usually highest at the lowest trophic levels; (7) toxic and sublethal properties of Cr are modified by a variety of biological and abiotic factors; and (8) sensitivity to Cr varies widely, even among closely related species. As reported here, adverse effects of Cr to sensitive species have been documented at 10.0 ug/L (ppb) of Cr+6 and 30.0 ug/L of Cr+3 in freshwater and 5.0 ug/L of Cr+6 in saltwater and, to wildlife, 5.1 and 10.0 mg of Cr+6 and Cr+3, respectively, per kilogram of diet (ppm). Tissue levels in excess of 4.0 mg total Cr/kg dry weight should be viewed as presumptive evidence of Cr contamination, although the significance of tissue Cr residues is unclear. Some of these findings are in sharp contrast to Cr criteria proposed by regulatory agencies.

This report should be cited as:

Eisler, R. 1986. Chromium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.6). 60 pp).

TABLES

INTRODUCTION

Environmental effects of chromium (Cr) have been extensively reviewed (NAS 1974; Steven et al. 1976; Snyder et al. 1977; Towill et al. 1978; Taylor and Parr 1978Langard and Norseth 1979; Post and Campbell 1980; Hatherill 1981; Ecological Analysts 1981). These authorities agree that Cr is used widely in domestic and industrial products and that some of its chemical forms, primarily hexavalent chromium (Cr+6) and trivalent chromium (Cr+3), are toxic. In North America, thousands of tons of Cr ore and concentrates are imported annually for the production of stainless steels, chrome plated metals, pigments for inks and paints, and a wide variety of chemicals. Reports from Europe, Scandinavia, Asia, and North America all emphasize the high incidence of lung cancer and other respiratory diseases among workers involved in the manufacture of chromates. Others document that land dumping of wastes from chromate production and electroplating operations have been responsible for groundwater contamination; that discharge of Cr wastes into streams and lakes has caused damage to aquatic ecosystems and accidental poisoning of livestock; and that large amounts of Cr+3 and Cr+6 are reintroduced into the environment as sewage and solid wastes by the disposal of consumer products containing Cr.

In this account I briefly review the ecological and toxicological effects of Cr to fish and wildlife, with emphasis on migratory species, their predators, and their prey, and also provide current recommendations for the protection of sensitive species of concern to the U.S. Fish and Wildlife Service. This report is part of a continuing series of synoptic reviews prepared in response to informational requests from FWS environmental specialists.

ENVIRONMENTAL CHEMISTRY

The annual world production of chromium is estimated at 7 million metric tons; most of the ore, in the form of chromite ($FeOCr_2O_3$), is produced by the USSR and the Republic of South Africa. In the United States, chromium is used principally in metallurgy and chemical industries (Langard and Norseth 1979). Although natural mobilization of Cr by weathering processes is estimated at 32 thousand tons/year, the amounts of Cr added to the environment as a result of anthropogenic activities are far greater. New York City alone contributes about 440 tons of Cr annually to the environment (Steven et al. 1976). Major atmospheric emissions of Cr are from the chromium alloy and metal producing industries; lesser amounts come from coal combustion, municipal incinerators, cement production, and cooling towers (Towill et al. 1978). Atmospheric emissions contribute 4 to 6 times more Cr to aquatic ecosystems than do liquid wastes (Ecological Analysts 1981). In aquatic environments, the major sources of chromium are the electroplating and metal finishing industries and publicly owned treatment plants; relatively minor sources (other than localized contamination) are iron and steel foundries, inorganic chemical plants, tanneries, textile manufacturing, and runoff from urban and residential areas (Towill et al. 1978; Ecological Analysts 1981). Chromium in phosphates used as fertilizers may be an important source of Cr in soil, water, and some foods (Langard and Norseth 1979). In general, elevated levels of Cr in biological or other samples have been positively correlated with increased industrial and other uses of the element—especially uses associated with plating and foundry applications, chemical manufacturing, and corrosion inhibition (Taylor and Parr 1978).

Chromium, in the crystalline form, is a steel-gray, lustrous, hard metal characterized by an atomic weight of 51.996, an atomic number of 24, a density of 7.14, a melting point of 1900°C, and a boiling point of 2642°C. Four Cr isotopes occur naturally—Cr-50 (4.3%), -52 (83.8%), -53 (9.6%), and -54 (2.4%)—and seven are man-made. Elemental Cr is very stable, but is not usually found pure in nature. Chromium can exist in oxidation states ranging from -2 to +6, but is most frequently found in the environment in the trivalent (+3) and hexavalent (+6) oxidation states. The +3 and +6 forms are the most important because the +2, +4, and +5 forms are unstable and are rapidly converted to +3, which in turn is oxidized to +6 (Towill et al. 1978; Langard and Norseth 1979; Ecological Analysts 1981).

Most compounds prepared from chromite ore contain Cr in the more stable +3 and +6 states. The Cr in essentially all environmentally important Cr compounds is in one of these two oxidation states. Chromium in biological materials is usually in the +3 form (Langard and Norseth 1979), and is the form that functions as an essential element in mammals by maintaining efficient glucose, lipid, and protein metabolism (Steven et al. 1976). In general, the toxicity of trivalent chromium to mammals is low because its membrane permeability is poor and it is noncorrosive; further, there is little tendency for Cr+3 to biomagnify in food chains in the inorganic form. However, organo-trivalent Cr compounds may have significantly different accumulation tendencies

although little is known about these compounds (Steven et al. 1976). Hexavalent chromium is more toxic than the +3 form because its oxidizing potential is high and it easily penetrates biological membranes (Steven et al. 1976; Taylor and Parr 1978; Langard and Norseth 1979; Ecological Analysts 1981). Most of the Cr+6 found in nature is a result of domestic and industrial emissions (Steven et al. 1976). Interaction of +6 chromic oxide, dichromate, or chromate compounds with organic compounds can result in reduction to the comparatively less toxic trivalent form (Taylor and Parr 1978).

Little is known about the relation between concentrations of total Cr in a given environment and biological effects on the organisms living there. Depending on the physical and chemical state of the Cr, the same element concentration has a wide variety of mobilities and reactivities and thus has different effects (Steven et al. 1976). Chromium toxicity to aquatic biota is significantly influenced by abiotic variables such as hardness, temperature, pH, and salinity of water; and biological factors such as species, life stage, and potential differences in sensitivities of local populations (Ecological Analysts 1981). In both freshwater and marine environments, hydrolysis and precipitation are the most important processes that determine the fate and effects of chromium, whereas adsorption and bioaccumulation are relatively minor (Ecological Analysts 1981). Both Cr+3 and Cr+6 can exist in water with little organic matter; Cr+6 is usually the major species in seawater (Towill et al. 1978). Under oxygenated conditions, Cr+6 is the dominant dissolved stable Cr species in aquatic systems. The hexavalent form exists as a component of a complex anion that varies with pH and may take the form of chromate (CrO_4^{-2}), hydrochromate ($HCrO_4^{-1}$), or dichromate ($Cr_2O_7^{-2}$). These ionic Cr+6 forms are highly soluble in water and thus mobile in the aquatic environment. All stable Cr+6 anionic compounds strongly oxidize organic matter on contact and yield oxidized organic matter and Cr+3 (Ecological Analysts 1981). Trivalent Cr tends to form stable complexes with negatively charged inorganic or organic compounds, and thus is unlikely to be found uncomplexed in aqueous solution if anionic or particulate compounds (such as decaying plant or animal tissues, or silt or clay particles) are present (Steven et al. 1976; Pfeiffer et al. 1980; Ecological Analysts 1981). Precipitated Cr+3 hydroxides remain in the sediments under aerobic conditions; under low pH and anoxic conditions, however, Cr+3 hydroxides may solubilize and remain as ionic Cr+3 unless oxidized to Cr+6 through mixing and aeration (Ecological Analysts 1981). Among estuarine sediments, Cr content tends to be highest in those of small grain size and high organic and iron content; concentrations in European estuaries ranged from 3.9 mg/kg in intertidal sands to 162.0 mg/kg in anaerobic muds (Rehm et al. 1984). Adsorption of Cr by sediments is salinity-dependent; adsorption is greatest at salinities of 0.1 to 1.0 ‰ (Mayer and Schick 1981). Colloidal iron strongly scavenges Cr+3 from river water; flocculation of the colloids when they are mixed with seawater, coupled with lack of removal of the colloids to the sediments by gravitational settling or scavenging by suspended sediments, promotes the flux of Cr+3 through the estuary to the open ocean (Mayer et al. 1981).

The solubility and potential bioavailability of waste Cr added to soils through sewage sludge, animal manures, and industrial wastewater are modified by soil pH and organic complexing substances (James and Bartlett 1983a, 1983b). Although soil pH can affect oxidation rates of Cr+6 to Cr+3, organic complexes appear to play a more significant role. For example, organically complexed Cr+3 added to soils may remain soluble for at least a year, whereas the free Cr+3 metal ion in the absence of soluble complexing ligands quickly becomes adsorbed, or hydrolyzed and precipitated. The biological effects of organochromium compounds, which are not well documented, appear to be high-priority subjects for further research.

All toxic effects of Cr+6 seem to be related to the strong oxidizing action of chromates, and all biological interactions of chromates seem to result in reduction to the Cr+3 form and subsequent coordination to organic molecules (Langard and Norseth 1979).

Data on the environmental cycling of Cr are lacking, and those on the biochemistry of Cr are incomplete and sparse (Towill et al. 1978); it is clear that these two subjects merit additional research. Furthermore, there is increasing concern about the uncertainties in the analysis of some types of biological and environmental samples (Towill et al. 1978; Taylor and Parr 1978). For example, collaborating laboratories have reported order-of-magnitude differences in persistence of Cr in standard bovine liver. Until more is learned about the reasons for these differences, caution should be exercised in interpreting past analytical results.

BACKGROUND CONCENTRATIONS

Chromium concentrations in selected nonbiological materials are elevated in the vicinity of industrial operations and municipal waste treatment facilities where chromium is a significant component of wastes discharged into the environment (Tables 1 and 2). The bioavailability of Cr in these materials was mentioned earlier, but the mechanism still remains largely unknown. It is generally agreed that suspended particulates are a major source of transport in aquatic systems, that most Cr in soil and sediment is unavailable to living organisms, that Cr+6 in air and water is hazardous to fish and wildlife, and that the grossly elevated levels of Cr (especially inorganic fractions) in sludge components may have serious implications to wildlife when the sludge is applied to croplands.

Concentrations of Cr in representative species of plants and animals collected worldwide are shown in Table 3. Additional and more comprehensive data were given by Jenkins (1980) and Eisler (1981). Chromium concentrations in species of individual taxonomic groups tended to be elevated when collection localities were near electroplating plants, tanneries, oil drilling operations, sewage outfalls, drift cooling towers, dump sites, or other sources of Cr-containing wastes that were being discharged into the environment.

Among marine algae and invertebrates, for example, comparatively high concentrations of Cr were recorded in algae, clams, and annelids from the vicinity of electroplating plants; in crabs collected near an ocean dump site receiving large quantities of metals; and in algae and echinoderms near urbanized areas in Puerto Rico. Grossly elevated levels of Cr were also noted (Table 3) in selected plasma fractions of tunicate blood, in scales from a few species of teleosts, and in corals from Cr-rich areas containing high concentrations of scandium and titanium; however, these accumulations were not attributed to anthropogenic activities. Many factors are known to modify Cr levels. In marine molluscs, as one example, Cr concentrations tended to increase with the age of the organism (Eisler et al. 1978), but uptake was significantly inhibited at high salinities (Olson and Harrel 1973). Accidental contamination of field samples by metal particles in the samples, rust from stainless hydrowire, or flaking paint from the hull of the collecting ship may also constitute significant sources of elevated Cr residues (Martin and Knauer 1973). In terrestrial ecosystems, elevated Cr levels were reported in cotton rats and plants collected near drift cooling towers and in earthworms and plants from sludge-amended soils (Table 3). However, the high levels of Cr reported in the hair of pronghorns and elk (Table 3) require verification.

A major source of concern at present is the accuracy and precision of chromium analyses in biological samples. One interlaboratory calibration study, involving 87 laboratories, showed that an oyster homogenate averaged 1.1 ppm dry weight, with a standard deviation of 0.5 ppm (Fukai et al. 1978). This means that about 67% of the laboratories were in the range of 0.6 to 1.6 ppm and about 33% of the laboratories reporting were outside this range. It seems clear that more rigorous and more standardized sample preparation techniques and analyses for chromium are needed.

BENEFICIAL AND PROTECTIVE PROPERTIES

Chromium is essential for normal metabolism of insulin and glucose in humans (Langard and Norseth 1979) and for regulating carbohydrate metabolism in mammals (Preston et al. 1976; Onkelinx 1977; Gale 1978; Towill et al. 1978; Post and Campbell 1980). Chromium deficiency has been described in rats, guinea pigs, and squirrel monkeys; signs include reduced growth, decreased life span, elevated serum cholesterol, increased formation of aortic plaques, and signs resembling those of diabetes mellitus. Subjecting Cr-deficient animals to stress can exacerbate the signs (Preston et al. 1976). In humans, Cr deficiency has been suggested as a possible factor in the incidence of diabetes and atherosclerosis. Autopsy data from 31 areas of the world suggested that many Americans, but few non-Americans, were deficient in Cr. One characteristic feature of Cr levels in human tissues is a decline with increasing age (Onkelinx 1977).

Table 1. Chromium concentration in nonbiological materials collected worldwide.

Sample (units in parentheses)	Concentration	Reference[a]
Terrestrial (mg/kg)		
Earth's crust	100–300	1
"	mean, 125	2
Soils	5–300	3
"	trace to 250	2
Granite and limestones	10	3
Serpentine materials	1,800	3
Marsh sediments		
Receiving fertilizers containing sewage sludge, for		
7 years (total dose of 10,300 mg Cr/m^2)	2,150–4,750	4
Control areas	50–54	4
Aquatic		
Suspended particulates (mg/kg)		
Atlantic coastal streams	≤460	5
United States	37–2,000	3
Brazil, electroplating plant		
Distance from discharge site (meters)		
0	2,210–61,070	6
50	15,260	6
600	18,620	6
Sediments (mg/kg)		
Freshwater		
Maine, receiving tannery wastes	≤25,000	7
California	90–140	3
Wisconsin	1–49	3
Rhine River, Germany	max. 1,240	3
Brazil, electroplating plan, distance from discharge site (meters)		
0	1,420–54,300	6
50	24,820	6
600	1,700	6
Marine		
United Kingdom	30–52	8
Rhode Island, near electroplating plant	60–80	9
Maine, near tanneries	80–3,000	10
Water (µg/L)		
Freshwater		
Rivers and lakes	1–10	2
Streams	0–112, mean 9.7	3
Drinking water	Usually <8; rarely >50	3
Untreated industrial effluents	≤5,000,000	11
Vicinity Brazilian electroplating plant		
Waste stream	1,290,000	6
At discharge	≤80,000	6
50 m downstream	54	6
600 m downstream	0.23	6
Seawater	<1–5	2
Seawater	0–0.5	3

Air (μg/m^3)		
Background level	0.001	11
Urban	0.06	11
Occupational exposure, chromate plants	≤1,000	11
Rural areas	≤0.01	2

[a]References: 1, Ecological Analysts 1981; 2, Langard and Norseth 1979; 3, Towill et al. 1978; 4, Giblin et al. 1980; 5, Turekian and Scott 1967; 6, Pfeiffer et al. 1980; 7, Duval et al. 1980; 8, Bryan et al. 1983; 9, Eisler et al. 1977; 10, Mayer et al. 1981; 11, Steven et al. 1976.

Table 2. Concentrations of total Cr and Cr+6 in air, water, soil, and sludge near industrial sites and sewage outfalls in the United States (modified from Snyder et al. 1977).

	Air (μg/m^3)		Water				Soil	Sludge (mg/L)	
			Filtered (mg/L)		Particulates	Sediments	Total	Inorganic	Organic
Industry	Total	Cr+6	Total	Cr+6	Total (mg/L)	Total (mg/kg)	(mg/kg)	Total	Total
Chromium pigment producer	13.5	2.1	3.3	1.3	59.6	568.0	41.0	-	-
Chromium plating facility	1.1	-	0.6	0.6	0.14	1.2	36.9	-	-
Tanning operation	<0.2	-	2.3	0.1	10.8	14.8	-	-	-
Sewage treatment plant									
Receiving tannery wastes	<0.4	-	0.05	0.001	0.5	23.2	-	13,950.0	101.0
Not receiving tannery wastes	<0.2	-	0.04	<0.001	0.09	-	-	911.0	8.6

Table 3. Chromium concentration in field collections of selected species of marine, freshwater, and terrestrial flora and fauna. Values shown are in mg Cr/kg (ppm) whole organism or designated body part fresh weight (FW), dry weight (DW), or ash weight (AW); ND = nondetectable.

Ecosystem, taxonomic group organism, tissue, location and other variables	Concentration (ppm)	Reference[a]
MARINE		
Algae and macrophytes		
Algae, whole		
Sea of Japan, 12 spp.	1.0-14.0 DW	1
United Kingdom, 11 sp.	2.8-30.0 DW	2
Algae and macrophytes, whole		
Puerto Rico, 18 spp.	0.4-110.0 DW	3
Knotted wrack, *Ascophyllum nodosum*		

Whole		
Norway	4.0 DW	4
Great Britain	1.1-10.0 DW	5,6
Bladder wrack, *Fucus vesiculosus*		
Whole		
United Kingdom	2.6-4.5 DW	4,5,6
Phytoplankton, whole		
Narragansett Bay, RI	4.3-73.3 DW	7
Seaweeds, whole		
Japan, 44 spp.	0.1-2.5 DW	8
Korea, 20 spp.	0.7-7.4 DW	9
Marsh grasses, *Spartina* spp., whole		
Control areas	2.3-3.1 DW	10
From areas treated with sewage-amended sludge		
at 10,300 mg Cr/m^2 over 7-year period	31.0-44.0 DW	10
Coelenterates		
Corals, 34 spp.		
Deep open ocean	0.8-3.0 DW	11
Shallow open ocean	2.0-35.0 DW	11
Shallow coastal zone	0.2-23.0 DW	11
Molluscs		
Red abalone, *Haliotis rufescens*		
Gill	0.6-4.0 DW	12
Mantle	0.0-12.6 DW	12
Digestive gland	2.0-13.2 DW	12
Foot	ND	12
Hardshell clam, *Mercenaria mercenaria*		
Soft parts	3.3-24.7 DW	7
Soft parts	0.2-5.8 FW	13
Soft parts	0.8 DW	14
Shell	0.4 DW	14
Periwinkle, *Littorina littorea*		
Soft parts, United Kingdom	<0.1-1.6 DW	15
Common mussel, *Mytilus edulis*		
Soft parts	0.9-2.7 DW	14,16,17,18,19
Soft parts	0.4-21.0 DW	20
Shell	0.1 DW	18
Shell	1.0-2.0 DW	4
Digestive gland	7.4 FW	21
Hepatopancreas	3.5-15.0 DW	22
Gonad	3.0 FW	21
Muscle	11.0 FW	21
Clam, *Pitar morrhuana*		
Soft parts	14.2 DW	23
Squid, unidentified		
Various tissues	3.1-5.4 DW	24
Crustaceans		
Edible tissues		
7 spp.	0.1-0.2 FW	25
9 spp.	0.2-0.3 FW	25
Crab, *Cancer irroratus*		
Flesh	<0.3-0.6 FW	26
Digestive gland	<0.5-1.2 FW	26
Gills	0.8-2.5 FW	26
Annelids		
Polychaete annelids		

Whole	8.1-14.7 DW	27
Whole	23.8-38.0 DW	7
Annelid worm, *Nereis diversicolor*		
Whole	0.6 DW	19
Echinoderms		
U.K., whole, 5 spp.	DW	28
Puerto Rico, whole, 2 spp.	24.2-43.2 FW	3
Greece, whole, 7 spp.	0.5-13.0 DW	29
Sea cucumber, *Holothuria forskalii*		
Muscle	0.3 DW	16
Tunicates		
Tunicates, whole		
Greece, 2 spp.	5.5-6.6 DW;	30
	0.2-1.1 FW	30
Tunicate, *Podoclavella moluccensis*		
Blood		
Plasma, whole	0.4 DW	31
Plasma fractions 9-12	940.0 DW	31
Cell residues	22.0 DW	31
Elasmobranchs		
Smooth dogfish, *Mustelus canis*		
New York Bight		
Muscle	<0.3 FW	32
Liver	<0.8 FW	32
Fish		
Gills, 7 spp.	<0.1-0.6 FW	33
Gonad, 7 spp.	<0.1-0.3 FW	33
Heart, 7 spp.	<0.1-0.8 FW	33
Kidney, 7 spp.	<0.1-0.3 FW	33
Liver, 86 spp.	<0.1-0.4 FW	25,33
Liver, 4 spp.	0.4-2.0 FW	25
Muscle, 196 spp.	<0.1-1.9 FW	25,33,34,35,36
Muscle, 31 spp.	0.2-7.3 DW	24,35,37
Otoliths, 8 spp.	2.5-6.9 DW	38
Scales, 6 spp.	0.6-97.0 DW	38
Skin, 8 spp.	3.1-8.1 DW	24
Spleen, 7 spp.	<0.1-4.8 FW	34
Vertebrae, 8 spp.	<0.1-1.2 FW	34
Viscera	<0.1-4.5 DW	24,27
Whole, 17 spp.	<0.1-0.8 FW	25
Mammals		
Harbor seal, *Phoca groenlandica*		
Kidney	0.2-0.6 FW	39
Heart	0.7-1.2 FW	39
Spleen	0.8-1.4 FW	39
Brain	1.0-2.8 FW	39
Blubber	<0.5 FW	39
FRESHWATER		
Molluscs		
Snails, 8-9 km below electroplating plant discharge		
Soft parts	450.0 DW	40
Amphibians		
Anurans, Laurel, Maryland		
Tadpoles		

Whole, 2 spp.	1.6-3.8 FW	41
Adults		
Whole, 3 spp.	1.8-5.4 FW	41
Frog, *Rana pipiens*		
Whole	0.5 FW	41
Fish		
Alewife, *Alosa pseudoharengus*		
Whole	1.1 FW	42
Pumpkinseed, *Lepomis gibbosus*		
Whole, Laurel, Maryland	5.7 FW	41
Lake trout, *Salvelinus namaycush*		
Lake Cayuga, New York		
Whole		
Ages 1-10 years	<0.013 FW	43
Age 11	0.032 FW	43
Age 12	0.09 FW	43
Eastern mudminnow, *Umbra pygmaea*		
Whole, Laurel, Maryland	0.9 FW	41
Fish		
Muscle, 12 spp.	0.03-1.1 FW	44
TERRESTRIAL		
Plants		
Big sagebrush, *Artemisia tridentata*		
Whole, Idaho		
Distance from phosphate plant		
Downwind 3 km	270.0-400.0 DW	45
Upwind 3 km	77.0-117.0 DW	45
Fescue, *Festuca arundinacea*		
Distance downwind from drift of cooling towers		
15 meters	342.0 DW	46
130 meters	15.0 DW	46
Control areas	0.6 DW	46
Tobacco, *Nicotiana tabacum*		
Kentucky		
Burley leaf	2.5 DW	47
Cigarette leaf	0.3-6.5 DW	47
Pipe leaf	2.8 DW	47
Cigar leaf	3.1-6.2 DW	47
Rye, *Secale cerealis*		
United States		
Seed	0.05 FW	48
Whole	0.04 FW	48
Ontario, Canada, on sludge-amended soil		
Whole	2.2-3.3 DW	49
Corn, *Zea mays*		
Seed	0.25 DW	44
Kernel	0.02 FW	44
Oil	0.47 FW	44
Meal	0.06-0.13 DW	44
Grain	0.1 DW; 3.4 AW	44
Insects		
Termites, Rhodesia, 2 spp.		
Worker	1,500.0 DW	44
Soldier	300.0 DW	44

Queen	20.0 DW	44
Annelids		
Earthworms		
Whole, 2 spp.	5.0-10.2 DW	44
Earthworm, *Eisenia foetida*		
From sewage treatment plant sludge containing 299-650 ppm Cr		
Whole less gut		
2 weeks residence	1.0 DW	50
28 weeks residence	13.0 DW	50
Grain fed worms	0.8 DW	50
Feeding on cattle manures	ND	50
Birds		
American black duck, *Anas rubripes*		
Egg	0.6 FW	51
Canvasback, *Aythya valisineria*		
Liver	0.02 FW	52
Lesser black-backed gull, *Larus fuscus*		
Muscle, liver, kidney, and egg	<1.0 DW	4
Osprey, *Pandion haliaetus*		
Liver	0.2 FW	54
Brown pelican, Pelecanus occidentalis		
Liver	<0.2 FW	54
Common eider, *Somateria mollissima*		
Muscle, liver, kidney, and egg	<1.0 DW	4
Waterfowl		
Feathers, 4 spp.	<0.05 DW	55
Mammals		
Pronghorn, *Antilocapra americana*		
Hair		
Idaho	1.9-640.0 DW	44
Wyoming	0.3-130.0 DW	44
Coyote, *Canis latrans*		
Hair	0.7-12.0 DW	44
Elk, *Cervus canadensis*		
Hair	1.9-570.0 DW	44
Bighorn sheep, *Ovis canadensis*		
Hair	<0.1 DW	44
Cotton rat, *Sigmodon hispidus*		
Controls		
Bone	0.2 DW	46,56
Pelt	0.1 DW	46,56
Hair	0.4 DW	46,56
GI tract	1.1 DW	46,56
Whole	0.06 FW; 0.19 DW	46,56
Collected 100-130 m from cooling tower drift		
Bone	0.5 DW	46,56
Pelt	1.1 DW	46,56
Hair	4.4 DW	46,56
GI tract	1.0 DW	46,56
Whole	0.12 FW; 0.40 DW	46,56
Western jumping mouse, *Zapus princeps*		
Hair	23.0-45.0 DW	44

[a]References: 1, Gryzhankova et al. 1973; 2, Riley and Roth 1971; 3, Bernhard and Zattera 1975; 4, Lande

1977; 5, Foster 1976; 6, Bryan and Uysal 1978; 7, Phelps et al. 1975; 8, Ishibashi and Yamamoto 1960; 9, Pak et al. 1977; 10, Giblin et al. 1980; 11, Livingston and Thompson, 1971; 12, Anderlini 1974; 13, Shuster and Pringle 1968; 14, Segar et al. 1971; 15, Bryan et al. 1983; 16, Fukai 1965; 17, Graham 1972; 18, Bertine and Goldberg 1972; 19, Bryan and Hummerstone 1977; 20, Karbe et al. 1977; 21, Young and McDermott 1975; 22, Young et al. 1979; 23, Eisler et al. 1978; 24, Horowitz and Presley 1977; 25, Hall et al. 1978; 26, Greig et al. 1977; 27, Fukai and Broquet 1965; 28, Riley and Segar 1970; 29, Papadopoulu et al. 1976; 30, Papadopoulu and Kanias 1977; 31, Hawkins et al. 1980; 32, Greig and Wenzloff 1977; 33, Brooks and Rumsey 1974; 34, Van As et al. 1973; 35, Plaskett and Potter 1979; 36, De Clerck et al. 1979; 37, Roth and Hornung 1977; 38, Papadopoulu and Kassimati 1977; 39, Duinker et al. 1979; 40, Duval et al. 1980; 41, Hall and Mulhern 1984; 42, Lucas et al. 1970; 43, Tong et al. 1974; 44, Jenkins 1980; 45, Gough and Severson 1976; 46, Taylor and Parr 1978; 47, Nadkarni and Ehmann 1970; 48, Schroeder et al. 1962; 49, Bates et al. 1975; 50, Hartenstein et al. 1980; 51, Haseltine et al. 1980; 52, White et al. 1980; 53, Wiemeyer et al. 1980; 54, Blus et al. 1977; 55, Kelsall 1970; 56, Taylor et al. 1975.

Chromium is beneficial but not essential to growth in higher plants. Residues in plants seldom exceed a few parts per million, except in plants living on infertile serpentine soils containing high Cr concentrations, or grown on soils amended with sewage sludge. Plants with elevated Cr residues show no toxic effects, although concentrations in excess of 1 ppm in the aqueous medium may inhibit germination of the seed and growth of roots and shoots (Towill et al. 1978).

Chromium has proved effective in counteracting the deleterious effects of cadmium in rats and of vanadium in chickens. High mortality rates and testicular atrophy occurred in rats subjected to an intraperitoneal injection of cadmium salts; however, pretreatment with Cr ameliorated these effects (Stacey et al. 1983). In chickens, 10 ppm of dietary Cr counteracted adverse effects on albumin metabolism and egg shell quality induced by 10 ppm of vanadium salts (Jensen and Maurice 1980).

Additional research on the beneficial aspects of Cr in living resources appears warranted, especially where the organism is subjected to complex mixtures containing Cr and other potentially toxic heavy metals.

TOXICITY

GENERAL

Biocidal properties of chromium salts to aquatic organisms are modified, sometimes by an order of magnitude or more, by a variety of biological and abiotic factors. These include the species, age, and developmental stage of the organism; the temperature, pH, salinity, and alkalinity of the medium; interaction effects of Cr with other contaminants; duration of exposure; and chemical form of Cr tested. For hexavalent chromium, LC-50 (96 h) values for sensitive freshwater and marine species were between 445 and 2,000 ppb. For trivalent chromium, LC-50 (96 h) concentrations were 2,000 to 3,200 ppb for sensitive freshwater organisms and 3,300 to 7,500 ppb for marine biota.

Among warm-blooded organisms, hexavalent chromium was fatal to dogs in 3 months at 100 ppm in their food and killed most mammalian experimental animals at injected doses of 1 to 5 mg Cr/kg body weight, but had no measurable effect on chickens at dietary levels of 100 ppm over a 32-day period. Trivalent chromium compounds were generally less toxic than hexavalent chromium compounds, but significant differences may occur in uptake of anionic and cationic Cr+3 species, and this difference may affect survival.

AQUATIC ORGANISMS

Records of acute toxicities of hexavalent and trivalent chromium salts to representative species of aquatic life (Table 4) make it clear that Cr+6 is the more toxic to freshwater biota in comparatively soft and acidic waters, that younger life stages are more sensitive than older organisms, and that 96 h is insufficient to attain stable mortality patterns. There are at least five ionic species of hexavalent Cr, of which two—the hydrochromate ion and the chromate ion—are the predominant species and probably the agents that are toxic to freshwater life (Van der Putte et al. 1981b). However, water pH dramatically affects the concentration of each: as pH decreased from 7.8 to 6.5 the hydrochromate ion increased by a factor of about 3, and the chromate ion decreased by a factor of about 6.8 (Van der Putte et al. 1981b). More research is needed to fully elucidate chromium's mode of action. The organisms most sensitive to Cr+6, as judged by 96-h LC-50 values, were freshwater crustaceans and rotifers, and marine crustaceans, for which LC-50 values were 445 to 3,100 ppb;

longer exposures of 28 to 84 days produced LC-50 values of 200 to 500 ppb (Table 4). Other investigators had confirmed that Cr+6 is more toxic to freshwater daphnids and teleosts in water of comparatively low alkalinity, low pH, and low total hardness (Muller 1980). In marine teleosts, the toxicity of Cr+6 increased at elevated temperatures; furthermore, Cr was additive in toxicity when present as a component in a complex mixture of cadmium, zinc, and Cr+6 salts, (Negelski 1976).

For trivalent chromium and freshwater biota, toxicity was significantly increased in comparatively soft waters; this pattern was especially pronounced for daphnids (Table 4). Among freshwater teleosts, survival was reduced at comparatively low pH (EPA 1980). Also, organisms exposed previously to Cr+3 salts were not unusually sensitive or resistant when subjected to additional Cr+3—suggesting that they were unable to acclimatize or to become sensitized to Cr+3 (Stevens and Chapman 1984). As judged by 96-h LC-50 values, Cr+3 was toxic to sensitive freshwater organisms at concentrations of 2,000-3,000 ppb, or slightly less toxic than Cr+6 (Table 4). Toxicity of Cr+3, like that of Cr+6 increased with increasing exposure in rainbow trout. However, Cr+3 was significantly less toxic than Cr+6 in freshwater to salmon fingerlings, and was dramatically less toxic than Cr+6 to polychaetes and crustaceans (but not to molluscs or teleosts) in saltwater (Table 4).

Table 4. Acute toxicities of hexavalent and trivalent chromium to aquatic life.

Chemical species, ecosystem, taxonomic group, organism, modifiers, and other information	Acute toxicity: Concentration (µg/L)	Percent dead	Duration of test[a]	Reference[b]
Hexavalent Chromium				
Freshwater				
Plants	2,500-25,000	50	96 h	1
Rotifers				
Philodena acuticornis				
Water hardness, in mg $CaCO_3$/L				
25	3,100	50	96 h	2
81	15,000	50	96 h	2
Molluscs				
Snail, *Physa heterostropha*				
Water hardness, in mg $CaCO_3$/L				
45	17,300	50	96 h	3
171	31,600-40,600	50	96 h	3
Crustaceans				
Amphipod, *Gammarus pseudolimnaeus*	67,000	50	96 h	3
Freshwater prawn, *Machrobrachium lamarrei*	1,840	50	96 h	4
Cladoceran, *Daphnia magna*	435	50	24 h	5
Fish				
Mud skipper, *Bolephthalmus dussumieri*	30,500	50	96 h	6
Rainbow trout, *Salmo gairdneri*				
Weight 0.2 g				
Water pH 7.8	12,200	50	96 h	7
Water pH 7.0	7,600	50	96 h	7
Water pH 6.5	3,400	50	96 h	7
Weight 25 g				
Water pH 7.8	65,500	50	96 h	7
Water pH 7.0	45,000	50	96 h	7

Water pH 6.5	20,200	50	96 h	7
Fish				
2 spp.	17,600-118,000	50	96 h	8
3 spp.				
Softwater	<18,000	50	96 h	9
Hardwater	>133,000	50	96 h	9
Salmon fingerlings, *Oncorhynchus* sp.	200	53	12 w	9
Goldfish, *Carssius auratus*	110,000	50	96 h	10
Water hardness, in mg $CaCO_3$/L				
20	37,500	50	96 h	3
220	>90,000	50	96 h	3
Bluegill, *Lepomis macrochirus*				
Water hardness, in mg $CaCO_3$/L				
20	118,000	50	96 h	3
44	113,000	50	96 h	3
45	110,000-170,000	50	96 h	3
120	213,000	50	96 h	3
171	130,000-135,000	50	96 h	3
360	133,000	50	96 h	3
Striped bass, *Morone saxatilis*	30,400	50	96 h	3
Marine				
Molluscs				
3 spp.	14,000-105,000	50	96 h	3
Annelids				
Polychaetes				
Neanthes arenaceodentata	550	50	28 d	11
Neanthes arenaceodentata	200	50	56 d	11
Nereis virens	1,000	50	21 d	11
Capitella capitita	280	50	28 d	11
Capitella capitita	5,000	50	96 h	11
4 spp.	2,000-7,500	50	96 h	3
Echinoderms				
Starfish, *Asterias forbesi*	32,000	50	96 h	3
Crustaceans				
7 spp.	2,000-98,000	50	96 h	3
Copepod, *Tisbe holothuriae*	8,100	50	48 h	12
Copepod, *Acartia clausi*	8,830-19,270	50	48 h	13
Blue crab, *Callinectes sapidus*				
Early life stages	930	50	96 h	14
Early life stages	320	50	40 d	14
Fish				
Small-mouthed hardy head, *Atherinasoma*	36,000	50	96 h	8
microstoma	19,300	0	168 h	8
Yellow-eye mullet, *Aldrichetta*	24,000	50	96 h	8
forsteri	17,900	0	96 h	8
Atlantic silverside, *Menidia menidia*				
Larva	12,400-14,300	50	96 h	3
Juvenile	20,100	50	96 h	3
Mummichog, *Fundulus heteroclitus*	91,000	50	96 h	3

Speckled sanddab, *Citharichthys stigmaeus*	30,000-31,000	50	96 h	3
Trivalent chromium				
Freshwater				
Molluscs				
Snail, *Amnicola* sp.	8,400	50	96 h	3
Annelids				
Worm, *Nais* sp.	9,300	50	96 h	3
Arthropods				
Cladoceran, *Daphnia magna*				
Water hardness, in mg $CaCO_3$/L				
48	2,000	50	96 h	3
52	16,800	50	96 h	3
99	27,400	50	96 h	3
110	26,300	50	96 h	3
195	51,400	50	96 h	3
215	58,700	50	96 h	3
Amphiod, *Gammarus* sp.	3,200	50	96 h	3
Insects, 4 spp.	2,000-64,000	50	96 h	3
Fish				
9 spp.	3,300-71,900	50	96 h	3
3 spp.				
Soft water	< 3,000	50	96 h	9
Hard water	72,000	50	96 h	9
Salmon fingerlings	200	0	12 w	9
Rainbow trout				
Juveniles	4,400	50	96 h	15
Eggs	495	100	30 d	15
Fathead minnow				
Water hardness, mg $CaCO_3$/L				
20	5,070	50	96 h	3
203	7,000-29,000	50	96 h	3
360	67,400	50	96 h	3
Marine				
Molluscs				
American oyster, *Crassostrea virginica*	10,300	50	96 h	3
Annelids				
Polychaete, *Neanthes arenaceodentata*	12,500	0	21 d	11
Crustaceans				
Crab, *Sesarma haematocheir*, zoea	56,000	50	96 h	3
Copepod, *Acartia clausi*	17,000	0	48 h	13
Fish				
Yellow-eye mullet	53,000	50	96 h	8
2 spp.	3,300-7,500	50	96 h	8

[a]Abbreviations: h = hour; d = day; w = week.

[b]Reference: 1, Mangi et al. 1978; 2, Buikema et al. 1974; 3, EPA 1980; 4, Murti et al. 1983; 5, Jouany et al. 1982; 6, Krishnaja and Rege 1982; 7, Van der Putte 1981b; 8, Negelski 1976; 9, Steven et al. 1976; 10, Riva et al. 1981; 11, Reish 1977; 12, Moraitou-Apostolopoulou and Verriopoulos 1982a; 13, Moraitou-Apostolopoulou and Verriopoulos 1982b; 14, Bookhout et al. 1984; 15, Stevens and Chapman 1984.

Maximum acceptable toxicant concentrations (MATC) of chromium to aquatic life were derived from life cycle or partial life cycle exposures, and expressed as the highest concentration tested having no significant adverse effect on the characteristics measured—usually survival, growth, and reproduction—and the lowest concentration at which these effects were observed. For Cr and freshwater teleosts, MATC values ranged from as low as 51 to 105 ppb in rainbow trout to as high as 1,000 to 31,950 ppb in fathead minnows (Table 5). The most sensitive saltwater organism tested was a polychaete worm with a MATC range of 17 to 38 ppb (Table 5). For Cr+3 the MATC range for freshwater organisms was 47 to 1,400 ppb, which was quite similar to that for Cr+6 for freshwater life. No MATC data were available for Cr+3 and marine biota.

TERRESTRIAL INVERTEBRATES

Data on toxicity of Cr to terrestrial invertebrates are sparse. Studies conducted in India showed that a concentration of 10 to 15 ppm of Cr+6 in irrigation water, when applied to soils for agricultural purposes, was lethal to two species of earthworms in 58 to 60 days (Soni and Abbasi 1981; Abbasi and Soni 1983).

Table 5. Maximum acceptable toxicant concentration (MATC) values for hexavalent and trivalent chromium to aquatic life based on life cycle or partial life cycle exposures.

Chemical species, ecosystem, organism	MATC (µg/L, ppb)	Reference[a]
Hexavalent chromium		
Freshwater		
Rainbow trout, *Salmo gairdneri*		
Water hardness, mg $CaCO_3$/L		
34	51-105	1
45	200-350	2
Brook trout, *Salvelinus fontinalis*	200-350	2
Fathead minnow, *Pimephales promelas*	1,000-3,950	3
Lake trout, *Salvelinus namaycush*	105-194	1
Channel catfish, *Ictalurus punctatus*	150-305	1
Bluegill, *Lepomis macrochirus*	522-1,122	1
White sucker, *Catostomus commersoni*	290-538	1
Northern pike, *Esox lucius*	538-963	1
Walleye, *Stizostedion vitreum*	>2,161	1
Saltwater		
Polychaete worm, *Neanthes arenaceodentata*	17-38	4
Mysid shrimp, *Mysidopsis bahia*	88-198	2
Trivalent chromium		
Freshwater		
Cladoceran, *Daphnia magna*	47-93	2
Fathead minnow	750-1,400	2
Rainbow trout	30-157	5

[a]References; 1, Sauter et al. 1976; 2, EPA 1980; 3, Pickering 1980; 4, Reish 1977; 5, Stevens and Chapman 1984.

MAMMALS AND BIRDS

Acute and chronic adverse effects of chromium to warm-blooded organisms are caused mainly by Cr+6 compounds; there is little conclusive evidence of toxic effects caused by Cr+2 or Cr+3 compounds (Langard and Norseth 1979). Most investigators agree that chromium in biological materials is probably always in the trivalent state, that greatest exposures of Cr+3 in the general human population are through the diet (but no adverse effects have been reported from such exposures), and that no organic trivalent chromium complexes of toxicological importance have been described. Studies with guinea pigs fed Cr+3 for 21 weeks at concentrations up to 50 ppm dietary Cr+3 showed no adverse effects (Preston et al. 1976). Domestic cats were apparently

unaffected after exposure to aerosol levels of 80 to 115 mg Cr+3/m^3 for 1 h daily for 4 months, or after consuming diets with high amounts of chromic (Cr+3) salts over a similar period (Langard and Norseth 1979). When chromium was administered by injection, trivalent salts were substantially less toxic than hexavalent salts in producing effects in embryos of golden hamsters (Gale 1978). A similar pattern was evident in mice and in embryos of chickens. The LD-50's for mice were 260 mg/kg body weight for Cr+3, but only 5 mg/kg body weight for Cr+6 (Steven et al. 1976). For chicken embryos, the LD-50 values (mg/kg body weight) were 22.9 for Cr+3 and 1.7 for Cr+6 (Ridgeway and Karnofsky 1952). However, survival was depressed in young American black ducks fed 10 or 50 ppm dietary Cr+3 for 10 weeks—suggesting that black duck broods along the Atlantic coast (an area of high anthropogenic chromium discharge) may be adversely affected if they remain in contaminated areas for extended periods (Haseltine et al. 1985). In the black duck study, the authors administered chromium in the form of $CrK(SO_4)_2$ 12 H_2O; absorption of this anionic trivalent chromium compound (and an anionic hexavalent Cr compound) through black duck intestine was superior to that of cationic forms (Eastin et al. 1980).

Steven et al. (1976), in studies with Cr+6 and dogs, showed that 100 ppm in food for 3 months was fatal, that 11.2 ppm in drinking water was not lethal over a 4-year period (although significant accumulation was observed), and that 6.0 ppm in drinking water for 4 years had no measurable effects. In rats, 1,000 ppm dietary Cr+6 represented the toxic threshold, but all animals survived 134 ppm Cr+6 in drinking water for 3 months (Steven et al. 1976). For most mammalian experimental animals, including mice, dogs, rabbits, cats, and guinea pigs, the minimum injected fatal dose of Cr+6 ranged from 1 to 5 mg/kg body weight—although doses of 0.2 to 0.5 mg/kg body weight produced marked kidney damage (Steven et al. 1976). Repeated sublethal injections of Cr+6 did not promote tolerance in mice, but rather decreased the minimum lethal dose, suggesting that the animals were unable to develop tolerance to repeated chromium exposures (Steven et al. 1976). Investigators have not yet been able to identify a specific hexavalent Cr compound, or group of compounds, that could account for the most pronounced biological activity (Langard and Norseth 1979). A lethal oral dose of Cr+6 for a 14-year-old boy was estimated to be 10 mg/kg body weight—much lower than that tolerated by test animals on a repeated basis over a period of several months (Steven et al. 1976). Domestic chickens appear to be more resistant than mammals. No adverse effects were observed in chickens exposed to 100 ppm dietary Cr+6 in a 32-day study (Bosomer et al. 1961), although embryolethal and teratogenic effects have been observed in the range of 0.2 mg/kg (Gilani and Marano 1979) to 1.7-22.9 mg/kg (Ridgeway and Karnofsky 1952), depending on the method of administration.

SUBLETHAL EFFECTS

GENERAL

Under laboratory conditions, chromium is mutagenic, carcinogenic, and teratogenic to a wide variety of organisms, and Cr+6 has the greatest biological activity. However, information is lacking on the biological activities of water soluble Cr+3 compounds, organochromium compounds, and their ionic states. Aquatic plants and marine polychaete worms appear to be the most sensitive groups tested. In exposures to Cr+6, growth of algae was inhibited at 10.0 ppb, and reproduction of worms at 12.5 ppb. At higher concentrations, Cr+6 is associated with abnormal enzyme activities, altered blood chemistry, lowered resistance to pathogenic organisms, behavioral modifications, disrupted feeding, histopathology, osmoregulatory upset, alterations in population structure and species diversity indices, and inhibition of photosynthesis. Not all sublethal effects observed were permanent, but the potential for acclimatization of organisms to Cr is not well documented. The great variability among species and tissues in the accumulation or concentration of Cr is attributed partly to the route of administration, partly to the concentration of Cr and its chemical species, and partly to numerous biotic and physicochemical modifiers. High accumulations of Cr have been recorded among organisms from the lower trophic levels, but there is little evidence of biomagnification through food chains. Marine bivalve molluscs, for example, accumulated measurable concentrations at ambient water concentrations of 5.0 ppb of Cr+6, but the significance of Cr residues in molluscs and other organisms is not well understood. Depuration of accumulated Cr among organisms differs markedly, but usually follows a complex multicompartmental excretion pattern.

AQUATIC ORGANISMS: FRESHWATER

BACTERIA

The role of sewage bacteria in Cr kinetics and cycling is unresolved and promises to be a fruitful field of research. Of 362 bacterial isolates from Cr+6 liquid sanitary sewage and chemical waste sludges, only 1—an

isolate of *Arthrobacter* sp.—could tolerate 400 ppm of Cr+6 (Coleman and Paran 1983); however, this isolate could not effectively accumulate Cr at low ambient levels of 5 ppm of Cr+6, whereas *Agrobacter* sp., another isolate, could. Hexavalent Cr in a wide array of forms showed dose dependent responses for mutagenic activity in the bacterium *Salmonella typhimurium* (Del Carratore et al. 1984); moreover, among 56 metal compounds tested, Cr+6 elicited the strongest mutagenic responses in *Bacillus subtilis* (Hatherill 1981). In some tests, Cr+3 was genetically active, but only when present as a stable organic complex (Del Carratore et al. 1984).

ALGAE AND MACROPHYTES

Growth of freshwater algae was reduced at Cr+6 concentrations of 10 ppb for *Chlamydomonas reinhardi* and >45 ppb for other species tested; effects were most pronounced in water of low alkalinity (EPA 1980). Frond growth of the common duckweed, *Lemna minor*, the most sensitive aquatic plant tested, was reduced at 10 ppb Cr+6 in days (Mangi et al. 1978). Jouany et al. (1982) reported that a green alga, *Chlorella vulgaris*, biomagnified Cr+6 from the medium about 1000X in 28 days at ambient concentrations of 300 ppb; growth was inhibited at 445 ppb Cr+6 in 96 hours, and adenosine triphosphate (ATP) production was reduced at 470 ppb in 24 hours. At 10 ppb Cr+6 in the medium, bioconcentration factors for the chlorophytes *Hydrodictyon reticulatum* and *Oedogonium* sp. ranged from 200 to 600X in 14 days (Mangi et al. 1978). Accumulation of Cr by living and dead plant tissue is extensive, uptake linearly approximating concentration on a logarithmic basis (Mangi et al. 1978).

Trivalent chromium is far less effective than Cr+6 in producing root weight inhibition in Eurasian watermilfoil, *Myriophyllum spicatum*: 9,900 ppb Cr+3 vs. 1,900 ppb Cr+6 (EPA 1980).

INVERTEBRATES

Hexavalent chromium was associated with adverse effects in invertebrates of widely separated taxa: reduced survival and fecundity of the cladoceran *Daphnia magna* at a concentration of 10 ppb and exposure for 32 days (EPA 1980); growth inhibition of the protozoan *Chilomonas paramecium* at 1,100-3,000 ppb at temperatures of 10-30 °C during exposures of 19-163 h (Honig et al. 1980); abnormal movement patterns of larvae of the midge *Chironomus tentans* at 100 ppb in 48 h (Catalan 1982); and a temporary decrease in hemolymph glucose levels in the freshwater prawn *Macrobrachium lamarrei* surviving 1,840 ppb Cr+6 for 96 h (Murti et al. 1983).

Trivalent Cr was less effective than Cr+6 in reducing fecundity of *Daphnia magna*: 44 ppb Cr+3 vs. 10 ppb Cr+6 (EPA 1980). Annelid worms (*Tubifex* sp.) accumulated about 1 ppm Cr during exposure for 2 weeks in sediments containing 175 ppm Cr+3, suggesting that benthic invertebrates have only a limited ability to accumulate chromium from sediments or clays (Neff et al. 1978).

FISH

Among sensitive species of freshwater teleosts, Cr+6 concentrations of 16 to 21 ppb in the medium resulted in reduced growth of rainbow trout and chinook salmon fingerlings during exposure of 14 to 16 weeks, and altered plasma cortisol metabolism in rainbow trout after 7 days; locomotor activity in bluegills increased after 2 weeks in 50 ppb Cr+6 (EPA 1980). Long-term exposure of rainbow trout by Calamari et al. (1982) for 180 days to high, but environmentally realistic, concentrations of 0.2 ppm Cr+6 resulted in elevated levels of Cr in kidney (3.5 mg/kg fresh weight), liver (2.0), and muscle (0.6); after 90 days in Cr-free media, Cr levels were 1.6, 1.3, and 0.5, respectively. Time required to reach median asymptotic uptake ranged from 36 to 55 days for various tissues; extrapolated values for almost complete equilibrium were 237 to 365 days (Calamari et al. 1982). The rudd (*Scardinus erythrophthalmus*), exposed to Cr+6 for 24 hours, did not accumulate detectable levels of Cr in tissues during exposure to 16 ppm, but did during exposures to 20 ppm; the kidney contained the highest residues—10.3 mg Cr/kg fresh weight (Van Hoof and Van San 1981).

At high environmental concentrations of Cr+6 (i.e., 2.0 ppm in water) and at alkaline pH, concentrations in rainbow trout tissues were greatest in gill, liver, kidney, and digestive tract; after transfer of the fish to Cr-free media, residues tended to remain high in kidney and liver; concentration in gill tissues tended to be greater at pH 7.8 than at pH 6.5 (Van der Putte et al. 1981a). Studies with perfused gills showed that the transfer of Cr was directly coupled with the transfer of oxygen from the external solution to the internal perfusion medium and that this transfer was significantly more rapid at pH 6.5 than at alkaline pH (Van der Putte and Part 1982). Uptake rate of Cr+6 was rapid, equilibrium usually being reached in 2 to 4 days of exposure for various tissues,

except for gill, which continued to accumulate Cr with increasing exposure at acidic pH. In rainbow trout, the excretion pattern was biphasic. The biological half-life of the short-lived component (34% of the total Cr) was 1.0 day, and that of the long-lived component was 25.6 days (Van der Putte et al. 1981a). Other sublethal effects were observed in freshwater teleosts following Cr+6 insult. In the snakehead (*Channa punctatus*), enzyme activities were altered in a wide variety of organs and tissues after exposure for 30 days to 2.6 ppm (Sastry and Sunita 1984); the effects became life threatening after exposure for 120 days (Sastry and Tyagi 1982; Sastry and Sunita 1982,1983). In the mud skipper (*Boleophthalmus dussumieri*), chromosomal aberrations in the gill increased after injection of 1.0 mg/kg body weight, or exposure to 24 ppm in the medium for 24 h (Krishnaja and Rege 1982). In juvenile coho salmon (*Oncorhynchus kisutch*), disease resistance and serum agglutinin production both decreased after 2 weeks in water containing 0.5 ppm (Sugatt 1980b). In seaward migrating coho salmon, salinity tolerance and serum osmolality were impaired during exposure to 0.23 ppm Cr+6 for 4 weeks (Sugatt 1980a).

Chromium uptakes and effects in teleosts were modified significantly by many biological and abiotic variables, including water temperature and pH, the presence of other contaminants or compounds, and sex and tissue specificity. In rainbow trout, only males showed significant changes in liver enzyme activity during exposure to 0.2 ppm Cr+6 for 6 months; the effects were intensified by the presence of nickel and cadmium salts in solution (Arillo et al. 1982). Rainbow trout are able to regulate Cr somewhat, either actively, by reduced absorption or increased excretion, or passively, by the limitation of binding sites for Cr *in vivo* (Buhler et al. 1977). Tests with goldfish and high Cr+6 concentrations indicated that toxic and sublethal effects were more pronounced at comparatively high water temperatures and reduced pH; further, Cr residue levels were abnormally high in dead or moribund fish, suggesting that residue values from dead or dying fish should be interpreted with extreme caution (Riva et al. 1981). In rainbow trout, acute Cr poisoning caused morphological changes in gills, kidney, and stomach tissues at pH 7.8, but only in the gills at pH 6.5 (Van der Putte et al. 1981b). Chromium uptake in trout increased when 10 ppb of ionic cadmium was present in solution (Calamari et al. 1982)—again demonstrating that uptake patterns are not necessarily predictable for single components in complex mixtures.

AQUATIC ORGANISMS: MARINE

ALGAE AND MACROPHYTES

Algae and higher plants accumulated chromium from seawater by factors up to 8,600 (Van As et al. 1973), and from solutions containing 50 ppm Cr by a factor of 18 in 48 h (Sivalingam 1978). Algae also accumulated Cr from sewage sludge, showing increases in Cr of 25 to 60 mg/kg dry weight (Montgomery et al. 1978). The unusually high Cr concentrations observed in some species of algae and macrophytes from Narragansett Bay, Rhode Island (Phelps et al. 1975) and from Puerto Rico (Bernhard and Zattera 1975) almost certainly came from chromium wastes discharged from electroplaters (in Narragansett Bay) and from other anthropogenic sources (in Puerto Rico). A similar situation probably exists wherever grossly elevated Cr levels are observed.

Although chromium is abundant in primary producers, there is little evidence of biomagnification through marine food chains consisting of herbivores and carnivores (Osterberg et al. 1964). Baptist and Lewis (1969) followed the transfer of assimilated and unassimilated radiochromium through an experimental food chain that included phytoplankton, brine shrimp, postlarval fish, and adult fish. When chromium was successively transferred through each of the four trophic levels, concentrations declined after each transfer. Comparisons of the results from the food chain with laboratory studies on chromium uptake from seawater suggest that the food chain, despite the successive declines, was generally the more efficient pathway for uptake of chromium by all trophic levels.

Among sensitive species of marine algae, concentrations of 10 ppb of Cr+6 partly inhibited growth of *Olisthodiscus lutens*. All cultures, including those in which growth was inhibited, contained viable, active (75%) cells at the end of 10 days. Inhibitory effects were reversed by chelators such as EDTA (Mahoney 1982), suggesting that naturally occurring ligands and sequestering agents in seawater may alleviate the toxicity of Cr+6, and perhaps other metals. In the giant kelp (*Macrocystis pyrifera*), photosynthesis was inhibited 20% in 5 days at 1,000 ppb of Cr+6, and 50% in 4 days at 5,000 ppb (EPA 1980); this kelp appears to be one of the more resistant aquatic plants.

MOLLUSCS

Edible tissues of commercially important North American molluscs contained 0.1 to 0.6 mg Cr/kg fresh weight (Hall et al. 1978). Although this concentration is in general agreement with molluscan data from other geographic areas (Eisler 1981), Shuster and Pringle (1968) reported values (mg Cr/kg fresh weight) in edible portions as high as 3.4 in oysters (*Crassostrea virginica*), 5.8 in hardshell clams (*Mercenaria mercenaria*), and 5.0 in softshell clams (*Mya arenaria*). The ability of marine molluscs to accumulate Cr far in excess of that in ambient seawater was documented by Papadopoulu (1973), who found that the Cr concentration in 5 species of bivalves from Greek waters exceeded that in seawater by 16,000 times (*Pinna nobilis*) to 260,000 times (*Astralium rogosum*). No deleterious health effects have been reported among consumers of molluscs that contained occasional high Cr residues. Anthropogenic and natural chromium gradients in sediments or the water column were reflected in the wide range of values reported for this element in field collections of clams (Phelps et al. 1975; Eisler et al. 1978) and mussels (Alexander and Young 1976; Fowler and Oregioni 1976; Lande 1977; Karbe et al. 1977).

Two factors known to modify Cr accumulations in molluscs are the weight of the organism and the salinity of the medium. Concentrations of Cr in clams were reported to decrease with increasing body weight (Eisler et al. 1978) and increasing salinity (Olson and Harrel 1973). Accumulation of Cr by oysters (*Crassostrea gigas*) was independent of sediment Cr levels and dependent on organism size—suggesting some homeostatic regulation of this metal (Ayling 1974). In a 20-week laboratory study of chromium accumulation rates by oysters (Shuster and Pringle (1969) continuously subjected the animals to seawater solutions containing 50 or 100 ppb Cr+6. After 5, 10, or 20 weeks in 50 ppb, maximum whole body concentrations (mg Cr/kg fresh weight) were 2.4, 3.7, and 6.3, respectively (up from control values of <0.12); in 100 ppb, the values were 4.4 (5 weeks), 6.4 (10 weeks), and 11.5 (20 weeks). Preston (1971) concluded that *C. virginica*, under laboratory conditions, accumulated Cr more readily by direct absorption from the medium than from ingestion of radiochromium-labeled algae (*Chlamydomonas* spp.). In natural environments, however, Cr concentration is likely to be greater in the food supply than in the water. As a consequence, food might be the primary source of Cr to oysters, even though accumulation occurs more readily by direct absorption (Preston 1971).

Clams, oysters, and mussels accumulate Cr from the medium or from contaminated sediments at comparatively low concentrations. For example, oysters subjected to 5.0 ppb of Cr+6 for 12 weeks contained 3.1 mg Cr/kg dry weight in soft parts and retained 52% of the accumulated Cr after they were transferred to Cr-free seawater for 28 weeks (Zaroogian and Johnson 1983). Mussels (*Mytilus edulis*) subjected to the same dose-time regimen contained 4.8 mg/kg, but retained only 39% after 28 weeks of depuration. Both oysters and mussels contained higher residues after exposure to 10.0 ppb Cr+6 for 12 weeks—5.6 and 9.4 mg Cr/kg dry weight in soft parts, respectively—and both contained substantial (30-58%) residues after 28 weeks in a Cr-free environment (Zaroogian and Johnson 1983). In studies with mussels and softshell clams (*Mya arenaria*), Capuzzo and Sasner (1977) demonstrated that Cr in New Hampshire sediments (contaminated with Cr+3 from tannery wastes) was bioavailable to clams by diffusion from seawater, and that both diffusion and particulate uptake were important pathways for mussels. Accumulation was observed at sediment Cr concentrations as low as 150 ppm. Kaolinite sediments containing up to 1,200 ppm of Cr+3 produced the most pronounced adverse effects on filtration rates and ciliary activity of bivalve molluscs, leading the authors to conclude that Cr that has accumulated in areas affected by industrial wastes might have serious consequences to filter feeding bivalves.

It is emphasized that Cr+3, probably because of its very low solubility in seawater, appears to have a much lower bioavailability to most groups of marine animals than Cr+6, which is more water soluble (Carr et al. 1982). The clam *Rangia cuneata* appears to be an exception: it accumulated up to 19 mg Cr/kg in soft parts, on a dry weight basis, during exposure for 16 days to chromium-contaminated muds, and retained most of it for an extended period; the estimated biological half-time was 11 days (Carr et al. 1982). In general, benthic invertebrates rarely accumulate Cr from contaminated sediments (82-188 ppm Cr+3); only a few examples have been recorded (Neff et al. 1978).

NEMATODES

Representatives of this phylum have been used extensively as indicators of stressed environments. Population structure and species diversity of free-living nematodes inhabiting sediments in the New York Bight were moderately influenced by the heavy metal content of sands. In medium-grained sands, species diversity was inversely correlated with increased concentrations of Cr and other metals. Sands containing 3.0 to 21.5 mg

Cr/kg were also marked by high relative abundances of one or two nematode species; the tolerance of these species to Cr stress probably exceeded that of the normal nematode inhabitants of such sediments (Tietjen 1980).

CRUSTACEANS

In general, chromium seldom exceeds 0.3 mg/kg fresh weight in edible crustacean tissues (Eisler 1981). The highest value (0.6 mg Cr/kg fresh weight) reported in muscle of rock crab (*Cancer irroratus*) was from specimens collected near an ocean dump site receiving large quantities of metals. Digestive glands and gills from these crabs also contained the highest Cr residues for these tissues in crustaceans (Greig et al. 1977).

Sather (1967) observed that uptake and loss of radiochromium by the crab *Podophthalmus vigil* was independent of sex and eyestalk hormone influences. Most of the radiochromium accumulated in gills. Equilibrium was reached in gill and muscle in 2-3 days, but in midgut and hemolymph in 4-5 days. Iron interfered with chromium uptake and retention. Tennant and Forster (1969) demonstrated that Cr concentrated in setae, gills, and hepatopancreas of Dungeness crab (*Cancer magister*) and suggested that surface adsorption and physiological processes were both instrumental in Cr accumulation. Barnacles (*Balanus* sp.) incorporated Cr+6 in soft tissues up to 1,000X over ambient concentrations, reaching equilibrium in 7 days (biological half-life for some components was 120 days); however, Cr+3, which precipitates in seawater, was quickly removed by filtering activity, was not concentrated in soft tissues, and was rapidly excreted by way of the digestive system (^{51}Cr (VI) and ^{51}Cr (III) by barnacles (van Weerelt et al. 1984).

Sediment Cr concentrations of 3,200 ppm in the New Bedford (Massachusetts) Acushnet estuary, and 100 ppm in the New York Bight have been recorded (Doughtie et al. 1983). Massive cuticular lesions suggestive of shell disease characterized up to 30% of the lobsters, crabs, and shrimp collected from the New York Bight, and these lesions could also be induced in crustaceans exposed to New York Bight sediments in the laboratory. This shell disease syndrome has been induced in 41% of grass shrimp (*Palaemonetes pugio*) during exposure to 0.5 ppm Cr+6 for 28 days (Doughtie et al. 1983). It is proposed that Cr interferes with the normal functions of subcuticular epithelium, particularly cuticle formation, and subsequently causes structural weaknesses or perforations to develop in the cuticle of newly molted shrimp. Because of these Cr-induced exoskeletal deficiencies, a viaduct for pathogenic bacteria and direct Cr influx is formed that perpetuates the development of the lesion.

Of the 65,000 tons of Cr compounds used annually in exploratory oil drilling, a significant portion enters the marine environment through the discharge of used drilling muds. It has been estimated that more than 225 tons of drilling mud may be used in a single 3,000-m well (Carr et al. 1982). One of the most frequently used muds in offshore drilling operations is a chrome lignosulphonate mud containing barium sulphonate, bentonite clay, and ferrochrome or chrome lignosulphonates (Carr et al. 1982). The bioavailability of Cr to grass shrimp from used chrome lignosulphonate drilling muds is most pronounced at the mud aqueous layers. At Cr concentrations of 248 ppb in the mud aqueous fraction, grass shrimp accumulated 23.7 mg Cr/kg dry weight whole body after 7 days (Carr et al. 1982). Concentrations of drilling mud of 1% or greater in seawater were toxic to sensitive species of crustaceans (Neff et al. 1981); uptake of 4 to 5 mg/kg was reported in grass shrimp exposed to sediments containing 188 ppm Cr (Neff et al. 1978). The toxicity of Cr-contaminated drilling muds to grass shrimp may sometimes be attributable to large residuals of petroleum hydrocarbons in the sediments (Conklin et al. 1983).

ANNELIDS

Uptake and excretion studies of Cr+3 by *Hermione hystrix* (Chipman 1967) showed that Cr+3 was not readily accumulated from seawater, owing to the formation of particles and surface adsorption phenomena; furthermore, little accumulation was evident on contact with contaminated sediments. Hexavalent chromium in the medium was readily accumulated by *Hermione*; the process was slow and only small amounts were taken up in 19 days—i.e., 0.03 to 0.10 mg/kg fresh weight from media containing 3 to 10 ppb Cr+6. Higher body burdens of 0.5 to 1.8 mg Cr/kg fresh body weight were reported at 100 to 500 ppb of Cr+6, but some deaths were noted at these concentrations. Chromium accumulation by *Hermione* is a passive process and directly related to Cr+6 concentration in the medium. At least two rates of biological loss are involved—one of 8 days and another of 123 days. Chipman (1967) concluded that most of the Cr accumulated by *Hermione* from long exposure is bound in a body component having a slow turnover rate and an estimated biological half-life of

about 123 days.

Uptake of Cr+6 from seawater has been reported for *Neanthes arenaceodentata*. Whole *Neanthes* contained 30.0 mg Cr/kg dry weight after exposure for 150 days in ppb of Cr+6 (Mearns and Young 1977) and 0.5 to 1.6 mg Cr/kg fresh weight after exposure for 440 days (Oshida et al. 1976); both of these observations were similar to those of Chipman (1967), after adjustment for wet and dry weights. Concentrations as low as 12.5 ppb of Cr+6 decreased brood size in *Neanthes* (Mearns et al. 1976; Oshida et al. 1976), although no significant body residues were evident. Uptake of Cr+6 by *Neanthes* was related to dose at low ambient Cr concentrations. Worms subjected to 2.6, 4.5, 9.8, or 16.6 ppb Cr+6 for 309 days contained 0.5, 0.7, 2.2, and 2.5 mg Cr/kg whole fresh organism, respectively (Oshida and Word 1982). There was no direct relationship between tissue concentration and brood size, suggesting that Cr in *Neanthes* attaches to proteins in the body wall, gut, and parapodial regions (Oshida and Word 1982).

Neanthes arenaceodentata is the most sensitive marine organism yet tested. In worms exposed to sublethal concentrations of Cr+6, feeding was disrupted after 14 days at 79 ppb (EPA 1980), reproduction ceased after 440 days (three generations) at 100 ppb (Oshida et al. 1981), brood size was reduced after 309 to 440 days at 12.5 to 16.0 ppb (Oshida et al. 1981; Oshida and Word 1982), and abnormalities in larval development increased after 5 months at 25 ppb (Reish 1977). On the other hand, exposure for 293 days (two generations) in 50,400 ppb Cr+3 caused no adverse effects on survival, maturation time required for spawning, or brood size (Oshida et al. 1981). The polychaete *Capitella capitata* was more resistant than *Neanthes*; a decrease in brood size was noted only after exposure for 5 months to 50 and 100 ppb Cr+6 (EPA 1980).

ECHINODERMS

With the exception of two sea urchin samples collected from Puerto Rico, most Cr residues reported in echinoderms have been less than 1.0 mg/kg dry weight (Eisler 1981). The exceptions—elevated levels of 24 and 43 mg/kg fresh weight of whole organism in Puerto Rican sea urchins—were not reflected in sea cucumber muscle from the same vicinity (Fukai 1965), and thus should be viewed with caution. Echinoderms from the United Kingdom and environs were comparatively low in chromium; concentrations were less than 0.46 mg Cr/kg dry weight whole organism (Riley and Segar 1970). Embryos of a sea urchin (*Anthocidaris* sp.) developed normally in solutions containing 3.2 to 4.2 mg Cr/L, but failed to develop at 8.4-10.0 mg Cr/L (Okubo and Okubo 1962; Kobayashi 1971). Larvae of another species of sea urchin (*Hemicentrotus* sp.) were more sensitive, showing abnormal development or dying within 24 h at concentrations of less than 1.0 mg Cr/L (Okubo and Okubo 1962). Hexavalent chromium at 6.0 mg/L was associated with abnormal development in embryos of *Anthocidaris crassispina* (Kobayashi 1977).

FISH

Individual tissues of most species of finfishes contained between 0.1 and 0.6 mg Cr/kg fresh weight (Hall et al. 1978). For still unexplained reasons, chromium concentrated in the scales of some species collected in Greek waters, values ranging up to 97.0 mg Cr/kg dry weight (Papadopoulu and Kassimati 1977). Chromium concentrations also vary significantly among different species of fish collected from the same geographic area. For example, muscle Cr concentration was 1,430X greater in a porgy (*Pachymetopan qrande*) than in a goosefish (*Lophius piscatorius*) from the same collection (Van As et al. 1973).

Accumulation of chromium under controlled conditions has been documented for speckled sanddab (Mearns and Young 1977) and Atlantic croaker (Baptist et al. 1970). Sanddabs held in seawater solutions containing 3 to 5 ppm Cr+6 contained up to 100 mg Cr/kg intestine (dry weight), 10 in liver, and 3 in muscle (Mearns and Young 1977). Sanddabs accumulated significant concentrations of Cr in various tissues during long-term exposure in seawater concentrations as low as 16 ppb Cr+6 (Mearns and Young 1977). Baptist et al. (1970), who studied the retention of radiochromium-51 in croakers following a single intraperitoneal injection, wrote that retention was expressed as two exponential rate functions: 70 days for the long-lived component and 20 days for the short-lived component.

BIRDS

Male domestic chickens fed diets containing up to 100 ppm of Cr+6 for 32 days showed no adverse effects in survival, growth, or food utilization efficiency (Rosomer et al. 1961). However, teratogenic effects were documented in chicken embryos after eggs had been injected with Cr+6. Deformities included short and twisted

limbs, microphthalmia, exencephaly, everted viscera, growth stunting, and parrot beaks (Ridgeway and Karnofsky 1952; Gilani and Marano 1979). The highest incidence of teratogenic effects was observed at Cr+6 concentrations that caused some deaths, and when the administration route was through the chorioallantoic membrane as opposed to the yolk; no teratogenic effects were observed with Cr+3 salts (Ridgeway and Karnofsky 1952).

Young American black ducks (*Anas rubripes*) absorbed anionic Cr species more readily than cationic forms from the intestines, strongly indicating that ionic Cr state should be considered when avian dietary toxicity studies are being planned (Eastin et al. 1980). Adult black ducks fed diets containing 10 or 50 ppm anionic Cr+3, as Cr $K(SO_4)_2.12\ H_2O$, for 5 months were normal in survival, reproduction, and blood chemistry. However, in ducklings from treated groups that were fed Cr-contaminated diets at original parental dosages, growth patterns were altered and survival was reduced (Haseltine et al. 1985). In another study with black ducks, adults were fed diets containing 0, 20, or 100 ppm anionic Cr+3 and ducklings from these pairs were fed the same diets for 7 days; tests of avoidance responses of the ducklings to a fright stimulus showed that the Cr had no significant effect on their behavior (Heinz and Haseltine 1981).

MAMMALS

Chromium is causally associated with mutations and malignancy (Leonard and Lawerys 1980; Norseth 1981). Under appropriate conditions, Cr is a human and animal carcinogenic agent; its biological effects depend on chemical form, solubility, and valence. In general, Cr+6 compounds are hazardous to animals, whereas metallic Cr and Cr+3 are essentially nontoxic (Gale 1978); however, exposure to water solubilized Cr+3 has caused cancers and dermatitis in workers, and toxicity in rabbits (Hatherill 1981). In the chromate producing industry workers who developed respiratory cancer had been exposed to 30 to 1,100 ug/m^3 Cr in air for periods of 4 to 24 years, and workers producing chromate pigment who developed respiratory cancer had been subjected to an estimated Cr+6 exposure of 500 to 1,500 ug/m^3 for 6 to 9 years. Carcinogens released in the chromate manufacturing process have not yet been identified (Post and Campbell 1980). Levels as low as 10 ug/m^3 of Cr+6 in air produced strong irritation in nasal membranes, even after short exposures. In some persons whose lower respiratory tissues became Cr-sensitized, asthmatic attacks occurred at levels of Cr+6 as low as 2.5 ug/m^3 (Steven et al. 1976). There is no evidence of Cr sensitization in mammals other than humans. In the only animal study demonstrating a carcinogenic effect of an inhaled chromate, adenocarcinomas were reported in the bronchial tree of mice exposed throughout life to $CaCrO_4$ dust at 13 mg/m^3 (4,330 ug Cr+6/m^3) for 35 h weekly (Langard and Norseth 1979). Trivalent Cr compounds did not produce respiratory cancers (Steven et al. 1976). In rabbits, both Cr+3 and Cr+6, given 1.7 mg/kg body weight daily for 6 weeks, adversely affected blood and serum chemistry, and both produced significant morphological changes in liver (Tandon et al. 1978); similar results were observed in rats (Laj et al. 1984). Although damage effects and residue accumulations were greater in rabbits treated with Cr+6, water soluble Cr+3 compounds also may have significant biological activity (Tandon et al. 1978).

Hexavalent Cr compounds may cause skin ulceration, irritative dermatitis, ulcerations in mucous membranes, and perforations of the nasal septum. That inhalation of Cr+6 compounds may cause bronchial carcinomas has been well documented in humans (Langard and Norseth 1979). Skin lesions or ulcers were produced in guinea pigs when solutions containing 30,000 ppm of Cr+6 were applied to abraded skin or if the natural oils were removed from the skin beforehand; Cr+3 in concentrations as high as 100,000 ppm had no ulcerogenic effects (Steven et al. 1976). Allergic guinea pigs developed dermatitis when exposed to solutions of either Cr+6 or Cr+3 at concentrations as low as 10 ppb (Steven et al. 1976). In nonallergic animals, these effects were observed after repeated exposures to solutions containing 1,000 to 3,000 ppm of Cr+3 or Cr+6 salts. Local sarcomas in muscle and local carcinomas of the skin have also been demonstrated in small laboratory animals exposed to Cr+6 (Langard and Norseth 1979). Kidney and liver lesions in rats were observed when the drinking water contained 134 ppm of Cr+6 for 2 to 3 months (Steven et al. 1976).

Hexavalent Cr has established its mutagenic activity in a wide array of screening tests, whereas insoluble Cr+3 forms appear to be inactive, in analogous evaluations—perhaps because Cr+3 absorption is poor in the systems analyzed (Hatherill 1981). Studies with tissue cultures of ovary cells of the Chinese hamster showed that the addition of 52 ppb of Cr+6 not only induced sister chromatid exchanges but also inhibited cell

proliferation; there was no measurable effect at 0.52 ppb Cr+6. Trivalent Cr at 520 ppb did not measurably affect cell proliferation or chromatid exchanges (Uyeki and Nishio 1983). Genotoxic effects of Cr+6 are reversed by the addition of reducing agents or ascorbic acid (Hatherill 1981; Uyeki and Nishio 1983). Chromosomal rearrangements and aberrations were recorded in rabbit cells after exposure to Cr+6 (Hatherill 1981). Teratogenic effects induced by intravenous administration of 5 mg Cr+6/kg body weight to pregnant golden hamsters included cleft palates and defects in the ossification of the skeletal system (Gale 1978).

Accumulations of Cr in tissues and organism depend heavily on its chemical form, route of entry, and amount administered (Yamaguchi et al. 1983). Tissue accumulations were significant in dogs exposed to drinking water concentrations of 11.2 ppm Cr; but were nil at 6 ppm (Steven et al. 1976). Although both Cr+3 and +6 accumulated in brain, kidney, and myocardium of rabbits, the accumulation of Cr+6 was highest in brain and that of Cr+3 in kidney; for both valence states there was no correlation between dose and concentration of stored Cr, or extent of tissue damage (Hatherill 1981). Tissue residues in mice given 0.1 ppm Cr+6 in food and water during lifetime exposure ranged from 0.1 mg Cr/kg fresh weight in liver to 0.7 in heart; mice given 5.1 ppm for a similar period contained 0.5 to 1.8 mg Cr/kg fresh weight in tissues, the residues being highest in the heart and spleen (Schroeder et al. 1964). Trivalent Cr was poorly absorbed from the intestinal tract of rats (<1% of an oral dose), whereas absorption of Cr+6 ranged from 3 to 6% (Langard and Norseth 1979). However, both Cr+3 and Cr+6 traverse placental barriers in mice when administered intravenously (Steven et al. 1976; Langard and Norseth 1979). All chemical forms of chromium, except chromates, cleared rapidly from the blood of rats. At dose levels of 60 to 250 ug/kg body weight, Cr+6 tended to accumulate in the reticuloendothelial system, liver, spleen, and bone marrow; at the much lower doses of 10 and 1 ug/kg body weight, major accumulation sites were the bone, marrow, spleen, testes, and epididymis (Langard and Norseth 1979). Female rats given a single i.v. injection of radiochromium-51 depurated the isotope primarily by urinary clearance, and secondarily by fecal and residual clearances over an 11-day period. Retained radiochromium-51 accumulated over time in bone, kidney, spleen, and liver (Onkelinx 1977). For multicompartmental excretion patterns recorded in rats, biological half-lives of the three components were estimated to be 0.5, 5.9, and 83.4 days; in mammals, Cr is excreted primarily in urine (Langard and Norseth 1979). At least three distinct Cr+6 excretion patterns exist in rats: blood has a single component, with a biological half-life of 13.9 days; testes, brain, kidney and lung have two components; and liver has three components with half-lives of 2.4 hours, 52.8 hours, and 15.7 days (Yamaguchi et al. 1983). Excretion patterns for Cr+3 in rats were unpredictable and impossible to calculate (Yamaguchi et al. 1983). The excretion patterns for fecal Cr among 40 grazing Angus cows given 20 g dietary Cr_2O_3 (13.6 g Cr+3) daily for 72 days was diurnal; excretion was lowest at 8 p.m. and highest at 9 a.m. (Hopper et al. 1978).

FIELD INVESTIGATIONS

There is a wealth of data concerning the effects of chromium on living organisms under laboratory conditions simulating those encountered in the vicinity of high Cr discharges and accumulations typical of electroplating plants, tanneries, ocean dumping sites, and municipal waste outfalls. However, little research has been conducted under actual field conditions, except in three general fields: occupational exposures of humans in the chromate industry (discussed earlier), accidental poisoning of livestock resulting from oil-field activities, and Cr accumulations in ecosystems impacted by discharges associated with cooling waters or cooling towers.

All cases of accidental chromate poisoning in cattle have resulted from the exposure of animals to chromate compounds associated with oil field activities. Chromates are used as a corrosion inhibitor between the pipe and casing and are often added to drilling fluids (in the form of chromelignosulfonate) to improve thermal stability. One recorded case involved 20 mature cows and their 8-month-old calves, grazing in a native pasture where an oil well had just been completed. One cow and calf died and another cow and calf became uncoordinated and thin, and the feces contained bloody mucous. The calf soon died. The cow aborted, but appeared to recover completely. Liver from the dead calf had 14.8 mg Cr/kg fresh weight vs 1.8 in controls; levels of arsenic and lead were not elevated (Reagor and McDonald 1980). The cause of death was the consumption by the animals of concentrated sodium chromate found near the well site. In other cases, 2 of 80 heifers died after consuming concentrated zinc chromate, and 10 cows and one calf died after they had ingested ammonium chromate. In poisoned cows, Cr concentrations were 500 mg/kg in stomach contents, 15.8 ppm fresh weight in kidney vs. 3.0 ppm in controls, and 1.1 ppm in blood vs. 0.02 ppm for controls (Kerr and Edwards 1981).

Chromium is widely used as a corrosion inhibitor in cooling waters by the electric power industry. Its use in this capacity involves addition of a Cr+6 salt, typically sodium dichromate, which forms an oxide on metal

surfaces. Chromates are subsequently released to surface waters in high concentrations, compared with background levels of Cr in most freshwaters. In White Oak Lake (Eastern Tennessee), which received chronic inputs of chromates from cooling towers located on two tributary streams, typical Cr+6 concentrations of 3 to 10 ppm in waste effluents produced 100 to 300 ppb of Cr+6 in White Oak Lake vs. 5 ppb in a control area (Elwood et al. 1980). Concentrations of Cr in muscle of bluegills and largemouth bass from White Oak Lake did not differ significantly from those in fish from a control site—suggesting that these species either effectively regulated Cr concentration or that the elevated Cr levels in White Oak Lake (where 20 to 73% of the total chromium was Cr+6) were in a form that was unavailable for absorption into tissues. Elwood et al. (1980) suggested that Cr is an element with a determinant concentration in fish, and that accumulation is independent of environmental concentration. This concept requires validation. Noteworthy is the observation that Cr concentrations were lower in muscle and body of older freshwater teleosts—an observation consistent with the findings of Eisler (1984), who noted that liver Cr decreased with increasing age in marine teleosts.

Cooling towers of uranium enrichment facilities and gaseous diffusion plants, similar to those of 1,000-MW conventional steam electric stations, contain a chromate zinc-phosphate compound to inhibit corrosion and fouling within the cooling system. A small fraction of the cooling water, containing about 20 ppm of Cr+6, becomes entrained within the exit air flow and is deposited as drift on the landscape, together with other salts found in the recirculating water system, such as sodium pentachlorophenate, chromated copper arsenate, and acid copper chromate. Effects of the Cr component on biological systems have been under investigation in Kentucky and Tennessee for many years (Taylor and Parr 1978; Taylor 1980;Taylor et al. 1975, 1979, 1983). Analysis of vegetation along distance gradients from the cooling towers identified areas of significant drift deposition, accumulation, and magnitude of atmospheric transport over the landscape. At 13 m downwind from the point source, plant foliar concentrations of Cr were highest in winter at 1,390 ppm dry weight, decreasing to 190 in spring, and to 173 in summer as the demand for cooling—and hence the operation time of the facility—decreased. Decreased accumulations on foliage probably reflected high mobility due to leaching, and the short life span of individual leaves. In contrast, Cr concentrations in plant litter at 13 m increased from 894 ppm dry weight during winter to 1,890 ppm in summer and 2,140 ppm in autumn. Accumulation of Cr in the litter was probably related to the higher surface-to-volume ratio in the litter biomass resulting from seasonal senescence of foliage. Taylor and his coworkers emphasized that no adverse biological effects were observed in native vegetation bearing high Cr residues. Concentrations in plants and litter decreased with increasing distance from the cooling towers: concentrations in foliage at 168, 530, and 923 m downwind were 157, 10, and 1.3 ppm (dry weight), respectively; for litter, these values were 421, 24, and 5.8. Potted tobacco plants (*Nicotiana tabacum*) proved to be sensitive indicators of Cr contamination. Tobacco plants placed 15 m from the towers contained 30X background levels after 1 week and up to 237 ppm dry weight in 5 weeks; in plants placed 200 m downwind, leaf growth was reduced 75% after 7 weeks. Beetles and crickets collected near the towers contained 9 to 37 ppm Cr in gut contents (vs. 0.5 to 0.8 ppm for controls); however, assimilation rates were not measured. Cotton rats trapped in a fescue field adjacent to a large mechanical draft cooling tower contained up to 10X more Cr in hair, pelt, and bone than controls, but accumulations were negligible in viscera and other internal organs. Licking of the coat by rats appeared to be a primary route of Cr uptake—a likelihood confirmed experimentally by Langard and Nordhagen (1980). Feeding of radiochromium-51 to cotton rats demonstrated low assimilation (0.8%), and rapid initial loss of Cr+6 (99% in 1 day)—suggesting that Cr is neither essential to cotton rats nor accumulated to any great extent through ingestion of drift-contaminated vegetation or inhalation of drift-contaminated air (Taylor 1980). Biological half times of Cr assimilated by man and cotton rats were similar: 616 and 693 days, respectively. The magnitude of the half times suggests that Cr derived from a chromate has a high potential for biological interaction, but that fractional assimilation is very low—thus reducing the likelihood of toxic effects.

CURRENT RECOMMENDATIONS

As reported here, sensitive species of freshwater aquatic organisms showed reduced growth, inhibited reproduction, and increased bioaccumulation at 10.0 ug/L of Cr+6, and other adverse effects at 30.0 ug/L of Cr+3. Among marine organisms, measurable accumulations were recorded in oysters and worms at 5.0 ug/L of Cr+6, algal growth was reduced at 10.0 ug/L, and reproduction of polychaete annelid worms was inhibited at 12.5 ug/L; in all situations, Cr+3 was less damaging than Cr+6. For birds and mammals, dietary levels of 10.0 mg Cr+3/kg adversely affected young black ducks, and 5.1 mg Cr+6/kg in food and water of mice was associated with elevated tissue residues. The significance of Cr residues is unclear, but available evidence suggests that organs and tissues of fish and wildlife that contain 4.0 mg total Cr/kg dry weight should be viewed

as presumptive evidence of Cr contamination. Aerosol concentrations in excess of 10.0 ug Cr+6/m^3 are potentially harmful to human health; in the absence of supporting data, this value is recommended for protection of sensitive species of wildlife, especially migratory waterfowl.

Proposed criteria for the protection of various environmental compartments against chromium are numerous, disparate, and often contradictory (Table 6). Some of this confusion may be attributable to the general lack of confidence in analyses of chromium residues conducted some years ago, and some to the continued inability to quantify chemical species and ionic states of Cr. Uncertainties about the metabolic role of organochromium compounds, water soluble Cr+3 species, and their interactions with other components in complex and potentially toxic mixtures, further confound the issue. The essentiality of Cr to some, but not all, species of mammals is recognized, but comparable data for other groups of organisms are missing. Finally, the wide range in sensitivities and accumulation rates documented between different taxonomic groups, and even among closely related species, to Cr+3 and Cr+6 salts merits elucidation. Until these questions are resolved, the acceptance of uniform Cr criteria is debatable, and their passage to administratively legislated standards is contraindicated.

Table 6. Proposed chromium criteria for protection of selected resources.

Category and criterion (units in parentheses)	Chromium concentration	Reference[a]
Freshwater aquatic life protection (µg/L)		
USA	<0.29 Cr+6 as 24 h average; not to exceed 21 Cr+6 at any time	1
Water hardness, in mg $CaCO_3$/L		
50	<2,200 Cr+3 at any time	1
100	<4,700 Cr+3 at any time	1
200	<9,900 Cr+3 at any time	1
Colorado	<25 Cr+6; <100 Cr+3	2
Florida		
Effluent discharges	<500 Cr+6; <1,000 total Cr	2
Recovery waters	<50 total Cr	
Indiana		
Most waters	Not to exceed 0.1X 96-h LC-50 of aquatic species	2
Lake Michigan	<50 total Cr	2
Marine aquatic life protection (µg/L)		
USA	<18 Cr+6 as 24 h average; not to exceed 1,260 Cr+6 at any time	1
USA	Insufficient data base for Cr+3 at this time, but presumably less stringent than Cr+6	1
California	<2 total Cr, 6 month median; <8 total Cr, daily maximum; <20 total Cr, instantaneous mix	2
California		
Waste discharges into marine waters	<5 total Cr for 50% of measurements; <10 for 10% of measurements	3
Drinking water (µg/L)		
USA	<50 Cr+6; <170,000 Cr+3	1
California	<50 total Cr	2
Colorado	<50 Cr+6; <50 Cr+3	2
Florida	<50 total Cr	2
Brazil	<50 total Cr	4
USSR	<600 total Cr	4
Agricultural water (µg/L)		
Irrigation Colorado	<100 of Cr+6; <100 of Cr+3	2
Groundwater Florida	<50 total Cr	2
Diet		
Human health protection		
Normal dietary intake	50 to 70 g Cr+3 daily	2
"	30 to 100 µg total Cr daily	5
Food stuffs	100 to 300 g total Cr/kg fresh weight	2
Tissue residues (µg/kg fresh weight)		
Human soft tissues	<30 total Cr	2
Animal tissues	<200 total Cr	2
Air (µg/m^3)		
USA	<50 total Cr	6

[a]References: 1, EPA 1980; 2, Ecological Analysts 1981; 3, Reish 1977; 4, Pfeiffer et al. 1980; 5, Langard and Norseth 1979; 6, Steven et al. 1976.

ACKNOWLEDGMENTS

I thank I. Moore for secretarial help; L. J. Garrett, M. Shawe, and B. Graff for literature retrieval; B. A. Rattner, J. B. Hunn, and J. F. Moore for reviewing the manuscript; and P. H. Eschmeyer and J. R. Zuboy for editorial services.

LITERATURE CITED

Abbasi, S. A., and R. Soni. 1983. Stress-induced enhancement of reproduction in earthworm *Octochaetus pattoni* exposed to chromium (VI) and mercury (II)—implications in environmental management. Int. J. Environ. Stud. 22:43-47.

Alexander, G. V., and D. R. Young. 1976. Trace metals in southern California mussels. Mar. Pollut. Bull. 7:7-9.

Anderlini, V. 1974. The distribution of heavy metals in the red abalone, *Haliotis rufescens*, on the California coast. Arch. Environ. Contam. Toxicol. 2:253-265.

Arillo, A., C. Margiocco, F. Melodia, and P. Mensi. 1982. Biochemical effects of long term exposure to Cr, Cd, Ni on rainbow trout (*Salmo gairdneri* Rich.): influence of sex and season. Chemosphere 11:47-57.

Ayling, G. M. 1974. Uptake of cadmium, zinc, copper, lead and chromium in the Pacific oyster, *Crassostrea gigas*, grown in the Tamar River, Tasmania. Water Res. 8:729-738.

Baptist, J. P., D. E. Hoss, and C. W. Lewis. 1970. Retention of chromium-51, iron-59, cobalt-60, zinc-65, strontium-85, niobium-95, indium-114m, and iodine-131 by the Atlantic croaker (*Micropogon undulatus*). Health Phys. 18:141-148.

Baptist, J. P., and C. W. Lewis. 1969. Transfer of Zn and Cr through an estuarine food chain. Proc. 2nd Nat. Symp. Radioecology. U.S. Atom. Ener. Comm. Conf. 670503:420-430.

Bates, T. E., A. Haq, Y. K. Soon, and J. R. Moyer. 1975. Uptake of metals from sewage sludge amended soils. Int. Conf. Heavy Metals in the Environment. Symp. Proc. (Toronto) 2(1):403-416.

Bernhard, M., and A. Zattera. 1975. Major pollutants in the marine environment. Pages 195-300 *in* E. A. Pearson and E. D. Frangipane (eds.). Marine pollution and marine waste disposal. Pergamon Press, New York.

Bertine, K. K., and E. D. Goldberg. 1972. Trace elements in clams, mussels, and shrimp. Limnol. Ocean. 17:877-884.

Blus, L. J., B. S. Neely, Jr., T. G. Lamont, and B. M. Mulhern. 1977. Residues of organochlorines and heavy metals in tissues and eggs of brown pelicans, 1969-1973. Pestic. Monitor. J. 11:40-53.

Bookhout, C. G., R. J. Monroe, R. B. Forward, Jr., and J. D. Costlow, Jr. 1984. Effects of hexavalent chromium on development of crabs, *Rithropanopeus harrisii* and *Callinectes sapidus*. Water, Air, Soil Pollut. 21:199-216.

Brooks, R. R., and D. Rumsey. 1974. Heavy metals in some New Zealand commercial sea fishes. N.Z. J. Mar. Freshwater Res. 8:155-166.

Bryan, G. W., and L. G. Hummerstone. 1977. Indicators of heavy metal contamination in the Looe estuary (Cornwall) with particular regard to silver and lead. J. Mar. Biol. Assoc. U.K. 57:75-92.

Bryan, G. W., W. J. Langston, L. G. Hummerstone, G. R. Burt, and Y. B. Ho. 1983. An assessment of the gastropod, *Littorina littorea*, as an indicator of heavy-metal contamination in United Kingdom estuaries. J. Mar. Biol. Assoc. U.K. 63:327-345.

Bryan, G. W., and H. Uysal. 1978. Heavy metals in the burrowing bivalve *Scrobicularia plana* from the Tamar estuary in relation to environmental levels. J. Mar. Biol. Assoc. U.K. 58:89-108.

Buhler, D. R., R. M. Stokes, and R. S. Caldwell. 1977. Tissue accumulation and enzymatic effects of hexavalent chromium in rainbow trout (*Salmo gairdneri*). J. Fish. Res. Board Canada 34:9-18.

Buikema, A. L., Jr., J. Cairns, Jr., and, G. W. Sullivan. 1974. Evaluation of *Philodena acuticornis* (Rotifera) as a bioassay organism for heavy metals. Water Resour. Bull. 10:648-661.

Calamari, D., G. F. Gaggino, and G. Pacchetti. 1982. Toxicokinetics of low levels of Cd, Cr, Ni and their mixture in long-term treatment on *Salmo gairdneri* Rich. Chemosphere 11:59-70.

Capuzzo, J. M., and J. J. Sasner, Jr. 1977. The effect of chromium on filtration rates and metabolic activity of *Mytilus edulis* L. and *Mya arenaria* L. Pages 225-237 *in* F. J. Vernberg, A. Calabrese, F. P. Thurberg, and W. B. Vernberg (eds.). Physiological responses of marine biota to pollutants. Academic Press, New York.

Carr, R. S., W. L. McCullough, and J. M. Neff. 1982. Bioavailability of chromium from a used chrome lignosulphonate drilling mud to five species of marine invertebrates. Mar. Environ. Res. 6:189-203.

Catalan, Z. B. 1982. Behavioral responses of *Chironomus tentans* to stress as determined by an optical fiber monitoring system. Ph.D. thesis, Univ. Michigan, Ann Arbor. 94 pp.

Chipman, W. A. 1967. Some aspects of the accumulation of chromium-51 by marine organisms. Proc. Int. Symp. Radioecol. Conc. Proc., 1966 (Stockholm):931-941.

Coleman, R. N., and J. H. Paran. 1983. Accumulation of hexavalent chromium by selected bacteria. Environ. Technol. Lett. 4:149-156.

Conklin, P. J., D. Drysdale, D. G. Doughtie, K. R. Rao, J. P. Kakareka, T. R. Gilbert, and R. F. Shokes. 1983. Comparative toxicity of drilling muds: role of chromium and petroleum hydrocarbons. Mar. Environ. Res. 10:105-125.

DeClerck, R., R. Vanderstappen, W. Vyncke, and P. Van Hoeyweghen. 1979. La teneur en metaux lourdes dans les organismes marins provenant de la capture accessoire de la peche coteire belg. Rev. Agric. (Brussels) 3(32):793-801.

Del Carratore, R., E. Cundari, C. Morganti, J. Moretton, C. Bauer, C. Corsil, R. Nieri, M. Paolini, and G. Bronzetti. 1984. Detection of mutagens in leather and tannery industry assay of 28 commercial mixtures. Bull. Environ. Contam. Toxicol. 32:400-404.

Doughtie, D. G., P. J. Conklin, and K. R. Rao. 1983. Cuticular lesions induced in grass shrimp exposed to hexavalent chromium. J. Invert. Pathol. 42:249-258.

Duinker, J. C., M. T. J. Hillebrand, and R. F. Nolting. 1979. Organochlorines and metals in harbour seals (Dutch Wadden Sea). Mar. Pollut. Bull. 10:360-364.

Duval, R. L., C. R. Ferris, R. B. Owen, Jr., K. E. Gibbs, L. K. Fink, Jr., and F. E. Woodward. 1980. Effects of a cattle skin tannery on stream quality and benthic macroinvertebrates in central Maine. Bull. Environ. Contam. Toxicol. 25:269-276.

Eastin, W. C., Jr., S. D. Haseltine, and H. C. Murray. 1980. Intestinal absorption of 5 chromium compounds in young black ducks (*Anas rubripes*). Toxicol. Lett. 6:193-197.

Ecological Analysts, Inc. 1981. The sources, chemistry, fate, and effects of chromium in aquatic environments. Avail. from American Petroleum Institute, 2101 L St., N.W., Washington, DC 20037. 207 pp.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. Biol. Trace Elem. Res. 6:165-180.

Eisler, R., M. M. Barry, R. L. Lapan, Jr., G. Telek, E. W. Davey, and A. E. Soper. 1978. Metal survey of the marine clam *Pitar morrhuana* collected near a Rhode Island (USA) electroplating plant. Mar. Bio. 45:311-317.

Eisler, R., R. L. Lapan, Jr., G. Telek, E. W. Davey, A. E. Soper, and M. Barry. 1977. Survey of metals in sediments near Quonset Point, Rhode Island. Mar. Pollut. Bull. 8:260-264.

Elwood, J. W., J. J. Beauchamp, and C. P. Allen. 1980. Chromium levels in fish from a lake chronically contaminated with chromates from cooling towers. Int. J. Environ. Stud. 14:289-298.

EPA. 1980. Ambient water quality criteria for chromium. U.S. Environ. Protection Agency Rep. 440/5-80-035.

Foster, P. 1976. Concentrations and concentration factors of heavy metals in brown algae. Environ. Pollut. 10:45-53.

Fowler, S. W., and B. Oregioni. 1976. Trace metals in mussels from the N.W. Mediterranean. Mar. Pollut. Bull. 7:26-29.

Fukai, R. 1965. Analysis of trace amounts of chromium in marine organisms by the isotope dilution of Cr-51. Pages 335-351 *in* Radiochemical methods of analysis. Int. Atom. Ener. Agen. (Vienna).

Fukai, R., and D. Broquet. 1965. Distribution of chromium in marine organisms. Bull. Inst. Ocean. (Monaco) 65(1336):1-19.

Fukai, R., B. Oregioni, and D. Vas. 1978. Interlaboratory comparability of measurements of trace elements in marine organisms: results of intercalibration exercise on oyster homogenate. Ocean. Acta 1:391-396.

Gale, T. F. 1978. Embryotoxic effects of chromium trioxide in hamsters. Environ. Res. 16:101-109.

Giblin, A. E., A. Bourg, I. Valiela, and J. M. Teal. 1980. Uptake and losses of metals in sewage sludge by a New England salt marsh. Am. J. Bot. 67:1059-1068.

Gilani, S. H., and M. Marano. 1979. Chromium poisoning and chick embryogenesis. Environ. Res. 19:427-431.

Gough, L. P., and R. C. Severson. 1976. Impact of point source emissions from phosphate processing on the element content of plants and soils, Soda Springs, Idaho. Pages 225-233 *in* D. D. Hemphill (ed.). Trace substances in environmental health. Vol. X, Univ. Missouri, Columbia.

Graham, D. L. 1972. Trace metal levels in intertidal mollusks of California. Veliger 14:365-372.

Greig, R., and D. Wenzloff. 1977. Final report on heavy metals in small pelagic finfish, euphausid crustaceans and apex predators, including sharks, as well as on heavy metals and hydrocarbons (C 15+) in sediments collected at stations in and near deepwater dumpsite 106. Vol. III. Contaminant inputs and chemical characteristics. Pages 547-564 *in* U.S. Dep. Com. NOAA, Rockville, MD, Baseline report of the environmental conditions on deepwater dumpsite 106.

Greig, R. A., D. R. Wenzloff, A. Adams, B. Nelson, and C. Shelpuk. 1977. Trace metals in organisms from ocean disposal sites of the middle eastern United States. Arch. Environ. Contam. Toxicol. 6:395-409.

Gryzhankova, L. N., G. N. Sayenko, A. V. Karyakin, and N. V. Laktionova. 1973. Concentrations of some metals in the algae of the Sea of Japan. Oceanology 13:206-210.

Hall, R. A., E. G. Zook, and G. M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resources. U.S. Dep. Comm. NOAA Tech. Rep. NMFS SSRF-721. 313 pp.

Hall, R. J., and B. M. Mulhern. 1984. Are anuran amphibians heavy metal accumulators? Pages 123-133 *in* R. A. Seigel, L. E. Hunt, J. L. Knight, L. Malaret, and N. L. Zuschlag (eds.). Vertebrate ecology and systematics—a tribute to Henry S. Fitch. Mus. Nat. Hist., Univ. Kansas, Lawrence.

Hartenstein, R., E. F. Neuhauser, and J. Collier. 1980. Accumulation of heavy metals in the earthworm *Eisenia foetida*. J. Environ. Qual. 9:23-26.

Haseltine, S. D., B. M. Mulhern, and C. Stafford. 1980. Organochlorine and heavy metal residues in black duck eggs from the Atlantic flyway, 1978. Pestic. Monitor. J. 14:53-57.

Haseltine, S. D., L. Sileo, D. J. Hoffman, and B. M. Mulhern. 1985. Effects of chromium on reproduction and growth of black ducks. Manuscript in preparation.

Hatherill, J. R. 1981. A review of the mutagenicity of chromium. Drug Chem. Toxicol. 4:185-195.

Hawkins, C. J., D. L. Parry, and C. Pierce. 1980. Chemistry of the blood of the ascidian *Podoclavella moluccensis*. Biol. Bull. 159:669-680.

Heinz, G. H., and S. D. Haseltine. 1981. Avoidance behavior of young black ducks treated with chromium. Toxicol. Lett. 8:307-310.

Honig, R. A., M. J. McGinniss, A. L. Buikema, Jr., and J. Cairns, Jr. 1980. Toxicity tests of aquatic pollutants using *Chilomonas paramecium* Ehrenberg (Flagellata) populations. Bull. Environ. Contam. Toxicol. 25:169-175.

Hopper, J. T., J. W. Holloway, and W. T. Butts, Jr. 1978. Animal variation in chromium sesquioxide excretion patterns of grazing cows. J. Anim. Sci. 46:1096-1102.

Horowitz, A., and B. J. Presley. 1977. Trace metal concentrations and partitioning in zooplankton, neuston, and benthos from the South Texas Outer Continental Shelf. Arch. Environ. Contam. Toxicol. 5:241-255.

Ishibashi, M., and T. Yamamoto. 1960. Inorganic constituents in seaweeds. Rec. Ocean. Wks. Japan 5:55-62.

James, B. R., and R. J. Bartlett. 1983a. Behavior of chromium in soils: V. Fate of organically complexed Cr (III) added to soil. J. Environ. Qual. 12:169-172.

James, B. R., and R. J. Bartlett. 1983b. Behavior of chromium in soils. VI. Interactions between oxidation-reduction and organic complexation. J. Environ. Qual. 12:173-176.

Jenkins, D. W. 1980. Biological monitoring of toxic trace metals. Vol. 2. Toxic trace metals in plants and animals of the world. Part I. U.S. Environ. Protection Agency Rep. 600/3-80-090:364-443.

Jensen, L. S., and D. Maurice. 1980. Dietary chromium and interior egg quality. Poult. Sci. 59:341-346.

Jouany, J. M., P. Vasseur, and J. F. Ferard. 1982. Ecotoxicite directe et integree du chrome hexavalent sur deux niveaux trophiques associes: *Chlorella vulgaris* et *Daphnia magna*. Environ. Pollut. 27A:207-221.

Karbe, L., C. Schnier, and H. O. Siewers. 1977. Trace elements in mussels (*Mytilus edulis*) from coastal areas of the North Sea and the Baltic. Multielement analysis using instrumental neutron activation analysis. J. Radioanal. Chem. 37:927-943.

Kelsall, J. P. 1970. Chemical elements in waterfowl flight feathers. Prog. Notes, Canad. Wildl. Serv. 17:1-11.

Kerr, L. A., and W. C. Edwards. 1981. Chromate poisoning in livestock from oil field wastes. Veterin. Human Toxicol. 23:401-402.

Kobayashi, N. 1971. Fertilized sea urchin eggs as an indicatory material for marine pollution bioassays, preliminary experiments. Publ. Seto Mar. Biol. Lab. 18:379-406.

Kobayashi, N. 1977. Preliminary experiments with sea urchin pluteus and metamorphosis in marine pollution bioassay. Publ. Seto Mar. Biol. Lab. 24:9-21.

Krishnaja, A. P., and M. S. Rege. 1982. Induction of chromosomal aberrations in fish *Boleophthalmus dussumieri* after exposure in vivo to mitomycin C and heavy metals mercury, selenium and chromium.

Mutat. Res. 102:71-82.

Laj, S., V. K. Jain, and S. K. Tandon. 1984. Comparative toxicity of trivalent and hexavalent chromium IV: biochemical changes in blood and liver of rat. J. Environ. Biol. 5:29-35.

Lande, E. 1977. Heavy metal pollution in Trondheimsfjorden, Norway, and the recorded effects on the fauna and flora. Environ. Pollut. 12:187-198.

Langard, S., and A.-L. Nordhagen. 1980. Small animal inhalation chambers and the significance of dust ingestion from the contaminated coat when exposing rats to zinc chromate. Acta Pharmacol. Toxicol. 46:43-46.

Langard, S., and T. Norseth. 1979. Chromium. Pages 383-397 *in* L. Friberg, G. F. Nordberg, and V. B. Vouk (eds.). Handbook on the toxicology of metals. Elsevier/North Holland Biomedical Press.

Leonard, A., and R. R. Lauwerys. 1980. Carcinogenicity and mutagenicity of chromium. Mutat. Res. 76:227-239.

Livingston, H. D., and G. Thompson. 1971. Trace element concentrations in some modern corals. Limnol. Ocean. 16:786-795.

Lucas, H. F., D. N. Edgington, and P. J. Colby. 1970. Concentrations of trace elements in Great Lakes fishes. J. Fish. Res. Board Canada 27:677-684.

Mahoney, J. B. 1982. The effects of trace metals on growth of a phytoflagellate *Olisthodiscus luteus*, which blooms in lower New York Bay. Bull. N.J. Acad. Sci. 27:53-57.

Mangi, J., K. Schmidt, J. Pankow, L. Gaines, and P. Turner. 1978. Effects of chromium on some aquatic plants. Environ. Pollut. 16:285-291.

Martin, J. H., and G. A. Knauer. 1973. The elemental composition of plankton. Geochim. Cosmochim. Acta 37:1639-1653.

Mayer, L. M., and L. L. Schick. 1981. Removal of hexavalent chromium from estuarine waters by model substrates and natural sediments. Environ. Sci. Technol. 15:1482-1484.

Mayer, L. M., L. L. Schick, P. M. Rossi, H. H. Patterson, C. A. Chang, D. E. Bause, and L. K. Fink, Jr. 1981. Analysis, distribution, and interactions of chromium in the aquatic environment. Univ. Maine at Orono, Land and Water Res. Cent., Compl. Rep. Proj. B-016-ME. 58 pp.

Mearns, A. J., P. S. Oshida, M. J. Sherwood, D. R. Young, and D. J. Reish. 1976. Chromium effects on coastal organisms. J. Water Pollut. Control Feder. 48:1929-1939.

Mearns, A. J., and D. R. Young. 1977. Chromium in the southern California marine environment. Pages 125-142 *in* C. S. Giam (ed.). Pollutant effects on marine organisms. D.C. Heath, Lexington, Massachusetts.

Montgomery, J. R., M. Price, J. Thurston, G. L. de Castro, L. L. Cruz, and D. D. Zimmerman. 1978. Biological availability of pollutants to marine organisms. U.S. Environ. Protection Agency Rep. 600/3-78-035. 134 pp.

Moraitou-Apostolopoulou, M., and G. Verriopoulos. 1982a. Individual and combined toxicity of three heavy metals, Cu, Cd and Cr for the marine copepod *Tisbe holothuriae*. Hydrobiologia 87:83-87.

Moraitou-Apostolopoulou, M., and G. Verriopoulos. 1982b. Toxicity of chromium to the marine planktonic copepod *Acartia clausi*, Giesbrecht. Hydrobiologia 96:121-127.

Muller, H. G. 1980. Acute toxicity of potassium dichromate to *Daphnia magna* as a function of water quality. Bull. Environ. Contam. Toxicol. 25:113-117.

Murti, R., O. Omkar, and G. S. Shukla. 1983. Chromium toxicity to a freshwater prawn *Macrobrachium lamarrei* (H. M. Edwards). Toxicol. Lett. 18:257-261.

Nadkarni, R. A., and W. D. Ehmann. 1970. Trace element determination in biological materials by neutron activation analysis. Pages 407-419 *in* D. D. Hemphill (ed.). Trace substances in environmental health IV. Univ. Missouri, Columbia.

NAS. 1974. Medical and biologic effects of environmental pollutants. Chromium. Nat. Acad. Sci., Div. Med. Sci., Nat. Res. Coun., Washington, DC. 155 pp.

Neff, J. M., R. S. Carr, and W. L. McCullough. 1981. Acute toxicity of a used chrome lignosulfonate drilling mud to several species of marine invertebrates. Mar. Environ. Res. 4:251-266.

Neff, J. M., R. S. Foster, and J. F. Slowey. 1978. Availability of sediment-absorbed heavy metals to benthos with particular emphasis on deposit-feeding infauna. Tech. Rep. D-78-42, U.S. Army Waterways Exp. Sta., Vicksburg, Mississippi. 286 pp.

Negilski, D. S. 1976. Acute toxicity of zinc, cadmium and chromium to the marine fishes, yellow-eye mullet (*Aldrichetta forsteri* C. & V.) and small-mouthed hardyhead *Atherinasoma microstoma* Whitley). Aust. J. Mar. Freshwater Res. 27:137-149.

Norseth, T. 1981. The carcinogenicity of chromium. Environ. Health Perspect. 40:121-130.

Okubo, K., and T. Okubo. 1962. Study on the bioassay method for the evaluation of water pollution—II. Use of the fertilized eggs of sea urchin and bivalves. Bull. Tokai Reg. Fish. Res. Lab. 32:131-140.

Olson, K. R., and R. C. Harrel. 1973. Effect of salinity on acute toxicity of mercury, copper, and chromium for *Rangia cuneata* (Pelecypoda, Mactridae). Contrib. Mar. Sci. 17:9-13.

Onkelinx, C. 1977. Compartment analysis of metabolism of chromium (III) in rats of various ages. Am. J. Physiol. 232:E478-E484.

Oshida, P. S., A. J. Mearns, D. J. Reish, and L. S. Word. 1976. The effects of hexavalent and trivalent chromium on *Neanthes arenaceodentata* (Polychaeta: Annelida). S. Calif. Coastal Water Res. Proj., 1500 E. Imperial Hwy., El Segundo, Calif., TM 225. 58 pp.

Oshida, P. S., and L. S. Word. 1982. Bioaccumulation of chromium and its effects on reproduction in *Neanthes arenaceodentata* (Polychaeta). Mar. Environ. Res. 7:167-174.

Oshida, P. S., L. S. Word, and A. J. Mearns. 1981. Effects of hexavalent and trivalent chromium on the reproduction of *Neanthes arenaceodentata* (Polychaeta). Mar. Environ. Res. 5:41-49.

Osterberg, C., W. G. Pearcy, and H. J. Curl. 1964. Radioactivity and its relation to oceanic food chains. J. Mar. Res. 22:2-12.

Pak, C. K., K. R. Yang, and I. K. Lee. 1977. Trace metals in several edible marine algae of Korea. J. Oceanol. Soc. Korea 12:41-47.

Papadopoulu, C. 1973. The elementary composition of marine invertebrates as a contribution to the sea pollution investigation. Proc. MAMBO meeting, Castellabate, Italy, June 18-22, 1973. 18 pp.

Papadopoulu, C., and G. D. Kanias. 1977. Tunicate species as marine pollution indicators. Mar. Pollut. Bull. 8:229-231.

Papadopoulu, C., G. D. Kanias, and E. M. Kassimati. 1976. Stable elements of radioecological importance in certain echinoderm species. Mar. Pollut. Bull. 7:143-144.

Papadopoulu, C., and E. M. Kassimati. 1977. Stable elements in skeletal formations of fish species from Greek waters. Thal. Jugoslavica 13:187-192.

Pfeiffer, W. C., M. Fiszman, and N. Carbonell. 1980. Fate of chromium in a tributary of the Iraja River, Rio de Janeiro. Environ. Pollut. 1B:117-126.

Phelps, D. K., G. Telek, and R. L. Lapan, Jr. 1975. Assessment of heavy metal distribution within the food web. Pages 341-348 *in* E. A. Pearson, and E. D. Frangipane (eds.). Marine pollution and marine waste disposal. Pergamon Press, New York.

Pickering, Q. H. 1980. Chronic toxicity of hexavalent chromium to the fathead minnow. Arch. Environ. Contam. Toxicol. 9:405-413.

Plaskett, D., and I. C. Potter. 1979. Heavy metal concentrations in the muscle tissue of 12 species of teleost from Cockburn Sound, Western Australia. Aust. J. Mar. Freshwater Res. 30:607-616.

Post, M. A., and P. G. Campbell. 1980. Lead chromate pigments—a literature survey on environmental and toxic effects. U.S. Dep. Comm. Nat. Bur. Stand. Rep. NBSIR 80-1974. 38 pp.

Preston, A. M., R. P. Dowdy, M. A. Preston, and J. N. Freeman. 1976. Effect of dietary chromium on glucose tolerance and serum cholesterol in guinea pigs. J. Nutr. 106:1391-1397.

Preston, E. M. 1971. The importance of ingestion in chromium-51 accumulation by *Crassostrea virginica* (Gmelin). J. Exp. Mar. Biol. Ecol. 6:47-54.

Reagor, J. C., and D. McDonald. 1980. Chromate poisoning in cattle—a case report. Southwest. Veterin. 33:10-11.

Rehm, E., M. Schulz-Baldes, and B. Rehm. 1984. Geochemical factors controlling the distribution of Fe, Mn, Pb, Cd, Cu and Cr in Wadden areas of the Weser estuary (German Bight). Veroff. Inst. Meeresforsch. Bremerh. 20:75-102.

Reish, D. J. 1977. Effects of chromium on the, life history of *Capitella capitata* (Annelida: Polychaeta). Pages 199-207 *in* F. J. Vernberg, A. Calabrese, F. P. Thurberg, and W. B. Vernberg (eds.). Physiological responses of marine biota to pollutants. Academic Press, New York.

Ridgeway, L. P., and D. A. Karnofsky. 1952. The effects of metals on the chick embryo: toxicity and production of abnormalities in development. Ann. N.Y. Acad. Sci. 55:203-215.

Riley, J. P., and I. Roth. 1971. The distribution of trace elements in some species of phytoplankton grown in culture. J. Mar. Biol. Assoc. UK 51:63-72.

Riley, J. P., and D. A. Segar. 1970. The distribution of the major and some minor elements in marine animals. I. Echinoderms and coelenterates. J. Mar. Biol. Assoc. UK 50:721-730.

Riva, M. C., R. Flos, M. Crespi, and J. Balasch. 1981. Lethal potassium dichromate and whitening (blankophor) exposure of goldfish (*Carassius auratus*): chromium levels in gills. Comp. Biochem. Physiol. 68C:161-165.

Rosomer, G. L., W. A. Dudley, L. J. Machlin, and L. Loveless. 1961. Toxicity of vanadium and chromium for the growing chick. Poult. Sci. 40:1171-1173.

Roth, I., and H. Hornung. 1977. Heavy metal concentrations in water, sediments, and fish from Mediterranean coastal area, Israel. Environ. Sci. Tech. 11:265-269.

Sastry, K. V., and K. Sunita. 1982. Effect of cadmium and chromium on the intestinal absorption of glucose in the snakehead fish, *Channa punctatus*. Toxicol. Lett. 10:293-296.

Sastry, K. V., and K. Sunita. 1983. Enzymological and biochemical changes produced by chronic chromium exposure in a teleost fish, *Channa punctatus*. Toxicol. Lett. 16:9-15.

Sastry, K. V., and K. Sunita. 1984. Chronic toxic effects of chromium in *Channa punctatus*. J. Environ. Biol. 5:47-52.

Sastry, K. V., and S. Tyagi. 1982. Toxic effects of chromium in a freshwater teleost fish, *Channa punctatus*. Toxicol. Lett. 11:17-21.

Sather, B. T. 1967. Chromium absorption and metabolism by the crab *Podophthalmus vigil*. Proc. Int. Symp. Radioecol. Conc. Proc., 1966, Stockholm, Sweden: 943-976.

Sauter, S., K. S. Buxton, K. J. Macek, and S. R. Petrocelli. 1976. Effects of exposure to heavy metals on selected freshwater fish. Toxicity of copper, cadmium, chromium and lead to eggs and fry of seven fish species. U.S. Environ. Protection Agency Rep. 600/3-76-105. 75 pp.

Schroeder, H. A., J. J. Balassa, and I. H. Tipton. 1962. Abnormal trace metals in man—chromium. J. Chron. Dis. 15:941-964.

Schroeder, H. A., J. J. Balassa, and W. H. Vinton, Jr. 1964. Chromium, lead, cadmium, nickel and titanium in mice: effect on mortality, tumors, and tissue levels. J. Nutr. 83:239-250.

Segar, D. A., J. D. Collins, and J. P. Riley. 1971. The distribution of the major and some minor elements in marine animals. Part II. Molluscs. J. Mar. Biol. Assoc. U.K. 51:131-136.

Shuster, C. N., Jr., and B. H. Pringle. 1968. Effects of trace metals on estuarine molluscs. Proc. First Mid-Atl. Indus. Waste Conf. 13-15 Nov. 1967:285-304. Avail. from Dept. Civil Engin., Univ. Delaware, Newark, Del.

Shuster, C. N., Jr. and B. H. Pringle. 1969. Trace metal accumulation by the American oyster, *Crassostrea virginica*. Proc. Nat. Shellfish. Assoc. 59:91-103.

Sivalingam, P. M. 1978. Effects of high concentration stress of trace metals on their biodeposition modes in *Ulva reticulata* Forskal. Jpn. J. Phycol. 26:157-160.

Snyder, A. D., D. G. DeAngelis, E. C. Eimutus, D. M. Haile, J. C. Ochsner, R. B. Reznik, and H. D. Troy. 1977. Environmental monitoring near industrial sites: chromium. U.S. Environ. Protection Agency Rep. 560/6-77-016. 56 pp. plus Appendices.

Soni, R., and S. A. Abbasi. 1981. Mortality and reproduction in earthworms *Pheritima posthuma* exposed to chromium (VI). Int. J. Environ. Stud. 17:147-149.

Stacey, N. H., K-L. Wong, and C. D. Klaassen. 1983. Protective effects of chromium on the toxicity of cadmium in vivo. Toxicology 28:147-153.

Steven, J. D., L. J. Davies, E. K. Stanley, R. A. Abbott, M. Ihnat, L. Bidstrup, and J. F. Jaworski. 1976. Effects of chromium in the Canadian environment. Nat. Res. Coun. Canada, NRCC No. 15017. 168 pp. Avail. from Publications, NRCC/CNRC, Ottawa, Canada, K1A OR6.

Stevens, D. G., and G. A. Chapman. 1984. Toxicity of trivalent chromium to early life stages of steelhead trout. Environ. Toxicol. Chem. 3:125-133.

Sugatt, R. H. 1980a. Effects of sublethal sodium dichromate exposure in freshwater on the salinity tolerance and serum osmolality of juvenile coho salmon *Oncorhynchus kisutch*, in seawater. Arch. Environ. Contam. Toxicol. 9:41-52.

Sugatt, R. H. 1980b. Effects of sodium dichromate exposure on the immune responses of juvenile coho salmon *Oncorhynchus kisutch*, against *Vibrio anguillarum*. Arch. Environ. Contam. Toxicol. 9:207-216.

Tandon, S. K., D. K. Saxena, J. S. Gaur, and S. V. Chandra. 1978. Comparative toxicity of trivalent and hexavalent chromium. Alterations in blood and liver. Environ. Res. 15:90-99.

Taylor, F. G., Jr. 1980. Chromated cooling tower drift and the terrestrial environment: a review. Nuclear Safety 21:495-508.

Taylor, F. G., S. R. Hanna, and P. D. Parr. 1979. Cooling tower drift studies at the Paducah, Kentucky gaseous diffusion plant. U.S. Dep. Ener. Conf. 790109-1, Oak Ridge National Lab. 31 pp.

Taylor, F. G., L. K. Mann, R. C. Dahlman, and F. L. Miller. 1975. Environmental effects of chromium and zinc in cooling-water drift. Pages 408-425 *in* Cooling Tower Environment. 1974. U.S. Ener. Res. Serv. Admin.,

Conf. Rept. 740302, Washington, DC.

Taylor, F. G., Jr., and P. D. Parr. 1978. Distribution of chromium in vegetation and small mammals adjacent to cooling towers. J. Tenn. Acad. Sci. 53:87-91.

Taylor, F. G., J. A. Watts, and P. D. Parr. 1983. Seasonality of cooling tower drift in vegetation at ORGDP. Environ. Int. 9:149-152.

Tennant, D. A., and W. D. Forster. 1969. Seasonal variation and distribution of 65-Zn, 54-Mn, and 51-Cr in tissues of the crab *Cancer magister* Dana. Health Phys. 18:649-659.

Tietjen, J. H. 1980. Population structure and species composition of the free-living nematodes inhabiting sands of the New York Bight Apex. Estuar. Coast. Mar. Sci. 10:61-73.

Tong, S. S. C., W. D. Youngs, W. H. Gutenmann, and D. J. Lisk. 1974. Trace metals in Lake Cayuga lake trout (*Salvelinus namaycush*) in relation to age. J. Fish. Res. Board Canada 31:238-239.

Towill, L. E., C. R. Shriner, J. S. Drury, A. S. Hammons, and J. W. Holleman. 1978. Reviews of the environmental effects of pollutants: III chromium. U.S. Environ. Protection Agency Rep. 600/1-78-023. 287 pp.

Turekian, K. K., and M. R. Scott. 1967. Concentrations of Cr, Hg, Mo, Ni, Co, Mn in suspended material of streams. Environ. Sci. Technol. 1:940-942.

Uyeki, E. M., and A. Nishio. 1983. Antiproliferative and genotoxic effects of chromium on cultured mammalian cells. J. Toxicol. Environ. Health 11:227-235.

Van As, D., H. O. Fourie, and C. M. Vlegaar. 1973. Accumulation of certain trace elements in the marine organisms from the sea around the Cape of Good Hope. Pages 615-624 *in* Radioactive contamination of the marine environment. Int. Atom. Ener. Agen. (Vienna).

Van der Putte, I., J. Lubbers, and Z. Kolar. 1981a. Effect of pH on uptake, tissue distribution and retention of hexavalent chromium in rainbow trout (*Salmo gairdneri*). Aquatic Toxicol. 1:3-18.

Van der Putte, I., M. A. Brinkhorst, and J. H. Koeman. 1981b. Effect of pH on the acute toxicity of hexavalent chromium to rainbow trout (*Salmo gairdneri*). Aquatic Toxicol. 1:129-142.

Van der Putte, I., and P. Part. 1982. Oxygen and chromium transfer in perfused gills of rainbow trout (*Salmo gairdneri*) exposed to hexavalent chromium at two different pH levels. Aquatic Toxicol. 2:31-45.

Van Hoof, F., and M. Van San. 1981. Analysis of copper, zinc, cadmium and chromium in fish tissues. A tool for detecting metal caused fish kills. Chemosphere 10:1127-1135.

van Weerelt, M., W. C. Preiffer, and M. Fiszman. 1984. Uptake and release of ^{51}Cr (VI) and ^{51}Cr (III) by barnacles (*Balanus* sp). Mar. Environ. Res. 11:201-211.

White, D. H., K. A. King, and R. M. Prouty. 1980. Significance of organochlorine and heavy metal residues in wintering shorebirds at Corpus Christi, Texas, 1976-77. Pestic. Monitor. J. 14:58-63.

Wiemeyer, S. N., T. G. Lamont, and L. N. Locke. 1980. Residues of environmental pollutants and necropsy data for eastern United States ospreys, 1964-1973. Estuaries 3:155-167.

Yamaguchi, S., K. Sano, and N. Shimojo. 1983. On the biological half-time of hexavalent chromium in rats. Industr. Health 21:25-34.

Young, D. R., G. V. Alexander, D. McDermott-Ehrlich. 1979. Vessel-related contamination of southern California harbours by copper and other metals. Mar. Pollut. Bull. 10:50-56.

Young, D. R., and D. J. McDermott. 1975. Trace metals in harbor mussels. Ann. Rept. S. Calif. Coast. Water Res. Proj., El Segundo, CA:139-142.

Zaroogian, G. E., and M. Johnson. 1983. Chromium uptake and loss in the bivalves *Crassostrea virginica* and *Mytilus edulis*. Mar. Ecol. Prog. Ser. 12:167-173.

Biological Report 85(1.7)
April 1986

Contaminant Hazard Reviews
Report No. 7

POLYCHLORINATED BIPHENYL HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

This account summarizes recent technical literature on the environmental chemistry of polychlorinated biphenyls (PCBs); lists PCB background concentrations in fish, wildlife, and invertebrates; documents their toxic and sublethal properties; and reviews and provides recommendations for the protection of sensitive species of aquatic organisms and wildlife.

PCBs, a group of 209 synthetic halogenated aromatic hydrocarbons, have been used extensively in the electricity generating industry as insulating or cooling agents in transformers and capacitors. Due to human activities and the chemical characteristics of the products, PCBs are now distributed worldwide, with measurable concentrations reported in aquatic organisms and wildlife from North America, Europe, the United Kingdom, and the Atlantic and Pacific oceans. PCBs elicit a variety of biologic and toxic effects including death, birth defects, reproductive failure, liver damage, tumors, and a wasting syndrome. They are known to bioaccumulate and to biomagnify within the food chain. As a result of legislation, virtually all uses of PCBs and their manufacture have been prohibited in the United States since 1979. In general, the ban has been accompanied by declines in PCB residues in fishery and wildlife resources. However, the current environmental burden of PCBs in water, sediments, disposal sites, deployed transformers, and other PCB containers is now estimated at more than 82 million kg, much of it localized, and this continues to represent a potential hazard to associated fish and wildlife.

The toxicological properties of individual PCBs are influenced primarily by two factors: the partition coefficient based on solubility in N-octanol/water (Kow); and steric factors, resulting from different patterns of chlorine substitution. In general, PCB isomers with high Kow values, and high numbers of substituted chlorines in adjacent positions, constitute the greatest environmental concern. Unfortunately, basic chemical information is lacking on many isomers. Also, biological responses to individual isomers or mixtures vary widely, even among closely related taxonomic species. The issue is further confounded by the presence of toxic impurities, such as polychlorinated dibenzofurans, which may have been formed during the PCB manufacturing process, or result from product usage. At this time, total PCB residues give a more reliable measure of environmental PCB contamination than do measurements of any Aroclor or other commercial mixtures. In view of the demonstrated differential toxicities within the array of PCB congeners, it may finally become necessary to modify existing standards and criteria based on the more toxic PCBS.

For aquatic life, water concentrations of less than 0.014 ug total PCBs/1 (ppb) appear to afford a satisfactory degree of protection, although concentrations as low as 0.006 ug/l resulted in measurable accumulation by various species of filter-feeding shellfish. Among sensitive species of teleosts, total PCB residues (in ug/kg fresh weight) in excess of 500 in diets, 400 in whole body, and 300 in eggs were demonstrably harmful, and should be considered as presumptive evidence of significant PCB contamination. Among small mammals, the mink (*Mustela vison*) is one of the most susceptible species tested; dietary levels as low as 100 ug PCBs/kg fresh weight caused death and reproductive toxicity. A tolerable daily limit for mink has been estimated at less than 1.5 ug total PCBs/kg body weight. Tolerable daily PCB levels for rhesus monkey (*Macaca mulatta*) dog (*Canis* sp.), and rat (*Rattus* spp.) were 1.0, 2. , and 5.0 ug/kg body weight, respectively. For birds, total PCB levels (in ug/kg fresh weight) in excess of 3,000 in diet, 16,000 in egg, or 54,000 in brain were frequently associated with PCB poisoning.

DISCLAIMER

Mention of trade names or commercial products does not constitute endorsement or recommendation for use by the Division of Biological Services, Research and Development, Fish and Wildlife Service, U.S. Department of the Interior.

This report should be cited as:

Eisler, R. 1986. Polychlorinated biphenyl hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85(1.7).

TABLES

ACKNOWLEDGMENTS

I thank L.J. Garrett, J.E. Haber, and B. Graff for library services; I.E. Moore for secretarial help; T.W. Custer, G.H. Heinz, J.B. Hunn, and L.M. Smith for constructively reviewing the manuscript; and C.H. Halvorson and J.R. Zuboy for editorial assistance.

INTRODUCTION

As a result of human activity, polychlorinated biphenyls (PCBS) are now distributed worldwide, with measurable concentrations reported in polar bears (*Ursus martinus*) from the Canadian Arctic, birds and fish from the Great Lakes, wildlife in Europe, Scandinavia, and the United Kingdom, marine organisms of the Atlantic and Pacific Oceans, and up to 91% of the adult human population in the United States. Their presence in the organisms has been shown to cause reproductive failure, birth defects, skin lesions, tumors, liver disorders, and, among sensitive species, death. PCB toxicity is further enhanced by their ability to bioaccumulate and to biomagnify within the food chain due to extremely high liposolubility. These, and other, biological effects of PCBs have been extensively reviewed by Ayer (1976), Roberts et al. (1978), NAS (1979), EPA (1980), Pal et al. (1980), D'Itri and Kamrin (1983), Fleming et al. (1983), Ernst (1984), Stickel et al. (1984), Safe (1984), Simmons (1984), and Lucier and Hook (1985a,b).

PCBs, a group of synthetic halogenated aromatic hydrocarbons, were first prepared in 1881, and since 1930 have been in general use in products that include heat transfer agents, lubricants, dielectric agents, flame retardants, plasticizers, and waterproofing materials (Roberts et al. 1978). After 1971, they were used almost exclusively as insulating or cooling agents in closed electrical systems, such as transformers and capacitors (NAS 1979). Environmental contamination resulted from industrial discharges, from leaks of supposedly closed systems, from disposal of PCB wastes to municipal sewage treatment plants, landfills, and equipment dumps, and especially through atmospheric transport of incompletely incinerated PCBS. Long-range atmospheric transport of PCBs by wind, rain, and snow is now well documented (NAS 1979). PCBs tend to bond tightly to particulate matter, notably soils and sediments of lakes, estuaries, and rivers, where they may remain available for resuspension for at least 8 to 15 years (Swain 1983). The North Atlantic Ocean seems to be the dominant sink for PCBs, accounting for 50 to 80% of the PCBs in the environment, while freshwater sediment is a major continental reservoir (NAS 1979). Other significant reservoirs of mobile PCBs still exist along with even larger, currently immobile, pools. The latter includes those materials containing PCBs that are still in service, and those deposited in landfills and dumps.

Between 1930 and 1975, more than 630 million kg of PCBs were manufactured domestically (Safe 1984). At present, PCBs are not produced in the United States. PCB legislation under the Toxic Substances Control Act, effective January 1977, required the U.S. Environmental Protection Agency (EPA) to establish labeling and disposal requirements for PCBs, and mandated an eventual ban on the manufacture and processing of PCBs (Bremer 1983). Effective July 1979, the final PCB ban rule was implemented, which prohibits the manufacture, processing, distribution in commerce, and use of PCBs except in a totally enclosed system, unless specifically exempted by EPA (Bremer 1983). Although the ban has been in effect for about 6 years, the current environmental burden of PCBs in water, sediments, disposal sites, and in deployed transformers and other containers is sufficiently large, estimated at 82 million kg (D'Itri and Kamrin 1983), to present potentially significant hazards to fish and wildlife resources.

In this account, I summarize the recent technical literature documenting environmental hazards associated with PCBs, with emphasis on aquatic organisms and wildlife, and review quality criteria recommendations for the protection of sensitive species. This account is part of a continuing series of synoptic reviews prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service.

ENVIRONMENTAL CHEMISTRY

PCBs are organic compounds commercially produced by chlorination of a biphenyl (BP) with anhydrous chlorine in the presence of iron filings or ferric chloride as the catalyst. The purified product is a complex mixture of chlorobiphenyls containing 18 to 79% chlorine; the precise composition depends on the conditions under which chlorination occurred (EPA 1980). Ten possible degrees of chlorination of the biphenyl molecule give rise to ten PCB congener groups: mono-, di-, tri-, tetra-, penta-, hexa-, hepta-, octa-, nona-, and decachlorobiphenyl (Figure 1). Within any congener group, a number of positional isomers (discrete chemical compounds) are possible, depending on the number of chlorines in the molecule. For example, the tetrachloro- and pentachlorobiphenyl congener groups are composed of 30 and 46 possible isomers, respectively. Not all 209 possible isomers are likely to be formed during the manufacturing process. In general, the most common ones are those that have either an equal number of chlorine atoms on both rings, or a difference of only one

chlorine atom between rings (NAS 1979). Although chlorine substitution is favored at the ortho and para positions (Figure 1), the commercial products are complex mixtures of isomers and congeners with no apparent positional preference for halogen substitution (Safe 1984).

Recent advances in the identification and quantification of PCB isomers through mathematical and computer-assisted techniques (Dunn et al. 1984; Schwartz et al. 1984) will prove useful in data interpretation of metabolic fate studies. Unfortunately, the results of PCB analyses vary widely among cooperating laboratories. An interlaboratory comparison of spiked and unspiked samples of herring oil by 23 participating European and North American laboratories showed that calculated spike recoveries ranged from 23 to 136% (Musial and Uthe 1983). This was attributed to serious deficiencies in most steps in the analytical procedures. It seems that until these deficiencies are corrected, PCB analyses will have credibility from only a few selected laboratories.

Toxic materials as impurities in PCBs include polychlorinated dibenzofurans (PCDF) in some domestic and foreign mixtures at levels of 0.8 to 33 mg/kg. The concentrations of PCDFs in Great Lakes fish were related to the concentrations of PCBs (Stalling et al. 1983). Sometimes, PCBs used in electrical capacitors and transformers are converted under the action of heat or electrical arcing to form PCDFs including 2,3,7,8-tetrachlorobenzofuran and 2,3,4,7,8-pentachlorobenzofuran. Kanechlor 400 (Table 1), for example, with an initial PCDF content of 20 mg/kg, yielded fluid with a PCDF content of 4,975 to 11,765 mg/kg after use as a heat transfer fluid in a heat exchanger. These PCDFs were identified as the agents that poisoned more than one thousand humans in Japan in 1968 (EPA 1980; Lucier and Hook 1985a,b). Additional research is needed on PCDFs and other toxic impurities in PCBS.

PCBs are extremely stable compounds, and slow to chemically degrade under environmental conditions. Microbial degradation of PCBs depends on the degree of chlorination and the position of the chlorine atom on the biphenyl molecule; lower chlorinated BPs are readily transformed by bacteria, but not the higher chlorinated compounds (NAS 1979). Higher chlorobiphenyls, i.e., those with five or more chlorine atoms, were more persistent in the environment than those with three or less chlorine atoms; tetrachloro BPs were intermediate in persistence (EPA 1980). Passage of PCBs through activated sludge in sewage treatment plants for 48 hours resulted in 81% degradation for Aroclor 1221 (21% chlorine by weight), 26% for Aroclor 1242 (42% chlorine), and only 15% for Aroclor 1254 (54% chlorine) (NAS 1979). Because of their wide range of physical properties, their chemical stability, and their miscibility with organic compounds, PCBs have been used extensively as hydraulic fluids, plasticizers, adhesives, heat transfer fluids, wax extenders, dedusting agents, lubricants, flame retardants, and especially as dielectric fluids in capacitors and transformers. The current uses of PCBs in the United States have been severely curtailed and production was stopped during the 1970's, although significant quantities of PCBs are still used as dielectric fluids in older transformers and capacitors (Safe 1984).

Commercial PCB formulations are sold under a variety of trade names (Roberts et al. 1978; NAS 1979; EPA 1980; D'Itri and Kamrin 1983; Safe 1984). In the United States, Aroclor is the most familiar requested trademark, but PCBs have also been marketed as Chloretol, Dyknol, Inerteem, Noflamol, and Pyranol. In other countries, PCB formulations have been sold as Pyralene (France), Phenoclor (France), Kanechlor (Japan), Santotherm (Japan), Fenclor (Italy), Apirolio (Italy), Soval (USSR), Delor (Czechoslovakia), and Clophen (West Germany). Some formulations are similar; for example, Kanechlor 600, Phenoclor DP6, Clophen A60, and Aroclor 1260 all contain an average of 60% chlorine, although the former three preparations are composed of a mixture of hexachloro BPs, while Aroclor 1260 contains a variety of forms (Table 1; NAS 1979; EPA 1980).

Chlorination levels of PCB formulations differ markedly (Table 1). Among Aroclor formulations commercially produced by the Monsanto Corporation, Aroclor 1221 contained an average of 21% chlorine by weight and was a clear mobile oil. Aroclor 1254 contained 54% chlorine and was a yellow viscous liquid; 1260 contained 60% chlorine by weight and resembled a yellow sticky resin; and Aroclor 1268 was a white solid (Safe 1984). Aroclor 1254 contained less than 1% of biphenyl and monochloro BP, 0.5% dichloro BP, 1% trichloro BP, 21% tetrachloro BP, 48% pentachloro BP, 24% hexachloro BP, and 6% heptachloro BP (NAS 1979). Aroclor 1016 was similar to Aroclor 1242, with both containing an average of about 42% chlorine by weight, although 1242 contained 9% PCBs with five or more chlorines and 1016 only 5% (Roberts et al. 1978). In general, PCBs are relatively insoluble in water but freely soluble in nonpolar organic solvents and in biological lipids (EPA 1980). Monochlorobiphenyls are comparatively soluble in water (1,190-5,900 ug/1), but this decreases rapidly with increasing chlorination: dichlorobiphenyls, 80 to 1,880 ug/l; trichloro BP, about 8 ug/l; and tetrachloro BP, 3 to 170 ug/l (NAS 1979). The solubilities of various PCB isomers in water also decreased with increasing chlorine

content: 2, 4'-dichloro BP was soluble to 637 ug/l; 2,2',5-trichloro BP to 248 ug/l; 2,2',5,5'-tetrachloro BP to 26.5; 2,2',4,5,5'-pentachloro BP to 10.3; and 2,2',4,4',5,5'-hexachloro BP to 0.95 ug/l (Menzie 1978). Water solubilities of various Aroclor formulations, in ug/l, were 240 for 1242, 50 for 1248, 10 for 1254, and 3 for 1260 (NAS 1979). PCB octanol/water partition coefficients ranged between 10,000 and 20,000 for representative tri-, tetra-, and pentachlorobiphenyls. High partition coefficients with this biphasic solvent system correlate well with PCB biomagnification in fatty tissues of aquatic organisms (EPA 1980), and with incorporation into sediments (Fox et al. 1983). In fact, PCBs are strongly adsorbed on soils, sediments, and particulates in the environment, with levels usually highest in aquatic sediments containing microparticulates (EPA 1980; Duinker et al. 1983) and high organic or clay content (NAS 1979). Uptake of PCBs from contaminated marine sediments by benthic invertebrates is governed by processes that include ingestion of contaminated sediment particles, and exchange of PCBs directly from sediment particles (Larsson 1984). PCB-laden sediments of Raritan Bay, New Jersey, and lower New York Harbor were effective in producing population perturbations of benthic marine invertebrates when sediments contained high silt and clay composition; low silt and clay sediments were ineffective (Stainken 1984).

The number and position of the chlorine atoms on the biphenyl rings affects the biological properties of the compound. For example, PCBs with hydrogen atoms on two adjacent carbon atoms in one or both rings are more readily metabolized than those with hydrogen atoms adjacent only to chlorines, due to metabolic reactions involving arene oxide intermediates (EPA 1980). Furthermore, PCBs with chlorines in the 2 and 6 (ortho) positions are easily metabolized by humans while those with chlorines in the 4 and 4' (para) positions or 3, 4, or 3, 4, 5 positions on one or both rings tend to be biologically active and well-retained in tissues (EPA 1980).

In mammals, PCBs are readily absorbed through the gut, respiratory system, and skin. Initally, PCBs concentrate in liver, blood, and muscle; eventually, accumulations are highest in adipose tissue and skin. Phenolic derivatives or dihydrodiols are the major metabolites, but susceptibility of individual PCB isomers to metabolism is a function of the number of chlorine atoms present on the biphenyl rings and their arrangement. In general, most readily metabolized PCBs are also rapidly excreted in urine and bile. The highly chlorinated isomers are difficult to metabolize and accumulate almost indefinitely. PCBs can be transferred to young mammals either transplacentally or in breast milk. Retention of PCBs is highly species specific: nonhuman primates, for example, retained PCBs more efficiently than rodents (EPA 1980). PCB patterns, especially in warm-blooded animals, only vaguely resemble the mixture from which they originated (Hansen et al. 1983; Ernst 1984). Subtle differences between chlorobiphenyls are further amplified by differences among various animals to absorb, distribute, biotransform, and excrete individual PCB isomers (Hansen et al. 1983).

Biological activities of PCB isomers differ substantially. Among three symmetrical hexachlorobiphenyl (HCBP) isomers, 3,4,5,3',4',5'-HCBP was the most toxic in dietary lethal studies to domestic chickens (*Gallus* spp.), 2,4,5,21,4',5'-HCBP was least toxic, and 2,4,6,2',4',6'-HCBP intermediate in toxicity (Ayer 1976). A tetrachlorobiphenyl (3,4,3',4') was more than 1000 times more potent in producing effects in chicks than 2,4,5,2',4',5'-HCBP both as an hepatotoxin and as an inducer of cytochrome P mediated mixed function oxidases (Rifkind et al. 1984). The biological half-life of intravenously administered PCB formulations in liver of rat (*Rattus* spp.) increased with increasing chlorination: half-lives of 86 hours were determined for 4-monochlorobiphenyl, 99 hours for 4,4'-dichlorobiphenyl, 193 hours for 2,2',4,5,5'-pentachlorobiphenyl, and 1,308 hours for 2,2',4,4',5,5'-hexachlorobiphenyl (Menzie 1978).

PCBs are usually taken up by animals and stored in lipids under circumstances of increasing lipid content in organs. However, recent studies with marine fishes indicate that PCB components remain mobilizable from organs whose lipid contents increased (Boon et al. 1984). The degree of mobilization in codfish (*Gadus morhua*) and sole (*Solea solea*) appeared to be related to polar lipid components such as phospholipids and glycerols. In other aquatic species, the role of diet and tissue specific sites are important. The patterns of pentachloro BP and higher chlorinated BP (not present in seawater) were equal in marine clams, worms, and sediments, and strongly indicate that uptake was via the diet or from sediments (Duinker et al. 1983). In freshwater fishes, direct partitioning across the gill membrane of the blood:water interface controls PCB accumulation; however, dietary PCBs may significantly affect accumulation and exchange rates at the gill membrane (Rohrer et al. 1982).

Biological availability and uptake of individual PCBs from aqueous solution are influenced primarily by two factors: the partition coefficient (Kow) based on the solubilities of compounds in N-octanol/water; and steric

factors resulting from different patterns of chlorine substitution. Log Kow values for various isomers of Aroclors 1242, 1254, and 1260 are high, varying from 4.0 to 9.35, indicating high biological uptake potential. Steric effect coefficients are based on the number of chlorine atoms in the biphenyl molecule and their arrangement (Shaw and Connell 1982). For example, three chlorines in the ortho positions were assigned a steric effect coefficient of 0.3; four chlorines in the ortho postions 0.2; three or four adjacent chlorines on one ring 0.6, and on both rings 0.3; chlorines in the meta position on one ring 0.8, and on both rings 0.6. The product of log Kow and the steric effect coefficient seem to be directly related to bioaccumulation (Shaw and Connell 1982). Thus, maximum uptake was found with penta- and hexachlorobiphenyls predominant in Aroclor 1254, which have high values for log Kow and for steric effect coefficients. Comparatively less uptake was found with di-, tri-, and tetrachlorobiphenyls, typical of Aroclor 1242, which have lower values for log Kow, and with hepta- and octachlorobiphenyls, predominant in Aroclor 1260, which have lower steric effect coefficients. Structure-activity relationships, particularly for PCBS, can be applied to predictive models of contaminant cycling and biomagnification--and promises to become a fruitful research area.

Pal et al. (1980), in a review of PCBs in plant-soil systems, indicated three important research needs. First, many isomers of several PCB formulations have not been studied with respect to their biotransformation, volatilization, photodecomposition, adsorption, and transport. Second, highly chlorinated biphenyls, especially tetra-, penta-, and hexachlorobiphenyls, have not been evaluated for uptake by crops, volatilization, or distribution in soil layers. The relative build up and assimilation in soil-plant systems of hepta-, octa-, nona-, and decachlorobiphenyls have not been evaluated or studied. Finally, data are lacking on partition coefficients of PCBs between soil and water, water and atmosphere, atmosphere and plant populations, and during flow in food chains. A similar case can be made for most fish and wildlife species of current concern.

BACKGROUND CONCENTRATIONS

GENERAL

PCB concentrations have been determined for a variety of flora and fauna, and in certain nonbiological materials (Table 2). These selected data seem to represent current state-of-the-art analytical procedures for accurate and precise measurement of PCBs at detection limits of less than 0.01 ppm for most isomers. Characterization of Aroclor PCB residues in living and nonliving resources is difficult due to the chemical, physical, and metabolic transformations between product manufacture and detection in environmental samples. Schmitt et al. (1985) suggest that total PCBs in samples is a more reliable measure of environmental contamination than measurements of any commercial PCB mixtures such as Aroclor PCBS. Also, Brown et al. (1985) indicated that only a few PCB congeners (i.e., those most toxic) are appropriate for meaningful interpretation of PCB residues in biota.

There is general agreement that more samples from recent collections have detectable PCB residues, that absolute concentrations seem to be declining in some areas of known high PCB contamination, and that lower chlorinated PCBs--resembling Aroclor 1242--are disappearing. Nevertheless, many fish and wildlife species, including salmon, trout, turtles, eagles, herons, fish-eating birds, mink (*Mustela vison*), river otters (*Lutra canadensis*), and bats, all contain measurable, and in some cases potentially harmful, PCB residues, especially in adipose (fatty) tissues.

ALGAE AND TERRESTRIAL MACROPHYTES

In the Great Lakes, atmospheric deposition of PCBs is the most significant source of contamination. More than 90% of atmospheric PCBs are transported in the vapor phase and deposited by turbulent impaction. Deposition of PCBs is also associated with particulate matter, as well as direct partitioning from the vapor phase into the surface organic microlayer at the air-water interface, and these account for the remaining input (Rohrer et al. 1982). Once in the water column, the hydrophobic PCBs partition into the more apolar compartments of the ecosystem or are physically adsorbed on particulate matter. Transfer of PCBs on microparticulate materials and into phytoplankton is well documented, as is partitioning from aqueous solution into algal lipids (Rohrer et al. 1982). PCBs incorporated into phytoplankton exert inhibitory effects on photosynthesis and cell motility. In addition to direct toxic effects on algae, accumulated PCBs are readily introduced into the aquatic food chain (Rohrer et al. 1982).

Selected species of terrestrial plants collected in upstate New York showed decreases in total PCB concentrations of 42% between 1978 and 1980; however, levels in hay in 1979 varied between 0.08 and 0.10 ppm dry weight, or nearly half the Food and Drug Administration (FDA) limit of 0.2 ppm for PCBs in feeds for livestock (Buckley 1983). Plants grown on soils amended with lake sediments contaminated with Aroclors 1248, 1254, and 1260, accumulated PCBs (Sawhney and Hankin 1984). Uptake of Aroclors by beets (*Beta vulgaris*), turnips (*Brassica rapa*), and beans (*Phaseolus vulgaris*) was in the order 1248>1254>1260, indicating that lower chlorinated isomers (which are more soluble in water and more volatile) were more abundant in crop plants than higher chlorinated isomers. Based on these studies, continued monitoring of plants used as forage for livestock and wildlife appears necessary, especially in locations where soils are amended with PCB-contaminated aquatic sediments or sewage sludges.

INVERTEBRATES

Aquatic invertebrates assume an important role in the cycling of PCBs within and between ecosystems. Mysid crustaceans from Lake Michigan appear to have a low assimilation efficiency for PCBs and a high efficiency for fecal excretion of ingested PCBS; fecal pellets sink rapidly (80-170 m/day) and many probably reach the sediments intact before the onset of microbial degradation (Evans et al. 1982). By vertically migrating to the surface at night, mysids may transport PCBs into the upper regions; the PCBs will continue to recycle through the Lake Michigan ecosystem if the PCBs are excreted, egested, lost with molts, or if the mysid is consumed by fish. PCB levels of freshwater oligochaete worms from the Niagara River in New York State were positively correlated with sediment PCB levels (Fox et al. 1983). Uptake of PCBs from the sediment by chironomid (*Chironomus plumosus* - type) larvae was also directly related to the concentration of PCBs in the sediment (Larsson 1984). When larvae metamorphosed to adults, PCB compounds were concentrated and transferred from the aquatic to the terrestrial environment. In a field study near a Swedish sewage plant outfall, transport of PCBs by chironomids from the aquatic to the terrestrial environment was estimated at 20 ug of PCBs per m2 annually. Terrestrial predators that feed on emerging aquatic insects whose larval stage inhabits PCB-contaminated sediments may be exposed to PCBs (Larsson 1984).

FISH

Trace concentrations of the more persistent, more highly chlorinated PCBs are detected in fish from almost every major river in the United States (Schmitt et al. 1983, 1985). The ubiquity of PCB residues probably results from the dispersal of contaminated sediments, from atmospheric transport, and from patterns of continued use and disposal. Maximum concentrations in whole fish did not change appreciably at most locations in recent years; concentrations approaching 100 ppm fresh weight and 500 ppm in lipids were measured as recently as 1978 (Schmitt et al. 1983). Residues of PCBs in fish were more widely distributed than reported previously, but appeared to be declining in some areas of high concentration, and the less chlorinated PCBs (resembling Aroclor 1242) were disappearing. PCB concentrations in whole fish, collected Nationwide between 1976 and 1979, tended to be highest in the industrialized regions of the Northeast and the Midwest. Fish from the Hudson River, near Poughkeepsie, New York, contained 4 to 6X more PCBs than any of the other 108 stations analyzed; mean residue levels were 33.9 ppm fresh weight in 1976-1977 and 44.1 in 1978-1979 (Schmitt et al. 1983). However, data from 1982 (Brown et al. 1985) indicated a general decline in PCB content of fish from the Hudson River (although levels in some species remained substantially higher than the 5.0 ppm temporary tolerance level established by the U.S. Food and Drug Administration); this was attributed primarily to declines in the less chlorinated PCB congeners, especially Aroclor 1016. Accumulations in excess of 1.0 ppm PCBs fresh weight were reported in fish from stations in the Northeast, the Ohio River system, the Missouri River system, the Great Lakes, portions of the Mississippi River in Wisconsin, and from the Manoa Stream near Honolulu, Hawaii (Schmitt et al. 1983). In general, frequency of detectable PCB residues and total PCB residue levels in fish did not change significantly from 1974 to 1979. One exception to this pattern was the decline in residues resembling Aroclor 1242 from 14% of all samples in 1973, to 5% in 1974, to zero in 1976-1977; apparently, components most prevalent in the 1242 mixture are rapidly degraded. Furthermore, the continuing presence of residues resembling Aroclor 1248 suggest that relatively unaltered PCBs continue to enter the environment (Schmitt et al. 1983). The most recent Nationwide monitoring survey (Schmitt et al. 1985) demonstrated a significant downward trend in whole fish body burdens of PCBs in 1981-1982, with no significant increases at any station, confirming that residues were highest at stations in the industrialized regions of the Northeast, the Great Lakes, the Upper Mississippi River System, the Ohio River System, and the Cape

Fear River in North Carolina. Schmitt et al. (1985) suggested that total PCBs measure environmental PCB contamination more reliably than do measurements of any commercial mixtures such as Aroclor PCBs.

About 10% of coho salmon (*Oncorhynchus kisutch*) and 58% of chinook salmon (*0. tshawytscha*) collected in 1980 from the Great Lakes exceeded the current FDA action lever of 5.0 ppm total PCBs on a fresh weight basis. All chinook and about half the coho salmon exceeded the proposed FDA action level of 2.0 ppm total PCBs in fillets (Rohrer et al. 1982). PCBs detected in salmon from the Great Lakes in 1980 most closely resembled Aroclor 1254, although higher and lower chlorohomologues were present. PCBs resembling Aroclor 1260 were detected in only 10% of coho salmon from Lake Huron and may be the result of widespread historical use of Aroclor 1254 and more limited use of Aroclor 1260 (Rohrer et al. 1982). Marked variations in PCB content of selected tissues were evident; skinless fillets of Great Lakes salmon contained significantly lower PCB residues than skin-on fillets, with Aroclor 1254 concentrations 3.5 to 4X lower in the skinless fillets (Table 2). Also, a strong correlation was observed between the concentration of PCBs and DDE in Great Lakes salmon collected in 1980 (Rohrer et al. 1982), probably due to the chemicals' similar polarity and molecular size. The chemical interactions of PCBs with other chlorinated hydrocarbon contaminants, and their biological properties, are areas requiring additional research effort.

Although diet is a major route of PCB uptake in many species of fish, there are notable exceptions--even among closely related species. In lake trout (*Salvelinus namaycush*), for example, most (more than 99%) accumulated PCBs are from the diet and less than 1% from the medium. However, water is the major PCB uptake route in coho salmon (Rohrer et al. 1982). In the windowpane (*Scopthalmus aquosus*), a marine flounder from Long Island Sound, New York, stomach contents contained up to 0.45 ppm of PCBs fresh weight, suggesting a potentially large amount of dietary PCBs available to this species (Greig et al. 1983).

Elevated levels of PCBs (mostly Aroclor 1254) found in gonads of striped bass (*Morone saxatilis*), up to 1.4 ppm fresh weight and 2.3 on a lipid basis, may be associated with poor reproductive success of this species in Nova Scotia (Ray et al. 1984). This is similar to levels of 2.8 ppm PCBs in lipids of eggs of rainbow trout (*Salmo gairdneri*) that experienced heavy fry mortality (Rohrer et al. 1982), and to levels of 0.12 ppm PCBs on a fresh weight basis in gonads of flounder (*Platichthys flesus*) with inhibited reproduction (Ray et al. 1984). However, eggs of Atlantic salmon (*Salmo salar*) with 6.0 ppm PCBs in lipids hatched normally (Ray et al. 1984). It is clear that considerable interspecies differences exist in the responses of teleosts to PCB loadings.

Equilibrium levels of stable lipophilic contaminants in fish are directly proportional to the ambient water concentration of the chemical. Atmospheric deposition and high sediment contamination have also been implicated as major sources of PCB contamination (Rohrer et al. 1982). Lowest PCB levels in Great Lakes salmon were at stations with high flushing and high sedimentation rates (Rohrer et al. 1982). PCBs were detectable at low concentrations in brook trout (*Salvelinus fontinalis*) from remote New England lakes, tending to confirm that PCBS, and other recorded contaminants, reached the lakes by atmospheric deposition (Haines 1983).

REPTILES

Water snakes (*Nerodia* spp.) collected in Louisiana reflected PCB levels similar to those of CB residues in their prey species, primarily fresh- and brackish-water teleosts. PCBs in water snakes were detected in 95% of all fat samples and 52% of liver and muscle tissues; Aroclor 1260 accounted for most of the PCBs (Sabourin et al. 1984). Snapping turtles (*Chelydra serpentia*) are capable of storing high concentrations of PCBs in their fat without any apparent detrimental effects, and may be useful as biological indicators for lipophilic substances, including PCBs (Olafsson et al. 1983). Sea turtles contain relatively lower levels of PCBs than snapping turtles (Table 2). PCB concentrations were higher in saltwater loggerhead turtles (*Caretta caretta*), an omnivore, than green turtles (*Chelonia mydas*), which are vegetarians, again demonstrating that diet is an important route of PCB transfer (McKim and Johnson 1983).

BIRDS

In general, most bird tissues and eggs collected had measurable concentrations of PCBS, and the frequency of occurrence appears to be increasing. In 1976, 21% of European starlings (*Sturnus vulgaris*) collected Nationwide had detectable PCBS; in 1979 it was 83% (Cain and Bunck 1983). For mallards (*Anas platyrhynchos*), PCBs were detected in 39% of wing tissues in 1976-1977, and 95% In 1979-1980 (Fleming et

al. 1983). PCBs were detected in all of the eggs of six species of South African seabirds and in the majority of eggs from a seventh species in 1981-1983 (de Kock and Randall 1984); in 50 to 55% of eggs of the black-crowned night-heron (*Nycticorax nycticorax*) from Colorado, Wyoming, Washington, and Nevada taken in 1978-1980 (McEwen et al. 1984; Henny et al. 1984); in all Norwegian seabird fledglings in 1976-1977 (Fimreite and Bjerk 1983); in 77% of eggs of the black skimmer (*Rynchops nigra*) from Texas in 1981 (White et al. 1984); in 85 to 100% of all game bird tissues examined in West Germany during 1982 (Brunn et al. 1985); and in 99% of the eggs of the endangered American bald eagle (*Haliaeetus leucocephalus*), including 89% occurrence in breeding areas (Wiemeyer et al. 1984).

Populations of double-crested cormorants (*Phalacrocorax auritus*) from Lake Huron are now recovering rapidly, presumably due to a decrease in CB and other contaminant residues in eggs (Weseloh et al. 1983). In the late 1960's and early 1970's, cormorants nesting on the Great Lakes, and in particular Lake Huron, had eggs that were more highly contaminated with PCBS, DDE, and mercury, than did cormorant eggs from anywhere else in Canada. Concomitantly, egg survival, reproductive success, and colony size were either dangerously low or decreasing. In .1972, colonies were small, they showed high egg breakage and egg loss (95%), and nearly total reproductive failure (less than 0.11 young/nest). Eggshells were about 24% thinner than normal. Levels of DDE (14.5 ppm fresh weight) and PCBs (23.8) in eggs collected in 1972 were higher than other Canadian cormorant populations (Weseloh et al. 1983).

In the past, PCB residues in birds tended to be higher in areas of local contamination and heavy industrial use or discharge. But with the current stringent restrictions on PCB use, geographical distinctions are not as clear (Custer et al. 1983a; McLane et al. 1984), although residues in birds from industrialized areas still remain comparatively high (Fleming et al. 1983; White et al. 1984). For example, birds collected near the Sheboygan River, Wisconsin, contained PCB residues that would be considered harmful to some species tested in the laboratory (Table 2). The main source of PCBs at that location was a diecasting plant. Granular oil absorbent material behind the plant contained up to 120,000 ppm of PCBS; runoff and seepage from rain and floodwaters carried PCBs into the river, subsequently contaminating fish, especially carp (*Cyprinus carpio*). Whole fresh carp from the Sheboygan River contained more than 155 ppm of PCBs (as quoted in Heinz et al. 1984), suggesting that fish-eating birds may be especially at risk.

In 1981 and 1982, duck hunters in New York and New Jersey were cautioned about the consumption of wild waterfowl. At the time, waterfowl from the Hudson and Niagara rivers contained PCBs in excess of tolerances established by FDA for poultry (more than 5 ppm fresh weight), although PCB concentrations found in these waterfowl were below the levels associated with reproductive impairment or decreased survival of birds (Fleming et al. 1983).

Residues of PCBs in birds are modified by numerous biotic factors including fat content, tissue specificity, sex, and developmental stage. PCB residues in birds may also reflect levels due to aerosol transport of these compounds (Weber 1983), as well as water transport (Norheim and Kjos-Hanssen 1984). Highest PCB residues were in birds with low fat content and in poor condition on capture (Falandysz and Szefer 1984). Sexual differences in PCB content are pronounced due to the female's ability to shed a significant portion of the PCB burden into eggs (Lemmetyinen and Rantamaki 1980). Developmental stage is an important consideration when collecting bird samples for PCB analysis (Lemetyinen and Rantamaki 1980); for example, PCB level is reduced from egg to fledgling (Fimreite and Bjerk 1983). Finally, residues in brain appear to be good indicators of PCB stress in birds (Stickel et al. 1984). Concentrations greater than 300 ppm of PCBs in brain (fresh weight) were consistently recorded in dead or dying ring-billed gulls (*Larus delawarensis*) and ring-necked pheasants (*Phasianus colchicus*) poisoned by PCBs, as quoted in Heinz et al. (1984).

MAMMALS

Among mammals, the mink is especially sensitive to PCBS; only 0.64 ppm PCBs in their diets caused reproductive failure, and 1.0 ppm caused death (as quoted in Fleming et al. 1983). In western Maryland and in northern Oregon during 1978-1979 (areas with no recognized large-scale PCB pollution), levels of PCBs in livers of some wild mink were comparable to those reported for female ranch mink that failed to reproduce after eating a diet contaminated with 0.64 ppm of PCBs for 160 days (O'Shea et al. 1981; Henny et al. 1981). Some fish from the Oregon collection sites contained PCB residues (0.24-2.8 ppm fresh weight) that were equivalent to, or higher, than dietary levels fed to mink under controlled conditions (Henny et al. 1981).

PCB concentrations in river otters from the Columbia River, Oregon, during 1978 and 1979, were substantially higher than those reported in the same species from Alabama. The significance of this is not clear, but declining harvests of Columbia River otter populations (as opposed to upward trends elsewhere in Oregon) suggest that PCBs may be a contributory agent (Henny et al. 1981).

In little brown bats (*Myotis lucifugus*) and big brown bats (*Eptesicus fuscus*) from Maryland, pups found dead at birth had significantly more Aroclor than live littermates; moreover, females with elevated Aroclor 1260 residues tended to produce litters with a greater frequency of stillbirths (Clark and Lamont 1976; Clark and Krynitsky 1978).

PCBs were recently detected in 13 of 26 Florida manatees (*Trichechus manatus*), an endangered species. All individuals with detectable PCB residues were recovered from locations in the relatively urbanized areas of northeastern Florida, primarily in the lower St. Johns River and Brevard County (O'Shea et al. 1984).

In harbor seals (*Phoca vitulina*), PCB concentrations decrease with increasing blubber thickness (Van Der Zande and De Ruiter 1983). As expected, lower chlorinated PCBs were eliminated more rapidly from blubber lipids than higher chlorinated PCBS. For harbor seals in particular, blubber PCB residues contained a small fraction of lower chlorinated components when compared to PCB residues in fish that they eat (Van Der Zande and De Ruiter 1983). PCBs in adult Weddell seals (*Leptonychotes weddelli*) were predominantly penta- and hexachlorobiphenyls; a slightly higher amount of lower chlorinated biphenyls were found in newborns (Hidaka et al. 1983), suggesting that lower chlorinated biphenyls are more easily transferred from mother to pup through transplacental action than higher chlorinated biphenyls. Weddell seals contain low concentrations of PCBs in blubber compared to 10 other pinniped species and small cetaceans. This probably reflects the low PCB burdens in their diets attributed, in part, to the heavy ice and snow cover during much of the year that prevents atmospheric deposition of PCBs from entering the water and contaminating their diet (Hidaka et al. 1983).

INTEGRATED STUDIES

Biomagnification of PCBs through marine food chains in an Australian estuary became increasingly important with upper level carnivores such as gulls and pelicans, but was relatively unimportant at lower trophic levels (Shaw and Connell 1982). A similar situation was observed in Central Puget Sound in Washington in 1979 (Malins et al. 1980). PCB body burdens in marine organisms, especially benthic organisms, were directly related to the log of PCB concentration in sediments (Shaw and Connell 1982). Furthermore, PCBs were found in every tissue analyzed from fish and invertebrates in Puget Sound in 1979 (Malins et al. 1980). High PCB levels, especially in sediments, have been recorded from highly industrialized areas worldwide (Baldi et al. 1983).

PCBs used in the manufacture of electrical equipment at two facilities located on the upper Hudson River in Washington County, New York, have resulted in severe PCB contamination of the sediments--reportedly more than 100X greater than any other major river system (Sloan et al. 1983). Edible portions of fish collected from this area often exceeded the FDA tolerance level of 5.0 ppm fresh weight (Sloan et al. 1983). Carcich and Tofflemire (1982) estimated that more than 272,000 kg (perhaps as much as 603,000 kg) of PCBs were discharged into the River, and that most still resides in sediments north of Troy, New York. In the Hudson River, levels of higher chlorinated PCB components typical of Aroclor 1254 have stabilized during 1977 to 1981, suggesting that a dynamic equilibrium has been reached, and that these compounds may continue to exist at concentrations close to present levels (Sloan et al. 1983). Removal of PCB contaminated sediments by dredging from the Hudson River is now being studied, with greatest effort confined to the most highly contaminated 8% of the river bed. Disposal, by total containment and isolation of contaminated materials within a land burial facility, is one of the more preferred options (Carcich and Tofflemire 1982).

TOXICITY

AQUATIC ORGANISMS

LC-50 values of sensitive species of freshwater and marine organisms subjected to various Aroclor PCBs varied from 0.1 to 10.0 ug/l during exposure of 7 to 38 days (Table 3). In general, toxicity increased with increasing exposure, crustaceans and younger developmental stages were the most sensitive groups tested, and lower chlorinated biphenyls were more toxic than higher chlorinated biphenyls. In most toxicity tests, mortality patterns in PCB-exposed fish did not stabilize within 30 days (Johnson and Finley 1980).

BIRDS

As a group, birds were more resistant to acutely toxic effects of PCBs than mammals (Table 4). LD-50s for various species of birds varied from 604 to more than 6,000 mg Aroclor/kg diet, and for mallards more than 2,000 mg/kg body weight administered orally (Table 4). Signs of PCB poisoning among birds included morbidity, tremors (which may become continuous),. beak pointed upwards, and muscular incoordination. At necropsy, the liver frequently contained hemorrhagic areas and the gastrointestinal tract was filled with blackish fluid (Stickel et al. 1984).

For all avian species, PCB residues of 310 mg/kg fresh weight or higher in brain were associated with an increased likelihood of death from PCB poisoning. Residues in brains of starlings, red-winged blackbirds (*Agelaius phoeniceus*), common grackles (*Quiscalus quiscula*), and brown-headed cowbirds (*Molothrus ater*), that died after eating diets containing 1,500 mg Aroclor 1254/kg, varied from 349 to 763 mg/kg; surviving birds, at the 50% mortality point, contained 54 to 301 mg/kg (Stickel et al. 1984). Similar results are reported for ringed turtle-doves (*Streptopelia risoria*) after 105 days fed a 10 mg Aroclor 1254/kg diet, chickens fed Phenoclor, Clophen, and Aroclor PCBS, and finches and cormorants fed Aroclor 1254 (as quoted in Stickel et al. 1984). In the field, PCBs were the probable cause of mortality of many ring-billed gulls that died in southern Ontario in late summer and early autumn of 1969 and 1973; PCB residues in brains were 310 to 1,110 mg/kg fresh weight in 67% of the samples analyzed, and 200 to 310 in the remainder (as quoted in Stickel et al. 1984).

MAMMALS

The mink is the most sensitive wildlife species tested for which data are available (Table 4). Diets containing 6.7 to 8.6 mg Aroclor PCBs/kg fresh weight killed 50% of the mink in 9 months; single dosages administered orally produced LD-50 values of 750 to 4,000 mg/kg body weight, those administered intraperitoneally produced LD-50s between 500 and 2,250 mg/kg body weight (Table 4). Recent data (Aulerich et al. 1985) indicate that certain hexachlorobiphenyls (HCBP), such as 3,4,5,3',4',5' HCBP, are extremely toxic to mink; concentrations as low as 0.1 mg/kg fresh weight diet produced an LD-50 in 3 months, and completely inhibited reproduction in survivors. However, other HCBPS, such as 2,4,5,2',4',5' HCBP and 2,3,6,2',3',6' HCBP, were not fatal to mink under similar conditions, and did not produce adverse reproductive effects (Aulerich et al. 1985). Additional research is needed on the toxicodynamics of PCB congeners. Signs of PCB poisoning in mink included anorexia, bloody stools, fatty liver, kidney degeneration, and hemorrhagic gastric ulcers (Aulerich and Ringer 1977). The reasons for mink sensitivity to PCBs are unknown, but large variations in sensitivity to PCBs among species are common, even among those closely-related taxonomically. The European ferret (*Mustela putorius furo*), for example, is at least three times more resistant than mink to Aroclor 1242 (Table 4).

Rats fed diets containing 1,000 mg of Aroclor 1254/kg diet all died in 53 days; mortality started at day 28 (Hudson et al. 1984). These, and other feeding studies, suggest that a total intake of about 500 to 2,000 mg of Aroclor 1254 per kg body weight is the lethal level in rats for dietary exposures of 1 to 7 weeks. Prior to death, rats showed lack of muscular coordination, eyelid drooping, blanched retinas, morbidity, nasal secretions, and (with Aroclor 1268) a reddish exudate from their eyes (Hudson et al. 1984). Some rats died at 100 mg Aroclor 1254/kg body weight administered orally, or about 1/5 of the dietary LD-50 (Hudson et al. 1984).

SUBLETHAL EFFECTS

GENERAL

PCBs elicit a variety of biologic and toxic effects including skin lesions, a wasting syndrome, immunotoxicity, reproductive toxicity, genotoxic and epigenetic effects, hepatomegaly and related liver damage, and the induction of hepatic and extrahepatic drug-metabolizing enzymes. PCB accumulations from the diet and from other sources are high, and retention is lengthy in fatty tissues. Interspecies differences in sensitivity to PCBs are large, even between species that are closely related taxonomically.

TERRESTRIAL MACROPHYTES

A 5X increase in somatic mutations was observed in ostrich ferns (*Matteuccia struthiopteris*) growing near the Housatonic River in Pittsfield, Massachusetts, on sediments containing mean PCB residues of 26 mg/kg (mostly as Aroclor 1254), when compared to ostrich ferns from control areas (Klekowski 1982). No attempt was

made to duplicate these observations under controlled conditions, and no evidence of genetic damage to other plants of the PCB-contaminated area was found (Klekowski 1982).

AQUATIC ORGANISMS

Bioconcentration of Aroclor 1254 from the medium by selected species of freshwater and marine organisms varied from 60 to 340,000X (Table 5). Various species of algae also concentrate PCBs over water levels by 10,000 to 100,000X (Ernst 1984). Oysters (*Crassostrea virginica*) held for 65 days in seawater solutions containing 0.0055 to 0.06 ug/l of di-, tri-, tetra-, penta-, or hexachlorobiphenyls had bioconcentration factors of 1,200 to 4,800X; uptake was lowest for dichlorobiphenyls and became progressively higher with increasing chlorination of PCB congeners (Ernst 1984). Similar results were recorded for *Daphnia magna* exposed to five different C-14 labeled PCBs for 24 hours. BCFs varied from 473 to 11,232; formulations lowest in water solubilty (highest chlorination) were accumulated most readily (Zhang et al. 1983). For all PCBS, BCFs were generally higher with increasing exposure period, with increasing PCB concentration, and with increasing chlorination of PCB congeners (NAS 1979; Johnson and Finley 1980; EPA 1980).

Since PCBs are highly lipophilic, greatest concentrations were expected, and occurred, in fatty tissues. For example, lipid content in muscle of brown trout (*Salmo trutta*) was the best correlate of PCB concentration in muscle (Spigarelli et al. 1983). Differences in PCB content of tissue lipids were negatively correlated with phospholipid fractions in total lipid extracts; the higher the phospholipid fraction, the lower the PCB content in organ lipids. This has been verified experimentally in codfish and other species of marine teleosts (Boon et al. 1984), and probably should be explored in greater detail for other trophic levels. Other factors known to modify PCB accumulations in aquatic biota include: temperature magnitude and variation for trout (Spigarelli et al. 1983); time of incubation and age of larvae for mosquitos (Gooch and Hamdy 1983); presence of mineral oils on PCB-contaminated substrates for chironomid larvae (Meier and Rediske 1984); and diet for teleosts (Pizza and O'Connor 1983; Spigarelli et al. 1983; O'Connor and Pizza 1984). Of these, diet contributes most of the total PCB body burdens of upper level carnivores. For example, diet accounted for 90% of the total PCB body burden in brown trout (Spigarelli et al. 1983), and 51 to 83% in striped bass (Pizza and O'Connor 1983). PCB body burdens in striped bass were lower in winter during nonfeeding periods, and lower when fish migrated to a new area where dietary PCB levels were lower (O'Connor and Pizza 1984). Prey species of carnivores accumulate PCBs through contaminated sediments. PCB transfer through aquatic ecosystems has been reported in the Great Lakes using a sediment-lake trout model (Jensen 1984), and in New York Harbor from contaminated sediments to clams, shrimp, and especially nereid worms (Rubenstein et al. 1983).

Depuration of accumulated PCBs is slow, and slower yet at reduced temperatures (Zhang et al. 1983). Larvae of codfish exposed to PCBs as eggs showed no elimination after 12 days. Uptake of PCBs by yolk sac larvae was higher than in eggs; 60% of the PCBs remained after 15 days (Solbakken et al. 1984b). Larvae of chironomids (*Glyptotendipes barbipes*), held for 24 days in substrates containing 1,000 mg Aroclor 1242/kg, contained 18.0 mg Aroclor 1242/kg fresh weight; 7 days later, larvae still retained 97.8% of the total (Meier and Rediske 1984). Tissue samples of a Bermuda brain coral (*Diploria strigosa*) taken 9 months after initial exposure for 24 hours to radiolabeled 2,4,5,2',4',5'-hexachlorobiphenyl contained 84% of the original radioactivity (Solbakken et al. 1984a). Rainbow trout fed 1,150 mg Aroclor 1254/kg body weight contained high residues in various tissues 38 days posttreatment: 70 mg/kg in muscle on a fresh weight basis, 33 in liver, and 6 in gill filament (Kiessling et al. 1983). Factors affecting elimination of Aroclor 1254 by marine crustacean copepods (*Acartia tonsa*) include diet and reproductive state (McManus et al. 1983). Copepods fed during depuration eliminated PCBs more rapidly than unfed copepods. PCBs in copepod eggs were up to 4X the concentration in females producing them. Females eliminated PCBs twice as rapidly as males, indicating that egg production is an important route for PCB elimination. Fecal pellets were the most significant elimination route, but levels in fecal pellets from both sexes decreased over time suggesting a multiphasic elimination pattern. In fish, egg maturation and spawning result in a significant reduction in the body burden of persistent PCBs such as 2,5,2',5'-tetrachloro BP (Vodicnik and Peterson 1985). The percent lipid, and the percent of total lipid deposited in their eggs, markedly influences PCB transfer from fish to eggs (Niimi 1983). Mean percent PCB residue levels translocated to eggs in five species of Great Lakes fish varied from a low of 5.4 in rainbow trout to a high of 29.3 in yellow perch, and these (and intermediate) percentages reflected lipid percent levels transferred (Niimi 1983). Structural features in PCB forms and congeners cause different elimination rates between individual components in fish, resulting in differences in PCB composition between tissues and the source of uptake (Boon et al. 1984).

Decreased growth of aquatic organisms during exposure to PCBs is well documented. Concentrations as low as 0.1 ug/l of Aroclor 1254 produced growth reductions in marine diatoms and a freshwater alga (*Scenedesmus quadricauda*), and altered the population structure of phytoplankton communities (EPA 1980). Among sensitive species of freshwater algae treated with Aroclor 1242, including *S. quadricauda*, disruption of internal chloroplast membranes and failure of cytokinesis were the major changes observed (Mahanty et al. 1983). Marine algae exhibited greater-than-expected reductions in photosynthesis when stressed with mixtures of PCBs and DDE (Ernst 1984), and demonstrates the importance of toxicant evaluation of complex mixtures containing PCBs. Decreased shell growth of oysters was reported in acute tests with Aroclor 1016 at 10.1 ug/l, with Aroclor 1248 at 17.0 ug/l, with Aroclor 1254 at 14.0 ug/l, and with Aroclor 1260 at 60.0 ug/l (EPA 1980); similar results were reported for shrimp (Ernst 1984). Fry of brook trout held for 48 days at 1.5 ug Aroclor 1254/1 also showed decreased growth (Johnson and Finley 1980).

Reproductive toxicity of PCBs is reported for Baltic flounder (*Platichthys flesus*) when ovaries exceeded 0.12 mg of PCBs/kg fresh weight, and for cyprinid minnows (*Phoxinus phoxinus*) when gonads contained more than 24 mg PCBs/kg fresh weight; these are the threshold values beyond which reduced survival of developing eggs can be expected in those species Ernst 1984). Gonadal levels of 24 mg/kg in minnows were obtained with diets of 20 mg Clophen A-50/kg for 40 days, followed by 260 days on untreated diets (Ernst 1984). Rainbow trout with whole body residues of 0.4 mg Aroclor 1242/kg fresh weight produced eggs with low survival, and numerous (70%) fry deformities (EPA 1980). Rainbow trout eggs with 0.33 mg Aroclor 1254/kg fresh weight incurred 10 to 28% mortality prehatch, and numerous posthatch deformities (Niimi 1983). Eggs and fry of Atlantic salmon with PCB contents of 0.6 to 1.9 mg/kg fresh weight, or 14.4-34.0 mg/kg lipid weight, experienced 46 to 100% mortality (Niimi 1983). Embryos of sheepshead minnow (*Cyprinodon variegatus*) containing 7 mg Aroclor 1254/kg fresh weight had low survival; these values were effected through exposure of parent fish to 0.14 ug Aroclor 1254/1 for 28 days (EPA 1980). Brook trout experienced complete reproductive failure during exposure to 200 ug Aroclor 1254/1 for 71 weeks; the no effect level was 0.94 ug/l (EPA 1980). Eggs of the sea urchin, *Arbacia punctulata*, exposed for one hour to 0.5 mg Aroclor 1254/1 prior to fertilization showed reduced fertilization success and lowered survival; eggs were markedly more resistant to PCBs at the time of insemination and afterwards (Aroclor 1254) on early development and mortality in Arbacia eggs. (Adams 1983).

Mutagenic properties of Aroclor 1221 and 4-monochlorobiphenyl to bacteria were indicated by positive Ames tests, and Aroclor 1260 and Kanechlor 500 were demonstrably carcinogenic to mice and rats (NAS 1979). Unexpectedly, Aroclor 1254 prevented carcinogenesis and mutagenesis in rainbow trout. Trout fed 100 ppm dietary Aroclor 1254 for 3 months were significantly more resistant to liver carcinomas (induced by dietary aflatoxins) when PCBs were prefed prior to carcinogenic insult (Shelton et al. 1983). At the time of aflatoxin administration, trout contained 594 mg/kg PCBs in fat which declined rapidly over the next 12 months to 3.9 mg/kg. Aflatoxin-induced mutagenesis in trout liver cells was also significantly inhibited (67%) by Aroclor 1254 under similar conditions (Shelton et al. 1983).

Histopathology was reported in sensitive marine teleosts following exposure for 2 weeks to PCB concentrations of 0.5 ug/l; similar damage effects were recorded in oysters held for 24 weeks in 5 ug/l of Aroclor 1254, but not for 30 weeks in 1 ug/l (Ernst 1984).

A wide variety of biochemical perturbations were recorded among teleosts stressed by PCBS. The primary biochemical effect of PCBs is to induce hepatic mixed function oxidase systems, thus increasing the organism's capacity to biotransform or to detoxify xenobiotic chemicals and endogenous steroids (Melancon and Lech 1983; Shelton et al. 1983). Coho salmon injected intraperitoneally with 50 to 100 ug Aroclor 1254/kg body weight just prior to smoltification contained elevated levels of PCBs in liver (500 to 1,200 ppb) 2 weeks after injection when compared to controls (25 to 45 ppb), showed depressed gill Na-K ATPase and plasma thyroxin levels, and experienced great difficulty in adapting to seawater (Folmar et al. 1982). Biochemical indicators suggested that tissue accumulations of PCBs (at concentrations that clearly could be derived through a contaminated diet or from water column exposure) delayed events preparatory to, and involved in, saltwater adaptation in coho salmon. Mixtures of Aroclor 1242 and 1254 fed to rainbow trout and coho salmon at dietary concentrations of 500 ppm PCBs for 7 to 10 weeks produced inhibited growth, enlarged livers, elevated muscle water content, and lowered muscle lipid content (Leatherland and Sonstegard 1981). Salmon showed disrupted calcium and magnesium metabolism in blood, muscle, and skeleton. After about a week on PCB diets, both trout and salmon showed signs of poor muscle coordination and tetany, accompanied by lateral or ventral caudal flexion (scoliosis or lordosis). Brown trout fed diets containing 10 ppm of Clophen A-50 for 43 days were

anemic, hyperglycemic, and showed altered cholesterol metabolism (EPA 1980). Brook trout held in Aroclor 1254 solutions of more than 0.43 ug/l for 48 days had decreased concentrations of hydroxyproline in collagen isolated from the backbone (Johnson and Finley 1980). However, Aroclor 1254 did not markedly affect adrenaline response in gills of rainbow trout, or glycogen storage in muscle (Kiessling et al. 1983).

Maximum Acceptable Toxicant Concentration (MATC) values bracket the "no effect," and "measurable effect" levels, and are based on chronic exposure, and variables such as growth, reproduction, and metabolic upset. MATC values for selected species of aquatic organisms and Aroclor PCBS, with one exception, varied from 0.1 to 5.4 ug/l for the no effect level, and from 0.4 to 15.0 ug/l for measurable effects (Table 6). The exception was larvae of the sheepshead minnow (which was especially sensitive) with an MATC of 0.06 to 0.16 ug/l for Aroclor 1254 (Table 6).

BIRDS

Among sensitive avian species, PCBs disrupt normal patterns of growth, reproduction, metabolism, and behavior. In general, PCB accumulation is rapid and depuration is lengthy. Diet is an important route of PCB accumulation. Concentrations in liver (mg/kg fresh weight) were highest (900) in birds that fed on fish, followed by species that feed on small birds and mammals (50), worms and insects (0.65), and lowest (0.2) in herbivorous species (NAS 1979).

Delayed reproductive impairment was documented in ringed turtle-doves given 10 ppm of dietary Aroclor 1254 for 3 months; residues in the fat of adults was 736 ppm, and in their eggs 16 ppm fresh weight (as quoted in Heinz et al. 1984). Hatchability of ringed turtle-dove eggs from the first clutch was not reduced by consumption of Aroclor by the adults. However, 6 months later, the hatchability of the second clutch (accompanied by abnormal incubation behavior) was reduced to 10% of controls; embryos also contained chromosomal aberrations (Peakall et al. 1972). Mourning doves (*Zanaida macroura carolinensis*) given dietary Aroclor 1254 for 6 weeks at 0, 16, or ppm were observed for courtship behavior and reproductive effort during days 14 to 44 posttreatment (Tori and Peterle 1983). Doves fed 10 ppm spent twice as much time as controls in the courtship phase (billing, cooing, nest site selection), but only 50% of these pairs completed the courtship phase and progressed into nest building and incubation; of those that nested, nest initiation was significantly delayed. Doves fed 40 ppm spent the 30 days posttreatment in courtship without nesting; most of this group, especially females, did not respond normally to the presence of a mate. Tori and Peterle (1983) suggested that the disrupted reproductive behavior observed in PCB-treated doves was due to reduced estrogen and androgen levels. PCBs have been shown to degrade estrogens and androgens by increasing the activity of hepatic microsomal enzymes (as quoted in Tori and Peterle 1983). Hatchability of chicken eggs was reduced when hens were fed diets containing 20 ppm of various Aroclor PCBs (1232, 1242, 1248, or 1254). PCB residues in samples of fat from treated hens varied from 45 to 125 ppm, and in their eggs from 3 to 14 ppm (as quoted in Heinz et al. 1984). Reproductive impairment in chickens was recorded at Aroclor dietary levels as low as 5 ppm; effects at the 2 ppm level were not significant (Heinz et al. 1984). American kestrels (*Falco sparverius*) given 33 ppm of dietary Aroclor 1254 for 62 to 69 days (equivalent to 9 to 10 mg/kg body weight/daily), showed a significant decline in sperm concentration, but no compensatory increase in semen volume (Bird et al. 1983). PCB residues in treated kestrels, in ppm lipid weight, were 107 in muscle and 128 in testes; for controls, these values were 0.4 in muscle and 1.0 in testes. These results suggest that migratory flesh-eating birds feeding on a PCB-contaminated food chain might consume enough toxicant to alter their semen quality in that breeding season; when coupled with altered courtship, this could reduce the fertility of the eggs and reproductive fitness of the individual (Bird et al. 1983).

Among comparatively resistant species of birds, no significant reproductive effects were observed during long-term exposures at high Aroclor 1254 feeding levels in Japanese quail *Coturnix coturnix* (50 ppm in diets), northern bobwhites *Colinus virginianus* (50 ppm) 979), and mallards (25 ppm) (Custer and Heinz 1980). Screech owls (*Otus asio*), given 3 ppm of Aroclor 1248 in their diets for two breeding seasons, laid eggs containing 3.9 to 17.8 mg PCBs/kg fresh weight compared to control values of 0.0 to 0.6; however, reproductive variables, including eggs per clutch, hatchability, chick malformations, survival, and eggshell thickness, were not affected (McLane and Hughes 1980).

For most avian species, a reduction in eggshell thickness of 15 to 20% is suggested as a critical value beyond which population numbers will decline (Nygard 1983). Pheasants fed 50 mg of Aroclor 1254 weekly produced fewer eggs, but an effect on eggshell thinning was not apparent before other effects became obvious

(Roberts et al. 1978). However, eggshell thickness of the peregrine falcon (*Falco peregrinus*) from Norway declined 85% between 1854 and 1976; addled eggs containing dead embryos collected in 1976 had 724 ppm of PCBs in lipids, and up to 110 ppm on a fresh weight basis (Nygard 1983) Peregrine populations have declined in Norway, but the high DDT levels (which cause eggshell thinning) in tissues and eggs--together with measurable residues of dieldrin and mercury--made it difficult to ascribe thinning or population declines exclusively to PCBs (Nygard 1983). Mean PCB residues were significantly lower in eggs from successful nests of the American bald eagle than unsuccessful nests (1.3 ppm fresh weight vs. 7.2), and may be associated with eggshell thinning (Wiemeyer et al. 1984). PCB concentrations in eggs were inversely correlated with shell thickness in the bald eagle (Wiemeyer et al. 1984) as well as the black-crowned night-heron (McEwen et al. 1984; Henny et al. 1984). However, PCB content is frequently correlated positively with DDE content- (Norheim and Kjos-Hanssen 1984), which is known to interfere with avian calcium metabolism and to induce thin eggshells. The observed thickening of eggshells in black-crowned night-heron eggs between 1973 and 1979 in colonies from Rhode Island locations was associated with marked reductions in both PCBs and DDE (Custer et al. 1983a,b). At present, the evidence implicating PCBs as a major source of eggshell thinning is inconclusive.

Loss rates were followed in common grackles fed 150 ppm dietary Aroclor 1254 for 8 days, then given untreated food and killed at 1 to 32 weeks posttreatment (Stickel et al. 1984). PCB levels in bodies of grackles declined from 1,300 ppm fresh weight on the day clean food was restored, to 169 ppm 32 weeks later. The overall loss rate was estimated at 0.77% daily with a calculated biological half-life of 89 days. Similar loss rates were observed in pheasants given a single capsule dosage of Aroclor 1254 (as quoted in Stickel et al. 1984). In general, PCB residues in brain are good indicators of PCB exposure. For example, Japanese quail fed 1,000 ppm of Aroclor 1260, and that subsequently died, contained 780 ppm in brain; treated survivors contained 250 ppm (as quoted in Heinz et al. 1984). Also, various species of small birds that were killed by dietary exposure to Aroclor 1254 had PCB brain residues of 349 to 763 ppm (Heinz et al. 1984).

PCBs are associated with a variety of biochemical, histopathological, and behavioral responses in birds. PCBs affect zinc and calcium metabolism in chickens, disrupt vitamin A use in quail, and potentiate vitamin A deficiency in chickens by interfering with selenium use (Roberts et al. 1978). Body temperature, serum chemistry, and thyroid function of ringed turtle-doves was significantly altered by 3,4,3',4'-tetrachlorobiphenyl (Spear and Moon 1985). Metabolism of various respiratory pigments was disrupted by PCBs in birds and mammals (Roberts et al. 1978). PCBs are good inducers of drug-metabolizing enzymes that are vital in detoxification processes. Aroclor 1254 injected once into liver parenchymal tissue of the barn owl (*Tyto alba*), at 30 mg/kg body weight, produced increases in the levels of liver cytochrome P-450 activities (Rinzky and Perry 1983). Ringed turtle-doves fed 10 or 100 ppm of dietary Aroclor 1254 showed depressed levels of dopamine and norepinephrine; PCB residues in the brains of these doves averaged 2.8 in the 10 ppm group, and 18.3 ppm in the 100 ppm group (Heinz et al. 1984). Pelicans (Pelecanus sp.) fed 100 ppm of dietary Aroclor 1254 for 10 weeks showed increase liver histopathology (NAS 1979). Certain PCB congeners produce acute histopathologic changes in chick embryo liver, and these same congeners selectively induce cytochrome P-448 mediated mixed function oxidases; adverse effects were noted within 24 hours at concentrations as low as 146 mg of 3,4,3',4'-tetrachlorobiphenyl and 3,4,5,3',4',5'-hexachlorobiphenyl on a whole egg fresh weight basis (Rifkind et al. 1984). PCBs also have been associated with abnormal behavior in European robins (*Erithacus rubecula*), pheasants, quail, and other avian species according to Heinz et al. (1984).

MAMMALS

The mink is one of the most sensitive mammalian species to PCBs (Aulerich et al. 1985). Signs of PCB poisoning in mink include anorexia, weight loss, lethargy, and unthrifty appearance; prior to death, dark fecal stools indicative of the presence of blood from the upper gastrointestinal tract (confirmed by necropsy) was observed. Enlarged livers of mink given PCB diets were typical; a similar pattern has been associated in practically all species studied. PCB residues (10 to 15 ppm whole body fresh weight) within Great Lakes fish incorporated into the diet of mink caused reproductive problems and death in commercially ranched mink as long ago as 1965. Diets supplemented with as little as 2 ppm of Aroclor 1254 for 8 months, or 5 ppm for 4 months, resulted in near reproductive failure--with normal breeding and whelping, but a high death rate of kits; reproduction was not affected at dietary levels of 1 ppm of Aroclor 1254. Certain hexachlorobiphenyl isomers can produce death and reproductive toxicity in mink at dietary concentrations as low as 0.1 mg/kg, while other hexachlorobiphenyls are relatively innocuous (Aulerich et al. 1985). Biologically modified PCBs are more toxic to mink than corresponding technical mixtures. For example, tissues from cattle that had been dosed with

Aroclor 1254 and fed to mink at levels as low as 0.64 ppm fresh weight of diet caused severe reproductive effects, possibly because cattle tissues retained more of the highly chlorinated congeners of the PCB mixture once they have been metabolized. But Aroclors 1016 and 1221, at dietary concentrations of 2 ppm, produced no adverse reproductive effects in mink over a 9-month period, nor did Aroclor 1242 at 5 ppm during a similar period; the reasons for this are unknown but may be due to the ability of mink to metabolize selected PCB congeners. Mink, for example, easily eliminate 2,2',4,4',5,5'-hexachlorobiphenyl, but in rats, domestic pigeons (*Columba livia*), and trout, this congener remains almost indefinitely (Hornshaw et al. 1983). Placental transfer of PCBs occurs in mink, as has been demonstrated for rats, rabbits, cattle, rhesus monkeys, ferrets, and humans, and gives rise to the embryotoxicity demonstrated by these species (Ringer 1983). A significantly greater quantity of PCBs enters the growing offspring of mink from mammary transfer than from placental transfer. This PCB transfer by the lactating mink probably resulted in the high offspring mortality observed when Great Lakes fish were fed to commercial ranch mink in the late 1960's. Aroclor 1254 residues in subcutaneous fat of adult mink was up to 38X dietary levels, and some individual congeners accumulated up to 200X. The time for 50% elimination of PCBs from adipose tissues was about 98 days, and about 199 days for 100% elimination. Comparable data for other mammals indicate that PCBs are eliminated more rapidly by these species than mink, with 50% half-life times of 33 hours to 69 days for tissues of rat and dairy cows (EPA 1980; Stickel et al. 1984). In general, PCB residues in fat of mink were highest in winter when fat deposits were mobilized during cold weather and PCB residues were concentrated in remaining fat stores; this is consistent with the results obtained from pigeons subjected to low temperatures and starvation (Hornshaw et al. 1983).

The European ferret was significantly more resistant to PCBs than mink, and demonstrates that interspecies sensitivity to PCBs varies widely, even among taxonomically close species (Ringer 1983; Bleavins et al. 1984). In ferrets, total reproductive failure was documented in 9-month feeding studies of Aroclor 1242 at dietary levels of 20 ppm, but Aroclor 1016 at 20 ppm did not affect reproduction during a similar period. PCBs in maternal body fat stores of ferrets represent a reservoir that can be transferred to the developing fetus and growing neonate (Aroclor 1254) in the European ferret (Bleavins et al. 1984). Placental transfer of Aroclor 1254 to kits of the European ferret was about 0.01% per kit of the female's absorbed dietary dose when exposure occurred during the first trimester of pregnancy, and 0.04% when PCBs were administered during the third trimester. Transfer of PCBs through the dam's milk was also documented, and this route was 6 to 15X more effective than placental transfer.

The rhesus monkey (*Macaca mulatta*) is extremely sensitive to PCBs (Roberts et al. 1978; NAS 1979 EPA 1980; Safe 1984). Females fed diets containing 2.5 to 5.0 ppm of Aroclor 1248 for 6 months showed altered menstrual cycles, an increased frequency of stillbirths and abortions, a lowered birth rate, hyperpigmentation, skin eruptions, eye problems, and negatively altered behavioral patterns. Males were less sensitive than females; however, when fed diets containing 300 ppm of Aroclor 1248 for one month, both sexes showed hair loss, purulent discharges from the eyes, acneform skin eruptions, and hypertrophy of the liver and gastric mucosa. Rhesus monkeys can efficiently absorb Aroclor 1248 from the gut; 90% of a single oral dose of 1,500 or 3,000 mg/kg body weight was reported absorbed from the gastrointestinal tract. This, and the fact that rhesus monkeys were unable to efficiently eliminate or metabolize certain PCB congeners (i.e., 2,5,2',5'-tetrachlorobiphenyl) when compared to other species, may partially account for the sensitivity of this species. Infant rhesus monkeys, born to mothers exposed to 2.5 ppm of Aroclor 1248 in the diet during pregnancy and lactation, survived over 4 months; PCB levels in their fat declined over a period of 8 to 23 months.

In Japan, humans were accidentally poisoned by rice oil containing 2 to 3 mg of Kanechlor 400/kg (EPA 1980; Lucier and Hook 1985a,b). Symptoms included increased eye discharges and swelling of upper eyelids, acneform skin eruptions, skin pigmentation, hearing and vision problems, gastrointestinal disturbances, and altered blood chemistry. Infants born of Japanese women married to afflicted males were small for their age, had unusual pigmentation, premature eruption of teeth, and exophthalmia (popeyes). Three years after exposure, 50% of the patients were improving, 40% were unchanged, and 10% were worse. Even among those said to be improving, many still complained of headaches, fatigue, weakness and numbness of the limbs, and weight loss. Impurities in the Kanechlor 400 mixture included polychlorinated dibenzofurans and dioxins at levels up to 5 ppm, and these may be responsible, in part, for the observed symptoms in victims.

Mutagenic, carcinogenic, and teratogenic properties of PCBs are documented. Certain PCB congeners, such as 4-chlorobiphenyl, were highly mutagenic to *Salmonella typhimurium* in Ames tests (EPA 1980). Aroclor 1221 was less mutagenic, while Aroclors 1254 and 1268 were essentially inactive. In general, mutagenic

activity tends to decrease with increasing chlorination (EPA 1980). The carcinogenic effects of PCBs have been established in mice and rats with various Aroclor and Kanechlor PCBs and these, in turn, may enhance the carcinogenicity of other chemicals (EPA 1980). Experimental data clearly shows that commercial PCBs cause liver damage which leads to putative preneoplastic changes and hepatocellular carcinomas; however, these lesions are observed only after lengthy (11 to 21 months) exposures to relatively high doses (100 to 1,200 ppm in diets) of these chemicals (NAS 1979; Safe 1984). PCBs were also shown to inhibit the growth of experimental tumors in rats (EPA 1980); administration of Aroclor 1254 (either dietary or injected) for 5 days before or after tumor inoculation was more effective than administration between days 5 and 10. Teratogenic effects of PCBs observed in monkeys and rabbits include abnormal skull formation of fetuses exposed to high levels of Aroclor 1254 in utero, and retarded growth (EPA 1980).

Aroclor 1254 at dietary levels of 25 to 100 ppm for up to 3 weeks can significantly reduce sleeping times in animals that normally aestivate or hibernate, such as white-footed mice, *Peromyscus leucopus* (Sanders and Kirkpatrick 1977), and raccoons, *Procyon lotor* (Montz et al. 1982). The implications of this are not clear, and additional research is needed. Other systemic effects of PCBs that occur in a wide variety of animal species include hepatic disorders distinguished by altered porphyrin metabolism, increased thyroxin metabolism and ultrastructural changes in the thyroid, inhibition of ATPases, interference with oxidative phosphorylation, alterations in steroid hormone activities, immunosuppressive effects, and altered vitamin A metabolism (EPA 1980; Safe 1984).

CURRENT RECOMMENDATIONS

Effective July 1979, under Section 6e of the Toxic Substances Control Act, and unless specifically exempted by the U.S. Environmental Protection Agency, the manufacturing, processing, commercial distribution, and use of PCBs (except in a totally enclosed system) were prohibited (Bremer 1983). Similar actions had been initiated by Michigan, Wisconsin, and Minnesota in 1977 (Bremer 1983). However, PCBs remain universally distributed in the environment, and releases still include those from manufacturing, leaks from supposedly closed systems, and disposal of PCBs manufactured prior to 1971 (Ayer 1976). PCB burdens in waters, sediments, soils, disposal sites, and in deployed transformers and other containers of PCB is estimated at 82 million kg (D'Itri and Kamrin 1983). At this time, total PCB residues in organisms appear to be a more reliable measure of environmental PCB levels than measurements of any commercial mixtures (Schmitt et al. 1985). In light of the demonstrated differential toxicities within the array of PCB congeners, existing standards and criteria may need to be modified in order to reflect the more toxic PCBs (Brown et al. 1985).

PCB tolerance levels have been recommended for protection of various environmental resources and human health (Table 7). The recommended freshwater aquatic life protection criterion of 0.014 ug/l (24-hour average) is lower than 0.1 ug/l, a concentration known to adversely affect the growth of freshwater algae and fish (EPA 1980). This criterion would probably afford a satisfactory degree of protection to freshwater life if it were changed from 0.014 ug/l (24-hour average) to 0.014 ug/l (maximum). Criteria based on average daily concentrations usually indicate that high doses of toxicants may occur within a short period. Unfortunately, data bases existing for PCBs are inadequate to predict long-term effects on growth, uptake, and other variables when repeated high doses occur in short intervals.

The criterion of 0.03 ug/l (24-hour average) recommended for saltwater aquatic life protection is unsatisfactory. Concentrations of 0.1 ug/l of Aroclor 1254 are fatal to sheepshead minnows in 21 days, and concentrations as low as 0.006 ug/l result in significant uptake by oysters over a period of 65 days (Ernst 1984). Until additional data become available, the saltwater aquatic life protection criterion should not differ from the freshwater criterion (0.014 ug/l, maximum).

Fish diets containing 1.0 mg of Aroclor 1254 per kg fresh weight produced pathological changes in the kidney of rainbow trout after 11 months, and diets containing 1.2 mg Aroclor 1248/kg fresh weight produced progressive degenerative changes in the liver of lake trout after 9 months (Roberts et al. 1978). The current recommended level for PCBs in fish diets of less than 0.5 mg/kg fresh weight is based on investigations with striped bass by O'Connor and Pizza (1984). They found that food items containing less than 0.5 mg/kg fresh weight will not, in the course of one growing season, cause body burdens in striped bass to exceed 2 mg/kg fresh weight, a proposed Food and Drug Administration guideline for PCB burdens in fish. Striped bass are mobile, pelagic, and highly migratory; accordingly, dietary levels may have to be revised downwards for benthic, nonmigratory species that frequent localized areas of high PCB contamination (O'Connor and Pizza 1984).

Whole body residues of 0.4 mg PCBs/kg fresh weight are associated with reproductive toxicity in rainbow trout (EPA 1980). The large discrepancy between this value and the current recommended level of 5.0 mg/kg fresh weight in fish and shellfish (Table 7) will be discussed later. Eggs of rainbow trout containing 0.33 mg PCBs/kg fresh weight showed reduced hatch, and a significant increase in larval deformities (Niimi 1983). PCB residues of 0.12 mg/kg fresh weight in gonads of field-collected Baltic flounders may be associated with population declines of that species (Ernst 1984), but this needs to be verified experimentally.

Birds seem relatively resistant to PCBS. Among sensitive species, female screech owls fed 3.0 mg of PCBs/kg fresh weight diet laid eggs containing up to 17.8 mg/kg fresh weight; however, no other adverse effects were observed in either parents or progeny (McLane and Hughes 1980). Higher dietary exposures of 5 mg/kg in chickens, and 10 mg/kg in mourning doves resulted in reproductive impairment (Tori and Peterle 1983; as quoted in Heinz et al. 1984). Fertilized eggs of ringed turtle-doves containing 16.0 mg PCBs/kg fresh weight showed delays in growth and development (Peakall et al. 1972), and residues of this magnitude should be considered as presumptive evidence of significant PCB contamination. Residues in brain appear to be good indicators of PCB exposure in birds. Concentrations in excess of 301 mg PCBs/kg brain fresh weight is strong evidence of PCB poisoning, while concentrations in excess of 54 mg/kg fresh weight were common in brain of various avian species that survived high PCB dosages (Stickel et al. 1984).

Rats and dogs (*Canis* sp.) fed various Aroclor PCBs for 2 years showed no measurable effects at dietary levels equivalent to 0.255 (dogs) and 0.5 (rats) mg/kg body weight daily. Using a safety factor of 100, tolerable exposure limits of 2.5 (dog) and 5.0 (rat) ug PCBs/kg body weight daily were derived (Table 7). For the rhesus monkey, a comparatively sensitive species, the new temporary tolerance exposure is 1.0 ug/kg body weight daily (Grant 1983). The mink is the most sensitive animal tested to PCBs, with death and reproductive toxicity documented at 100 to 640 ug PCBs/kg fresh weight of diet (Table 7). The feeding level at which no measurable effects occur is not known with certainty. However, the calculated maximum tolerance level for mink is less than 1.54 ug PCBs/kg body weight daily. This value was derived by known growth rates of female mink between ages 7 and 31 weeks (NAS 1968)--when their body weight increased from 560 g to 1,130 g--by the percent of body weight consumed as food on a daily basis (16.4 to 27.2), and by a safety factor of 100 applied to a dietary level of 0.64 mg PCBs/kg fresh weight of diet. Since safety factors are usually applied to the no observed effect levels, a tolerable level of PCBs for mink may be less than 1.0 ug/kg body weight daily. Other species of mammalian wildlife tested were more resistant to PCBs than mink, and tolerance levels for livestock (Table 7) may also afford a reasonable degree of protection for wildlife, except mink.

Sound management of fishery and wildlife resources--including those resources that are artificially propagated and released--requires noninterference with desired uses such as health and well being of humans and other organisms at various trophic levels. Prior to the legislative restrictions on PCB use, Substantial losses to the atmosphere resulted from evaporation of plasticizers and from improper incineration, directly impacting occupational workers (EPA 1980), as well as aquatic ecosystems (Ayer 1976). In recent years, PCB levels have significantly declined in all human food items, with the possible exception of fish; most samples of fish containing more than 5.0 mg PCBs/kg fresh weight originated from the Great Lakes area (Hoeting 1983). In Michigan, all of a sample of 1,057 mothers had measurable PCBs in their breast milk at an average level of 2.3 mg/kg. Nursing infants from Michigan mothers might consume 10 to 25X the maximum daily dose rate of 1.0 ug PCBs/kg body weight that is currently recommended by the U.S. Food and Drug Administration for human adult intake (Swain 1983). The Michigan Department of Public Health has since established a Public Health Advisory related to fish consumption. They recommend that children, pregnant women, nursing mothers, and women who expect to bear children should not consume fish from the Great Lakes area (Swain 1983). Canadian PCB tolerance levels in food items for human health protection are markedly lower than those of the United States (Table 7). In one case, the current USA health tolerance level of 5.0 mg/kg fresh weight in fish and shellfish presents a distinct hazard to piscivorous teleosts and to fish-eating birds and mammals. A lowering from 5.0 to 2.0 mg PCBs/kg fresh weight in fish and shellfish has been proposed by FDA, but the tolerance level has not yet been changed; the delay appears to be based on economic reasons (Hoeting 1983). In the Great Lakes, for example, 55% of the domestic fish samples collected in 1979-1980 exceeded 2.0 mg PCBs/kg fresh weight; in 1980-1981, this was 17%; and in 1981-1982, 10% of the samples exceeded 2 mg/kg, including chinook salmon and their eggs, and lake trout (Hoeting 1983). In every collection year, measurable PCB residues were recorded in at least 28% of the Great Lakes fish samples collected (Hoeting 1983). At present, three courses of action appear warranted: continuation of the Nationwide monitoring program of fish and wildlife for PCBs and other environmental pollutants (O'Shea and Ludke 1979), additional investigations on the fate of PCBs under

conditions prevailing in the natural environment, and controlled studies on the toxicological significance of chlorinated dibenzofurans and other trace impurities found in commercial PCB mixtures and used PCB containing fluids.

LITERATURE CITED

Adams, J.A. 1983. Effect of PCB (Aroclor 1254) on early development and mortality in *Arbacia* eggs. Water, Air, Soil Pollut. 20:1-5.

Adams, J.A., and H.M. Haileselassie. 1984. The effects of polychlorinated biphenyls (AroclorsO 1016 and 1254) on mortality, reproduction, and regeneration in *Hydra oligactis*. Arch. Environ. Contam. Toxicol. 13:493-499.

Aguilar, A. 1983. Organochlorine pollution in sperm whales *Physeter macrocephalus*, from the temperate waters of the eastern North Atlantic. Mar. Pollut. Bull. 14:349-352.

Aulerich, R.J., S.J. Bursian, W.J. Breslin, B.A. Olson, and R.K. Ringer. 1985. Toxicological manifestations of 2,4,5,2',4',5'-, 2,3,6,2',3',6'-, and 3,4,5,3',4',5'- hexachlorobiphenyl and Aroclor 1254 in mink. J. Toxicol. Environ. Health 15:63.79.

Aulerich, R.J., and R.K. Ringer. 1977. Current status of PCB toxicity to mink, and effect on their reproduction. Arch. Environ. Contam. Toxicol. 6:279-292.

Ayer, F.A. (compiler). 1976. National conference on polychlorinated biphenyls. U.S. Environ. Protection Agency Rep. 560/6-75-004. 487 pp.

Baldi, F., R. Bargagli, S. Focardi, and C. Fossi. 1983. Mercury and chlorinated hydrocarbons in sediments from the Bay of Naples and adjacent marine areas. Mar. Pollut. Bull. 14:108-111.

Bird, D.M., P.H. Tucker, G.A. Fox, and P.C. Lague. 1983. Synergistic effects of Aroclor ® 1254 and mirex on the semen characteristics of American kestrels. Arch. Environ. Contam. Toxicol. 12:633-640.

Bleavins, M.R., W.J. Breslin, R.J. Aulerich, and R.K. Ringer. 1984. Placental and mammary transfer of a polychlorinated biphenyl mixture (Aroclor 1254) in the European ferret (*Mustela putorius furo*). Environ. Toxicol. Chem. 3:637-644.

Boon, J.P., R.C.H.M. Oudejans, and J.C. Duinker. 1984. Kinetics of polychlorinated biphenyl (PCB) components in juvenile sole (*Solea solea*) in relation to their concentrations in food and to lipid metabolism. Comp. Biochem. Physiol. 79C:131-142.

Bowes, G.W., and J.A. Lewis. 1974. Extraction of polychlorinated biphenyls: evaluation of a column technique applied to polar bear and seal tissue. J. Assoc. Off. Anal. Chem. 57:138-144.

Bremer, K.E. 1983. Dealing with multi-agency and multi-state regulation of polychlorinated biphenyls. Pages 367-373 *in* F.M. D'Itri and M.A. Kamrin (eds.). PCBS: human and environmental hazards. Butterworth Publ., Woburn, MA.

Brown, M.P., M.B. Werner, R.J. Sloan, and K.W. Simpson. 1985. Polychlorinated biphenyls in the Hudson River. Environ. Sci. Technol. 19:656-661.

Brunn, H., H.D. Berlich, and F.J. Muller. 1985. Residues of pesticides and polychlorinated biphenyls in game animals. Bull. Environ. Contam. Toxicol. 34:527-532.

Buckley, E.H. 1983. Decline of background PCB concentrations in vegetation in New York State. Northeast. Environ. Sci. 2:181-187.

Cain, B.W., and C.M. Bunck. 1983. Residues of organochlorine compounds in starlings (*Sturnus vulgaris*), 1979. Environ. Monitor. Assess. 3:161-172.

Carcich, I.G., and T.J. Tofflemire. 1982. Distribution and concentration of PCB in the Hudson River and associated management problems. Environ. Int. 7:73-85.

Chovelon. A., L. George, C. Gulayets, Y. Hoyano, E. McGuinness, J. Moore, S. Ramamoorthy, Su. Ramamoorthy, P. Singer, K. Smiley, and A. Wheatley. 1984. Pesticide and PCB levels in fish from Alberta (Canada). Chemosphere 13:19-32.

Clark, D.R., Jr., and A. Krynitsky. 1978. Organochlorine residues and reproduction in the little brown bat, Laurel, Maryland-June 1976. Pestic. Monitor. J. 12:113-116.

Clark, D.R., Jr., and T.G. Lamont. 1976. Organochlorine residues and reproduction in the big brown bat. J. Wildl. Manage. 40:249-254.

Clark, D.R., Jr., R.K. LaVal, and A.J. Krynitsky. 1980. Dieldrin and heptachlor residues in dead gray bats, Franklin County, Missouri- 1976 versus 1977. Pestic. Monitor. J. 13:137-140.

Clark, D.R., Jr., and R.M. Prouty. 1976. Organochlorine residues in three bat species from four localities in Maryland and West Virginia, 1973. Pestic. Monitor. J. 10:44-53.

Custer, T.W., C.M. Bunck, and T.E. Kaiser. 1983a. Organochlorine residues in Atlantic coast black-crowned night-heron eggs, 1979. Colonial Waterbirds 6:160-167.

Custer, T.W., and G.H. Heinz. 1980. Reproductive success and nest attentiveness of mallard ducks fed Aroclor 1254. Environ. Pollut. 21:313-318.

Custer, T.W., G.L. Hensler, and T.E. Kaiser. 1983b. Clutch size, reproductive success, and organochlorine contaminants in Atlantic coast black-crowned night-herons. Auk 100:699-710.

De Vault, D.S. 1985. Contaminants in fish from Great Lakes harbors and tributary mouths. Arch. Environ. Contam. Toxicol. 14:587-594.

D'Itri, F.M., and M.A. Kamrin (eds.). 1983. PCBS: human and environmental hazards. Butterworth Publ., Woburn, MA. 443 pp.

Duinker, J.C., M.T.J. Hillebrand, and J. P. Boon. 1983. Organochlorines in benthic invertebrates and sediments from the Dutch Wadden Sea; identification of individual PCB components. Neth. J. Sea Res. 17:19-38.

Dunn, W.J., III, D.L. Stalling, T.R. Schwartz, J.W. Hogan, and J.D. Petty. 1984. Pattern recognition for classification and determination of polychlorinated biphenyls in environmental samples. Anal. Chem. 56:1308-1313.

Edwards, W.R., R.E. Duzan, and R.J. Siemers. 1983. Organochlorine insecticide residues and PCBs in tissues of woodcock, mourning doves, and robins from east-central Illinois, 1978-79. Bull. Environ. Contam. Toxicol. 31:407-414.

EPA. 1980. Ambient water quality criteria for polychlorinated biphenyls. U.S. Environ. Protection Agency Rep. 440/5-80-068. 211 pp.

Ernst, W. 1984. Pesticides and technical organic chemicals. Pages 1617-1709 in 0. Kinne (ed.). Marine ecology. Vol. V, Part 4. John Wiley, New York.

Evans, M.S., R.W. Bathelt, and C.P. Rice. 1982. PCBs and other toxicants in *Mysis relicta*. Hydrobiol. 93:205-215.

Falandysz, J., and P. Szefer. 1984. Chlorinated hydrocarbons in fish-eating birds wintering in the Gdansk Bay, 1981-82 and 1982-83. Mar. Pollut. Bull. 15:298-301.

Fimreite, N., and J.E. Bjerk. 1983. Residues of DDE and PCBs in Norwegian seabirds' fledglings, compared to those in their eggs. Astarte 12:49-51.

Fleming, W.J., D.R. Clark, Jr., and C.J. Henny. 1983. Organochlorine pesticides and PCB's: a continuing problem for the 1980s. Trans. North Am. Wildl. Natur. Resour. Conf. 48:186-199.

Flickinger, E.L., and D.M. Swineford. 1983. Environmental contaminant hazards to Attwater's greater prairie-chickens. J. Wildl. Manage. 47:1132-1137.

Folmar, L.C., W.W. Dickhoff, W.S. Zaugg, and H.O. Hodgkins. 1982. The effects of Aroclor 1254 and No. 2 fuel oil on smoltification and sea-water adaptation of coho salmon (*Oncorhynchus kisutch*). Aquat. Toxicol. 2:291-299.

Fox, M.E., J.H. Carey, and B.G. Oliver. 1983. Compartmental distribution of organochlorine contaminants in the Niagara River and the western basin of Lake Ontario. J. Great Lakes Res. 9:287-294.

Friedman, M.A., F.D. Griffith, and S. Woods. 1977. Pathologic analysis of mink mortality in New England mink. Arch. Environ. Contam. Toxicol. 5:457-469.

Gooch, J.A., and M.K. Hamdy. 1983. Uptake and concentration factor of Aroclor 1254 in aquatic organisms. Bull. Environ. Contam. Toxicol. 31:445-452.

Grant, D.L. 1983. Regulation of PCBs in Canada. Pages 383-392 *in* F.M. D'Itri and M.A. Kamrin (eds.). PCBS: human and environmental hazards. Butterworth Publ., Woburn, MA.

Greig, R.A., S. Schurman, J. Pereira, and P. Naples. 1983. Metals and PCB concentrations in windowpane flounder from Long Island Sound. Bull. Environ. Contam. Toxicol. 31:257-962.

Haines, T.A. 1983. Organochlorine residues in brook trout from remote lakes in the northeastern United States. Water, Air, Soil Pollut. 20:47-54.

Hansen, L.G., L.G.M.T. Tuinstra, C.A. Kan, J.J.T.W.A. Strik, and J.H. Koeman. 1983. Accumulation of chlorobiphenyls in chicken fat and liver after feeding Aroclor 1254 directly or fat from swine fed Aroclor 1254. J. Agric. Food Chem. 31:254-260.

Heath, R.G., J.W. Spann, E.F. Hill, and J.F. Kreitzer. 1972. Comparative dietary toxicities of pesticides to birds. U.S. Fish Wildl. Serv. Spec. Sci. Rep. - Wildl. 152. 57 pp.

Heinz, G.H., T.C. Erdman, S.D. Haseltine, and C. Stafford. 1985. Contaminant levels in colonial waterbirds from Green Bay and Lake Michigan, 1975-80. Environ. Monitor. Assess. 5:223-236.

Heinz, G.H., D.M. Swineford, and D.E. Katsma. 1984. High PCB residues in birds from the Sheboygan River, Wisconsin. Environ. Monitor. Assess 4:155-161.

Henny, C.J., L.J. Blus, S.V. Gregory, and C.J. Stafford. 1981. PCBs and organochlorine pesticides in wild mink and river otters from Oregon. Pages 1763-1780 *in* J.A. Chapman and D. Pursley (eds.). Worldwide furbearer conference proceedings. Vol. III. Frostburg, MD.

Henny, C.J., L.J. Blus, A.J. Krynitsky, and C.M. Bunck. 1984. Current impact of DDE on black-crowned night-herons in the intermountain West. J. Wildl. Manage. 48:1-13.

Hidaka, H., S. Tanake, and R. Tatsukawa. 1983. DDT compounds and PCB isomers and congeners in Weddell seals and their fate in the Antarctic marine ecosystem. Agric. Biol. Chem. 47:2009-2017.

Hoeting, A.L. 1983. FDA regulation of PCB in food. Pages 393-407 *in* F.M. D'Itri and M.A. Kamrin (eds.). PCBS: human and environmental hazards. Butterworth Publ., Woburn, MA.

Hornshaw, T.C., R.J. Aulerich, and H.E. Johnson. 1983. Feeding Great Lakes fish to mink: effects on mink and accumulation and elimination of PCBs by mink. J. Toxicol. Environ. Health 11:933-946.

Hudson R.H., R.K. Tucker, and M.A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. Second edition. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp.

Jensen, A.L. 1984. PCB uptake and transfer to humans by lake trout. Environ. Pollut. 34A:73-82.

Johnson, W.W., and M.T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. Summaries of toxicity tests conducted at Columbia National Fisheries Research Laboratory, 1965-78. U.S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Kiessling, A., P. Part, 0. Ring, and K. Lindahl-Kiessling. 1983. Effects of PCB on the adrenergic response in perfused gills and on levels of muscle glycogen in rainbow trout (*Salmo gairdneri* Rich.). Bull. Environ. Contam. Toxicol. 31:712-718.

Kim, H.T., K.S. Kim, J.S. Kim, and W.B. Stone. 1985. Levels of polychlorinated biphenyls (PCBs), DDE, and mirex in waterfowl collected in New York State, 1981-1982. Arch. Environ. Contam. Toxicol. 14:13-18.

Kim, K.S., M.J. Pastel, J.S. Kim, and W.B. Stone. 1984. Levels of polychlorinated biphenyls, DDE, and mirex in waterfowl collected in New York State, 1979-1980. Arch. Environ. Contam. Toxicol. 13:373-381.

Klekowski, E.J. 1982. Mutation in ferns growing in an environment contaminated with polychlorinated biphenyls. Water Resour. Res. Cent. Univ. Massachusetts, Amherst, Compl. Rep. A-129-MASS. 23 pp.

Knap, A.H., and T.D. Jickells. 1983. Trace metals and organochlorines in the goosebeaked whale. Mar. Pollut. Bull. 14:271-174.

de Kock, A.C., and R.M. Randall. 1984. Organochlorine insecticide and polychlorinated biphenyl residues in eggs of coastal birds from the eastern Cape, South Africa. Environ. Pollut. 35A:193-201.

Koeman, J.H. 1973. PCB in mammals and birds in the Netherlands. Pages 35-43 in S. Lundstrom (ed.). PCB conference II. Nat. Swedish Environ. Protection Board, Publ. 1973:4E.

Kuehl, D.W., E.N. Leonard, B.C. Butterworth, and K.L. Johnson. 1983. Polychlorinated chemical residues in fish from major watersheds near the Great Lakes, 1979. Environ. Int. 9:293-299.

Larsson, P. 1984. Transport of PCBs from aquatic to terrestrial environments by emerging chironomids. Environ. Pollut. 34A:283-289.

Leatherland, J.F., and R.A. Sonstegard. 1981. Effect of dietary mirex and PCB's on calcium and magnesium metabolism in rainbow trout, *Salmo gairdneri* and coho salmon, *Oncorhynchus kisutch*; a comparison with Great Lakes coho salmon. Comp. Biochem. Physiol. 69C:345-351.

Lemmetyinen, R., and P. Rantamaki. 1980. DDT and PCB residues in the arctic tern (*Sterna paradisaea*) nesting in the archipelago of southwestern Finland. Ann. Zool. Fennici 17:141-146.

Lucier, G.W., and G.E.R. Hook (eds.). 1985a. Japan - U.S joint seminar: toxicity of chlorinated biphenyls, dibenzofurans, dibenzodioxins and related compounds. Environ. Health Perspec. 59. 181 pp.

Lucier, G.W., and G.E.R. Hook (eds.). 1985b. Potential health effects of polychlorinated biphenyls and related persistent halogenated hydrocarbons: U.S. symposium. Environ. Health Petspec. 60:1-221.

Mahanty, H.K., B.A. Fineran, and P.M. Gresshoff. 1983. Effects of polychlorinated biphenyls (Aroclor 1242) on the ultrastructure of certain planktonic algae. Bot. Gaz. 144:56-61.

Malins, D.C., B. B. McCain, D.W. Brown, A.K. Sparks, and A.0. Hodgkins. 1980. Chemical contaminants and biological abnormalities in Central and Southern Puget Sound. U.S. Dep. Comm., NOAA Tech. Mem. OMPA-2. 295 pp.

McEwen, L.C., C.J. Stafford, and G.L. Hensler. 1984. Organochlorine residues in eggs of black-crowned night-herons from Colorado and Wyoming. Environ. Toxicol. Chem. 3:367-376.

McKim, J.M., Jr., and K.L. Johnson. 1983. Polychlorinated biphenyls and p,p'-DDE in loggerhead and green postyearling Atlantic sea turtles. Bull. Environ. Contam. Toxicol. 31:53-60.

McLane, M.A.R., and D.L. Hughes. 1980. Reproductive success of screech owls fed Aroclor® 1248. Arch. Environ. Contam. Toxicol. 9:661-665.

McLane, M.A., D.L. Hughes, and G.H. Heinz. 1984. Changes in levels of organochlorines in woodcock wings from 1971 to 1975. Environ. Monitor. Assess. 4:105-111.

McManus, G.B., K.B. Wyman, W.T. Peterson, and C.F. Wurster. 1983. Factors affecting the elimination of PCBs in the marine copepod *Acartia tonsa*. Estuar. Coast. Shelf Sci. 17:421-430.

Meier, P.G., and R.R. Rediske. 1984. Oil and PCB interactions on the uptake and excretion in midges. Bull. Environ. Contam. Toxicol. 33:225-232.

Melancon, M.J., and J.J. Lech. 1983. Dose-effect relationship for induction of hepatic monooxygenase activity in rainbow trout and carp by Aroclor 1254. Aquat. Toxicol. 4:51-61.

Menzie, C.M. 1978. Metabolism of pesticides, update II. U.S. Fish Wildl. Serv. Spec. Sci. Rep.-Wildl. 212:206-218.

Montz, W.E., W.C. Card, and R.L. Kirkpatrick. 1982. Effects of polychlorinated biphenyls and nutritional restriction on barbituate-induced sleeping times and selected blood characteristics in raccoons (*Procyon lotor*). Bull. Environ. Contam. Toxicol. 28:578-583.

Musial, C.J., and J.F. lithe. 1983. Interlaboratory calibration results of polychlorinated biphenyl analyses in herring. J. Assoc. Off. Anal. Chem. 66:22-31.

NAS. 1968. Nutrient requirements of mink and foxes. Publ. 1676. Nat. Acad. Sci., Washington DC. 46 pp.

NAS. 1979. Polychlorinated biphenyls. Rep. Comm. Assess. PCBs in Environ., Environ. Stud. Bd., Comm. Nat. Resour., Nat. Res. Coun., Nat. Acad. Sci., Washington DC. 182 pp.

Niethammer, K.R., T.S. Baskett, and D.H. White. 1984. Organochlorine residues in three heron species as related to diet and age. Bull. Environ. Contam. Toxicol. 33:491-498.

Niimi, A.J. 1983. Biological and toxicological effects of environmental contaminants in fish and their eggs. Can. J. Fish. Aquat. Sci. 40:306-312.

Norheim, G., and B. Kjos-Hanssen. 1984. Persistent chlorinated hydrocarbons and mercury in birds caught off the west coast of Spitzbergen. Environ. Pollut. 33A:143-152.

Nygard, T. 1983. Pesticide residues and shell thinning in eggs of peregrines in Norway. Ornis Scand. 14:161-166.

O'Connor, J.M., and J.C. Pizza. 1984. Eco-kinetic model for the accumulation of PCB in marine fishes. Pages 285-303 *in* T.R. Patin (ed.). Management of bottom sediments containing toxic substances. U.S. Army Corps Engin., Wat. Res. Supp. Cen. Avail from Nat. Tech. Infor. Serv., 5285 Port Royal Road, Springfield, VA.

Ohlendorf, H.M., and M.R. Miller. 1984. Organochlorine contaminants in California waterfowl. J. Wildl. Manage. 48:867-877.

Olafsson, P.G., A.M. Bryan, B. Bush, and W. Stone. 1983. Snapping turtles a biological screen for PCB's. Chemosphere 12:1525-1532.

O'Shea, T.J., T.E. Kaiser, G.R. Askins, and J.A. Chapman. 1981. Polychlorinated biphenyls in a wild mink population. Pages 1746-1752 *in* J.A. Chapman and D. Pursley (eds.). Worldwide furbearer conference proceedings. Vol. 111. Frostburg, MD.

O'Shea, T.J., and J.L. Ludke. 1979. Monitoring fish and wildlife for environmental pollutants. U.S. Fish Wildl. Serv. 12 pp. Available from U.S. Govt. Printing Office, Washington DC, as Stock No. 024-010-00512-2.

O'Shea, T.J., J.F. Moore, and H.I. Kochman. 1984. Contaminant concentrations in manatees in Florida. J. Wildl. Manage. 48:741-748.

Pal, D., J.B. Weber, and M.R. Overcash. 1980. Fate of polychlorinated biphenyls (PCBs) in soil-plant systems. Residue Rev. 74:45-98.

Pattee, O.H., M.R. Fuller, and T.E. Kaiser. 1985. Environmental contaminants in eastern Cooper's hawk eggs. J. Wildl. Manage. 49:1040-1044.

Peakall, D.B., J.L. Lincer, and S.E. Bloom. 1972. Embryonic mortality and chromosomal alterations caused by Aroclor 1254 in ring doves. Environ. Health Perspect. 1:103-104.

Pizza, J.C., and J.M. O'Connor. 1983. PCB dynamics in Hudson River striped bass. II. Accumulation from dietary sources. Aquat. Toxicol. 3:313-327.

Ray, S., B.M. Jessop, J. Coffin, and D.A. Swetnam. 1984. Mercury and polychlorinated biphenyls in striped bass (*Morone saxatilis*) from two Nova Scotia rivers. Water, Air, Soil Pollut. 21:15-23

Rifkind, A.B., A. Firpo, Jr., and D.R. Alonso. 1984. Coordinate induction of cytochrome P-448 mediated mixed function oxidases and histopathologic changes produced acutely in chick embryo liver by polychlorinated biphenyl congeners. Toxicol. Appl. Pharmacol. 72:343-354.

Ringer, R.K. 1983. Toxicology of PCBs in mink and ferrets. Pages 227-240 *in* F.M. D'Itri and M.A. Kamrin (eds.). PCBS: human and environmental hazards. Butterworth Publ., Woburn, MA.

Rinzky, A., and A.S. Perry. 1983. Postnatal development of the mixed function oxidase system in nestling barn owls and baby chicks and induction of this system in the mature forms by Aroclor 1254. Comp. Biochem. Physiol. 75C:51-55.

Roberts, J.R., D.W. Rodgers, J.R. Bailey, and M.A. Rorke. 1978. Polychlorinated biphenyls: biological criteria for an assessment of their effects on environmental quality. Nat. Res. Coun. Canada, Rep. 16077. 172 pp.

Rohrer, T.K., J.C. Forney, and J.H. Hartig. 1982. Organochlorine and heavy metal residues in standard fillets of coho and chinook salmon of the Great Lakes-1980. J. Great Lakes Res. 8:623-634.

Rubenstein, N.I., E. Lores, and N.R. Gregory. 1983. Accumulation of PCBS, mercury and cadmium by *Nereis virens, Mercenaria mercenaria* and *Palaemonetes pugio* from contaminated harbor sediments. Aquat. Toxicol. 3:249-260

Sabourin, T.D., W.B. Stickle, T.C. Michot, C.E. Villars, D.W. Garton, and H.R. Mushinsky. 1984. Organochlorine residue levels in Mississippi River water snakes in southern Louisiana. Bull. Environ. Contam. Toxicol. 32:460-468.

Safe, S. 1984. Polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs): biochemistry, toxicology, and mechanism of action. CRC Crit. Rev. Toxicol. 13:319-393.

Sanders, O.T., and R.L. Kirkpatrick. 1977. Reproductive characteristics and corticoid levels of female white-footed mice fed *ad libitum* and restricted diets containing a polychlorinated biphenyl. Environ. Res. 13:358-363.

Sawhney, B.L., and L. Hankin. 1984. Plant contamination by PCBs from amended soils. J. Food Prot. 47:232-236.

Schmitt, C.J., M.A. Ribick, J.L. Ludke, and T.W. May. 1983. National Pesticide Monitoring Program: organochlorine residues in freshwater fish, 1976-79. U.S. Fish Wild. Serv. Resour. Publ. 152. 62 pp.

Schmitt, C.J., J.L. Zajicek, and M.A. Ribick 1985. National Pesticide Monitoring Program: residues of organochlorine chemicals in freshwater fish, 1980-81. Arch. Environ. Contam. Toxicol. 14:225-260.

Schwartz, T.R., R.D. Campbell, D.L. Stalling, R.L. Little, J.D. Petty, J.W. Hogan, and E.M. Kaiser. 1984. Laboratory data base for isomer-specific determination of polychlorinated biphenyls. Anal. Chem. 56:1303-1308.

Shaw, G.R., and D.W. Connell. 1982. Factors influencing polychlorinated biphenyls in organisms from an estuarine ecosystem. Aust. J. Mar. Freshwater Res. 33:1057-1070.

Shelton, D.W., R.A. Coulombe, C.B. Pereira, J.L. Casteel, and J.D. Hendricks. 1983. Inhibitory effect of Aroclor 1254 on aflatoxin-initiated carcinogenesis in rainbow trout and mutagenesis using a *Salmonella*/trout hepatic activation system. Aquat. Toxicol. 3:229-238.

Simmons, M.S. 1984. PCB contamination in the Great Lakes. Pages 287-309 in J.O. Nriagu and M.S. Simmons (eds.). Toxic contamination in the Great Lakes. John Wiley, New York.

Sloan, R.J., K.W. Simpson, R.A. Schroeder, and C.R. Barnes. 1983. Temporal trends toward stability of Hudson River PCB contamination. Bull. Environ. Contam. Toxicol. 31:377-385.

Solbakken, J.E., A.H. Kinapp, T.D. Sleeter, C.E. Searle, and K.H. Palmork. 1984a. Investigation into the fate of ^{14}C-labelled xenobiotics (naphthalene, phenanthrene, 2,4,5,2',4',5'-hexachlorobiphenyl, octachlorostyrene) in Bermudian corals. Mar. Ecol. - Prog. Ser. 16:149-154.

Solbakken, J.E., S. Tilseth, and K. H. Palmork. 1984b. Uptake and elimination of aromatic hydrocarbons and a chlorinated biphenyl in eggs and larvae of cod *Gadus morrhua*. Mar. Ecol. - Prog. Ser. 16:297-301.

Spear, P.A., and T.W. Moon. 1985. Low dietary iodine and thyroid anomalies in ring doves, *Streptopelia risoria*, exposed to 3,4,3',4'-tetrachlorobiphenyl. Arch. Environ. Contam. Toxicol. 14:547-553.

Spigarelli, S.A., M.M. Thommes, and W. Prepejchal. 1983. Thermal and metabolic factors affecting PCB uptake by adult brown trout. Environ. Sci. Technol. 17:88-94.

Stainken, D.M. 1984. Organic pollution and the macrobenthos of Raritan Bay. Environ. Toxicol. Chem. 3:95-111.

Stalling, D.L., L.M. Smith, J.D. Petty, J.W. Hogan, J.L. Johnson, C. Rappe, and H.R. Buser. 1983. Residues of polychlorinated dibenzo-p-dioxins and dibenzofurans in Laurentian Great Lakes fish. Pages 221-240 in R.E. Tucker, A.L. Young and A.P. Gray (eds.). Human and environmental risks of chlorinated dioxins and related compounds. Plenum Publ., New York.

Stickel, W.H., L.F. Stickel, R.A. Dyrland, and D.L. Hughes. 1984. Aroclor 1254® residues in birds: lethal levels and loss rates. Arch. Environ. Contam. Toxicol. 13:7-13.

Stone, W.B., and J.C. Okoniewski. 1983. Organochlorine toxicants in great horned owls from New York, 1981-82. Northeast. Environ. Sci. 2:1-7.

Swain, W.R. 1983. An overview of the scientific basis for concern with polychlorinated biphenyls in the Great Lakes. Pages 11-48 *in* F.M. D'Itri and M.A. Kamrin (eds.). PCBs: human and environmental hazards. Butterworth Publ., Woburn, MA.

Talcott, P.A., and L.D. Koller. 1983. The effect of inorganic lead and/or a polychlorinated biphenyl on the developing immune system of mice. J. Toxicol. Environ. Health 12:337-352.

Tori, G.M., and T.J. Peterle. 1983. Effects of PCBs on mourning dove courtship behavior. Bull. Environ. Contam. Toxicol. 30:44-49.

Van Der Zande, T., and E. De Ruiter. 1983. The quantification of technical mixtures of PCBs by microwave plasma detection and the analysis of PCBs in the blubber lipid from harbour seals (*Phoca vitulina*). Sci. Total Environ. 27:133-147

Vodicnik, M.J., and R.E. Peterson. 1985. The enhancing effect of spawning on elimination of a persistent polychlorinated biphenyl from female yellow perch. Fundam. Appl. Toxicol. 5:770-776.

Weber, R.F. 1983. DDT and PCBs in equatorial Atlantic organisms. Mar. Pollut. Bull. 14:274-275.

Weseloh, D.V., S.M. Teeple, and M. Gilbertson. 1983. Double-crested cormorants of the Great Lakes: egg-laying parameters, reproductive failure, and contaminant residues in eggs, Lake Huron 1972-1973. Can. J. Zool. 61:427-436.

White, D.H., C.A. Mitchell, and C.J. Stafford. 1985. Organochlorine concentrations, whole body weights, and lipid content of black skimmers wintering in Mexico and in south Texas, 1983. Bull. Environ. Contam. Toxicol. 34:513-517.

White, D.H., C.A. Mitchell, and D.M. Swineford. 1984. Reproductive success of black skimmers in Texas relative to environmental pollutants. J. Field Ornithol. 55:18-30.

Wiemeyer, S.N., T.G. Lamont, C.M. Bunck, C.R. Sindelar, F.J. Gramlich, J.D. Fraser, and M.A. Byrd. 1984. Organochlorine pesticide, polychlorobiphenyl, and mercury residues in bald eagle eggs -1966-1979- and their relationships to shell thinning and reproduction. Arch. Environ. Contam. Toxicol. 13:529-549.

Zepp, R.L., Jr., and R.L. Kirkpatrick. 1976. Reproduction in cottontails fed diets containing a PCB. J. Wildl. Manage. 40:491-495.

Zhang, Y., B. Rott, and D. Freitag. 1983. Accumulation and elimination of ^{14}C-PCBs by *Daphnia magna* Straus 1820. Chemosphere 12:1645-1651.

Table 1. Average chlorine content, chlorine atoms per molecule, and molecular weight of selected Aroclor and Kanechlor PCB formulations (after Roberts et al. 1978).

Trade name and formulation		Percent chlorine	Mean no. chlorine atoms per molecule	Mean molecular weight
Aroclor	Kanechlor			
1221	---	20.5-21.5	1.15	192
1232	200	31.5-32.5	2.04	221
1242	300	42	3.10	261
1248	400	48	3.90	288
1254	500	54	4.96	327
1260	600	60	6.30	372
1262	---	61.5-62.5	6.80	389
1268	---	68	8.70	453

Table 2. PCB concentrations in field collections of selected species of flora and fauna. Values shown are in mg/kg (ppm) fresh weight (FW), dry weight (DW), or lipid weight (LW).

Taxonomic group, organism tissue, location and other variables	Concentration[a] (ppm)	Reference[b]
Plants		
Northeast and central New York		
18 spp., 1979		
Foliage	0.03-0.29 DW	Buckley 1983
Hay	0.08-0.10 DW	
Brome grass, *Bromus inermis*		
Hay, 1979	0.14 DW	
Perennial rye, *Lolium perenne*		
Hay, 1979	0.08 DW	
Timothy, *Phleum pratense*		
Hay, 1979	0.10 DW	
Trembling aspen, *Populus tremuloides*		
Leaves		
1978	0.12 DW	
1979	0.09 DW	
1980	0.07 DW	
Goldenrod, *Solidago graminifolia*		
Leaves		
1978	0.32 DW	
1979	0.25 DW	
1980	0.18 DW	

Invertebrates		
Chironomid, *Chironomus plumosus*,		
near Swedish sewage plant outfall		
From sediments with	0.04 FW; 0.3 DW	Larsson 1984
Larvae	0.1 FW; 10.0 LW	
Adults	0.2 FW; 8.9 LW	
From sediments with	0.6 FW; 4.2 DW	
Larvae	8.6 FW; 757.0 LW	
Adults	19.4 FW; 665.0 LW	
From sediments with	7.0 FW; 28.0 DW	
Larvae	35.5 FW; 3,583.0 LW	
Adults	124.0 FW; 4,234.0 LW	
Mysid, *Mysis relicta*		
Lake Michigan, 1980-1981		
Whole	0.1-0.5 DW	Evans et al. 1982
Fecal pellets		
Aroclor 1254	1.3 DW	
Aroclor 1242	1.2 DW	
Fish		
Goldfish, *Carassius auratus*		
Hudson River, New York		
Whole		
1979	6,761.0 LW	Brown et al. 1985
1982	310.0 LW	
Brown bullhead, *Ictalurus nebulosus*		
Hudson River, New York		
Whole		
1979	2,510.0 LW	
1982	428.0 LW	
Pumpkinseed, *Lepomis gibbosus*		
Hudson River, New York		
Whole		
1979	1,079.0 LW	
1982	36.0 LW	
Largemouth bass, *Micropterus salmoides*		
Hudson River, New York		
Muscle		
1977	29.5-145.3 FW	
1981	<1.0-10.2 FW	
Whole		
1979	6,010.0 LW	
1982	1,000.0 LW	
Brook trout, *Salvelinus fontinalis*		

Whole, 1979-1980		
New Hampshire	0.08 FW	Haines 1983
Maine and Vermont	<0.03 FW	
Codfish, *Gadus morhua*		
Liver		
Fish weight (g)		
86	9.3 LW	Ernst 1984
243	8.9 LW	
471	10.0 LW	
917	21.0 LW	
2,628	22.0 LW	
North Sea, 1974-1976		
Muscle	<0.001 FW	
Liver	0.03 FW	
Windowpane flounder, *Scopthalmus aquosus*		
Long Island Sound, New York, 1980-1982		
Liver	0.9-1.9 FW	Greig et al. 1983
Stomach contents	0.03-0.45 FW	
Striped bass, *Morone saxatilis*		
Nova Scotia		
Muscle	0.02 (Max. 0.09) FW; 0.22 (Max. 0.73) LW	Ray et al. 1984
Gonad	0.04-1.4 FW; 0.08-2.3 LW	
Hudson River, New York		
Muscle		
1978	9.9 FW	Brown et al. 1985
1982	2.6 FW	
USA, Nationwide, 109 stations		
Whole		
Aroclor 1248		
1976-1977	0.15 (Max. 51.9) FW; 0.64 (Max. 465.0) LW	Schmitt et al. 1983
1978-1979	0.14 (Max. 66.9) FW; 0.73 (Max. 348.0) LW	
1980-1981	0.1 (Max. 8.5) FW; 0.8 (Max. 143.8) LW	Schmitt et al. 1985
Aroclor 1254		
1976-1977	0.47 (Max. 16.4) FW; 4.0 (Max. 278.0) LW	Schmitt et al. 1983
1978-1979	0.46 (Max. 22.0) FW; 4.7 (Max. 115.0) LW	
1980-1981	0.2 (Max. 4.2) FW; 2.1 (Max. 87.5) LW	Schmitt et al. 1985

Aroclor 1260		
1976-1977	0.87 (Max. 70.6) FW; 8.0 (Max. 738.0) LW	Schmitt et al. 1983
1978-1979	0.84 (Max. 92.3) FW; 8.8 (Max. 483.0) LW	
1980-1981	0.3 (Max. 2.6) FW 2.6 (Max. 61.0) LW	Schmitt et al. 1985
Total PCBs		
1976-1977	1.5 FW; 12.6 LW	Schmitt et al. 1983
1978-1979	1.4 FW; 14.2 LW	
Great Lakes, 48 watersheds, 1979		
Whole		
16 watersheds	<2.0 FW	Kuehl et al. 1983
13 watersheds	2.0-5.0 FW	
17 watersheds	5.0-20.0 FW	
2 watersheds	>20.0 FW	
Antioch, Illinois		
Walleye, *Stizostedion vitreum vitreum*		
Aroclor 1242	18.0 FW	
Aroclor 1248	22.0 FW	
Aroclor 1254	7.3 FW	
Total PCBs	47.3 FW	
Monroe, Michigan		
Carp, *Cyprinus carpio*		
Aroclor 1242	77.0 FW	
Aroclor 1248	27.0 FW	
Aroclor 1254	7.7 FW	
Total PCBs	111.7 FW	
Great Lakes, tributaries, 1980		
Coho salmon, *Oncorhynchus kisutch*		
Fillets, skin-on	Max. 6.1 FW	Rohrer et al. 1982
Fillets, skinless	Max. 1.6 FW	
Great Lakes area, 1980-1981		
Whole		
Ohio		
Astabula River	1.7-10.7 FW	De Vault 1985
Black River	1.3 FW	
Wisconsin		
Sheboygan River		
Total PCBs	38.6-98.4 FW	
Aroclor 1248	21.3-51.4 FW	
Aroclor 1254	15.8-42.4 FW	
Aroclor 1260	1.5-4.7 FW	

Milwaukee River	6.6-15.5 FW	
Menominee River	0.8-3.2 FW	
Kinnickinnic River	17.7 FW	
Fox River	2.0-20.9 FW	
Wolf River	0.2-0.8 FW	
Chequamegon Bay	0.4-0.7 FW	
North Saskatchewan River, Alberta, Canada, 5 spp.		
Fat	Max. 81.3 FW	Chovelon et al. 1984
Muscle	ND-0.3 FW	
Reptiles		
Loggerhead sea turtle, *Caretta caretta* Florida, east coast		
Muscle	0.005-0.046 FW	McKim and Johnson
Liver	0.008-0.182 FW	1983
Green sea turtle, *Chelonia mydas*		
Florida, east coast		
Muscle	0.005-0.009 FW	
Liver	0.043-0.080 FW	
Snapping turtle, *Chelydra serpentia*		
Fat		
Upper Hudson River	3,608.0 LW	Olafsson et al.
Lake Ontario	633.0 LW	1983
Water snake, *Nerodia cyclopion*		
Louisiana, near Baton Rouge, 1977-1979		
Whole, less skin and head	0.3 FW	Sabourin et al. 1984
Embryo	1.3 FW	
Water snake, *Nerodia rhombifera*		
Louisiana, near Baton Rouge, 1977-1979		
Fat	5.2-8.2 LW	
Liver	0.2-0.7 FW	
Muscle	up to 0.2 FW	
Whole, less skin and head	0.3-0.6 FW	
Embryo	0.8-1.3 FW	
Birds		
Cooper's hawk, *Accipiter cooperii*		
Egg, 1980		
Wisconsin	Max. 2.9 FW	Pattee et al. 1985
Maryland	Max. 4.0 FW	
Michigan	Max. 4.0 FW	
Connecticut	Max. 6.4 FW	
Pennsylvania	Max. 25.0 FW	
Spotted sandpiper, *Actitis macularia*		
Sheboygan River, Wisconsin, August 1979		
Carcass	28.0-106.0 FW	Heinz et al. 1984

Northern pintail, *Anas acuta*		
California, 1980-1981		Ohlendorf and Miller
Wings	0.07-0.74 FW	1984
Northern shoveler, *Anas clypeata*		
California, 1980-1981		
Carcass		
Males	0.33 (0.18-0.63) FW	
Females	0.11 (0.04-0.31) FW	
Mallard, Anas platyrhynchos		
New York, 1981-1982		
Subcutaneous fat	0.3-14.0 LW	Kim et al. 1985
New York, 1979-1980		
Subcutaneous fat	Max. 26.0 LW	Kim et al. 1984
Breast muscle	Max. 0.8 FW	
Liver	Max. 1.6 FW	
Brain	Max. 3.0 FW	
American black duck, *Anas rubripes*		
New York, 1979-1980		
Subcutaneous fat	Max. 19.0 LW	
Breast muscle	Max. 0.3 FW	
Liver	Max. 1.0 FW	
Brain	Max. 0.9 FW	
Great blue heron, *Ardea herodias*		
Sheboygan River, Wisconsin		
Dead on collection		
Brain, 1976	220.0 FW	Heinz et al. 1984
Brain, 1980	50.0 FW	
Carcass, 1980	23.0 FW	
Alive when captured		
Carcass, 1979	36.0 FW	
Stomach contents, 1979	20.0 FW	
Long-eared owl, *Asio otus*, Netherlands		
Liver		
1968-1969	191.0 FW	Koeman 1973
1969-1970	84.8 FW	
1970-1971	6.9 FW	
Lesser scaup, *Aythya affinis*		
California, 1980-1981		Ohlendorf and Miller
Wings	0.17-1.25 FW	1984
Canvasback, *Aythya valisineria*		
California, 1980-1981		
Wings		
San Francisco Bay		

Males	1.6 FW	
Females	0.3 FW	
Salton Sea	0.3 FW	
Canada goose, *Branta canadensis*		
New York, 1979-1980		
Breast muscle	Max. 0.5 FW	Kim et al. 1984
Liver	Max. 0.4 FW	
Great horned owl, *Bubo virginianus*		
New York, 1981		Stone and Okoniewski
Brain	360.0 LW	1983
Green-backed heron, *Butorides striatus*		
Northeastern Louisiana, 1980		
Adults		
Whole	0.7 (0.2-4.8) FW	Niethammer et al.
Muscle	0.1 FW	1984
Liver	0.2 FW	
Fat	6.0 FW	
Immature		
Whole	0.4 (ND-2.0) FW	
Belted kingfisher, *Ceryle alcyon*		
Sheboygan River, Wisconsin, August 1979		
Carcass	65.0-218.0 FW	Heinz et al. 1984
Stomach contents	12.0-58.0 FW	
Northern bobwhite, *Colinus virginianus*		
Southeastern Texas 1975-1981		Flickinger and
Carcass	<0.5 LW	Swineford 1983
Kestrel, *Falco tinnunculus*, Netherlands		
Liver		
1968-1969	21.4 FW	Koeman 1973
1969-1970	18.7 FW	
1970-1971	44.1 FW	
American bald eagle, *Haliaeetus leucocephalus*		
Egg		
Alaska		
1975	Max. 2.5 FW	Wiemeyer et al. 1984
1976	Max. 4.8 FW	
Arizona, 1977	Max. 8.5 FW	
California, 1977	Max. 2.6 FW	
Delaware		
1977	Max. 52.0 FW	
1978	Max. 32.0 FW	
Florida		
1975	Max. 16.0 FW	

1976	Max. 28.0 FW
1977	Max. 8.1 FW
1979	Max. 5.7 FW
Louisiana, 1979	Max. 7.4 FW
Maine	
1974	Max. 75.0 FW
1975	Max. 45.0 FW
1976	Max. 39.0 FW
1977	Max. 20.0 FW
1978	Max. 11.0 FW
1979	Max. 36.0 FW
Maryland	
1973	Max. 8.9 FW
1977	Max. 64.0 FW
1978	Max. 35.0 FW
1979	Max. 5.7 FW
Michigan	
1969	Max. 30.0 FW
1974	Max. 7.0 FW
1978	Max. 37.0 FW
Minnesota	
1972	Max. 44.0 FW
1976	6.1 (Max. 18.0) FW
1977	4.2 (Max. 13.0) FW
1978	4.7 (Max. 19.0) FW
1979	Max. 12.0 FW
New York	
1971	Max. 9.6 FW
1977	Max. 6.2 FW
1978	Max. 3.2 FW
Ohio, 1976	Max. 67.0 FW
Oregon, 1979	Max. 5.6 FW
Virginia	
1976	Max. 56.0 FW
1977	23.0-218.0 FW
1979	Max. 81.0 FW
Wisconsin	
1976	12.0 (Max. 61.0) FW
1977	5.4 (Max. 33.0) FW
1978	14.0 (Max. 98.0) FW
1979	3.0 (Max. 68.0) FW
Herring gull, *Larus argentatus*	
Lake Michigan and Green Bay	

Egg		
1977	100.0 (77.0-136.0) FW	Heinz et al. 1985
1978	65.0 (40.0-160.0) FW	
1980	54.0 (28.0-76.0) FW	
Norway, 1976-1977		
Fledgling	0.6-1.2 FW	Fimreite and Bjerk
Egg	7.0-9.8 FW	1983
Great Lakes, 1981		
Egg		
Snake Island,		
Lake Ontario	86.0 (45.0-127.0) FW	Fleming et al. 1983
Other colonies	23.0 FW	
Hooded merganser, *Lophodytes cacullatus*		
New York, 1981-1982		
Subcutaneous fat	45.0 LW	Kim et al. 1985
Common merganser, *Mergus merganser*		
New York, 1981-1982		
Subcutaneous fat	124.0 LW	
New York, 1979-1980		
Subcutaneous fat	Max. 9.8 LW	Kim et al. 1984
Breast muscle	Max. 20.0 FW	
Liver	Max. 2.9 FW	
Brain	Max. 2.3 FW	
Red-breasted merganser, *Mergus serrator*		
Lake Michigan, 1977-1978		
Egg	4.9-229.0 FW	Fleming et al. 1983
Black-crowned night-heron, *Nycticorax nycticorax*		
Carcass		
Lake Michigan, 1978	23.0-127.0 FW	Heinz et al. 1985
Brain, Lake Michigan, 1978	4.0-160.0 FW	
Egg		
New England, 1979		
Laid during different quarters of breeding season		
1st	8.4 FW	Custer et al. 1983b
2nd	8.1 FW	
3rd	6.9 FW	
4th	5.5 FW	
North Carolina, 1979		
Laid during different quarters of breeding season		
1st	2.6 FW	
2nd	2.0 FW	
3rd	1.4 FW	
4th	0.6 FW	

Rhode Island		
Gould Island		
1973	10.3 FW	Custer et al. 1983a
1979	6.1 FW	
Hope Island, 1979	10.0 FW	
Massachusetts, Clark's Island		
1973	7.2 FW	
1979	6.2 FW	
North Carolina		
Middle Marsh, 1979	2.4 FW	
Annex, 1979	0.8 FW	
Washington, Oregon, Nevada		
1979-1980	2.0-19.0 FW	Henny et al. 1984
Colorado, Wyoming		
1979	1.0 (0.4-7.0) FW	McEwen et al. 1984
Lake Michigan and Green Bay		
1977	92.0 FW	Heinz et al. 1985
1978	15.0-23.0 FW	
1980	24.0 FW	
Gray partridge, *Perdix perdix*		
Breast		
Low chlorinated PCBs		
Fat	7.8 FW	Brunn et al. 1985
Nonfat	0.04 FW	
High chlorinated PCBs		
Fat	0.8 FW	
Nonfat	0.001 FW	
Double-crested cormorant, *Phalacrocorax auritus*		
Lake Michigan and Green Bay		
Egg		
1977	12.0-16.5 FW	Heinz et al. 1985
1978	4.4-11.0 FW	
1980	2.0 FW	
Lake Huron 1972		
Egg	23.8 (10.3-25.6) FW	Weseloh et al. 1983
Cormorant, *Phalacrocorax carbo*, Netherlands, 1970		
Adults		
Liver	320.0 (93.0-470.0) FW	Koeman 1973
Whole body	29.0-460.0 FW	
Brain	190.0 FW	
Nestlings		
Liver	0.4 FW	
Whole body	2.4 FW	

Brain	0.7 FW	
Ring-necked pheasant, *Phasianus colchicus*		
Breast		
Low chlorinated PCBs		
Fat	6.4 FW	Brunn et al. 1985
Nonfat	0.03 FW	
High chlorinated PCBs		
Fat	4.9 FW	
Nonfat	0.007 FW	
Woodcock, *Philohela minor*		
Wing lipids		
17 States		
1971	5.7 LW	McLane et al. 1984
1972	1.7 LW	
1975	2.8 LW	
Fat, East Central Illinois		
1978-1979	Max. 12.5 LW	Edwards et al. 1983
Kittiwake, *Rissa tridactyla*		
Norway, 1976-1977		
Fledgling	0.65 FW	Fimreite and Bjerk
Egg	2.1 FW	1983
Black skimmer, *Rynchops niger*		
Egg		
Corpus Christi, Texas		
1978	7.2 (4.3-12.0) FW	White et al. 1984
1979	4.1 (1.4-9.0) FW	
1980	3.2 (1.0-20.0) FW	
1981	2.6 (0.8-5.0) FW	
Carcass		
Texas, 1983	1.6 (<0.5-10.0) FW	White et al. 1985
Mexico, 1983	1.0 (<0.5-16.0) FW	
Seabirds		
Baltic Sea, 1981-1983		
Adipose fat		
Auks, Family Alcidae		
4 spp.	92.0 (trace-1,100.O) LW	Falandysz and Szefer
Mergansers, *Mergus* spp.	54.0 LW	1984
Black-throated diver,		
Colymbus arcticus	19.0 LW	
Grebes, *Podiceps* spp.	16.0 LW	
West Coast Spitzbergen, 5 spp., 1979-1980		
Liver	<0.1-6.1 FW	Norheim and Kjos-
Fat	3.1-82.0 LW	Hanssen 1984

Eastern Cape, South Africa, 7 spp.		de Kock and Randall
Egg, 1981-1983	0.05-0.9 FW	1984
Arctic tern, *Sterna paradisaea*		
Finland, 1969-1974		
Liver		
Males	80.1 LW; 4.4 FW	Lemmetyinen and
Females	38.7 LW; 1.7 FW	Rantamaki 1980
Muscle		
Males	74.6 LW; 4.0 FW	
Females	40.3 LW; 2.1 FW	
Egg		27.7 LW; 2.9 FW
Chicks		
Liver		
Newly-hatched	44.0 LW; 4.3 FW	
Age 2-3 weeks	10.8 LW; 0.3 FW	
Muscle		
Age 2-3 weeks	14.1 LW; 0.6 FW	
European starling, *Sturnus vulgaris*		
Whole, minus feet, beak, wing tips, and skin		
Nationwide, USA		
1976	0.01 (ND-0.9) FW	Cain and Bunck 1983
1979	0.05 (ND-2.2) FW	
Wisconsin	1.6 FW	
North Carolina	2.2 FW	
Alabama	1.0 FW	
Maryland	0.8 FW	
Brown booby, *Sula leucogaster*		
Equatorial Atlantic, 1979-1980		
Muscle	0.2 FW; 0.2 DW	Weber 1983
Egg	0.1 FW; 0.1 DW	
Solitary sandpiper, *Tringa solitaria*		
Sheboygan River, Wisconsin, August 1979		
Carcass	23.0 FW	Heinz et al. 1984
Robin, *Turdus migratorius*		
East central Illinois, 1978-1979		
Fat	Max. 6.7 LW	Edwards et al. 1983
Attwater's greater prairie chicken, *Tympanuchus cupido attwateri*		
Southeastern Texas, 1975-1981		Flickinger and
Carcass	<0.5 LW	Swineford 1983
Guillemot, *Uria aalge*		
Norway, 1976-1977		
Fledgling	0.5-0.6 FW	Fimreite and

Egg	2.0-3.6 FW	Bjerk 1983
Waterfowl		
New York, 1979-1980, 17 spp.		
Subcutaneous fat	7.5 LW; 8.1 DW	Kim et al. 1984
Muscle	1.3 FW; 4.2 DW	
Liver	0.8 FW; 2.7 DW	
Brain	0.6 FW; 2.4 DW	
New York, 1981-1982, 9 spp.		
Subcutaneous fat	6.1 LW; 10.1 DW	Kim et al. 1985
Breast muscle	0.3 FW; 0.8 DW	
Mourning dove, *Zenaidura macroura*		
East central Illinois, 1978-1979		
Fat	Max. 0.4 LW	Edwards et al. 1983
Mammals		
Big brown bat, *Eptesicus fuscus*		
Laurel, Maryland		
May 1974		
Adult females, whole	1.3 (1.1-1.6) FW	Clark and Lamont
Young, whole	0.4 (0.2-3.3) FW	1976
June 1974		
Adult females, whole	2.0 (1.6-2.4) FW	
Young, whole	1.2 (0.8-1.7) FW	
Hare, *Lepas europans*		
Muscle		
Low chlorinated PCBs		
Fat	8.5 FW	Brunn et al. 1985
Nonfat	0.02 FW	
High chlorinated PCBs		
Fat	2.0 FW	
Nonfat	0.003 FW	
River otter, *Lutra canadensis*		
Lower Columbia River, Oregon, 1978-1979		
Liver		
Males	9.3 (4.8-23.0) FW	Henny et al. 1981
Females	3.5 (1.7-7.0) FW	
Muscle		
Males	3.7 (1.1-8.3) FW	
Females	2.7 (1.6-4.5) FW	
Mink, *Mustela vison*		
Oregon, 1978-1979		
Liver		
Males	0.5-3.5 FW	
Females	0.7-1.7 FW	

Muscle	0.6-1.6 FW	
Western Maryland, 1978-1979		
Liver		
Males	1.5 (1.1-2.0) FW	O'Shea et al. 1981
Females	1.4 (0.6-2.4) FW	
Atlantic Coast, 1970		
Fat		
Massachusetts		
Dead on collection	6.0-60.0 FW	Friedman et al. 1977
Healthy	0.3-0.5 FW	
Virginia		
Healthy	0.4-0.5 FW	
Gray bat, *Myotis grisescens*		
Missouri		
Brain		
1976	ND	Clark et al. 1980
1977	ND-9.3 FW	
Carcass		
1976	163.0 (71.0-425.0) LW	
1977	295.0 (86.0-1,000.0) LW	
Little brown bat, *Myotis lucifugus*		
Laurel, Maryland, 1976, carcass		
Adult females	11.4 (3.6-24.0) FW	Clark and Krynitsky
Young	4.2 (ND-25.0) FW	1978
Maryland and West Virginia, 1973		
Adults		
Carcass	3.2-11.6 FW	Clark and Prouty
Stomach contents	1.4 FW	1976
Guano	0.5-1.0 FW	
Ringed seal, *Phoca hispida*		
Liver	0.2 FW	Bowes and Lewis
Fat	0.6 FW	1974
Harbor seal, *Phoca vitulina*		
Dutch coast, 1981		
Blubber		
Age 1 year	31.0 LW	Van Der Zande and
Age 3 years	65.0 LW	De Ruiter 1983
Age 4 years	35.0 LW	
Age 5 years	55.0 LW	
Sperm whale, *Physeter macrocephalus*, Spain		
Males		
Blubber	9.9 LW	Aguilar 1983
Muscle	24.0 LW	

Sperm oil	10.5 LW	
Liver	30.1 LW	
Kidneys	9.4 LW	
Brain	1.4 LW	
Females		
Blubber	15.5 LW	
Muscle	30.7 LW	
Sperm oil	5.0 LW	
Liver	18.6 LW	
Kidneys	9.2 LW	
Brain	1.1 LW	
Milk	4.7 LW	
Manatee, *Trichechus manatus*		
Florida, 1977-1981, dead on collection		
Blubber	1.4 (0.5-4.6) FW	O'Shea et al. 1984
Polar bear, *Ursus martinus*		
Liver	4.0-4.9 FW	Bowes and Lewis
Fat	17.4-19.4 FW	1974
Cuvier's goosebeaked whale, *Ziphius cavirostris*		
Blubber	9.4 (7.9-12.3) LW	
Flesh	0.16 FW	Knap and Jickells
Liver	0.25 FW	1983
Kidney	0.10 FW	
Heart	0.04 FW	
Integrated studies		
Upper Hudson River, New York		
Water		
1977	0.00054 FW	Sloan et al. 1983
1978	0.00042 FW	
1979	0.00039 FW	
1980	0.00026 FW	
1981	0.00013 FW	
1982	0.00011 FW	Brown et al. 1985
Water column, including organisms, silt, and detritus		
1977	671.0 LW	Sloan et al. 1983
1978	792.0 LW	
1979	267.0 LW	
1980	186.0 LW	
1981	626.0 LW	
Fish, whole		
1977	4,217.0 LW	
1978	3,951.0 LW	
1979	1,332.0 LW	

1980	1,431.0 LW	
Aroclor 1221	33.0 LW	
Aroclor 1016	664.0 LW	
Aroclor 1254	734.0 LW	
Sediments	20.0-150.0 DW	Carcich and
Water column	0.0001-0.001 FW	Tofflemire 1982
Fish	10.0-130.0 FW	
Macroinvertebrates	3.0-10.0 FW	
Dredge spoils	5.0-50.0 DW	
Industrial landfills		
Waste material	500.0-5,000.0 DW	
Leachate	0.05-0.5 FW	
Dust	17.0 DW	
Plants		
Near industrial landfill	10.0-500.0 FW	
Near dredge spoil area	0.2-1.3 FW	
Lower Hudson River, New York		
Fish		
1977	1,604.0 LW	Sloan et al. 1983
1978	969.0 LW	
1979	371.0 LW	
1980	327.0 LW	
Aroclor 1221	36.0 LW	
Aroclor 1016	106.0 LW	
Aroclor 1254	185.0 LW	
1981	319.0 LW	
Aroclor 1221	19.0 LW	
Aroclor 1016	87.0 LW	
Aroclor 1254	213.0 LW	
Sediments	1.0-15.0 DW	Carcich and
Water column	ND-0.0008 FW	Tofflemire 1982
Fish		
Resident	5.0-10.0 FW	
Migratory	0.5-15.0 FW	
Macroinvertebrates	1.0-13.0 FW	
Turtles		
Muscle	5.0 FW	
Eggs	25.0 FW	
Lake Ontario, 1981		
Surficial sediments	0.3-0.8 DW	Fox et al. 1983
Oligochaetes	1.5-5.3 DW	
Amphipods	2.6-11.0 DW	
Mysid shrimp	3.0 DW	

Lake trout, whole, Age 1+	6.3 DW	
Australian estuary		
Muscle		
Herbivores Shaw and Connell	0.3 FW; 11.5 LW	
Omnivores 1982	1.2 FW; 16.3 LW	
Lower carnivores	0.9 FW; 26.8 LW	
Middle carnivores	0.1 FW; 41.0 LW	
Top carnivores	8.2 FW; 170.0 LW	
Central Puget Sound, Washington, 1979		
Sediments	<0.001-1.2 DW	Malins et al. 1980
Clam, soft parts	0.02-1.3 DW	
Shrimp, whole	0.1-3.0 DW	
Worms, whole	0.2-1.8 DW	
Crab, hepatopancreas	0.4-33.0 DW	
Fish, liver	0.6-35.0 DW	
Escambia Bay and River, Florida		
Sediments		
1970	Max. 78.0 DW	NAS 1979
1971	Max. 8.1 DW	
1972	Max. 5.8 DW	

[a]Concentrations are listed as mean, minimum-maximum, or maximum (Max.) values recorded.

[b]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

Table 3. Acute toxicities of Aroclor PCBs to selected aquatic species.

Ecosystem, organism, compound tested	Exposure period (days)	LC-50 (ug/l)	Reference[a]
Freshwater			
Invertebrates			
Crayfish, *Orconectes nais*			
1242	7	30	NAS 1979
1254	7	80-100	
Scud, *Gammarus pseudolimnaeus*			
1242	4	10	
1242	10	5	
1248	4	52	
1254	4	2,400	
Glass shrimp, *Palaemonetes kadiakensis*			

1254	7	3	
Damselfly, *Ischnura verticalis*			
1242	4	400	Johnson and Finley 1980
1254	4	200	
Dragonfly, *Macromia* sp.			
1242	4	800	
1254	5	800	
Cladoceran, *Daphnia magna*			
1254	14	1.8-24.0	EPA 1980
1254	21	1.3	
Stonefly, *Pteronarcella badia*			
1016	4	424-878	Johnson and Finley 1980
Hydra, *Hydra oligactis*			
1016	3	5,000	Adams and Haileselassie 1984
1254	3	10,000	
Fish			
Rainbow trout, *Salmo gairdneri*			
1016	4	114-159	Johnson and Finley 1980
1242	5	67	
1248	5	54	
1254	5	142	
1254	10	8	NAS 1979
1260	20	21	
Bluegill, *Lepomis macrochirus*			
1016	4	390-540	Johnson and Finley 1980
1242	5	125	
1242	15	54	NAS 1979
1248	20	10	
1254	25	54	
1260	30	150	
Channel catfish, *Ictalurus punctatus*			
1016	4	340-560	Johnson and Finley 1980
1242	15	110	NAS 1979
1248	15	130	
1254	15	740	
1260	30	140	
Salmonids, 4 spp.			
1016	4	134-1,154	Johnson and Finley 1980
Catostomids, 2 spp.			
1016	4	222-582	
Cutthroat trout, *Salmo clarki*			
1221	4	1,170	

1232	4	2,500	
1242	4	5,420	
1248	4	5,750	
1254	4	42,500	
1260	4	60,900	
1262	4	>50,000	
1268	4	>50,000	
Yellow perch, *Perca flavescens*			
1016	4	240	
1242	4	>150	
1248	4	>100	
1254	4	>150	
1260	4	>200	
Marine			
Invertebrates			
Grass shrimp, *Palaemonetes pugio*			
1254	4	6.1-7.8	Ernst 1984
1016	4	12.5	EPA 1980
Brown shrimp, *Penaeus aztecus*			
1016	4	10.5	
Pink shrimp, *Penaeus duorarum*			
1254	12	1.0	
Fish			
Sheepshead minnow, *Cyprinodon variegatus*			
1254			
Fry	21	0.1-0.32	Ernst 1984
Adult	21	0.9	EPA 1980
Spot, *Leiostomus xanthurus*			
1254	38	0.5	Ernst 1984
Pinfish, *Lagodon rhomboides*			
1254	12	0.5	

[a]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

Table 4. Toxicities of Aroclor PCBs to selected species of birds and mammals administered via dietary, oral, dermal, or intraperitoneal routes.

Taxonomic group, route of administration, units, organism, and compound	Exposure period	.LD-50	Reference[a]
Birds			
Dietary (mg/kg diet)			

Northern bobwhite, *Colinus virginianus*			
1221	5 days on	>6,000	Heath et al. 1972
1232	treated diet	3,002	
1242	plus 3 days	2,098	
1248	untreated	1,175	
1254		604	
1260		747	
1262		871	
Mallard, *Anas platyrhynchos*			
1242	5 days on	3,182	
1248	treated diet	2,798	
1254	plus 3 days	2,699	
1260	untreated	1,975	
1262		3,004	
Ring-necked pheasant, *Phasianus colchicus*			
1221	5 days on	>4,000	
1232	treated diet	3,146	
1242	plus 3 days	2,078	
1248	untreated	1,312	
1254		1,091	
1260		1,260	
1262		1,234	
Japanese quail, *Coturnix coturnix japonica*			
1221	5 days on	>6,000	
1232	treated diet	>5,000	
1242	plus 3 days	>6,000	
1248	untreated	4,844	
1254		2,898	
1260		2,186	
1262		2,291	
European starling, *Sturnus vulgaris*			
1254	4 days	1,500	Stickel et al. 1984
Red-winged blackbird, *Agelaius phoeniceus*			
1254	6 days	1,500	
Brown-headed cowbird, *Molothrus ater*			
1254	7 days	1,500	
Oral (grams/kg body weight)			
Mallard			
1242	Single dose	>2	NAS 1979
1254	"	>2	
1260	"	>2	
1268	"	>2	
Mammals			

Dietary (mg/kg diet)			
Mink, *Mustela vison*			
1242	9 months	8.6	Ringer 1983
1254	9 months	6.7	
European ferret, *Mustela putorius furo*			
1242	9 months	>20	
White-footed mice, *Peromyscus leucopus*			
1254	3 weeks	>100	Sanders and Kirkpatrick 1977
Rat, *Rattus norvegicus*			
1254	6 days	>75	Hudson et al. 1984
Mice, Swiss-Webster PCB-resistant strain			
1254	18 weeks	>250	Talcott and Koller 1983
Raccoon, *Procyon lotor*			
1254	8 days	>50	Montz et al. 1982
Cottontail rabbit, *Sylvilagus floridanus*			
1254	12 weeks	>10	Zepp and Kirkpatrick 1976
Oral (grams/kg body weight)			
Rat			
1221	Single dose	1.0- 4.0	EPA 1980; NAS 1979
1232	"	1.3- 4.5	
1242	"	0.8- 8.7	
1248	"	0.8-11.0	
1260	"	1.3-10.0	
1262	"	1.3- 3.2	
1268	"	2.5-11.3	
Various	"	1.0-12.0	Safe 1984
1254	"	0.5-1.4	Hudson et al. 1984
Mink			
1221	Single dose	0.75-1.0	Aulerich and Ringer
1242	"	3.0	1977; Ringer 1983
1254	"	4.0	
Dermal (grams/kg body weight)			
Rabbit			
1221	Single dose	4.0	EPA 1980
1232	"	4.5	
1242	"	8.7	
1248	"	11.0	
1260	"	10.0	
1262	"	11.3	

1268	"	10.9	
Rat			
Various	Single dose	0.8-3.2	Safe 1984
Intraperitoneal (grams/kg body weight)			
Mink			
1221	Single dose	0.5-0.75	Aulerich and Ringer
1242	"	1.0	1977
1254	"	1.25-2.25	

[a]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

Table 5. Aroclor 1254 bioconcentration factors (BCF) for selected species of whole aquatic organisms.

Ecosystem, organism, exposure duration in days, (tissue)	Aroclor 1254 concentration in medium (ug/l)	BCF	Reference[a]
Freshwater			
Invertebrates			
Daphnid, *Daphnia magna*			
4 (whole)	1.1	47,000	NAS 1979
Phantom midge, *Chaoborus punctipennis*			
4 (whole)	1.3	23,000	
14 (whole)	1.3	25,000	
Scud, *Gammarus pseudolimnaeus*			
4 (whole)	1.6	24,000	
21 (whole)	1.6	27,000	
Mosquito larvae, *Culex tarsalis*			
4 (whole)	1.5	18,000	
Crayfish, *Orconectes nais*			
4 (whole)	1.2	1,700	
21 (whole)	1.2	5,100	
Glass shrimp, *Palaemonetes kodiakensis*			
4 (whole)	1.3	12,000	
21 (whole)	1.3	17,000	
Protozoan, *Tetrahymena pyriformis*			
4 (whole)	1.0	60	EPA 1980
Vertebrates			
Fish			
Cichlid, *Cichlasoma facetum*			
3 (spleen)	isotope	1,862	Gooch and
3 (fins)	"	268	Hamdy 1983

3 (liver)	"	173	
3 (muscle)	"	164	
Marine			
Invertebrates			
American oyster, *Crassostrea virginica*			
168 (soft parts)	5.0	85,000	Ernst 1984
Rotifer, *Brachionus plicatilis*			
45 (Lipid)	-	340,000	EPA 1980
45 (Dry tissue)	-	51,000	
Vertebrates			
Fish			
Pinfish, *Lagodon rhomboides*			
35 (whole)	5.0	21,800	Ernst 1984
Spot, *Leiostomus xanthurus*			
56 (whole)	1.0	27,800	

[a]Each reference applies to data in the same row and in other rows that immediately follow for which no reference is indicated.

Table 6. Maximum acceptable toxicant concentration (MATC) values for Aroclor PCBs and selected species of aquatic organisms, based on exposure for life cycle, partial life cycle, or early life stage (from EPA 1980).

Ecosystem, organism, Aroclor PCB	MATC[a] (ug/l)
Freshwater	
Cladoceran, *Daphnia magna*	
1248	1.2-3.5
1254	2.5-7.5
Amphipod, *Gammarus pseudolimnaeus*	
1242	2.8-8.7
1248	2.5-5.1
Insect (midge), *Tanytarsus dissimilis*	
1254	0.5-1.2
Brook trout, *Salvelinus fontinalis*	
1254	0.7-1.5
Fathead minnow, *Pimephales promelas*	
1242	5.4-15.0
1248	0.1-0.4
1254	1.8-4.6
1260	1.3-4.0

Marine	
Sheepshead minnow, *Cyprinodon variegatus*	
Early life stage	
1016	3.4-15.0
1254	0.06-0.16

[a]Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, reproduction, survival, and metabolic upset during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Table 7. Proposed PCB criteria for protection of various resources and human health.

Resource and criterion	PCB concentration[a]	Reference[b]
Aquatic life		
Freshwater	<0.014 ug/l, 24-h average	EPA 1980
Saltwater	<0.030 ug/l, 24-h average	
Fish		
Diets	<0.5 mg/kg FW	O'Connor and
Residues		Pizza 1984
Whole body	<0.4 mg/kg FW	EPA 1980
Eggs	<0.33 mg/kg FW	Niimi 1983
Laboratory Animals		
Rat	<5.0 ug/kg BW daily	Grant 1983
Dog	<2.5 ug/kg BW daily	
Rhesus monkey	<1.0 ug/kg BW daily	
Livestock		
Finished animal feedsc[c]	<0.2 mg/kg FW	Hoeting 1983
Animal feed components[d]	<2.0 mg/kg FW	
Food packaging materials[e]	<10.0 mg/kg	
Wildlife		
Mink	<100 ug/kg FW diet	Aulerich et al. 1985
Mink	<640 ug/kg FW diet;	Ringer 1983;
<1.5 ug/kg BW daily	Hornshaw et al. 1983	
Birds		
Diet	<3.0 mg/kg FW	McLane and Hughes
Residues		1980
Egg	<16.0 mg/kg FW	Peakall et al. 1972
Brain	<54.0 mg/kg FW	Stickel et al. 1984

Human health		
Adult daily intake	<1.0 ug/kg BW	Swain 1983
Fish and shellfish[f]		
USA	<5.0 mg/kg FW	Hoeting 1983
Canada	<2.0 mg/kg FW	Grant 1983
Poultry		
USA	<3.0 mg/kg LW	Hoeting 1983; Kim et al. 1985
Canada	<0.5 mg/kg LW	Grant 1983
Eggs, whole less shell		
USA	<0.3 mg/kg FW	Hoeting 1983
Canada	<0.1 mg/kg FW	Grant 1983
Dairy products		
USA	<1.5 mg/kg LW	Hoeting 1983
Canada	<0.2 mg/kg LW	Grant 1983
Fish oil		
Canada	<2.0 mg/kg LW	
Beef		
Canada	<2.0 mg/kg LW	
Infant and junior foods	<0.2 mg/kg FW	Hoeting 1983
Drinking water [g]	zero	EPA 1980
Lifetime safety limit	200 mg	Rohrer et al. 1982
Overt human effects	500 mg	
Air		
Occupational, 40-h week	<1.0 ug/m^3	EPA 1980

[a] FW = fresh weight; BW = body weight; LW = lipid weight.

[b] Each reference applies to data in the same row and in other rows that immediately follow for which no reference is indicated.

[c] Except feed concentrates, feed supplements, and feed premixes.

[d] Including fish meal and other byproducts of marine origin, and finished feed concentrates, supplements, and premixes.

[e] Paper products intended for use in contact with human food and finished animal feed.

[f] Excluding heads, scales, viscera, and inedible bones.

[g] The zero drinking water criterion for human health protection is based on the nonthreshold assumption for PCBs. However, a zero level threshold may not be attainable at this time. A measurable reduction in potential carcinogenic effects due to exposure of PCBs through ingestion of contaminated water may be affected through ingestion of water containing less than 0.0008 ug PCBs/1.

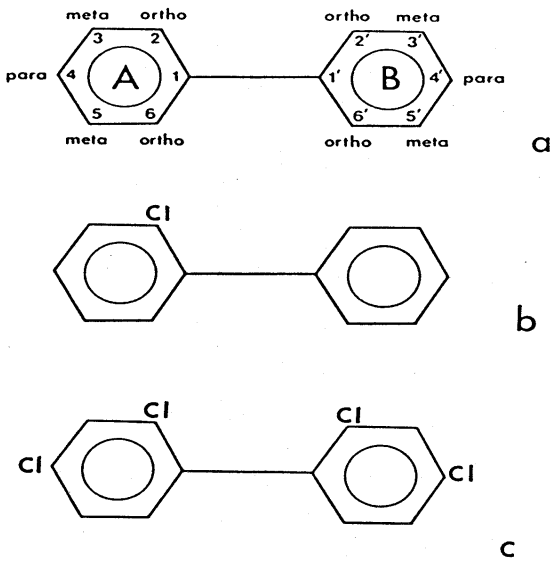


Figure 1. a = Structure of biphenyl (modified from Safe 1984); b= 2-monochlorobiphenyl; c= 2,2',4,4'=tetrachlorobiphenyl.

Biological Report 85 (1.8)
May 1986

Contaminant Hazard Reviews
Report No. 8

DIOXIN HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

By

Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Polychlorinated dibenzo- *para*- dioxins (PCDDS) are present as trace impurities in some manufactured chemicals and industrial wastes. The chemical and environmental stability of PCDDs and their tendency to accumulate in fat have resulted in their detection within many ecosystems. In general, wherever high levels of PCDDs have been detected, the source has been a hazardous waste dump, an industrial discharge, or an application of PCDD-contaminated herbicide.

There are 75 PCDD isomers; some are extremely toxic, while others are believed to be relatively innocuous. The most toxic and most extensively studied PCDD isomer is 2,3,7,8-tetrachlorodibenzo- *para*- dioxin (2,3,7,8-TCDD). In the United States and elsewhere, accidental contamination of the environment by 2,3,7,8-TCDD has resulted in deaths in many species of wildlife and domestic animals. High residues of 2,3,7,8-TCDD in fish, i.e., more than 50 parts-per-trillion (ppt) wet weight, have resulted in closing rivers to fishing. In the most seriously affected areas, hospitalization and permanent evacuation of humans has been necessary. Laboratory studies with birds, mammals, aquatic organisms, and other species have demonstrated that exposure to 2,3,7,8-TCDD can result in acute and delayed mortality as well as carcinogenic, teratogenic, mutagenic, histopathologic, immunotoxic, and reproductive effects. These effects varied greatly among species.

No regulations governing PCDD contamination exist at present to protect sensitive species of wildlife and aquatic organisms. However, the limited data available suggest that 2,3,7,8-TCDD concentrations in water should not exceed 0.01 ppt to protect aquatic life, or 10 to 12 ppt in food items of birds and other wildlife. Additional data are needed in several areas: background levels of PCDDs in natural systems; identification of fish and wildlife populations at risk; relative importance of PCDD sources; toxicological effects of various PCDDs to aquatic biota and wildlife, especially reproductive and immunosuppressive effects; and toxic and other interaction effects of PCDDs with other groups of polychlorinated chemicals having similar structure and properties, such as biphenyls, dibenzofurans, and biphenylenes.

DISCLAIMER

Mention of trade names or commercial products does not constitute endorsement or recommendation for use by the Division of Biological Services, Research and Development, Fish and Wildlife Service, U.S. Department of the Interior.

This report should be cited as:

Eisler, R. 1986. Dioxin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report. 85(1.8).

TABLES

ACKNOWLEDGMENTS

I thank L.J. Garrett and J.E. Haber for library services; I.E. Moore for secretarial help; D.L. Stalling, C.E. Grue, and D.M. Swineford for reviewing the manuscript; and C.H. Halvorson and J.R. Zuboy for editorial assistance.

INTRODUCTION

Accidental contamination of the environment by polychlorinated dibenzopara- dioxins (PCDDs), especially 2,3,7,8-tetrachlorodibenzo -*para*- dioxin (2,3,7,8-TCDD), has been associated with poor reproduction of herring gulls (*Larus argentatus*) in Lake Ontario (Stolzenburg and Sullivan 1983), with the closure of selected rivers in Missouri to anglers due to high residues in fish (Powell 1984), with the destruction of fish and wildlife in Vietnam during. military defoliation operations using phenoxy herbicides (Rappe 1984), and with the death of livestock and wildlife in Missouri (Powell 1984) and Italy (Fanelli et al. 1980b). For example, in 1976, massive kills of small animals (predominantly rabbits and poultry) occurred within the first few weeks after a chemical plant explosion in Seveso, Italy, in which 2,3,7,8-TCDD was released; many humans were hospitalized (Fanelli et al. 1980b). Levels of 2,3,7,8-TCDD in milk from dairy cows and tissues of pigs, chickens, cattle, goats, and sheep from Seveso were sufficiently elevated to pose a risk to human health. Accordingly, all domestic livestock in the most seriously afflicted areas were destroyed. In eastern Missouri during 1971, waste oil contaminated with 2,3,7,8-TCDD was applied to control road dust (Powell 1984). Later, hundreds of horses kept in riding arenas became sick, and 75 died; deaths were also observed among dogs, rodents, chickens, cats, and birds near the treated areas. Soils in Times Beach, Missouri were so heavily contaminated with 2,3,7,8-TCDD that it was permanently evacuated in December 1982. The U.S. Environmental Protection Agency had earlier announced that they would buy the dioxin-contaminated city of Times Beach; once purchase is completed the city will no longer exist officially (Powell 1984). Approximately 22 kg (48.4 pounds) of 2,3,7,8-TCDD were involved in the Times Beach incident (Westing 1978).

PCDDs are present as trace impurities in some commercial herbicides and chlorophenols. They can be formed as a result of photochemical and thermal reactions in fly ash and other incineration products. Their presence in manufactured chemicals and industrial wastes is neither intentional nor desired. The chemical and environmental stability of PCDDs coupled with their potential to accumulate in fat has resulted in their detection throughout the global ecosystem. The number of chlorine atoms in PCDDs can vary between one and eight to produce up to 75 positional isomers. Some of these isomers are extremely toxic, while others are believed to be relatively innocuous. The most toxic and extensively studied PCDD isomer is 2,3,7,8-TCDD. In fact, it is the most toxic synthetic compound ever tested under laboratory conditions. This isomer is produced during the synthesis of 2,4,5-trichlorophenol, which is used in the manufacture of the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), and other trichlorophenoxy acids, and the germicide hexachlorophene. There is general agreement that 2,3,7,8-TCDD is exceedingly stable, readily incorporated into aquatic and terrestrial ecosystems, extraordinarily persistent, and virtually impossible to destroy. PCDD-contaminated phenoxy herbicides are not the only sources of 2,3,7,8-TCDD, others include polychlorinated biphenyls and pentachlorophenols. The other 74 isomers enter the biosphere from a variety of sources (NRCC 1981). The fate and effects of PCDDs--with special reference to 2,3,7,8-TCDD and its role in poisonings of humans, aquatic organisms, wildlife, livestock, poultry, and its contamination of vegetation, soils, and sediments--have been extensively reviewed (Blair 1973; Cattebeni et al. 1978; Ramel 1978; Nicholson and Moore 1979; NRCC 1981; Hay 1982; Kociba and Schwetz 1982a,b; Choudhary et al. 1983; Josephson 1983; Long et al. 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Nriagu and Simmons 1984; Rappe 1984; Webb 1984; Kamrin and Rodgers 1985; Stalling et al. 1985a,b; Young and Cockerham 1985).

This account summarizes available data on ecological and toxicological aspects of PCDDs in the environment, with special reference to fish, wildlife, and their diets. In addition, it reviews and provides recommendations for the protection of sensitive species of wildlife and aquatic biota. This report is part of a continuing series of synoptic reviews prepared in response to requests for information from Resource Contaminant Specialists of the U.S. Fish and Wildlife Service.

ENVIRONMENTAL CHEMISTRY

The PCDDs consist of 75 isomers that differ in the number and position of attached chlorine atoms; each isomer has its own unique identity and toxicological properties. The most toxic of the chlorinated dioxin isomers is 2,3,7,8-TCDD (Figure 1). It is one of 22 possible congeners of tetrachlorodibenzo- *p*- dioxin. There is general agreement that PCDDS, including 2,3,7,8-TCDD, are (or were, until recently) found in chlorophenols, especially trichlorophenol and pentachlorophenol (Table 1), in certain phenoxy pesticides (2,4,5-T; 2,4-D; Fenoprop; Silvex; Ronnel; Erbon; Agent Orange), in hexachlorophene, and in polychlorinated biphenyls (used in electrical transformers and capacitors, and contaminated with trichlorobenzenes). PCDDs enter the environment through accidental release during chlorophenol production, through aerial application of some phenoxy herbicides, and through improper disposal of wastes into terrestrial and aquatic ecosystems (Ramel 1978; NRCC 1981; Ogilvie 1981: Choudhary et al. 1983; Josephson 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Rappe 1984;

Kamrin and Rodgers 1985). The PCDD content of technical products varies between manufacturers, between lots and grades, and between various formulations of pesticidal chemicals (NRCC 1981). More recently, PCDDs have been identified in effluents from combustion products of municipal and industrial incinerators, including fly ash and flue gas (Czuczwa and Hites 1984). These PCDDs may be associated with small particles which have long residence times in the atmosphere and can become distributed over large areas. For example, in the Great Lakes atmospheric transport of combustion products is the major source of PCDDs (mostly octa-, hepta-, and hexa-CDDs) in sediments (Czuczwa et al. 1984). High-temperature combustion of bituminous coal in an oxidized and chlorinated atmosphere (produced experimentally) yielded chlorodioxins, mostly octa-, hepta-, and hexa-CDDs and measurable quantities of tetra-CDDs (Mahle and Whiting 1980). Other potential sources of PCDDs include fossil fuel power plants, internal combustion engines, home fireplaces, and cigarette smoke (Kociba and Schwetz 1982a,b), but they require verification.

In general, PCDDs exhibit a relative inertness to acids, bases, oxidation, reduction, and heat. With increasing halogen content, they become more environmentally and chemically stabile (NRCC 1981). PCDDs are usually destroyed at temperatures greater than 1,000 C. They are resistant to biological breakdown, concentrated in fat, not readily excreted, extremely toxic to some animals, and the cumulative effects of small doses to both animals and humans are a source of increasing concern (Stolzenburg and Sullivan 1983). Most PCDDs are relatively insoluble in water, sparingly soluble in organic solvents, and will decompose on exposure to UV light, including sunlight (NIOSH 1984), or to hydroxyl compounds (Josephson 1983). The isomer 2,3,7,8-TCDD is a colorless crystalline solid at room temperature and decomposes when heated at greater than 700 C (Table 2).

Data on the bioavailability of PCDDs are scarce. It is known that PCDDs incorporated into wood as a result of chlorophenol (preservative) treatement are bioavailable. Swine and poultry using chlorophenol-treated wooden pens or litter have been found to be contaminated with PCDDs (NRCC 1981). Toxicities of individual PCDD isomers can vary by a factor of 1,000 to 10,000 for isomers as closely related as 2,3,7,8-TCDD and 1,2,3,8-TCDD or 1,2,3,7,8-penta CDD and 1,2,4,7,8-penta CDD (Rappe 1984). Isomers with the hightest biological activity and acute toxicity have 4 to 6 chlorine atoms, and all lateral (i.e., 2,3,7, and 8) positions substituted with chlorine. On this basis, the most toxic PCDD isomers are 2,3,7,8-TCDD, 1,2,3,7,8-penta CDD, 1,2,3,6,7,8-hexa CDD, 1,2,3,7,8,9-hexa CDD, and 1,2,3,4,7,8-hexa CDD (Rappe 1984).

Although PCDDs are highly persistent, volatilization and photolysis are major removal processes (NRCC 1981). In soils, 2,3,7,8-TCDD undergoes photolysis rapidly on the surface in a few hours, but more deeply buried 2,3,7,8-TCDD could have a chemical half-time greater than 10 years (NRCC 1981). Microbial degradation of 2,3,7,8-TCDD in soils is slow, with biological half-times estimated at 1.0 to 1.5 years (Ramel 1978). However 2,3,7,8-TCDD was detected in northwestern Florida from samples of soils, rodents, birds, lizards, fishes, and insects 12 years after application. This half-time in soil was estimated at 2.9 years (Westing 1978). Uptake of 2,3,7,8-TCDD from soils by vegetation is considered negligible (Blair 1973;Ramel 1978).

Other than 2,3,7,8-TCDD, identification difficulties with specific isomers make quantification difficult. To date, there has been little effort towards resolution of deficiencies in analytical methodology (NRCC 1981). A detection level of 1 pg (10^{-12}g), or lower, might be requried to find 2,3,7,8-TCDD in a one gram sample. Analyses at such low levels are complicated by interference from a multitude of other compounds, as well as by the large number of PCDD isomers and their variation in chemical properties (Rappe 1984). Although 2,3,7,8-TCDD is the most extensively studied PCDD isomer, data on its fate and persistence are generally poor, interpretations are frequently absent, and extrapolations from case to case usually impossible. The general result is a qualitative concept of this compound's behavior in environmental situations (NRCC 1981). This issue is further confounded by the presence in biological and abiotic samples of chemicals of similar structure and toxicological properties to that of 2,3,7,8-TCDD. These isosteric compounds include: 2,3,6,7-tetrachlorobiphenylene; 2,3,7,8-chlorine substituted dibenzofurans; and 3,3',4,4'-tetra-, 3,3',4,4',5-penta-, and 3,3',4,4',5,5'-hexachlorobiphenyl (Stalling et al. 1985a,b). For example, analytical results of fish, birds, and sediments indicated that every sample that was positive for 2,3,7,8-TCDD also contained 2,3,7,8-chlorine substituted dibenzofurans (Stalling et al 1985a,b).

Table 1. Levels of PCDDs in commercial chlorinated phenols, and levels of 2,3,7,8-TCDD in 2,4,5-T acid and ester formulations (Hardell 1983).

Formulation	Geographic locale (year)	Concentration, in mg/kg (ppm) PCDDs	2,3,7,8-TCDD
2,4,5-T Acid	Sweden (1952)	-	1.10
2,4,5-T Ester	Sweden (1960)	-	0.40
2,4,5-T Ester	Finland (1962)	-	0.95
2,4,5-T Ester.	Finland (1967)	-	0.22
2,4,5-T Acid	USA (1964)	-	4.8
2,4,5-T Acid	USA (1969)	-	6.0
Agent Orange	USA (-)	-	0.12
Agent Orange	USA (-)	-	5.1
2,4,6-trichlorophenol	Sweden (-)	3.0	-
2,4,6-trichlorophenol	USA (-)	0.3	-
2,3,4,6-tetrachlorophenol	England (-)	12.0	-
Pentachlorophenol	USA (-)	1,900-2,625	-
Pentachlorophenol	Germany (-)	6.8	-

Table 2. Chemical and physical properties of 2,3,7,8-TCDD, also known as CAS Registry No. 1746-01-6 (NIOSH 1984).

Criterion	Property
Empirical formula	$C_{12}H_4Cl_40_2$
Percent by weight	
Carbon	44.70
Oxygen	9.95
Hydrogen	1.25
Chlorine	44.1
Molecular weight	322
Vapor pressure, mm Hg at 25 C	$1.7x10^{-6}$
Melting point, C	305
Decomposition temperature, C	>700
Solubilities, g/liter	
o - dichlorobenzene	1.4
Chlorobenzene	0.72
Benzene	0.57
Chloroform	0.37
n - octanol	0.05
Methanol	0.01
Acetone	0.11
Water	$2.0x10^{-7}$

BACKGROUND CONCENTRATIONS

Data are accumulating that indicate many PCDDS, in addition to 2,3,7,8-TCDD, are present in biological and abiotic samples (NRCC 1981; O'Keefe et al. 1983; Petty et al. 1983; Stalling et al. 1983; Czuczwa et al. 1984; Lamparski et al. 1984; Kamrin-and Rodgers 1985; Stalling et al. 1985a). In general, wherever high levels of dioxins have been detected in the environment, a local application of TCDD-contaminated herbicide, hazardous waste site, or industrial discharge has usually been implicated as the source (Stolzenburg and Sullivan 1983). At Eglin Air Force Base (EAFB), located in northwestern Florida, contamination of a 208 hectare section with 2.778 kg of 2,3,7,8-TCDD (equivalent to 13 mg/ha) occurred between 1962 and 1970 as a result of repeated, massive herbicide applications (Young and Cockerham 1985). The 2,3,7,8-TCDD isomer was present as an impurity in 76,740 kg of 2,4-D and 73,010 kg of 2,4,5-T applied to this section of EAFB during the 9-year span. Ecological surveys conducted between 1970 and 1975 showed an apparently healthy and diverse wildlife fauna, although soil levels of 520 ppt of 2,3,7,8-TCDD were frequently encountered, and 2,3,7,8-TCDD residues were elevated in some species examined. The highest residues recorded in various trophic levels were 283 ppt in whole beetle grubs, up to 1,360 ppt in whole southern toads (*Bufo terrestris*), 360 ppt in viscera and 430 ppt in-carcass of a lizard, the six-lined racerunner (*Cnemidophorus sexlineatus*), 18 ppt in gonad and 85 ppt in gut contents of the spotted sunfish (*Lepomis punctatus*), 100 to 1,200 ppt in stomach contents of the southern meadowlark (*Sturnella magna argutula*), and 300 to 2,900 ppt in liver and 130 to 200 ppt in pelt of a beachmouse (*Peromyscus polionotus*) (Young and Cockerham 1985). The significance of these elevated residues will be discussed later.

In some cases, 2,3,7,8-TCDD has constituted up to 95% of the total body PCDD burden, as was true in lake trout, *Salvelinus namaycush* (O'Keefe et al. 1983), and rainbow trout, *Salmo gairdneri* (Petty et al. 1983) from Lake Ontario. Concentrations of 2,3,7,8-TCDD in whole carp (*Cyprinus carpio*), varied from 24% of total body PCDDs in Saginaw Bay, Michigan (Stalling et al. 1983), to 45 to 56% in the Niagara River (NRCC 1981). In herring gulls from Saginaw Bay, 2,3,7,8-TCDD comprised 40 to 60% of the whole body PCDD content (NRCC 1981; Petty et al. 1983), and 72 to 78% in gulls from Lakes Huron and Ontario (Stalling et al. 1983, 1985a). In 1983, Forster's tern (*Sterna forsteri*) from Green Bay, Wisconsin, contained 114 ppt of PCDDs in egg, of which 41% was 2,3,7,8-TCDD; double-crested cormorants (*Phalacrocorax auritus*) from the same area contained 25 to 214 ppt of PCDDs in whole body, of which only 10 to 31% was 2,3,7,8-TCDD (Stalling et al. 1985a). The causes of the observed variations are not known, but may be associated with localized inputs from municipal sewage treatment plants (Lamparski et al. 1984) and with atmospheric transport of incinerated domestic and industrial chemical wastes (Czuczwa et al. 1984). For example, the PCDD composition of sewage sludge from Milwaukee, Wisconsin, was relatively constant, as judged by analysis of samples from 1933, 1981, and 1982 (Lamparski et al. 1984). Total PCDD content in these samples ranged between 60,950 and 70,191 ppt, of which the great majority was in the form of octa-CDDs (82-86%), hepta-CDDs (11.0-15.4%), and hexa-CDDs (1.3-2.1%). However, the tetra-CDDs increased from 34 ppt in 1933, to 138 in 1981, and to 222 in 1981; corresponding values for the 2,3,7,8-TCDD isomer in 1933, 1981 and 1982 were 2.2, 11.0, and 16.0 ppt, respectively. Other TCDD isomers also showed increases from 6 ppt in 1933 to 22 ppt in 1982 (1,3,7,8-TCDD), and during that same period from 2.2 ppt to 140 ppt (1,2,3,7-, and 1,2,3,8-TCDD). It seems that chlorinated dibenzodioxins have been present in dried sludge from this plant for at least 50 years. Their presence in this material suggests that they may have been formed by the condensation of chlorophenols resulting from the chlorination of naturally occurring phenolic compounds (Lamparski et al. 1984). PCDDs were also found in sediments from Siskiwit Lake on Isle Royale in Lake Superior, a location which can receive only atmospheric inputs. The source of these compounds is the atmospheric transport of dioxins formed by combustion of domestic and chemical wastes. For example, particulates from a chemical waste incinerator in Midland, Michigan had 260,000,000 ppt of octa-CDDs and 170,000,000 ppt of hepta-CDDs; lower, but still elevated levels of 440,000 ppt of octa-CDDs and 310,000 ppt of hepta-CDDs were measured in municipal trash incinerator particulates (Czuczwa et al. 1984).

Data are limited on 2,3,7,8-TCDD concentrations in field collections of biological and other materials (Table 3). In the Great Lakes area, fish from the Tittabawasee and Saginaw Rivers, two tributaries of Lake Huron's Saginaw Bay, contained up to 695 ppt of 2,3,7,8-TCDD (Stolzenburg and Sullivan 1983). High 2,3,7,8-TCDD levels (87 to 162 ppt) were also recorded in fish. from the Niagara River, New York, and from parts of Lake Ontario; lower concentrations (2 to 28 ppt) were noted in fish from Lakes Erie, Huron, Michigan, and Superior (Stolzenburg and Sullivan 1983). Muscle from larger specimens of commercial fish collected from Lake Ontario in 1980 had higher levels of 2,3,7,8-TCDD than smaller fish (Ryan et al. 1984), suggesting that accumulation increases with age. The larger fish also contained high concentrations (1.2 to 4.9 parts per million, fresh weight)

of polychlorinated biphenyls (Ryan et al. 1984), demonstrating a need to elucidate TCDD interaction kinetics with other contaminants. Bottom-feeding fish, such as carp and catfish, from rivers in Michigan during 1978, contained higher 2,3,7,8-TCDD residues than surface feeders (Marless et al. 1982), indicating an association with contaminated sediments. Sediments from the Spring River, Missouri, contained 12 ppt of 2,3,7,8-TCDD immediately downstream of a now defunct hexachlorophene facility (Kleopfer and Zirschky 1983); concentrations in fish were measurable 111 km downstream from this disposal site (Table 3). Fish from the Spring River (and also the Meremac River, Missouri) contained inordinately high levels of 18 to 78 ppt of 2,3,7,8-TCDD, prompting the U.S. Food and Drug Administration to issue a health advisory in 1982 against fish consumption from these areas (Powell 1984). In Massachusetts, 6 ponds were surveyed for 2,3,7,8-TCDD in 1983 after prior treatment with phenoxy herbicides between 1958 and 1978 (Anon. 1984). Only one fish, a brown bullhead (*Ictalurus nebulosus*), age 3+ years, contained measurable (25 ppt) dioxin levels. Residues were not detectable in other species of fish sampled, including several species of ictalurid catfish, yellow perch (*Perca flavescens*), and chain pickerel (*Esox niger*). Negative results (less than 10 ppt 2,3,7,8-TCDD) were also documented in freshwater fish from Arkansas and Texas following spraying of the herbicide 2,4,5-T (Shadoff et al. 1977).

In birds, the levels of 2,3,7,8-TCDD have been decreasing, according to analysis of herring gull eggs from Lake Ontario. During the decade 1970-1980, there was a reduction of about 50% in 2,3,7,8-TCDD levels every two years (Ogilvie 1981; NRCC 1981; Nriagu and Simmons 1984). The reasons for the decline are unknown, and the relevance to higher-chlorinated PCDDs has not yet been determined. Until these questions are resolved and more substantative data are acquired on dioxin residues in birds, the current predictive trends on decline rates should be interpreted with caution.

Table 3. Concentrations of 2,3,7,8-TCDD measured in selected organisms and nonbiological materials collected from various locales. All values are in parts-per-trillion (ng/kg) fresh weight.

Ecosystem, taxonomic group, collection locale, year of collection, species, tissue, and other variables	Concentration[a] (ppt)	Reference[b]
Aquatic organisms		
Amphibians		
Seveso, Italy, 1978		
Toad, *Bufo* sp., whole	200	Fanelli et al. 1980c
Molluscs		
South Vietnam, during military defoliation operations with 2,4,5-T		
Various species, whole	Max. 810	Ramel 1978
Fish		
Massachusetts, 1983		
Lake Winthrop		
Muscle with skin		
Brown bullhead, *Ictalurus nebulosus*	25	Anon. 1984
Other fish species	ND	
Other bodies of water (5)		
Muscle with skin, 8 spp.	ND	
Missouri, 1982		
Spring River		

Whole fish	26	Powell 1984
Fillets	18	
Meremac River		
Whole	78	
Missouri, 1981		
Spring River, whole		
Distance, in km downstream from hexachlorophene manufacturing facility		
1	19	Kleopfer and Zirschky
5	37	1983
9	36	
74	1.1	
111	0.8	
Niagara River, New York, 1981		
Spottail shiner, *Notropis hudsonius*		
Whole	(4–60)	Suns et al. 1983
Cayuga Creek, New York, 1980		
Fillets, 4 spp.	(12–27)	O'Keefe et al. 1983
Coho salmon, *Oncorhynchus kisutch*		
Fillet	21	
Lake Ontario, 1980		
Muscle fillet, skinless		
White sucker, *Catostomus commersoni*	3 (2–4)	Ryan et al. 1984
Yellow perch, *Perca flavescens*	3.8 (3.2–4.3)	
Brown bullhead, *Ictalurus nebulosus*	6.0 (3.4–8.6)	
Channel catfish, *Ictalurus punctatus*	15.5 (12.8–17.7)	
American eel, *Anguilla rostrata*	19.8 (6.4–38.5)	
Rainbow smelt, *Osmerus mordax*	20.0 (11.3–32.9)	
Rainbow trout, *Salmo gairdneri*	32	O'Keefe et al. 1983
Lake trout, *Salvelinus namaycush*	41	NRCC 1981
Whole		
Lake trout	51	O'Keefe et al. 1983
Lake Ontario, 1979		
Rainbow trout		
Muscle	17	O'Keefe et al. 1983
Lake Ontario, 1978		
Lake trout		
Muscle	107	NRCC 1981

Brown trout, *Salmo trutta fario*		
Muscle	162	
Michigan Rivers, 1978		
Muscle, edible		
Lake trout	ND	Harless et al. 1982
Smallmouth bass,		
Micropterus dolomieui	8 (7–8)	
Catostomids	11 (4–21)	
Yellow perch	14 (10–20)	
Carp,		
Cyprinus carpio	55 (20–153)	
Channel catfish	157 (28–695)	
Cayuga Creek, New York 1978		
Coho salmon		
Fillet	20	O'Keefe et al. 1983
Amsterdam, Netherlands		
Eel, *Anguilla anguilla*		
From sediments containing		
5,000 ppt (dry weight)		
Whole	1.1	Heida 1983
Fat	3.9	
Terrestrial organisms		
Higher plants		
Seveso, Italy, 1976		
Various species, leaves	Max. 50,000,000	Ramel 1978
Annelids		
Seveso, Italy, 1978		
Earthworms, whole	12,000	Fanelli et al. 1980c
Reptiles		
Seveso, Italy, 1978		
Snakes, various spp.		
Liver	2,700	
Adipose tissue	16,000	
Mammals		
Seveso, Italy, 1978		
Field mouse, *Microtus arvalis*		
Whole	1,200 (70–49,000)	
Rabbit, *Lepus* sp.		
Liver	7,700 (2,700–13,000)	
Seveso, Italy, 1976		
Domestic goat, *Capra* sp.		
Liver	1,253	Fanelli et al. 1980b
Rabbit		
Liver		

Precontamination	13 (0.3–55)	
Postcontamination	85 (3.7–633)	
Cow, *Bos* sp.		
Milk		
July 9	ND	Fanelli et al. 1980a
July 28	7,900	
August 2	5,100	
August 10	2,500	
Birds		
Herring gull, *Larus argentatus*		
Egg		
Lake Ontario		
1983	90	Stalling et al. 1985a
1980	(44–68)	Ogilvie 1981
1971–72	(800–1,000)	
1970	1,200	Nriagu and Simmons 1984
Other Great Lakes		
1980	(2–14)	Ogilvie 1981
Saginaw Bay		
1980	(43–86)	
Great Lakes area,		
Green Bay and Lake Michigan		
Black-crowned night-heron,		
Nycticorax nycticorax		
Whole		
1982	21	Stalling et al. 1985a
1978	(12–59)	
Double-crested cormorant,		
Phalacrocorax auritus		
Whole, 1983	4	
Forster's tern, *Sterna forsteri*		
Wisconsin, 1983		
Egg		
Green Bay	47	
Lake Poygan	9	
Nonbiological materials		
Soils		
Seveso, Italy		
1978	3,500 (10–12,000)	Fanelli et al. 1980c
1976		
Precontamination	ND	Fanelli et al. 1980b
Postcontamination	2,300 (<0.75–51,000)	
Southwest Missouri		
1974	(220,000–440,000)	Kimbrough 1984

1971	(31,800,000–33,000,000)	
Pond sediments		
Massachusetts, 1983		
Lake Winthrop	5.9	Anon. 1984
Other ponds (5)	ND	
Municipal sewage sludge		
Milwaukee, Wisconsin		
1933	2	Lamparski et al. 1984
1981	11	
1982	16	
Industrial chemical and sludge samples		
Trichlorophenol process		
Still, bottom	111,000,000	Van Ness et al. 1980
Sump fluid		
Upper layer	63	
Lower layer	676,000	
Sludge		
Liquid	445,000	
Solid	374,000	
Process	79	
Discharge	22,000	

[a]Concentrations are listed as mean, (minimum-maximum), maximum=max., or nondetectable=ND, values recorded.

[b]Each reference applies to the values in the same row, and in the rows that follow for which no other reference is indicated.

Much of the information on 2,3,7,8-TCDD levels in wildlife and domestic livestock are from the vicinity of Seveso, Italy (Table 3). There, on July 10, 1976, a chemical cloud containing 2,3,7,8-TCDD was released as a result of an industrial accident. It contaminated the food (hay, grass, cut-up corn) of dairy cows (Fanelli et al. 1980a). Grossly elevated levels (7,900 ppt) were measured in milk from these herds at concentrations considered hazardous to human health, i.e., more than 7,000 ppt (Fanelli et al. 1980a). Wildlife from the most heavily-contaminated area appeared to accumulate 2,3,7,8-TCDD. Field mice (*Microtus arvalis*), for example, contained very high whole body concentrations of 2,3,7,8-TCDD (up to 49,000 ppt) almost 2 years after the critical contamination. The mechanisms for this phenomenon included ingestion of contaminated soil and licking of their dioxin-contaminated pelt (Fanelli et al. 1980c). In another study, no 2,3,7,8-TCDD was detected in livers of mountain beavers (*Aplodontia rufa*) that fed for 45 to 60 days in Oregon forests that had been sprayed with 2.2 kg of 2,4,5-T/ha (Newton and Snyder 1978). Although it was presumed that the herbicide was heavily contaminated with dioxins, no chemical analysis of the 2,4,5-T was performed.

TOXIC AND SUBLETHAL EFFECTS

GENERAL

Information is lacking or scarce on the biological properties of PCDD isomers, except 2,3,7,8-TCDD. The latter has been associated with lethal, carcinogenic, teratogenic, reproductive, mutagenic, histopathologic, and immunotoxic effects. There are substantial inter- and intraspecies differences in sensitivity and toxic responses to 2,3,7,8-TCDD. Typically, animals poisoned by 2,3,7,8-TCDD exhibit weight loss, atrophy of the thymus gland, and eventually death. The toxicological mechanisms are imperfectly understood.

TERRESTRIAL INVERTEBRATES

Reinecke and Nash (1984) reported that two species of earthworms (*Allolobophophora caliginosa, Lumbricus rubellus*) showed no adverse effects when held for 85 days in soils containing grossly elevated levels

of 5 ppm of 2,3,7,8-TCDD, but both species died at 10 ppm. In soils containing lower concentrations of 50 ppb of 2,3,7,8-TCDD, earthworms accumulated 5X soil levels in 7 days. There was no avoidance of soils contaminated with 2,3,7,8-TCDD, suggesting indifference. No surface penetration of dioxins into the body of earthworms was noted, and there was no biological breakdown of 2,3,7,8-TCDD during digestion as judged by the absence of mono-, di-, and tri-CDD's in excrement. Worm-worked soils had 2,3,7,8-TCDD retention times of 80 to 400 days, suggesting that earthworms may significantly alter half-time patterns of 2,3,7,8-TCDD in soils (Reinecke and Nash 1984).

Mutagenic responses were produced in *Escherichia coli* and certain strains of *Salmonella typhimurium* bacteria by 2,3,7,8-TCM,- but not by octa-CDD (Vos 1978). Further, chromosomal aberrations were induced in at least one species of higher plant and mammal (Ramel 1978). It must be concluded at this time that 2,3,7,8-TCDD is mutagenic or has mutagenic potential.

AQUATIC ORGANISMS

No data were available on lethal and sublethal effects of any PCDD isomer to aquatic organisms, except for 2,3,7,8-TCDD and freshwater biota (Table 4); 2,3,7,8-TCDD and liver microsomal enzyme activities in two marine species: winter flounder, *Pseudopleuronectes americanus*, and the little skate, *Raja erinacea* (Pohl et al. 1976); and 1,3,6,8-TCDD uptake and elimination by fathead minnows and rainbow trout (Corbet et al. 1983).

Sensitive species of teleosts exhibited reduced growth and fin necrosis at concentrations as low as 0.1 ppt of 2,3,7,8-TCDD after exposure for 24 to 96 hours. Concentrations of 1.0 ppt and higher were eventually fatal, and exposure to lower concentrations of 0.01 ppt for 24 hours had no measurable effect (Table 4). A typical 2.,3,7,8-TCDD poisoning sequence in guppies (*Poecilia reticulatus*) and coho salmon (*Oncorhynchus kisutch*) during a postexposure observation period included: declining interest in feeding (5-8 days postexposure); skin discoloration and fin necrosis (30 days), with caudal fin most severely affected; reduced resistance to fungal infestations; reduced swimming; and, finally, death several weeks to months after exposure (Miller et al. 1973). In general, older and larger fish die last, and smaller or younger specimens succumb first (Norris and Miller 1974).

Histopathologic and teratogenic effects were noted in fry of rainbow trout (*Salmo gairdneri*) exposed to 10 ppt of 2,3,7,8-TCDD for 96 hours as eggs, or is yolk-sac fry Helder 1981). Some fry showed extensive degeneration and necrosis of the liver, and subsequently developed edema prior to death. The remaining fry showed a high incidence of teratogenic changes, including opercular defects, and foreshortened maxillas.

Invertebrates, plants, and amphibians were comparatively resistant to 2,3,7,8-TCDD. For example, there were no adverse effects on growth, reproduction, or food consumption of algae, daphnids, and snails during immersion for 32 days in solutions containing 2.4 to 4.2 ppt of 2,3,7,8-TCDD (Yockim et al. 1978).

Accumulation of 2,3,7,8-TCDD from the aquatic environment was evident for all species examined (Table 4). The isomer 1,3,6,8-TCDD was also accumulated from the environment by freshwater teleosts, but accumulations were much lower than predicted when compared to 2,3,7,8-TCDD, and elimination was 10 to 15 times more rapid than. 2,3,7,8-TCDD (Corbet et al. 1983). In outdoor pond studies, a major portion of the added 2,3,7,8-TCDD concentrated in aquatic plants and at the sediment-water interface (Tsushimoto et al. 1982); however, most (85-99%) of the 2,3,7,8-TCDD originally added to the ecosystem remained in the sediments at the end of the study (Isensee and Jones 1975). Among teleosts, body burdens of 2,3,7,8-TCDD increased with increasing concentration in the water column and with increasing duration of exposure; on removal to uncontaminated water, less than 50% was lost in 109 days (Miller et al. 1979). The significance of 2,3,7,8-TCDD residues in aquatic organisms is not clear, and loss-rate kinetics are not fully documented; both areas merit additional research.

BIRDS

LD-50 values computed 37 days after a single oral dose of 2,3,7,8-TCDD varied from 15 ug/kg body weight in Northern bobwhite (*Colinus virginianus*), with 95% confidence limits of 9.2 and 24.5 ug/kg, to more than 810 ug/kg bodyweight for the ringed turtle-dove (*Streptopelia risoria*). Mallards (*Anas platyrhynchos*) were intermediate in sensitivity with an acute oral LD-50 value of more than 108 ug/kg body weight (Hudson et al. 1984). For all 3 species, death occurred 13 to 37 days after treatment; remission in survivors had apparently occurred by day 30 posttreatment. Gross necropsy of ringed turtle-doves that survived treatment showed enlarged livers, about twice normal size. Bobwhites showed severe emaciation, high accumulations of uric acid salts in connective tissues, and fluid accumulations in the pericardial and abdominal cavities (Hudson et al.

1984). Some birds regurgitated within a few minutes after treatment. Signs of intoxication that began 7 days after treatment included excessive drinking, loss of appetite, hypoactivity, emaciation, weakness, debility, muscular incoordination, increased reaction to stimuli, fluffed feathers, huddled position, unkempt appearance, falling, tremors, spasms, convulsions, and immobility (Hudson et al. 1984).

Table 4. Effects of 2,3,7,8-TCDD on selected species of freshwater organisms.

Taxonomic group, organism, and other variables	Dose[a]	Duration of exposure	Effects	Reference[b]
Algae and macrophytes	2.4–4.2 ppt (M)	32 days	Bioconcentration factor (BCF)	
Alga, *Odegonium cardiacum*			of 6X water at day 1; 654 to 2,083 at days 3 to 32; 500 at day 7 post-exposure (pe); 230 at day 14 pe	1
Pondweeds, *Elodea* sp. and *Ceratophyllum* sp.	53.7 ppt (M)	30 days	Residues of 7,000 ppt in 5 days; 2,500 ppt in 30 days	2
Molluscs				
Snail, *Helisoma* sp.	2.4–4.2 ppt (M)	32 days	Maximum BCF of 3,731	1
Snail, *Physa* sp.	200 ppt (M)	36 days	Reduced reproduction at day 12 pe	3
Annelids				
Worm, *Paranais* sp.	200 ppt (M)	55 days	Reduced reproduction	3
Arthropods				
Mosquito, *Aedes aegypti*				
Larvae	200 ppt (M)	17 days	No effect at day 30 pe	3
Cladoceran, *Daphnia magna*	2.4–4.2 ppt (M)	32 days	Maximum BCF of 7,125	3
Amphibians				
Bullfrog, *Rana catesbeiana*				
Tadpole	500 µg/kg (BW)	Single dose, injected intra-peritoneally (ip)	No effect through metamorphosis	4
Adult	500 µg/kg (BW)	Single dose, injected ip	No effect at day 35 pe	4

Fish				
Northern pike, *Esox lucius*				
Eggs and fry	0.1 ppt (M)	96 h	Growth retardation	5
Rainbow trout, *Salmo gairdneri*				
Eggs	0.1 ppt (M)	96 h	Growth retardation of fry at day 72 pe	6
Juveniles	10 ppt (M)	96 h	Growth retardation, edma; 26% dead at day 72 pe	6
Immature	107 ppt (M)	2 h	Whole body residues of 1,010 ppt	7
Immature	107 ppt (M)	6 h	Some deaths beginning at day 78 pe. At day 136 pe, survivors showed reduced growth and enlarged livers; tissue residues, in ppt fresh weight, were 650 in whole trout, 260 in muscle, 3,710 in liver, and 3,880 in fat	7
Juveniles	6.3 µg/kg (BW), oral route	33 days	Fin necrosis in 14 days; some deaths at day 33	3
Juveniles	0.0063 µg/kg (BW), oral route	33 days	No effect	3
Immature	1.2 µg/kg (BW)	Single dose, injected ip	Elevated liver cytochrome P-450 content	8
Guppy, *Poecilia reticulatus*	1.1 ppt (M)	24 h	Fin disease after 42 days	9
"	1.0 ppt (M)	24 h	LC-50 at day 42 pe	9
"	0.01 ppt (M)	24 h	No effect at day 32 pe	9
"	100 ppt (M)	24 h	Fin necrosis in 10 days; all dead at day 32 pe	10
Coho salmon, *Oncorhynchus kisutch*				
Juveniles	0.56 ppt (M)	48 h	12% dead in 60 days	3
Juveniles	5.6 ppt (M)	96 h	55% dead in 60 days	3
Juveniles	56 ppt (M)	24 h	All dead in 40 days	3
Juveniles	2.05 ppt (M)	96 h	Whole body residues of 125 ppt at day 114 pe	9
Juveniles	10.53 ppt (M)	96 h	Whole body residues of 2,177 ppt at day 114 pe; reduced growth and survival	9
Mosquitofish, *Gambusia affinis*	2.4–4.2 ppt (M)	15 days	BCF of 676 at day 1; 1,482 at day 7. All dead at day 15, preceded by	

			nasal bleeding and listless swimming	1
Channel catfish, *Ictalurus punctatus*	2.4–4.2 ppt (M)	20 days	Fin necrosis, erratic swimming, hemorrhaging from anus and lower jaw, BCF of 2,181; all dead between days 15 and 20	1
Fathead minnow, *Pimephales promelas*	53.7 ppt (M)	40 days	Whole body residues of 8,500 ppt in 10 days, 2,500 ppt in 40 days	2

[a]M=concentration in ambient medium at start; BW=body weight.

[b]References: 1, Yockim et al. 1978; 2, Tsushimoto et al. 1982; 3, Miller et al. 1973; 4, Neal et al. 1979; 5, Helder 1980; 6, Helder 1981; 7, Branson et al. 1985; 8, Vodicnik et al. 1981; 9, Miller et al. 1979; 10, Norris and Miller 1974.

Domestic chickens were relatively sensitive to PCDDS, especially 2,3,7,8-TCDD, with an estimated 2,3,7,8-TCDD oral LD-50 range of 25 to 50 ug/kg body weight (Kociba and Schwetz 1982a,b). Chickens fed 1 or 10 ug of 2,3,7,8-TCDD, 1,2,3,7,8,9-hexa CDD, or hepta-CDDs per kg body weight daily for 21 days showed signs of chick edema disease, i.e., pericardial, subcutaneous, and peritoneal edema; liver enlargement and necrosis with fatty degeneration; and frequently resulted in death (NRCC 1981; Gilbertson 1983). Autopsies of poultry killed by 2,3,7,8-TCDD in Seveso, Italy, in 1976 showed signs characteristic of chick edema disease (Fanelli et al. 1980b). Pathological signs of chick edema disease were also seen in herring gull chicks on the lower Great Lakes in the early 1970's (Gilbertson 1983). Concentrations of 2,3,7,8-TCDD in eggs of the herring gull declined from about 1,000 ppt in 1971 to less than 80 ppt in 1981. This was accompanied by a decrease in the frequency of chick edema disease (Gilbertson 1983). Decreases in levels of other contaminants notably mirex were probably more important to the survival of gulls in these colonies than 2,3,7,8-TCDD (Eisler 1985); however, little data exist on the interaction of PCDDS, including 2,3,7,8-TCDD, with other contaminants appearing concomitantly in bird tissues or their diets.

Although there presently is no evidence of biomagnification of PCDDs in birds (Gilbertson 1983), it is speculated that piscivorous birds have a greater potential to accumulate PCDDs than the fish that they eat (NRCC 1981).

MAMMALS

The greater toxic potential of certain PCDD isomers involves two properties: halogen atoms occupying at least 3 of the 4 lateral ring positions (2,3,7, 8 positions) and at least one of the adjacent ring positions being nonhalogenated (Kociba and Schwetz 1982a,b). Comparative toxicity data for selected PCDD isomers to the guinea pig (*Cavia* sp.) and the mouse (*Mus* sp.) confirmed this generalization and demonstrated significant interspecies differences in sensitivity (Table 5). Other PCDD isomers tested (2,8-di CDD, octa-CDD) were relatively nontoxic to mice and guinea pigs (NRCC 1981).

Acute toxicity studies with 2.,3,7,8-TCDD have shown marked differences--up to 8,400X--between the single oral LD-50 dose for the guinea pig and the hamster (*Cricetus* sp.) (Table 6). The acute oral LD-50 value of 0.6 ug/kg body weight for guinea pigs, suggests that 2,3,7,8-TCDD may be the most toxic compound ever tested on small laboratory animals. The unusual resistance of hamsters may be associated with its enhanced rate of metabolism and excretion of 2,3,7,8-TCDD relative to other PCDD isomers examined (Olson et al. 1980b; NRCC 1981). Poisoning in mammals by 2,3,7,8-TCDD is typically characterized by loss of body weight and delayed lethality; large interspecies differences exist in lethal dosages and toxic effects (Vos 1978; Neal et al. 1979; Kociba and Schwetz 1982a,b; Josephson 1983; Matsumura 1983; Kimbrough 1984; Seefeld et al. 1984). For example, 2,3,7,8-TCDD produces prominent chloracne-type skin lesions in man and monkeys, edema formation in birds, and severe liver damage in rats, mice, and rabbits.

Table 5. Acute toxicities of selected PCDD isomers to the guinea pig and the mouse (Kociba and Schwetz 1982b).

PCDD isomer	Oral LD-50, in µg/kg body weight Guinea pig	Mouse
2,8-di CDD	>300,000	-
2,3,7-tri CDD	29,444	>3,000
2,3,7,8-TCDD	2	284
1,2,3,7,8-penta CDD	3	338
1,2,4,7,8-penta CDD	1,125	>5,000
1,2,3,4,7,8-hexa CDD	73	825
1,2,3,6,7,8-hexa CDD	70–100	1,250
1,2,3,7,8,9-hexa CDD	60–100	>1,440
1,2,3,4,6,7,8-hepta CDD	>600	-

Table 6. Acute oral toxicities of 2,3,7,8-TCDD to mammals.

Organism	LD-50, in µg/kg body weight (ppb)	Reference[a]
Guinea pig	0.6- 2	1, 2
In corn oil	2.5	3
In aqueous methyl cellulose	19	3
Rat	22 - 45	2
Rhesus monkey	<70	4
Dog	100 - 200	2
Mouse	114 - 284	2
Rabbit	115	4
Hamster	1,157 -5,051	2

[a]References: 1, Harless et al. 1982; 2, Kociba and Schwetz 1982a, b; 3, Silkworth et al. 1982; 4, Olson et al. 1980a, b.

Intraspecies differences in sensitivity to 2,3,7,8-TCDD--up to 14 fold--were recently reported among 3 strains of mice; no reasons were given to account for these differences. Oral LD-50 (30 day) values varied from 182 ug 2,3,7,8-TCDD per kg body weight in strain C57, the most sensitive strain tested, and 296 for strain BD6, to 2,570 for strain DBA (Chapman and Schiller 1985). All 3 strains of mice evidenced a 25 to 34% weight loss prior to death; however, there was no measurable decline in food consumption.

Atrophy of the thymus is a consistent finding in mammals poisoned by 2,3,7,8-TCDD, and suppression of thymus-dependent cellular immunity, particularly in young animals, may contribute to their death. Although the mechanisms of 2,3,7,8-TCDD toxicity are unclear, current research areas include the role of thyroid hormones (Rozman et al. 1984), interference with plasma membrane functions (Matsumura 1983), alterations in, ligand receptors (Vickers et al. 1985), the causes of hypophagia (reduced desire for food) and subsequent attempts to alter or reverse the pattern of weight loss (Courtney et al. 1978; Seefeld et al. 1984; Seefeld and Peterson 1984), and excretion kinetics of biotransformed metabolites (Koshakji et al. 1984).

Developing mammalian fetuses are especially sensitive to 2,3,7,8-TCDD, and maternal exposure results in increased frequencies of stillbirths. Among live births, exposure to it produces teratogenic effects such as cystic kidney, cleft palate, and spinal column deformities (Ramel 1978). Effects of 2,3,7,8-TCDD on reproduction are reported for rats (McNulty 1977; Murray et al. 1979; Kociba and Schwetz 1982a,b) and monkeys (Ramel 1978; Barsotti et al. 1979; NRCC 1981; Kociba and Schwetz 1982a,b). In a 3-generation study with rats, daily dose levels of 0.01 ug of 2,3,7,8-TCDD/kg body weight (equivalent to 120 to 290 ppt or ng/kg in the diet), produce decreased litter size at birth, increased number of stillborns, and reduced survival and growth of young in both the Fl and F2 generations. Reproduction was not affected in rats at daily dosages of 0.001 ug/kg body weight, which are equivalent to 12 to 30 ppt or ng/kg of 2,3,7,8-TCDD in the diet. Abortion and weight loss were reported in rhesus monkeys (*Macaca mulatta*) at dietary levels as low as 50 ppt 2,3,7,8-TCDD (about 0.0017 ug/kg body weight daily) after 7 to 29 months. However, comparatively high dosages (200 ppt in diets equivalent to 0.0095 ug/kg body weight daily) could be tolerated by monkeys for short periods (3X weekly for 3 weeks) with no adverse effects on reproduction. Higher dose levels for extended periods (i.e., 500 ppt in diets equivalent to about 0.011 ug/kg body weight daily for 9 months) caused death (63%) or, among survivors, abortion, chloracne, nail loss, scaly and dry skin, and progressive weakness. Most treated monkeys remained fairly alert to external stimuli until just prior to death. On removal from the 500 ppt 2,3,7,8-TCDD diet and transfer to an uncontaminated diet, a severely affected monkey became pregnant and gave birth to a well-developed infant after an uneventful gestation. This suggests that some 2,3,7,8-TCDD damage effects are not permanent.

Androgenic deficiency in male rats given a single oral dose of 15 ug 2,3,7,8-TCDD/kg BW was evident as early as 2 days posttreatment, with persistence up to 12 days. These deficiencies may account for male reproductive pathology and dysfunction in rats treated with overtly toxic doses of TCDD. Findings included depression in plasma testosterone concentrations, as well as decreased weight of seminal vesicles (by 68%), ventral prostate gland (by 48%), testes, and epididymis (Moore et al. 1985).

Accumulation of 2,3,7,8-TCDD is reported in the liver of rats during lifetime exposure to diets containing 0.022 ug 2,3,7,8-TCDD/kg (Newton and Snyder 1978), or when administered orally at 0.01 ug/kg body weight once a week for 45 weeks (Cantoni et al. 1981). Liver residues of rats fed 2,3,7,8-TCDD were 0.54 ug/kg, or about 25X dietary levels; livers of rats dosed orally contained 1.05 ug/kg, or about 2.3X the total dose received on a unit weight basis.

Unlike toxicity, elimination rates of accumulated 2,3,7,8-TCDD were within a relatively narrow range. The estimated retention times of 2,3,7,8-TCDD in small laboratory mammals (rats, mice, guinea pigs, and hamsters) extended from 10.8 to 30.2 days for 50% elimination and seemed to be little influenced by species, concentration administered, duration of dose, or route of administration (Blair 1973; Olson et al. 1980b; NRCC 1981; Koshakji et al. 1984).

Histopathological effects have been reported in rabbits and horses poisoned by 2,3,7,8-TCDD. Rabbits surviving exposure to an industrial accident in Seveso, Italy, in which 2,3,7,8-TCDD was released, had edema, hemorrhagic tracheitis, pleural hemorrhage, and dystrophic lesions of hepatic tissue (Fanelli et al. 1980b). Horses from Missouri that died after waste oil contaminated with 2,3,7,8-TCDD was applied as a dust control agent in riding arenas had liver lesions, skin hyperkeratosis, gastric ulcers, and lung and kidney lesions (Kimbrough 1984). Since 2,3,7,8-TCDD is an extremely potent porphyrogenic agent, it is probable that these animals also exhibited porphyria, a condition characterized by fragility of the skin, photosensitivity, and accumulation of porphyrins in the liver (Cantoni et al. 1981).

Teratogenic and fetotoxic effects of 2,3,7,8-TCDD are well-documented in several species of animals (Marless et al. 1982; Kociba and Schwetz 1982a,b; Kimbrough 1984; Weber et al. 1985). Cleft palate in young mice was associated with daily dosages of 1.0 ug 2,3,7,8-TCDD per kg body weight in pregnant females (no-effect level at 0.1 ug/kg), and intestinal hemorrhage was found in sensitive strains of rats given daily dosages of 0.125 ug/kg body weight (no-effect level at 0.03 ug/kg) (Kociba and Schwetz 1982a,b). The 2,3,7,8-TCDD isomer has been studied for carcinogenic potential in rats and mice. There is a good correlation between carcinogenicity in both species and long-term ingestion of higher dose levels that induce toxicity. In rats, carcinomas in liver, pharynx, skin, lung, and thyroid were documented at daily dosages of 0.01 to 0.1 ug of 2,3,7,8-TCDD/kg body weight; comparable values for mice were 0.03 to 0.07 ug/kg body weight (Kociba and Schwetz 1982a,b). No response occurred at continuous daily dose levels of 0.001 to 0.0014 ug/kg body weight in rats and 0.001 to 0.03 in mice. Carcinogenic or cocarcinogenic effects were also induced by 1,2,3,6,7,8-hexa CDD and 1,2,3,7,8,9-hexa CDD, but only at higher dose levels (Rappe 1984). It appears that 2,3,7,8-TCDD has

a greater effect on growth, survival, and reproduction of animals than on tumor formation.

Interaction effects of PCDDs with other polychlorinated compounds or mixtures are not extensively documented. For example, certain polychlorinated hexachlorobiphenyls (PCBs) have a low toxic potency to induce cleft palate deformities in mice (Birnbaum et al. 1985). However, mixtures of 2,3,7,8-TCDD and 2,3,4,5,3',4' hexachlorobiphenyl resulted in a 10-fold increase in incidence of cleft palate in mice. Thus, the toxicity of compounds such as 2,3,7,8-TCDD may be enhanced by compounds of relatively low acute toxicity such as selected PCBs. Birnbaum et al. (1985) concluded that the widespread environmental occurrence of such combinations suggests a need for further evaluation of the mechanism of this interaction.

CURRENT RECOMMENDATIONS

At present, there are no criteria or standards promulgated for any of the 75 PCDD isomers, by any regulatory agency, for the protection of sensitive species of wildlife and aquatic organisms. Data are scarce or missing on the distribution and upper limits of background levels of PCDDs in natural resources, on the identification of fish and wildlife resources potentially at risk, on the relative importance of PCDD sources, and on the comparative toxicities of various PCDDs to fish and wildlife, especially reproductive and immunosuppressive toxicities (NRCC 1981). A similar situation exists for human health protection, except for the 2,3,7,8-TCDD isomer.

For protection of human health, concentrations of 2,3,7,8-TCDD (in ppt fresh weight) in fish muscle (and presumably other food items) considered acceptable are 10 in New York State (Kleopfer and Zirschky 1983), 20 in Canada (Kleopfer and Zirschky 1983), and 25 in other States within the U.S., according to the U.S. Food and Drug Administration (Stolzenburg and Sullivan 1983). Food items containing more than 50 ppt are considered unsafe for human consumption, but fish fillets containing between 25 and 50 ppt of 2,3,7,8-TCDD may be eaten once weekly by occasional consumers of fish, and twice monthly for those who eat contaminated fish year round (Stolzenburg and Sullivan 1983). It is not known at this time whether residues of 10 to 50 ppt (or higher) of 2,3,7,8-TCDD in fish flesh represents an unacceptable risk to the growth, survival, reproduction, metabolism, or behavior of the teleost, or to its predators; clearly, this is a high priority research topic.

For protection of aquatic life, it is conservatively estimated that water levels of 2,3,7,8-TCDD should not exceed 0.01 ppt as judged by laboratory studies with freshwater teleosts. The highest 2,3,7,8-TCDD concentration tested to date which has no measurable adverse effect on freshwater fish is 0.01 ppt (Miller et al. 1979). The next highest concentration tested, 0.1 ppt, was associated with fin disease in guppies (Miller et al. 1979) and reduced growth of northern pike (Helder 1981).

Diets containing up to 10 or 12 ppt of 2,3,7,8-TCDD may prove to be nonhazardous to birds and other wildlife, as judged by the results of laboratory studies with rats, monkeys, and chickens, and by the recommendations of New York State for human health protection. Higher dietary levels of 12 to 30 ppt of 2,3,7,8-TCDD (equivalent to about 1.0 ng/kg body weight daily) are not harmful to rats, based on the results of a 3-generation study (McNulty 1977; Murray et al. 1979). However, domestic chickens are relatively sensitive, with adverse effects recorded at daily dietary levels equivalent to almost 1.0 ng/kg body weight (NRCC 1981; Gilbertson 1983). Unacceptable dietary levels of 50 ppt (equivalent to 1.7 ng/kg body weight daily) are recorded for monkeys (Ramel 1978; Barsotti et al. 1979; NRCC 1981).

In the past, the major source of 2,3,7,8-TCDD in the environment was as a contaminant in phenoxy herbicides (such as 2,4,5-T; Silvex; 2,4-D; and Agent Orange), in hexachlorophene, and in other chlorophenol-type compounds. Concentrations of 2,3,7,8-TCDD in some of these products exceeded 60,000 ppb. However, this situation has been largely corrected by new manufacturing processes and by increasingly stringent Federal regulations (NRCC 1981; Choudhary et al. 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Rappe 1984). For example, 2,3,7,8-TCDD level in 2,4,5-T has decreased from 60,000 ppb in 1957 to 2,000 ppb in 1965 as a result of new manufacturing processes, and it was limited to 500 ppb in 1970 by the Canadian Federal Government. In 1970, the U.S. Department of Defense halted the spraying of Agent Orange. In 1972, the U.S. Food and Drug Administration banned the use of hexachlorophene in nonprescription soaps and deodorants. In 1978, 7 of 14 major producers of 2,4,5-T no longer manufactured this product, and the remainder claimed that their products contained less than 100 ppb of 2,3,7,8-TCDD. In 1979, production of 2,4,5-T and Silvex ceased in the United States, although stockpiles of both are still being distributed and permitted for use on rice fields, sugarcane fields, orchards, fence rows, vacant lots, and lumber yards. In 1982, the EPA required some industries to certify that chlorophenol-type compounds were no longer used as slime control agents. On

October 18, 1983, EPA published its intent to cancel the registration of pesticide products containing 2,4,5-T and Silvex, and to prohibit the transfer, distribution, sale, or importation of any unregistered product containing 2,4,5-T, Silvex, or their derivatives (NIOSH 1984).

At present, burning or heating of commercial and purified chlorophenates, and pyrolysis of polychlorinated biphenyls contaminated with trichlorobenzenes can result in the production of 2,3,7,8-TCDD and other PCDDs (NIOSH 1984). These sources together with discharges from various municipal and industrial incinerators of chlorinated compounds probably constitute the largest source of PCDDs in the environment today. In 1983, the U.S. Environmental Protection Agency proposed to monitor 2,3,7,8-TCDD in the environment (Stolzenburg and Sullivan 1983). Specific goals of the monitoring program include: determination of 2,3,7,8-TCDD concentrations in soils and biota, with emphasis on geographic areas where PCDDs may have been manufactured, used, or stored--and where concentrations may be in excess of 1,000 ppt; monitoring of industrial and municipal incinerators for TCDD emissions; and establishment of background levels for PCDDs in areas where these compounds are not expected to occur in high levels. It seems that information is also needed on the toxicological interactions of groups of polychlorinated chemicals (such as certain biphenyls, biphenylenes, and dibenzofurans) known to be isosteric with 2,3,7,8-TCDD and which frequently coexist with 2,3,7,8-TCDD in environmental samples. Acquisition of these data should provide the basis of a risk assessment analysis for dioxin and fishery and wildlife resources.

LITERATURE CITED

Anon. 1984. Six ponds dioxin survey 1983. Publ. 13,669-38-50-7-84-CR, Massachusetts Dep. Environ. Qual. Engin., Westborough. 29 pp. plus Appendix.

Barsotti, D.A., L.J. Abrahamson, and J.R. Allen. 1979. Hormonal alterations in female rhesus monkeys fed a diet containing 2,3,7,8-tetrachlorodibenzo-p-dioxin. Bull. Environ. Contam. Toxicol. 21:463-469.

Birnbaum, L.S., H. Weber, M.W. Harris, J.C. Lamb IV, and J.D. McKinney. 1985. Toxic interaction of specific polychlorinated biphenyls and 2,3,7,8-tetrachlorodibenzo-p-dioxin: increased incidence of cleft palate in mice. Toxicol. Appl. Pharmacol. 77:292-302.

Blair, E.H. (ed.) 1973. Chlorodioxins - origin and fate. Adv. Chem. Ser. 120, Am. Chem. Soc., Washington, DC. 141 pp.

Branson, D.R., I.T. Takahashi, W.M. Parker, and G.E. Blau. 1985. Bioconcentration kinetics of 2,3,7,8-tetrachlorodibenzo- p- dioxin in rainbow trout. Environ. Toxicol. Chem. 4:779-788.

Cantoni, L., M. Salmons, and M. Rizzardini. 1981. Porphyrogenic effect of chronic treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin in female rats. Dose-effect relationship following urinary excretion of porphyrins. Toxicol. Appl. Pharmacol. 57:156-163.

Cattebeni, F., A. Cavallaro, and G. Galli (eds.). 1978. Dioxin: toxicological and chemical aspects. Spectrum Publ., New York. 222 pp,.

Chapman, D.E., and C.M. Schiller. 1985. Dose-related effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in C57BL/6J and DBA/2J mice. Toxicol. Appl. Pharmacol. 78:147-157.

Choudhary, G., L.H. Keith, and C. Rappe. (eds.). 1983. Chlorinated dioxins and dibenzofurans in the total environment. Butterworth Publ., Woburn, MA. 416 pp.

Corbet, R.L., D.C.G. Muir, and G.R.B. Webster. 1983. Fate of 1,3,6,8-T_4CDD in an outdoor aquatic system. Chemosphere 12:523-527.

Courtney, K.D., J.P. Putnam, and J.E. Andrews. 1978. Metabolic studies with TCDD (dioxin) treated rats. Arch. Environ. Contam. Toxicol. 7:385-396.

Czuczwa, J.M., and R.M. Hites. 1984. Environmental fate of combustion-generated polychlorinated dioxins and furans. Environ. Sci. Technol. 18:444-450.

Czuczwa, J.M., B.D. McVeety, and R.A. Hites. 1984-. Polychlorinated dibenzo-p-dioxins and dibenzofurans in sediments from Siskiwit Lake, Isle Royale. Science 226:568-569.

Eisler, R. 1985. Mirex hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.1). 42 pp.

Fanelli, R., M.P. Bertoni, M. Bonfanti, M.G. Castelli, C. Chiabrando, G.P. Martelli, M.A. Noe, A. Noseda, S. Garattini, C. Binaghi, V. Marazza, F., Pezza, D. Pozzoli, and G. Cigognetti. 1980a. 2,3,7,8-tetrachlorodibenzo-p-dioxin in cow's milk from the contaminated area of Seveso, Italy. Bull. Environ. Contam. Toxicol. 24:634-639.

Fanelli, R., M.P. Bertoni, M.G. Castelli, C. Chiabrando, G.P. Martelli, A. Noseda, S. Garattini, C. Binaghi, V. Marazza, and F. Pezza. 1980b. 2,3,7,8-tetrachlorodibenzo-p-dioxin toxic effects and tissue levels in animals from the contaminated area of Seveso, Italy. Arch. Environ. Contam. Toxicol. 9:569-577.

Fanelli, R., M.G. Castelli, G.P. Martelli, A. Noseda, and S. Garattini. 1980c. Presence of 2,3,7,8-tetrachlorodibenzo-p-dioxin in wildlife living near Seveso, Italy: a preliminary study. Bull. Environ. Contam. Toxicol. 24:460-462.

Gilbertson M. 1983. Etiology of chick edema disease in herring gulls in the lower Great Lakes. Chemosphere 12:357-370.

Hardell, L. 1983. Epidemiological studies on soft-tissue sarcoma, malignant lymphoma, nasal and nasopharyngeal cancer, and their relation to phenoxy acid or chlorophenol exposure. Pages 367-374 in G. Choudhary, L.H. Keith and C. Rappe (eds.). Chlorinated dioxins and dibenzofurans in the total environment. Butterworth Publ., Woburn, MA.

Harless, R.L., E.O. Oswald, R.G. Lewis, A.E. Dupuy, Jr., D.D. McDaniel, and H. Tai. 1982. Determination of 2,3,7,8-tetrachlorodibenzo-p-dioxin in fresh water fish. Chemosphere 11:193-198.

Hay, A. 1982. The chemical scythe: lessons of 2,4,5-T and dioxin. Plenum Press, New York. 264 pp.

Heida, H. 1983. TCDD in bottom sediments and eel around a refuse dump near Amsterdam, Holland. Chemosphere 12:503-509.

Helder, T. 1980. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on early life stages of the pike (*Esox lucius* L.). Sci. Total Environ. 14:255-264.

Helder, T. 1981. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on early life stages of rainbow trout (*Salmo gairdneri*, Richardson). Toxicology 19:101-112.

Hudson, R.H., R.K. Tucker, and M.A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp.

Isensee, A.R., and G.E. Jones. 1975. Distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in aquatic model ecosystem. Environ. Sci. Technol. 9:668-672.

Josephson, J. 1983. Chlorinated dioxins and furans in the environment. Environ. Sci. Technol. 17:124A-128A.

Kamrin, M.A., and P.W. Rodgers (eds.). 1985. Dioxins in the environment. Hemisphere Publ. Corp., New York. 328 pp.

Kimbrough, R.D. 1984. The epidemiology and toxicology of TCDD. Bull. Environ. Contam. Toxicol. 33:636-647.

Kleopfer, R.O., and J. Zirschky. 1983. TCDD distribution in the Spring River, Southwestern Missouri. Environ. Int. 9:249-253.

Kociba, R.J., and B.A. Schwetz. 1982a. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Drug Metabol. Rev. 13:387-406.

Kociba, R.J., and B.A. Schwetz. 1982b. A review of the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) with a comparison to the toxicity of other chlorinated dioxin isomers. Assoc. Food Drug Off. Quart. Bull. 46:168-188.

Koshakji, R.P., R. D. Harbison, and M.T. Bush. 1984. Studies on the metabolic fate of [^{14}C]2,3,7,8-tetrachlorodibenzo- p -dioxin (TCDD) in the mouse. Toxicol. Appl. Pharmacol. 73:69-77.

Lamparski, L.L., T.J. Nestrick, and V.A. Stenger. 1984. Presence of chlorodibenzo dioxins in a sealed 1933 sample of dried municipal sewage sludge. Chemosphere 13:361-365.

Long, J.R., D.J. Hanson, R.L. Rawis, W. Worthy, D. Webber, and P.L. Layman. 1983. Dioxin report. Chem. Eng. News 61(23):20-64.

Mahle, N.H., and L.F. Whiting. 1980. The formation of chlorodibenzo-p-dioxins by air oxidation and chlorination of bituminous coal. Chemosphere 9:693-699.

Matsumura, F. 1983. Biochemical aspects of action mechanisms of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related chemicals in animals. Pharmac. Ther. 19:195-209.

McNulty, W.P. 1977. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin for rhesus monkeys: brief report. Bull. Environ. Contam. Toxicol. 18:108-109.

Miller, R.A., L.A. Norris, and C.L. Hawkes. 1973. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in aquatic organisms. Environ. Health Perspec. 5:177-186.

Miller, R.A., L.A. Norris, and B.R. Loper. 1979. The response of coho salmon and guppies to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in water. Trans. Am. Fish. Soc. 108:401-407.

Moore, R.W., C.L. Potter, H.M. Theobald, J.A. Robinson, and R.E. Peterson. 1985. Androgenic deficiency in male rats treated with 2,3,7,8-tetrachlorodibenzo- p -dioxin. Toxicol. Appl. Pharmacol. 79:99-111.

Murray, F.J., F.A. Smith, K.D. Nitschke, C.G. Humiston, R.J. Kociba, and B.A. Schwetz. 1979. Three-generation reproduction study of rats given 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the diet. Toxicol. Appl. Pharmacol. 50:241-252.

Neal, R.A., P.W. Beatty, and T.A. Gasiewicz. 1979. Studies of the mechanisms of toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Ann. N.Y. Acad. Sci. 320:204-213.

Newton, M., and S.P. Snyder. 1978. Exposure of forest herbivores to 2,3,7,8-tetrachlorodibenzo- p -dioxin (TCDD) in areas sprayed with 2,4,5-T. Bull. Environ. Contam. Toxicol. 20:743-750.

Nicholson, W.J., and J.A. Moore (eds.). 1979. Health effects of halogenated aromatic hydrocarbons. Ann. N.Y. Acad. Sci. 320. 730 pp.

NIOSH. 1984. Current intelligence bulletin 40, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, "dioxin"). U.S. Dep. Health Human Serv., NIOSH Publ. 84-104. 20 pp.

Norris, L.A., and R.A. Miller. 1974. The toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in guppies (*Poecilia reticulatus* Peters). Bull. Environ. Contam. Toxicol. 12:76-80.

NRCC. 1981. Polychlorinated dibenzo-p-dioxins: criteria for their effects on man and his environment. Natl. Res. Coun. Canada, Publ. NRCC No. 18574. 251 pp.

Nriagu, J.O., and M.S. Simmons (eds.). 1984. Toxic contaminants in the Great Lakes. John Wiley, New York. 527 pp.

Ogilvie, D. 1981. Dioxin found in the Great Lakes basin. Ambio 10:38-39.

O'Keefe, P., C. Meyer, D. Hilker, K. Aldous, B. Jelus-Tyror, K. Dillon, and R. Donnelly. 1983. Analysis of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Great Lakes fish. Chemosphere 12:325-332.

Olson, J.R., M.A. Holscher, and R.A. Neal. 1980a. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the golden Syrian hamster. Toxicol. Appl. Pharmacol. 55:67-78.

Olson, J.R., T.A. Gasiewicz, and R.A. Neal. 1980b. Tissue distribution, excretion, and metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the golden Syrian hamster. Toxicol. Appl. Pharmacol. 56:78-85.

Petty, J.D., D.L. Stalling, L.M. Smith, and J.L. Johnson. 1983. Occurrence and potential impact of PCDF's and PCDD's in aquatic ecosystems. Pages 96-102 in D.D. Hemphill (ed.). Trace substances in environmental health XVII. Univ. Missouri, Columbia.

Pohl, R.J., M.O. James, J.R. Fouts, and J.R. Bend. 1976. Xenobiotic metabolism in marine fish treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 3-methylcholanthrene (3-MC), or 1,2,3,4-dibenzanthracene (DBA). Pharmacologist 18:207.

Powell, R.L. 1984. Dioxin in Missouri: 1971-1983. Bull. Environ. Contam. Toxicol. 33:648-654.

Ramel, C. (ed.). 1978. Chlorinated phenoxy acids and their dioxins. Ecol. Bull. (Stockholm) 27. 302 pp.

Rappe, C. 1984. Analysis of polychlorinated dioxins and furans. Environ. Sci. Technol. 18:78A-90A.

Reinecke, A.J., and R.G. Nash. 1984. Toxicity of 2,3,7,8-TCDD and short-term bioaccumulation by earthworms (Oligochaeta). Soil Biol. Biochem. 16:45-49.

Rozman, K., T. Rozman, and H. Greim. 1984. Effect of thyroidectomy and thyroxine on 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) induced toxicity. Toxicol. Appl. Pharmacol. 72:372-376.

Ryan, J.J., P.Y. Lau, J. C. Pilon, D. Lewis, H.A. McLeod, and A. Gervais. 1984. Incidence and levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Lake Ontario commercial fish. Environ. Sci. Technol. 18:719-721.

Seefeld, M;D., S.W. Corbett, R.E. Keesey, and R.E. Peterson. 1984. Characterization of the wasting syndrome in rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Toxicol. Appl. Pharmacol. 73:311-322.

Seefeld, M.D., and R.E. Peterson. 1984. Digestible energy and efficiency of feed utilization in rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Toxicol. Appl. Pharmacol. 74:214-222.

Shadoff, L.A., R.A. Hummel, L. Lamparski, and J.H. Davidson. 1977. A search for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in an environment exposed annually to 2,4,5-trichlorophenoxyacetic acid ester (2,4,5-T) herbicides. Bull. Environ. Contam. Toxicol. 18:478-485.

Silkworth, J., D. McMartin, A. DeCaprio, R. Rej, P. O'Keefe, and L. Kaminsky. 1982. Acute toxicity in guinea pigs and rabbits of soot from a polychlorinated biphenyl-containing transformer fire. Toxicol. Appl. Pharmacol. 65:425-439.

Stalling, D.L., R.J. Norstrom, L.M. Smith, and M. Simon. 1985a. Patterns of PCDD, PCDF, and PCB contamination in Great Lakes fish and birds and their characterization by principal components analysis. Chemosphere 14:627-643.

Stalling, D.L., J.D. Petty, L.M. Smith, and W.J. Dunn, III. 1985b. Dioxins and furans in the environment: a problem for chemometrics. Pages 101-126 *in* M.A. Kamrin and P.W. Rodgers (eds.). Dioxins in the environment. Hemisphere Publ. Corp., New York.

Stalling, D.L., L.M. Smith, J.D. Petty, J.W. Hogan, J.L. Johnson, C. Rappe, and H.R. Buser. 1983. Residues of polychlorinated dibenzo-p-dioxins and dibenzofurans in Laurentian Great Lakes fish. Pages 221-240 *in* R.E. Tucker, A.L. Young and A.P. Gray (eds.). Human and environmental risks of chlorinated dioxins and related compounds. Plenum Publ. Corp., New York.

Stolzenburg, T., and J. Sullivan. 1983. Dioxin: a cause for concern? Publ. WIS-SG-83-141. Univ. Wisconsin, Madison. 21 pp.

Suns, K., G.R. Craig, G. Crawford, G.A. Rees, H. Tosine, and J. Osborne. 1983. Organochlorine contaminant residues in spottail shiners (*Notropis hudsonius*) from the Niagara River. J. Great Lakes Res. 9:335-340.

Tsushimoto, G., F. Matsumura, and R. Sago. 1982. Fate of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in an outdoor pond and in model aquatic ecosystems. Environ. Toxicol. Chem. 1:61-68.

Van Ness, G.F., J.G. Solch, M.L. Taylor, and T.O. Tiernan. 1980. Tetrachlorodibenzo-p-dioxins in chemical wastes, aqueous effluents and soils. Chemosphere 9:553-563.

Vickers, A.E.M., T.C. Sloop, and G.W. Lucier. 1985. Mechanism of action of toxic halogenated aromatics. Environ. Health Perspec. 59:121-128.

Vodicnik, M.J., C.R. Elcombe, and J.J. Lech. 1981. The effect of various types of inducing agents on hepatic microsomal monooxygenase activity in rainbow trout. Toxicol. Appl. Pharmacol. 59:364-374.

Vos, J.G. 1978. 2,3,7,8-tetrachlorodibenzo-*para*-dioxin: effects and mechanisms. Pages 165-176 *in* C. Ramel (ed.). Chlorinated phenoxy acids and their dioxins. Ecol. Bull. (Stockholm) 27.

Webb, K.E. (ed.). 1984. Dioxin: lessons from the Missouri experience. Bull. Environ. Contam. Toxicol. 33:629-734.

Weber, H., M.W. Harris, J.K. Haseman, and L.S. Birnbaum. 1985. Teratogenic potency of TCDD, TCDF, and TCDD-TCDF combinations in C57BL/6N mice. Toxicol. Lett. 26:159-167.

Westing, A.H. 1978. Ecological considerations regarding massive environmental contamination with 2,3,7,8-tetrachlorodibenzo- para -dioxin. Pages 285-294 *in* C. Ramel (ed.). Chlorinated phenoxy acids and their dioxins. Ecol. Full. (Stockholm) 27.

Yockim, R.S., A.R. Isensee, and G.E. Jones. 1978. Distribution and toxicity of TCDD and 2,4,5-T in an aquatic model ecosystem. Chemosphere 3:215-220.

Young, A.L., and L.G. Cockerham. 1985. Fate of TCDD in field ecosystems assessment and significance for human exposures. Pages 153-171 *in* M.A. Kamrin and P.W. Rodgers (eds.). Dioxins in the environment. Hemisphere Publ. Corp., New York.

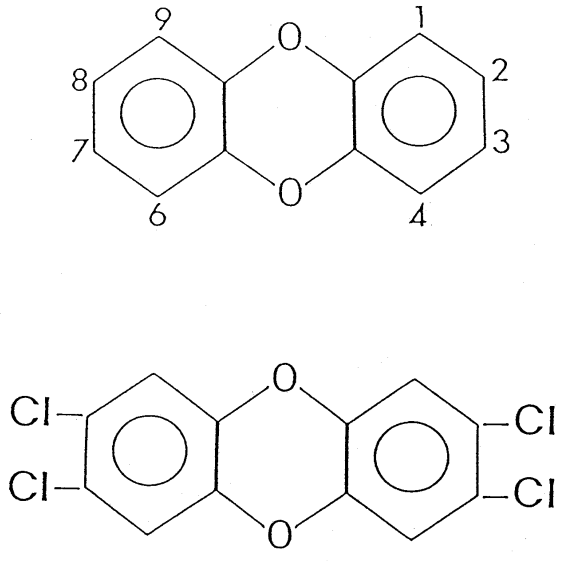


Figure 1. Upper. Numbering system used for identification of individual PCDD isomers. Lower. The isomer 2, 3, 7, 8-tetrachlorodibenzo-*para*-dioxin (2, 3, 7, 8-TCDD).

Biological Report 85(1.9)
August 1986

Contaminant Hazard Reviews
Report No. 9

DIAZINON HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Diazinon (phosphorothioic acid 0,0- diethyl 0- (6-methyl-2-(1-methylethyl)-4-pyrimidinyl) ester) is an organophosphorus compound with an anticholinesterase mode of action. It is used extensively to control flies, lice, insect pests of ornamental plants and food crops, as well as nematodes and soil insects in lawns and croplands. Diazinon degrades rapidly in the environment, with half-time persistence usually less than 14 days. But under conditions of low temperature, low moisture, high alkalinity, and lack of suitable microbial degraders, diazinon may remain biologically active in soils for 6 months or longer.

At recommended treatment levels, diazinon-related kills have been noted for songbirds, honeybees, and especially waterfowl that consume diazinon-treated grass; however, incidents involving agricultural applications may be underreported. Accidental deaths through misapplication of diazinon have also been recorded in domestic poultry, monkeys, and humans. It has been suggested, but not yet verified, that wildlife partially disabled in the field as a result of diazinon poisoning would be more likely to die of exposure, predation, starvation, or dehydration, or face behaviorial modifications, learning impairments, and reproductive declines than would similarly treated domestic or laboratory animals.

Among sensitive aquatic organisms, LC-50 (96 h) values of 1.2 to 2.0 ug/l were derived for freshwater cladocerans, and 4.1 to 5.9 ug/l for marine shrimps; freshwater teleosts were comparatively resistant, with all LC-50 (96 h) values greater than 90 ug/l. Sublethal effects were recorded at 0.3 to 3.2 ug diazinon/l and included reduced emergence of stream insects (0.3 ug/1), reduced fecundity of a marine fish (0.47 ug/1), significant accumulations in freshwater teleosts (0.55 ug/1), daphnid immobilization (1.0 ug/1), potential mutagenicity in a freshwater fish (1.6 ug/1), and spinal deformities in teleosts (3.2 ug/1). Exposure to diazinon during spawning caused temporary, but complete, inhibition of reproduction at concentrations which did not produce this effect in fish exposed continuously since hatch.

Acute oral LD-50's of about 2,500 to 3,500 ug diazinon/kg body weight were determined for goslings *(Anser* spp.), ducks *(Anas* spp.), domestic turkey (*Meleagris gallopavo)*, and the red-winged blackbird (*Agelaius phoeniceus*), the most sensitive birds tested. A dietary LD-50 of 167,000 ug diazinon/kg was determined for Japanese quail (*Corturnix japonica)*. Diazinon produced marked teratogenic effects in embryos of the domestic chicken (*Gallus gallus*) at 6.2 to 25 ug/embryo, reduced egg deposition in the ring-necked pheasant (*Phasianus colchicus*) at more than 1,050 ug/bird, and (empirically) decreased food consumption and increased weight loss in the northern bobwhite (*Colinus virginianus*) at greater than 17,500 ug diazinon/kg diet.

The rat (*Rattus rattus*) was the most sensitive mammal tested in acute oral toxicity screenings, with an LD-50 of 224,000 ug diazinon/kg body weight. Chronic oral toxicity tests with swine (*Sus scrofa*) indicated that death was probable if daily intakes were greater than 5,000 ug diazinon/kg body weight. Measurable adverse effects of diazinon have been recorded in rodents, the most sensitive mammalian group tested, at: 500 ug/kg in diets fed to rats for 5 weeks, causing blood cholinesterase inhibition; 180 ug/kg body weight administered daily to pregnant mice (*Mus musculus*) during gestation, inducing behaviorial modifications and delayed sexual maturity of progeny; and single oral doses of 1,800 and 2,300 ug/kg body weight in rats and white-footed mice (*Peromyscus leucopus*), respectively, which produced altered blood chemistry and brain cholinesterase inhibition.

For protection of sensitive aquatic organisms, diazinon concentrations in water should not exceed 0.08 ug/l; however, more data are needed on effects of fluctuating and intermittent chronic exposures of diazinon on reproduction of fish and aquatic invertebrates. Granular formulations of diazinon seem to be especially hazardous to seed-eating birds, suggesting a need to control or eliminate granular applications when these species are present. For additional protection of birds, diazinon should be used with extreme caution in areas where waterfowl feed, and in large-scale spray applications such as grasshopper control. Diazinon in combination with some agricultural chemicals produced more-than-additive adverse effects on bird growth and fecundity; accordingly, more research is needed on effects of complex mixtures of pesticides that contain diazinon. Most investigators agreed that mammals were less susceptible to diazinon than were birds, at least under controlled environmental regimens. Data are lacking on diazinon impacts to mammals under field conditions; acquisition of these data should constitute a priority research area.

DISCLAIMER

Mention of trade names or commercial products does not constitute endorsement or recommendation for use by the Division of Biological Services, Research and Development, Fish and Wildlife Service, U.S. Department of the Interior.

This report should be cited as:

Eisler, R. 1986. Diazinon hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85(1.9).

TABLES

FIGURES

ACKNOWLEDGMENTS

I thank Lynda J. Garrett, Joyce E. Haber, and Brenda Graff for library services; Irene E. Moore for secretarial help; Joseph B. Hunn, Matthew C. Perry, Kenneth L. Stromborg, and Donald H. White for reviewing the manuscript; and Paul A. Opler and James R. Zuboy for editorial services.

INTRODUCTION

Diazinon, an organophosphorus compound with an anticholinesterase mode of action, was released for experimental evaluation in the early 1950's. Today, diazinon is used extensively by commercial and home applicators in a variety of formulations to control flies, cockroaches, lice on sheep, insect pests of ornamental plants and food crops (especially corn, rice, onions, and sweet potatoes), forage crops such as alfalfa, and nematodes and soil insects in turf, lawns, and croplands (Anon. 1972; Meier et al. 1976; Allison and Hermanutz 1977; Berg 1984; Stone and Gradoni 1985).

Waterfowl and other wildlife may acquire diazinon by drinking contaminated water, by absorbing it through legs and feet, by consuming treated grass or grain, or by ingestion of pesticide-impregnated carrier particles (Stone and Knoch 1982; Stone and Gradoni 1985). Diazinon poisonings of birds--involving 54 incidents in 17 States--have been recorded for at least 23 species, especially among waterfowl feeding on recently treated turfgrass; incidents involving agricultural applications may be less conspicuous, and thus not as well-documented (Stone and Gradoni 1985). Kills of Canada geese (*Branta canadensis*), brant (*Branta bernicla*), mallard (*Anas platyrhynchos*), American black duck (*Anas rubripes*), other species of waterfowl, and songbirds have all been associated with consumption of grass or grain shortly after diazinon application (Schobert 1974; Zinkl et al. 1978; Stone 1980; Stone and Knoch 1982). Fatal diazinon poisonings have also been recorded in humans (Soliman et al. 1982; Lox 1983), domestic chickens (*Gallus gallus*) (Sokkar et al. 1975), domestic ducklings (*Anas* spp.) and goslings (*Anser* spp.) (Egyed et al. 1974, 1976), in laboratory monkey colonies of the tamarin (*Saguinus fuscicollis*) and the common marmoset (*Callithrix jacchus*) (Brack and Rothe 1982), and the honeybee (*Apis mellifera*) (Anderson and Glowa 1984). Mammals seem to be less sensitive than birds to diazinon poisoning (Stone and Gradoni 1985). The lack of reported mammalian mortalities (only one suspected case of a pocket gopher, *Thomomys* sp., found dead in a park at Yakima, Washington, following aerial spraying of diazinon on shade trees) is consistent with the general findings of Grue et al. (1983) for organophosphorus insecticides. Sublethal effects such as reduced hatch, retarded growth, and spinal deformities in fish (Allison and Hermanutz 1977), reduced food consumption and egg production in the ring-necked pheasant (*Phasianus colchicus*) (Stromborg 1977), and behavioral modifications, reduced food intake, alterations in liver enzyme activities, reductions in vitamin concentrations, reduced body temperature, and lowered resistance to cold stress in white-footed mice (*Peromyscus leucopus*) (Montz and Kirkpatrick 1985) have been noted at diazinon concentrations markedly lower than those causing acute mortality. It has been suggested, but not proven, that wildlife partially disabled in the field as a result of diazinon poisoning would be more likely to die of exposure, predation, starvation, or dehydration, or face behaviorial abnormalities learning, impairments, and reproductive declines than would similarly treated domestic or laboratory animals, (Montz 1983; Montz and Kirkpatrick 1985).

In this account, I summarize available data on the environmental fate and effects of diazinon, with emphasis on fish and wildlife resources. Also included are recommendations for the protection of sensitive species of concern to the U.S. Fish and Wildlife Service. This report is part of a continuing series of synoptic reviews prepared in response to requests for information from Service environmental specialists.

ENVIRONMENTAL CHEMISTRY

Diazinon is a broad spectrum insecticide that is effective against a variety of orchard, vegetable, and soil pests, ectoparasites, flies, lice, and fleas. It exists as a technical grade product, a wettable powder, an emulsifiable concentrate, as granules, and in a variety of other formulations (Negherbon 1959; Anon. 1972; Eberle 1974; Berg 1984). The active ingredient in diazinon is phosphorothioic acid 0,0- diethyl 0- (6-methyl-2-1(methylethyl)-4-pyrimidinyl) ester (Figure 1). Its molecular formula and molecular weight are $C_{12}H_{2l}N_2O_3PS$, and 304.35. The technical grade is light amber to dark brown, and boils at 83 to 84 C. Diazinon is soluble in water to 40 mg/l, and dissolves readily in aliphatic and aromatic solvents, alcohols, and ketones. Diazinon may be stored on the shelf for at least 3 years with negligible degradation. Diazinon is also known as G-24480, Sarolex, Spectracide (Anon. 1972), AG-500, Alfa-tox, Basudin, Dazzel, Diazajet, Diazide, Diazol, ENT 19507, Gardentox, Neocidol, Nucidol, CAS 333-41-5 (Hudson et al. 1984), Diagran, Dianon, DiaterrFos, Diazatol, Dizinon, Dyzol, D.z.n., Fezudin, Kayazinon, Kayazol, Knox Out, and Nipsan (Berg 1984).

Some diazinon formulations contain 0.2 to 0.7% (2,000 to 7,000 mg/kg) of Sulfotep (tetraethyl dithiopyrophosphate) as a manufacturing impurity; Sulfotep is reportedly at least 100 times more toxic than diazinon to some organisms (Jarvinen and Tanner 1982). It seems that additional, research is warranted on diazinon/Sulfotep interactions.

Diazinon degrades rapidly in plants, with half-time persistence usually less than 14 days; however, persistence increases as temperatures decrease, and is longer in crops with a high oil content (Table 1). In water, diazinon breaks down to comparatively nontoxic compounds with little known hazard potential to aquatic species (Meier et al. 1976; Jarvinen and Tanner 1982), although the degradation rate is highly dependent on pH (Table 1). In soils, diazinon seldom penetrates below the top 1.3 cm (Kuhr and Tashiro 1978; Branham and Wehner 1985). But diazinon may remain biologically available in soils for 6 months or longer at low temperature, low moisture, high alkalinity, and lack of suitable microbial degraders (Anon. 1972; Bartsch 1974; Meier et al. 1976; Allison and Hermanutz 1977; Menzie 1978; Forrest et al. 1981; Branham and Wehner 1985). Bacterial enzymes, derived from *Pseudomonas* sp., can be used to hydrolyze diazinon in soil, although costs are prohibitive except in treating emergency situations involving spills of concentrated diazinon solutions. In one case, diazinon was enzymatically hydrolyzed within 24 hours in an agricultural sandy soil at concentrations as high as 10,000 mg/kg (Barik and Munnecke 1982).

Table 1. Persistence of diazinon in plants, soil, and water.

Sample type and other variables	Time for 50% persistence	Reference[a]
Plants		
Cabbage leaves		
Summer	14 days	1
Winter	>14 days	1
Leafy vegetables, forage crops	<2 days	2
Other vegetables, cereal products	<7 days	2
Fruits	4 days	2
Carrots, oil seed plants	> 4 days	2
Grass	7 days	3
Soil	2 to 4 weeks	2, 4
Water		
Lake Superior	30 days (14–184 days)	5
River water	39 days	6
Effect of pH		
3.1	12 h	7
6.0	2 weeks	8
7.4	6 months	8
9.0	4 months	8
10.4	6 days	7

[a]References: 1, Montz 1983; 2, Bartsch 1974; 3, Kuhr and Tashiro 1978; 4, Branham and Wehner 1985; 5, Jarvinen and Tanner 1982; 6, Arthur et al. 1983; 7, Meier et al. 1976; 8, Allison and Hermanutz 1977.

In almost every instance of diazinon poisoning, there has been a general reduction in cholinesterase activity levels, especially in brain and blood. Diazinon exerts its toxicity by binding to the neuronal enzyme acetylcholinesterase (AChE) for a considerable time postexposure (Montz 1983). It is emphasized that all organophosphorus pesticide compounds, in sufficient dose, inhibit AChE in vivo, and all share a common

mechanism of acute toxic action (Murphy 1975). AChE inhibition results in the accumulation of endogenous acetylcholine-in nerve tissues and effector organs, resulting in signs that mimic the muscarinic, nicotinic, and central nervous system (CNS) actions of acetylcholine. The immediate cause of death in fatal organophosphorus compound poisonings, including diazinon, is asphyxia resulting from respiratory failure. Contributing factors are the muscarinic actions of bronchoconstriction and increased bronchial secretions, nicotinic actions leading to paralysis of the respiratory muscles, and the CNS action of depression and paralysis of the respiratory center (Murphy 1975).

Diazinon is not a potent inhibitor of cholinesterase, and must be converted to its oxygen analogues (oxons), especially diazoxon (diethyl 2-isopropyl-6-methylpyrimidin-4-yl phosphate) in vivo before poisoning can occur (Wahla et al. 1976). Diazoxon is about 10,000 times more effective in reducing cholinesterase activity levels than diazinon (Fog and Asaka 1982). At least eight diazinon metabolites have been identified in vertebrates, of which four are oxons (Machin et al. 1975; Menzie 1978; Seguchi and Asaka 1981). It is generally agreed that diazinon is metabolized to diazoxon through the action of liver mixed-function oxidases and nicotinic adenine nucleotide phosphate (Menzie 1978; McLean et al. 1984). Diazinon toxicity will depend to some extent upon the relation between the rates of activation of diazinon to diazoxon, and of decomposition of the latter to harmless products (Fujii and Asaka 1982). Birds are more sensitive to diazinon than mammals, probably because mammalian blood enzymes hydrolyze diazoxon rapidly, whereas bird blood has virtually no hydrolytic activity. It seems that diazoxon stability in blood is a major factor affecting susceptibility of birds and mammals to diazinon poisoning (Machin et al. 1975).

Diazinon poisoning effects in animals can be delayed or prevented by treatment with a variety of compounds. For example, AChE in diazinon-stressed birds can be reactivated by pralidoxime (Egyed et al. 1976; Fleming and Bradbury 1981; Misawa et al. 1982). Furthermore, pretreatment of large white butterfly (*Pieris brassicae*) larvae with methylene dioxyphenyl compounds will inhibit the diazinon to diazoxon activation (Wahla et al. 1976). Added tryptophan and its metabolites may prevent teratogenic defects by maintaining nicotinic adenine nucleotide (NAD) levels in diazinon-treated chicken embryos; diazinon reportedly acts to decrease the availability of tryptophan to bird embryos, subsequently interfering with NAD metabolism and causing birth defects (Henderson and Kitos 1982). NAD metabolism in diazinon-stressed birds may also be maintained with nicotinamide (Misawa et al. 1982). In contrast to many other organophosphorus insecticides, organisms that survive diazinon-inhibited cholinesterase levels can undergo considerable spontaneous reactivation (dephosphorylation), indicating that its dephosphorylation occurs more readily than that of cholinesterase inhibited by other organophosphorus compounds (Fleming and Bradbury 1981).

ACUTE AND CHRONIC TOXICITY

GENERAL

Diazinon toxicity varies widely within and among species, and is modified by organism age, sex, and body size, climatic conditions, pesticide formulation, chemistry of the environment, and other factors (Montz 1983). Nevertheless, several trends are apparent as judged by available data. Among aquatic organisms, for example, freshwater cladocerans and marine shrimps were the most sensitive species tested, with LC-50 (96 h) values of less than 5 ug/l; freshwater teleosts were more resistant, with the lowest LC-50 (96 h) value recorded being 90 ug/l. Diazinon has considerable potential for causing acute avian poisoning episodes; sensitive species of birds, including ducks, turkey (*Meleagris gallopavo*), and red-winged blackbird (*Agelaius phoeniceus*), died at single oral doses of 2 mg of diazinon/kg body weight. Mammals are more resistant than birds to diazinon; the lowest LD-50 (acute oral) value recorded is 224 mg/kg body weight for female rats (*Rattus rattus*). Chronic oral toxicity tests with mammals suggest that daily intake exceeding 5 or 10 mg diazinon/kg body weight is probably fatal over time to swine (*Sus scrofa*) and dogs (*Canis familiaris*), respectively. Finally, 9 mg/kg of dietary diazinon fed during gestation to pregnant mice (*Mus musculus*) was associated with significant mortality of pups prior to weaning.

AQUATIC ORGANISMS

Freshwater cladocerans and marine crustaceans were the most sensitive groups tested, with LC-50(96 h) values of less than 5 ug/l for the more sensitive species (Table 2). Rainbow trout (*Salmo gairdneri*) and bluegill (*Lepomis macrochirus*) seemed to be the least resistant freshwater teleosts tested, with LC-50(96 h) values

between 90 and 120 ug/l; however, the postlarval and juvenile stages of the striped knifejaw (*Oplegnathus fasciatus*) --a marine fish cultured intensively in Japan-- were unusually sensitive (Table 2). In general, technical grade formulations of diazinon seem to be more toxic than emulsifiable concentrates, dusts, and oil solutions (Table 2). Also, large variations in acute toxicity values were evident, even among closely related species (Table 2).

Outward signs of diazinon poisoning in fish included lethargy, forward extension of pectoral fins, darkened areas on posterior part of body, hyperexcitability when startled, sudden rapid swimming in circles, and severe muscular contractions (Goodman et al. 1979). Internally, physiological mechanisms in teleosts preceding death involved the following sequence: cholinesterase inhibition, acetylcholine accumulation, disruption of nerve functions, respiratory failure, and asphyxia (Sastry and Sharma 1980).

Limited data indicated that the yellowtail (*Seriola quinqueradiata*), a marine teleost, was 84X more sensitive to diazinon than were 4 species of freshwater fishes, as judged by LC-50(48 h) values, and by its inability to biotransform diazinon to nontoxic metabolites within one hour (Fujii and Asaka 1982). Diazinon has not been detected in marine waters, but the potential exists for contamination of estuarine areas from agricultural and urban runoff (Goodman et al. 1979).

BIRDS

Diazinon adversely affects survival of developing mallard embryos when the eggshell surface is subjected for 30 seconds to concentrations 25 to 34 times higher than recommended field application rates; mortality patterns were similar for solutions applied in water or in oil (Table 3). This laboratory finding suggests that eggs of mallards, and probably other birds, are protected when diazinon is applied according to label directions. Chickens dipped in solutions containing 1,000 mg of diazinon/l, an accidentally high formulation, experienced 60% mortality within 3 days; no other deaths occurred during the next 4 months (Sokkar et al. 1975).

Results of 5-day feeding trials with 2-week-old Japanese quail (*Coturnix japonica*), followed by 3 days on untreated feed, showed an LD-50 of 167 mg diazinon/kg diet -- a concentration considered "very toxic". No deaths were observed at dietary levels of 85 mg diazinon/kg, but 53% died at 170 mg/kg, and 87% at 240 mg/kg (Hill and Camardese 1986).

Diazinon has a potential for causing acute avian poisoning episodes (Schafer et al. 1983). Ingestion of 5 granules of Diazinon 14G (14.3% diazinon) killed 80% of house sparrows (*Passer domesticus*), and all red-winged blackbirds to which they were administered (Balcomb et al. 1984). Ingestion of fewer than 5 granules of Diazinon 14G, each containing about 215 ug of diazinon, could be lethal to sparrow-sized birds (i.e., 15 to 35 g body weight), especially juveniles of seed-eaters (Hill and Camardese 1984). Acute oral LD-50's indicate that 15 mg of diazinon/kg body weight is fatal to virtually all species tested, and that 2 to 5 mg/kg is lethal to the more sensitive species (Table 4). Signs of diazinon poisoning in birds included muscular incoordination, wing spasms, wing-drop, hunched back, labored breathing, spasmodic contractions of the anal sphincter, diarrhea, salivation, lacrimation (tear production), eyelid drooping, prostration, and arching of the neck over the back (Hudson et al. 1984). Most of these signs have been observed in birds poisoned by compounds other than diazinon; these compounds also act via an anticholinesterase mode of action (Hudson et al. 1984).

Table 2. Acute toxicity of diazinon to aquatic organisms. All values shown are in micrograms of diazinon (active ingredients)/liter of medium fatal to 50% in 96 hours.

Ecosystem, taxonomic group organism, and other variables	LC-50 (96 h), in µg/L	Reference[a]
Freshwater		
Invertebrates		
Daphnid, *Daphnia magna*		
Dust (27%)	1.2	1
Emulsifiable concentrate (47.5%)	1.3	1
Technical grade (91.9%)	2.0	1
Oil solution (0.5%)	13.0	1
Cladoceran, *Simocephalus serrulatus*	1.4[b]	2
Stonefly, *Pteronarcys californica*	25	2
Amphipod, *Gammarus fasciatus*	200	2
Daphnid, *Daphnia pulex*	800[b]	2
Fish		
Rainbow trout, *Salmo gairdneri*	90–400	2, 3
Technical grade	110	1
Emulsifiable concentrate	3,000	1
Dust	3,200	1
Oil solution	19,000	1
Bluegill, *Lepomis macrochirus*	120–670	2, 3, 4
Technical grade	120	1
Emulsifiable concentrate	530	1
Dust	170	1
Oil solution	160	1
Lake trout, *Salvelinus namaycush*	602	2
Brook trout, *Salvelinus fontinalis*	770	4
Flagfish, *Jordanella floridae*	1,600	4
Cutthroat trout, *Salmo clarki*	1,700	2
Murrel, *Channa punctatus*	3,100	5
Fathead minnow, *Pimephales promelas*	5,100–15,000	4, 6
Goldfish, *Carassius auratus*	9,000	3
Amphibians		
Bullfrog, *Rana catesbeiana*	>2,000,000[c]	7
Marine		
Invertebrates		
Mysid shrimp, *Mysidopsis bahia*	4.8	8

Penaeid shrimp, *Penaeus aztecus*	28[b]	8
Fish		
Sheepshead minnow, *Cyprinodon variegatus*	1,470	9
Striped knifejaw, *Opelgnathus fasciatus*		
Egg	3,200[d]	10
Prelarvae	5,500[d]	10
Postlarvae	25.1[d]	10
Juvenile	27.8[d]	10

[a]References: 1, Meier et al. 1976; 2, Johnson and Finley 1980; 3, Anon. 1972; 4, Allison and Hermanutz 1977; 5, Sastry and Malik 1982; 6, Jarvinen and Tanner 1982; 7, Hudson et al. 1984; 8, Nimmo et al. 1981; 9, Goodman et al. 1979; 10, Seikai 1982.

[b]48 h value.

[c]Single oral dose, in g/kg body weight.

[d]24 h value.

Table 3. Mortality of mallard embryos after immersion for 30 seconds in graded strength diazinon solutions (after Hoffman and Eastin 1981).

Age of eggs (days)	Solution vehicle (water or oil)	Diazinon concentration (mg/L)	Percent dead	Approximate field application rate
3	Water	11	none	0.5
3	Water	110	3	5
3	Water	542	50	25
8	Water	597	50	27
3	Oil	13	none	0.6
3	Oil	133	7	6
3	Oil	648	50	29
8	Oil	741	50	34

MAMMALS

Signs of diazinon poisoning in mammals included a reduction in blood and brain cholinesterase activity, diarrhea, sweating, vomiting, salivation, cyanosis, muscle twitches, convulsions, loss of reflexes, loss of sphincter control, and coma (Anon. 1972). Other compounds that produce their toxic effects by inhibiting AChE, such as organophosphorus pesticides and many carbamates, show similar effects (Murphy 1975). Two species of marmoset accidentally poisoned by diazinon exhibited, prior to death, high-pitched voices, trembling, frog-like jumping, a stiff gait, and pale oral mucous membranes; internally, bone marrow necrosis and hemorrhages in several organs were evident (Brack and Rothe 1982). Internal damage was also observed in swine and dogs that died following controlled administration of diazinon. Swine showed histopathology of liver and intestinal tract, and duodenal ulcers; dogs showed occasional rupture of the intestinal wall, and testicular atrophy (Earl et al. 1971).

Results of acute oral toxicity tests indicated that the rat was the most sensitive mammalian species tested, with an acute oral LD-50 of 224 mg diazinon/kg body weight (Table 4). It is clear that mammals are significantly more resistant to acute oral poisoning by diazinon than birds (Table 4). Diazinon was also toxic to mammals when administered dermally, through inhalation, and in the diet (Table 5). The lowest dermal LD-50 recorded was 600 mg diazinon/kg body weight for rabbits (*Lepus* sp.) using an emulsifiable (4E) formulation. The single datum for inhalation toxicity indicated that 27.2 mg of diazinon/l of air killed 50% of test rabbits after exposure for 4 hours (Table 5). Pregnant mice fed diets containing 9 mg of diazinon/kg during gestation all survived, but some pups died prior to weaning (Table 5). Results of chronic oral toxicity tests of diazinon indicated that death was probable if daily doses exceeded 5 mg/mg body weight for swine, or 10 mg/kg for dogs (Table 5).

TERRESTRIAL INVERTEBRATES

Accidental spraying of beehives in Connecticut with diazinon resulted in a complete kill of resident honeybees. Dead bees contained up to 3 mg/kg of diazinon (Anderson and Glowa 1984). Diazinon is an an effective insecticide. LD-50 values for diazinon and adult houseflies (*Musca domestica*), applied topically, were 0.4 ug/insect, or 4.6 mg/kg body weight (Negherbon 1959). LD-50 values for larvae of the large white butterfly, applied topically, were 8.8 mg/kg body weight for diazinon, and 11.0 mg/kg body weight for diazoxon (Wahla et al. 1976). Pretreatment of larvae with methylene dioxyphenyl compounds antagonized the action of diazinon by a factor of about 2, but synergized the action of diazoxon by an order of magnitude (Wahla et al. 1976).

Table 4. Acute oral toxicity of diazinon to birds and mammals. All values shown are in milligrams of diazinon/kg body weight fatal to 50% after a single oral dose.

Taxonomic group, organism and other variables	LD-50 (range), in mg/kg body weight	Reference[a]
Birds		
Turkey, *Meleagris gallopavo*	2.5	1
Red-winged blackbird, *Agelaius phoeniceus*	2.6	2
Goslings, *Anser* spp.	2.7	1
Turkey	3.5	3
Ducks, *Anas* spp.	3.5	3
Mallard, *Anas platyrhynchos*	3.5 (2.4–5.3)	4, 5
European quail, *Coturnix coturnix*	4.2	2
Ring-necked pheasant, *Phasianus colchicus*	4.3 (3.0–6.2)	4, 5
Northern bobwhite, *Colinus virginianus*	5.0[b]	6
Chicks, *Gallus gallus*	5.0[c]	1
Chicken, *Gallus gallus*	9.0	3
Turkey	10.0[c]	1
Ducklings	14.0	1
Northern bobwhite	14.7	6
Northern bobwhite	25.0[c]	6
European starling, *Sturnus vulgaris*	213	2
Mammals		

Rat, *Rattus rattus*	425	3, 5
Technical grade	350	7
AG 500 (granule)	327	7
4 E (emulsion)	542	7
4 S (spray)	735	7
50 W (wettable)		
Males	521	7
Females	224	7
Pig, *Sus scrofa*	400	3
Guinea pig, *Cavia cobaya*	450	3
Dog, *Canis familiaris*	>500	8
Sheep, *Ovis aries*	>1,000	3

[a]References: 1, Egyed et al. 1974; 2, Schaefer et al. 1983; 3, Machin et al. 1975; 4, Hudson et al. 1984; 5, Zinkl et al. 1978; 6, Hill et al. 1984; 7, Anon. 1972; 8, Earl et al. 1971.

[b]No mortality seen. [c]All animals tested died.

Table 5. Toxicity of diazinon to laboratory animals via dermal, inhalation, dietary, and chronic oral routes of administration.

Mode of administration, units, organism, formulations, and other variables	Dose	Effect	Reference[a]
Dermal, in mg/kg body weight			
Rabbit, *Lepus* sp.			
AG-500 (granule	900	LD-50	1
4 E (emulsion)	600	LD-50	1
4 S (spray)	735	LD-50	1
14 G (granule)	>15,400	LD-50	1
50 W (wettable)	>2,000	LD-50	1
Mice, *Mus musculus*			
Technical diazinon	2,750	LD-50	2
Inhalation, in mg/L air			
Rabbit[b]	27.2	LC-50	1
Dietary, in mg/kg diet, during gestation only			
Mice	0.18	No pup deaths at weaning	3
"	9	12% of pups dead prior to weaning	3
Chronic oral, in mg/kg body weight daily			
Dog, *Canis familiaris*	10	None dead in 8 months	4
"	20	All dead in 30 days	4
"	25	None dead in 15 days	4

"	50	None dead in 4 days	4
Swine, *Sus scrofa*	5	None dead in 8 months	4
"	10	75% dead in 30 days	4

[a]References: 1, Anon., 1972; 2, Skinner and Kilgore 1982; 3, Barnett et al. 1980; 4, Earl et al. 1971.

[b]Exposure for 4 h to 4% aqueous suspension.

SUBLETHAL EFFECTS

GENERAL

Among sensitive species of aquatic organisms, diazinon was associated with reduced growth and reproduction in marine and freshwater invertebrates and teleosts, spinal deformities in fish, reduced emergence in stream insects, measurable accumulations in tissues, increased numbers of stream macroinvertebrates carried downstream by currents (drift), possible mutagenicity in fish, and interference with algal-invertebrate interactions. In birds, diazinon is a known teratogen; it also is associated with reduced egg production, decreased food intake, and loss in body weight. Diazinon fed to pregnant mice resulted in offspring with brain pathology, delayed sexual maturity, and adverse behavioral modifications that became apparent late in life. For all groups tested, diazinon directly or indirectly inhibited cholinesterase activity.

AQUATIC ORGANISMS

Spinal deformities, mostly lordosis and scoliosis, were among the more insidious effects documented for diazinon. Malformations were observed in fathead minnows (*Pimephales promelas*) after 19 weeks in water containing 3.2 ug diazinon/l (Allison and Hermanutz 1977), in yearling brook trout (*Salvelinus fontinalis*) within a few weeks at 4.8 ug/l (Allison and Hermanutz 1977), and in various species of freshwater teleosts after exposure for 7 days to 50 ug diazinon/l (Kanazawa 1978).

Diazinon is a noncarcinogen and reportedly has no significant mutagenic activity in microbial systems, yeast, and mammals including humans (as quoted in Vigfusson et al. 1983). However, Vigfusson et al. (1983) have measured a significant increase in the frequency of sister chromatid exchange in central mud minnows (*Umbra limi*) that were exposed *in vivo* for 11 days to solutions containing 0.16 to 1.6 ug of diazinon/l. This finding requires verification.

Diazinon in water is bioconcentrated by brook trout at levels as low as 0.55 ug/l, but tissue residues for all aquatic organisms did not exceed 213 times that of ambient water, even after months of continuous exposure (Table 6). Diazinon and its metabolites are excreted rapidly posttreatment; the loss rate is approximately linear (Kanazawa 1978). The enzyme system responsible for diazinon metabolism in fish liver microsomes required NADPH and oxygen for the oxidative desulfuration of diazinon to diazoxon (Hogan and Knowles 1972). Fish with high fat content contained greater residues of diazinon in fatty tissues than fish with comparatively low lipid content (Seguchi and Asaka 1981), and this could account, in part, for inter-and intraspecies variations in uptake and depuration. Some organisms, such as the sheepshead minnow (*Cyprinodon variegatus*), have measurable diazinon residues during initial exposure to 6.5 ug/l, but no detectable residues after lengthy exposure (Goodman et al. 1979), suggesting that physiological adaptation resulting in rapid detoxication is possible.

Freshwater and marine alga were unaffected at water diazinon concentrations, that were fatal (i.e., 1,000 ug/l) to aquatic invertebrates (Stadnyk and Campbell 1971; Shacklock and Croft 1981). However, diazinon at 1.0 ug/l induced extensive clumping of a freshwater alga (*Chlorella pyrenoidosa*) onto the antennae of *Daphnia magna* within 24 hours (Stratton and Corke 1981). The affected daphnids were immobilized and settled to the bottom of the test containers. The causes of particulate matter adhesion are open to speculation, and additional research is merited.

Freshwater macroinvertebrates were comparatively sensitive to diazinon (Table 7). Results of large scale experimental stream studies (Arthur et al. 1983) showed that dose levels of 0.3 ug diazinon/l caused a 5 to 8-fold reduction in emergence of mayflies and caddisflies within 3 weeks; after 12 weeks, mayflies, damselflies, caddisflies, and amphipods were absent from benthic samples. Elevated (and catastrophic) drift of stream

invertebrates also was documented in diazinon-treated streams, especially for amphipods, leeches, and snails (Arthur et al. 1983).

Freshwater fish populations can be directly damaged by prolonged exposure to diazinon at concentrations up to several hundred times lower than those causing acute mortality (Sastry and Sharma 1980; Sastry and Malik 1982; Table 7). Impaired reproduction and AChE inhibition occurs concurrently in teleosts during long-term exposure to diazinon, but reproduction can be impaired for at least 3 weeks after fish are placed in uncontaminated water, even though AChE is normal and they contained no detectable diazinon residues (Goodman et al. 1979). Furthermore, diazinon exposure during spawning caused complete, but temporary, inhibition of reproduction at concentrations which did not produce this effect in fish exposed since hatch (Allison 1977). This could severely impact aquatic species with a short reproductive period (Allison 1977).

BIRDS

Diazinon produces visible Type I and II teratisms when injected into chicken embryos (Misawa et al. 1981, 1982; Henderson and Kitos 1982; Wyttenbach and Hwang 1984). Type I teratisms (related to tissue NAD depression) included abnormal beaks, abnormal feathering, and shortened limbs. Type II teratisms, which included short and wry neck, leg musculature hypoplasia, and rumplessness were associated with disruptions in the nicotinic cholinergic system. The severity of effects depended on embryo age and was dose-related. Chick embryos (age 48 hours) receiving 25 ug or more of diazinon/embryo had cervical notochord and neural tube malformations at 96 hours, and short neck at 19 days (Wyttenbach and Hwang 1984). Wry neck occurred at doses ranging from 6.2 to 100 ug/embryo, but was more frequent at higher doses. Type II teratisms were attributed to disruption of notochord sheath formation. Coinjection of 2-pyridinealdoxime methochloride (2-PAM) along with 200 ug of diazinon/embryo markedly reduced notochord and neural tube deformations (Wyttenbach and Hwang 1984). Similarly, the copresence of tryptophan--or its metabolites L-kynurenine, 3-hydroxyanthronilic acid, quinolinic acid--maintained NAD levels of diazinon-treated embryos close to, or above, normal, and significantly alleviated the symptoms of Type I teratisms (Henderson and Kitos 1982).

Table 6. Accumulation of diazinon by aquatic organisms.

Ecosystem, taxonomic group, organism, and other variables	Diazinon concentration in water (ug/l)	Exposure period (d = days, m = months)	Concentration factor	Reference[a]
Freshwater				
Invertebrates				
Crayfish, *Procambarus clarkii*				
Whole	10	7 d	5	1
Pond snail, *Cipangopaludina malleata*				
Whole	10	7 d	6	1
Red snail, *Indoplanorbis exustus*				
Whole	10	7 d	17	1
Shrimp, *Penaeopsis joyneri*				
Whole	20	14 d	3	2
Whole	20	14 d + 7 d posttreatment (pt)	<1	2
Fish				
4 spp., whole	10	7 d	18–152	1
3 spp., whole	20	14 d	26–120	2

3 spp., whole	20	14 d + 7 d pt	<1	2
Topmouth gudgeon,				
Pseudorasbora parva				
Whole	10	14 d	173	1
Whole	10	14 d + 1 d pt	72	1
Whole	10	14 d + 4 pt	8	1
Whole	10	14 d + 8 d pt	<1	1
Brook trout, *Salvelinus fontinalis*				
Adult				
Muscle	0.55	8 m	25	3
Blood	1.1	6 m	17	3
Muscle	1.1	8 m	25	3
Muscle	2.4	8 m	35	3
Blood	4.8	6 m	13	3
Muscle				
Mature male	4.8	8 m	24	3
Spawned female	4.8	8 m	19	3
Immature male				
Muscle	4.8	8 m	51	3
Adult female				
Egg	9.6	8 m	151	3
Muscle	9.6	8 m	34	3
Marine				
Fish				
Sheepshead minnow,				
Cyprinodon variegatus				
Whole	1.8	4 d	147	4
Whole	3.5	4 d	147	4
Whole	6.5	4 d	213	4
Whole	6.5	4 d + 8 d pt	<1	4
Whole	6.5	108 d	<1	4
Egg	<0.98	LC[b]	<1	4
Egg	1.8–6.5	LC[b]	10–13	4

[a]References: 1, Kanazawa 1978; 2, Seguchi and Asaka 1981; 3, Allison and Hermanutz 1977; 4, Goodman et al. 1979.

[b]LC = life cycle.

Table 7. Lowest tested diazinon concentrations that produce significant biological effects to aquatic organisms.

Ecosystem, and taxonomic group	Water concentration in µg/L	Effect	Reference[a]
Freshwater			
Invertebrates			
Insects	0.3	Lowered emergence	1
Amphipods	0.3	Elevated drift	1
Daphnids	1.0	Immobilization	2
Fish			
Brook trout, *Salvelinus fontinalis*	0.55	Reduced growth of progeny	3
Fathead minnow, *Pimephales promelas*	3.2	Reduced hatching success	3
Flagfish, *Jordanella floridae*	14.0	Reduced larval growth	4
Marine			
Invertebrates			
Mysid shrimp, *Mysidopsis bahia*	3.2	Reduced growth and reproduction	5
Fish			
Sheepshead minnow, *Cyprinodon variegatus*	0.47	Reduced fecundity	3

[a]References: 1, Arthur et al. 1983; 2, Stratton and Corke 1981; 3, Goodman et al. 1979; 4, Allison and Hermanutz 1977; 5, Nimmo et al. 1981.

Reduced egg production, depressed food consumption, and loss in body weight have been observed in ring-necked pheasants at daily diazinon intakes greater than 1.05 mg/bird; a dose-related delay in recovery of egg laying was noted after termination of diazinon treatment (Stromborg 1977, 1979). Threshold levels in ring-necked pheasants of 1.05 and 2.1 mg of diazinon daily corresponded to 1/16 and 1/8 of daily ration (70 g) treated at commercial application rates. Food consumption of ring-necked pheasants was reduced significantly when only food treated with diazinon was available; pheasants avoided diazinon-treated food if suitable alternatives existed (Stromborg 1977; Bennett and Prince 1981). Dietary levels above 50 mg/kg were associated with reduced food consumption, weight loss, and reduction in egg production in northern bobwhites (Stromborg 1981). If food reduction is important, then diets containing more than 17.5 mg diazinon/kg (based on, empirical calculations) were potentially harmful to bobwhites (Stromborg 1981). The mechanisms accounting for reduction in egg deposition are not clear, but are probably related primarily to decreased food intake. They may also be associated with diazinon-induced pituitary hypofunction at the level of the hypothalamus, resulting in reduced synthesis and secretion of gonadotrophic, thyrotrophic, and adrenocorticotrophic hormones (Sokkar et al. 1975).

MAMMALS

Diazinon exerts its toxic effects by binding to the neuronal enzyme acetylcholinesterase (AChE) for long periods after exposure. Diazinon, in turn, is converted to diazoxon, which has a higher affinity for AChE (and thus greater toxicity) than the parent compound. There is a latent period in white-footed mice in reduction of

cholinesterase activities, sometimes up to 6 hours, until diazinon is converted to diazoxon (Montz 1983). Effects of multiple doses of diazinon to mammals are not clear, e.g., rats exposed to a high dose of diazinon did not respond fully to a second dose until one month later (Kikuchi et al. 1981). It is difficult to ascertain when complete recovery of diazinon-poisoned animals has occurred. It is speculated, but not verified, that wildlife recovering from diazinon poisoning may face increased predation, aberrant behavior, learning disabilities, hypothermia, and reproductive impairments (Montz 1983). Data are now lacking on recovery aspects of diazinon-poisoned native mammal populations (Montz and Kirkpatrick 1985).

Diazinon is rapidly biotransformed and excreted in mammals. Estimated half-times of diazinon persistence were 6 to 12 hours in rats (Anon. 1972) and dogs (Iverson et al. 1975). Most of the diazinon metabolites were excreted in the urine as diethyl phosphoric acid and diethyl phosphorothioic acid in dogs (Iverson et al. 1975), and as hydroxy diazinon and dehydrodiazinon in sheep (Machin et al. 1974).

Determination of AChE activity in selected tissues following diazinon exposure provided an estimate of potential toxicity, but tissue sensitivity varied widely between and among taxa. In sheep, brain cholinesterase inhibition was pronounced after diazinon insult, and metabolism of diazinon in, or close to, the brain was the most likely, source of toxicologically effective diazoxon (Machin et al. 1974, 1975). In rat, diazinon effectively reduced blood cholinesterase levels, with inhibition significantly more evident in erythrocytes than in plasma (Tomokuni and Hasegawa 1985). All mammalian bloods hydrolyze diazoxon rapidly, whereas birds have virtually no hydrolytic activity in their blood, and, as a result, were more susceptible than mammals. The stability of diazoxon in the blood appears to be a primary factor in susceptibility to diazinon poisoning (Machin et al. 1975). In species lacking blood oxonases, the liver was probably the most important site of diazinon metabolism (Machin et al. 1975). Diazinon that accumulated in rat liver was biotransformed, usually within 24 hours, by microsomal mixed-function oxidases and glutathione S-transferases; however, diazinon residues in rat kidney were almost 500 times those in liver (and 11 times brain), and were measurable in kidney but not in liver (Tomokuni and Hasegawa 1985). It now seems that diazinon residues in kidney, and cholinesterase inhibition in erythrocytes are the most useful indicators of acute diazinon poisoning in mammals.

Sublethal effects of diazinon have been recorded in rodents, the most sensitive mammal group tested. Effects were measured at 0.5 mg diazinon/kg in diets of rats for 5 weeks, at 0.18 mg/kg body weight administered daily to pregnant mice, and at single doses of 1.8 mg/kg body weight for rat and 2.3 mg/kg body weight for white-footed mice (Table 8). Many variables modify diazinon-induced responses, including the organism's sex. For example, female rats and dogs were more sensitive to diazinon than males (Earl et al. 1971; Davies and Holub 1980a, 1980b; Kikuchi et al. 1981), but male swine were more sensitive than females (Earl et al. 1971).

Table 8. Sublethal effects of diazinon to selected mammals.

Organism and dose (D = mg/kg diet; BW = mg/kg body weight daily)	Exposure period	Effect	Reference[a]
Rat, *Rattus rattus*			
0.009 (BW)	5 weeks	No effect	1
0.1 (D)	5 weeks	No effect	1
0.5 (D)	5 weeks	Depressed plasma cholinesterase	1
1.8 (BW)	Single dose	Elevated serum glucuronidase	2
2 (D)	1 week	Depressed plasma cholinesterase (females only)	3
3.8 (BW)	Single dose	Altered blood chemistry	4
10 (D)	2 years	Cholinesterase inhibition	5
1,000 (D)	2 years	Reduced growth	5
1,000 (D)	3 generations	No malformations, no effect on reproduction	5
Mice, *Mus musculus* (pregnant)			
0.18 (BW)	2.8 weeks	Altered behavior and delayed sexual maturity of progeny	6
9 (BW)	Throughout gestation	Reduced growth and altered serum immunoglobulins of progeny; some deaths	7
Mice (juveniles)			
0.18 (BW)	14.4 weeks	Impaired endurance and coordination	6
9 (BW)	14.4 weeks	Brain pathology	6
White-footed mice, *Peromyscus leucopus*			
2.3 (BW)	Single dose	9% depression in brain AChE in 24 h	8
17.3 (BW)	Single dose	60% depression in brain AChE in 6 h	9
Dog, *Canis familiaris*			
4 (BW)	Single dose	39% reduction in serum cholinesterase in 10 min; 50% reduction in 3.5 h	10
4.3–5.3 (BW)	43 weeks	Cholinesterase inhibition	5

10 (BW)	8 months	Testicular atrophy, cholinesterase inhibition	11
75 (BW)	Single dose	Acute pancreatitis	12
Swine, *Sus scrofa*			
5 (BW)	8 months	Cholinesterase inhibition, duodenal ulcers, liver pathology	11
Sheep, *Ovis aries*			
Sprayed with 100 ppm diazinon solutions	4 min	Effective lice control for 3 weeks, partial protection for 8.6 weeks	13
450–650 (BW)	Single dose	Flesh unfit for human consumption for several weeks (high fat residues of 333–520 mg/kg)	14
Monkeys, several species			
0.5 (BW)	2.04 years	None	5
5 (BW)	2.04 years	Cholinesterase inhibition	5

[a]References: 1, Davies and Holub 1980a; 2, Kikuchi et al. 1981; 3, Davies and Holub 1980b; 4, Lox 1983; 5, Anon. 1972; 6, Spyker and Avery 1977; 7, Barnett et al. 1980; 8, Montz 1983; 9, Montz and Kirkpatrick 1985; 10, Iverson et al. 1975; 11, Earl et al. 1971; 12, Dressel et al. 1982; 13, Wilkinson 1980; 14, Machin et al. 1974.

Behavioral deficits observed in offspring of mice exposed to diazinon during gestation indicated that prenatal exposure may produce subtle dysfunctions not apparent until later in life (Spyker and Avery 1977). Pregnant mice given a daily dose of 0.18 or 9 mg diazinon per kg body weight throughout gestation gave birth to viable, overtly normal, offspring. But, pups born to mothers of the 9 mg/kg groups grew more slowly than controls and were significantly smaller at 1 month than controls (Spyker and Avery 1977). Offspring of mothers receiving 0.18 mg/kg body weight exhibited significant delays in the appearance of the contact placing reflex, and in descent of testes or vaginal opening. Mature offspring of mothers exposed to either dose level displayed impaired endurance and coordination on rod cling and inclined plane tests of neuromuscular function (Table 8). In addition, offspring of the 9 mg/kg dose had slower running speeds and less endurance in a swimming test than controls. At 101 days, forebrain neuropathology was evident in the 9 mg/kg dose, but not in the 0.18 mg/kg group. The mechanisms responsible for these effects are unknown (Spyker and Avery 1977).

Diazinon is nonmutagenic to mammals, as judged by its inability to induce sister chromatid exchanges (SCE) in Chinese hamster ovary cells (CHOC) at 80 mg/kg culture medium; most organophosphorus insecticides tested induced SCE in CHOC at this concentration (Nishio and Uyeki 1981; Chen et al. 1982). Diazoxon, an oxygen analog of diazinon, did produce SCE at 304 mg/kg, but was 3 to 10X less effective than oxygen analogs of other organophosphorus compounds screened (Nishio and Uyeki 1981).

TERRESTRIAL INVERTEBRATES

Tobacco hornworms (*Manduca sexta*) from a field sprayed with 840 mg diazinon/ha contained no detectable residues of diazoxon. Only one sample, collected about 4 hours after spraying, exceeded 1.0 mg diazinon/kg body weight. No diazinon residues in these insects were detectable after 18 days. It was concluded that the potential hazard to birds eating hornworms was minimal (Stromborg et al. 1982). In contrast, diazinon residues in molluscan slugs (*Agriolimax reticulatus*), collected from plats of spring wheat sprayed with 8,000 mg diazinon/ha, increased linearly to about 200 mg/kg at 6 weeks postapplication, then declined to background levels after 16 weeks (Edwards 1976). During this same period, soil residues decreased from about 4 mg/kg immediately after application, to about 1 mg/kg at 6 weeks, and were not detectable after 12 weeks. The high

residues observed in slugs may be due, in part, to physical adsorption of diazinon to slug mucus. Edwards (1976) concluded that slugs heavily contaminated by diazinon constituted a serious danger to birds and mammals feeding on them.

Depuration rates of diazinon differed significantly for two species of nematodes, *Panagrellus redivivus* and *Bursaphelenchus xylophilus* (Al-Attar and Knowles 1982). Both species showed maximum uptake of radiolabeled diazinon between 6 and 12 hours, and both metabolized diazinon to diazoxon and pyrimidinol. By 96 hours, 95% of the diazinon in *P. redivivus* had been metabolized, but only 26% was transformed in *B. xylophilus*, again demonstrating variability in diazinon metabolism between related species.

RECOMMENDATIONS

Certain aquatic organisms were impacted by diazinon water concentrations between 0.3 and 1.2 ug/l; effects included lowered emergence and elevated drift of stream insects (0.3 ug/l), reduced fecundity of marine minnows (0.47 ug/l), accumulations in freshwater teleosts (0.55 ug/l), and daphnid immobilization (1.0 ug/l) and death (1.2 ug/l). For protection of sensitive aquatic organisms, Arthur et al. (1983) recommended that water diazinon levels should not exceed 0.08 ug/l. This value represents a safety factor of about 4 over the lowest recorded adverse effect level of 0.3 ug/l. The safety factor may require adjustment, probably upwards, as additional data become available. Establishment of safe levels is complicated by the fact that diazinon can persist many months in neutral or basic waters, including seawater (Kanazawa 1978), but hydrolyzes rapidly in acidic waters (Allison and Hermanutz 1977). Data on chronic effects of fluctuating and intermittent exposures of fishes and invertebrates to diazinon are also needed, and these will aid in the establishment of safe concentrations for this organophosphorus pesticide (Allison and Hermanutz 1977).

Granular formulations were especially hazardous to seed-eating birds; ingestion of fewer than 5 granules of a Diazinon 14G formulation could be lethal (Hill and Camardese 1984). A reduction in diazinon content of existing granular formulations may become necessary in application areas frequented by high densities of seed-eating birds. Stone and Gradoni (1985) recommend that diazinon should not be used in areas where waterfowl feed, especially turfgrass. Suggested alternatives to diazinon for turfgrass use include Dursban (0,0- diethyl 0-(3,5,6-trichloro-2- pyridyl)-phosphorothioate), Dylox (dimethyl (2,2,2-trichloro-l-hydroxyethyl) phosphonate), Carbaryl (1-naphthyl N-methylcarbamate), and Lannate (S-methyl-N-((methylcarbamoyl) oxy)- thioacetimidate) (Stone 1980; Stone and Gradoni 1985). Diazinon should be used with caution in large-scale spray applications--such as grasshopper control--as judged by some deaths of horned larks (*Eremophila alpestris*), lark buntings (*Calamospiza melanocorys*), western meadowlarks (*Sturnella neglecta*). and chestnut-collared longspurs (*Calcarius ornatus*) when used for this purpose in Wyoming (McEwen et al. 1972). Diazinon applications to agricultural crops comprised a relatively small percentage of the reported mortality incidents, but it is likely that this category is underreported since such incidents were probably less conspicuous than those noted on lawns and golf courses (Stone and Gradoni 1985). Also, diazinon interactions with other agricultural chemicals, such as Captan (cis -N-((trichloromethyl)thio)-4-cyclohexene- 1,2-dicarboximide), may produce more-than-additive (but reversible) adverse effects on food consumption and egg production of ring-necked pheasants (Stromborg 1977). More research is needed on complex mixtures of agricultural pesticides that contain diazinon.

In female rats, the no-observable-effect level (NOEL) is 0.1 mg/kg of dietary diazinon; at 0.5 mg/kg there was a marked lowering of plasma cholinesterase activity in 5 weeks (Davies and Holub 1980a). But studies with male rats indicate that the NOEL is 2 mg/kg of dietary diazinon, or about 20X higher than female rats (Davies and Holub 1980b). Accordingly, future studies should consider sex as a variable in toxicity evaluation of diazinon. It is generally agreed that mammals are more resistant than birds to diazinon owing, in part, to their ability to rapidly metabolize diazoxon. However, data are missing on the effects of diazinon to native mammals under field conditions, and this should constitute a priority research area.

LITERATURE CITED

Al-Attar, H.J., and C.O. Knowles. 1982. Diazinon uptake, metabolism, and elimination by nematodes. Arch. Environ. Contam. Toxicol. 11:669-673.

Allison, D.T. 1977. Use of exposure units for estimating aquatic toxicity of organophosphate pesticides. U.S. Environ. Protection Agency Rep. 600/3-77-077. 25 pp.

Allison, D.T., and R.O. Hermanutz. 1977. Toxicity of diazinon to brook trout and fathead minnows. U.S. Environ. Protection Agency Rep. 600/3-77-060. 69 pp.

Anderson, J.W., and W. Glowa. 1984. Insecticidal poisoning of honey bees in Connecticut. Environ. Entomol. 13:70-74.

Anon. 1972. Diazinon insecticide. Tech. Bull., CIBA-GEIGY, Agric. Div., Ardsley, New York.

Arthur, J.W., J.A. Zischke, K.N. Allen, and R.O. Hermanutz. 1983. Effects of diazinon on macroinvertebrates and insect emergence in outdoor experimental channels. Aquat. Toxicol. 4:283-301.

Balcomb, R., R. Stevens, and C. Bowen II. 1984. Toxicity of 16 granular insecticides to wild-caught songbirds. Bull. Environ. Contam. Toxicol. 33:302-307.

Barik, S., and D.M. Munnecke. 1982. Enzymatic hydrolysis of concentrated diazinon in soil. Bull. Environ. Contam. Toxicol. 29:235-239.

Barnett, J.B., J.M. Spyker-Cranmer, D.L. Avery, and A.M. Haberman. 1980. Immunocompetence over the lifespan of mice exposed in utero to carbofuran or diazinon: I. Changes in serum immunoglobulin concentrations. J. Environ. Pathol. Toxicol. 4(5&6):53-63.

Bartsch, E. 1974. Diazinon. II. Residues in plants, soil, and water. Residue Rev. 51:37-68.

Bennett, R.S., Jr., and H.H. Prince. 1981. Influence of agricultural pesticides on food preference and consumption by ring-necked pheasants. J. Wildl. Manage. 45:74-82.

Berg, G.L. (ed.). 1984. Farm chemicals handbook. Meister Publ. Co., Willoughby, Ohio. 501 pp.

Brack, M., and H. Rothe. 1982. Organophosphate poisoning in marmosets. Lab. Anim. 16:186-188.

Branham, B.E., and D.J. Wehner. 1985. The fate of diazinon applied to thatched turf. Agron. J. 77:101-104.

Chen, H.H., S.R. Sirianni, and C.C. Huang. 1982. Sister chromatid exchanges in Chinese hamster cells treated with seventeen organophosphorus compounds in the presence of a metabolic activation system. Environ. Mutagen. 4:621-624.

Davies, D.B., and B.J. Holub. 1980a. Toxicological evaluation of dietary diazinon in the rat. Arch. Environ. Contam. Toxicol. 9:637-650.

Davies, D.B., and B. J. Holub. 1980b. Comparative subacute toxicity of dietary diazinon in the male and female rat. Toxicol. Appl. Pharmacol. 54:359-367.

Dressel, T.D., R.L- Goodale, B. Zweker, and J.W. Borner. 1982. The effect of atropine and duct decompression on the evaluation of diazinon - induced acute canine pancreatitis. Ann. Surg. 195:424-434.

Earl, F.L., B.E. Melveger, J.E. Reinwall, G.W. Bierbower, and J.M. Curtis. 1971. Diazinon toxicity - comparative studies in dogs and miniature swine. Toxicol. Appl. Pharmacol. 18:285-295.

Eberle, D.O. 1974. Diazinon. I. Analysis of technical grade product, formulations, and residues. Residue Rev. 51:1-35.

Edwards, C.A. 1976. The uptake of two organophosphorus insecticides by slugs. Bull. Environ. Contam. Toxicol. 16:406-410.

Egyed, M.N., M. Malkinson, A. Eilat, and A. Shlosberg. 1974. Basudin (diazinon) poisoning in goslings. Refuah Veterin. 31:22-26.

Egyed, M.N., A. Shlosberg, M. Malkinson, and A. Eilat. 1976. Some considerations in the treatment of diazinon poisoned goslings. Clin. Toxicol. 9:245-249.

Fleming, W.J., and S.P. Bradbury. 1981. Recovery of cholinesterase activity in mallard ducklings administered organophosphorus pesticides. J. Toxicol. Environ. Health 8:885-897.

Forrest, M., K.A. Lord, N. Walker, and H.C. Woodville. 1981. The influence of soil treatments on the bacterial degradation of diazinon and other organophosphorus insecticides. Environ. Pollut. 24A:93-104.

Fujii, Y., and S. Asaka. 1982. Metabolism of diazinon and diazoxon in fish liver preparations. Bull. Environ. Contam. Toxicol. 29:453-460.

Goodman, L.R., D.J. Hansen, D.L. Coppage, J.C. Moore, and E. Matthews. 1979. Diazinon: chronic toxicity to, and brain acetylcholinesterase inhibition in, the sheepshead minnow, *Cyprinodon variegatus.* Trans. Am. Fish. Soc. 108:479-488.

Grue, C.E., W.J. Fleming, D.G. Bushy, and E.F. Hill. 1983. Assessing hazards of organophosphate insecticides to wildlife. Trans. North Am. Wildl. Nat. Res. Conf. 48:200-220.

Henderson, M., and P.A. Kitos. 1982. Do organophosphate insecticides inhibit the conversion of tryptophan to NAD+ in ovo? Teratology 26:173-181.

Hill, E.F., and M.B. Camardese. 1984. Toxicity of anticholinesterase insecticides to birds: technical grade versus granular formulations. Ecotoxicol. Environ. Safety 8:551-563.

Hill, E.F., and M.B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to coturnix. U.S. Fish Wildl. Serv. Tech. Rep. 2. 147 pp.

Hill, E.F., M.B. Camardese, G. H. Heinz, J.W. Spann, and A.B. DeBevec. 1984. Acute toxicity of diazinon is similar for eight stocks of bobwhite. Environ. Toxicol. Chem. 3:61-66.

Hoffman, D.J., and W.C. Eastin, Jr. 1981. Effects of malathion, diazinon, and parathion on mallard embryo development and cholinesterase activity. Environ. Res. 26:472-485.

Hogan, J.W., and C.O. Knowles. 1972. Metabolism of diazinon by fish liver microsomes. Bull. Environ. Contam. Toxicol. 8:61-64.

Hudson, R.H., R.K. Tucker, and M.A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp.

Iverson, F., D.L. Grant and J. Lacroix. 1975. Diazinon metabolism in the dog. Bull. Environ. Contam. Toxicol. 13:611-618.

Jarvinen, A.W., and D.K. Tanner. 1982. Toxicity of selected controlled release and corresponding unformulated technical grade pesticides to the fathead minnow *Pimephales promelas*. Environ. Pollut. 27A:179-195.

Johnson, W.W., and M.T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Kanazawa, J. 1978. Bioconcentration ratio of diazinon by freshwater fish and snail. Bull. Environ. Contam. Toxicol- 20:613-617.

Kikuchi, H., Y. Suzuki, and Y. Hashimoto. 1981. Increase of B-glucuronidase activity in the serum of rats administered organophosphate and carbamate insecticides. J. Toxicol. Sci. 6:27-35.

Kuhr, R.J., and H. Tashiro. 1978. Distribution and persistence of chlorpyrifos and diazinon applied to turf. Bull. Environ. Contam. Toxicol. 20:652-656.

Lox, C.D. 1983. Effects of acute pesticide poisoning on blood clotting in the rat. Ecotoxicol. Environ. Safety 7:451-454.

Machin, A.F., P.H. Anderson, and C.N. Hebert. 1974. Residue levels and cholinesterase activities in sheep poisoned experimentally with diazinon. Pestic. Sci. 5:49-56.

Machin, A.F., H. Rogers, A.J. Cross, M.P. Quick, L.C. Howells, and N.F. Janes. 1975. Metabolic aspects of the toxicology of diazinon. I. Hepatic metabolism in the sheep, cow, pig, guinea-pig, rat, turkey, chicken and duck. Pestic. Sci. 6:461-473.

McEwen, L.C., C.E. Knittle, and M.L. Richmond. 1972. Wildlife effects from grasshopper insecticides sprayed on short-grass range. J. Range Manage. 25:188-195.

McLean, S., M. Sameshina, T. Katayama, J. Iwata, C.E. Olney, and K.L. Simpson. 1984. A rapid method to determine microsomal metabolism of organophosphate pesticides. Bull. Jpn. Soc. Sci. Fish. 50:1419-1423.

Meier, E.P., M.C. Warner, W.H. Dennis, W.F. Randall, and T.A. Miller. 1976. Chemical degradation of military standard formulations of organophosphate and carbamate pesticides. I. Chemical hydrolysis of diazinon. U.S. Army Med. Bioengin. Res. Dev. Lab., Fort Detrick, Frederick, MD. Tech. Rep. 7611. 32 pp.

Menzie, C.M. 1978. Metabolism of pesticides. Update II. U.S. Fish Wild. Serv. Spec. Sci. Rep. - Wildl. No. 212. 381 pp.

Misawa, M., J. Doull, P.A. Kitos, and E.M. Uyeki. 1981. Teratogenic effects of cholinergic insecticides in chick embryos. I. Diazinon treatment on acetylcholinesterase and choline acetyltransferase activities. Toxicol. Appl. Pharmacol. 57:20-29.

Misawa, M., J. Doull, and E.M. Uyeki. 1982. Teratogenic effects of cholinergic insecticides in chick embryo-T. III. Development of cartilage and bone. J. Toxicol. Environ. Health 10:551-563.

Montz, W.E., Jr. 1983. Effects of organophosphate insecticides on aspects of reproduction and survival in small mammals. Ph.D. Thesis. Virginia Polytechnic Institute and State University, Blacksburg. 176 pp.

Montz, W.E., Jr., and R.L. Kirkpatrick. 1985. Temporal patterns of brain cholinesterase activities of white-footed mice (*Peromyscus leucopus*) following dosing with diazinon or parathion. Arch. Environ. Contam. Toxicol. 14:19-24.

Murphy, S.D. 1975. Pesticides. Pages 408-453 *in* L.J. Casarett and J. Doull (eds.). Toxicology: the basic science of poisons. Macmillan Publ. Co., New York.

Negherbon, W.O. 1959. Handbook of toxicology. Volume III. Insecticides, a compendium. Natl. Acad. Sci., Natl. Res. Coun., Div. Biol. Agric., WADC Tech. Rep. 55-16:252-261.

Nimmo, D.R., T.L. Hamaker, E. Matthews, and J.C. Moore. 1981. An overview of the acute and chronic effects of first and second generation pesticides on an estuarine mysid. Pages 3-19 *in* J. Vernberg, A. Calabrese, F.P. Thurberg and W.B. Vernberg (eds.). Biological monitoring of marine pollutants. Academic Press, New York.

Nishio, A., and E.M. Uyeki. 1981. Induction of sister chromatid exchanges in Chinese hamster ovary cells by organophosphate insecticides and their oxygen analogs. J. Toxicol. Environ. Health 8:939-946.

Sastry, K.V., and P.V. Malik. 1982. Acute and chronic effects of diazinon on the activities of three dehydrogenases in the digestive system of a freshwater teleost fish *Channa punctatus*. Toxicol. Lett. 10:55-59.

Sastry, K. V., and K. Sharma. 1980. Diazinon effect on the activities of brain enzymes from *Ophiocephalus* (*Channa*) *punctatus*. Bull. Environ. Contam. Toxicol. 24:326-332.

Schafer, E.W., Jr., W.A. Bowles, Jr., and J. Hurlbert. 1983. The acute oral toxicity, repellency, and hazard potential of 998 chemicals to one or more species of wild and domestic birds. Arch. Environ. Contam. Toxicol. 12:355-382.

Schobert, E.E. 1974. Ingested insecticide poisoning in waterfowl. J. Zoo Anim. Med. 5:20.

Seguchi, K., and S. Asaka. 1981. Intake and excretion of diazinon in freshwater fishes. Bull. Environ. Contam. Toxicol. 27:244-249.

Seikai, T. 1982. Acute toxicity of organophosphorus insecticides on the developmental stages of eggs, larvae and juveniles of Japanese striped knifejaw *Oplegnathus fasciatus*. Bull. Jpn. Soc. Sci. Fish. 48:599-603.

Shacklock, P.F., and G.B. Croft. 1981. Effect of grazers on *Chondrus crispus* in culture. Aquaculture 22:331-342.

Skinner, C.S., and W. W. Kilgore. 1982. Acute dermal toxicities of various organophosphate insecticides in mice. J. Toxicol. Environ. Health 9:491-497.

Sokkar, S.M., M. A. Mohammed, and F.A. Soliman. 1975. Toxic effects of diazinon on the gonads of fowl. Zbl. Vet. Med. 22A:557-563.

Soliman, S.A., G.W. Sovocool, A. Curley, N.S. Ahmed, S. El-Fiki, and A-K. El-Sebae. 1982. Two acute human poisoning cases resulting from exposure to diazinon transformation products in Egypt. Arch. Environ. Health 37:207-212.

Spyker, J.M., and D.L. Avery. 1977. Neurobehavioral effects of prenatal exposure to the organophosphate diazinon in mice. J. Toxicol. Environ. Health 3:989-1002.

Stadnyk, L., and R..S. Campbell. 1971. Pesticide effect on growth and assimilation in a freshwater alga. Bull. Environ. Contam. Toxicol. 6:1-8.

Stone, W.B. 1980. Bird deaths caused by pesticides used on turfgrass. N.Y. State Turfgrass Conf. Proc. 4:58-62.

Stone, W.B., and P.B. Gradoni. 1985. Wildlife mortality related to use of the pesticide diazinon. Northeast. Environ. Sci. 4:30-38.

Stone, W.B., and H. Knoch. 1982. American brant killed on golf courses by diazinon. N.Y. Fish Game J. 29:95-96.

Stratton, G.W., and C.T. Corke. 1981. Interaction of permethrin with *Daphnia magna* in the presence and absence of particulate material. Environ. Pollut. 24A:135-144.

Stromborg, K.L. 1977. Seed treatment pesticide effects on pheasant reproduction at sublethal doses. J. Wildl. Manage. 41:632-642.

Stromborg, K.L. 1979. Pheasant food habits in spring and consumption of seed treatment pesticides. J. Wildl. Manage. 43:214-219.

Stromborg, K.L. 1981. Reproductive tests of diazinon on bobwhite quail. Pages 19-30 *in* P.W. Lamb and E.E. Kenaga (eds.). Avian and mammalian wildlife toxicology: second conference. ASTM STP 757, American Society for Testing and Materials. Philadelphia.

Stromborg, K.L., W.N. Beyer, and E. Kolbe. 1982. Diazinon residues in insects from sprayed tobacco. Pages 93-97 *in* Chemistry in ecology, Vol. 1. Gordon and Breach Science Publishers, Great Britain.

Tomokuni, K., and T. Hasegawa. 1985. Diazinon concentrations and blood cholinesterase activities in rats exposed to diazinon. Toxicol. Lett. 25:7-10.

Vigfusson, N.V., E.R. Vyse, C.A. Pernsteiner, and R.J. Dawson. 1983. In vivo induction of sister-chromatid exchange in *Umbra limi* by the insecticides endrin, chlordane, diazinon and guthion. Mutat. Res. 118:61-68.

Wahla, M.A., G. Gibbs, and J.B. Ford. 1976. Diazinon poisoning in large white butterfly larvae and the influence of sesamex and piperonyl butoxide. Pestic. Sci. 7:367-371.

Wilkinson, F.C. 1980. The uptake of dipping fluid and persistence of diazinon on shower-dipped sheep. Aust. Veterin. J. 56:561-562.

Wyttenbach, C.R., and J.D. Hwang. 1984. Relationship between insecticide-induced short and wry neck and cervical defects visible histologically shortly after treatment of chick embryos. J. Exp. Zool. 229:437-446.

Zinkl, J.G., J. Rathert, and R.R. Hudson. 1978. Diazinon poisoning in wild Canada geese. J. Wildl. Manage. 42:406-408.

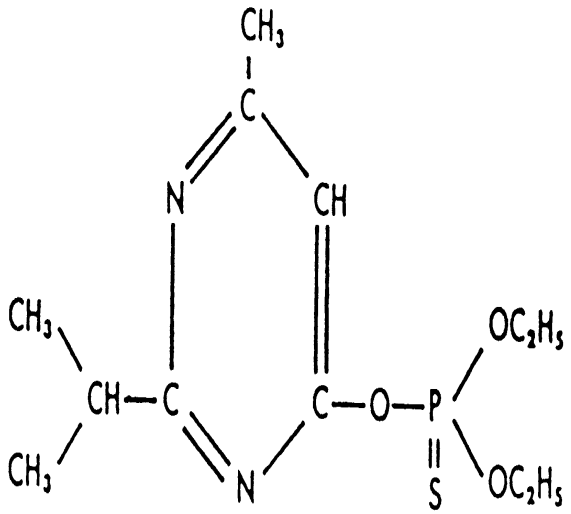


Figure 1. Structural formula of diazinon.

Biological Report 85(1.10)
April 1987

Contaminant Hazard Reviews
Report No. 10

MERCURY HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

U. S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

Available literature on the ecological and toxicological aspects of mercury (Hg) in the environment, with special reference to fish and wildlife resources, is reviewed and summarized. Subdivisions include sources, chemical properties, background concentrations, acute and chronic toxicity, sublethal effects, and proposed criteria to protect sensitive resources.

Mercury has been used by man for at least 2,300 years, most recently as a fungicide in agriculture, in the manufacture of chlorine and sodium hydroxide, as a slime control agent in the pulp and paper industry, in the production of plastics and electrical apparatus, and in mining and smelting operations. Mercury burdens in some environmental compartments are estimated to have increased up to 5X precultural levels, primarily as a result of man's activities. The construction of artificial reservoirs, for example, which releases Hg from flooded soils, has contributed to the observed elevation of Hg concentrations in fish tissues from these localities. Elevated levels of Hg in living organisms in Hg-contaminated areas may persist for as long as 100 years after the source of pollution has been discontinued. One major consequence of increased mercury use, coupled with careless waste disposal practices, has been a sharp increase in the number of epidemics of fatal mercury poisonings in humans, wildlife, and aquatic organisms.

Most authorities agree on six points: (1) mercury and its compounds have no known biological function, and the presence of the metal in the cells of living organisms is undesirable and potentially hazardous; (2) forms of mercury with relatively low toxicity can be transformed into forms of very high toxicity, such as methylmercury, through biological and other processes; (3) mercury can be bioconcentrated in organisms and biomagnified through food chains; (4) mercury is a mutagen, teratogen, and carcinogen, and causes embryocidal, cytochemical, and histopathological effects; (5) some species of fish and wildlife contain high concentrations of Hg that are not attributable to human activities; (6) anthropogenic use of Hg should be curtailed, as the difference between tolerable natural background levels of Hg and harmful effects in the environment is exceptionally small.

Concentrations of total Hg lethal to sensitive, representative, nonhuman species range from 0.1 to 2.0 ug/l (ppb) of medium for aquatic organisms; from 2,200 to 31,000 ug/kg body weight (acute oral) and 4,000 to 40,000 ug/kg (dietary) for birds; and from 100 to 500 ug/kg body weight (daily dose) and 1,000 to 5,000 ug/kg diet for mammals. Organomercury compounds, especially methylmercury, are always more toxic than inorganic Hg compounds. Numerous biological and abiotic factors modify the toxicity of Hg compounds--sometimes by an order of magnitude or more--but the mechanisms of action are not clear. Significant adverse sublethal effects were observed among selected aquatic species at water concentrations of 0.03 to 0.1 ug Hg/l. For some birds, adverse effects--predominantly on reproduction--have been associated with total Hg concentrations (in ug/kg fresh weight) of 5,000 in feather, 900 in egg, and 50 to 100 in diet; and with daily intakes of 640 ug/kg body weight. Sensitive nonhuman mammals showed significant adverse effects of Hg when daily intakes were 250 ug/kg body weight, when dietary levels were 1,100 ug/kg, or when tissue concentrations exceeded 1,100 ug/kg.

The most recent mercury criteria proposed by the U.S. Environmental Protection Agency for protection of freshwater aquatic life are 0.012 ug/l medium (4-day average), not to exceed 2.4 ug/l on an hourly average; however, these criteria offer only limited protection to freshwater ecosystems. The saltwater criteria of 0.025 ug Hg/l medium (4-day average), not to exceed 2.1 ug/l hourly, are unsatisfactory for the protection of marine life. For the protection of sensitive species of mammals and birds that regularly consume fish and other aquatic organisms, total Hg concentrations in these prey items should probably not exceed 100 ug/kg fresh weight for birds, and 1,100 ug/kg for small mammals. The significance of elevated Hg levels in tissues of fish and wildlife is not fully understood; some species of marine pinnipeds, for example, normally contain high concentrations of Hg in various tissues without apparent adverse effects. Usually, however, concentrations in excess of 1,100 ug/kg fresh weight of tissue (liver, kidney, blood, brain, hair) should be considered as presumptive evidence of an environmental mercury problem.

Four courses of action now seem warranted. First, toxic mercurials in agriculture and industry should be replaced by less toxic substitutes. Second, controls should be applied at the point of origin to prevent the discharge of potentially harmful Hg wastes. Third, continued periodic monitoring of Hg in fish and wildlife is needed for identification of potential problem areas., and for evaluation of ongoing mercury curtailment programs. And fourth, additional research is merited on mechanisms of mercury accumulation and detoxication in comparatively pristine ecosystems.

This report should be cited as follows:

Eisler, R. 1987. Mercury hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85(1.10).

TABLES

FIGURES

ACKNOWLEDGMENTS

I thank J. Higgis and I. Moore for secretarial help; L.J. Garrett and J.E. Haber for literature retrieval; W.N. Beyer, T.A. Haines, M.C. Perry, J.G. Wiener, and M.R. Winfrey for reviewing the manuscript; and P.H. Eschmeyer and J.R. Zuboy for editorial services.

INTRODUCTION

The element mercury (Hg) and its compounds have no known normal metabolic function. Their presence in the cells of living organisms represents contamination from natural and anthropogenic sources; all such contamination must be regarded as undesirable and potentially hazardous (NAS 1978).

The most important ore of mercury, cinnabar (mercuric sulfide), has been mined continuously since 415 BC (Clarkson and Marsh 1982). In the period before the industrial revolution, Hg was used extensively in gold extraction and in the manufacture of felt hats and mirrors; in the 1800's, it was used in the chloralkali industry, in the manufacture of electrical instruments, and as a medical antiseptic; and since 1900, it has been used in pharmaceuticals, in agricultural fungicides, in the pulp and paper industry as a slimicide, and in the production of plastics (Clarkson and Marsh 1982). Current world use of mercury is estimated at 10,000 to 15,000 metric tons annually (Boudou and Ribeyre 1983), of which the United States accounts for about 18% (Clarkson and Marsh 1982).

The first cases of fatal mercury poisoning were reported for two men in a European chemical laboratory in 1865 (Das et al. 1982). The first documented human poisoning from an agricultural exposure to methylmercury occurred in 1940 (Das et al. 1982). As summarized by Elhassani (1983), exposure of humans to mercury compounds may result from dermal application (e.g., 1,600 infants in Argentina showed symptoms of Hg poisoning after a laundry treated their diapers with a Hg disinfectant), from diet (i.e., ingestion of Hg-contaminated fish, pork, seafoods, or grains), and from contact by respiratory routes (e.g., occupational exposure of mercury fungicide applicators in Nicaragua). Sporadic incidences of human poisonings have occurred in the United States, the Soviet Union, and Canada; and major epidemics have been reported in Japan, Pakistan, Guatemala, Ghana, Yugoslavia, and Iraq (Clarkson and Marsh 1982; Das et al. 1982; Elhassani 1983; Greener and Kochen 1983). In 1972, for example, there were 6,530 hospital admissions within 18 months (459 hospital deaths) among Iraqi farmers who ate bread made from seed wheat treated with a methylmercury fungicide. A water soluble red dye was washed off the wheat, with the assumption that the mercury would be equally soluble. Before the wheat was consumed by humans, it was fed (without apparent effect) to chickens and other :livestock for only a few days; it was not realized that a lengthy latency period was involved (Das et al. 1982; Elhassani 1983). There is no effective antidote to counteract the effects of methylmercury on the central nervous system (Elhassani 1983).

Poisoning of game birds and other wildlife in Sweden, apparently by seeds treated with organomercurials, was noticed in 1960 (Das et al 1982). Massive kills of the grey heron (*Ardea cinerea*) in the Netherlands during 1976, were attributed to a combination of low temperatures, undernourishment, and high body burdens of mercury (Van der Molen et al. 1982). Mercury contamination has resulted in the closure of pheasant and partridge hunting areas in Alberta, Canada (Mullins et al. 1977). In 1967, the Swedish medical board banned the sale of fish that contained high concentrations of organomercury salts, originating from about 40 lakes and rivers (Das et al. 1982). In 1970, after the discovery of high levels of mercury in fish from Lake St. Clair, Canada, restrictions on fishing and the sale of fish were imposed in many areas of the United States and Canada (Das et al. 1982). Since 1970, a total of 26 of the 48 States in the conterminous United States have reported mercury pollution in their waters as a direct result of human activities. These States have banned sport or commercial fishing in Hg-contaminated waters, or have issued health warnings about the consequences of eating Hg-contaminated fish or seafood from selected water courses, or have placed restrictions on fish consumption from certain streams, lakes, or rivers polluted with mercury (NAS 1978). In general, the number of Hg-contaminated fish and wildlife habitats has progressively increased--almost all as a direct result of anthropogenic activities (Boudou and Ribeyre 1983).

Most authorities on Hg ecotoxicology agree on six points. First, Hg and its compounds have no known biological function, and its presence in living organisms is undesirable and potentially hazardous. Second, forms of mercury with relatively low toxicity can be transformed into forms with very high toxicity through biological and other processes. Third, methylmercury can be bioconcentrated in organisms and biomagnified through food chains, returning mercury directly to man and other upper trophic level consumers in concentrated form. Fourth, mercury is a mutagen, teratogen, and carcinogen, and causes embryocidal, cytochemical, and histopathological effects. Fifth, high body burdens of mercury normally encountered in some species of fish and wildlife from remote locations emphasize the complexity of natural mercury cycles and human impacts on these cycles. And finally, the anthropogenic use of mercury should be curtailed, because the difference between

tolerable natural background levels of mercury and harmful effects in the environment is exceptionally small. These, and other aspects of mercury and its compounds in the environment as a result of anthropogenic or natural processes, have been the subject of many reviews, including those by Montague and Montague (1971), D'Itri (1972), Friberg and Vostal (1972), Jernelov et al. (1972, 1975), Keckes and Miettinen (1972), Buhler (1973), Holden (1973), D'Itri and D'Itri (1977), Eisler (1978, 1981), NAS (1978), Birge et al. (1979),.Magos and Webb (1979), Nriagu (1979), EPA (1980, 1985), Jenkins (1980), Clarkson and Marsh (1982), Das et al. (1982), Boudou and Ribeyre (1983), Elhassani (1983), Clarkson et al. (1984), Robinson and Touvinen (1984), and Wren (1986).

This report was prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service. it is part of a continuing series of synoptic reviews on chemical contaminants and natural resources.

SOURCES OF ENVIRONMENTAL MERCURY

As a direct result of human activities, mercury levels in river sediments have increased fourfold since precultural times, and twofold to fivefold in sediment cores from lakes and estuaries (Das et al. 1982). During the past 100 years, it has been estimated that more than 500,000 metric tons of Hg entered the atmosphere, hydrosphere, and surface soils, with eventual deposition in subsurface soils and sediments (Das et al. 1982). Several activities that contribute significantly to the global input of Hg include the combustion of fossil fuels; mining and reprocessing of gold, copper, and lead; operation of chloralkali plants; and disposal of batteries and fluorescent lamps (NAS 1978; Das et al. 1982). The atmosphere plays an important role in the mobilization of Hg; 25% to 30% of the total atmospheric Hg burden is of anthropogenic origin (NAS 1978).

In the United States, mercury consumption rose from 1,305 metric tons in 1959 to 2,359 tons in 1969 (Table 1). The major use of mercury has been as a cathode in the electrolytic preparation of chlorine and caustic (Nriagu 1979). In 1968 this use accounted for about 33% of the total U.S. demand for Hg (EPA 1980). Of recent U.S. mercury consumption, electrical apparatus have accounted for about 27%; industrial and control instruments, such as switches, thermometers, and barometers, and general laboratory appliances, 14%; antifouling and mildew-proofing paints, 12%; Hg formulations to control fungal diseases of seeds, bulbs, and vegetables, 5%; and dental amalgams, pulp and paper manufacturers, pharmaceuticals, metallurgy and mining, and catalysts, 9% (EPA 1980). Mercury, however, is no longer registered for use in antifouling paints, or for the control of fungal diseases of bulbs (EPA 1980).

Mercury from natural sources enters the biosphere directly as a gas, in lava (from terrestrial and oceanic volcanic activity), in solution, or in particulate form; cinnabar (HgS), for example, is a common mineral in hot spring deposits and a major natural source of mercury (Das et al. 1982). The global cycle of Hg involves degassing of the element from the Earth's crust and evaporation from natural bodies of water, atmospheric transport (mainly in the form of Hg vapor), and deposition of Hg back onto land and water. Oceanic effluxes of Hg are tied to equatorial upwelling and phytoplankton activity and may significantly affect the global cycling of this metal. If volatilization of Hg is proportional to primary production in the world's oceans, oceanic phytoplankton activity represents about 36% of the yearly Hg flow to the atmosphere, or about 2,400 tons per year (Kim and Fitzgerald 1986). Mercury finds its way into sediments, particularly oceanic sediments, where the retention time can be lengthy (Table 2), and where it may continue to contaminate aquatic organisms (Lindsay and Dimmick 1983). Estimates of the quantities of Hg entering the atmosphere from degassing of the surface of the planet vary widely, but a commonly quoted figure is 30,000 tons annually (Clarkson et al. 1984). In aquatic ecosystems, removal of the source of anthropogenic Hg results in a slow decrease in the Hg content of sediments and biota (NAS 1978). The rate of loss depends, in part, on the initial degree of contamination, the chemical form of Hg, physical and chemical conditions of the system, and the hydraulic turnover time (NAS 1978).

Table 1. Industrial and other uses of mercury in the United States in 1959 and in 1969. All values are in metric tons (modified from Montague and Montague 1971).

	1959		1969	
Use	Tons	Percent	Tons	Percent
Chloralkali process	201	15.5	716	30.4
Electrical apparatus	308	23.6	644	27.3
Antifouling and mildew paints	121	9.3	336	14.2
Control devices	213	16.3	241	10.2
Dental preparations	63	4.8	105	4.5
Catalysts	33	2.5	102	4.3
Agriculture	110	8.4	93	3.9
Laboratory	38	2.9	71	3.0
Pharmaceuticals	59	4.5	25	1.1
Pulp and paper mill	150	11.5	19	0.8
Metal amalgamation	9	0.7	7	0.3
Total	1,305		2,359	

Table 2. Amount of mercury in some global reservoirs (NAS 1978), and residence time (Clarkson et al. 1984).

Reservoir	Hg content (metric tons)	Residence time
Atmosphere	850	6 to 90 days
Soils	21,000,000	1,000 years
Freshwater	200	-
Freshwater biota (living)	4	-
Ocean water	4,150,000,000	2,000 years
Oceanic biota (living)	3	-
Ocean sediments	330,000,000,000	>1 million years

CHEMICAL PROPERTIES

Mercury, a silver-white metal that is liquid at room temperature and is highly volatile, can exist in three oxidation states: elemental mercury (Hg^0), mercurous ion (Hg_2^{2+}), and mercuric ion (Hg^{2+}). It can be part of both inorganic and organic compounds (EPA 1980; Clarkson et al. 1984; Table 3). All mercury compounds interfere with thiol metabolism, causing inhibition or inactivation of proteins containing thiol ligands and ultimately leading to mitotic disturbances (Das et al. 1982; Elhassani 1983). The mercuric species is the most toxic inorganic chemical form, but all three forms of inorganic Hg may have a common molecular mechanism of damage in which Hg^{2+} is the toxic species (Clarkson and Marsh 1982; Figure 1).

Chemical speciation is probably the most important variable influencing ecotoxicology of Hg, but Hg speciation is difficult, especially in natural environments (Boudou and Ribeyre 1983). Mercury compounds in an aqueous solution are chemically complex. Depending on pH, alkalinity, redox, and other variables, a wide

variety of chemical species are liable to be formed, having different electrical charges and solubilities. For example, $HgCl_2$ in solution can speciate into $Hg(OH)_2$, Hg^{2+}, $HgCl^+$, $Hg(OH)^-$, $HgCl_3^-$, and $HgCl_4^{2-}$; anionic forms predominate in saline environments (Boudou and Ribeyre 1983). In the aquatic environment, under naturally occurring conditions of pH and temperature, Hg may also become methylated by biological or chemical processes, or both (Beijer and Jernelov 1979; EPA 1980; Ramamoorthy and Blumhagen 1984; Figure 1) -- although abiological methylation is limited (Callister and Winfrey 1986). Methylmercury is the most hazardous mercury species due to its high stability, its lipid solubility, and its possession of ionic properties that lead to a high ability to penetrate membranes in living organisms (Beijer and Jernelov 1979).

All mercury discharged into rivers, bays, or estuaries as elemental (metallic) mercury, inorganic divalent mercury, phenylmercury, or alkoxyalkyl mercury can be converted into methylmercury compounds by natural processes (Jernelov 1969). The mercury methylation in ecosystems depends on mercury loadings, microbial activity, nutrient content, pH and redox condition, suspended sediment load, sedimentation rates, and other variables (NAS 1978; Compeau and Bartha 1984; Berman and Bartha 1986; Callister and Winfrey 1986; Jackson 1986). The finding that certain microorganisms are able to convert inorganic and organic forms of Hg into the highly toxic methylmercury or dimethylmercury has made it clear that any form of Hg is highly hazardous to the environment (EPA 1980, 1985). The synthesis of methylmercury by bacteria from inorganic Hg compounds present in the water or in the sediments is the major source of this molecule in aquatic environments (Boudou and Ribeyre 1983). This process can occur under both aerobic and anaerobic conditions (Beijer and Jernelov 1979; Clarkson et al. 1984), but seems to favor anaerobic conditions (Olson and Cooper 1976; Callister and Winfrey 1986). Transformation of inorganic mercury to an organic form by bacteria alters its biochemical reactivity and hence its fate (Windom and Kendall 1979; Figure 1). Methylmercury is decomposed by bacteria in two phases. First, hydrolytic enzymes cleave the C-Hg bond, releasing the methyl group. Second, a reductase enzyme converts the ionic Hg to the elemental form, which is then free to diffuse from the aquatic environment into the vapor phase. These demethylating microbes appear to be widespread in the environment; they have been isolated from water, sediments, and soils and from the gastrointestinal tract of mammals--including humans (Clarkson et. al. 1984).

Table 3. Some properties of mercury and its compounds.[a]

Property	Elemental mercury	Mercurous chloride	Mercuric chloride	Methylmercury chloride
Empirical formula	Hg	Hg_2Cl_2	$HgCl_2$	CH_3HgCl
Molecular weight	200.59	472.09	271.52	251.09[c]
Chlorine, %	0	15.02	26.12	14.12[c]
Mercury, %	100	84.98	73.88	79.89[c]
Melting point, ° C	–38.87	sublimes at 400–500	277	170[c]
Density	13.534	7.15	5.4	4.063[c]
Solubility, mg/L (ppm)				
In water	0.056	2.0	74,070	~1,016[d]
In benzene	2.387[b]	insol.	5,000	~6,535[e]

[a]All data from Merck Index (1976), except where indicated.

[b]Spencer and Voigt (1968).

[c]Weast and Astle (1982).

[d]Eisler (unpubl.), 72 h equilibrium value.

[e]Eisler (unpubl.), 24 h equilibrium value.

Methylmercury is produced by methylation of inorganic mercury present in both freshwater and saltwater sediments, and accumulates in aquatic food chains in which the top-level predators usually contain the highest concentrations (Clarkson and Marsh 1982). Organomercury compounds other than methylmercury decompose rapidly in the environment, and behave much like inorganic Hg compounds (Beijer and Jernelov 1979). In organisms near the top of the food chain, such as carnivorous fishes, almost all Hg accumulated is in the methylated form, primarily as a result of the consumption of prey containing methylmercury; methylation also occurs at the organism level by way of mucous, intestinal bacteria, and enzymatic processes, but these pathways are not as important as diet (Huckabee et al. 1979; Boudou and Ribeyre 1983).

The biological cycle of Hg is delicately balanced, and small changes in input rates and the chemical form of Hg may result in increased methylation rates in sensitive systems (NAS 1978). For example, the acidification of natural bodies of freshwater is statistically associated with elevated concentrations of methylmercury in the edible tissues of predatory fishes (Clarkson et al. 1984). In chemically sensitive waterways, such as poorly buffered lakes, the combined effects of acid precipitation and increased emissions of Hg to the atmosphere (with subsequent deposition) pose a serious threat to the biota if optimal biomethylation conditions are met (NAS 1978).

Mercury binds strongly with sulfhydryl groups, and has many potential target sites during embryogenesis; phenylmercury and methylmercury compounds are among the strongest known inhibitors of cell division (Birge et al. 1979). Organomercury compounds, especially methylmercury, cross placental barriers and can enter mammals by way of the respiratory tract, gastrointestinal tract, skin, or mucous membranes (Elhassani 1983). When compared with inorganic mercury compounds, organomercurials are more completely absorbed, are more soluble in organic solvents and lipids, pass more readily through biological membranes, and are slower to be excreted (Clarkson and Marsh 1982; Elhassani 1983; Greener and Kochen 1983). Biological membranes, including those at the blood-brain interface and placenta, tend to discriminate against ionic and inorganic Hg, but allow relatively easy passage of methylmercury and dissolved Hg vapor (Greener and Kochen 1983). As judged by membrane model studies, it appears that electrically neutral mercurials are responsible for most of the diffusion transport of Hg, although this movement is modified significantly by pH and Hg speciation. It seems, however, that the liposolubility of methylmercury is not the entire reason for its toxicity and does not play a major role in its transport. This hypothesis needs to be examined further in studies with living membranes (Boudou et al. 1983).

Mercury-antagonistic drugs include 2,3-dimercaptopropanol, polythiol resins, selenium salts, vitamin E, and sulfhydral agents (in J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.Magos and Webb 1979; Elhassani 1983). Thiols (R-SH), which compete with Hg for protein binding sites, are the most important antagonists of inorganic mercury salts, and have been used extensively in attempts to counteract Hg poisoning in humans (Das et al. 1982). The protective action of selenium (Se) against adverse or lethal effects induced by inorganic or organic mercury salts has been reported for algae, aquatic invertebrates, fish, and mammals (Magos and Webb 1979; Heisinger 1979; Chang et al. 1981; Lawrence and Holoka 1981; Das et al. 1982; Gotsis 1982; Eisler 1985; Satoh et al. 1985). Selenite salts can release methylmercury from its linkage to proteins, and there is general agreement that a true antagonism exists between Se and Hg, although the exact mechanism is not fully established (Das et al. 1982). In marine mammals and humans, for example, Se and Hg concentrations are closely related, almost linearly in a 1:1 molar ratio, but this relation blurs in teleosts (in which Se is abundant) and fails in birds (Eisler 1985).

MERCURY IN MINAMATA, JAPAN

One of the earliest and most extensively documented cases of mercury poisoning occurred in the 1950's at Minamata Bay, in southwestern Kyushu, Japan--especially among fishermen and their families (Fujiki 1963, 1980; Irukayama 1967; Matida and Kumada 1969; Kojima and Fujita 1973; NAS 1978; Elhassani 1983; Nishimura and Kumagai 1983; Doi et al. 1984). The source of the mercury was in waste discharged from an acetaldehyde plant that used inorganic Hg as a catalyst; between 1932 and 1968, Minamata Bay received at least 260 tons of mercury, and perhaps as much as 600 tons. A severe neurological disorder was recognized in late 1953 and had reached epidemic proportions by 1956; 111 cases of poisoning were reported by the end of 1960 and 41 deaths by August 1965. By 1982, there were 1,800 verified human victims of mercury poisoning in a total regional population of 200,000; however, the total number of victims remains unconfirmed. Symptoms evidenced by human victims included sensory impairment, constriction of visual fields, hearing loss, ataxia, and

speech disturbances. Congenital cases were accompanied by disturbance of physical and mental development; about 6% of babies born in Minamata had cerebral palsy (vs. 0.5% elsewhere).

"Minamata disease" resulted from the discharge of methylmercury from chemical factories into Minamata Bay. Once diluted and diffused in the water, it was concentrated to a high level in fish and filter-feeding shellfish by several routes, including bioconcentration and food chain biomagnification. When these fish and shellfish were consumed by humans, methylmercury gradually accumulated to exceed a threshold value, causing intoxication. Spontaneously poisoned cats, dogs, rats, waterfowl, and pigs behaved erratically and died; flying crows and grebes suddenly fell into the sea and drowned; and large numbers of dead fish were seen floating on the sea surface (Doi et al. 1984). In laboratory studies, cats and rats fed shellfish from the Bay developed the same signs as those seen in animals affected spontaneously. Abnormal Hg content--i.e., more than 30 mg/kg fresh weight--was measured in fish, shellfish, and muds from the Bay, and in organs of necropsied humans and cats that had succumbed to the disease. Mercury contamination of fish and sediments was still evident in 1981, although discharges from the acetaldehyde plant ceased in 1971 (Doi et al. 1984).

There is a strong relation between the food of birds from Minamata and the Hg content in feathers; the content is highest in fish-eating seabirds and lowest in herbivorous waterfowl (Doi et al. 1984; Table 4). This same relation held in birds collected from China and Korea, although concentrations were significantly lower (Doi et al. 1984). There are close correlations between Hg contents of zooplankton and suspended particulate matter, and of sediments and fish muscle, suggesting a pathway from sediment to fish by way of suspended matter and zooplankton. The conversion from inorganic Hg to methylmercury is believed to have occurred primarily in zooplankton (Nishimura and Kumagai 1983).

Table 4. Mercury concentrations in selected biological and nonbiological materials collected from Minamata Bay, Japan and environs. Concentrations are in mg Hg/kg (ppm) fresh weight (FW), or dry weight (DW).

Sample, year of collection, and other variables	Concentration (mg/kg)	Reference[a]
Phytoplankton		
1974	Max. 0.32 DW	Nishimura and Kumagai 1983
Invertebrates		
1961		
Coelenterates	9.6 DW	Matida and
Tunicates	35–56 DW	Kumada 1969
Molluscs		
Pacific scallop, *Chlamys ferrei nipponensis*		
Soft parts	48 DW	
Pacific oyster, *Crassostrea gigas*		
Soft parts	10 DW; 5.6 FW	
Clam, *Hormomya mutabilis*		
Foot	18–48 DW	Fujiki 1963
Ganglion	181 DW	

Other tissues	20–73 DW	
Crustacean		
Crab, *Neptunus pelagicus*		
Muscle	39 DW	
Filter-feeding molluscs		
Soft parts		
1962	Max. 43 DW	Fujiki 1980
1963	Max. 40 DW	
1965	Max. 35 DW	
1967	Max. 60 DW	
1969	Max. 16 DW	
1971	Max. 16 DW	
1972	Max. 4 DW	
Zooplankton		
1974	Max. 1.1 DW	Nishimura and Kumagai 1983
Fish		
1961		
Largescale blackfish,		
Girella punctata		
Viscera	18–27 DW	Matida and
Muscle	12–20 DW	Kumada 1969
Scarbreast tuskfish,		
Choerodon azurio		
Muscle	309.1 DW	Fujiki 1963
Liver	85.0 DW	
Heart	36.4 DW	
Gill	13.3 DW	
Digestive gland	1.3 DW	
Black porgy, *Sparus macrocephalus*		
Muscle	16.5 DW	
Liver	32.2 DW	
Heart	18.3 DW	
Gill	9.1 DW	
Digestive gland	4.0 DW	
Muscle		
1961	23.0 DW	Fujiki 1980
1963	3.5 DW	
1965	11.5 DW	
1966–72	<0.6 DW	
1974	Max. 0.6 FW	Nishimura and Kumagai 1983
Birds		

1955–80		
Feather		
Fish-eating seabirds	7.1 DW	Doi
Omnivorous waterfowl	5.5 DW	et al. 1984
Predators	3.6 DW	
Omnivorous terrestrial birds	1.5 DW	
Herbivorous waterfowl	0.9 DW	
1965-66, found dead		
Feather	4.6–13.4 FW	Kojima and Fujita 1973
Mammals		
Cat, *Felis domesticus*, 1961		
Hair		
Naturally poisoned	40–52 DW	Jenkins 1980
Experimentally poisoned	22–70 DW	
Seawater		
1961		
Total	0.0016–0.0036 FW	EPA 1980
1974		
Filtered	0.0001 FW	Nishimura and
Suspended particulates	0.000075 FW	Kumagai 1983
Mud		
1963	28–713 DW	Fujiki 1980
1969	19–908 DW	
1970	8–253 DW	
1971	14–586 DW	
Sediments		
1973	>15–600 DW	Nishimura and Kumagai 1983

[a]Each reference applies to the values in the same row and in the rows that follow for which no other reference is indicated.

In aquatic environments where point sources of industrial contamination have been identified, the elimination of Hg discharges has usually improved environmental quality. Such improvement has been reported for Minamata Bay (Table 4); for sediments in Saguenay Fjord, Quebec, when chloralkali wastes were limited; for fish residues in Canada's Lake St. Clair after two chloralkali plants were closed; and in various sections of Europe and North America when industrial discharges were eliminated (Barber et al. 1984).

BACKGROUND CONCENTRATIONS

GENERAL

Mercury burdens in sediments and other nonbiological materials are estimated to have increased up to 5X prehuman levels, primarily as a result of man's activities (NAS 1978). The residence time of mercury is comparatively short (about 11 days) in the atmosphere, but is much longer (at least 1,000 years) in oceanic waters, soils, and sediments (Clarkson 1984).

An elevated concentration of mercury (i.e., >1.0 mg/kg fresh weight), usually as methylmercury, in any biological sample is often associated with proximity to human use of mercury. The elimination of Hg point-source discharges has usually been successful in improving environmental quality. However, elevated levels of mercury in biota may persist in contaminated areas long after the source of pollution has been discontinued (Rada et al. 1986). For example, Hg remains elevated today in resident biota of Lahontan Reservoir, Nevada, which received about 7,500 tons of mercury as a result of gold and silver mining operations during the period 1865 to 1895 (Cooper 1983). It is noteworthy that some groups of organisms with consistently elevated Hg residues may have acquired these concentrations as a result of natural processes, rather than from anthropogenic activities. These groups include older specimens of long-lived predatory fishes, marine mammals (especially pinnipeds), and organisms living near natural Hg-ore-cinnabar deposits.

NONBIOLOGICAL

Mercury burdens have increased 2X to 5X precultural levels in freshwater and estuarine sediments and freshwater lakes and rivers, but estimated increases in oceanic waters and terrestrial soils have been negligible (NAS 1978). Total mercury concentrations in uncontaminated natural waters (presumably unfiltered) now range from about 0.001 to 0.050 ug/l (Table 5). In sediments that were anthropogenically contaminated with Hg, concentrations were significantly elevated (usually >20.0 mg/kg) when compared with uncontaminated sediments (usually <1.0 mg/kg). The residence time of Hg in nonbiological materials is variable, and depends on a number of physicochemical conditions. Estimated half-time residence values for Hg are 11 days in the atmosphere, 1,000 years in terrestrial soils, 2,100 to 3,200 years in ocean waters, And >250 million years in oceanic sediments (NAS 1978, as quoted in Boudou and Ribeyre 1983); the estimate was 1 month to 5 years for water from the contaminated Saguenay River in Quebec (Smith and Loring 1981).

Table 5. Mercury concentrations in water and sediments.

Material (units)	Concentration	Reference[a]
Water (µg/L)		
Open ocean	0.0053 ± 0.0022	Nishimura et al. 1983
Open ocean	<0.01	Fitzgerald 1979
Coastal seawater	<0.02	
Estuarine seawater	<0.05	
Rivers and lakes	0.01 (Max. 0.05)	
Rainwater		
Open ocean	0.001	
Coastal ocean	0.01	
Continents	Often >0.05	
Sediment interstitial water	0.1	
Glacial waters	0.01	
Ground waters	0.05	
Sediments (mg/kg)		
Contaminated areas		
Near chloralkali plant		
Quebec, Canada	12.0	Smith and Loring 1981
Norway	250 (90.0–350.0)	Skei 1978
Thailand	8.4–58.0	Suckcharoen and Lodenius 1980

Near gold mining operations		
South Dakota	0.1–4.1	Martin and Hartman 1984
Australia	120.0	Bycroft et al. 1982
Near Hg-fungicide plant		
Denmark	22.0	Kiorboe et al. 1983
Near acetaldehyde plant		
Minamata Bay, Japan	28.0–713.0	Skei 1978
Near pulp and paper mill		
Finland	746.0	Paasivirta et al. 1983
Uncontaminated areas		
North Central U.S.	0.02–0.06 (Max. 0.11)	Martin and Hartman 1984
South Dakota	0.02–0.1	
Thailand	0.03	Suckcharoen and
Finland	0.02	Lodenius 1980
Various lakes	Usually <10.0, frequently <1.0	Skei 1978

[a]Each reference applies to the value in the same row and in the rows that follow for which no other reference is indicated.

Levels of mercury in sediments may be reflected by an increased mercury content in epibenthic fauna. For example, Hg concentrations in sediments near the Hyperion sewer outfall in Los Angeles, which ranged up to 820 ug/kg and decreased with increasing distance from the outfall, were reflected in the Hg content of crabs, scallops, and whelks. Concentrations of Hg were highest in organisms collected nearest the discharge, and lowest in those collected tens of kilometers away (Klein and Goldberg 1970).

BIOLOGICAL

Information on mercury residues in field collections of living organisms is especially abundant; accordingly, only a few selected data points are shown in Table 6. Additional, more extensive, information was given by Jenkins (1980), Eisler (1981), and Wren (1986).

In general, mercury concentrations in biota were usually <1.0 mg/kg fresh weight tissue in organisms collected from locations not directly affected by man's use of the element. However, they exceed 1.0 mg/kg--and are sometimes markedly higher--in animals and vegetation from the vicinity of chloralkali plants; agricultural users of mercury; smelteries; mining operations; pulp and paper mills; factories producing Hg-containing paints, fertilizers, and insecticides; sewer outfalls; sludge disposal areas; and other anthropogenic point sources of mercury. (Several notable exceptions to this generalization are discussed later.)

Certain species of macrophytes strongly influence mercury cycling. For example, *Spartina alterniflora*--a dominant salt marsh plant in Georgia estuaries--accounted for almost half the total mercury budget in that ecosystem (Windom et al. 1976). Mangrove vegetation plays a similarly important role in mercury cycling in the Florida Everglades (Tripp and Harriss 1976). These findings suggest that more research is needed on the role of higher plants in the mercury cycle.

Mercury was detectable in the tissues of almost all freshwater fishes examined, with the majority of the Hg (>80%) present as methylmercury (Huckabee et al. 1979). Methylmercury is absorbed more efficiently than inorganic Hg from water, and probably from food, and is retained longer regardless of the uptake pathway (Huckabee et al. 1979). Reservoir construction has often been inferred to be a cause of elevated mercury concentrations in fish. It is hypothesized that increases in mercury levels observed in fish were due to bacterial methylation of naturally occurring Hg in the flooded soils (Bodaly et al. 1984). Other factors that enhance accumulation of Hg in predatory teleosts from recently created reservoirs include low pH, high humus content, and low bioproduction (Lodenius 1983; Lodenius et al. 1983). In general, mercury levels are higher in fish from younger oligotrophic reservoirs, and lower in fish from older eutrophic reservoirs; in both situations, tissue Hg levels usually decline as the reservoirs age (Abernathy and Cumbie 1977). Concentrations >0.5 mg/kg (but <1.0 mg/kg) fresh weight have been reported in trout from several wilderness lakes in northern Maine (Akielaszak and Haines 1981) and from the Adirondacks region of New York (Sloan and Schofield 1983); these values are considerably higher than might be expected for fish inhabiting remote lakes. These elevated concentrations were usually associated with lakes of low pH, low calcium, low dissolved organic carbon concentrations, and low water hardness and alkalinity.

Table 6. Mercury concentrations in field collections of selected species of flora and fauna. Values shown are in mg Hg/kg fresh weight (FW), or dry weight (DW).

Taxonomic group, organism, tissue, and other variables	Concentration[a] (ppm)	Reference[b]
Fungi, Lichens, Mosses, Plants		
Mandarin orange, *Citrus tachibana*		
Japan		
Sprayed with Hg		
Fruit skin	0.03–0.24 FW	Jenkins 1980
Fruit pulp	0.01-0.4 FW	
Unsprayed		
Skin and pulp	0.01–0.05 FW	
Fungi, *Cortinarius* spp.		
Near smelter	9.5–35.0 DW	
Moss, *Dicranum scoparium*, whole		
Tennessee		
Exposed to fly ash	1.1 DW	
Remote areas	0.1 DW	
Great Smoky Mountains	0.07 DW	
Hawaii	0.16 DW	
Iceland	0.03 DW	
Water hyacinth, *Eichhornia crassipes*		
From sewage lagoon in		
Bay St. Louis, Mississippi		
Leaves	70.0 DW	Chigbo et al. 1982
Lichen, *Hypogymnia physodes*, whole		
Finland, 1982–83		
Distance, in km, from		
chloralkali plant		

0–1	18.0 FW	Lodenius and
1–5	2.0 FW	Tulisalo 1984
5–20	0.4 FW	
20–100	0.3 FW	
>100	0.3 FW	
Labrador tea, *Ledum* sp.		
Alaska, over cinnabar deposit		
Stem	1.0–3.5 DW	Jenkins 1980
Alfalfa, *Medicago sativa*		
From soil containing 0.4 ppm Hg		
Root	90.0 FW	
Leaf	0.13–0.4 FW	
From soil with <0.4 ppm Hg		
Leaf	0.16 FW	
Tobacco, *Nicotiana tabacum*		
Leaf		
Treated with Hg (Japan)	1.0–1.6 FW	
Untreated (USA)	<0.2 FW	
Rice, *Oryza sativa*, grain		
Sprayed with Hg	0.1–0.7 FW	
Unsprayed	0.02–0.1 FW	
Marine flowering plant, *Posidonia oceanica*		
Near sewer outfall, Marseilles, France		
Rhizomes	2.5 DW	Augier
Leaves	51.5 DW	et al. 1978
Roots	0.6 DW	
Cherry, *Prunus avium*		
Europe (Slovenia), bark		
Uncontaminated areas	0.06 FW	Jenkins 1980
High Hg in soil	6.0 FW	
Factory area	59.0 FW	
Mosses, *Sphagnum* spp., whole		
Finland, 1982–83		
Distance (km) from chloralkali plant		
0–1	3.8 (1.5–16.0) FW	Lodenius and
1–5	0.8 (0.2–2.6) FW	Tulisalo 1984
5–20	0.09 (0.04–0.2) FW	
20–100	0.05 (0.0–0.8) FW	
>100	0.02 FW	

Aquatic Invertebrates

Freshwater		
Annelids, 2 families		
From Hg-contaminated areas	0.3–0.6 FW	Huckabee
From uncontaminated areas	0.03–0.05 FW	et al. 1979
Arthropods		
Sow bug, *Asellus* sp.		
Sweden, whole		
20 km below paper mill	1.9 FW	Jenkins 1980
1–15 km above paper mill	0.06 FW	
Crustaceans, 2 families		
From Hg-contaminated areas	1.9–10.0 FW	Huckabee
From uncontaminated areas	0.06–0.56 FW	et al. 1979
Insects, 8 families		
From Hg-contaminated areas	0.5–5.0 FW	
From uncontaminated areas	0.05–0.21 FW	
Stonefly, *Isoperla* sp.		
Whole, Sweden		
17 km below paper mill	2.4 FW	Jenkins 1980
15 km above paper mill	0.07 FW	
Crayfish, *Orconectes virilis*		
Ontario, whole		
Central location	0.09–0.49 FW	
From chloralkali plant location	1.4–7.4 FW	
Crayfish, *Pacifiastacus* sp.		
Lahontan Reservoir, Nevada, 1981		
Abdomen	5.7 FW	Cooper 1983
Molluscs		
From Hg-contaminated areas	0.02–2.1 FW	Huckabee
From uncontaminated areas	0.05 FW	et al. 1979
Marine		
Annelids, whole, 3 spp.		
Georgia, USA, estuaries		
Hg-contaminated estuary		
Total Hg	0.7–4.5 DW	Windom and
Methyl Hg	Max. 0.8 DW	Kendall 1979
Control estuary		
Total Hg	0.1–0.6 DW	
Methyl Hg	Max. 0.13 DW	
Arthropods		
Crustaceans, whole, 2 spp.		
Georgia, USA, estuaries		

Hg-contaminated estuary		
Total Hg	0.4–1.8 DW	
Methyl Hg	Max. 1.0 DW	
Control estuary		
Total Hg	0.1–0.4 DW	
Methyl Hg	Max 0.05 DW	
American lobster, *Homarus americanus*		
Muscle		
Chesapeake Bay	0.03–0.06 FW	Jenkins 1980
NW Atlantic	0.25–1.6 DW	
Nova Scotia	0.15–1.5 FW	
Spiny lobster, *Nephrops norvegicus*		
Tyrrhenian Sea, 1981		
Muscle	2.9 FW	Schreiber 1983
Shrimp		
Edible portions		
Total Hg	0.77 FW	Cappon
Methyl Hg	0.4 FW	and Smith 1982
Echinoderms		
Sea stars, 3 spp., 1981		
Venezuela, polluted area		
Gonads	3.8–8.7 DW; 0.9–1.6 FW	Iglesias and Panchaszadeh 1983
Molluscs		
From vicinity chloralkali plant, Israel, 1980–82, soft parts		
Gastropod, *Arcularia gibbosula*	18.2–38.7 DW	Hornung et al. 1984
Bivalve, *Donax venustus*	Max. 6.4 DW	
Bivalves, soft parts		
From Hg-polluted area, Denmark		
Deposit feeders	1.4–4.4 FW	Kiorboe
Suspension feeders	0.9–1.9 FW	et al. 1983
Edible portions		
Total Hg	0.04–0.22 FW	Cappon and
Methyl Hg	Max. 0.09 FW	Smith 1982
Soft parts, 2 spp.		
Georgia, USA, estuaries		

Hg-contaminated estuary	0.5–1.2 DW	Windom and
Control estuary	0.1–0.2 DW	Kendall 1979
Mussel, *Mytilus californianus*		
Soft parts		
Nationwide	<0.4 DW	Flegal
California	0.6–2.5 DW	et al. 1981
Mussel, *Mytilus edulis*		
Soft parts		
Belgium	1.0 DW	
Spain	1.5 DW	
New Brunswick	0.1 FW	
Netherlands	0.1–0.3 FW	
Great Britain	0.02–0.7 FW	
New Zealand	0.02–0.48 FW	
Norway	0.2–0.65 DW	
Softshell clam, *Mya arenaria*		
Soft parts		
Chesapeake Bay, MD	0.01–0.05 FW	
Nova Scotia	0.03–0.13 FW	
New Brunswick		
3 km below pulp mill	0.9 FW	
3 km below chloralkali plant	3.6 FW	
Terrestrial Invertebrates		
Aphid, *Macrosiphium gei*		
Whole, Illinois		
Fed on Hg-treated tomato plants	0.3–11.5 FW	
Control	0.08–0.81 FW	
Lacewing, *Chrysopa carnea*		
Whole, Illinois		
Fed on Hg-treated tomato plants	0.6–31.4 FW	
Control	0.0–1.1 FW	
Fish		
Rock bass, *Ambloplites rupestris*		
Muscle		
Ontario	0.6–4.6 FW	
Michigan	0.4 FW	
Western Ontario	1.1–10.9 FW	
Lake St. Clair	0.5–2.0 FW	
Blue hake, *Antimora rostrata*		
NW Atlantic, 2500 m depth		

Muscle		
1880	0.51 FW	Barber
1970	0.34 FW	et al. 1984
Freshwater drum, *Aplodinotus grunniens*		
Whole		
Age 0	0.05 FW	Busch 1983
Age I	0.13 FW	
Age II	0.18 FW	
Blacktail, *Diplodus sargus*, muscle		
Hg-polluted area	0.3–1.7 FW	Hornung
Unpolluted area	0.04–0.64 FW	et al. 1984
Northern pike, *Esox lucius*, muscle		
Sweden	0.2–9.8 FW	Jenkins 1980
Quebec	0.3–0.8 FW	
Norway	0.1 FW	
Saskatchewan	0.7–10.6 FW	
Canada (normal)	0.1 FW	
Canada (polluted)	0.5–0.7 FW	
Lake St. Clair	2.0–3.0 FW	
NW Ontario mining area	5.6 FW	
Wisconsin	0.9–1.4 FW	
Manitoba, manmade reservoir		
Preimpoundment (1971–73)	0.25–0.35 FW	Bodaly
Postimpoundment (1979–82)	0.67–0.95 FW	et al. 1985
Fish		
Muscle		
Freshwater		
Total Hg	0.27–1.7 FW	Cappon and
Methyl Hg	Max. 1.4 FW	Smith 1982
Marine		
Total Hg	0.11–5.7 FW	
Methyl Hg	Max. 4.5 FW	
Lahontan Reservoir, Nevada, 1981		
Muscle, 5 spp.	Max. 2.3–3.9 FW	Cooper 1983
Liver, 5 spp.	Max. 2.4–8.3 FW	
Heart, 4 spp.	Max. 1.1–2.1 FW	
Louisiana, Atchafalaya River, 1981		
Whole, 8 spp.	0.06–0.79 FW	Winger and Andreasen 1985
Nationwide, USA, whole		
1969–70	0.26 (0.05–1.7) FW	Henderson and
Pacific Coast and Alaska	0.25 (0.05–1.7) FW	Shanks 1973
Southwest	0.08 (<0.05–0.14) FW	

North Central	0.20 (<0.05–0.05) FW	
Northeast	0.23 (<0.05–0.08) FW	
Southeast	0.23 (<0.05–1.0) FW	
1972	0.15 FW	
1976–77	0.11 FW	Lowe et al.
1978–79	0.11 (0.01–1.1) FW	1985
1980–81	0.11 (0.01–0.77) FW	
Thailand		
Muscle		
Near chloralkali plant		
No waste water system, 1975–76	0.32–3.6 FW	Suckcharoen and Lodenius 1980
With waste water system, 1978	0.1–1.4 FW	
Control location	0.01–0.3 FW	
Various species		
Muscle		
From unpolluted areas	0.04–0.15 FW	NAS 1978
From moderately Hg-polluted areas	>1.0 FW	
From highly polluted areas	10.0–24.0 FW	
Blackfish, *Gadopsis marmoratus*		
Muscle		
From Hg-contaminated sediments	Max. 0.64 FW	Bycroft et al. 1982
From uncontaminated sediments	Max. 0.06 FW	
Channel catfish, *Ictalurus punctatus*		
Muscle		
Lake Erie	0.3–1.8 FW	Jenkins 1980
Lake St. Clair	0.5–2.0 FW	
Ohio	0.1–0.4 FW	
Illinois	0.03–0.2 FW	
Oregon	0.02–1.5 FW	
Georgia	0.1–1.9 FW	
Texas	0.2–2.5 FW	
Pumkinseed, *Lepomis gibbosus*		
16 lakes, Ontario, Canada, 1981		
Muscle	0.09–0.54 FW	Wren and MacCrimmon 1984
Black marlin, *Makaira indica*		
Muscle		
Pacific Ocean	0.6–4.3	Cappon and Smith 1982
NE Australia	0.5–16.5 FW	
Blue marlin, *Makaira nigricans*		

Muscle		
Hawaii	0.4–14.0 FW	
Total Hg	0.4–0.9 FW	
Methyl Hg	Max. 0.16 FW	
Largemouth bass, *Micropterus salmoides*		
Muscle		
Texas	0.1 FW	Jenkins 1980
Utah	0.3–7.3 FW	
California	0.1–0.6 FW	
Oregon	0.2–1.8 FW	
Washington	0.1–0.3 FW	
Georgia	0.1–5.4 FW	
Michigan	0.2–0.9 FW	
Illinois	0.03–1.2 FW	
Arizona	0.3 FW	
Striped bass, *Morone saxatilis*		
Lahontan Reservoir, Nevada, 1981		
Single specimen, 16 years old		
Muscle	9.5 FW	Cooper 1983
Heart	5.6 FW	
Liver	23.7 FW	
Muscle		
Body weight		
<3.2 kg	<0.5 FW	Alexander
3.2–5.7 kg	0.5 FW	et al. 1973
>5.7 kg	>0.5 FW	
Yellow perch, *Perca flavescens*		
Whole		
Age 0	0.07 FW	Busch 1983
Age I	0.13 FW	
Age II	0.22 FW	
Round whitefish, *Prosopium cylindraceum*		
Saginaw Bay, Michigan		
1977–78		
Fillets		
Methyl Hg	Max. 0.05 FW	Miller and
Total Hg	Max. 0.1 FW	Jude 1984
Trout, *Salmo* spp.		
Missouri		
Liver and muscle		

1946–50	3.0 FW	Lloyd
1973	0.1–0.3 FW	et al. 1977
Brook trout, *Salvelinus fontinalis*		
Adirondack lakes (15), New York		
Whole	<1.0 FW	Sloan and Schofield 1983
Lake trout, *Salvelinus namaycush*		
Muscle		
British Columbia	1.1–10.5 FW	Jenkins 1980
Ontario	0.3–1.3 FW	
Quebec	0.3–1.2 FW	
New York	0.3–0.6 FW	
Sharks, Australia, 1980		
Muscle, 7 spp.		
Carcharhinus spp.	Max. 4.3 FW	Lyle 1984
Sphyrna spp.	Max. 4.9 FW	
Walleye,		
Stizostedion vitreum vitreum		
Manitoba, manmade reservoir		
Muscle		
Preimpoundment (1971–77)	0.2–0.3 FW	Bodaly
Postimpoundment		et al. 1984
(1978–92)	0.6–0.8 FW	
Tunas, 1981, 5 spp.		
Muscle	1.0–6.3 FW	Schreiber 1983
Swordfish, *Xiphias gladius*		
Muscle		
NW Atlantic	2.0 FW; 8.1 DW	Jenkins 1980
Peru	1.1–1.8 FW	
Pacific	0.5–1.7 FW	
W. Atlantic	0.05–4.9 FW	
Gibralter Strait	1.0–2.0 FW	
Amphibians and Reptiles		
European toad, *Bufo bufo*		
Yugoslavia		
Control area		
Liver	1.5 FW	
Kidney	1.2 FW	
Lung	0.2 FW	
Muscle	0.2 FW	
Egg	0.06 FW	
Polluted mercury mining area		
Liver	21.8–25.5 FW	Jenkins 1980;
Kidney	22.8–24.0 FW	Terhivuo et al. 1985

Lung	1.7 FW	
Muscle	2.3–2.9 FW	
Egg	2.3 FW	
Loggerhead sea turtle, *Caretta caretta*		
Egg	0.01 FW	Hall 1980
Crocodile, *Crocodylus acutus*		
Egg	0.7 FW	
Bullfrog, *Rana catesbeiana*		
Lake St. Clair		
Carcass	0.1 FW	Jenkins 1980
Liver	0.3 FW	
Leopard frog, *Rana pipiens*		
Lake St. Clair		
Carcass	0.1–0.2 FW	
Liver	0.5–1.1 FW	
Florida		
Liver	0.1 FW	
Frog, *Rana temporaria*		
Yugoslavia, 1975		
From Hg-mining area		
Liver	21.0 FW	Terhivuo
Kidney	16.2 FW	et al. 1984
Muscle	3.4 FW	
Egg	1.3 FW	
From uncontaminated area		
All tissues	<0.08 FW	
Birds		
Goshawk, *Accipiter gentilis*		
Sweden		
Feather		
1860–1946	2.2 FW	Jenkins 1980
1947–65	29.0 FW	
1967–69	3.1–5.1 FW	
Finnish sparrowhawk, *Accipiter nisus*		
Feather		
Finland		
1899–1960	4.1 (2.1–7.7) DW	Solonen and
1961–70	11.1 (2.3–42.0) DW	Lodenius 1984
1971–82	7.4 (1.0–29.0) DW	
Germany		
1972–73	4.9 (0.4–20.3) DW	

Norway		
1976	2.0–20.0 DW	
Wood duck, *Aix sponsa*		
Tennessee, 1972–73		
Juveniles		
Liver	0.4 (0.1–1.1) FW	Lindsay and
Muscle	0.1 (0.05–0.4) FW	Dimmick 1983
Fat	0.1 (0.01–0.4)	
Adults		
Liver	0.2 (0.1–0.3) FW	
Muscle	0.08 (0.06–0.11) FW	
Fat	0.06 (0.01–0.11) FW	
Blue-winged teal, *Anas discors*		
Muscle		
Lake St. Clair	0.1–2.3 FW	Jenkins 1980
Ontario	3.8–10.4 FW	
Wisconsin	0.0–0.5 FW	
Illinois	0.05 FW	
Great blue heron, *Ardea herodius*		
Liver		
Lake St. Clair	97.0 (14.6–175.0) FW	
New Brunswick	4.5 FW	
Lake Erie	0.7–4.3 FW	
Wisconsin	0.5 (0.2–1.1) FW	
Birds		
Antarctic		
Liver		
1977–79		
4 spp.	0.5–1.3 FW	Norheim
3 spp.	2.7–2.9 FW	et al. 1982
1980		
5 spp.	0.5–2.1 FW	Norheim and Kjos-Hanssen 1984
Belgium, 1970–81		
Liver, 30 spp.		
Aquatic birds	0.11–35.0 FW	Delbeke
Terrestrial birds	ND-14.0 FW	et al. 1984
Hawaiian, 1980		
Egg, 3 spp.	0.12–0.36 FW	Ohlendorf and Harrison 1986
North America		
Feather		

From areas with mercury-treated seed dressing		
Seed-eating songbirds	1.6 DW	NAS 1978
Upland game birds	1.9 DW	
From untreated areas		
Seed-eating songbirds	0.03 DW	
Upland game birds	0.35 DW	
Northwestern Ontario, Canada		
From a heavily mercury-contaminated freshwater system		
Liver		
Scavengers	57.0 (13.8–121) FW	Fimreite 1979
Fish eaters	39.5 (1.7–91) FW	
Omnivores	26.6 (9.5–53) FW	
Invertebrate feeders	12.4 (3.2–28) FW	
Vegetarians	6.2 (1.9–28) FW	
Diving ducks	Max. 175.0	NAS 1978
Muscle		
Diving ducks	Max. 23.0 FW	
Mallard, *Anas platyrhynchos*	Max. 6.1 FW	
Eagle-owl, *Bubo bubo*		
Sweden, 1963–76		
Feather		
Inland populations	3.2 DW	Broo and
Coastal populations	6.5 DW	Odsjo 1981
1829–1933	0.3–3.6 FW	Jenkins 1980
1964–65	12.8–41.0 FW	
Peregrine, *Falco peregrinus*		
Feather		
1834–1849	2.5 DW	NAS 1978
1941–65	>40.0 DW	
Swedish gyrfalcon, *Falco rusticolus*		
Nestlings, feather		
Percent aquatic birds in diet		
None	0.035 FW	Lindberg 1984
4.8% biomass	0.66 FW	
10.6% biomass	1.22 FW	
American bald eagle, *Haliaeetus leucocephalus*		
Egg		
Maine (highest concentrations Nationwide)		
1974	0.35–0.58 FW	Wiemeyer

1975	0.22–0.63 FW	et al. 1984
1976	0.22–0.66 FW	
1977	0.28–0.90 FW	
1978	0.30 FW	
1979	0.84–1.2 FW	
Ringed herring gull,		
Larus argentatus		
Denmark, 1975–76		
Liver	0.65 (0.08–2.34) FW	Karlog and Clausen 1983
Ontario		
Egg	1.5–15.8 FW	Jenkins 1980
Albumin	16.1–22.7 FW	
Yolk	3.4–3.5 FW	
California seagull,		
Larus californicus		
Lahontan Reservoir, Nevada, 1981		
Muscle	0.4 FW	Cooper 1983
Liver	1.0 FW	
Egg	0.1–0.2 FW	
Osprey, *Pandion haliaetus*		
Sweden		
Feather		
1840–1940	3.5–5.0 FW	Jenkins 1980
1940–66	>17.0 FW	
Brown pelican,		
Pelecanus occidentalis		
Egg		
South Carolina	0.3–0.5 FW	
Florida	0.4 FW	
California	0.4 FW	
Liver	0.75 DW	Ohlendorf et al. 1985
Kidney	0.68 DW	
Feather	0.97 DW	
Ring-necked pheasant,		
Phasianus colchicus		
Muscle		
Denmark	0.01 FW	Jenkins 1980
Idaho	0.0–15.0 FW	
Indiana	0.06 FW	
Oregon	<0.5 FW	
Wyoming	0.2–0.6 FW	
Colorado	0.04–0.6 FW	

Utah	0.15 (0.01–2.1) FW	
California	1.6–4.7 FW	
Wisconsin	0.01–0.08 FW	
Illinois	0.02–0.03 FW	
Great crested grebe,		
Podiceps cristata		
Sweden		
Feather		
1865–1940	<10.0 FW	
1940–66	>14.0 FW	
Mourning dove, *Zenaida macroura*		
Liver		
Eastern United States	0.07–0.67 FW	
Mammals		
Australian fur seal,		
Arctocephalus pusillus		
Muscle	0.9 (0.1–1.9) FW	Bacher 1985
Liver	62.3 (1.0–170.0) FW	
Kidney	0.6 (0.1–1.7) FW	
Spleen	1.3 (0.0–3.8) FW	
Brain	0.7 (0.0–2.5) FW	
Hair	9.6 (1.1–19.8) DW	
Woodmouse, *Apodemus sylvaticus*		
Great Britain		
In field with Hg-treated		
wheat seed		
Liver	Max. 7.1 FW	Jenkins 1980
Kidney	Max. 11.7 FW	
In chloralkali area		
Liver	Max. 0.5 FW	
Kidney	Max. 1.3 FW	
Control area		
Liver	Max. 0.07 FW	
Kidney	Max. 0.3 FW	
Roe deer, *Capreolus capreolus*		
Males, Poland, 1977–78		
From Hg-contaminated habitat		
Muscle	0.047 FW	Krynski
Liver	0.036 FW	et al. 1982
Kidney	0.053 FW	
From uncontaminated area		
Muscle	0.013 FW	
Liver	0.015 FW	

Kidney	0.027 FW	
Beaver, *Castor canadensis*		
Wisconsin, 1972–75		
All tissues	<0.09 FW	Sheffy and St. Amant 1982
Cat, *Felis domesticus*		
Ate fish from below chloralkali plant, NW Ontario		
Brain	6.9–16.4 FW	Jenkins 1980
Pancreas	4.3–4.9 FW	
Kidney	0.8–13.4 FW	
Liver	14.2–67.1 FW	
Fur	121.0–392.0 FW	
River otter, *Lutra canadensis*		
Winnipeg River,		
Manitoba, Canada, 1979–81		
Males		
Liver	Max. 8.9 FW	Kucera 1983
Kidney	Max. 6.5 FW	
Brain	Max. 3.1 FW	
Females		
Liver	Max. 3.9 FW	
Kidney	Max. 1.8 FW	
Brain	Max. 0.6 FW	
Wisconsin, 1972–75		
Brain	0.7 FW	Sheffy and St. Amant 1982
Muscle	1.4 FW	
Liver	3.3 (Max. 23.6) FW	
Kidney	8.5 (Max. 20.9) FW	
Fur		
Industrial area	9.5 (Max. 63.2) FW	
Nonindustrial area	3.8 FW	
Bobcat, *Lynx rufus*		
Hair		
Georgia USA		
Upper coastal plain	13.1 DW	Jenkins 1980
Lower coastal plain	0.9 DW	
Mink, *Mustela vision*		
Wisconsin, 1972–75		
Brain	0.5 FW	Sheffy and St. Amant 1982
Muscle	1.3 FW	
Liver	2.1 (Max. 17.4) FW	
Kidney	2.3 (Max. 12.5) FW	

Fur		
Industrial area	10.5 (Max. 41.2) FW	
Nonindustrial area	3.0 FW	
Winnipeg River,		
Manitoba, Canada, 1979–81		
Males		
Liver	Max. 9.9 FW	Kucera 1983
Kidney	Max. 6.4 FW	
Brain	Max. 2.4 FW	
Females		
Liver	Max. 10.7 FW	
Kidney	Max. 8.1 FW	
Brain	Max. 2.1 FW	
Muskrat, *Ondatra zibethicus*		
Wisconsin, 1972–75		
All tissues	<0.06 FW	Sheffy and St. Amant 1982
Sheep, *Ovis aries*		
Grazing for 23 months on		
Hg-contaminated field		
Diet (grass)		
Winter	6.5 DW	Edwards and
Summer	1.9 DW	Pumphery 1982
Lung	Max. 4.0 FW	
Kidney	Max. 3.1 FW	
Liver	Max. 2.4 FW	
Brain	Max. 1.1 FW	
Flesh	<1.0 FW	
Harbor seal, *Phoca vitulina richardi*		
Liver		
California	269.0 (81.0–700.0) FW	Jenkins 1980
Oregon	0.3–68.0 FW	
Washington	1.3–60.0 FW	
Pribilof Islands	0.6–8.9 FW	
Raccoon, *Procyon lotor*		
Wisconsin, 1972–75		
Brain	<0.02 FW	Sheffy and
Muscle	0.08 FW	St. Amant 1982
Kidney	1.4 FW	
Liver	2.0 FW	
Fur	3.8 FW	
Gray squirrel, *Sciurus carolinensis*		

Hair, Florida, 1974		
Rural areas	0.43 FW	Jenkins 1980
Urban		
Age 0–1	1.0 (0.07–6.7) FW	
Age >2	2.7 (0.30–9.2) FW	
Striped dolphin, *Stenella coeruleoalba*		
Adults, Japan, 1977–80		
Muscle		
Total Hg	15.2 FW	Itano
Methyl Hg	5.3 FW	et al. 1984a
Liver		
Total Hg	205.0 FW	
Methyl Hg	7.0 FW	
Kidney		
Total Hg	14.7 FW	
Methyl Hg	3.2 FW	
Whole body		
Age 1 year		
Total Hg	0.8 FW	Itano
Methyl Hg	0.4 FW	et al. 1984b
Age 3 years		
Total Hg	1.8 FW	
Methyl Hg	1.0 FW	
Age 4 years		
Total Hg	3.0 FW	
Methyl Hg	1.5 FW	
Age 14 years		
Total Hg	4.5 FW	
Methyl Hg	2.6 FW	
Age 20 years		
Total Hg	10.7 FW	
Methyl Hg	3.5 FW	
Red fox, *Vulpes vulpes*		
Hair		
Georgia, USA		
Upper coastal plain	2.3 DW	Jenkins 1980
Lower coastal plain	0.5 DW	
Wisconsin, 1972–75		
Fur	0.6 FW	Sheffy and
Other tissues	<0.14 FW	St. Amant 1982
California sea lion, *Zalophus californianus*		

Liver		
Mother	73.0–1,026.0 DW	Jenkins 1980
Pup	0.9–16.0 DW	
Kidney		
Mother	4.1–43.2 DW	
Pup	0.6–6.7 DW	

[a]Concentrations are listed as mean, range, or maximum (Max.).

[b]Each reference applies to the value in the same row and in the rows that follow for which no other reference is indicated.

Nationwide monitoring of whole fish during the period 1969 to 1981 demonstrated that the highest Hg concentrations (0.33 to 1.7 mg/kg FW) were in northern squawfish (*Ptychocheilus oregonensis*) from the Columbia River basin in the Pacific Northwest (Henderson and Shanks 1973; Lowe et al. 1985). Elevated Hg concentrations in this piscivorous species were attributed primarily to the presence of major cinnabar deposits and with Hg use associated with mineral mining in the Columbia River basin. Northern squawfish may have a natural tendency to accumulate high concentrations of mercury in their flesh--as is well known for older specimens of long-lived predatory fishes such as tunas, billfishes, bluefish (*Pomatomus saltatrix*), striped bass (*Morone saxatilis*), northern pike (*Esox lucius*), and many species of sharks--but Hg uptake kinetics in squawfish requires further research (Lowe et al. 1985).

Of 159 species of finfish and sharks from the coastal waters of Alaska, Hawaii, and the conterminous United States, mercury concentrations in muscle were usually less than 0.3 mg/kg fresh weight (Hall et al. 1978). Mean Hg concentrations in excess of 0.5 mg/kg fresh weight muscle were recorded in 31 species, including 10 species of sharks and 4 species of billfishes; however, these 31 species accounted for less than 0.65% of the catch intended for human consumption (Hall et al. 1978).

In birds, it is generally acknowledged that mercury concentrations are highest in species that eat fish and other birds. Residues were highest in kidney and liver, but total Hg contents were significantly modified by food preference and availability, and by migratory patterns (NAS 1978; Delbeke et al. 1984). Also, there is an inverse relationship between total Hg and percent methylmercury in tissues of various avian species (Norheim et al. 1982; Karlog and Clausen 1983)--a pattern that seems to hold for all vertebrate organisms for which data are available. Diet and migration are the most important Hg modifiers in birds. For example, the higher levels of Hg in juvenile than in adult wood ducks (*Aix sponsa*) from Tennessee were related to dietary patterns: juveniles preferred insects, whereas adults preferred pondweed tubers; Hg residues were higher in the insects than in the pondweeds (Lindsay and Dimmick 1983). Concentrations of Hg in livers of Antarctic birds reflected Hg body burdens accumulated during migration, while the birds were overwintering near industrialized areas. Concentrations were highest in species that ate higher trophic levels of prey and were especially pronounced for skuas, *Catharacta* spp.; however, significant inherent interspecies differences were evident (Norheim et al. 1982; Norheim and Kjos-Hanssen 1984).

The significance of Hg residues in birds is not fully understood. For example, all eggs of the American bald eagle (*Haliaeetus leucocephalus*) collected Nationwide contained detectable levels of Hg, but the mean was 0.15 mg Hg/kg (fresh weight basis) in eggs from unsuccessful nests vs. 0.11 in eggs from successful nests (Wiemeyer et al. 1984). Many other contaminants--especially organochlorine compounds--were in eagle eggs, and several were present at levels that potentially interfere with eagle reproduction (Wiemeyer et al. 1984). It is not now possible to implicate Hg as a major cause of unsuccessful eagle reproduction.

Bird feathers have been used for some time as indicators of Hg loadings in terrestrial and marine environments. The keratin in bird feathers is not easily degradable, and Hg is probably associated firmly with the disulphide bonds of keratin. Consequently, it has been possible to compare Hg contents of feathers recently sampled with those from museum birds, thereby establishing a time series (Applequist et al. 1984). The most probable source of recent elevated Hg residues in feathers of the Finnish sparrowhawk (*Accipiter nisus*) was from consumption of avian granivores that had become contaminated as a result of eating seeds treated with

organomercury compounds; in 1981, 5.6 tons of methoxyethylmercury compounds were used in Finnish agriculture for protection of seeds against fungi (Solonen and Lodenius 1984). Captive Swedish eagle-owls (*Bubo bubo*), with low Hg content in feathers (<1.0 mg/kg DW), that were introduced into coastal areas quickly reflected the high (6.5 mg/kg) Hg levels in feathers of wild eagle-owls from that region. Captive birds released into inland territories, where Hg levels were near background, did not accumulate Hg in feathers (Broo and Odsjo 1981). Mercury levels in feathers of nestling Swedish gyrfalcons (*Falco rusticolus*) showed a better correlation with Hg levels in actual food items than with levels based on adult feathers. Mercury concentrations in feathers were higher in nestlings fed partly with aquatic bird species containing >0.07 mg Hg/kg in pectoral muscle than in nestlings fed willow grouse (*Lagopus lagopus*) and ptarmigan (*Lagopus mutus*), both of which contained <0.01 mg Hg/kg in pectoral muscle (Lindberg 1984). In some instances there was a substantial time lag, up to 10 years, between the introduction of a pesticide, such as alkylmercury, its subsequent banning, and measurable declines of Hg in feathers of several species of Swedish raptors; this was the case for various species of *Falco, Haliaeetus*, *Bubo, Buteo*, and *Accipiter* (Wallin 1984). Accordingly, a reduction in Hg content in feathers of free-living birds may be sufficient to establish an improved situation.

Among mammals, marine pinnipeds usually contained the highest reported concentrations of Hg in tissues (Table 6). The relatively high concentrations appeared to be a result of natural processes rather than of anthropogenic activities, however, and probably did not represent a significant risk to pinniped health. In general, Hg concentrations increased significantly with increasing age of the organism, as shown (Figure 2) in the livers of harbor seal (*Phoca groenlandica*), grey seal (*Halichoerus grypus*), California sea lion (*Zalophus californianus*), and northern fur seal (*Callorhinus ursinus*). The mechanisms to account for this phenomenon in pinnipeds are similar to those reported by Itano et al. (1984 a,b, c) for the striped dolphin (*Stenella coeruleoalba*). They showed that tissue concentrations of mercury in striped dolphins increased with increasing age of the animal, reaching a plateau in 20 to 25 years; were highest in liver, although muscle accounted for about 90% of the total body Hg burden; were present in the methylated form in fetal and suckling stages, but the proportion of methylmercury decreased over time with no absolute increase after age 10 years; were excreted slowly by all developmental stages, and slowest in older dolphins (resulting in higher accumulations); and were correlated strongly with selenium concentrations in all age groups. It is probable that inorganic Hg and selenium were complexed in a 1:1 molar ratio, in a form biologically unavailable to marine mammals (and probably other mammals), thereby significantly decreasing the risk of mercury toxicosis to individuals with grossly elevated Hg body burdens (Eisler 1984, 1985). Large colonies of pinnipeds and, to a lesser extent, marine birds along the western coast of the United States may make Hg available to mussels (*Mytilus californianus*) through fecal elimination of large amounts of Hg, resulting in abnormally high Hg levels in mussels from several west coast sites (Flegal et al. 1981).

Among furbearers in the Wisconsin River drainage system, Hg burdens were higher in fish-eating than in herbivorous species--i.e., river otter (*Lutra canadensis*) > mink (*Mustela vison*) > raccoon (*Procyon lotor*) > red fox (*Vulpes fulva*) > muskrat (*Ondatra zibethicus*) > beaver (*Castor canadensis*) (Sheffy and St. Amant 1982). In general, fur contained the highest Hg levels, followed by liver, kidney, muscle, and brain, in that order (Table 6; Sheffy and St. Amant 1982). Mercury levels in piscivorous furbearers collected from the Wisconsin River basin paralleled Hg levels in fish, crayfish, and bottom sediments from that system; levels in all compartments were highest about 30 km downstream from an area that supported 16 pulp and paper mills and a chloralkali plant (Sheffy and St. Amant 1982). Mink and river otter accumulated about 10X more Hg than did predatory fishes from the same drainage areas--suggesting that these furbearers can serve as sensitive indicators of mercury, even at very low levels of Hg contamination (Kucera 1983).

Domestic sheep (*Ovis* sp.) allowed to graze for 23 months on grass contaminated with Hg (up to 6.5 mg/kg dry weight) caused by atmospheric emissions of a nearby chloralkali site, retained about 0.1% of the total Hg taken in by ingestion and inhalation, although residues in flesh were negligible (Edwards and Pumphery 1982). It was concluded that contamination of grass as a result of atmospheric discharges of inorganic He from

chloralkali sites causes no hazard, either directly to grazing animals or indirectly to humans who might ultimately consume their flesh.

ACUTE AND CHRONIC TOXICITY

GENERAL

For all organisms tested, early developmental stages were the most sensitive, and organomercury compounds--especially methylmercury--were more toxic than inorganic forms. Numerous biological and abiotic factors modify the toxicity of Hg compounds, sometimes by an order of magnitude or more, but the mechanisms of action are not clear.

Lethal concentrations of total Hg to sensitive, representative organisms varied from 0.1 to 2.0 ug/l of medium for aquatic fauna; from 2.2 to 31.0 mg/kg body weight (acute oral) and 4.0 to 40.0 mg/kg (dietary) for birds; and from 0.1 to 0.5 mg/kg body weight (daily dose) and 1.0 to 5.0 mg/kg (dietary) for mammals.

AQUATIC ORGANISMS

Toxic concentrations of mercury salts ranged from less than 0.1 ug/l to more than 200 ug/l for representative species of marine and freshwater organisms (Table 7). The lower concentrations of <2.0 ug/l recorded were usually associated with early developmental stages, long exposures, and flowthrough tests (Table 7). Among metals tested, mercury was the most toxic to aquatic organisms, and organomercury compounds showed the greatest biocidal potential (Eisler 1981). In general, toxicity was higher at elevated temperatures (Armstrong 1979), at reduced salinities in marine organisms (McKenney and Costlow 1981), and in the presence of other metals such as zinc and lead (Parker 1979).

Signs of acute mercury poisoning in fish included flaring of gill covers, increased frequency of respiratory movements, loss of equilibrium, and sluggishness (Armstrong 1979). Signs of chronic mercury poisoning included emaciation (due to appetite loss), brain lesions, cataracts, diminished response to change in light intensity, inability to capture food, abnormal motor coordination, and various erratic behaviors (Armstrong 1979; Hawryshyn et al. 1982). Mercury residues in severely poisoned fish that died soon thereafter ranged (in mg/kg fresh weight) from 26 to 68 in liver, 16 to 20 in brain, and 5 to 7 in whole body (Armstrong 1979).

Table 7. Toxicities of inorganic and organic mercury compounds to selected species of aquatic organisms.

Chemical species, ecosystem, taxonomic group, species, and other variables	Effect[a]	Concentration (µg Hg/L medium)	Reference
Inorganic Mercury			
Freshwater			
Crustaceans			
Crayfish, *Orconectes limosus*	LC-50 (30 d)	2.0	EPA 1980
Cladoceran, *Daphnia magna*	LC-50 (96 h)	5.0	EPA 1980
Cladoceran, *Daphnia magna*	LC-50 (LT)	1.3–1.8	EPA 1980
Scud, *Gammarus pseudolimnaeus*	LC-50 (96 h)	10.0	EPA 1980
Fish			
Rainbow trout, *Salmo gairdneri*			
Juveniles	LC-50 (96 h)	155.0–200.0	EPA 1980
Embryo-larva			
Static test	LC-50 (28 d)	4.7	Birge et al. 1979
Flowthrough test	LC-50 (28 d)	<0.1	Birge et al. 1979
Channel catfish, *Ictalurus punctatus*			
Embryo-larva			

Static test	LC-50 (10 d)	30.0	Birge et al. 1979
Flowthrough test	LC-50 (10 d)	0.3	Birge et al. 1979
Largemouth bass, *Micropterus salmoides*			
Embryo-larva			
Static test	LC-50 (8 d)	140.0	Birge et al. 1979
Flowthrough test	LC-50 (8 d)	5.3	Birge et al. 1979
Brook trout, *Salvelinus fontinalis*	LC-50 (LT)	0.3–0.9	EPA 1980
Fish, *Notopterus notopterus*	LC-50 (96 h)	440.0	Verma and Tonk 1983
Amphibians			
Narrow-mouthed toad, *Gastrophryne carolinensis*			
Embryo-larva	LC-50 (96 h)	1.3	Birge et al. 1979
Treefrogs, *Hyla* spp.			
Embryo-larva, 5 spp.	LC-50 (96 h)	2.4–2.8	Birge et al. 1979
Leopard frog, *Rana pipiens*			
Embryo-larva	LC-50 (96 h)	7.3	Birge et al. 1979
Cricket frog, *Acris* sp.			
Embryo-larva	LC-50 (96 h)	10.4	Birge et al. 1979
Anurans, 4 spp.			
Embryo-larva	LC-50 (96 h)	36.8–67.2	Birge et al. 1979
Marbled salamander, *Ambystoma opacum*			
Embryo-larva	LC-50 (96 h)	107.5	Birge et al. 1979
Marine			
Protozoans			
Ciliate, *Uronema marinum*	LC-50 (24 h)	6.0	Parker 1979
Molluscs			
Softshell clam, *Mya arenaria*	LC-50 (168 h)	4.0	Eisler and Hennekey 197
Hardshell clam, *Mercenaria mercenaria*			
Larva	LC-50 (48 h)	4.8	EPA 1980
Larva	LC-5 (9 d)	4.0	EPA 1980
American oyster, *Crassostrea virginica*			
Embryo	LC-5 (12 d)	3.3	EPA 1980
Larva	LC-50 (48 h)	5.6	EPA 1980
Adults	LC-50 (48 h)	5.5–10.2	EPA 1980
Blue mussel, *Mytilus edulis*	LC-50 (96 h)	5.8	EPA 1985
Slipper limpet, *Crepidula fornicata*			
Larva	LC-50 (96 h)	60.0	Thain 1984
Adults	LC-50 (96 h)	330.0	Thain 1984
Bay scallop, *Argopecten irradians*			
Juveniles	LC-50 (96 h)	89.0	Nelson et al. 1976
Crustaceans			

Fiddler crab, *Uca pugilator*			
Zoea	LC-50 (8 d)	1.8	EPA 1980
Mysid shrimp, *Mysidopsis bahia*			
Juveniles	LC-50 (96 h)	3.5	Gentile et al. 1983
Egg to egg	LC-50 (LT)	1.8	Gentile et al. 1983
Dungeness crab, *Cancer magister*			
Larva	LC-50 (96 h)	6.6	Glickstein 1978
Copepod, *Acartia tonsa*, adult	LC-50 (96 h)	10.0–15.0	EPA 1980
Prawn, *Penaeus indicus*			
Postlarva	LC-50 (48 h)	16.1	McClurg 1984
Postlarva	LC-50 (96 h)	15.3	McClurg 1984
Annelids			
Polychaete, *Capitella capitata*			
Larva	LC-50 (96 h)	14.0	EPA 1980
Fish			
Haddock, *Melanogrammus aeglifinus*			
Larvae	LC-50 (96 h)	98.0	EPA 1980
Organic Mercury			
Freshwater			
Planarians			
Flatworm, *Dugesia dorotocephala*			
Adult	LC-0 (10 d)	200.0	Best et al. 1981
Adult	LC-100 (5 d)	500.0	Best et al. 1981
Crustaceans			
Cladoceran, *Daphnia magna*	LC-50 (LT)	0.9–3.2	EPA 1980
Fish			
Rainbow trout			
Larva	LC-50 (96 h)	24.0	EPA 1980
Juvenile	LC-50 (96 h)	5.0–42.0	EPA 1980
Brook trout			
Yearling	LC-50 (96 h)	65.0	EPA 1980
Marine			
Crustaceans			
Amphipod, *Gammarus duebeni*	LC-50 (96 h)	150.0	EPA 1980

[a]Abbreviations: LT = lifetime exposure; h = hours; d = days.

BIRDS

Signs of mercury poisoning in birds included muscular incoordination, falling, slowness, fluffed feathers, calmness, withdrawal, hyporeactivity, hypoactivity, and eyelid drooping. In acute oral exposures, signs appeared as soon as 20 minutes postadministration in mallards and 2.5 hours in pheasants. Deaths occurred between 4 and 48 hours in mallards and 2 and 6 days in pheasants; remission took up to 7 days (Hudson et al. 1984). In studies with coturnix (*Coturnix coturnix coturnix*), (Hill 1981) found that methylmercury was always more toxic than inorganic mercury, and that young birds were usually more sensitive than older birds. Furthermore, some birds poisoned by inorganic mercury recovered after treatment was withdrawn, but chicks that were fed

methylmercury and later developed toxic signs usually died, even if treated feed was removed. Coturnix subjected to inorganic mercury, regardless of route of administration, showed a violent neurological dysfunction that ended in death 2 to 6 hours posttreatment. The withdrawal syndrome in coturnix poisoned by Hg 2^+ was usually preceded by intermittent, nearly undetectable tremors, coupled with aggressiveness towards cohorts; time from onset to remission was usually 3 to 5 days, but sometimes extended to 7 days. Coturnix poisoned by methylmercury appeared normal until 2 to 5 days posttreatment; then, ataxia and low body carriage with outstretched neck were often associated with walking. In advanced stages, coturnix lost locomotor coordination and did not recover; in mild to moderate clinical signs, recovery usually took at least 1 week (Hill 1981).

Mercury toxicity to birds varies with the form of the element, dose, route of administration, species, sex, age, and physiological condition (.Fimreite 1979). For example, in northern bobwhite chicks fed diets containing methylmercury chloride, mortality was significantly lower when the solvent was acetone than when it was another carrier such as propylene glycol or corn oil (Spann et al. 1986). In addition, organomercury compounds interact with elevated temperatures and pesticides, such as DDE and parathion, to produce additive or more-than-additive toxicity, and with selenium to produce less-than-additive toxicity (*Fimreite* 1979). Acute oral toxicities of various mercury formulations ranged between 2.2 and about 31.0 mg/kg body weight for most avian species tested (Table 8). Similar data for other routes of administration were 4.0 to 40.0 mg/kg for diet and 8.0 to 15.0 mg/kg body weight for intramuscular injection (Table 8).

Residues of mercury in experimentally poisoned passerine birds usually exceeded 20 mg/kg fresh weight, and were similar to concentrations reported in wild birds that died of mercury poisoning (Finley et al. 1979). Mercury levels in tissues of poisoned wild birds were highest (45 to 126 mg/kg fresh weight) in red-winged blackbirds (*Agelaius phoeniceus*), intermediate in starlings (*Sturnus vulgaris*) and cowbirds (*Molothrus ater*), and lowest (21 to 54) in grackles (*Quiscalus quiscula*); in general, Hg residues were highest in the brain, followed by the liver, kidney, muscle, and carcass. Some avian species are more sensitive than passerines (Solonen and Lodenius 1984): liver residues (in mg Hg/kg dry weight) in birds experimentally killed by methylmercury ranged from 17 in red-tailed hawks (*Buto jamaicensis*) to 70 in jackdaws (*Corvus monedula*); and values were intermediate in ring-necked pheasants, kestrels (*Falco tinnunculus*), and magpies (*Pica pica*). Experimentally poisoned grey herons (*Ardea cinerea*) seemed to be unusually resistant to Hg; lethal doses produced residues of 415 to 752 mg Hg/kg dry weight of liver (Van der Molen et al. 1982). However, levels of this magnitude were frequently encountered in livers from grey herons collected during a massive die-off in the Netherlands during a cold spell in 1976; the interaction effects of cold stress, mercury loading, and poor physical condition of the herons are unknown ((*Ardea cinerea*) in the Netherlands. Ardea 70:173-184Van der Molen et al. 1982).

Table 8. Toxicity to birds of mercury administered by oral, dietary, or other routes.

Route of administration (units), organism, and mercury formulation	Concentration	Exposure interval	Effect	Reference[a]
Acute oral (mg Hg/kg body weight)				
Chukar, *Alectoris chukar*				
Ethyl	26.9	Within 14 d posttreatment	LD-50	Hudson et al. 1984
Mallard, *Anas platyrhynchos*				
Methyl	2.2–23.5	"	LD-50	
Ethyl	75.7	"	LD-50	
Phenyl	524.7	"	LD-50	
Northern bobwhite, *Colinus virginianus*				

Methyl	23.8	"	LD-50	
Coturnix, *Coturnix coturnix coturnix*				
Methyl	11.0–27.0	"	LD-50	Hill 1981
Inorganic	26.0–54.0	"	LD-50	
Japanese quail, *Coturnix japonica*				
Methyl	14.4–33.7	"	LD-50	Hill and Soares 1984; Hudson et al. 1984
Ethyl	21.4	"	LD-50	Hudson et al. 1984
Inorganic	31.1	"	LD-50	Hill and Soares 1984
Rock dove, *Columba livia*				
Ethyl	22.8	"	LD-50	Hudson et al. 1984
Fulvous whistling duck, *Dendrocygna bicolor*				
Methyl	37.8	"	LD-50	
Domestic chicken, *Gallus domesticus*				
Phenyl	60.0	"	LD-50	Mullins et al. 1977
House sparrow, *Passer domesticus*				
Methyl	12.6–37.8	Within 14 d posttreatment	LD-50	Hudson et al. 1984
Gray partridge, *Perdix perdix*				
Ethyl	17.6	"	LD-50	
Ring-necked pheasant, *Phasianus colchicus*				
Ethyl	11.5	"	LD-50	
Methyl	11.5–26.8	"	LD-50	
Phenyl	65.0–101.0	"	LD-50	Mullins et al. 1977; Hudson et al. 1984
Prairie chicken, *Tympanuchus cupido*				
Ethyl	11.5	"	LD-50	Hudson et al. 1984

Dietary (mg Hg/kg diet)				
Coturnix				
Inorganic	32.0	Hatch-9 weeks	LD-0	Hill 1981
Inorganic	2,956–5,086	5 d + 7 d pt	LD-50	
Methyl	4.0	Hatch-9 weeks	LD-0	
Methyl	8.0	5 d	Some deaths	Hill and Soares 1984
Methyl	31.0–47.0	5 d + 7 d pt	LD-50	Hill 1981
Ring-necked pheasant				
Ethyl	4.2	70 d	LD-0[b]	Spann
Ethyl	12.5	70 d	LD-50	et al. 1972
Ethyl	37.4	28 d	LD-50	
Ethyl	112.0	15 d	LD-50	
Japanese quail				
Inorganic				
In dry salt	500	28 d	LD-86	El-Begearmi
In ethanol, methanol, or water	500	28 d	LD-55	et al. 1980
In casein premix	500	28 d	LD-33	
Birds, 4 spp.				
Methyl	40.0	6 to 11 d	LD-33	Finley et al. 1979
Intramuscular injection (mg Hg/kg body weight)				
Coturnix				
Methyl	8.0–33.0	Single dose	LD-50	Hill 1981
Inorganic	15.0–50.0	Single dose	LD-50	
Rock dove				
Inorganic	10.0	Daily, 17 d	Some deaths	Leander et al. 1977
Yolk sac injection (ug Hg/egg)				
Chicken				
Methyl	15.0	Single dose	Some deaths	Greener and Kochen 1983
Methyl	40.0-50.0	Single dose	LD-50	
Applied to Egg Surface ug Hg/egg				
Mallard				
Methyl	3.0	Single dose	LD-0	Hoffman and
Methyl	9.0	Single dose	Some deaths	Moore 1979

In drinking water (mg Hg/L)				
Chicken				
Inorganic	500.0	3 d	Some deaths	Grissom and Thaxton 1985

[a]Reference cited applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

[b]Reduction in egg production, 55% to 80%; embryonic survival sharply reduced.

Table 9. Toxicity of organomercury compounds to selected mammalian species.

Organism	Dose, route of administration, and other variables	Effects	Reference
Dog, *Canis familiaris*	0.1 to 0.25 mg/kg body weight during entire pregnancy; oral route	High incidence of stillbirths	Khera 1979
Cat, *Felis domesticus*	0.25 mg/kg body weight daily for 90 days (total 80–90 mg Hg); dietary route	Mean survival time 78 days. Convulsions starting at day 68; all with signs by day 90. Liver residues of survivors were 40.2 and 18.1 mg/kg fresh weight for total mercury and inorganic mercury, respectively	Eaton et al. 1980
Pig, *Sus* spp.	0.5 mg/kg body weight during pregnancy; oral route	High incidence of stillbirths	Khera 1979
Rhesus monkey, *Macaca mulatta*	0.5 mg/kg body weight during days 20–30 of pregnancy	Maternally toxic, and abortient	Khera 1979
Mink, *Mustela vison*	1.0 mg/kg in diet	Fatal to 100% in about 2 months 2 months	Sheffy and St. Amant 1982
River otter,	>2.0 mg/kg in diet	Fatal	Kucera 1983

Lutra canadensis			
Mink	5.0 mg/kg in diet	All dead in 30 to 37 days. Elevated residues in kidney (37.7 mg/kg fresh weight) and liver (55.6) prior to death	Sheffy and St. Amant 1982
Humans	Various	Lethal residues in tissues, in mg/kg fresh weight, were >6.0 in brain, >10.0 in liver, and >17.0 in whole body	Khera 1979
Mule deer, *Odocoileus hemionus hemionus*	17.88 mg/kg body weight; single oral dose	LD-50	Hudson et al. 1984
Harp seal, *Pagophilus groenlandicus*	25.0 mg/kg body weight daily; oral route	Dead in 20 to 26 days. Blood Hg levels just before death were 26.8 to 30.3 mg/L	Ronald et al. 1977

MAMMALS

Methylmercury affects the central nervous system in man--especially the sensory, visual, and auditory areas concerned with coordination; the most severe effects lead to widespread brain damage, resulting in mental derangement, coma, and death (Clarkson and Marsh 1982). In mule deer (*Odocoileus hemionus hemionus*), after acute oral Hg poisoning was induced experimentally, additional signs included belching, bloody diarrhea, piloerection (hair more erect than usual), and loss of appetite (Hudson et al. 1984). The kidney is the probable critical organ in adult mammals due to the rapid degradation of phenylmercurials and methoxyethylmercurials to inorganic Hg compounds and subsequent translocation to the kidney (Suzuki 1979), whereas in the fetus the brain is the principal target (Khera 1979). Most human poisonings were associated with organomercury compounds used in agriculture as fungicides to protect cereal seed grain (Elhassani 1983); judging from anecdotal evidence, many wildlife species may have been similarly afflicted. Organomercury compounds, especially methylmercury, were the most toxic mercury species tested. Among sensitive species of mammals, death occurred at daily organomercury concentrations of 0.1 to 0.5 mg/kg body weight, or 1.0 to 5.0 mg/kg in the diet (Table 9). Larger animals such as mule deer and harp seals appear to be more resistant to Hg than smaller mammals such as mink, cats, dogs, pigs, monkeys, and river otters; the reasons for this difference are unknown, but may be related to differences in metabolism and detoxication rates. Tissue residues in fatally poisoned mammals (in mg Hg/kg fresh weight) were 6.0 in brain, 10.0 to 55.6 in liver, 17.0 in whole body, about 30.0 in blood, and 37.7 in kidney (Table 9).

OTHER GROUPS

Methylmercury compounds at concentrations of 25.0 mg Hg/kg in soil were fatal to all tiger worms (*Eisenia foetida*) in 12 weeks; at 5.0 mg/kg, however, only 21% died in a similar period (Beyer et al. 1985). Inorganic mercury compounds were also toxic to earthworms (*Octochaetus pattoni*); in 60 days, 50% died at soil Hg levels of 0.79 mg/kg, and all died at 5.0 mg/kg (Abbasi and Soni 1983).

SUBLETHAL EFFECTS

GENERAL

Mercury is a known mutagen, teratogen, and carcinogen. At comparatively low concentrations in birds and mammals, it adversely affects reproduction, growth and development, behavior, blood and serum chemistry, motor coordination, vision, hearing, histology, and metabolism. It has a high potential for bioaccumulation and biomagnification, and is slow to depurate. Organomercury compounds were more effective in producing adverse effects than were inorganic Hg compounds; however, effects were significantly enhanced or ameliorated by numerous biotic and nonbiological modifiers. For sensitive aquatic species, adverse effects were observed at water concentrations of 0.03 to 0.1 ug Hg/l. For sensitive species of birds, harmful levels were 640 ug Hg/kg body weight daily, or 50 to 500 ug Hg/kg in the diet; for sensitive mammals, these levels were 250 ug Hg/kg body weight daily, or 1,100 ug Hg/kg diet.

AQUATIC ORGANISMS

Mercury at comparatively low concentrations adversely affects the reproduction, growth, behavior, metabolism, blood chemistry, osmoregulation, and oxygen exchange of marine and freshwater organisms. In general, the accumulation of mercury by aquatic biota is rapid, and depuration is slow. It is emphasized that organomercury compounds, especially methylmercury, were significantly more effective than inorganic mercury compounds in producing adverse effects and accumulations.

Reproduction was inhibited among sensitive species of aquatic organisms at water concentrations of 0.03 to 1.6 ug Hg/l. In the planarian (Best et al. 1981); in the slipper limpet (*Crepidula fornicata*), spawning was delayed and fecundity was decreased at 0.25 ug Hg^{2+}/l (Thain 1984); in the zebrafish (*Brachydanio rerio*), hatching success was reduced at 0.1 ug Hg^{2+}/l and egg deposition was reduced at 0.8 ug/l (Armstrong 1979); fathead minnows (*Pimephales promelas*) exposed to 0.12 ug methylmercury/l for 3 months failed to reproduce (Birge et al. 1979); the leopard frog (*Rana pipiens*) did not metamorphose during exposure to 1.0 ug methylmercury/l for 4 months (EPA 1980); and in the mysid shrimp (*Mysidopsis bahia*), the abortion rate increased and population size decreased after lifetime (i.e., 28 days) exposure to 1.6 ug/l of mercury as mercuric chloride (Gentile et al. 1983). For sensitive marine invertebrates such as hydroids, protozoans, and mysid shrimp, reproduction was inhibited at concentrations between 1.1 and 2.5 ug Hg^{2+}/l; this range was 5 to 71 ug/l for more resistant species of marine invertebrates (Gentile et al. 1983).

Reduced growth of sensitive species of aquatic organisms has been recorded at water concentrations of 0.04 to 1.0 ug Hg/l. The rainbow trout (*Salmo gairdneri*) was the most sensitive species tested; growth reduction was observed after 64 days in 0.04 ug Hg/l as methylmercury, or 0.11 ug Hg/l as phenylmercury (EPA 1980). In adults of the marine mollusc *Crepidula fornicata*, growth was reduced after 16 weeks in 0.25 ug Hg^{2+}/1 (Thain 1984). Growth inhibition was recorded in freshwater algae after exposure of 24 hours to 10 days to 0.3 to 0.6 ug organomercury/l, in brook trout (*Salvelinus fontinalis*) alevins after exposure for 21 days to 0.79 ug organomercury/l (EPA 1980), and in the marine alga *Scripsiella faeroense* exposed to 1.0 ug Hg^{2+}/l for 24 hours (Kayser 1976).

Adverse effects of mercury to aquatic organisms, in addition to those listed on reproduction and growth, have been documented at water concentrations of 0.88 to 5.0 ug/l: enzyme disruption in brook trout (*Salvelinus fontinalis*) embryos immersed for 17 days in solutions containing 0.88 ug/l, as methylmercury (EPA 1980); an increased incidence of frustule abnormalities and burst thecae in two species of marine algae during exposure to 1.0 ug Hg^{2+}/l for 24 hours (Kayser 1976; Saboski 1977); arrested development of sea urchin larvae at 3.0 ug Hg^{2+}/l for 40 hours (EPA 1980); decreased rate of intestinal transport of glucose, fructose, glycine, and

tryptophan in the murrel (*Channa punctatus*) at 3.0 ug Hg^{2+}/l for 30 days (Sastry et al. 1982); altered blood chemistry in striped bass (*Morone saxatilis*) at 5.0 ug Hg^{2+}/l in 60 days (Dawson 1982); and decreased respiration in striped bass 30 days postexposure after immersion for 30 to 120 days in 5.0 ug Hg^{2+}/l (Armstrong 1979; EPA 1980). In marine molluscs exposed to water concentrations of 6 to 10 ug Hg^{2+}/l for 96 hours, the feeding of adults ceased and the swimming rate of larval stages declined (Thain 1984). At 44 ug Hg^{2+}/l for 30 days, the freshwater fish *Notopterus notopterus* showed generalized metabolic derangement (Verma and Tonk 1983). In freshwater planarians exposed to 80 to 100 ug/l as methylmercury, behavior was modified and regeneration retarded (Best et al. 1981). And at high sublethal concentrations of methylmercury, rainbow trout were listless and darkly pigmented; appetite was reduced, and digestion was poor (Rodgers and Beamish 1982).

At lower trophic levels, the efficiency of mercury transfer was low through natural aquatic food chains; however, in animals of higher trophic levels, such as predatory teleosts and fish-eating birds and mammals, the transfer was markedly amplified (Eisler 1978, 1981).

High uptake and accumulation of mercury from the medium by representative species of marine and freshwater teleosts and invertebrates have been documented (Kopfler 1974; Eisler 1978, 1981; Birge et al. 1979; Huckabee et al. 1979; EPA 1980, EPA. 1985; Stokes et al. 1981; Rodgers and Beamish 1982; Hirota et al. 1983; Clarkson et al. 1984; McClurg 1984; Niimi and Lowe-Jinde 1984; Ramamoorthy and Blumhagen 1984; Ribeyre and Boudou 1984; Thain 1984). Accumulation patterns were enhanced or significantly modified by numerous biological and abiotic factors (NAS 1978; Eisler 1978, 1981, 1984, 1985; EPA 1980, 1985; Stokes et al. 1981;Rodgers and Beamish 1982; Clarkson et al. 1984; Ramamoorthy and Blumhagen 1984; Ribeyre and Boudou 1984). In general, the accumulation of mercury was markedly enhanced at elevated water temperatures, reduced water salinity or hardness, reduced water pH, increased age of the organism, and reduced organic matter content of the medium; in the presence of zinc, cadmium, or selenium in solution; after increased duration. of exposure; and in the presence of increased nominal concentrations of protein-bound mercury. Uptake patterns were significantly modified by sex, sexual condition, prior history of exposure to Hg salts, the presence of complexing and chelating agents in solution, dietary composition, feeding niche, tissue specificity, and metabolism; however, trends were not consistent between species and it is difficult to generalize. In one example, Ribeyre and Boudou (1984) immersed rainbow trout in solutions containing 0.1 ug Hg/l, as methylmercury: after 30 days, bioconcentration factors (BCF) ranged from 28,300 for brain to 238,000 for spleen; values were intermediate for muscle (30,000), whole fish (36,000), blood (102,000), liver (110,000), kidney (137,000), and gill (163,000). The values may have been higher if exposure had extended beyond 30 days; Rodgers and Beamish (1982) showed that whole body Hg residues in rainbow trout subjected to mercury insult continued to increase for the first 66 days before stabilizing. When mercury was presented as inorganic mercuric ion at 0.1 ug/l for 30 days, BCF values were usually lower than in trout exposed to methylmercury: 2,300 for muscle; 6,800 for brain; 7,000 for whole trout; 14,300 for blood; 25,000 for liver; 53,000 for kidney; 68,600 for gill; and 521,000 for spleen (Ribeyre and Boudou 1984). The high BCF values recorded for rainbow trout were probably due to efficient uptake from water, coupled with slow depuration (Rodgers and Beamish 1982). Whole body levels up to 100 mg Hg/kg were reportedly not lethal to rainbow trout, although 20 to 30 mg/kg were associated with reduced appetite, loss of equilibrium, and hyperplasia of gill epithelium (Niimi and Lowe-Jinde 1984). However, brook trout showed toxic signs and death at whole body residues of only 5 to 7 mg/kg (Armstrong 1979). In another example, the marine copepod *Acartia clausi*, subjected to 0.05 ug/l of mercury and higher, reached equilibrium with the medium in only 24 hours. In that study (Hirota et al. 1983), BCF values for whole *Acartia* after 24-hour exposures were 14,360 for inorganic mercuric ion (0.05 ug/l) and, for methylmercury, 179,200 (0.05 ug/l) and 181,000 (0.1 ug/l).

Elimination of accumulated mercury, both organic and inorganic, from aquatic organisms is a complex multicompartmental process, but appears to be largely dependent on its rate of biological assimilation. This rate, in turn, varies widely (20% to 90%) between species, for reasons as yet unexplained (NAS 1978). For example, mercury associated with dietary components that are not assimilated is eliminated rapidly with feces. The rest is absorbed across the gut and incorporated into tissues. This assimilated fraction of mercury is depurated much more slowly, at a rate positively correlated with the organism's metabolism (NAS 1978; Rodgers and Beamish 1982). Time to eliminate 50% of biologically assimilated mercury and its compounds (Tb 1/2) is variable. Among various species of freshwater teleosts, Tb 1/2 values (in days) were 20 for guppies

Poecilia reticulatus, 23 for goldfish *Carassius auratus*, 100 for northern pike, and 1,000 each for mosquitofish *Gambusia affinis*, brook trout, and rainbow trout (Huckabee et al. 1979). similar range in. Tb 1/2 values was recorded for invertebrates and marine fishes: 297 days for the crayfish *Astacus fluviatilis*, 435 days for mussel, 481 days for the clam *Tapes decussatus* 1,030 days for the eel *Anguilla vulgaris*, and 1,200 days for the flounder *Pleuronectes flesus* (NAS 1978).

Mercury-tolerant strains of bacteria (Colwell et al. 1976), protozoa (Berk et al. 1978), crustaceans (Green et al. 1976; Weis 1976), and fish (Weis 1984) have been reported. It has been suggested that the mercury-resistant strains of bacteria that have been cultured or discovered may have application in mobilization or fixation of mercury from contaminated aquatic environments to the extent that polluted areas may become innocuous (Colwell et al. 1976). The marine protozoan *Uronemia nigricans*, after feeding on Hg-laden bacteria, acquired mercury tolerance within a single generation (Berk et al. 1978). The white shrimp (*Penaeus setiferus*), preexposed for 57 days to 1 ug Hg/l, did not differ from controls during either exposure or subsequent Hg stress experiments (Green et al. 1976); this observation suggested that nonsensitization or adaptation mechanisms are involved. The fiddler crab (*Uca pugilator*) seemed unusually resistant and showed negligible uptake or effects during exposure to 100 ug Hg/l for 2 weeks (Weis 1976). Reasons to account for Hg adaptation of the estuarine cyprinodontiform teleost *Fundulus heteroclitus* to both methylmercury and inorganic mercury are under investigation (Weis 1984).

BIRDS

Sublethal effects of mercury on birds, administered by a variety of routes, included adverse effects on growth, development, reproduction, blood and tissue chemistry, metabolism, and behavior; histopathology and bioaccumulation were also noted.

The dietary route of administration is the most extensively studied pathway of avian Hg intake. Domestic chickens fed diets containing as little as 50 ug/kg of mercury, as methylmercury, contained elevated total Hg (2.0 mg/kg fresh weight) residues in liver and kidney after 28 weeks; at 150 ug/kg, residues ranged from 1.3 to 3.7 mg/kg in heart, muscle, brain, kidney, and liver, in that general order; at 450 ug/kg in diets, residues in edible chicken tissues (3.3 to 8.2 mg/kg) were considered hazardous to human consumers, although no overt signs of mercury toxicosis were observed in the chickens (March et al. 1983). High inorganic mercury levels (500 mg/l) in drinking water of chickens decreased growth rate and food and water consumption, and elevated hemoglobin, hematocrit, and erythrocyte content within 3 days (Grissom and Thaxton 1985). The dietary concentration of 0.5 mg Hg/kg dry weight (equivalent to about 0.1 mg/kg fresh weight) in the form of methylmercury was fed to three generations of mallards (Heinz 1979). Females laid a greater percentage of their eggs outside nest boxes than did controls, and also laid fewer eggs and produced fewer ducklings. Ducklings from parents fed methylmercury were less responsive than controls to tape-recorded maternal calls, but were hyperresponsive to a fright stimulus in avoidance tests. The tissues and eggs of ducks and other species of birds collected in the wild have sometimes contained levels of mercury equal to, or far exceeding, those associated with reproductive and behavioral deficiencies in domestic mallards (e.g., 9 to 11 mg/kg in feathers; >2.0 mg/kg in other tissues); therefore, it is possible that reproduction and behavior of wild birds have been modified by methylmercury contamination (Heinz 1979). Tissue mercury residues of wild-strain mallards and game-farm mallards were not significantly different after the birds were fed diets containing 0.5 mg Hg/kg as methylmercury for extended periods--indicating that game-farm mallards are suitable substitutes for wild mallards in toxicological evaluations (Heinz 1980). Dietary concentrations of 1.1 mg total Hg/kg have been associated with kidney lesions in juvenile starlings (*Sturnus vulgaris*) and with elevated residues in the liver (6.5 mg/kg dry weight and kidney (36.3 mg/kg), after exposure for 8 >weeks (Nicholson and Osborn 1984). In American black ducks (*Anas rubripes*) fed diets containing 3.0 mg Hg/kg as methylmercury for 28 weeks, reproduction was significantly inhibited; tissue residues were elevated in kidney (16.0 mg/kg fresh weight) and liver (23.0 mg/kg); and brain lesions characteristic of mercury poisoning were present (Finley and Stendell 1978). Japanese quail (*Coturnix japonica*) fed diets containing 8 mg Hg/kg of inorganic mercury for 3 weeks had depressed gonad weights; those fed 3 mg/kg inorganic mercury or 1 mg/kg methylmercury for 9 weeks showed alterations in brain and plasma enzyme activities (Hill and Soares 1984). Grossly elevated tissue residues of 400 mg/kg in feathers and 17 to 130 mg/kg in other tissues were measured in gray partridge (*Perdix perdix*) after dietary exposure of 20 to 25 mg total Hg/kg for 4 weeks (McEwen et al. 1973).

Mercury exposure by immersion and oral administration have caused reproductive and behavorial modifications. Brief immersion of mallard eggs in solutions of methylmercury resulted in a significant incidence of skeletal embryonic aberrations at dosages of 1.0 ug Hg/egg, and higher; no increases in embryonic malformations were noted at 0.3 ug Hg/egg (Hoffman and Moore 1979). Reduced reproductive ability was noted in grey pheasants ingesting 640 ug Hg (as organomercury)/kg body weight daily for 30 days (McEwen et al. 1973); similar results were observed in ring-necked pheasants (Spann et al. 1972; Mullins et al. 1977). Behavioral alterations were noted in pigeons (*Columba livia*) given 3,000 ug inorganic Hg/kg body daily for 17 days (Leander et al. 1977) or 1,000 ug/kg body weight of methylmercury for 5 weeks (Evans et al. 1982). Observed behavioral changes in posture and motor coordination of pigeons were permanent after the brain accumulated >12,000 ug Hg/kg fresh weight, and were similar to the "spastic paralysis" observed in wild crows during the Minamata, Japan, outbreak of the 1950's, although both species survived for years with these signs (Evans et al. 1982).

Mercury residues of 790 to 2,000 ug/kg in egg, and 5,000 to 40,000 ug/kg in feathers, are linked to impaired reproduction in various bird species (Spann et al. 1972; NAS 1978; Heinz 1979; Fimreite 1979; Solonen and Lodenius 1984). Residues in eggs of 1,300 to 2,000 ug Hg/kg fresh weight were associated with reduced hatching success in white-tailed sea-eagles (*Haliaeetus albicilla*), the common loon (*Gavia immer*), and in several seed-eating species (Fimreite 1979); this range was 900 to 3,100 ug/kg for ring-necked pheasant (Spann et al. 1972), and 790 to 860 ug/kg for mallards (Heinz 1979). Residues of 5,000 to 11,000 ug Hg/kg in feathers of various species of birds have been associated with reduced hatch of eggs and with sterility (NAS 1978). Sterility was observed in the Finnish sparrow hawk (*Accipiter nisus*) at mercury concentrations of 40,000 ug/kg in feathers (Solonen and Lodenius 1984). Chicks of the common tern (*Sterna hirundo*) from a colony in Long Island, New York, with abnormal feather loss, had significantly elevated mercury levels in blood and liver (Gochfeld 1980); however, the linkage of feather loss to mercury contamination requires further examination.

Interaction effects of mercury with other contaminants, such as herbicides and pesticides, could intensify hazards to avian populations (Mullins et al. 1977). For example, a striking parallel exists between levels of Hg and of DDT and its metabolites in birds of prey, suggesting the existence of common ecotoxicological mechanisms (Delbeke et al. 1984; Wiemeyer et al. 1984); additional research is clearly needed.

MAMMALS

Mercury has no known physiological function (EPA 1985). In humans and other mammals, it causes teratogenic, mutagenic, and carcinogenic effects; the fetus is the most sensitive life stage (NAS 1978; Chang 1979; Khera 1979; EPA 1980, 1985; Elhassani 1983; Greener and Kochen 1983; Clarkson et al. 1984). Methylmercury irreversibly destroys the neurons of the central nervous system. Frequently, a substantial latent period intervenes between the cessation of exposure to Hg and the onset of signs and symptoms; this interval is usually measured in weeks or months, but sometimes in years (Clarkson et al. 1984). At high sublethal doses in man, mercury causes cerebral palsy, gross motor and mental impairment, speech disturbances, blindness, deafness, microcephaly, intestinal disturbances, tremors, and tissue pathology (Chang 1979; EPA 1980, 1985; Elhassani 1983; Clarkson et al. 1984). Pathological and other effects of Hg may vary from organ to organ, depending on factors such as the effective toxic dose in the organ, the compound involved and its metabolism within the organ, the duration of exposure, and the other contaminants to which the animal is concurrently exposed (Chang 1979). Many compounds--especially salts of selenium--protect humans and other animals against mercury toxicity, although their mode of action is not clear (NAS 1978; Chang 1979; EPA 1980, 1985; Eisler 1985).

Adverse effects of organomercury compounds to selected species of mammals have been recorded at administered doses of 0.25 mg Hg/kg body weight daily, dietary levels of 1.1 mg/kg, and blood Hg levels of 1.2 mg/l (Table 10).

Mercury transfer and biomagnification through mammalian food chains is well documented (Galster 1976; NAS 1978; Eaton et al. 1980; Eisler 1981; Huckabee et al. 1981; Sheffy and St. Amant 1982; Kucera 1983; Clarkson et al. 1984; Wren 1986), but considerable variation exists. Among terrestrial mammals, for example, herbivores such as mule deer, moose (*Alces alces*), caribou (*Rangifer tarandus*), and various species of rabbits usually contained less than 1.0 mg Hg/kg fresh weight in liver and kidney, but carnivores such as the marten (*Martes martes*), polecat (*Mustela putorius*), and red fox (*Vulpes vulpes*) frequently contained more than 30 mg/kg NAS 1978). The usually higher mercury concentrations in fish-eating furbearers than in herbivorous

species seemed to reflect the amounts of fish and other aquatic organisms in the diet. In river otter and mink from the Wisconsin River drainage system, Hg levels paralleled those recorded in fish, crayfish, and bottom sediments at that location. Highest Hg levels in all samples were recorded about 30 km downstream from an area that supported 16 pulp and paper mills and a chloralkali plant; residues were highest in the fur, followed by the liver, kidney, muscle, and brain (Sheffy and St. Amant 1982).

In marine mammals, more than 90 % of the mercury content is inorganic; however, enough methylmercury occurs in selected tissues to result in the accumulation of high tissue concentrations of methylmercury in humans and wildlife consuming such meat (Clarkson et al. 1984). The liver of the ringed seal (*Phoca hispida*) normally contains 27,000 to 187,000 ug Hg/kg fresh weight, and is a traditional and common food of the coastal Inuit people (Eaton et al. 1980). Although levels of Hg in hair (109,000 ug/kg) and blood (37 ug/l) of Inuits were grossly elevated, no symptoms of Hg poisoning were evident in the coastal Inuits. Similar high concentrations have been reported for Alaskan Eskimo mothers who, during pregnancy, ate seal oil twice a day, and seal- meat or fish from the Yukon-Kuskokwim Coast every day (Galster 1976). Despite the extremely high total Hg content of seal liver, only the small organomercury component was absorbed and appeared in the tissues. Cats fed a diet of seal liver (26,000 ug Hg/kg fresh weight) for 90 days showed no neurologic or histopathologic signs (Eaton et al. 1980). It seems that the toxic potential of seal liver in terms of accumulated tissue levels in cats (up to 862 ug total Hg/l blood, and 7,600 ug total Hg/kg hair) is better indicated by the organomercury fraction in seal liver than by the concentration of total Hg (Eaton et al. 1980).

Table 10. Sublethal effects of organomercury compounds administered to selected species of mammals.

Organism	Dose, and other variables	Effect	Reference
Rhesus monkey, *Macaca mulatta*	16 µg/kg body weight daily on days 20 to 30 of pregnancy	No measurable eff ect on reproduction	Khera 1979
Human, adult	50 µg/day	Risk of paresthesia, 0.3% (burning-prickling sensation of skin)	Clarkson et al. 1984
Human, adult	200 µg/day	Risk of paresthesia, 8%	Clarkson et al. 1984
Cat, *Felis domesticus*	250 µg/kg body weight daily on days 10 to 58 of gestation; oral route	Increased incidence of anomalous fetuses	Khera 1979
Harp seal, *Pagophilus groenlandicus*	250 µg/kg body weight daily for 90 days; dietary route	Residues of 47,200 to 82,500 µg/kg fresh weight in liver, kidney, and muscle; histopathology	Ronald et al. 1977; Ramprashad and Ronald 1977

		of middle ear	
Rat, *Rattus* sp.	500 µg/kg body weight daily; oral route	Reduced fertility	Khera 1979
Human, adult	1,000 µg/day	Risk of paresthesia, 50%	Clarkson et al. 1984
Mink, *Mustela vison*	1,100 µg/kg in diet	Residues of 7,100 to 9,300 µg/kg in brain; signs of poisoning	Kucera 1983
Rat	2,000 µg/kg in diet (as Pacific blue marlin); gestation through post-natal day 16	Adverse behavioral changes in offspring	Suzuki 1979
Rat	13,300 to 50,000 µg/kg body weight daily for 5 days; subcutaneous injection	Impaired cutaneous sensitivity and hearing up to one year post-treatment	Wu et al. 1985
Monkeys, *Macaca* spp.	Various	Visual disturbances at blood Hg levels of 1,200 to 4,000 µg/L or brain Hg levels of 6,000 to 9,000 µg/kg; tremors at blood Hg levels of 2,000 to 10,000 µg/L; kidney pathology at brain Hg levels of 1,500 µg/kg	Suzuki 1979
Human, adult	Various	Symptoms of poisoning evident at residues of 1,200 µg Hg/L blood, 2,000 to 3,000 µg/kg whole body, or 3,400 µg/kg hair	Suzuki 1979

Mice, *Mus* spp.	Various	Residues of 2,000 to 5,000 µg/kg hair or >10,000 µg/kg brain associated with motor incoordination and decreased swimming ability; no observable effect at <2,000 µg/kg hair	Suzuki 1979
Human, infant	Various	Severe effects at blood Hg levels of 3,000 µg/L	Elhassani 1983

Retention of mercury by mammalian tissues is longer for organomercury compounds (especially methylmercury) than for inorganic mercury compounds (NAS 1978; Clarkson and Marsh 1982; Elhassani 1983; Clarkson et al. 1984). Excretion of all Hg species follows a complex, variable, multicompartmental pattern; the longer-lived chemical Hg species have a biological half-life that ranges from about 1.7 days in human lung to 1.36 years in whole body of various pinnipeds.

OTHER GROUPS

Methylmercury compounds have induced abnormal sex chromosomes in the fruit fly (*Drosophila melanogaster*) (NAS 1978; Khera 1979). Earthworms (*Eisenia foetida*) exposed to soil containing methylmercury concentrations of 5.0 mg Hg/kg--typical of soil Hg levels near chloralkali plants--showed a significant reduction in the number of segments regenerated after 12 weeks, and contained 85 mg Hg/kg on a whole body fresh weight basis. Regeneration was normal at soil Hg levels of 1.0 mg/kg, although body burdens up to 27 mg/kg were recorded. It was concluded that soil contaminated with methylmercury posed a greater hazard to the predators of earthworms than to the earthworms (Beyer et al. 1985). Studies with a different species of earthworm (*Octochaetus pattoni*) and mercuric chloride, demonstrated a progressive initial increase in reproduction as soil mercury levels increased from 0.0 to the 60-day lethal level of 5.0 mg/kg (Abbasi and Soni 1983).

CURRENT RECOMMENDATIONS

Proposed mercury criteria for the protection of sensitive aquatic organisms, birds, and mammals, as well as human health, are shown in Table 11. In almost every instance, these criteria are listed as concentrations of total Hg, with most, if not all, the Hg present as an organomercury species.

In 1980, the U.S. Environmental Protection Agency's proposed mercury criteria for freshwater aquatic life protection were 0.00057 ug/l (24-hour average), not to exceed 0.0017 ug/l at any time; these criteria seemed to afford a high degree of protection to freshwater biota, as judged by survival, bioconcentration, and biomagnification. Literature documented in this paper showed that mercury concentrations in water of 0.1 to 2.0 ug/l were fatal to sensitive aquatic species and that concentrations of 0.03 to 0.1 ug/l were associated with significant sublethal effects. The 1980 proposed freshwater criteria provided safety factors for acute toxicities of 175X to 3,508X based on the 24-hour average, and 58X to 1,176X based on the maximum permissible concentration (Table 11). For protection against sublethal effects, these values were 53X to 175X based on the 24-hour mean, and 18X to 59X based on the maximum permissible concentration (Table 11). However, the most current freshwater criteria of 0.012 ug/l, not to exceed 2.4 ug/l (Table 11; EPA 1985), dramatically reduces the level of protection afforded aquatic biota: safety factors for acute toxicities are now 8X to 167X based on the 96-hour average, and only 0.04X to 0.8X based on the maximum permissible concentration. For protection against sublethal effects, these values were 2X to 8X based on the 4-day average, and only 0.01X to 0.04X based on the maximum permissible concentration, or essentially no significant protection.

The proposed saltwater criteria of EPA (1980) for mercury and marine life were unsatisfactory. Proposed saltwater values of 0.025 ug/l (24-hour average), not to exceed 3.7 ug/l at any time (Table 11), provided safety factors of 4X to 80X against acute toxicity (based on 24-hour average), but less than 0.5X based on the maximum permissible level. For protection against sublethal damage effects, the safety factors computed were 1.2X to 4X (based on 24-hour average) and less than 0.03X (based on maximum allowable concentration). The most recent saltwater criteria of 0.025 ug/l, not to exceed 2.1 ug/l (Table 11; EPA 1985), does not appear to offer a substantive increase in protection to marine life, when compared to criteria proposed 5 years earlier (EPA 1980). It seems that some downward modification is needed in the proposed Hg saltwater criteria if marine and estuarine biota are to be provided even minimal protection.

Table 11. Proposed mercury criteria for protection of various resources and human health.

Resource and criterion (units in parentheses)	Mercury concentration	Reference
Aquatic life		
Freshwater (µg/L)	Total recoverable Hg <0.00057 (24 h average), not to exceed 0.0017 at any time	EPA 1980
	<0.012, 4-day average (not to be exceeded more than once every 3 years; <2.4, one-hour average (not to be exceeded more than once every 3 years)[a]	EPA 1985
Saltwater (µg/L)	Total recoverable Hg <0.025 (24 h average), not to exceed 3.7 at any time	EPA 1980
	<0.025, 4-day average (not to be exceeded more than once every 3 years); <2.1, one-hour average (not to be exceeded more than once every 3 years)[a]	EPA 1985
Freshwater (µg/L)		
Inland surface waters, India	<10.0 from point source discharge	Abbasi and Soni 1983
Fish (µg/kg fresh weight)		
Brook trout, *Salvelinus fontinalis*		

Whole body	<5,000	EPA 1980, 1985
Wildlife		
Birds		
Tissue residues (µg/kg fresh weight)		
Feather	<5,000	NAS 1978
Egg		
Mallard, *Anas platyrhynchos*	<900	Heinz 1979
Ring-necked pheasant, *Phasianus colchicus*	<900	Spann et al. 1972
Various species	1,300–2,000	Fimreite 1979
Diet (µg/kg fresh weight)	50 to <100	Heinz 1979; March et al. 1983
Daily dose (µg/kg body weight)		<640 Spann et al. 1972; McEwen et al. 1973; Mullins et al. 1977
Mammals		
Tissue residues (µg/kg fresh weight)		
Kidney	<1,100	EPA 1980
Blood	<1,200	Suzuki 1979
Brain	<1,500	Suzuki 1979
Hair		<2,000 Suzuki 1979
Diet (µg/kg fresh weight)	<1,100	Kucera 1979
Daily dosage (µg/kg body weight)	<250	Ramprashad and Ronald 1977; Ronald et al. 1977; Khera 1979
Human Health		
Tissue residues (µg/kg fresh weight)		
Blood	<200	Galster 1976
Hair		<6,000 Lodenius et al. 1983
Water (µg/L)		
Potable	<2.0	NAS 1978
Protection from toxic properties of Hg through consumption of contaminated aquatic organisms	<0.146	EPA 1980

Protection from toxic properties of Hg from ingestion of water plus consumption of resident aquatic organisms	<0.144	EPA 1980
Fish and seafood		
Acceptable intake (µg)		
Daily, 60 kg adult	25	Khera 1979
Weekly, 70 kg adult	200	Khera 1979
Weekly, adult	500	Lodenius et al. 1983
Pregnant women (µg/kg fresh weight)	<250	Khera 1979
Various locations (µg/kg fresh weight)		
Japan	<400	NAS 1978
Canada, West Germany, U.S.A.	<500	NAS 1978
Australia	<500 (mean), not to exceed 1,500 in any sample	Lyle 1984
Finland	<1,000	Lodenius et al. 1983
Scandinavia	<1,000	Suckcharoen and Lodenius 1983
Sweden	<1,000	NAS 1978
U.S.A.	<1,000	EPA 1980, 1985; Barber et al. 1984; Miller and Jude 1984
Foods of animal origin (µg/kg fresh weight)		
Livestock tissues	<500	Best et al. 1981
Wildlife tissues	<50	Krynski et al. 1982
Breast muscle		
Domestic poultry	<500	NAS 1978
Ducks (wildlife)	<1,000	Lindsay and Dimmick 1983
All foods		
Adult weekly intake (µg)		
As total Hg	<150	NAS 1978
As methylmercury	<100	NAS 1978
Various locations (µg/kg fresh weight)		
Australia	10 to 100	NAS 1978

Benelux countries	<30	NAS 1978
Brazil	<50	NAS 1978
Canada	<500	Bodaly et al. 1984
U.S.A.	<1,000	Bodaly et al. 1984

[a]All mercury that passes through a 0.45-mm membrane filter after the sample is acidified to pH 1.5 to 2.0 with nitric acid.

The significance of elevated Hg residues in tissues of aquatic organisms is not fully understood. Concentrations >1,000 ug Hg/kg fresh weight can occur in various tissues of selected species of fish and aquatic mammals eaten by humans. But it would be incorrect to assume that aquatic food chains--especially marine food chains--incorporate Hg exclusively from anthropogenic activities (Barber et al. 1984). Some organisms, however, do contain Hg tissue residues associated with known adverse effects to the organism and its predators. Thus, whole body residues of 5,000 to 7,000 ug Hg/kg fresh weight in brook trout eventually proved fatal to that species (EPA 1980). To protect sensitive species of mammals and birds that regularly consume fish and other aquatic organisms, total mercury concentrations in these food items should probably not exceed 100 ug/kg for avian protection, or 1,100 ug/kg for small mammals (Table 11). By comparison, proposed Hg levels in fish and seafood, in ug/kg fresh weight, for human health protection should not exceed 250 for expectant mothers, and 400 to 1,000 for adults worldwide (Table 11).

Since long-lived, slow-growing, high-trophic-positon aquatic organisms usually contain the highest tissue mercury residues, some fisheries managers have proposed a legal maximum limit based on fish length or body weight, or alternatively, constraining the mean Hg concentration of the entire catch to a nominated level. In the Australian shark fishery, for example, implementation of a maximum length restriction (to a nominated level of 500 ug Hg/kg), would result in retention of less than half of the present catch of seven species (Lyle 1984).

Among sensitive avian species, adverse effects--predominantly on reproduction--have been reported at mercury concentrations (in ug/kg fresh weight) of 5,000 in feather, 900 in egg, 50 to 100 in diet, and daily administered doses of 640 on a body weight basis (Table 11). Although low Hg concentrations--e.g., 50 ug/kg in the diets of domestic chickens--sometimes produced no adverse effects on chickens, the tissue residues of Hg were sufficiently elevated to pose a hazard to human consumers (March et al. 1983). In contrast, in eggs of the American bald eagle (with 150 ug Hg/kg and low hatch), other contaminants present--especially organochlorine compounds--probably had a greater effect on hatchability than did Hg (Wiemeyer et al. 1984).

Mammals, such as the domestic cat and the harp seal, showed birth defects, histopathology, and elevated tissue residues at doses of 250 ug Hg/kg body weight daily (Table 11). The mink, at dietary levels of 1,100 ug Hg/kg, had signs of mercury poisoning; Hg residues in mink brain at this dietary level ranged from 7,100 to 9,300 ug/kg (Kucera 1983). Tissue residues in kidney, blood, brain, and hair in excess of 1,100 ug Hg/kg in other nonhuman mammals are usually considered presumptive evidence of significant Hg contamination (Table 11).

At this point, it seems that four courses of action are warranted. First, toxic mercurials in agriculture and industry should be replaced by less toxic substitutes. Second, controls should be applied at the point of origin to prevent the discharge of potentially harmful Hg wastes. Third, continued periodic monitoring of fishery and wildlife resources is important, especially in areas with potential for reservoir development, in light of the hypothesis that increased flooding increases the availability of Hg to biota. And finally, additional research is needed on mercury accumulation and detoxication in comparatively pristine ecosystems.

LITERATURE CITED

Abbasi, S.A., and R. Soni. 1983. Stress-induced enhancement of reproduction in earthworms *Octochaetus pattoni* exposed to chromium (VI) and mercury (II) - implications in environmental management. Int. J. Environ. Stud. 22:43-47.

Abernathy, A.R., and P.M. Cumbie. 1977. Mercury accumulation by largemouth bass (*Micropterus salmoides*) in recently impounded reservoirs. Bull. Environ. Contam. Toxicol. 17:595-602.

Akielaszak, J.J., and T.A. Haines. 1981. Mercury in the muscle tissue of fish from three northern Maine lakes. Bull. Environ. Contam. Toxicol. 27:201-208.

Alexander, J.E., J. Foehrenbach, S. Fisher, and D. Sullivan. 1973. Mercury in striped bass and bluefish. N.Y. Fish Game J. 20:147-151.

Applequist, H., S. Asbirk, and I. Drabaek. 1984. Mercury monitoring: mercury stability in bird feathers. Mar. Pollut. Bull. 15:22-24.

Armstrong, F.A.J. 1979. Effects of mercury compounds on fish. Pages 657-670 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Augier, H., G. Gilles, and G. Ramonda. 1978. Recherche sur la pollution mercurielle du milieu maritime dans la region de Marseille (Mediterranee, France): 1, Degre de Contamination par le mercure de la phanerograme marine Posidonia oceanica delile a proximite du complexe portuaire et dans la zone de reject due grand collecteur disgouts de la ville de Marseille. Environ. Pollut. 17:269-285.

Bacher, G.J. 1985. Mercury concentrations in the Australian fur seal *Arctocephalus pusillus* from SE Australian waters. Bull. Environ. Contam. Toxicol. 35:490-495.

Barber, R.T., P.J. Whaling, and D.M. Cohen. 1984. Mercury in recent and century-old deep-sea fish. Environ. Sci. Technol. 18:552-555.

Beijer, K., and A. Jernelov. 1979. Methylation of mercury in natural waters. Pages 201-210 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Berk, S.G., A.L. Mills, D.L. Henricks, and R.R. Colwell. 1978. Effects of ingesting mercury containing bacteria on mercury tolerance and growth rate of ciliates. Microb. Ecol. 4:319-330.

Berman, M., and R. Bartha. 1986. Levels of chemical versus biological methylation of mercury in sediments. Bull. Environ. Contam. Toxicol. 36:401-404.

Best, J.B., M. Morita, J. Ragin, and J. Best, Jr. 1981. Acute toxic responses of the freshwater planarian, *Dugesia dorotocephala*, to methylmercury. Bull. Environ. Contam. Toxicol. 27:49-54.

Beyer, W.N., E. Cromartie, and G.B. Moment. 1985. Accumulation of methymercury in the earthworm, *Eisenia foetida*, and its effect on regeneration. Bull. Environ. Contam. Toxicol.-35:157-162.

Birge, W.J., J.A. Black, A.G. Westerman, and J.E. Hudson. 1979. The effect of mercury on reproduction of fish and amphibians. Pages 629-655 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Bodaly, R.A., R.E. Hecky, and R.J. P. Fudge. 1984. Increases in fish mercury levels in lakes flooded by the Churchill River diversion, northern Manitoba. Canad. J. Fish. Aquat. Sci. 41:682-691.

Boudou, A., D. Georgescauld, and J.P. Desmazes. 1983. Ecotoxicological role of the membrane barriers in transport and bioaccumulation of mercury compounds. Pages 117-136 *in* J.O. Nriagu (ed.). Aquatic toxicology. John Wiley, New York.

Boudou, A., and F. Ribeyre. 1983. Contamination of aquatic biocenoses by mercury compounds: an experimental toxicological approach. Pages 73-116 *in* J.O. Nriagu (ed.). Aquatic toxicology. John Wiley, New York.

Broo, B., and T. Odsjo. 1981. Mercury levels in feathers of eagle-owls *Bubo bubo* in a captive, a reintroduced and a native wild population in SW Sweden. Holarctic Ecol. 4:270-277.

Buhler, D.R. (ed.). 1973. Mercury in the western environment. Proceedings of a workshop, Portland, Oregon, February 25-26, 1971. Oregon State Univ., Corvallis. 360 pp.

Busch, W-D.N. 1983. Decline of mercury in young fishes from western Lake Erie between 1970-71 and 1974. Prog. Fish-Cult. 45:202-206.

Bycroft, B.M., B.A.W. Coller, G.B. Deacon, D.J. Coleman, and P.S- Lake. 1982. Mercury contamination of the Lerderderg River, Victoria, Australia, from an abandoned gold field. Environ. Pollut. 28A:135-147.

Callister, S.M., and H.R. Winfrey. 1986. Microbial methylation of mercury in upper Wisconsin River sediments. Water, Air, Soil Pollut. 29:453-465.

Cappon, C.J., and J.C. Smith. 1982. Chemical form and distribution of mercury and selenium in edible seafood. J. Anal. Toxicol. 6:10-21.

Chang, L.W. 1979. Pathological effects of mercury poisoning. Pages 519-580 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Chang, P.S.S., D.F. Malley, N.E. Strange, and J.F. Klaverkamp. 1981. The effects of low pH, selenium and calcium on the bioaccumulation of ^{203}Hg by seven tissues of the crayfish, *Orconectes virilis.* Canad. Tech. Rep. Fish. Aquat. Sci. 1151:45-67.

Chigbo, F.E., R.W. Smith, and F.L. Shore. 1982. Uptake of arsenic, cadmium, lead and mercury from polluted waters by the water hyacinth *Eichhornia crassipes*. Environ. Pollut. 27A:31-36.

Clarkson, T.W., R. Hamada, and L. Amin-Zaki. 1984. Mercury. Pages 285-309 *in* J.O. Nriagu (ed.). Changing metal cycles and human health. Springer-Verlag, Berlin.

Clarkson, T.W., and D.O. Marsh. 1982. Mercury toxicity in man. Pages 549-568 in A.S. Prasad (ed.). Clinical, biochemical, and nutritional aspects of trace elements, Vol. 6. Alan R. Liss, Inc., New York.

Colwell, R.R., G.S. Sayler, J.D. Nelson, Jr., and A. Justice. 1976. Microbial mobilization of mercury in the aquatic environment. Pages 437-487 *in* J.O. Nriagu (ed.). Environmental biogeochemistry, Vol. 2. Metals transfer and ecological mass balances. Ann Arbor Sci. Publ., Ann Arbor, Michigan.

Compeau, G., and R. Bartha. 1984. Methylation and demethylation of mercury under controlled redox, pH, and salinity conditions. Appl. Environ. Microbiol. 48:1202-1207.

Cooper, J.J. 1983. Total mercury in fishes and selected biota in Lahontan Reservoir, Nevada: 1981. Bull. Environ. Contam. Toxicol. 31:9-17.

Das, S.K., A Sharma, and G. Talukder. 1982. Effects of mercury on cellular systems in mammals - a review. Nucleus (Calcutta) 25:193-230.

Dawson, M.A. 1982. Effects of long-term mercury exposure on hematology of striped bass, *Morone saxatilis*. U.S. Natl. Mar. Fish. Serv., Fish. Bull. 80:389-392.

Delbeke, K., C. Joiris, and G. Decadt. 1984. Mercury contamination of the Belgian avifauna 1970-1981. Environ. Pollut. 7B:205-221.

D'Itri, F.M. 1972. Mercury in the aquatic ecosystem. Tech. Rep. 23, Inst. . Water Res., Michigan State Univ., Lansing. 101 pp.

D'Itri, P., and F.M. D'Itri. 1977. Mercury contamination: a human tragedy. John Wiley, New York. 311 pp.

Doi, R., H. Ohno, and M. Harada. 1984. Mercury in feathers of wild birds from the mercury-polluted area along the shore of the Shiranui Sea. Sci. Total Environ. 40:155-167.

Duncan, D.A., and J.F. Klaverkamp. 1983. Tolerance and resistance to cadmium in white suckers (*Catostomus commersoni*) previously exposed to cadmium, mercury, zinc, or selenium. Canad. J. Fish. Aquat. Sci. 40:128-138.

Eaton, R.D.P., D.C. Secord, and P. Hewitt. 1980. An experimental assessment of the toxic potential of mercury in ringed-seal liver for adult laboratory cats.. Toxicol. Appl. Pharmacol. 55:514-521.

Edwards, P.R., and N.W.J. Pumphery. 1982. Ingestion and retention of mercury by sheep grazing near a chlor-alkali plant. J. Sci. Food Agric. 33:237-243.

Eisler, R. 1978. Mercury contamination standards for marine environments. Pages 241-272 *in* J.H. Thorp and J.W. Gibbons (eds.). Energy and environmental stress in aquatic systems. U.S. Dep. Energy Symp. Ser. 48, CONF-771114. Available from Natl. Tech. Infor. Serv., U.S. Dep. Commerce, Springfield, Virginia 22161.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. Biol. Trace Elem. Res. 6:165-180.

Eisler, R. 1985. Selenium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.5). 57 pp.

Eisler. R. and R J. Hennekey. 1977. Acute toxicities of Cd^{2+}, Cr^{+6}, Hg^{2+},Ni^{2+}, and Zn^{2+} to estuarine macrofauna. Arch. Environ. Contam. Toxicol. 6:315-323.

El-Begearmi, M.M., H.E. Ganther, and M.L. Sunde. 1980. Toxicity of mercuric chloride in Japanese quail as affected by methods of incorporation into the diet. Poult. Sci. 59:2216-2220.

Elhassani, S.B. 1983. The many faces of methylmercury poisoning. J. Toxicol. 19:875-906.

EPA. 1980. Ambient water quality criteria for mercury. U.S. Environ. Protection Agency Rep. 440/5-80-058. Avail. from Natl. Tech. Infor. Serv., 5285 Port Royal Road, Springfield, Virginia 22161.

EPA. 1985. Ambient water quality criteria for mercury - 1984. U.S. Environ. Protection Agency Rep. 440/5-84-026. 136 pp. Avail from Natl. Tech. Infor. Serv., 5285 Port Royal Road, Springfield, Virginia 22161.

Evans, H.L., R. H. Garman, and V.3. Laties. 1982. Neurotoxicity of methylmercury in the pigeon. Neurotoxicology 3(3):21-36.

Fimreite, M. 1979. Accumulation and effects of mercury on birds. Pages 601-627 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Finley, M.T., and R.C. Stendell. 1978. Survival and reproductive success of black ducks fed methylmercury. Environ. Pollut. 16:51-64.

Finley, M.T., W.H. Stickel, and R.E. Christensen. 1979. Mercury residues in tissues of dead and surviving birds fed methylmercury. Bull. Environ. Contam. Toxicol. 21:105-110.

Fitzgerald, W.F. 1979. Distribution of mercury in natural waters. Pages 161-173 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Flegal, A.R., M. Stephenson, M.Martin, and J.H. Martin. 1981. Elevated concentrations of mercury in mussels (*Mytilus californianus*) associated with pinniped colonies. Mar. Biol. 65:45-48.

Friberg, L., and J. Vostal (eds.). 1972. Mercury in the environment. CRC Press, Cleveland, Ohio. 215 pp.

Fujiki, M. 1963. Studies on the course that the causative agent of Minamata disease was formed, especially on the accumulation of the mercury compound in the fish and shellfish of Minamata Bay. J. Kumamoto Med. Soc. 37:494-521.

Fujiki, N. 1980. The pollution of Minamata Bay by mercury and Minamata disease. Pages 493-500 *in* R.A. Baker (ed.). Contaminants and sediments, Vol. 2. Ann Arbor Science Publ., Ann Arbor, Michigan.

Galster, W.A. 1976. Mercury in Alaskan Eskimo mothers and infants. Environ. Health Perspec. 15:135-140.

Gentile, J.H., S.M. Gentile, G. Hoffman, J.F. Heltshe, and N. Hairston, Jr. 1983. The effects of a chronic mercury exposure on survival, reproduction and population dynamics of *Mysidopsis bahia*. Environ. Toxicol. Chem. 2:61-68.

Glickstein, N. 1978. Acute toxicity of mercury and selenium to *Crassostrea gigas* embryos and *Cancer magister* larvae. Mar. Biol. 49:113-117.

Gochfeld. M. 1980. Tissue distribution of mercury in normal and abnormal young common terns. Mar. Pollut. Bull. 11:362-366.

Gotsis, 0. 1982. Combined effects selenium/mercury and selenium/copper on the cell population of the alga *Dunaliella minuta*. Mar. Biol. 71:217-222.

Green, F.A., Jr., J.W. Anderson, S.R. Petrocelli, B.J. Presley, and R. Sims. 1976. Effect of mercury on the survival, respiration, and growth of postlarval white shrimp, *Penaeus setiferus*. Mar. Biol. 37:75-81.

Greener, Y., and J. A. Kochen. 1983. Methyl mercury toxicity in the chick embryo. Teratology 28:23-28.

Grissom, R.E., Jr., and J.P. Thaxton. 1985. Onset of mercury toxicity in young chickens. Arch. Environ. Contam. Toxicol. 14:193-196.

Hall, R.A., E.G. Zook, and G.M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resource. U.S. Dep. Commerce NOAA Tech. Rep. NMFS SSRF-721. 313 pp.

Hall, R.J. 1980. Effects of environmental contaminants on reptiles: a review. U.S. Fish Wildl. Serv. Spec. Sci. Rep. - Wildl. 228:1-12.

Hawryshyn, C.W., W.C. Mackay, and T.H. Nilsson. 1982. Methyl mercury induced visual deficits in rainbow trout. Canad. J. Zool. 60:3127-3133.

Heinz, G.H. 1979. Methylmercury: reproductive and behavioral effects on three generations of mallard ducks. J. Wildl. Manage. 43:394-401.

Heinz, G.H. 1980. Comparison of game-farm and wild-strain mallard ducks in accumulation of methylmercury. J. Environ. Pathol. Toxicol. 3:379-386.

Heisinger, J.F., C.D. Hansen, and J. H. Kim. 1979. Effect of selenium dioxide on the accumulation and acute toxicity of mercuric chloride in goldfish. Arch. Environ. Contam. Toxicol. 8:279-283.

Henderson, C., and W.E. Shanks. 1973. Mercury concentrations in fish. Pages 45-58 *in* D.R. Buhler (ed.). Mercury in the western environment. Oregon State Univ., Corvallis.

Hill, E.F. 1981. Inorganic and organic mercury chloride toxicity to coturnix: sensitivity related to age and quantal assessment of physiological responses. Ph.D. Thesis, Univ. Maryland, College Park. 221 pp

Hill, E.F., and J.H. Soares, Jr. 1984. Subchronic mercury exposure in *Coturnix* and a method of hazard evaluation. Environ. Toxicol. Chem. 3:489-502.

Hirota, R., J. Asada, S. Tajima, and M. Fujiki. 1983. Accumulation of mercury by the marine copepod *Acartia clausi*. Bull. Jpn. Soc. Sci. Fish. 49:1249-1251.

Hoffman, D.J., and J.M. Moore. 1979. Teratogenic effects of external egg applications of methyl mercury in the mallard, *Anas platyrhynchos*. Teratology 20:453-462.

Holden, A.V. 1973. Mercury in fish and shellfish, a review. J. Food Technol. 8:1-25.

Hornung, H., B.S. Krumgalz, and Y. Cohen. 1984. Mercury pollution in sediments, benthic organisms and inshore fishes of Haifa Bay, Israel. Mar. Environ. Res. 12:191-208.

Huckabee, J.W., J.W. Elwood, and S.G. Hildebrand. 1979. Accumulation of mercury in freshwater biota. Pages 277-302 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Huckabee, J.W., D.M. Lucas, and J.M. Baird. 1981. Occurrence of methylated mercury in a terrestrial food chain. Environ. Res. 26:174-181.

Hudson, R.H., R.K. Tucker, and M.A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp.

Iglesias, N., and P.E. Penchaszadeh. 1983. Mercury in sea stars from Golfo Triste, Venezuela. Mar. Pollut. Bull. 14:396-398.

Irukayama, K. 1967. The pollution of Minamata Bay and Minamata disease. Pages 153-180 *in* J.P. Maroto and F. Josa (eds.). Advances in water pollution research, Vol. 3. Proc. Third Int. Conf., Munich.

Itano, K., S. Kawai, N. Miyazaki, R. Tatsukawa, and T. Fujiyama. 1984a. Mercury and selenium levels in striped dolphins caught off the Pacific coast of Japan. Agric. Biol. Chem. 48:1109-1116.

Itano, K., S. Kawai, N. Miyazaki, R. Tatsukawa, and T. Fujiyama. 1984b. Body burdens and distribution of mercury and selenium in striped dolphins. Agric. Biol. Chem. 48:1117-1121.

Itano, K., S. Kawai, N. Miyazaka, R. Tatsukawa, and T. Fujiyama. 1984c. Mercury and selenium levels at the fetal and suckling stages of striped dolphin, *Stenella coeruleoalba*. Agric. Biol. Chem. 48:1691-1698.

Jackson, T.A. 1986. Methyl mercury levels in a polluted prairie river-lake system: seasonal and site-specific variations, and the dominant influence of trophic conditions. Canad. J. Fish. Aquat. Sci. 43:1873-1887.

Jenkins, D.W. 1980. Biological monitoring of toxic trace metals. Volume 2. Toxic trace metals in plants and animals of the world. Part II. Mercury. U.S. Environ. Protection Agency Rep. 600/3-80-091:779-982.

Jenkins, J.H., A.H. Davis, W.J. Bigler, and G.L. Hoff. 1980. Mercury and cesium-137 in urban gray squirrels. Bull. Environ. Contam. Toxicol. 25:321-324.

Jernelov, A., R. Hartung, P.B. Trost, and R.E. Bisque. 1972. Environmental dynamics of mercury. Pages 167-201 *in* R. Hartung and B.D. Dinman (eds.). Environmental mercury contamination. Ann Arbor Science Publ., Ann Arbor, Michigan.

Jernelov, A. 1969. Conversion of mercury compounds. Pages 68-74 *in* M.W. Miller and G.G. Berg (eds.). Chemical fallout, current research on persistent pesticides. Chas. C Thomas, Springfield, Illinois.

Jernelov, A., L. Landner, and T. Larsson. 1975. Swedish perspectives on mercury pollution. J. Water Pollut. Control Fed. 47:810-822.

Karlog,. O., and B. Clausen. 1983. Mercury and methylmercury in liver tissue from ringed herring gulls collected in three Danish localities. Nord. Vet. - Med. 35:245-250.

Kayser, H. 1976. Waste-water assay with continuous algal cultures: the effect of mercuric acetate on the growth of some marine dinoflagellates. Mar. Biol. 36:61-72.

Keckes, S., and J.J. Miettinen. 1972. Mercury as a marine pollutant. Pages 276-289 *in* M. Ruivo (ed.). Marine pollution and sea life. Fishing Trading News (books) Ltd., London.

Khera, K.S. 1979. Teratogenic and genetic effects of mercury toxicity. Pages 501-518 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press New York.

Kim, J.P., and W.F. Fitzgerald. 1986. Sea-air partitioning of mercury in the equatorial Pacific Ocean. Science 231:1131-1133.

Kiorboe, T., F. Mohlenberg, and H.U. Riisgard. 1983. Mercury levels in fish, invertebrates and sediment in a recently recorded polluted area (Nissum Broad, western Limfjord, Denmark). Mar. Pollut. Bull. 14:21-24.

Klein, D.H., and E.D. Goldberg. 1970. Mercury in the marine environment. Environ. Sci. Technol. 4:765-768.

Kojima, K., and M. Fujita. 1973. Summary of recent studies *in* Japan on methyl mercury poisoning. Toxicology 1:43-62.

Kopfler, F.C. 1974. The accumulation of organic and inorganic mercury compounds by the eastern oyster (*Crassostrea virginica*). Bull. Environ. Contam. Toxicol. 11:275-280.

Krynski, A., J. Kaluzinski, M. Wlazelko, and A. Adamowski. 1982. Contamination of roe deer by mercury compounds. Acta Theriol. 27:499-507.

Kucera, E. 1983. Mink and otter is indicators of mercury in Manitoba waters. Canad. J. Zool. 61:

2250-2256.

Lawrence, S.G., and M.H. Holoka. 1981. Effect of selenium on impounded zooplankton in a mercury contaminated lake. Canad. Tech. Rep. Fish. Aquat. Sci. 1151:83-92.

Leander, J.D., D.E. McMillan, and T.S. Barlow. 1977. Chronic mercuric chloride: behavioral effects in pigeons. Environ. Res. 14:424-435.

Lindberg, P. 1984. Mercury in feathers of Swedish gyrfalcons, *Falco rusticolus*, in relation to diet. Bull. Environ. Contam. Toxicol. 32:453-459.

Lindsay, R.C., and R.W. Dimmick. 1983. Mercury residues in wood ducks and wood duck foods in eastern Tennessee. J. Wildl. Dis. 19:114-117.

Lloyd, E.T., W.T. Schrenk, and J.O. Stoffer. 1977. Mercury accumulation in trout of southern Missouri. Environ. Res. 13:62-73.

Lodenius, M. 1983. The effects of peatland drainage on the mercury contents of fish. Suo 34:21-24.

Lodenius, M., A. Seppanen, and M. Herrnanen. 1983. Accumulation of mercury in fish and man from reservoirs in northern Finland. Water Air Soil Pollut. 19:237-246.

Lodenius, M., and E. Tulisalo. 1984. Environmental mercury contamination around a chlor-alkali plant. Bull. Environ. Contam. Toxicol. 32:439-444.

Lowe, T.P., T.W. May, W.G. Brumbaugh, and D.A. Kane. 1985. National Contaminant Biomonitoring Program: concentrations of seven elements in freshwater fish, 1978-1981. Arch. Environ. Contam. Toxicol. 14:363-388.

Lyle, J.M. 1984. Mercury concentrations in four carcharhinid and three hammerhead sharks from coastal waters of the Northern Territory. Aust. J. Mar. Freshwater Res. 35:441-451.

Magos, L., and M. Webb. 1979. Synergism and antagonism in the toxicology of mercury. Pages 581-599 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

March, B.E., R. Poon, and S. Chu. 1983. The dynamics of ingested methyl mercury in growing and laying chickens. Poult. Sci. 62:1000-1009.

Martin, D.B., and W.A. Hartman. 1984. Arsenic, cadmium, lead, mercury, and selenium in sediments of riverine and pothole wetlands of the north central United States. J. Assoc. Off. Anal. Chem. 67:1141-1146.

Matida, Y., and H. Kumada. 1969. Distribution of mercury in water, bottom mud and aquatic organisms of Minamata Bay, the River Agano and other water bodies in Japan. Bull. Freshwater Fish. Res. Lab. (Tokyo) 19(2):73-93.

McClurg, T.P. 1984. Effects of fluoride, cadmium and mercury on the estuarine prawn *Penaeus indicus.* Water SA 10:40-45.

McEwen, L.C., R.K. Tucker, J.O. Ells, and M.A. Haegele. 1973. Mercury-wildlife studies by the Denver Wildlife Research Center. Pages 146-156 *in* D.R. Buhler (ed.). Mercury in the western environment. Oregon State Univ., Corvallis.

McKenney, C.L., Jr., and J.D. Costlow, Jr. 1981. The effects of salinity and mercury on developing megalopae and early crab stages of the blue crab, *Callinectes sapidus* Rathbun. Pages 241-262 *in* F.J. Vernberg, A. Calabrese, F. P. Thurberg, and W.B. Vernberg (eds.). Biological monitoring of marine pollutants. Academic Press, New York.

Merck Index. 1976. The Merck Index, 9th edition. Merck and Co. Inc., Rahway, New Jersey.

Miller, T.J., and D.J. Jude. 1984. Organochlorine pesticides, PBBS, and mercury in round whitefish fillets from Saginaw Bay, Lake Huron, 1977-1978. J. Great Lakes Res. 10:215-220.

Montague, K., and P. Montague. 1971. Mercury. Sierra Club, New York. 158 pp.

Mullins, W.H., E.G. Bizeau, and W. W. Benson. 1977. Effects of phenyl mercury on captive game farm pheasants. J. Wildl. Manage. 41:302-308.

NAS. 1978. An assessment of mercury in the environment. Natl. Acad. Sci., Washington, DC. 185 pp.

Nelson, D.A., A. Calabrese, B.A. Nelson, J.R. MacInnes, and D.R. Wenzloff. 1976. Biological effects of heavy metals on juvenile bay scallops, *Argopecten irradians*, in short-term exposures. Bull. Environ. Contam. Toxicol. 16:275-282.

Nicholson, J.K., and D. Osborn. 1984. Kidney lesions in juvenile starlings *Sturnus vulgaris* fed on a mercury-contaminated synthetic diet. Environ. Pollut. 33A:195-206.

Niimi, A.J., and L. Lowe-Jinde. 1984. Differential blood cell ratios of rainbow trout (*Salmo gairdneri*) exposed to methylmercury and chlorobenzenes. Arch. Environ. Contam. Toxicol. 13:303-311.

Nishimura, H., and M. Kumagai. 1983. Mercury pollution of fishes in Minamata Bay and surrounding water: analysis of pathway of mercury. Water Air Soil Pollut. 20:401-411.

Nishimura, M., S. Konishi, K. Matsunaga, K. Hata, and T. Kosuga. 1983. Mercury concentration in the ocean. J. Oceanogr. Soc. Jpn. 39:2951-300.

Norheim, G., and B. Kjos-Hanssen. 1934. Persistent chlorinated hydrocarbons and mercury in birds caught off the west coast of Spitsbergen. Environ. Pollut. 33A:143-152.

Norheim, G., L. Some, and G. Holt. 1982. Mercury and persistent chlorinated hydrocarbons in Antarctic birds from Bouvetoya and Dronning Maud Land. Environ. Pollut. 28A:233-240.

Nriagu, J.O. (ed.). 1979. The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York. 696 pp.

Ohlendorf, H.M., D.W. Anderson, D.E. Boellstorff, and B.M. Mulhern. 1985. Tissue distribution of trace elements and DDE in brown pelicans. Bull. Environ. Contam. Toxicol. 35:183-192.

Ohlendorf, H.M., and C.S. Harrison. 1986. Mercury, selenium, cadmium and organochlorines in eggs of three Hawaiian seabird species. Environ. Pollut. 11B: 169-191.

Olson, B.H., and R.C. Cooper. 1976. Comparison of aerobic and anaerobic methylation of mercuric chloride by San Francisco Bay sediments. Water Res. 10:113-116.

Parker, J.G. 1979. Toxic effects of heavy metals upon cultures of *Uronema marinum* (Ciliophora: Uronematidae). Mar. Biol. 54:17-24.

Paasivirta, J., J. Sarkka, K. Surma-Aho, T. Humppi, T. Kuokkanen, and M. Marttinen. 1983. Food chain enrichment of organochlorine compounds and mercury in clean and polluted lakes of Finland. Chemosphere 12:239-252.

Rada, R.G., J.E. Findley, and J.G. Wiener. 1986. Environmental fate of mercury discharged into the upper Wisconsin River. Water Air Soil Pollut. 29:57-76.

Ramamoorthy, S., and K. Blumhagen. 1984. Uptake of Zn, Cd, and Hg by fish in the presence of competing compartments. Canad. J. Fish. Aquat. Sci. 41:750-756.

Ramprashad, F., and K. Ronald. 1977. A surface preparation study on the effect of methylmercury on the sensory hair cell population in the cochlea of the harp seal. Canad. J. Zool. 55:223-230.

Ribeyre, F., and A. Boudou. 1984. Bioaccumulation et repartition tissulaire du mercure-$HgCl_2$ et CH_3HgCl_2 - chez *Salmo gairdneri* apres contamination par voie directe. Water Air Soil Pollut. 23:169-186.

Robinson, J.B., and O.H. Touvinen. 1984. Mechanisms of microbial resistance and detoxification of mercury and organomercury compounds: physiological, biochemical and genetic analysis. Microbiol. Rev. 48:95-124.

Rodgers, D.W., and F.W.H. Beamish. 1982. Dynamics of dietary methylmercury in rainbow trout, *Salmo gairdneri*. Aquat. Toxicol. 2:271-290.

Ronald, K., S.V. Tessaro, J.F. Uthe, H.C. Freeman, and R. Frank. 1977. Methylmercury poisoning in the harp seal (*Pagophilus groenlandicus*). Sci. Total Environ. 8:1-11.

Saboski, E.M. 1977. Effects of mercury and tin on frustular ultrastructure of the marine diatom, *Nitzschia liebethrutti*. Water Air Soil Pollut. 8:461-466.

Sastry, K. V., D.R. Rao, and S.K. Singh. 1982. Mercury induced alterations in the intestinal absorption of nutrients in the fresh water murrel, *Channa punctatus*. Chemosphere 11:613-619.

Satoh, H., N. Yasuda, and S. Shimai. 1985. Development of reflexes in neonatal mice prenatally exposed to methylmercury and selenite. Toxicol. Lett. 25:199-203.

Schreiber, W. 1983. Mercury content of fishery products: data from the last decade. Sci. Total Environ. 31:283-300.

Sheffy, T.B., and J.R. St. Amant. 1982. Mercury burdens in furbearers in Wisconsin. J. Wildl. Manage. 46:1 17-1120.

Skei, J.H. 1978. Serious mercury contamination of sediments in a Norwegian semi-enclosed bay. Mar. Pollut. Bill. 9:191-193.

Sloan, R., and C.L. Schofield. 1983. Mercury levels in brook trout (*Salvelinus fontinalis*) from selected acid and limed Adirondack lakes. Northeast. Environ. Sci. 2:165-170.

Smith, J.N., and D. H. Loring. 1981. Geochronology for mercury pollution in the sediment of the Saguenay Fjord, Quebec. Environ. Sci. Technol. 15:944-951.

Solonen, T., and M. Lodenius. 1984. Mercury in Finnish sparrowhawks *Accipiter nisus*. Ornis Fennica 61:58-63.

Spann, J.W., R.G. Heath, J.F. Kreitzer, and L.N. Locke. 1972. Ethyl mercury p-toluene sulfonanilide: lethal and reproductive effects on pheasants. Science 175:328-331.

Spann, J.W., G.H. Heinz, and M.B. Camardese, E.F. Hill, J.F. Moore, and H.C. Murray. 1986. Differences in mortality among bobwhite fed methylmercury chloride dissolved in various carriers. Environ. Toxicol. Chem. 5:721-724.

Spencer, J.N., and A.F. Voigt. 1961. Thermodynamics of the solution of mercury metal. I. Tracer determination of the solubility in various liquids. J. Phys. Chem. 72:464-470.

Stokes, P.M., S.I. Dreier, N.V. Farkas, and R.A.N. McLean. 1981. Bioaccumulation of mercury by attached algae in acid stressed lakes, Canad. Tech. Rep. Fish. Aquat. Sci. 1151:136-148.

Suckcharoen, S., and M. Lodenius. 1980. Reduction of mercury pollution in the vicinity of a caustic soda plant in Thailand. Water, Air, Soil Pollut. 13:221-227.

Suzuki, T. 1979. Dose-effect and dose-response relationships of mercury and its derivatives. Pages 399-431 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Terhivuo, J., M. Lodenius, P. Nuortiva, and E. Tulisalo. 1984. Mercury content of common frogs (*Rana temporaria* L.) and common toads (*Bufo bufo* L.) collected in southern Finland. Ann. Zool. Fennici 21:41-44.

Thain, J.E. 1984. Effects of mercury on the prosobranch mollusc *Crepidula fornicata*: acute lethal toxicity and effects on growth and reproduction of chronic exposure. Mar. Environ. Res. 12:285-309.

Tripp, M., and R.C. Harriss. 1976. Role of mangrove vegetation in mercury cycling in the Florida Everglades. Pages 489-497 *in* J.O. Nriagu (ed.). Environmental biogeochemistry, Vol. 2. Metals transfer and ecological mass balances. Ann Arbor Sci. Publ., Ann Arbor, Michigan.

Van der Molen, E.J., A.A. Blok, and G.J. De Graaf. 1982. Winter starvation and mercury intoxication in grey herons (*Ardea cinerea*) in the Netherlands. Ardea 70:173-184.

Verma, S.R., and I.P. Tonk. 1983. Effect of sublethal concentrations of mercury on the composition of liver, muscles and ovary of *Notopterus notopterus*. Water Air Soil Pollut. 20:287-292.

Wallin, K. 1984. Decrease and recovery patterns of some raptors in relation to the introduction and ban of alkyl-mercury and DDT in Sweden. Ambio 13:263-265.

Weast, R.C., and M.J. Astle (eds.). 1982. CRC handbook of chemistry and physics. CRC Press, Boca Raton, Florida.

Weis, J.S. 1976. Effects of mercury, cadmium, and lead salts on regeneration and ecdysis in the fiddler crab, *Uca pugilator*. U.S. Natl. Mar. Fish. Serv., Fish. Bull. 74:464-467.

Weis, P. 1984. Metallothionein aid mercury tolerance in the killifish, *Fundulus heteroclitus*. Mar. Environ. Res. 14:153-166.

Wiemeyer, S.N.,, T.G. Lamont, C.M. Bunck, C.R. Sindelar, F.J. Gramlich, J.D. Fraser, and M.A. Byrd. 1984. organochlorine pesticide, polychlorobiphenyl, and mercury residues in bald eagle eggs--1969-79--and their relationships to shell thinning and reproduction. Arch. Environ. Contam. Toxicol. 13:529-549.

Windom, H., W. Gardner, J. Stephens, and F. Taylor. 1976. The role of methylmercury production in the transfer of mercury in a salt marsh ecosystem. Estuar. Coastal Mar. Sci. 4:579-583.

Windom, H.L., and D.R. Kendall. 1979. Accumulation and biotransformation of mercury in coastal and marine biota. Pages 301-323 *in* J.O. Nriagu (ed.). The biogeochemistry of mercury in the environment. Elsevier/North-Holland Biomedical Press, New York.

Winger, P.V., and J.K. Andreasen. 1985. Contaminant residues in fish and sediments from lakes in the Atchafalaya River basin (Louisiana). Arch. Environ. Contam. Toxicol. 14:579- 86.

Wren, C.D. 1986. A review of metal accumulation and toxicity in wild mammals. I. Mercury. Environ. Res. 40:210-244.

Wren, C.D., and H.R. Mac Crimmon. 1983. Mercury levels in the sunfish, *Lepomis gibbosus*, relative to pH and other environmental variables of precambrian shield lakes. Canad. J. Fish. Aquat. Sci. 40:1737-1744.

Wu, M-F., J.R. Ison, J.R. Wecker, and L.W. Lapham. 1985. Cutaneous and auditory function in rats following methyl mercury poisoning. Toxicol. Appl. Pharmacol. 79:377-388.

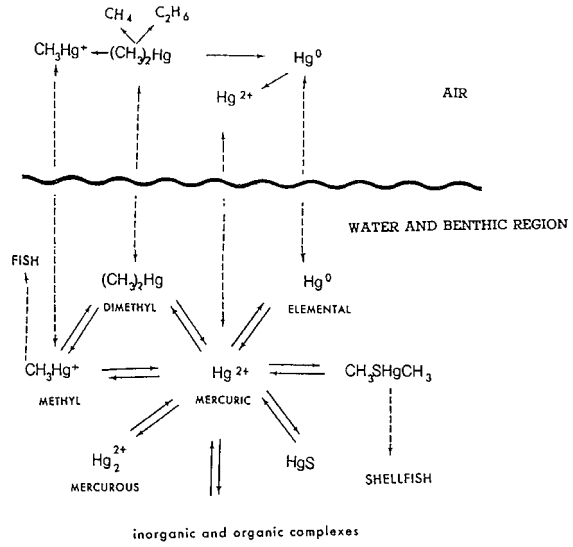


Figure 1. Major transformations of mercury in the environment (modified from Beijer and Jernelov 1979).

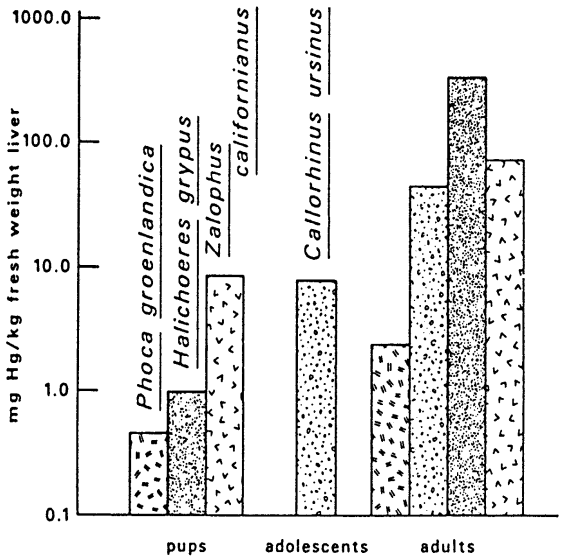


Figure 2. Mercury concentrations in livers of four species of pinniped mammals (from Eisler 1984).

Biological Report 85(1.11)
May 1987

Contaminant Hazard Reviews
Report No. 11

POLYCYCLIC AROMATIC HYDROCARBON HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

By

Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

This account synthesizes available technical literature on ecological and toxicological aspects of polycyclic aromatic hydrocarbons (PAHs) in the environment, with special reference to natural resources. Subtopics include: chemical properties, sources, and fate; background concentrations in biological and nonbiological samples; toxic and sublethal effects to flora and fauna; and proposed criteria and research needs for the protection of sensitive species.

PAHs consist of hydrogen and carbon arranged in the form of two or more fused benzene rings. There are thousands of PAH compounds, each differing in the number and position of aromatic rings, and in the position of substituents on the basic ring system. Environmental concern has focused on PAHs that range in molecular weight from 128.16 (naphthalene, 2-ring structure) to 300.36 (coronene, 7-ring structure). Unsubstituted lower molecular weight PAH compounds, containing 2 or 3 rings, exhibit significant acute toxicity and other adverse effects to some organisms, but are noncarcinogenic; the higher molecular weight PAHs, containing 4 to 7 rings, are significantly less toxic, but many of the 4- to 7-ring compounds are demonstrably carcinogenic, mutagenic, or teratogenic to a wide variety of organisms, including fish and other aquatic life, amphibians, birds, and mammals. In general, PAHs show little tendency to biomagnify in food chains, despite their high lipid solubility, probably because most PAHs are rapidly metabolized. Inter- and intraspecies responses to individual PAHs are quite variable, and are significantly modified by many inorganic and organic compounds, including other PAHs. Until these interaction effects are clarified, the results of single substance laboratory tests may be extremely difficult to apply to field situations of suspected PAH contamination.

PAHs are ubiquitous in nature--as evidenced by their detection in sediments, soils, air, surface waters, and plant and animal tissues--primarily as a result of natural processes such as forest fires, microbial synthesis, and volcanic activities. Anthropogenic activities associated with significant production of PAHs--leading, in some cases, to localized areas of high contamination--include high-temperature (>700 °C) pyrolysis of organic materials typical of some processes used in the iron and steel industry, heating and power generation, and petroleum refining. Aquatic environments may receive PAHs from accidental releases of petroleum and its products, from sewage effluents, and from other sources. Sediments heavily contaminated with industrial PAH wastes have directly caused elevated PAH body burdens and increased frequency of liver neoplasia in fishes.

At present, no criteria or standards have been promulgated for PAHs by any regulatory agency for the protection of sensitive species of aquatic organisms or wildlife. This observation was not unexpected in view of the paucity of data on PAH background concentrations in wildlife and other natural resources, the absence of information on results of chronic oral feeding studies of PAH mixtures, the lack of a representative PAH mixture for test purposes, and the demonstrable--and, as yet, poorly understood--effects of biological and nonbiological modifiers on PAH toxicity and metabolism. By contrast, criteria for human health protection and total PAHs, carcinogenic PAHs, and benzo(a)pyrene have been proposed for drinking water and air, and for total PAHs and benzo(a)pyrene in food: drinking water, 0.01 to <0.2 ug total PAHs/l, <0.002 ug carcinogenic PAHs/l, and <0.0006 ug benzo(a)pyrene/l; air, <0.01 ug total PAHs/m^3, <0.002 ug carcinogenic PAHs/m^3, and <0.0005 ug benzo(a)pyrene/m^3; food, 1.6 to <16.0 ug total PAHs daily, and 0.16 to <1.6 ug benzo(a)pyrene daily. In view of the carcinogenic characteristics of many PAH compounds and their increasing concentrations in the environment, it now seems prudent to reduce or eliminate them wherever possible, pending acquisition of more definitive ecotoxicological data.

DISCLAIMER

Mention of trade names or commercial products does not constitute U.S. Government endorsement or recommendation for use.

This report should be cited as follows:

Eisler, R. 1987. Polycyclic aromatic hydrocarbon hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85(1.11).

TABLES

FIGURES

ACKNOWLEDGMENTS

I thank Jean Higgis and Julia Armstrong for secretarial help; Lynda J. Garrett, Nancy A. Bushby, and Joyce E. Haber for literature retrieval; Matthew C. Perry, Martha L. Gay, David J. Hoffman, and Paul C. Baumann for constructively reviewing the manuscript; and Curtis H. Halvorson and James R. Zuboy for editorial services.

INTRODUCTION

Several polycyclic aromatic hydrocarbons (PAHs) are among the most potent carcinogens known to exist, producing tumors in some organisms through single exposures to microgram quantities. PAHs act at both the site of application and at organs distant to the site of absorption; their effects have been demonstrated in nearly every tissue and species tested, regardless of the route of administration (Lee and Grant 1981). The evidence implicating PAHs as an inducer of cancerous and precancerous lesions is becoming overwhelming, and this class of substances is probably a major contributor to the recent increase in cancer rates reported for industrialized nations (Cooke and Dennis 1984). PAHs were the first compounds known to be associated with carcinogenesis (Lee and Grant 1981). Occupational skin cancer was first documented in London chimney sweeps in 1775 and in German coal tar workers in the late 1800's. By the early 1900's,, soot, coal tar, and pitch were all found to be carcinogenic to humans. By 1918, it was shown that topical applications of coal tar produced skin tumors in mice and rabbits; benzo(a)pyrene, a PAH, was identified as one of the most carcinogenic compounds in coal tar (Dipple 1985). The carcinogenic activity to man of soots, tars, and oils is beyond dispute. In addition to the skin cancers noted initially, higher incidences of respiratory tract and upper gastrointestinal tract tumors were associated with occupational exposures to these carcinogens (Dipple 1985). PAH-induced cancers in laboratory animals is well documented. Benzo(a)pyrene, for example, has produced tumors in mice, rats, hamsters, guinea pigs, rabbits, ducks, and monkeys following administration by oral, dermal, and intraperitoneal routes (Pucknat 1981). Teratogenic or carcinogenic responses have been induced in sponges, planarians, echinoderm larvae, teleosts, amphibians, and plants by exposure to carcinogenic PAHs (Neff 1979, 1982b). An unusually high prevalence of oral, dermal, and hepatic neoplasms have been observed in bottom-dwelling fish from polluted sediments containing grossly-elevated PAH levels (Couch and Harshbarger 1985). PAH compounds have damaged chromosomes in cytogenetic tests, have produced mutations in mammalian cell culture systems, and have induced DNA repair synthesis in human fibroblast cultures (EPA 1980). While some PAHs are potent mutagens and carcinogens, others are less active or suspected carcinogens. Some, especially those of biological origin, are probably not carcinogens (Jackim and Lake 1978). Certain lower molecular weight, noncarcinogenic PAHs, at environmentally realistic levels, were acutely toxic to aquatic organisms, or produced deleterious sublethal responses (Neff 1985). However, few generalizations can be made about the class of PAH compounds because of the extreme variability in toxicity and physicochemical properties of PAHs and their various effects on individual species (Lee and Grant 1981).

PAHs are widely-distributed in the environment, almost ubiquitous, and have been detected in animal and plant tissues, sediments, soils, air, surface water, drinking water, industrial effluents, ambient river water, well water, and groundwater (EPA 1980). Man probably has always been exposed to PAHs from the natural background level in soils and plants (Harrison et al. 1975); avoiding exposure to nanogram quantities of these substances on a daily basis is now considered essentially impossible for all living resources (Dipple 1985). Ever since benzo(a)pyrene was recognized as a carcinogen at the beginning of this century, the presence of it and of other PAHs in the environment has received continuous attention. As one consequence, many reviews have been published on ecological and toxicological aspects of PAHs in the environment, with special reference to their carcinogenic properties. (Harrison et al. 1975; Barnett 1976; Suess 1976; Gelboin and Ts'o 1978a, 1978b, 1981; Jackim and Lake 1978; Jones and Freudenthal 1978; Lo and Sandi 1978; Jones and Leber 1979; Neff 1979, 1982a,1982b, 1985; Tsang and Griffin 1979; Bjorseth and Dennis 1980; EPA 1980; Cooke and Dennis 1981, 1983, 1984; Futoma et al. 1981; Lee and Grant 1981; Pucknat 1981; Sims and Grover 1981; Stegeman 1981; Cooke et al. 1982; Richards and Jackson 1982; Couch et al. 1983; Edwards 1983; Grimmer 1983; Quaghebeur et al. 1983; Sims and Overcash 1983; Couch and Harshbarger 1985; Harvey 1985; Johnson et al. 1985; Sugimura 1986.)

In this report, I summarize selected data on environmental aspects of PAHs, emphasizing PAH effects to aquatic and wildlife resources. This brief review is part of a continuing series prepared in response to informational requests from environmental specialists of the U. S. Fish and Wildlife Service.

ENVIRONMENTAL CHEMISTRY, SOURCES, AND FATE

PROPERTIES

Polycyclic aromatic hydrocarbons (PAHs), also known as polynuclear aromatic hydrocarbons (PNAs) and polycyclic organic matter (POM), are composed of hydrogen and carbon arranged in the form of two or more fused benzene rings in linear, angular, or cluster arrangements, which may or may not have substituted groups attached to one or more rings (Sims and Overcash 1983). In some cases, the newly defined substituted PAH has strikingly greater toxicological effects than does the parent compound (Cooke and Dennis 1984). The nomenclature of PAH compounds has been ambiguous in the past due to different peripheral numbering systems. The currently accepted nomenclature is shown in Figure 1.

Of major environmental concern are mobile PAHs that vary in molecular weight from 128.16 (naphthalene, $C_{10}H_8$) to 300.36 (coronene, $C_{24}H_{12}$). Higher molecular weight PAHs are relatively immobile because of their large molecular volumes and their extremely low volatility and solubility. Among the mobile forms are thousands of compounds that differ in the number and position of aromatic rings, and in the position of substituents on the basic ring system. The lower molecular weight unsubstituted PAH compounds, containing 2 to 3 rings, such as naphthalenes, fluorenes, phenanthrenes, and anthracenes (Figure 2), have significant acute toxicity to some organisms, whereas the higher molecular weight 4- to 7-ring aromatics do not. However, all known PAH carcinogens, cocarcinogens, and tumor producers are in the high molecular weight PAH group (Figure 3).

Physical and chemical characteristics of PAHs generally vary with molecular weight. With increasing molecular weight, aqueous solubility decreases, and melting point, boiling point, and the log Kow (octanol/water partition coefficient) increases (Table 1), suggesting increased solubility in fats, a decrease in resistance to oxidation and reduction, and a decrease in vapor pressure. Accordingly, PAHs of different molecular weight vary substantially in their behavior and distribution in the environment and in their biological effects. Additional and more comprehensive data on the physical and chemical properties of PAHs are given in Barnett (1976), Lo and Sandi (1978), Neff (1979, 1985), EPA (1980), Futoma et al. (1981), Lee and Grant (1981), Pucknat (1981), Edwards (1983), Grimmer (1983), Sims and Overcash (1983), and Whitehouse (1985).

Table 1. Some physical and chemical properties of selected PAHs.

Compound	Number of rings	Approximate molecular weight	Melting point (C)	Solubility in water (mg/l)	log Kow
Naphthalene	2	128	80	30.0	3.37
Anthracene	3	178	216	0.07	4.45
Benz(a)anthracene	4	228	158	0.014	5.61
Benzo(a)pyrene	5	252	179	0.0038	6.04
Benzo(g,h,i)perylene	6	276	222	0.00026	7.23

SOURCES

About 43,000 metric tons of PAHs are discharged into the atmosphere each year, and another 230,000 tons enter aquatic environments (Table 2). PAHs are ubiquitous in nature as a consequence of synthesis in terrestrial vegetation, microbial synthesis, and volcanic activity, but quantities formed by these natural processes are small in comparison with those produced from forest and prairie fires and anthropogenic sources (Barnett 1976; Suess 1976; Lo and Sandi 1978; Neff 1979, 1985; EPA 1980; Lee and Grant 1981; Pucknat 1981; Edwards 1983; Grimmer 1983; Sims and Overcash 1983). Anthropogenic activities associated with significant production of PAHs include: coke production in the iron and steel industry; catalytic cracking in the petroleum industry; the manufacture of carbon black, coil tar pitch, and asphalt; heating and power generation; controlled refuse incineration; open burning; and emissions from internal combustion engines used in transportation. Thus, the formation of PAHs in the environment is due to an endogenous synthesis by microorganisms, algae, and macrophytes which provide natural background, and to a second process which is connected to man-controlled high-temperature (>700 C) pyrolysis of organic materials, to open burning, and to natural volcanic activities. The discovery in fossil fuels of complex mixtures of PAHs spanning a wide range of molecular

weights has led to the conclusion that, given sufficient time (i.e., millions of years), pyrolysis of organic materials at temperatures as low as 100 to 150 °C can also lead to production of PAHs (Neff 1985).

Forest and prairie fires release much greater amounts of PAHs to the atmosphere than does fossil fuel burning. Nearly all of the airborne PAHs produced by flame pyrolysis are associated with the particulate fraction produced during combustion, and these are significantly modified by the chemical composition of the fuel, the pyrolysis temperature, the duration of exposure to elevated temperature;, and to other factors (Neff 1979; Edwards 1983). In one study, a PAH profile was established for a series of laboratory fires simulating the prescribed burning of pine needle litter (McMahon and Tsoukalas 1978). Heading fires (moving with wind) produced more total particulate matter than backing fires (moving against wind), but backing fires produced significantly higher amounts of PAHs, with the actual amounts formed dependent on fuel loading and the residence time of combustible gases in the burning zone. Emission factors for benzo(a)pyrene varied from 238 to 3,454 ug/kg in backing fires and 38 to 97 ug/kg in heading fires.

Table 2. Major sources of PAHs in atmospheric and aquatic environments (modified from Lo and Sandi 1978; Neff 1979; Edwards 1983; Sims and Overcash 1983).

Ecosystem and sources	Annual input, in metric tons
Atmosphere	
Total PAHs	
Forest and prairie fires	19,513
Agricultural burning	13,009
Refuse burning	4,769
Enclosed incineration	3,902
Heating and power	2,168
Benzo (a) pyrene	
Heating and power	
Worldwide	2,604
USA only	475
Industrial processes (mostly coke production)	
Worldwide	1,045
USA only	198
Refuse and open burning	
Worldwide	1,350
USA only	588
Motor vehicles	
Worldwide	45
USA only	22
Aquatic environments	
Total PAHs	
Petroleum spillage	170,000
Atmospheric deposition	50,000
Wastewaters	4,400
Surface land runoff	2,940
Biosynthesis	2,700
Total benzo (a) pyrene	700

PAHs present in the atmosphere enter rain as a result of in-cloud and below-cloud scavenging (van Noort and Wondergem 1985). Total PAHs deposited on land and water are almost equivalent to PAH content in rainfall; significant quantities of PAHs are found in presumed pollution-free areas, indicating the importance of rain in transport and distribution of PAHs (Quaghebeur et al. 1983).

PAHs may reach aquatic environments in domestic and industrial sewage effluents, in surface runoff from land, from deposition of airborne particulates, and especially from spillage of petroleum and petroleum products into water bodies (Jackim and Lake 1978; Lake et al. 1979; Neff 1979; EPA 1980; Martens 1982; Boehm and Farrington 1984; Hoffman et al. 1984; Prahl et al. 1984). The majority of PAHs entering aquatic environments remains close to sites of deposition, suggesting that lakes, rivers, estuaries, and coastal marine environments near centers of human populations are the primary repositories of aquatic PAHs (Neff 1979). Large variations in aquatic PAH contents were evident due to localized source inputs and physicochemical conditions. For example, urban runoff from stormwater and highways to Narragansett Bay, Rhode Island, accounted for 71% of the total inputs for higher molecular weight PAHs, and 36% of the total PAHs (Hoffman et al. 1984). More than 30% of all combustion-derived PAHs in coastal sediments of Washington State is supplied by riverine transport of suspended particulate materials, while direct atmospheric input accounts for a maximum of 10% (Prahl et al. 1984). In contrast, concentrations of PAHs in sediments from the vicinity of Georges Bank, off the US northeastern coast, varied from 1 to 100 ug/kg dry weight, and were directly related to total organic carbon, silt, and clay contents in sediments; combustion-derived PAHs dominated at the higher concentrations, while lower level were often associated with a fossil fuel origin (Boehm and Farrington 1984).

Discharge water from hydrostatic testing of natural gas pipelines is a significant source of PAH loading into aquatic environments, contributing as much as 32,000 ug PAHs/1 of discharge water, mostly as naphthalenes (Eiceman et al. 1984). More than 25 PAHs, primarily anthracenes and pyrenes, were detected in pipeline residues on inner walls of natural gas pipelines at concentrations up to 2,400 ug/m^2 of inner surface; the same compounds may be reasonably expected in aqueous waste from pipeline maintenance (Eiceman et al. 1985). Release of these, or similar, discharge waters directly into aquatic environments will result in contamination similar to that caused by oil spills; however, these sites for pollution may occur in locations far distant from oil production and refinery activities (Eiceman et al. 1984). PAHs are also present in tap water at concentrations of 0.1 to 1.0 ng/l, primarily as mono- and dichlorinated derivatives of naphthalene, phenanthrene, fluorene, and fluoranthene (Shiraishi et al. 1985). The presence of PAHs and chlorinated PAHs in tap water indicates the reaction of PAHs with chlorine; however, their significance to human health and to aquatic biota is unknown.

FATE

Concern about PAHs in the environment is due to their persistence and to the fact that some are known to be potent mammalian carcinogens, although environmental effects of most noncarcinogenic PAHs are poorly understood (Neff 1985). Prior to 1900, a natural balance existed between the production and the degradation of PAHs. Synthesis of PAHs by microorganisms and volcanic activity and production by man-made high temperature pyrolytic reactions and open burning seemed to be balanced by PAH destruction via photodegradation and microbial transformation. With increased industrial development and increased emphasis of fossil fuels as energy sources, the balance has been disturbed to the extent that PAH production and introduction into the environment greatly exceeds known PAH removal processes (Suess 1976; Sims and Overcash 1983).

When released into the atmosphere, PAH compounds will become associated with particulate materials. Their residence time in the atmosphere and transport to different geographic locations are governed by particle size, meteorological conditions, and atmospheric physics. The highly reactive PAHs photodecompose readily in the atmosphere by reaction with ozone and various oxidants; degradation times range from several days to six weeks for PAHs adsorbed onto particulates <1 um in diameter (in the absence of rainfall) to <1 day to several days for those adsorbed to larger particles (Suess 1976). Smaller atmospheric particulates containing PAHs are easily inhaled (Lee and Grant 1981), and may pose special problems, as yet unevaluated, for airborne organisms such as birds, insects, and bats. Photooxidation, one of the most important processes in the removal of PAHs from the atmosphere, can also produce reaction products that are carcinogenic or mutagenic, although little is known of their persistence (Edwards 1983): One of the more common photooxidation reactions of PAHs is the formation of endoperoxides that ultimately undergo a series of reactions to form quinones (Edwards 1983). Various parameters may modify chemical and photochemical transformation of PAHs in the atmosphere,

including light intensity, concentration of gaseous pollutants (0_3, NOx, SOx), and chemicophysical characteristics of particulates or substrates into which the PAHs are adsorbed; depending on these variables, the half-life of benzo(a)pyrene in the atmosphere varies from 10 minutes to 72 days (Valerio et al. 1984). Atmospheric PAHs are transported over relatively long distances from industrial areas and from natural forest and prairie fires (Edwards 1983); however, sites nearer urban centers have much higher PAH deposition rates than more rural areas (Hites and Gschwend 1982).

Much of the PAHs released into the atmosphere eventually reaches the soil by direct deposition or by deposition on vegetation. The PAHs may be adsorbed or assimilated by plant leaves before entering the animal food chain, although some adsorbed PAHs may be washed off by rain, chemically oxidized to other products, or returned to the soil as the plants decay. PAHs assimilated by vegetation may be translocated, metabolized, and possibly photodegraded within the plant. In some plants growing in highly contaminated areas, assimilation may exceed metabolism and degradation, resulting in an accumulation in plant tissues (Edwards 1983).

In water, PAHs may either evaporate, disperse into the water column, become incorporated into bottom sediments, concentrate in aquatic biota, or experience chemical oxidation and biodegradation (Suess 1976). The most important degradative processes for PAHs in aquatic systems are photooxidation, chemical oxidation, and biological transformation by bacteria and animals (Neff 1979). Most PAHs in aquatic environments are associated with particulate materials; only about 33% are present in dissolved form (Lee and Grant 1981). PAHs dissolved in the water column will probably degrade rapidly through photooxidation (EPA 1980), and degrade most rapidly at higher concentrations, at elevated temperatures, at elevated oxygen levels, and at higher incidences of solar radiation (McGinnes and Snoeyink 1974; Suess 1976; Bauer and Capone 1985). The ultimate fate of those PAHs that accumulate in sediments is believed to be biotransformation and biodegradation by benthic organisms (EPA 1980). PAHs in aquatic sediments, however, degrade very slowly in the absence of penetrating radiation and oxygen (Suess 1976), and may persist indefinitely in oxygen poor basins or in anoxic sediments (Neff 1979). PAH degradation in aquatic environments occurs at a slower rate than that in the atmosphere (Suess 1976), and the cycling of PAHs in aquatic environments, as is true for other ecological systems, is poorly understood (Neff 1979).

Animals and microorganisms can metabolize PAHs to products that may ultimately experience complete degradation. The degradation of most PAHs is not completely understood. Those in the soil may be assimilated by plants, degraded by soil microorganisms, or accumulated to relatively high levels in the soil. High PAH concentrations in soil can lead to increased populations of microorganisms capable of degrading the compounds. Of equal importance to PAH cycling dynamics is the physical state of the PAH, i.e., whether in vapor phase or associated with particles such as flyash. Particles may increase or decrease the susceptibility of PAHs to degradation, depending on the PAH and particles involved (Edwards 1983).

PAHs can be taken into the mammalian body by inhalation, skin contact, or ingestion, although they are poorly absorbed from the gastrointestinal tract. The main routes of elimination of PAHs and their metabolites include the hepatobiliary system and the gastrointestinal tract (Sims and Overcash 1983). In mammals, an enzyme system variously known as the cytochrome P-450-dependent mixed-function oxidase, mixed-function oxidase, mixed-function oxygenase, aryl hydrocarbon hydroxylase, or drug metabolizing system, is responsible for initiating the metabolism of various lipophilic organic compounds, including PAHs. The primary function of this system is to render poorly water soluble lipophilic materials more water soluble, and therefore more available for excretion. Some PAHs are transformed to intermediates, which are highly toxic, mutagenic, or carcinogenic to the host. Oxidative metabolism of PAHs in this system proceeds via high electrophilic intermediate arene oxides, some of which bind covalently to cellular macromolecules such as DNA, RNA, and protein. Most authorities agree that metabolic activation by the mixed-function oxidase system is a necessary prerequisite for PAH-induced carcinogenesis and mutagenesis (Neff 1979). This enzyme system is known to be present in rodent tissues, and human liver, skin, placenta, fetal liver, macrophages, lymphocytes, and monocytes (Lo and Sandi 1978). Studies with rodents have shown that the mixed-function oxidase system can convert PAHs to various hydroxylated derivatives including phenols, quinones, and epoxides, and can also activate PAHs to produce carcinogenic metabolites (Lo and Sandi 1978). Fish and most crustaceans tested to date possess the enzymes necessary for activation (Statham et al. 1976; Varanasi et al. 1980; Fabacher and Baumann 1985), but some molluscs and other invertebrates are unable to efficiently metabolize PAHs (Jackim and Lake 1978; Varanasi et al. 1985). Although many aquatic organisms possess the requisite enzyme

systems for metabolic activation of PAHs, it is not certain in most cases whether these enzymes produce the same metabolites as those produced by mammalian enzymes (Neff 1979).

PAHs are metabolized by liver mixed-function oxidases to epoxides, dihydrodiols, phenols, and quinones. The intermediate metabolites have been identified as the mutagenic, carcinogenic, and teratogenic agents (Sims and Overcash 1983). The activation mechanisms occur by hydroxylation or production of unstable epoxides of PAHs which damage DNA, initiating the carcinogenic process (Jackim and Lake 1978). Metabolic formation of bay region diol epoxides represents an important pathway by which PAHs are activated to carcinogens (Figure 4). Such metabolic activation proceeds via initial formation of the dihydrodiol with the bay region double bond, followed by subsequent oxidation of the dihydrodiol to the bay region diol epoxide (Sims and Overcash 1983). Active epoxides may be converted to less toxic products by various enzymatic and other reactions (Neff 1979). In the case of benzo(a)pyrene, the "ultimate circinogen" (7 beta, 8 alpha-dihydroxy-,7,8,9,10 tetrahydrobenzo(a)pyrene- 9 alpha, 10 alpha-epoxide) reacts with the guanine of RNA and DNA, the linkage taking place between the C-10 atom of benzo(a)pyrene and the C-2 amino group of guanine (Grimmer 1983; Dipple 1985; Figure 4). Additional information on actual and theoretical mechanisms involved in the metabolic activation of PAHs are given in Cavalieri et al. (1978, 1980), Bjorseth and Dennis (1980), Herd and Greene. (1980), Cooke and Dennis (1981), Sims and Grover (1981), Grimmer (1983), Szentpaly (1984), Harvey (1985), and Yan (1985).

BACKGROUND CONCENTRATIONS

GENERAL

PAHs are ubiquitous in the environment. In nonbiological materials, concentrations are elevated in the vicinity of urban industrialized locales, and from areas of significant wood burning activities such as forest fires and residential home heating. Terrestrial vegetation and aquatic invertebrates can accumulate significant concentrations of PAHs, possibly due to inefficient or missing mixed-function oxidase systems. Fish do not appear to contain grossly elevated PAH residues; this may be related to their efficient degradation system. At present, data are lacking or unavailable on PAH background concentrations in natural populations of birds and other wildlife --although it seems unlikely that significant accumulations will occur. Some investigators have shown that aquatic invertebrates, fish, and amphibians collected from areas of high sediment PAH content show elevated frequencies of hyperplasia and neoplasia (Rose 1977; Mix 1982; Black 1983; Malins et al. 1984, 1985a, 1985b; Black et al. 1985; Baumann et al., in press), and, recently, that hepatic carcinoma has been induced in rainbow trout (*Salmo gairdneri*) by benzo(a)pyrene through dietary and intraperitoneal injection routes (Hendricks et al. 1985).

More comprehensive information on PAH background levels in various biological and nonbiological compartments is given in Lo and Sandi (1978), Neff (1979, 1985), Pucknat (1981), Edwards (1983), Grimmer (1983), and Sims and Overcash (1983).

NONBIOLOGICAL SAMPLES

Total PAH levels in air are usually much higher in winter than in summer, higher in urban communities than in rural areas (Table 3; Grimmer 1983), and appear to be related primarily to the weight of total suspended particulates in the atmosphere (Hites and Gschwend 1982; Greenberg et al. 1985; Srivastava et al. 1985; Ang et al. 1986). PAH levels in precipitation are significantly higher in winter than in summer, primarily due to emissions from household heating (Quaghebeur et al. 1983; van Noort and Wondergem 1985). Among industrial sources, the production of metallurgical coke is the single most significant source of atmospheric PAHs in Ontario, Canada. Coke production in 1977 represented about 52% of all PAH emissions from Ontario sources versus about 46% formed as a result of forest fires (Potvin et al. 1981). Beyond 2 km distant from the coke point source, PAH concentrations in air were typical of those measured in major urban nonindustrialized areas (Table 3; Potvin et al. 1981). A variety of PAHs have been detected in ambient air in the USA and elsewhere. Benzo(a)pyrene, because of its carcinogenic properties, has been monitored extensively, and has frequently been used as an indicator of PAHs (EPA 1980). In general, total PAHs in air is about 10X higher than benzo(a)pyrene levels, although this relation is extremely variable (Lee and Grant 1981). Benzo(a)pyrene levels, like total PAHs, were higher in winter than summer, probably due to residential and industrial heating; air levels in urban areas with coke ovens were 40% to 70% higher than in cities without coke ovens, but this may be related to higher industrial emissions in those cities (Lee and Grant 1981). In one case, benzo(a)pyrene

levels in air from the center of a remote mountain community in Colorado were several times higher than what is usually found in U.S. metropolitan areas, and was attributed to extensive residential wood burning (in M. Cooke, A.J. Dennis, and G.L. Fisher (eds.). Polynuclear aromatic hydrocarbons: physical and biological chemistry. Battelle Press, Columbus, Ohio.Murphy et al. 1982). Average concentrations of benzo(a)pyrene in urban air Nationwide declined from 3.2 ng/m^3 in 1966 to 0.5 ng/m^3 in 1978, an 80% decrease (Lee and Grant 1981). These decreases are believed to be due primarily to decreases in coal consumption for commercial and residential heating, improved disposal of solid wastes, and restrictions on open burning (EPA 1980).

Table 3. PAH concentrations in selected nonbiological materials.

Material (units), and other variables	Concentration	Reference[a]
Air (ng/m^3)		
USA cities, 1959, total PAHs		
Detroit	95.1	EPA 1980
Birmingham	63.4	
Nashville	60.6	
New Orleans	33.6	
Los Angeles	31.8	
Atlanta	26.3	
San Francisco	13.7	
Sydney, Australia		
Winter	8.2	Barnett 1976
Summer	0.6	
USA cities, 1971–77		
Benzo (a) perylene = BaPER	0.2–9.2	EPA 1980
Benzo (e) pyrene = BeP	0.9–4.6	
Benzo (k) fluoranthene = BkFL	0.03–1.3	
Pyrene = PYR	0.18–5.2	
Coronene = COR	0.2–6.4	
Perylene = PER	0.01–1.2	
Anthracene = A	0.07–0.3	
Naphthalene = NA	Max. 0.4	
Benz (a) anthracene = BaA	Max. 4.6	
Indeno (1,2,3-cd) pyrene = IP	Max. 1.3	
Steel mill, Ontario, Canada, 1971–79		
Station 0.8 km distant		
Benzo (a) pyrene = BaP	9.4 (Max. 110.0)	Potvin
BkFL	8.9 (Max. 142.0)	et al. 1981
Fluoranthene = FL	7.0 (Max. 43.3)	
PER	9.1 (Max. 106.0)	
Benzo (g,h,i) perylene = BghiPER	13.7 (Max. 90.0)	

Station 2.8 km distant		
BaP	0.4 (Max. 7.9)	
BkFL	0.7 (Max. 5.1)	
FL	1.1 (Max. 4.8)	
PER	0.7 (Max. 9.1)	
BghiPER	1.4 (Max. 8.5)	
Benzo (a) pyrene = BaP		
Urban areas	0.1–61.0	Edwards 1983
Downwind from coal gasification		
plant, Yugoslavia	Max. 80.0	
Urban areas		
1966	3.2	EPA 1980
1970	2.1	
1976	0.5	
Rural areas	0.01–1.9	Edwards 1983
Rural areas		
1966	0.4	EPA 1980
1976	0.1	
Soils		
Near M6 Motorway, Lancaster, UK		
(maximum deposition rate, ng/m^2/week)		
Distance from roadway		
3.8 meters		
A	2,300	Johnston and
FL	15,200	Harrsion 1984
BaA	5,800	
Benzo (b) fluoranthene = BbFL	7,300	
BkFL	2,800	
BaP	4,900	
9.0 - 47 meters		
A	420	
FL	1,700	
BaA	260	
BbFL	690	
BkFL	470	
BaP	290	
Vicinity slash burn site, Oregon (g/ha)		
0–2 cm depth		
Preburn		
Phenanthrene = PHEN	0.5	Sullivan
FL	0.6	and Mix 1985
103 days postburn		

PHEN	9.8	
FL	3.6	
365 days postburn		
PHEN	ND	
FL	0.8	
2–5 cm depth		
105 days postburn		
PHEN	1.3	
FL	0.3	
365 days postburn		
PHEN	ND	
FL	ND	
BaP (g/kg)		
Rural areas	0.4	Barnett 1976
Industrial areas	400.0	
Nonpolluted areas	up to 1,000	Edwards 1983
Near known sources	>100,000	
Near coal-tar pitch disposal site, Germany	650,000	Lee and Grant 1981
Near recreation area, USSR	0.4	Harrison
Forest soil	1.5–4.0	et al. 1975
Litter		
Forest, Oregon (g/ha)		
3 days postburn		
PHEN	603	Sullivan and
FL	245	Mix 1985
32 days postburn		
PHEN	ND	
FL	ND	
Coniferous trees (g/kg)		
BghiPER	42	Thomas
BaP	51	et al. 1984
IP	47	
FL	164	
Sediments (µg/kg)		
Buffalo River, near Buffalo, NY		
Sediments		
BaA	7,300	Black 1983
Chrysene = CHRY	4,300	
BbFL		3,500
BaP	4,500	
Dibenz (a,h) anthracene = DBA	1,000	

IP	4,400	
Sediment extracts		
BaA	16,000	
CHRY	14,000	
BbFL	13,900	
BaP	15,400	
DBA	3,300	
IP	12,300	
Cayuga Lake, Ithaca, NY, 1978		
Total PAHs		
Within marinas	4,600–13,900	Heit 1985
Deepwater	1,260–2,500	
Near power plant	104–6,800	
FL		
Within marinas	1,700	
Deepwater	285	
Near power plant	8–1,000	
Penobscot Bay, Maine		
Total PAHs	286–8,794	Johnson
PHEN	17–252	et al. 1985
A	ND–49	
FL	156–3,700	
Pyrene	16–539	
BaA	14–540	
CHRY	9–578	
BbFL	17–1,000	
BkFL	14–696	
BaP	10–540	
DBA	2–120	
BghiPER	23–641	
IP	9–228	
Casco Bay, Maine, total PAHs	215–14,425	
Charles River, Mass., total PAHs	87,000–120,000	
Boston Harbor, Mass., total PAHs	8,500	
New Bedford Harbor, Mass., total PAHs	63,000	
Lake Erie, total PAHs	530–3,750	
Adirondack Lakes, total PAHs	4,070–12,807	
Alaska, total PAHs	5–113	
Tamar estuary, UK, total PAHs	4,900	
Southhampton estuary, UK, total PAHs	91,000–1,791,000	
Severn estuary, UK, total PAHs	1,600–25,700	
Monaco, total PAHs	5,200–12,100	
Gulf of Finland, total PAHs	437	

Norway, total PAHs	284–99,452	
Walvis Bay, Africa, total PAHs	68	
Amazon River system, total PAHs	ND–544	
Sewage		
Waters, worldwide, total PAHs (g/L)	100–500	Lee and Grant 1981
Sludge, total PAHs		
United Kingdom, 12 sites, (g/kg)		
Fresh weight	80–1,760	McIntyre
Dry weight	200–50,300	et al. 1981
Texas, Reese Air Force Base		
Effluent lagoon (g/kg fresh weight)		
PER	300.0	Rose 1977
PYR	5.8	
FL	5.7	
BaA	1.4	
CHRY	1.3	
BaP	0.5	
BeP	0.2	
A	0.2	
Motor oils (µg/L)		
Unused		
BaP	115	Pasquini and
CHRY	56	Monarca 1983
PER	11	
Used		
BaP	1,382	
CHRY	10,170	
PER	1,024	
Groundwater (µg/L)		
Worldwide		
Total PAHs	0.01–0.05	Lee and Grant 1981
Total PAHs	0.045–0.51	Harrison
Carcinogenic PAHs	0.00–0.081	et al. 1975
Germany		
Total PAHs	0.04	EPA 1980
Carcinogenic PAHs	0.003	
Champaign, Illinois		
Total PAHs	0.007	
Carcinogenic PAHs	0.003	
Elkhart, Indiana		
Total PAHs	0.02	

Carcinogenic PAHs	0.004	
Drinking water (µg/L)		
USA, total PAHs	0.015	Lee and
Europe, total PAHs	0.04–0.06	Grant 1981
Monongehla River, Pittsburgh, PA		
Untreated		
Total PAHs	0.6	EPA 1980
Carcinogenic	0.14	
Treated		
Total PAHs	0.003	
Carcinogenic PAHs	0.002	
Ohio River, Wheeling, WV		
Untreated		
Total PAHs	1.59	
Carcinogenic PAHs	0.57	
Treated		
Total PAHs	0.14	
Carcinogenic PAHs	0.011	
Lake Winnebago, Appleton, WI		
Untreated		
Total PAHs	0.007	
Carcinogenic PAHs	0.002	
Treated		
Total PAHs	0.006	
Carcinogenic PAHs	0.002	
Surface water (µg/L)		
Worldwide		
Low level contamination	0.05–0.25	Lee and
Medium polluted	0.2–1.0	Grant 1981
Germany, Rhine River		
Total PAHs	1.12	EPA 1980
Carcinogenic PAHs	0.49	
Thames River, UK		
Total PAHs	0.5–1.33	
Carcinogenic PAHs	0.18–0.56	

[a]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

A major source of PAHs in soils and soil litter is from emissions and deposition from forest fires. In a controlled burn study, Sullivan and Mix (1985) showed that lower molecular weight PAHs, such as phenanthrene and fluorene, which had been deposited in soil litter, degraded to nondetectable levels within 2 years after burning. Higher molecular weight PAHs such as benzo(k)fluorene, benzo(a)pyrene, benzo(g,h,i)perylene, perylene, and indeno(1,2,3-cd)pyrene, were more persistent in litter, decreasing after 5 years to about 20% of initial deposition. Although movement into the top 2 cm of the soil profile was initially

more pronounced for lower molecular weight PAHs, all compounds appeared to reach equilibrium between litter and soil on the basis of organic content within one year postburn. Differential persistence and fate of PAHs on slash burn sites is explained by solubility, Kow, and other physicochemical properties (Sullivan and Mix 1985). PAHs from vehicle emissions constitute a minor, but measurable, source of soil PAHs (Table 3). The majority of highway-derived PAHs appears to be deposited within 3.8 m of the road, but the influence of the highway may extend to nearly 70 m (Johnston and Harrison 1984). The use of composted municipal wastes for conditioning of agricultural soils is not recommended, as these contain at least nine identified carcinogenic PAHs (Martens 1982).

Some sediments were found to be highly contaminated with PAHs. Sediments and sediment extracts from the Buffalo River, New York, contained elevated levels of carcinogenic PAHs (1,000-16,000 ug/kg). Brown bullheads (*Ictalurus nebulosus*), in response to repeated applications of Buffalo River sediment extracts, showed epidermal hyperplasia and neoplasia when compared to controls (Black 1983). PAH concentrations in sediments from the Great Barrier Reef, Australia, were always <0.8 ug/kg dry weight, except in small areas close to sites frequently visited by power boats; in those instances, total PAH levels exceeded 13,400 ug/kg (Smith et al. 1985). Highest PAH levels measured in sediments of Cayuga Lake, New York, were found in marinas or areas of the lake receiving urban runoff, and were apparently not related to stack emissions from a nearby coal-fired power plant; Heit (1985) believed that stack emissions were either masked by other sources or were atmospherically transported and deposited elsewhere. Coastal and offshore sediments are subject to highly elevated PAH levels from a variety of sources, mostly unknown, relative to preindustrial times (Johnson et al. 1985). For example, PAH levels in sediments of Penobscot Bay, Maine, fell within the range found in sediments near industrialized regions, and were significantly higher than expected for an area previously considered to be uncontaminated (Table 3; Johnson et al. 1985).

Sewage effluents usually contained measurable levels of PAHs, although extreme variability between and among sites is common. For example, during a heavy storm, individual PAH levels in a sewage works may increase more than 100X over a dry weather period (Harrison et al. 1975). Conventional sewage treatment plant processes remove up to 90% of carcinogenic PAHs, and this may be increased to 99% using percolating filters and activated sludge processes (Harrison et al. 1975). Tiger salamanders (*Ambystoma tigrinum*), collected in 1975 from a 13 ha sewage effluent lagoon at Reese Air Force Base, Texas, showed a remarkably high incidence (53%) of neoplastic and other lesions (Rose 1977). Analysis of sludge composites showed elevated PAH levels, especially perylene; levels of organochlorine and organophosphorus pesticides, nitrosamines, and heavy metals were judged to be nonelevated (Rose 1977).

Careful disposal of used motor oils is warranted, as these contain high quantities of mutagenic and carcinogenic PAHs (Table 3; Pasquini and Monarca 1983).

All but the most heavily contaminated fresh and marine waters contain total PAH concentrations in the part-per-trillion or low part-per-billion range (Table 3; Neff 1982b). A large proportion of the PAH content in water is probably adsorbed onto suspended solids (Harrison et al. 1975). In Lake Michigan, concentrations of total PAHs in the surface microlayer varied from 0.15 to 0.45 ug/l, representing on a relative scale 106 times the concentration in air, suggesting that aerosols are a major source of these compounds and that the microlayer is a repository until the PAHs are removed by adsorption and sedimentation (Strand and Andren 1980).

BIOLOGICAL SAMPLES

Carcinogenic PAHs have been extracted from a large variety of fresh plants, including root and leaf vegetables, fruits, grains, and edible mushrooms, as well as from various marine bacteria and phytoplankton under circumstances suggesting that PAHs were present due to local biosynthesis (Suess 1976). Vegetation and soil near known PAH sources are more highly contaminated with PAHs than those collected at greater distances (Edwards 1983). PAH levels in lettuce (*Lactuca sativa*) grown in Sweden seemed to be directly related to its proximity to local recognized point sources of PAH emitters (Table 4; Larsson and Sahlberg 1982). Washing lettuce with water had little effect on phenanthrene levels, but significantly reduced other PAHs, such as benzo(a)pyrene, benz(a)anthracene, and benzo(g,h,i)perylene by 68% to 87% (Larsson and Sahlberg 1982). fruits and vegetables grown in polluted atmospheres may contain up to 100X higher levels of total PAHs than those grown in unpolluted environments (EPA 1980; Lee and Grant 1981). PAH concentrations for plants are generally greater on plant surfaces than internal tissues, greater in above ground plant parts than those below ground, and greater in plants with broad leaves (greater surface area) than those with narrow leaves (Edwards

1983). Plants can become contaminated with PAHs through environmental pollution, particularly through deposition from the atmosphere, and also through food processing. For example, the bran portion of milled wheat, as well as finished bran cereal, had a considerably higher PAH content than other fractions or finished products (Lawrence and Weber 1984b). Enrichment of PAHs in plants is associated with deposition of atmospheric particulate matter with relatively small particle sizes; thus, PAH content is usually in the order of humus > mosses > lichens (Thomas et al. 1984). Mosses appear to be good indicators of regional PAH air pollution and have been recommended for this purpose (Herrmann and Hubner 1984). Concentrations of total PAHs in soils, usually the sum of 5 to 20 PAHs, typically exceeded benzo(a)pyrene levels by at least one order of magnitude; however, concentrations of benzo(a)pyrene in vegetation were generally less than those in soil where plants were growing (Edwards 1983).

PAH accumulations in marine molluscs have been reported (Table 4); however, some of these data may be misleadingly low. For example, lengthy cold storage of 10 months can result in loss of volatile PAHs, such as anthracene, in tissues of mussels (Smith et al. 1984); accordingly, background concentrations in these organisms may be underreported. Bivalve molluscs tend to accumulate high PAH levels due to their inability to metabolize and excrete them (Lawrence and Weber 1984a), presumably due to inefficient or missing mixed-function oxidase systems (Sirota and lithe 1981). Cellular proliferative disorders, resembling neoplastic conditions in vertebrates, were found in mussels with the greatest PAH concentrations: 9.5% vs. 0.7% in control site (Mix 1982). Baseline levels of PAHs in indigenous bivalve molluscs reflected the degree of human onshore activity at the various sample sites, and presumably the level of water contamination; however, little relation was evident between accumulated levels of individual PAHs and total PAHs (Mix 1982). Elevated PAH concentrations, especially benz(a)anthracene, chrysene, fluorene, phenanthraene, and pyrene in oyster tissues and sediments were measured in samples from the vicinity of marinas, and were higher in oysters in cooler months, when lipids and glycogen were being stored preparatory to spawning (Marcus and Stokes 1985). In general, PAH concentrations in marine clams were highest in areas adjacent to industrialized bayfronts and lowest in clams inhabiting more remote areas; concentrations were lowest in autumn-winter, and highest during spring-summer (Mix and Schaffer 1983a). A similar pattern was observed in mussels, *Mytilus edulis*, with the more water soluble, lower molecular weight, PAHs bioconcentrated 10X to 100X above that of the higher molecular weight, less water soluble PAHs (Mix and Schaffer 1983b); PAH levels in mussels seemed to be independent of water salinity (Mix and Schaffer 1979). Clams contaminated with PAHs and removed to clean seawater for 24 hours showed significant depuration of unsubstituted 3- and 4-ring PAHs; in contrast, concentrations of all 5-, 6-, and 7-ring compounds, which includes most of the carcinogenic PAHs, were not significantly depurated (Mix 1982). A positive relation exists between PAH isomers in sediments, soft tissues of the mussel *Mytilus edulis*, and a seaweed (*Fucus* sp.) collected at Vancouver, British Columbia (Dunn 1980). For mussels, the general trend towards lower levels of higher molecular weight PAHs relative to levels in sediments suggests an uptake mechanism which involves the solution of PAHs in water; superimposed on this pattern is the more rapid turnover and shorter half-life of lower molecular weight PAHs in mussels (Dunn 1980).

PAH residues were higher than expected in American lobsters (*Homarus americanus*) collected offshore (mean weight 3.6 kg) when compared to smaller (0.6 kg) lobsters collected inshore (Sirota and Uthe 1981), suggesting that age or body size are important modifiers in PAH accumulation dynamics. PAH concentrations in sediments collected near a coking facility in Nova Scotia in 1980 contained up to 2,830 mg/kg dry weight, or more than 20X the levels recorded in Boston (Mass.) Harbor; concentrations in excess of 100 mg/kg dry weight sediment were recorded for phenanthrene, fluorene, pyrene, benz(a)anthracene, chrysene, benzo(e)pyrene, benzo(b)fluoranthene, and benzo(a)pyrene, and these seemed to reflect the elevated tissue levels in American lobsters collected from that locale (Sirota et al. 1983). PAH residues in digestive glands of American lobsters collected in 1979 in Nova Scotia from the vicinity of a major oil spill were higher than those from coastal control sites; however, PAH contents of edible muscle from control and oiled lobsters were similar (Sirota and Uthe 1981).

Table 4. PAH concentrations in field collections of selected biota. Values are shown in g/kg (ppb) fresh weight (FW), or dry weight (DW).

Taxonomic group, compound and other variables	Concentration	Reference[a]
Algae and other plants		
Marine algae, Greenland		
Total PAHs	60 FW	Harrison et al. 1975
Marine algae, Benzo (a) pyrene = BaP	Up to 60 DW	Lee and Grant 1981
Freshwater alga,		
Chlorella vulgaris, BaP	10–50 DW	Suess 1976
Bacteria, BaP	2–6 DW	
Moss, *Hypnum cupressiforme*		
Southern Finland, 1982		
Near center of		
industrial town		
BaP	110 DW	Herrmann
Fluoranthene = FL	250 DW	and Hubner 1984
Benzo (g,h,i) perylene = BghiPER	90 DW	
Indeno (1,2,3 cd) pyrene = IP	41 DW	
Vegetation		
Total PAHs		
Nonpolluted areas	20–1,000 DW	Edwards 1983
Near known source	25,000 DW	
BaP	0.1–150.0 DW	
Lettuce,		
Lactuca sativa, total PAHs		
Sweden, summer 1980		
Grown near highway		
8–15 m distant	50 FW	Larsson and
15–50 m distant	26 FW	Sahlberg 1982
Near airport, 150–800 m	24 FW	
Aluminum smelter		
0.5–1.5 km distant	654 FW	
2.0–6.5 km	128 FW	
Industrial areas	13 FW	
Residential areas		
Urban	13 FW	
Rural	12 FW	
Seedlings, wheat		
and rye, BaP	10–20 DW	Suess 1976

Invertebrates		
Rock crab, *Cancer irroratus*		
Edible portions, 1980		
New York Bight		
Total PAHs	1,600 FW	Humason and
BaP	1 FW	Gadbois 1982
Long Island Sound		
Total PAHs	1,290 FW	
BaP	ND	
American oyster,		
Crassostrea virginica, soft parts		
South Carolina, 1983,		
residential resorts		
Total PAHs		
Spring months		
Palmetto Bay	520 FW	Marcus and Stokes 1985
Outdoor Resorts	247 FW	
Fripp Island	55 FW	
Summer months		
Palmetto Bay	269 FW	
Outdoor Resorts	134 FW	
Fripp Island	21 FW	
American lobster, *Homarus americanus*		
Edible portions, 1980		
New York Bight		
Total PAHs	367 FW	Humason and
BaP	15 FW	Gadbois 1982
Long Island Sound		
Total PAHs	328 FW	
BaP	15 FW	
Softshell clam, *Mya arenaria*		
Coos bay, Oregon, 1978–79		
Soft parts		
Contaminated site		
Total PAHs	555 FW	Mix 1982
Phenanthrene = PHEN	155 FW	
FL	111 FW	
Pyrene = PYR	62 FW	
BaP	55 FW	
Benz (a) anthracene = BaA	42 FW	
Chrysene = CHRY	27 FW	
Benzo (b) fluoranthene = BbFL	12 FW	
Others	<10 FW	

Uncontaminated site		
Total PAHs	76 FW	
PHEN	12 FW	
FL	10 FW	
Others	<10 FW	
Bay mussel, *Mytilus edulis*		
Oregon, 1979–80		
Soft parts, total PAHs		
Near industrialized area	106–986 FW	Mix and Schaffer 1983b
Remote site	27–274 FW	
Sea scallop, *Placopecten magellanicus*		
Baltimore Canyon, east coast USA		
Muscle		
BaA	1 FW	Brown and
BaP	<1 FW	Pancirov 1979
PYR	4 FW	
New York Bight, 1980		
Edible portions		
Total PAHs	127 FW	Humason and
BaP	3 FW	Gadbois 1982
Clam, *Tridacna maxima*		
Australia, 1980–82, Great Barrier Reef		
Soft parts, total PAHs		
Pristine areas	<0.07 FW	Smith et al. 1984
Power boat areas	Up to 5 FW	
BaP		
Marine plankton		
Greenland	5 FW	Harrison et al. 1975
Italy	6–21 FW	
France	400 FW	
Worldwide	Up to 400 DW	Lee and Grant 1981
Mussel, *Mytilus* sp.		
Greenland		
Shell	60 FW	Harrison et al. 1975
Soft parts	18 FW	
Italy		
Shell	11 FW	
Soft parts	130–540 FW	
Bivalve molluscs, 5 spp.		
Edible portions	6 (Max. 36) FW	Stegeman 1981
Decapod crustaceans, 4 spp.		
Edible portions	2 (Max. 8) FW	
Softshell clam, *Mya arenaria*, soft parts		

Coos Bay, Oregon		
1976–78		
Near industrialized areas	6–20 FW	Mix and Schaffer 1983a
Remote areas	1–2 FW	
1978-79		
Near industrialized areas	9 FW	
Remote areas	4 FW	
Vertebrates		
Fish, muscle		
Lake Ontario, 6 spp., total PAH	3–8 FW	Lawrence and
Baltimore Canyon,		Weber 1984a
east coast, USA, 5 spp.		
BaA	Max. 0.3 FW	Brown and
BaP	Max. <5 FW	Pancirov 1979
PYR	Max. <5 FW	
Smoked		
FL	3 FW	EPA 1980
PYR	2 FW	
Nonsmoked		
FL	Max. 1.8 FW	
PYR	Max. 1.4 FW	
Winter flounder, *Pseudopleuronectes americanus*		
Edible portions, 1980		
New York Bight		
Total PAHs	315 FW	Humason and
BaP	21 FW	Gadbois 1982
Long Island Sound		
Total PAHs	103 FW	
BaP	ND	
Windowpane, *Scopthalmus aquosus*		
Edible portions, 1980		
New York Bight		
Total PAHs	536 FW	
BaP	4 FW	
Long Island Sound		
Total PAHs	86 FW	
BaP	ND	
Red hake, *Urophycus chuss*		
Edible portions, 1980		
New York Bight		
Total PAHs	412 FW	
BaP	22 FW	

Long Island Sound		
Total PAHs	124 FW	
BaP	5 FW	
BaP		
Fish		
Marine, edible portions		
9 spp.	Max. 3 FW	Stegeman 1981
Greenland	15 FW	Harrison et al. 1975
Italy	65 FW	
Steak, charcoal broiled	5–8 DW	Barnett 1976
Ribs, barbecued	11 DW	
Integrated studies		
Michigan, 1978, Hersey River		
Near wastewater treatment plant		
PHEN		
Sediments	4,097 FW	Black et al. 1981
Insects, whole	5,488 FW	
Crustaceans, muscle	447 FW	
Fish, muscle	28–15,313 FW	
BaA		
Sediments	3,504 FW	
Insects	2,893 FW	
Crustaceans	40 FW	
Fish	0.2–19 FW	
BaP		
Sediments	1,194 FW	
Insects	725 FW	
Crustaceans	8 FW	
Fish	0.07–1 FW	
Control location		
Sediments and biota		
PHEN	2–42 FW	
BaA	ND–6.7 FW	
BaP	0.04–1.2 FW	
Nova Scotia, 1980, total PAHs		
Near coking facility		
Sediments	2,830,000 DW	Sirota et al. 1983
American lobster, *Homarus americanus*		
Hepatopancreas	57,300–88,100 FW	
Tail muscle	1,910–2,670 FW	
Control area		
Sediments	<8,220 DW	

American lobster		
Hepatopancreas	1,185 FW	
Tail muscle	216 FW	
Black River, Ohio, contaminated		
area, total PAHs		
Sediments	6,700 DW	West et al. 1984
Brown bullhead,		
Ictalurus nebulosus	660 FW	
Water	153 FW	

[a]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

PAH levels in fish are usually low because this group rapidly metabolizes PAHs (Lawrence and Weber 1984a); furthermore, higher molecular weight PAHs, which include the largest class of chemical carcinogens, do not seem to accumulate in fish (West et al. 1984). Raw fish from unpolluted waters usually do not contain detectable amounts of PAHs, but smoked or cooked fish contain varying levels. The concentration of benzo(a)pyrene in skin of cooked fish was much higher than in other tissues, suggesting that skin may serve as a barrier to the migration of PAHs in body tissues (EPA 1980).

Sediments and biota collected from the Hersey River, Michigan, in 1978, were heavily contaminated with phenanthrene, benz(a)anthracene, and benzo(a)pyrene when compared to a control site. Elevated PAH concentrations were recorded in sediments, whole insect larvae, crayfish muscle, and flesh of lampreys (family Petromyzontidae), brown trout (*Salmo trutta*), and white suckers. (*Catostomus commersoni*), in that general order (Black et al. 1981). The polluted collection locale was the former site of a creosote wood preservation facility between 1902 and 1949, and, at the time of the study, received Reed City wastewater treatment plant effluent, described as an oily material with a naphthalene-like odor (Black et al. 1981). In many cases, aquatic organisms from PAH-contaminated environments have a higher incidence of tumors and hyperplastic diseases than those from nonpolluted environments. Carcinogenic PAHs have not been unequivocally identified as the causative agent for an increased incidence of cancer in any natural population of aquatic organisms, according to Neff (1982b). However, a growing body of evidence, mostly circumstantial, links PAHs to cancer in feral fish populations, especially bottom dwelling fish from areas with sediments heavily contaminated with PAHs (Baumann and Lech, in press).

TOXIC AND SUBLETHAL EFFECTS

GENERAL

A wide variety of PAH-caused adverse biological effects have been reported in numerous species of organisms under laboratory conditions, including effects on survival, growth, metabolism, and especially tumor formation. Inter- and intraspecies responses to carcinogenic PAHs were quite variable, and were significantly modified by many chemicals including other PAHs that are weakly carcinogenic or noncarcinogenic. Until these interaction effects are clarified, the results of single substance laboratory tests may be extremely difficult to apply to field situations of suspected PAH contamination.

FUNGI

Fungal degradation of PAHs may be important in the detoxification and elimination of PAHs in the environment. The fungus *Cunninghamella elegans*, for example, inhibited the mutagenic: activity of benzo(a)pyrene, 3 ethyl cholanthrene, benz(a)anthracene, and 7,12-dimethylbenz(a)anthracene, as judged by results of the Ames test using *Salmonella typhimurium* (Cerniglia et al. 1985). The rate of decrease in mutagenic activity in bacterial cultures incubated with PAHs was coincident with the rate of increase in fungal metabolism. *C. elegans* metabolized PAHs to dihydrodiols, phenols, quinones, and dihydrodiol epoxides, and to sulfate,, glucuronide, and glucoside conjugates of these primary metabolites in a manner similar to that reported

for mammalian enzyme systems, suggesting that this organism (and perhaps other fungi) is important in PAH metabolism and inactivation (Cerniglia et al. 1985).

TERRESTRIAL PLANTS

Biological effects of PAHs on terrestrial vegetation have been reviewed by EPA (1980), Lee and Grant (1981), Wang and Meresz (1982), Edwards (1983), and Sims and Overcash (1983). In general, these authorities agreed on several points. First, plants and vegetables can absorb PAHs from soils through their roots, and translocate them to other plant parts such as developing shoots. Uptake rates were governed in part, by PAH concentration, PAH water solubility, soil type, and PAH physicochemical state (vapor or particulate). Lower molecular weight PAHs were absorbed by plants more readily than higher molecular weight PAHs. Under laboratory conditions, some plants concentrated selected PAHs above that of their immediate geophysical surroundings, but this has not been conclusively demonstrated in field-grown cultivated crops or other vegetation. Second, above-ground parts of vegetables, especially the outer shell or skin, contained more PAHs than underground parts, and this was attributed to airborne deposition and subsequent adsorption. Externally deposited PAHs in vegetables were difficult to remove with cold water washings; not more than 25% were removed from lettuce, kale, spinach, leeks, and tomatoes using these procedures. Third, PAH-induced phytotoxic effects were rare; however, the data base on this subject is small. Fourth, most higher plants can catabolize benzo(a)pyrene, and possibly other PAHs, but metabolic pathways have not been clearly defined. Finally, the biomagnification potential of vegetation in terrestrial and aquatic food chains needs to be measured; this work should be conducted with a variety of PAHs in both field and laboratory experiments.

Some plants contain chemicals known to protect against PAH effects. Certain green plants contain ellagic acid, a substance that can destroy the diol epoxide form of benzo(a)pyrene, inactivating its carcinogenic and mutagenic potential (Edwards 1983). PAHs synthesized by plants may act as plant growth hormones (Edwards 1983). Some vegetables, such as cabbage, brussel sprouts, and cauliflower, contain naturally occurring antineoplastic compounds including benzyl isothiocyanate and phenethyl isothiocyanate; these compounds are known to inhibit mammary cancers, stomach tumors, and pulmonary edemas induced in rats by benzo(a)pyrene and 7,12-dimethylbenz(a)anthracene (EPA 1980). Decreased activation of carcinogens has also been demonstrated in animals fed diets that were high in protein, low in carbohydrate, and containing adequate choline; the reverse was observed in diets high in carbohydrate, low in protein, or containing certain organophosphorus insecticides, piperonyl butoxide carbon tetrachloride, nickel carbonyl, or tin (EPA 1980). In cases where dietary constituents can alter the metabolism of foreign agents, such as PAHs, the anticarcinogenic effect may result from an alteration of steady state levels of activated versus detoxified metabolites (EPA 1980). The implications of these observations to herbivorous wildlife are unknown at present.

AQUATIC BIOTA

PAHs vary substantially in their toxicity to aquatic organisms (Table 5). In general, toxicity increases as molecular weight increases (although high molecular weight PAHs have low acute toxicity, perhaps due to their low solubility in water) and with increasing alkyl substitution on the aromatic ring. Toxicity is most pronounced among crustaceans and least among teleosts (Neff 1979; Table 5). In all but a few cases, PAH concentrations that are acutely toxic to aquatic organisms are several orders of magnitude higher than concentrations found in even the most heavily polluted waters (Neff 1979). Sediments from polluted regions, however, may contain PAH concentrations similar to those which are acutely toxic, but their limited bioavailability would probably render them substantially less toxic than PAHs in solution (Neff 1979).

A growing literature exists on uptake, retention, and translocation of PAHs by aquatic plants and animals. Authorities generally agree that: most species of aquatic organisms studied to date rapidly accumulate (i.e., bioconcentrate) PAHs from low concentrations in the ambient medium; uptake of PAHs is highly species specific, being higher in algae, molluscs, and other species which are incapable of matabolizing PAHs; bioconcentration factors (BCF) tend to increase as the molecular weight of the PAH increases, with increasing octanol/water partition coefficient values, with time until approaching an apparent equilibrium level (sometimes within 24 hours), and with increases in dissolved organic matter in the medium, lipid content of organism, and a variety of endogenous and exogenous factors (Jackim and Lake 1978; Southworth et al. 1978; Lee and Grant 1981; Neff 1982a). BCF values have been determined for selected PAHs and aquatic organisms (Table 6); additional BCF data for aquatic biota are available for plants (Dobroski and Epifanio 1980; Boyle et al. 1984), crustaceans (Southworth 1979; Sirota and Uthe 1981; Fox and Rao 1982; Neff 1982a; Williams et al. 1985),

tunicates (Baird et al. 1982), molluscs (Jackim and Wilson 1979; Dobroski and Epifanio 1980; Neff 1982a), and fishes (Southworth 1979; Neff 1982a; Stoker et al. 1984). Algal accumulation of benzo(a)pyrene increased linearly in a 24-hour exposure period, and correlated positively with surface area (Leversee et al. 1981), suggesting adsorption rather than absorption. Algae readily transform benzo(a)pyrene to oxides, peroxides (Kirso et al. 1983), and dihydrodiols (Warshawsky et al. 1983). Photosynthetic rates of algae, and presumably PAH accumulations, were significantly modified by light regimens. For reasons still unexplained, algae grown in "white" light (major energy in blue-green portion of the spectrum) were more sensitive to benzo(a)pyrene than were cultures grown in "gold" light (Warshawsky et al. 1983; Schoeny et al. 1984). Accumulation by oysters (*Crassostrea virginica*) and clams (*Rangia cuneata*) of naphthalene, phenanthrene, fluorene, and their methylated derivatives increased with increasing methylation and PAH molecular weight; uptake was more rapid under conditions of continuous flow than in static tests (Neff et al. 1976). When returned to PAH-free seawater, molluscs released PAHs to non- detectable levels in about 60 days, with high molecular weight PAHs depurated more slowly than low molecular weight compounds; brown shrimp (*Penaeus aztecus*) and longnose killifish (*Fundulus similis*), which can metabolize PAHs, lost PAHs more quickly than clams and oysters, which apparently lack the detoxifying enzymes (Neff et al. 1976). Pink shrimp (*Penaeus duorarum*) exposed to 1.0 ug chrysene/l for 2 days and then transferred to unpolluted seawater for an additional 28 days contained concentrations of chrysene (91 ug/kg fresh weight in abdomen, 48 ug/kg in cephalothorax) that were considered potentially hazardous to human consumers over extended periods (Miller et al. 1982). Eggs of the sand sole (*Psettichthys melanostictus*) exposed to 0.1 ug benzo(a)pyrene /1 for 5 days showed reduced and delayed hatch and, when compared to controls, produced larvae with high accumulations (2.1 mg/kg fresh weight) and gross abnormalities, such as twinning and tissue overgrowths, in 50% of the test larvae (Hose et al. 1982). Naphthalene and benzo(a)pyrene were rapidly accumulated from the medium by three species of California marine teleosts; loss was rapid, being >90% for naphthalene in 24 hours, and 20% (muscle), to 90% (gill) for benzo (a)pyrene in a similar period (Lee et al. 1972). Phenanthrene is metabolized by many species of aquatic organisms, including fish. A marine flounder *Platichthys flesus*, given a single oral dose of 0.7 mg phenanthrene/kg body weight, contained elevated phenanthrene concentrations in lipids, melanin-rich tissues (such as skin), and the eye lens; most was eliminated within 2 weeks (Solbakken et al. 1984). Different rates of accumulation and depuration of benzo(a)pyrene and naphthalene in bluegill (*Lepomis macrochirus*) and *Daphnia magna* have been documented by McCarthy and Jimenez (1985) and McCarthy et al. (1985). Benzo(a)pyrene accumulations in bluegill, for example, were 10X greater than naphthalene, but benzo(a)pyrene is extensively metabolized, whereas naphthalene is not. Consequently, postexposure accumulations of naphthalene greatly exceeded that of the parent benzo(a)pyrene. Because the more hydrophobic PAHs, such as benzo(a)pyrene, show a high affinity for binding to dissolved humic materials and have comparatively rapid biotransformation rates, these interactions may lessen or negate bioaccumulation and food chain transfer of hydrophobic PAHs (McCarthy and Jimenez 1985; McCarthy et al. 1985).

Table 5. Toxicities of selected PAHs to aquatic organisms.

PAH compound, organism, and other variables	Concentration in medium (µg/L)	Effect[a]	Reference[b]
Benz (a) Anthracene			
Bluegill, *Lepomis macrochirus*	1,000	LC-87 (6 m)	EPA 1980
Benzo (a) pyrene			
Sandworm, *Neanthes arenceodentata*	>1,000	LC-50 (96 h)	Neff 1979
Chrysene			
Sandworm	>1,000	LC-50 (96 h)	

7,12-Dimethylbenz(a)anthracene			
Minnows, *Poeciliopsis* spp.			
Juveniles	250	LC-0 (20 h)	Schultz
Juveniles	500	LC-100 (20 h)	and Schultz 1982
Dibenz (a,h) anthracene			
Sandworm	>1,000	LC-50 (96 h)	Neff 1979
Fluoranthene			
Sandworm	500	LC-50 (96 h)	
Fluorene			
Grass shrimp, *Palaemonetes pugio*	320	LC-50 (96 h)	
Bluegill	500	LC-12 (30 d)	Finger et al. 1985
Amphipod, *Gammarus pseudolimnaeus*	600	LC-50 (96 h)	
Rainbow trout, *Salmo gairdneri*	820	LC-50 (96 h)	
Bluegill	910	LC-50 (96 h)	
Sandworm	1,000	LC-50 (96 h)	Neff 1979
Sheepshead minnow, *Cyprinodon variegatus*	1,680	LC-50 (96 h)	
Snail, *Mudalia potosensis*	5,600	LC-50 (96 h)	Finger et al. 1985
Mayfly, *Hexagenia bilineata*	5,800	LC-50 (120 h)	
Fathead minnow, *Pimephales promelas*	>100,000	LC-0 (96 h)	
Naphthalene			
Copepod, *Eurytemora affinis*	50	LC-30 (10 d)	Neff 1979
Pink salmon, *Oncorhynchus gorbuscha,* fry	920	LC-50 (24 h)	
Dungeness crab, *Cancer magister*	2,000	LC-50 (96 h)	Neff 1985
Grass shrimp	2,400	LC-50 (96 h)	Neff 1979
Sheepshead minnow	2,400	LC-50 (24 h)	
Brown shrimp, *Penaeus aztecus*	2,500	LC-50 (24 h)	
Amphipod, *Elasmopus*			

pectenicrus	2,680	LC-50 (96 h)	
Coho salmon, *Oncorhynchus* *kisutch,* fry	3,200	LC-50 (96 h)	Neff 1985
Sandworm	3,800	LC-50 (96 h)	Neff 1979
Mosquitofish, *Gambusia* *affinis*	150,000	LC-50 (96 h)	
1-Methylnaphthalene			
Dungeness crab, *Cancer* *magister*	1,900	LC-50 (96 h)	
Sheepshead minnow	3,400	LC-50 (24 h)	
2-Methylnaphthalene			
Grass shrimp	1,100	LC-50 (96 h)	Neff 1985
Dungeness crab	1,300	LC-50 (96 h)	
Sheepshead minnow	2,000	LC-50 (24 h)	Neff 1979
Trimethylnaphthalenes			
Copepod, *Eurytemora* *affinis*	320	LC-50 (24 h)	
Sandworm	2,000	LC-50 (96 h)	
Phenanthrene			
Grass shrimp	370	LC-50 (24 h)	
Sandworm	600	LC-50 (96 h)	EPA 1980
1-Methylphenanthrene			
Sandworm	300	LC-50 (96 h)	

[a]m = months, d = days, h = hours.

[b]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

Time to depurate or biotransform 50% of accumulated PAHs (Tb 1/2) varied widely. Tb 1/2 values for *Daphnia pulex* and all PAH compounds studied ranged between 0.4 and 0.5 hours (Southworth et al. 1978). For marine copepods and naphthalene, a Tb 1/2 of about 36 hours was recorded (Neff 1982a). For most marine bivalve molluscs, Tb 1/2 values ranged from 2 to 16 days. Some species, such as the hardshell clam (*Mercenaria mercenaria*), showed little or no depuration, while others, such as oysters, eliminated up to 90% of accumulated PAHs in 2 weeks--although the remaining 10% was released slowly, and traces may remain indefinitely (Jackim and Lake 1978). Percent loss of various PAHs in oysters (*Crassostrea virginica*), 7 days postexposure, ranged from no loss for benzo(a)pyrene to 98% for methylnaphthalene; intermediate were benz(a)anthracene (32%), fluoranthene (66%), anthracene (79%), dimethylnaphthalene (90%), and naphthalene (97%) (Neff 1982a). Teleosts and arthropods usually had low Tb 1/2 values. In bluegill, 89% loss of benzo(a)pyrene was recorded 4 hours postexposure; for midge larvae it was 72% in 8 hours, and for daphnids it was 21% in 18 hours (Leversee et al. 1981).

The role of sediments in PAH uptake kinetics should not be discounted. Sediment-associated anthracene contributed about 77% of the steady state body burden of this compound in the amphipod *Hyalella azteca* (Landrum and Scavia 1983). For benzo(a)pyrene and the amphipod *Pontoporeia hoyi*, the sediment source (including interstitial water) accounted for 53% in amphipods collected at 60 m, but only 9% at 23 to 45 m (Landrum et al. 1984). Benthos from the Great Lakes, such as oligochaete worms (*Limnodrilus* sp., *Stylodrilus* sp.) and amphipods (*Pontoporeia hoyi*), obtain a substantial fraction of their PAH body content from the water when sediment PAH concentrations are low. However, when sediment PAH concentrations are elevated, benthos obtain a majority of their PAHs from that source through their ability to mobilize PAHs from the. sediment/pore water matrix; the high concentrations of phenanthrene, fluorene, benzo(a)pyrene, and other PAHs measured in these organisms could provide a significant source of PAHs to predator fish (Eadie et al. 1983). Great Lakes benthos appear to contain as much PAHs as the fine grain fraction of the sediment which serves as their food, although overlying water or pore water appears to contribute a larger proportion of PAHs to the organism's body burden than does sediments (Eadie et al. 1984). Marine mussels (*Mytilus edulis*) and polychaete annelid worms (*Nereis virens*) exposed for 28 days to sediments heavily contaminated with various PAH compounds accumulated significant concentrations (up to 1,000X control levels) during the first 14 days of exposure, and little thereafter; during a 5-week postexposure period, depuration was rapid, with the more water soluble PAHs excreted most rapidly; PAH levels usually remained above control values to the end of the postexposure period (Lake et al. 1985). English sole (*Parophrys vetulus*), during exposure for 11 to 51 days to PAH-contaminated sediments, showed significant accumulations of naphthalenes in liver (up to 3.1 mg/kg dry weight) after 11 days, with concentrations declining markedly thereafter; uptake of phenanthrene, chrysene, and benzo(a)pyrene was negligible during the first 7 days (Neff 1982a).

Fluorene effects in freshwater pond ecosystems have recently been evaluated (Boyle et al. 1984, 1985; Finger et al. 1985). In ponds exposed to initial fluorene concentrations of 0.12 to 2.0 mg/l, Tb 1/2 values in water ranged from 6 to 11 days. Ten weeks after fluorene introduction, little degradation had occurred in th organic bottom sediments; fluorene residues were present in fish, invertebrates, and rooted submerged macrophytes. Studies with fingerling bluegills showed that 0.062 mg fluorene/l adversely affected their ability to capture chironomid prey, 0.12 mg/l reduced growth, and 1.0 mg fluorene/l increased their vulnerability to predation by largemouth bass (*Micropterus salmoides*). The authors concluded that fluorene, at concentrations well below its solubility and at levels that could realistically occur in the environment, represents a potential hazard to aquatic organisms.

Large interspecies differences in ability to absorb and assimilate PAHs from food have been reported. For example, crustaceans (Neff 1982a) and fish (Maccubbin et al. 1985; Malins et al. 1985a, 1985b) readily assimilated PAHs from contaminated food, whereas molluscs and polychaete annelids were limited (Neff 1982a). In all cases where assimilation of ingested PAHs was demonstrated, metabolism and excretion of PAHs were rapid (Neff 1982a). Thus, little potential exists for food chain biomagnification of PAHs (Southworth 1979; Dobroski and Epifanio 1980; Neff 1982a). In laboratory aquatic ecosystem studies, Lu et al. (1977 found that benzo(a)pyrene can be accumulated to high, and potentially hazardous, levels in fish and invertebrates. In the case of mosquitofish (*Gambusia affinis*), almost all of the accumulated benzo(a)pyrene was from its diet, with negligible accumulations from the medium. However, mosquitofish degraded benzo(a)pyrene about as rapidly as it was absorbed, in contrast to organisms such as snails (*Physa* sp.) which retained most (88%) of the accumulated benzo(a)pyrene for at least 3 days postexposure, presumably due to deficiencies in their mixed function oxidase detoxication system (Lu et al. 1977). Benzo(a)pyrene, when administered to northern pike (*Esox lucius*) through the diet or the medium, followed similar pathways: entry via the gills or gastrointestinal system, metabolism in the liver, and excretion in the urine and bile (Balk et al. 1984). Benthic marine fishes exposed to naphthalene or benzo(a)pyrene, either in diet or through contaminated sediments, accumulated substantial concentrations in tissues and body fluids (Varanasi and Gmur 1981). The tendency of fish to metabolize PAHs extensively and rapidly may explain why benzo(a)pyrene, for example, is frequently undetected, or only detected in low concentrations in livers of fish from environments heavily contaminated with PAHs (Varanasi and Gmur 1980, 1981). Extensive metabolism of benzo(a)pyrene plus the presence of large proportions of polyhydroxy metabolites in liver of English sole indicates the formation of reactive intermediates such as diol epoxides and phenol epoxides of benzo:a)pyrene, both of which are implicated in mammalian mutagenesis and carcinogenesis (Varanasi and Gmur 1981).

Table 6. PAH bioconcentration factors (BCF) for selected species of aquatic organisms.

PAH compound, organism, and other variables	Exposure period[a]	BCF	Reference[b]
Anthracene			
Cladoceran, *Daphnia magna*	60 m	200	EPA 1980
Fathead minnow, *Pimephales promelas*	2 to 3 d	485	Southworth 1979
Cladoceran, *Daphnia pulex*	24 h	760 to 1200	Southworth et al. 1978; Southworth 1979; EPA 1980; Neff 1985
Mayfly, *Hexagenia* sp.	28 h	3,500	EPA 1980
Rainbow trout, *Salmo gairdneri*	72 h	4,400 to 9,200	Linder et al. 1985
9-Methylanthracene			
Cladoceran, *Daphnia pulex*	24 h	4,583	Neff 1985
Benz(a)anthracene			
Cladoceran, *Daphnia pulex*	24 h	10,109	Southworth et al. 1978
Benzo(a)pyrene			
Teleosts, 3 spp., Muscle	1 h to 96 h	0.02 to 0.1	EPA 1980
Clam, *Rangia cuneata*	24 h	9 to 236	Neff 1979; EPA 1980
Bluegill, *Lepomis macrochirus*	4 h	12	Leversee et al. 1981
Atlantic salmon, *Salmo salar* Egg	168 h	71	Kuhnhold and Busch 1978
Midge, *Chironomus riparius,* larvae	8 h	166	Leversee et al. 1981
Rainbow trout, liver	10 d	182 to 920	Gerhart and Carlson 1978
Oyster, *Crassostrea virginica*	14 d	242	EPA 1980
Northern pike *Esox lucius*			
Bile and gallbladder	3.3 h	3,974	Balk et al. 1984
"	19.2 h	36,656	
"	8.5 d	82,916	
"	23 d	53,014	
Liver	3.3 h	259	
"	19.2 h	578	
"	8.5 d	1,376	

"	23 d	619	
Gills	3.3 h	283	
"	19.2 h	382	
"	8.5 d	372	
"	23 d	213	
Kidney	3.3 h	192	
"	19.2 h	872	
"	8.5 d	1,603	
Other tissues	3.3 h to 23 d	<55	
Mosquitofish, *Gambusia affinis*	3 d	930	Lu et al. 1977
Bluegill			
No dissolved humic material (DHM)	48 h	2,657	McCarthy and
20 mg/L	48 h	225	Jimenez 1985
Cladoceran, *Daphnia magna*	6 h	2,837	Leversee et al. 1981
Alga, *Oedogonium cardicacum*	3 d	5,258	Lu et al. 1977
Periphyton, mostly diatoms	24 h	9,600	Leversee et al. 1981
Mosquito, *Culex pipiens quinquefasciatus*	3 d	11,536	Lu et al. 1977
Sand sole, *Psettichthys melanostictus*			
Egg	6 d	21,000	Hose et al. 1982
Snail, *Physa* sp.	3 d	82,231	Lu et al. 1977
Cladoceran, *Daphnia pulex*	3 d	134,248	
Chrysene			
Clam, *Rangia cuneata*	24 h	8	Neff 1979
Mangrove snapper, *Lutjanus griseus*			
Liver	4 d	83 to 104	Miller et al. 1982
Liver	20 d	258 to 367	
Pink shrimp, *Penaeus duorarum*			
Cephalothorax	28 d	248 to 361	
Cephalothorax	28 d + 28 d Postexposure	21 to 48	
Abdomen	28 d	84 to 199	
Abdomen	28 d + 28 d postexposure	22 to 91	
Fluoranthene			
Rainbow trout, liver	21 d	379	Gerhart and Carlson 1978

Fluorene			
Bluegill	30 d	20 to 1,800	Finger et al. 1985
Naphthalene			
Clam, *Rangia cuneata*	24 h	6	Neff 1979
Sandworm, *Neanthes areaceodenta*	3 to 24 h	40	Neff 1982a
Sandworm	24 h + 300 h post- treatment	not detectable	
Atlantic salmon, egg	168 h	44 to 83	Kuhnhold and Busch 1978
Cladoceran, *Daphnia pulex*	24 h	131	Neff 1985
Crustaceans, 3 spp.	72 h	195 to 404	Neff 1979
Bluegill, whole	24 h	310	McCarthy and Jimenez 1985
Dimethylnaphthalenes			
Crustaceans, 3 spp.	72 h	967 to 1,625	Neff 1979
Perylene			
Cladoceran, *Daphnia pulex*	24 h	7,191	Neff 1985
Phenanthrene			
Clam, *Rangia cuneata*	24 h	32	Neff 1979
Cladoceran, *Daphnia pulex*	24 h	325	Neff 1985
Pyrene			
Cladoceran, *Daphnia pulex*	24 h	2,702	
Rainbow trout, liver	21 d	69	Gerhart and Carlson 1978

[a]m = minutes, h = hours, d = days.

[b]Each reference applies to the values in the same row and in the rows that follow for which no other reference is indicated.

Cytotoxic, mutagenic, and carcinogenic effects of many PAHs are generally believed to be mediated through active epoxides formed by interaction with microsomal monooxygenases. These highly active arene oxides can interact with macromolecular tissue components and can further be metabolized or rearranged to phenols or various conjugates. They can also be affected by epoxide hydrolase to form dihydrodiols, which are precursors of biologically active diol epoxides--a group that has been implicated as ultimate carcinogens. Investigators generally agree that marine and freshwater fishes are as well equipped as mammals with liver PAH-metabolizing enzymes; rapidly metabolize PAHs by liver mixed-function oxidases, with little evidence of accumulation; translocate conjugated PAH metabolites to the gall bladder prior to excretion in feces and urine; and have mixed-function oxidase degradation rates that are significantly modified by sex, age, diet, water temperature, dose-time relationships, and other variables. In addition, many species of fishes can convert PAHs, benzo(a)pyrene for example, to potent mutagenic metabolites, but because detection of the 7,8-dihydrodiol, 9,10-epoxide by analytical methods is extremely difficult, most, investigators must use biological assays, such as the Ames test, to detect mutagenic agents. At present, the interaction effects of PAHs with inorganic and other organic compounds are poorly understood. Specific examples of the above listed phenomena for PAH compounds and teleosts are documented for benzo(a)pyrene (Ahokas et al. 1975; Lu et al. 1977; Gerhart and Carlson 1978; Melius et al. 1980; Varanasi et al. 1980, 1984; Stegeman et al. 1982; Couch et al. 1983; in K.L. Hoover (ed.). National Cancer Institute Monograph 65, Washington, D.C.Hendricks 1984; Melius 1984; Schoor 1984; Schoor and Srivastava 1984; Hendricks et al. 1985; Neff 1985; Fair 1986; In vitro

metabolism and in vivo binding of benzo(a)pyrene in the California killifish (Fundulus parvipinnis) and speckled sanddab (von Hofe and Puffer 1986), 3-methylcholanthrene (Gerhart and Carlson 1978; Melius et al. 1980; Melius and Elam 1983; (Schoor and Srivastava 1984; Neff 1985), benz(a)anthracene, chrysene, and pyrene (Gerhart and Carlson 1978), and 7,12-dimethylbenz(a)anthracene (Stegeman et al. 1982).

Baumann et al. (1982) summarized reports on increasing frequencies of liver tumors in wild populations of fish during the past decade, especially in brown bullhead (*Ictalurus nebulosus*) from the Fox River, Illinois (12% tumor frequency), in Atlantic hagfish (*Myxine glutinosa*) from Swedish estuaries (6%), in English sole from the Duwamish estuary, Washington (32%), and in tomcod (*Microgadus tomcod*) from the Hudson River, New York (25%). In all of these instances, significant levels of contaminants were present in the sediments, including PAHs. PAHs have been identified as genotoxic pollutants in sediments from the Black River, Ohio, where a high incidence of hepatoma and other tumors has been observed in ictalurid fishes (West et al. 1984, 1986). Reports of tumors in Great Lakes fish populations have been increasing. Tumors of thyroid, gonad, skin, and liver are reported, with tumor frequency greatest near areas contaminated by industrial effluents such as PAHs; liver tumors were common among brown bullhead populations at sites with large amounts of PAHs in sediments (Baumann 1984). A positive relationship was finally established between sediment PAH levels and prevalence of liver lesions in English sole in Puget Sound, Washington (Malins et al. 1984; Varanasi et al. 1984), and sediment levels and liver tumor frequency in brown bullheads from the Black River, Ohio (Baumann and Harshbarger 1985; Black et al. 1985). Sediment PAH levels in the Black River, Ohio, from the vicinity of a coke plant outfall, were up to 10,000 times greater than those from a control location: concentrations were greater than 100 mg/kg for pyrene, fluoranthene, and phenanthrene; between 50 and 100 mg/kg for benz(a)anthracene, chrysene, and benzofluoranthenes; and between 10 and 50 mg/kg for individual naphthalenes, benzo(e)pyrene, benzo(a)pyrene, perylene, indeno(1,2,3-cd)pyrene, benzo(g,h,i)perylene, and anthanthrene (Baumann et al. 1982). Brown bullheads from this location contained >1.0 mg/kg of acenapthalene (2.4), phenanthrene (5.7), fluoranthene (1.9), and pyrene (1.1), and lower concentrations of heavier molecular weight PAHs; bullheads also exhibited a high (33%) liver tumor frequency, which seemed to correspond to their PAH body burdens. Investigators concluded that the elevated frequency of liver neoplasia in Black River bullheads was chemically induced, and was the result of exposure to PAHs (Baumann et al. 1982; Baumann and Harshbarger 1985).

Neoplasms in several species of fishes have been produced experimentally with 3-methylcholanthrene, acetylaminofluorene, benzo(a)pyrene, and 7, 12-dimethylbenz(a)anthracene, with tumors evident 3 to 12 months postexposure (Couch and Harshbarger 1985; Hendricks et al., 1985). Under laboratory conditions, liver neoplasms were induced in two species of minnows (*Poeciliopsis* spp.) by repeated short-term exposures (6 hours once a week, for 5 weeks) to an aqueous suspension of 5 mg/l of 7, 12-dimethylbenz(a)anthracene. About 44% of the fish surviving this treatment developed hepatocellular neoplasms 6 to 9 months postexposure (Schultz and Schultz 1982). Eastern mudminnows (*Umbra pygmaea*) kept in water containing up to 700 ug PAHs/l for 11 days showed increased frequencies of chromosomal aberrations in gills: 30% vs. 8% in controls (Prein et al. 1978). High dietary benzo(a)pyrene levels of 500 mg/kg produced significant elevations in hepatic mixed-function oxidase levels in rainbow trout after 9 weeks (Hendricks et al. 1985). Rainbow trout fed diets containing 1,006 mg benzo(a)pyrene/kg for 12 months developed liver tumors (Couch et al. 1983). About 25% of rainbow trout kept on diets containing 1,000 mg benzo(a)pyrene/kg for 18 months had histologically confirmed liver neoplasms as compared to 15% after 12 months, with no evidence of neoplasia in controls (Hendricks et al. 1985). Young English sole may activate and degrade carcinogenic PAHs, such as benzo(a)pyrene, to a greater extent than adults, but additional research is needed to determine if younger fish are at greater risk than older sole to PAH-induced toxicity (Varanasi et al. 1984). In English sole, a high significant positive correlation between PAH metabolites (1-and 3-hydroxy benzo(a)pyrene, hydroxy and dehydrodiol metabolites of pyrene and fluoranthene) in bile, and idiopathic liver lesions, prevalence of neoplasms, megalocytic hepatosis, and total number of hepatic lesions (Krahn et al. 1986) suggests that selected PAH metabolites and key organs or tissues may be the most effective monitors of PAH contamination in aquatic organisms.

In addition to those effects of PAHs emphasizing survival, uptake, depuration, and carcinogenesis previously listed, a wide variety of additional effects have been documented for aquatic organisms. These include: inhibited reproduction of daphnids and delayed emergence of larval midges by fluorene (Finger et al. 1985); decreased respiration and heart rate in mussels (*Mytilus californianus*) by benzo(a)pyrene (Sabourin and Tullis 1981); increased weight of liver, kidney, gall bladder, and spleen of sea catfish (*Arius felis*) by 3-methylcholanthrene, which was (dose-related (Melius and Elam 1983); photosynthetic inhibition of algae and

macrophytes by anthracene, naphthalene, phenanthrene, pyrene (Neff 1985) and fluorene (Finger et al. 1985); immobilization of the protozoan, *Paramecium caudatum*, by anthracene, with an EC-50 (60 min) of 0.1 ug/l EPA 1980); perylene accumulation by algae (Stegeman 1981); accumulation without activation of benzo(a)pyrene and benzo(a)anthracene by a marine protozoan (*Parauronema acutum*), and biotransformation of various fluorenes by *P. acutum* to mutagenic metabolites (Lindmark 1981); interference by toluene and anthracene with benzo(a)pyrene uptake by freshwater amphipods (Landrum 1983); abnormal blood chemistry in oysters (*Crassostrea virginica*) exposed for one year to 5 ug 3-methylcholanthrene/l (Couch et al. 1983); and enlarged livers in brown bullheads from a PAH-contaminated river (Fabacher and Baumann 1985).

AMPHIBIANS AND REPTILES

Limited data were available on biological effects of benzo(a)pyrene, 3-methylcholanthrene, and perylene to reptiles and amphibians (Balls 1964; Stegeman 1981; Anderson et al. 1982; Schwen and Mannering 1982a, 1982b; Couch et al. 1983).

Implantation of 1.5 mg of benzo(a)pyrene crystals into the abdominal cavity of adult South African clawed toads (Balls 1964). Immature toads were more resistant with only 45% bearing lymphoid tumors of liver, kidney, spleen, or abdominal muscle 272 to 310 days after implantation of 1.5 mg of benzo(a)pyrene crystals in the dorsal lymph sac or abdominal cavity. Implantation of 3-methylcholanthrene crystals into *X. laevis* provokes development of lymphoid tumors similar to those occurring naturally in this species; moreover, these tumors are readily transplantable into other *Xenopus* or into the urodele species *Triturus cristatus* (Balls 1964). Intraperitoneal injection of perylene into tiger salamanders can result in hepatic tumors (Couch et al. 1983).

A critical point of interaction between PAHs and reptiles/amphibians involves the transformation of these compounds by cytochrome P-450-dependent monooxygenase systems (Stegeman 1981 ;Schwen and Mannering 1982a). Mixed-function oxidation systems can be induced in liver and skin of tiger salamanders by perylene (Couch et al. 1983) and 3-methylcholanthrene (Anderson et al. 1982), and in liver of the leopard frog (*Rana pipiens*) and garter snake (*Thamnophis* sp.) by benzo(a)pyrene and 3-methylcholanthrene (Stegeman 1981; Schwen and Mannering 1982a, 1982b). A single dose of 40 mg/kg body weight of 3-methylcholanthrene was sufficient to induce mixed-function oxidase activity for several weeks in the leopard frog (Schwen and Mannering 1982b). Amphibians, including tiger salamanders, are quite resistant to PAH carcinogenesis when compared to mammals, according to Anderson et al. (1982). This conclusion was based on studies with *Ambystoma* hepatic microsomes and their inability to produce mutagenic metabolites of benzo(a)pyrene and perylene (as measured by bacterial *Salmonella typhimurium* strains used in the Ames test); however, rat liver preparations did produce mutagenic metabolites under these procedures (Anderson et al. 1982).

BIRDS

Only two articles were available on PAHs and avian wildlife, and both concerned mallards (*Anas platyrhynchos*). In one study, Patton and Dieter (1980) fed mallards diets that contained 4,000 mg PAHs/kg (mostly as naphthalenes, naphthenes, and phenanthrene) for a period of 7 months. No mortality or visible signs of toxicity were evident during exposure; however, liver weight increased 25% and blood flow to liver increased 30%, when compared to controls. In the second study, Hoffman and Gay (1981) measured embryotoxicity of various PAHs applied externally, in a comparatively innocuous synthetic petroleum mixture, to the surface of mallard eggs. The most embryotoxic PAH tested was 7,12-dimethylbenz(a)anthracene: approximately 0.002 ug/egg (equivalent to about 0.036 ug/kg fresh weight, based on an average weight of 55 g per egg) caused 26% mortality in 18 days, and, among survivors, produced significant reduction in embryonic growth and a significant increase in the percent of anomalies, e.g., incomplete skeletal ossification, defects in eye, brain, liver, feathers, and bill. At 0.01 ug 7,12-dimethylbenz(a)anthracene/egg, only 10% survived to day 18. Similar results were obtained with 0.015 ug (and higher) chrysene/egg. For benzo(a)pyrene, 0.002 ug/egg did not affect mallard survival, but did cause embryonic growth reduction and an increased incidence of abnormal survivors. At 0.01 ug benzo(a)pyrene/egg, 60% died in 18 days; at 0.05 ug/egg, 75% were dead within 3 days of treatment. Embryos may contain microsomal enzymes that can metabolize PAHs to more highly toxic intermediates than can adults, and avian embryos may have a greater capacity to metabolize PAHs in this manner than do mammalian embryos and fetuses (as quoted in Hoffman and Gay 1981); this observation warrants additional research. Several investigators have suggested that the presence of PAHs in petroleum, including benzo(a)pyrene, chrysene, and 7,12-dimethylbenz(a)anthracene, significantly enhances the overall embryotoxicity in avian species, and that the relatively small percent of the aromatic hydrocarbons contributed

by PAHs in petroleum may confer much of the adverse biological effects reported after eggs have been exposed to microliter quantities of polluting oils (Hoffman and Gay 1981; Albers 1983).

MAMMALS

Numerous PAH compounds are distinct in their ability to produce tumors in skin and in most epithelial tissues of practically all animal species tested; malignancies were often induced by acute exposures to microgram quantities. In some cases, the latency period car be as short as 4 to 8 weeks, with the tumors resembling human carcinomas (EPA 1980). Certain carcinogenic PAHs are capable of passage across skin, lungs, and intestine, and can enter the rat fetus, for example, following intragastric or intravenous administration to pregnant dams (EPA 1980). In most cases, the process of carcinogenesis occurs over a period of many months in experimental animals, and many years in man. The tissue affected is determined by the route of administration and species under investigation. Thus, 7,12-dimethylbenz(a)anthracene is a potent carcinogen for the mammary gland of young female rats after oral or intravenous administration; dietary benzo(a)pyrene leads to leukemia, lung adenoma, and stomach tumors in mice and both PAH compounds can induce hepatomas in skin of male mice when injected shortly after birth (Dipple 1985). Acute and chronic exposure to various carcinogenic PAHs have resulted in destruction of hematopoietic and lymphoid tissues, ovotoxicity, antispermatogonic effects, adrenal necrosis, changes in the intestinal and respiratory epithelia, and other affects (Table 7; EPA 1980; Lee and Grant 1981). For the most part, however, tissue damage occurs at dose levels that would also be expected to induce carcinomas, and thus the threat of malignancy predominates in evaluating PAH toxicity. There is a scarcity of data available on the toxicological properties of PAHs which are not demonstrably carcinogenic to mammals (EPA 1980; Lee and Grant 1981).

Target organs for PAH toxic action are diverse, due partly to extensive distribution in the body and also to selective attack by these chemicals on proliferating cells (EPA 1980). Damage to the hematopoietic and lymphoid system in experimental animals is a particularly common observation (EPA 1980). In rats, the target organs for 7,12-dimethylbenz(a)anthracene are skin, small intestine, kidney, and mammary gland, whereas in fish the primary target organ is liver (Schultz and Schultz 1982). Application of carcinogenic PAHs to mouse skin leads to destruction of sebaceous glands and to hyperplasia, hyperkeratosis, and ulceration (EPA 1980). Tumors are induced in mouse skin by the repeated application of small doses of PAHs, by a single application of a large dose, or by the single application of a subcarcinogenic dose (initiation) followed by repeated application of certain noncarcinogenic agents (promotion) (Dipple 1985). Newborn mice were highly susceptible to 3-methylcholanthrene, with many mice dying from acute or chronic wasting disease following treatment; some strains of mice eventually developed thynomas, but other strains showed no evidence despite serious damage to the thymus (EPA 1980).

In general, PAH carcinogens transform cells through genetic injury involving metabolism of the parent compound to a reactive diol epoxide. This, in turn, can then form adducts with cellular molecules, such as DNA, RNA, and proteins, resulting in cell transformation (Dipple 1985; Ward et al. 1985). In the case of benzo(a)pyrene, one isomer of the 7,8-diol, 9,10-epoxide is an exceptionally potent carcinogen to newborn mice and is believed to be the ultimate carcinogenic metabolite of this PAH (Slaga et al. 1978). One of the most toxicologically significant processes involved in the response to PAH absorption is the interaction with drug metabolizing enzyme systems (Lee and Grant 1981). Increased production of mixed-function oxidase enzymes in various small mammals has been induced by halogenated naphthalenes (Campbell et al. 1983), 3-methylcholanthrene (Miranda and Chhabra 1980), and numerous other PAHs (EPA 1980). PAH metabolites produced by microsomal enzymes in mammals can be arbitrarily divided into water soluble groups, and organosoluble groups such as phenols, dihydrodiols, hydroxymethyl derivatives, quinones, and epoxides (EPA 1980). In the case of benzo(a)pyrene, the diol epoxides are usually considered as the ultimate carcinogens. Other microsomal enzymes convert epoxide metabolites to easily excretable water soluble compounds, with excretion primarily through feces and the hepatobiliary system (EPA 1980). Interspecies differences in sensitivity to PAH-induced carcinogenesis are due largely to differences in levels of fixed function oxidase activities, and these will directly affect rates at which active metabolites are converted to less active products (Neff 1979).

Investigators agree that unsubstituted aromatic PAHs with less than 4 condensed rings have not shown tumorgenic activity; that many, but not all, 4-, 5-, and 6-ring PAH compounds are carcinogenic; and that only a few unsubstituted hydrocarbons with 7 rings or greater are tumorogenic or. carcinogenic (Neff 1979; EPA 198);

Dipple 1985). Many PAH compounds containing 4 and 5 rings and some containing 6 or more rings, provoke local tumors after repeated application to the dorsal skin of mice; the tumor incidence exhibited a significant dose-response relationship (Grimmer et al. 1985). Among unsubstituted PAHs containing a nonaromatic ring, e.g., cholanthrene and acenapthanthracene, all active carcinogens retained an intact phenanthrene segment (EPA 1980). The addition of alkyl substituentss in certain positions in the ring system of a fully aromatic PAH will often confer carcinogenic activity or dramatically enhance existing carcinogenic potency. For example, monomethyl substitution of benz(a)anthracene can lead to strong carcinogenicity in mice, with potency depending on the position of substitution in the order 7 > 6 > 8 = 12 > 9; a further enhancement of carcinogenic activity is produced by appropriate dimethyl substitution, with 7,12-dimethylbenz(a)anthracene among the most potent PAH carcinogens known. Alkyl substitution of partially aromatic condensed ring systems may also add considerable carcinogenic activity as is the case with 3-methylcholanthrene. With alkyl substitutes longer than methyl, carcinogenicity levels decrease, possibly due to a decrease in transport through cell membranes (EPA 1980).

Table 7. Some effects of PAHs on selected laboratory animals.

Effect (units), organism, PAH compound	Concentration	Reference[a]
LD-50, Acute oral		
(mg/kg body weight)		
Rodents (*Rattus* spp., *Mus* spp.)		
Benzo (a) pyrene	50	Sims and
Phenanthrene	700	Overcash 1978
Naphthalene	1,780	
Fluoranthene	2,000	
Carcinogenicity, chronic oral		
(mg/kg body weight)		
Rodents		
7,12-dimethylbenz (a) anthracene	0.00004-0.00025	Lo and Sandi 1978
Benzo (a) pyrene	0.002	Sims and Overcash 1978
Dibenz (a,h) anthracene	0.006	
Benz (a) anthracene	2.0	
Benzo (b) fluoranthene	40.0	
Benzo (k) fluoranthene	72.0	
Indeno (1,2,3-cd) pyrene	72.0	
Chrysene	99.0	
Anthracene	3,300.0	
Carcinogenicity, applied externally as topical (mg)		
Mice, *Mus* spp.		
Benzo (a) pyrene	0.001	Lo and Sandi 1978
Dibenz (a,c) anthracene	0.001	
7,12-dimethylbenz (a) anthracene	0.02	
Dibenz (a,j) anthracene	0.039	

Anthracene	0.08	
Benzo (g,h,i) perylene	0.8	
Benz (a) anthracene	1.0	
Carcinogenicity, subcutaneous (mg)		
Mice		
Dibenz (a,h) anthracene		
Adults	>0.0002	
Newborn	>0.00008	
Dibenzo (a,i) pyrene		
In sesame oil	0.05	
In peanut oil	0.6	
Benzo (a) pyrene	0.06	
Dibenzo (a,e) pyrene	>0.6	
Benzo (b) fluroanthene	1.8	
Benz (a) anthracene	5.0	
Dibenzo (a,h) pyrene	6.0	
Testicular damage (mg)		
Rat, *Rattus* spp.		
Benzo (a) pyrene, oral	100.0 (no effect)	EPA 1980
7,12-dimethylbenz (a) anthracene		
Intravenous		
Young rats	0.5–2.0	
Older rats	5.0	
Oral	20.0	
Oocyte and follicle destruction, single intraperitoneal injection (mg/kg body weight)		
Mice		
Benzo (a) pyrene	80.0	Mattison 1980
3-methylcholanthrene	80.0	
7,12-dimethylbenz (a) anthracene	80.0	
Altered blood serum chemistry and nephrotoxicity, single intraperitoneal injection (mg/kg body weight)		
Rat		
Phenanthrene	150.0	Yoshikawa
Pyrene	150.0	et al. 1985
Food consumption, daily for 5 days (mg/kg body weight)		
Deer mice, *Peromyscus maniculatus*		
2-methoxynaphthalene		
30% reduction	825	Schafer and
2-ethoxynaphthalene		Bowles 1985

3% reduction	1,213
House mice, *Mus musculus*	
2-methoxynaphthalene	
50% reduction	825
2-ethyoxynaphthalene	
50% reduction	1,213

[a]Each reference applies to the values in the same row, and in the rows that follow for which no other reference is indicated.

A good correlation exists between skin tumor initiating activities of various benzo(a)pyrene metabolites nd their mutagenic activity in mammalian cell mutagenesis systems (Slaga et al. 1978), although variations in chromosome number and structure may accompany tumors induced by various carcinogenic PAHs in rats, mice, and hamsters (Bayer 1978; EPA 1980). Active PAH metabolites, e.g., dihydrodiols or diol epoxides, can produce sister chromatid exchanges in Chinese hamster ovary cell (Bayer 1978; EPA 1980; Pal 1984). When exchanges were induced by the diol epoxide, a close relationship exists between the frequency of sister chromatid exchanges and the levels of deoxyribnucleoside-diol-epoxide adduct formation (Pal 1984). In general, noncarcinogenic PAHs were not mutagenic (EPA 1980).

Laboratory studies with mice have shown that many carcinogenic PAHs adversely affect the immune system, thus directly impacting an organism's general health, although noncarcinogenic analogues had no immunosuppressive effect; further, the more carcinogenic the PAH, the greater the immunosuppression (Ward et al. 1985).

Destruction of oocytes and follicles in mice ovary is documented following intraperitoneal injection of benzo(a)pyrene; 3-methylcholanthrene, and 7,12-dimethylbenz(a)anthracene; the rate of destruction was proportional to the activity of the ovarian cytochrome P-450 dependent monooxygenase, as well as the carcinogenicity of the PAH (Mattison 1980). However, no information is presently available to indicate whether PAHs present a hazard to reproductive success. In those cases where teratogenic effects are clearly evident, e.g., 7, 12-dimethylbenz(a)anthracene, the required doses were far in excess of realistic environmental exposures (Lee and Grant 1981).

Numerous studies show that unsubstituted PAHs do not accumulate in mammalian adipose tissues despite their high lipid solubility, probably because they tend to be rapidly and extensively metabolized (EPA 1980; Lee and Grant 1981).

Biological half-life (Tb 1/2) of PAHs is limited, as judged by rodent studies. In the case of benzo(a)pyrene and rat blood and liver, Tb 1/2 values of 5 to 10 minutes were recorded; the initial rapid elimination phase was followed by a slower disappearance phase lasting 6 hours or more (EPA 1980). Tb 1/2 values from the site of subcutaneous injection in mice were 1.75 weeks for benzo(a)pyrene, 3.5 weeks for 3-methylcholanthrene, and 12 weeks for dibenz(a,h)anthracene; the relative carcinogenicity of each compound was directly proportional to the time of retention at the injection site (Pucknat 1981).

Many chemicals are known to modify the action of carcinogenic PAHs in experimental animals, including other PAHs that are weakly carcinogenic or noncarcinogenic. The effects of these modifiers on PAH metabolism appear to fall into three major categories: those which alter the metabolism of the carcinogen, causing decreased activation or increased detoxification; those which scavenge active molecular species of carcinogens to prevent their reaching critical target sites in the cell; and those which exhibit competitive antagonism (DiGiovanni and Slaga 1981b). For example, benz(a)anthracene, a weak carcinogen when applied simultaneously with dibenz(a,h)anthracene, inhibited the carcinogenic action of the latter in mouse skin; a similar case is made for benzo(e)pyrene or dibenz(a,c)anthracene applied to mouse skin shortly prior to initiation with 7,12-dimethylbenz(a)anthracene, or 3-methylcholanthrene (DiGiovanni and Slaga 1981a). Benzo(a)pyrene, a known carcinogen, interacts synergistically with cyclopenta(cd)pyrene, a moderately strong carcinogen found in automobile exhausts, according to results of mouse skin carcinogenicity studies (Rogan et al. 1983). Other PAH combinations were cocarcinogenic, such as benzo(e)pyrene, pyrene, and fluoranthene

applied repeatedly with benzo(a)pyrene to the skins of mice (DiGiovanni and Slaga 1981a). Effective inhibitors of PAH-induced tumor development include selenium, vitamin E, ascorbic acid, butylated hydroxytoluene, and hydroxyanisole (EPA 1980). In addition, protective effects against PAH-induced tumor formation have been reported for various naturally occurring compounds such at flavones, retenoids, and vitamin A (EPA 1 80). Until these interaction effects are clarified, the results of single substance laboratory studies may be extremely difficult to apply to field situations of suspected PAH contamination. Additional work is also needed of PAH dose-response relationships, testing relevant environmental PAHs for carcinogenicity, and elucidating effects of PAH mixtures on tumor formation (Grimmer 1983).

RECOMMENDATIONS

At present, no criteria or standards have been promulgated for PAHs by any regulatory agency for the protection of sensitive species of aquatic organisms or wildlife. This observation is not unexpected in view of several factors: (1) the paucity of data on PAH background concentrations in wildlife and other natural resources; (2) the absence of information on results of chronic oral feeding studies of PAH mixtures and the lack of a representative PAH mixture for test purposes; and (3) the demonstrable--and as yet, poorly understood--effects of biological modifiers, such as sex, age, and diet, and interaction effects of PAHs with inorganic and other organic compounds, including other PAHs.

Nevertheless, the growing data base for aquatic life indicates a number of generalizations: (1) many PAHs are acutely toxic at concentrations between 50 and 1,000 ug/l; (2) deleterious sublethal responses are sometimes observed at concentrations in the range of 0.1 to 5.0 ug/l; (3) uptake can be substantial, but depuration is usually rapid except in some species of invertebrates; and (4) whole body burdens in excess of 300 ug benzo(a)pyrene/kg (and presumably other PAHs) in certain teleosts would be accompanied by a rise in the activity of detoxifying enzymes.

Current aquatic research has focused on PAHs because of their known relationship with carcinogenesis and mutagenesis. Many reports exist of high incidences of cancer-like growths and developmental anomalies in natural populations of aquatic animals and plants, but none conclusively demonstrate the induction of cancer by exposure of aquatic animals to environmentally realistic levels of carcinogenic PAHs in the water column, diet, or sediments (Neff 1982b, 1985). However, recent studies by Baumann, Malins, Black, Varanasi and their coworkers, among others, have now established that sediments heavily contaminated with PAHs from industrial sources were the direct cause of elevated PAH body burdens and elevated frequencies of liver neoplasia in fishes from these locales. At present, only a few sites containing high PAH concentrations in sediments have been identified (Couch and Harshbarger 1985), suggesting an urgent need to identify and to evaluate other PAH-contaminated aquatic sites. Most fishery products consumed by upper trophic levels, including man, contain PAH concentrations similar to those in green vegetables and smoked and charcoal-broiled meats, and would probably represent a minor source of PAH toxicity; however, consumption of aquatic organisms, especially filter-feeding bivalve molluscs, from regions severely contaminated with petroleum or PAH-containing industrial wastes, should be avoided (Jackim and Lake 1978; Neff 1982b). Neff (1982b) suggested that repeated consumption of PAH-contaminated shellfish may pose a cancer risk to humans. If true, this needs to be evaluated using seabirds, pinnipeds, and other wildlife groups which feed extensively on molluscs that are capable of accumulating high burdens of carcinogenic PAHs, in order to determine if similar risks exist.

For avian wildlife, data are missing on PAH background concentrations and on acute and chronic toxicity; these data should be collected posthaste. Studies with mallard embryos and PAHs applied to the egg surface showed toxic and adverse sublethal effects at concentrations between 0.036 and 0.18 ug PAH/kg whole egg (Hoffman and Gay 1981). Additional research is needed on petroleum-derived PAHs and their effects on developing embryos of seabirds and other waterfowl.

PAH criteria for human health protection (Table 8) were derived from tests with small laboratory mammals, primarily rodents. Accordingly, these proposed criteria should become interim guidelines for protection of nonhuman mammalian resources pending acquisition of more definitive data. The proposed PAH criteria are controversial. Pucknat (1981) states that there is no way at present to quantify the potential human health risks incurred by the interaction of any PAH with other PAHs or with other agents in the environment, including tumor initiators, promoters, and inhibitors. The problem arises primarily from the diversity of test systems and bioassay conditions used for determining carcinogenic potential of individual PAHs in experimental animals, and is confounded by the lack of a representative PAH mixture for test purposes, the absence of data for animal and

human chronic oral exposures to PAH mixtures, and the reliance on data derived from studies with benzo(a)pyrene to produce generalizations concerning environmental effects of PAHs--generalizations which may not be scientifically sound--according to Pucknat (1981). EPA (1980) emphasizes that only a small percentage of PAH compounds are known to be carcinogenic, and that measurements of total PAHs (i.e., the sum of all multiple fused-ring hydrocarbons having no heteroatoms) can not be equated with carcinogenic potential; furthermore, when the term "total PAHs" is used, the compounds being considered should be specified for each case. Lee and Grant (1981) state that an analysis of dose-response relationships for PAH-induced tumors in animals shows, in some cases, deviation from linearity in dose-response curves, especially at low doses, suggesting a two-stage model consistent with a linear nonthreshold pattern. Because overt tumor induction follows a dose-response relationship consistent with a multihit promotion process, the multihit component of carcinogenesis may be supplied by environmental stimuli not necessarily linked or related to PAH exposure.

The well-documented existence of carcinogenic and anticarcinogenic agents strongly suggests that a time assessment of carcinogenic risk for a particular PAH can be evaluated only through a multifactorial analysis (Lee and Grant 1981). One of the most toxicologically significant processes involved in the response to PAH absorption is the interaction with drug metabolizing enzyme systems. The induction of this enzyme activity in various body tissues by PAHs and other xenobiotics is probably critical to the generation of reactive PAH metabolites at the target site for tumor induction. At present, wide variations occur in human and animal carcinogen-metabolizing capacity. Moreover, it has not yet been possible to definitely correlate enzyme activity with susceptibility to carcinogenesis. The obligatory coupling of metabolic activation with PAH-induced neoplasia in animals indicates that the modulation of drug metabolizing enzymes is central to carcinogenesis (Lee and Grant 1981).

Table 8. Proposed PAH criteria for human health protection (modified from EPA 1980; Lee and Grant 1981; Pucknat 1981).

Criterion, PAH group, and units	Concentration
Drinking water	
Total PAHs	
µg/L[a]	0.0135–0.2
Daily intake, µg[a]	0.027–0.4
Yearly intake, µg	4.0
Benzo (a) pyrene	
µg/L	0.00055
Daily intake, µg	0.0011
Carcinogenic PAHs	
µg/L[b]	0.0021
Daily intake, µg[b]	0.0042
µg/L[c]	
Cancer risk 10^{-5}	0.028
Cancer risk 10^{-6}	0.0028
Cancer risk 10^{-7}	0.00028
Daily intake, g[c]	
Cancer risk 10^{-5}	0.056

Cancer risk 10^{-6}	0.0056
Cancer risk 10^{-7}	0.00056
Food	
Total PAHs	
Daily intake, g[d]	1.6–16.0
Yearly intake, g	4,150.0
Benzo (a) pyrene	
Daily intake, g[e]	0.16–1.6
Air	
Total PAHs	
$\mu g/m^3$	0.0109
Daily intake, µg[f]	0.164–0.251
Cyclohexane extractable fractions	
Coke oven emissions, coal tar products, $\mu g/m^3$, 8 to 10 hour-weighted average	100–150.0
Benzene soluble fractions	
Coal tar pitch volatiles, $\mu g/m^3$, 8-hour, time-weighted average	200.0
Benzo (a) pyrene	
$\mu g/m^3$	0.0005
Daily intake, µg[f]	0.005–0.0115
Carcinogenic PAHs	
$\mu g/m^3$	0.002
Daily intake, µg[f]	0.03–0.046
All sources	
Total PAHs	
Daily, µg	1.79–16.6
Benzo (a) pyrene	
Daily intake, µg	0.166–1.61
Daily allowable limit, µg[g]	0.048
Carcinogenic PAHs (except diet)	
Daily intake, µg[b]	0.086-0.102

[a]Total of 6 PAHs: fluoranthene, benzo (a) pyrene, benzo (g,h,i) perylene, benzo (b) fluoranthene, benzo (k) fluoranthene, and indeno (1,2,3-cd) pyrene.

[b]Total of 3 PAHs: benzo (a) pyrene, benzo (j) fluoranthene, and indeno (1,2,3-cd) pyrene.

[c]Based on all carcinogenic PAHs.

[d]Assuming 1,600 g food daily, 70 kg adult, 1 to 10 g total PAHs/diet.

[e]As above, except 0.1 to 1.0 g benzo (a) pyrene/diet.

[f]Assuming average of 15 to 23 m^3 of air inhaled daily.

[g]From Wang and Meresz (1982).

PAHs from drinking water contribute only a small proportion of the average total human intake (Harrison et al. 1975). The drinking water quality criterion for carcinogenic PAH compounds is based on the assumption that each compound is as potent as benzo(a)pyrene, and that the carcinogenic effect of the compounds is proportional to the sum of their concentrations (EPA 1980). Based on an oral feeding study of benzo(a)pyrene in mice, the concentration of this compound estimated to result in additional risk of one additional case for every 100,000 individuals exposed (i.e, 10^{-5}) is 0.028 ug/l. Therefore, with this assumption, the sum of the concentrations of all carcinogenic PAH compounds should be less than 0.028 ug/l in order to keep the lifetime cancer risk below 10^{-4} (EPA 1980). The corresponding recommended criteria which may result in an incremental cancer risk of 10^{-6} and 10^{-7} over the lifetime are 0.0028 and 0.00028 ug/l, respectively (Table 8). If the above estimates are made for consumption of aquatic organisms only, the levels are 0.311 (10^{-5}), 0.031(10^{-6}), and 0.003(10^{-7}) ug/kg, respectively (EPA 1980). The use of contaminated water for irrigation can also spread PAHs into other vegetable foodstuffs (EPA 1980). When vegetables grown in a PAH-polluted area are thoroughly washed and peeled, their contribution to total PAH intake in humans is not significant (Wang and Meresz 1982). Herbivorous wildlife, however, may ingest significant quantities of various PAHs from contaminated vegetables--but no data were available on this subject.

PAHs are widely distributed in the environment as evidenced by their detection in sediments, soils, air, surface waters, and plant and animal tissues. However, the ecological impact of PAHs is uncertain. PAHs show little tendency for bioconcentration despite their high lipid solubility (Pucknat 1981), probably because most PAHs are rapidly metabolized. Sims and Overcash (1983) list a variety of research needs regarding PAHs in soil-plant systems. Specifically, research is needed to establish: the rates of PAH decomposition in soils; the soil PAH levels above which PAH constituents adversely affects the food chain and enhancement factors that increase degradation rates of PAHs, especially PAHs with more than 3 rings. Once these factors have been determined, PAH disposal into soils may become feasible at environmentally nonhazardous levels.

Diet is the major source of PAHs to humans. Authorities agree that most foods contain 1 to 10 ug total PAHs/kg fresh weight, that smoking or barbecuing fish and meats increases total PAH content up to 100X, that contaminated molluscs and crustaceans may contribute significantly to PAH intake, and that PAH carcinogenic risk to humans has existed at least since man began to cook his food (Barnett 1976; EPA 1980; Lee and Grant 1981; Lawrence and Weber 1984a). A total of 22 PAHs has been identified in foods, of which 11 have been found to be carcinogenic in experimental animals. Of these, only 5 (benzo(a)pyrene, benz(a)anthracene, 3-methylcholanthrene, dibenz(a,h)anthracene, and 7,12-dimethylbenz(a)anthracene) have been demonstrated to induce tumors following oral administration to rats and mice, and only 3 of the 11 exhibited positive dose-response relationships in chronic studies with mice (Lo and Sandi 1978). At the present time, there is no evidence that any of the 11 known carcinogenic PAHs or their combinations can cause cancer in human beings via the oral route, especially in quantities likely to be present in foods (Lo and Sandi 1978).

In view of the carcinogenic characteristics of many PAH compounds, their increasing concentrations in the environment should be considered alarming, and efforts should be made to reduce or eliminate them wherever possible (Suess 1976).

LITERATURE CITED

Ahokas, J.T., O. Pelkonen, and N.T. Karki. 1975. Metabolism of polycyclic hydrocarbons by a highly active aryl hydrocarbon hydroxylase system in the liver of a trout species. Biochem. Biophys. Res. Comm. 63:635-641.

Albers, P.H. 1983. Effects of oil on avian reproduction: a review and discussion. Pages 78-96 *in* The effects of oil on birds. A multidiscipline symposium. Tri-State Bird Rescue and Research, Inc., Wilmington, Delaware.

Anderson, R.S., J.E. Doos, and F.L. Rose. 1982. Differential ability of *Ambystoma tigrinum* hepatic microsomes to produce mutagenic metabolites from polycyclic aromatic hydrocarbons and aromatic amines. Cancer Lett. 16:33-41.

Ang, K.P., H. Gunasingham, and B.T. Tay. 1986. The distribution of polynuclear aromatic hydrocarbons in ambient air particulates in Singapore. Environ. Monitor. Assess. 6:171-180.

Baird, W.M., R.A. Chemerys, L. Diamond, T.H. Meedel, and J.R. Whittaker. 1982. Metabolism of benzo(a)pyrene by *Ciona intestinalis*. Pages 191-200 *in* N.L. Richards and B.L. Jackson (eds.) Symposium: carcinogenic polynuclear aromatic hydrocarbons in the marine environment. U.S. Environ. Protection Agency Rep. 600/9-82-013.

Balk, L., J. Meijer, J.W. DePierre, and L.E. Appelgren. 1984. The uptake and distribution of (^{3}H) benzo(a)pyrene in the northern pike (*Esox lucius*). Examination by whole-body autoradiography and scintillation counting. Toxicol. Appl. Pharmacol. 74:430-449.

Balls, M. 1964. Benzpyrene-induced tumours in the clawed toad, *Xenopus laevis*. Experientia 20:143-145.

Barnett, D. 1976. Polycyclic aromatic hydrocarbons and foods. CSIRO Food Res. Quart. 36:8-12.

Bauer, J.E., and O.G. Capone. 1985. Degradation and mineralization of the polycyclic aromatic hydrocarbons anthracene and naphthalene in intertidal marine sediments. Appl. Environ. Microbiol. 50:81-90.

Baumann, P.C. 1984. Cancer in wild freshwater fish populations with emphasis on the Great Lakes. J. Great Lakes R,,s. 10:251-253.

Baumann, P.C., and J.C. Harshbarger. 1985. Frequencies of liver neoplasia in a feral fish population and associated carcinogens. Mar. Environ. Res. 17:324-327.

Baumann, P.C., and J.J. Lech. In press. PAH'S, metabolites, and neoplasia in feral fish populations. *in* U. Varanasi (ed.). PAH metabolism in the aquatic environment. CRC Press, Boca Raton, Florida.

Baumann, P.C., W.D. Smith, and W K. Parland. In press. Contaminant concentrations and tumor frequencies in brown bullhead from an industrialized river and a recreational lake. Trans. Am. Fish. Soc.

Baumann, P.C., W.D. Smith, and M. Ribick. 1982. Hepatic tumor rates and polynuclear aromatic hydrocarbon levels in two populations of brown bullhead (*Ictalurus nebulosus*). Pages 93-102

Bayer, U. 1978. *In* vivo induction of sister chromatid exchanges by three polyaromatic hydrocarbons. Pages 42-428 *in* P.W. Jones and R.I. Freudenthal (eds.) Carcinogenesis - a comprehensive survey. Vol. 3. Polynuclear aromatic hydrocarbons: second international symposium on analysis, chemistry, and biology. Raven Press, New York.

Bjorseth, A., and A.J. Dennis (eds.). 1980. Polynuclear aromatic hydrocarbons: chemistry and biological effects. Battelle Press, Columbus, Ohio. 1,097 pp.

Black, J., H. Fox, P. Black, and F. Bock. 1985. Carcinogenic effects of river sediment extracts in fish and mice. Pages 415-427 *in* R.L. Jolley, R.J. Bull, W.P. Davis, S. Katz, M.H. Roberts, Jr., and V.A. Jacobs (eds.). Water chlorination. Volume **5.** Lewis Publ., Chelsea, Michigan.

Black, J.J. 1983. Epidermal hyperplasia and neoplasia in brown bullheads (Ictalurus nebulosus) in response to repeated applications of a PAH containing extract of polluted river sediment. Pages 99-111 *in* M. Cooke (eds.). Polynuclear aromatic hydrocarbons: formation, and A.J. Dennis metabolism and measurement. Battelle Press, Columbus, Ohio.

Black, J.J., T.F. Hart, Jr., and E. Evans. 1981. HPLC studies of PAH pollution in a Michigan trout stream. Pages 343-355 *in* M. Cooke and A.J. Dennis (eds.). Chemical analysis and biological fate: polynuclear aromatic Battelle Press, Columbus, hydrocarbons. Fifth international symposium. Ohio.

Boehm, P.D., and J.W. Farrington. 1984. Aspects of the polycyclic aromatic hydrocarbon geochemistry of recent sediments in the Georges Bank region. Environ. Sci. Technol. 18:840-845.

Boyle, T.P., S.E. Finger, R.L. Paulson and C.F. Rabeni. 1985. Comparison of laboratory and field assessment of fluorene - Part II: effects on the ecological structure and function of experimental pond ecosystems. Pages 134-151 in T.P. Boyle (ed.). Validation and predictability of laboratory methods for assessing the fate and effects of contaminants in aquatic ecosystems. ASTM STP 865. American Society for Testing and Materials, Philadelphia, Pennsylvania.

Boyle, T.P., S.E. Finger, J.D. Petty, L.M. Smith, and J.N. Huckins. 1984. Distribution and rate of disappearance of fluorene in pond ecosystems. Chemosphere 13:997-1008.

Brown, R.A., and R.J. Pancirov. 1979. Polynuclear aromatic hydrocarbons in Baltimore Canyon fish. Environ. Sci. Technol. 13:878-879.

Campbell, M.A., S. Bandiera, L. Robertson, A. Parkinson, and S. Safe. 1983. Hepta-, hexa-, tetra- and dichloronaphthalene congeners as inducers of hepatic microsomal drug-metabolizing enzymes. Toxicology 26:193-205.

Cavalieri, E., R. Roth, E. Rogan C. Grandjean, and J. Althoff. 1978. Mechanisms of tumor initiation by polycyclic aromatic hydrocarbons. Pages 273-284 *in* P.W. Jones and R.I. Freudenthal (eds.). Carcinogenesis - a comprehensive survey. Vol. 3. Polynuclear aromatic hydrocarbons: second international symposium on analysts, chemistry, and biology. Raven Press, New York.

Cavalieri, E., D. Sinha, and E. Rogan. 1980. Rat mammary gland versus mouse skin: different mechanisms of activation of aromatic hydrocarbons. Pages 215-231 *in* A. Bjorseth and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: chemistry and biological effects. Battelle Press, Columbus, Ohio.

Cerniglia, C.E., G.L. White, and R.H. Heflich. 1985. Fungal metabolism and detoxification of polycyclic aromatic hydrocarbons. Arch. Microbiol. 143:105-110.

Cooke, M., and A.J. Dennis (eds.). 1981. Chemical analysis and biological fate: polynuclear aromatic hydrocarbons. Fifth international symposium. Battelle Press, Columbus, Ohio. 770 pp.

Cooke, M., and A.J. Dennis (eds.). 1983. Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio. 1,301 pp.

Cooke, M., and A.J. Dennis (eds.). 1984. Polynuclear aromatic hydrocarbons: mechanisms, methods and metabolism. Battelle Press, Columbus, Ohio. 1,464 pp.

Cooke, M., A.J. Dennis, and G.L. Fisher (eds.). 1982. Polynuclear aromatic hydrocarbons: physical and biological chemistry. Battelle Press, Columbus, Ohio. 947 pp.

Couch, J.A., and J.C. Harshbarger. 1985. Effects of carcinogenic agents on aquatic animals: an environmental and experimental overview. J. Environ. Sci. Health, Part C, Environ. Carcin. Rev. 3:63-105.

Couch, J.A., W.P. Schoor, W. Davis, and L. Courtney. 1983. Effects of carcinogens, mutagens, and teratogens on nonhuman species (aquatic animals). U.S. Environ. Protection Agency Rep. 600/9-83-005. 46 pp.

DiGiovanni, J., and T.J. Slaga. 1981a. Effects of benzo(e)pyrene [B(e)P] and dibenz(a,c)anthracene [DB(a,c)A] on the skin tumor-initiating activity of polycyclic aromatic hydrocarbons. Pages 17-31 *in* M. Cooke and A.J. Dennis (eds.). Chemical analysis and biological fate: polynuclear aromatic hydrocarbons. Fifth international symposium. Battelle Press, Columbus, Ohio.

DiGiovanni, J., and T.J. Slaga. 1981b. Modification of polycyclic aromatic hydrocarbon carcinogensis. Pages 259-292 *in* H.V. Gelboin and P.O. Ts'o (eds.). Polycyclic hydrocarbons and cancer. Vol. 3. Academic Press, New York.

Dipple, A. 1985. Polycyclic aromatic hydrocarbon carcinogensis: an introduction. Pages 1-17 *in* R.D. Harvey (ed.). Polycyclic hydrocarbons and carcinogensis. ACS Symp. Ser. 283. Amer. Chem. Soc., Washington, D.C.

Dobroski, C.J., Jr., and C.E. Epifanio. 1980. Accumulation of benzo(a)pyrene in a larval bivalve via trophic transfer. Canada. J. Fish. Aquatic Sci. 37:2318-2322.

Dunn, B.P. 1980. Polycyclic aromatic hydrocarbons in marine sediments, bivalves, and seaweeds: analysis by high-pressure liquid chromatography. Pages 367-377 *in* A. Bjorseth and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: chemistry and biological effects. Battelle Press, Columbus, Ohio.

Eadie, B.J., W.R. Faust, P.F. Landrum, and N.R. Morehead. 1984. Factors affecting bioconcentration of PAH by the dominant benthic organisms of the Great Lakes. Pages 363-377

Eadie, B.J., W.R. Faust, P.F. Landrum, N.R. Morehead, W.S. Gardner, and T. Nalepa. 1983. Bioconcentrations of PAH by some benthic organisms of the Great Lakes. Pages 437-449 *in* 4. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio.

Edwards, N.T. 1983. Polycyclic aromatic hydrocarbons (PAH's) in the terrestrial environment - a review. J. Environ. Qual. 12:427-441.

Eiceman, G.A., B. Davani, and J.A. Dodson. 1984. Discharge water from hydrostatic testing of natural gas pipelines as source of PAH loading into aquatic environments. Int. J. Environ. Anal. Chem. 19:27-39.

Eiceman, G.A., B. Davani, M.E. Wilcox, J.L. Gardea, and J.A. Dodson. 1985. High molecular weight hydrocarbons including polycyclic aromatic hydrocarbons in natural gas from consumer distribution pipelines and in pipeline sresidue. Environ. Sci. Technol. 19:603-608.

EPA. 1980. Ambient water quality criteria for polynuclear aromatic hydrocarbons. U.S. Environ. Protection Agency. Rep. 440/5-80-069. 193 PP-

Fabacher, D.L., and P.C. Baumann. 1985. Enlarged livers and hepatic microsomal mixed-function oxidase components in tumor-bearing brown bullheads from a chemically contaminated river. Environ. Toxicol. Chem. 4:703-710.

Fair, P.H. 1986. Interaction of benzo(a) pyrene and cadmium on GSH-S-transferase and benzo(a)pyrene hydroxylase in the black sea bass *Centropristis striata*. Arch. Environ. Contam. Toxicol. 15:257-263.

Finger, S.E., E.F. Little, M.G. Henry, J.F. Fairchild, and T.P. Boyle. 1985. Comparison of laboratory and field assessment of fluorene - Part I: effects of fluorene on the survival, growth, reproduction, and behavior of aquatic organisms in laboratory tests. Pages 120-133 *in* T.P. Boyle (ed.). Validation and predictability of laboratory methods for assessing the fate and effects of contaminants in aquatic ecosystems. ASTM STP 865. American Society for testing and Materials, Philadelphia, Pennsylvania.

Fox, F.R., and K.R. Rao. 1982. Accumulation, tissue distribution, and depuration of benzo(a)pyrene and benz(a)anthracene in the grass shrimp, *Palaemonetes pugio*. Pages 336-349 *in* N.L. Richards and B.L. Jackson (eds.). Symposium: carcinogenic polynuclear aromatic hydrocarbons in the marine environment. U.S. Environ. Protection Agency Rep. 600/9-82-013.

Futoma, D.J., S.R. Smith, T.E. Smith, and J. Tanaka. 1981. Polycyclic hydrocarbons in water systems. CRC Press, Boca Raton, Florida. 190 pp.

Gelboin, H.V., and P.O. Ts'o (eds.). 1978a. Polycyclic hydrocarbons and cancer. Vol. 1. Environment, chemistry, and metabolism. Academic Press, New York. 408 pp.

Gelboin, H.V., and P.O. Ts'o (eds.). 1978b. Polycyclic hydrocarbons and cancer. Vol. 2. Molecular and cell biology. Academic Press, New York. 452 pp.

Gelboin, H.V., and P.O. Ts'o (eds.). 1981. Polycyclic hydrocarbons and cancer. Vol. 3. Academic Press, New York. 351 pp.

Gerhart, E.H., and R.M. Carlson. 1978. Hepatic mixed-function oxidase activity in rainbow trout exposed to several polycyclic aromatic compounds. Environ. Res. 17:284-295.

Greenberg, A., F. Darack, R. Harkov, P. Lioy, and J. Daisey. 1985. Polycyclic aromatic hydrocarbons in New Jersey: a comparison of winter and summer concentrations over a two-year period. Atmospher. Environ. 19:1325-1339.

Grimmer, G. (ed.). 1983. Environmental carcinogens: polycyclic aromatic hydrocarbons. Chemistry, occurrence, biochemistry, carcinogenicity. CRC Press, Boca Raton, Florida. 261 pp.

Grimmer, G., H. Brune, R. Deutsch-Wenzel, G. Dettbarn, J. Misfeld, U. Able, and J. Timm. 1985. The contribution of polycyclic aromatic hydrocarbon fractions with different boiling ranges to the carcinogenic impact of emission condensate from coal fired residential furnaces as evaluated by topical application to the skin of mice. Cancer Lett. 28:203-211.

Harrison, R.M., R. Perry, and R.A. Wellings. 1975. Polynuclear aromatic hydrocarbons in raw, potable and waste waters. Water Res. 9:331-346.

Harvey, R.G. (ed.). 1985. Polycyclic hydrocarbons and carcinogensis. ACS Symp. Ser. 283. Amer. Chem. Soc., Washington, D.C. 406 pp.

Heit, M. 1985. The relationship of a coal fired power plant to the levels of polycyclic aromatic hydrocarbons (PAH) in the sediment of Cayuga Lake. Water, Air, Soil Pollut. 24:41-61.

Hendricks, J.D. 1984. Use of small fish species in carcinogenicity testing. Pages 397-404 *in* K.L. Hoover (ed.). National Cancer Institute Monograph 65, Washington, D.C.

Hendricks, J.D., T.R. Meyers, D.W. Shelton, J.L. Casteel, and G.S. Bailey. 1985. Hepatocarcinogenicity of benzo(a)pyrene to rainbow trout by dietary exposure and intraperitoneal injection. J. Natl. Cancer Inst. 74:839-851.

Herd, J.E., and F.E. Greene. 1980. Effects of perinatal exposure to benzo(a)pyrene on the aryl hydrocarbon hydroxylase system of adult rat liver. Biol. Neonate 38:291-299.

Herrmann, R., and D. Hubner. 1984. Concentrations of micropollutants (PAH, chlorinated hydrocarbons and trace metals) in the moss *Hypnum cupressiforme* in and around a small industrial town in southern Finland. Ann. Bot. Fennici 21:337-342.

Hites, R.A., and P.M. Gschwend. 1982. The ultimate fates of polycyclic aromatic hydrocarbons in marine and lacustrine sediments. Pages 357-365 *in* M. Cooke, A.J. Dennis, and F.L. Fisher (eds.). Polynuclear aromatic hydrocarbons: physical and biological chemistry. Battelle Press, Columbus, Ohio.

Hoffman,. D.J., and M.L. Gay. 1981. Embryotoxic effects of benzo(a)pyrene, chrysene, and 7,12-dimethylbenz(a)anthracene in petroleum hydrocarbon mixtures in mallard ducks. J. Toxicol. Environ. Health 7:775-787.

Hoffman, E.J., G.L. Mills, J.S. Latimer, and J.G. Quinn. 1984. Urban runoff as a source of polycyclic aromatic hydrocarbons to coastal waters. Environ. Sci. Technol. 18:580-587.

Hose, J.E., J.B. Hannah, D. DiJulio, M.L. Landolt, B.S. Miller, W.T. Iwaoka, and S.P. Felton. 1982. Effects of benzo(a)pyrene on early development of flatfish. Arch. Environ. Contam. Toxicol. 11:167-171.

Humason, A.W., and D.F. Gadbois. 1982. Determination of polynuclear aromatic hydrocarbons in-the New York Bight area. Mimeo MSG-506. Natl. Mar. Fish. Serv., Gloucester, Massachusetts.

Jackim, E., and C. Lake. 1978. Polynuclear aromatic hydrocarbons in estuarine and nearshore environments. Pages 415-428 *in* M.L. Wiley (ed.). Estuarine interactions. Academic Press, New York.

Jackim, E., and L. Wilson. 1979. Benzo(a)pyrene accumulation and depuration in the soft-shell clam (*Mya arenaria*). Pages 91-94 *in* D.S. Wilt (ed.). Proceedings tenth National Shellfish Sanitation workshop, Hunt Valley, Maryland.

Johnson, A.C., P.F. Larsen, D.F. Gadbois, and A.W. Humason. 1985. The distribution of polycyclic aromatic hydrocarbons in the surficial sediments of Penobscot Bay (Maine, USA) in relation to possible sources and to other sites worldwide. Mar. Environ. Res, 5:1-16.

Johnston, W.R., and R.M. Harrison. 1984. Deposition of metallic and organic pollutants alongside the M6 motorway. Sci. Total Environ. 33:119-127.

Jones, P.W., and R.I. Freudenthal (eds.). 1978. Carcinogensis - a comprehensive survey. Vol. 3. Polynuclear aromatic hydrocarbons: second international symposium on analysis, chemistry, and biology, Raven Press, New York. 487 pp.

Jones, P.W., and P. Leber (eds.). 1979. Polynuclear aromatic hydrocarbons. Third international symposium on chemistry and biology - carcinogenesis and mutagenesis. Ann Arbor Science Publ., Ann Arbor, Michigan. 892 pp.

Kirso, U., L. Belykh, D. Stom, N. Irha, and E. Urbas. 1983. Oxidation of benzo(a)pyrene by plant enzymes. Pages 679-687 *in* M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio.

Krahn, M.M., L.D. Rhodes, M.S. Myers L.K. Moore, W.D. MacLeod, Jr., and D.C. Malins. 1986. Associations between metabolites of aromatic compounds in bile and the occurrence of hepatic lesions in English sole (*Parophrys vetulus*) from Puget Sound, Washington. Arch. Environ. Contam. Toxicol. 15:61-67

Kuhnhold, W.W., and F. Busch. 1978. On the uptake of three different types of hydrocarbons by salmon eggs (*Salmo salar* L.). Meeresforsch. 26:50-59.

Lake, J., G.L. Hoffman, and S.C. Schimmel. 1985. Bioaccumulation of contaminants from Black Rock Harbor dredged material by mussels and polychaetes. U.S. Environ. Protection Agency Tech. Rep. D-85-2. 150 pp. Avail. from Natl. Tech. Infom. Serv., Springfield, Virginia.

Lake, J.L., C. Norwood, C. Dimock, and R. Bowen. 1979. Origins of polycyclic aromatic hydrocarbons in estuarine sediments. Geochim. Cosmochim. Acta 43:1847-1854.

Landrum, P.F. 1983. The effect of' co-contaminants on the bioavailability of polycyclic aromatic hydrocarbons to *Pontoporeia hoyi*. Pages 731-743 *in* M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio.

Landrum, P.F., B.J. Eadie, W.R. Faust, N.R. Morehead, and M.J. McCormick. 1984. Role of sediment in t e bioaccumulation of benzo(a)pyrene by the amphipod, *Pontoporeia hoyi*. Pages 799-812 *in* M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: mechanisms, methods and metabolism. Battelle Press, Columbus, Ohio.

Landrum, P.F., and D. Scavia. 1983. Influence of sediment on anthracene uptake, depuration, and biotransformation by the amphipod *Hyalella azteca*. Canada. J. Fish. Aquatic Sci. 40:298-305.

Larsson, B., and G. Sahlberg. 1982. Polycyclic aromatic hydrocarbons in lettuce. Influence of a highway and an aluminum smelter. Pages 417-426 *in* M. Cooke, A.J. Dennis, and G.L. Fisher (eds.). Polynuclear aromatic hydrocarbons: physical and biological chemistry. Battelle Press, Columbus, Ohio.

Lawrence J.F., and D.F. Weber. 1984a. Determination of polycyclic aromatic hydrocarbons in some Canadian commercial fish, shellfish, and meat products by liquid chromatography with confirmation by capillary gas chromatography-mass spectrometry. J. Agric. Food Chem. 32:789-794.

Lawrence, J.F., and D.F. Weber. 1984b. determination of polycyclic aromatic hydrocarbons in Canadian samples of processed vegetable and dairy products by liquid chromatography with fluorescence detection. J. Agric. Food Chem. 32:794-797.

Lee, R.F., R. Sauerheber, and G.D. Dobbs. 1972. Uptake, metabolism and discharge of polycyclic aromatic hydrocarbons by marine fish. Mar. Biol. 17:201-208.

Lee, S.D., and L. Grant (eds.). 1981. Health and ecological assessment of polynuclear aromatic hydrocarbons. Pathotex Publ., Park Forest South, Illinois. 364 pp.

Leversee, G.J., J.P. Geisy, P.F. Landrum, S. Bartell, S. Gerould, M. Bruno, A. Spacie, J. Bowling, J. Haddock, and T. Fannin. 1981. Disposition of benzo(a)pyrene in aquatic systems components: periphyton, chironomids, daphnia, fish. Pages 357-366 *in* M. Cooke and A.J. Dennis (eds.). Chemical analysis and biological fate: polynuclear aromatic hydrocarbons. Fifth international symposium. Battelle Press, Columbus, Ohio.

Linder, G., H.L. Bergman, and J.S. Meyer. 1985. Anthracene bioconcentration in rainbow trout during single-compound and complex-mixture exposures. Environ. Toxicol. Chem. 4:549-558.

Lindmark, D.G. 1981. Activation of polynuclear aromatic hydrocarbons to mutagens by the marine ciliate *Parauronema acutum*. Appl. Environ. Microbiol. 41:1238-1242.

Lo, M-T., and E. Sandi. 1978. Polycyclic aromatic hydrocarbons (polynuclears) in foods. Residue Rev. 69:35-86.

Lu, P-Y., R.L. Metcalf, N. Plummer, and D. Mandrel. 1977. The environmental fate of three carcinogens: benzo-(a)-pyrene, benzidine, and vinyl chloride evaluated in laboratory model ecosystems. Arch. Environ. Contam. Toxicol. 6:129-142.

Maccubbin, A.E., P. Black, L. Trzeciak, and J.J. Black. 1985. Evidence for polynuclear aromatic hydrocarbons in the diet of bottom-feeding fish. Bull. Environ. Contam. Toxicol. 34:876-882.

Malins, D.C., M.M. Krahn, D.W. Brown. L.D. Rhodes, M.S. Myers, B.B. McCain, and S. L. Chan. 1985a. Toxic chemicals in marine sediment and biota from Mukilteo, Washington: relationships with hepatic neoplasms and other hepatic lesions in English sole (*Parophrys vetulus*). J. Natl. Cancer Inst. 74:487-494.

Malins, D.C., M.M. Krahn, M.S. Myers, L.D. Rhodes, D.W. Brown, C.A. Krone, B.B. McCain, and S.-L. Chan. 1985b. Toxic chemicals in sediments and biota from a creosote-polluted harbor: relationships with hepatic neoplasms and other hepatic lesions in English sole (*Parophrys vetulus*). Carcinogenesis 6:1463-1469.

Malins, D.C., B.B. McCain, D.W. Brown, S. L. Chan, M.S. Myers, J.T. Landahl, P.G. Prohaska, A.J. Friedman, D. Rhodes, D.G. Burrows, W.D. Gronlund, and H.O. Hodgins. 1984. Chemical pollutants in sediments and diseases of bottom-dwelling fish in Puget Sound, Washington. Environ. Sci. Technol. 18:705-713.

Marcus, J.M., and T.P. Stokes. 1985. Polynuclear aromatic hydrocarbons in oyster tissue around three coastal marinas. Bull. Environ. Contam. Toxicol. 35:835-844.

Martens, R. 1982. Concentrations aid microbial mineralization of four to six ring polycyclic aromatic hydrocarbons in composted municipal waste. Chemosphere 11:761-770.

Mattison, D.R. 1980. Morphology of oocyte and follicle destruction by polycyclic aromatic hydrocarbons in mice. Toxicol. Appl. Pharmacol. 53:249-259.

McCarthy, J.F., and B.D. Jimenez 1985. Reduction in bioavailability to bluegills of polycyclic aromatic hydrocarbons bound to dissolved humic material. Environ. Toxicol. Chem. 4:511-521.

McCarthy, J.F., B.D. Jimenez, and T. Barbee. 1985. Effect of dissolved humic material on accumulation of polycyclic aromatic hydrocarbons: structure-activity relationships. Aquatic Toxicol. 7:15-24.

McGinnes, P.R., and V.L. Snoeyink. 1974. Determination of the fate of polynuclear aromatic hydrocarbons in natural water systems. Univ. Illinois at Urbana-Champaign, Water Res. Center, UILU-WRC--74-0080, Res. Rep. No. 80. 56 pp.

McIntyre, A.E., R. Perry, and J.N. Lester. 1981. Analysis of polynuclear aromatic hydrocarbons in sewage sludges. Anal. Lett. 14(A4):291-309.

McMahon, C.K., and S.N. Tsoukalas. 1978. Polynuclear aromatic hydrocarbons in forest fire smoke. Pages 61-73 *in* P.W. Jones and R.I. Freudenthal (eds.). Carcinogenesis - a comprehensive survey. Vol. 3. Polynuclear national symposium on analysis, chemistry, and biology. Raven Press, New York.

Melius, P. 1984. Comparative benzo(i)pyrene metabolite patterns in fish and rodents. Pages 387-390 *in* K.L. Hoover (ed.). Use of small fish in carcinogenicity testing. Natl. Cancer Inst. Mono. 65. Bethesda, Maryland.

Melius, P., and D.L. Elam. 1983. Mixed function oxidase in sea catfish. Pages 877-895 *in* M. Cooke and A J. Dennis (eds.). Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio.

Melius, P., D. Elam, M. Kilgore, B. Tan, and W.P. Schoor. 1980. Mixed function oxidase inducibility and polyaromatic hydrocarbon metabolism in the mullet, sea catfish, and Gulf killifish. Pages 1059-1075 *in* A. Bjorseth and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: chemistry and biological effects. Battelle Press, Columbus, Ohio.

Miller, D.L., J.P. Corliss, R.N. Farragut, and H.C. Thompson, Jr. 1982. Some aspects of the uptake and elimination of the polynuclear aromatic hydrocarbon chrysene by mangrove snapper, *Lutjanus griseus*. and pink shrimp, *Penaeus duorarum*. Pages 321-335 *in* N.L. Richards and B.L. Jackson (eds.). Symposium: carcinogenic polynuclear aromatic hydrocarbons in the marine environment. U.S. Environ. Protection Agency Rep. 600/9-82-013.

Miranda, C.L., and R.S. Chhabra. 1980. Species differences in stimulation of intestinal and hepatic microsomal nixed-function oxidase enzymes. Biochem. Pharmacol. 29:1161-1165.

Mix, M.C. 1982. Polynuclear aromatic hydrocarbons and cellular proliferative disorders in bivalve molluscs from Oregon estuaries. U.S. Environ. Protection Agency Rep. 600/4-82-026. 49 pp.

Mix, M.C., and R.L. Schaffer. 1979. Benzo(a)pyrene concentrations in mussels (*Mytilus edulis*) from Yaquina Bay, Oregon during June 1976 - May 1978. Bull. Environ. Contam. Toxicol. 23:677-684.

Mix, M.C., and R.L. Schaffer. 1983a. Concentrations of unsubstituted polycyclic aromatic hydrocarbons in softshell clams from Coos Bay, Oregon, USA. Mar. Pollut. Bull. 14:94-97.

Mix, M.C., and R.L. Schaffer. 1983b. Concentrations of unsubstituted polynuclear aromatic hydrocarbons if bay mussels (*Mytilus edulis*) from Oregon, USA. Mar. Environ. Res. 9:193-209.

Murphy, D.J., R.M. Buchan, and D.G. Fox. 1982. Ambient particulate and benzo(a)pyrene concentrations from residential wood combustion, in a mountain community. Pages 567-574 *in* M. Cooke, A.J. Dennis, and G.L. Fisher (eds.). Polynuclear aromatic hydrocarbons: physical and biological chemistry. Battelle Press, Columbus, Ohio.

Neff, J.M. 1979. Polycyclic aromatic hydrocarbons in the aquatic environment. Applied Science Publ. Ltd., London. 262 pp.

Neff, J.M. 1982a. Accumulation and release of polycyclic aromatic hydrocarbons from water, food, and sediment by marine animals. Pages 282-320 *in* N.L. Richards and B.L. Jackson (eds.). Symposium: carcinogenic polynuclear aromatic hydrocarbons n the marine environment. U.S. Environ. Protection Agency Rep. 600/9-82-013.

Neff, J.M. 1982b. Polycyclic aromatic hydrocarbons in the aquatic environment and cancer risk to aquatic organisms and man. Pages 385-409 *in* N.L Richards and B.L. Jackson (eds.). Symposium: carcinogenic polynuclear aromatic hydrocarbons in the marine environment. U.S. Environ. Protection Agency Rep. 600/9-82-013.

Neff, J.M. 1985. Polycyclic aromatic hydrocarbons. Pages 416-454 *in* G.M. Rand and S.R. Petrocelli (eds.). Fundamentals of aquatic toxicology. Hemisphere Publ. Corp., New York.

Neff, J.M., B.A. Cox, D. Dixit, and J.W. Anderson. 1976. Accumulation and release of petroleum derived aromatic hydrocarbons by four species of marine animals. Mar. Biol. 38:279-289.

Pal, K. 1984. The relationship between the levels of DNA-hydrocarbon adducts and the formation of sister-chromatid exchanges in Chinese hamster ovary cells treated with derivatives of polycyclic aromatic hydrocarbons. Mutat. Res. 129:365-372.

Pasquini, R., and S. Monarca. 1983,. Detection of mutagenic/carcinogenic compounds in unused and used motor oils. Sci. Total Environ. 32:55-64.

Patton, J.F., and M.P.. Dieter. 1980. Effects of petroleum hydrocarbons on hepatic function in the duck. Comp. Biochem. Physiol. 65C:33-36.

Potvin, R.R., E.G. Adamek, and D. Balsillie. 1981. Ambient PAH levels near a steel mill in northern Ontario. Page; 741-753 *in* M. Cooke and A.J. Dennis (eds.). Chemical analysis and biological fate: polynuclear aromatic hydrocarbons. Fifth international symposium. Battelle Press, Columbus, Ohio.

Prahl, F.G., E. Crecellus, and R. Carpenter. 1984. Polycyclic aromatic hydrocarbons in Washington coastal sediments: an evaluation of atmospheric and riverine routes of introduction. Environ. Sci. Technol. 18:687-693.

Prein, A.E., G.M. Thie, G.M. Alink, and J.H. Koeman. 1978. Cytogenetic changes in fish exposed to water of the River Rhine. Sci. Total Environ. 9:287-291.

Pucknat, A.W. (ed.). 1981. Health impacts of polynuclear aromatic hydrocarbons. Environmental Health Review No. 5. Noyes Data Corp., Park Ridge, New Jersey. 271 pp.

Quaghebeur, D, E. DeWulf, M.C. Ravelingien, and G. Janssens. 1983. Polycyclic aromatic hydrocarbons in rainwater. Sci. Total Environ. 32:35-54.

Richards, N.L., and B.L. Jackson (eds.). 1982. Symposium: carcinogenic polynuclear aromatic hydrocarbons in the marine environment. U.S. Environ. Protection Agency Rep. 60019-82-013. 409 pp.

Rogan, E., E. Cavalieri, A. Munhall, and S. Salmasi. 1983. Synergistic effect of the environmental contaminants cyclopenta(cd)pyrene and benzo(a)pyrene in mouse skin carcinogenicity. Pages 1035-1046 *in* M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio.

Rose, F.L. 1977. Tissue lesions of tiger salamander (*Ambystoma tigrinum*): relationship to sewage effluents. Ann. N.Y. Acad. Sci. 298:270-279.

Sabourin, T.D., and R.E. Tullis. 1981. Effect of three aromatic hydrocarbons on respiration and heart rates of the mussel, *Mytilus californianus*. Bull. Environ. Contam. Toxicol. 26:729-736.

Schafer, E.W., Jr., and W.A. Bowles, Jr. 1985. Acute oral toxicity and repellency of 933 chemicals to house and deer mice. Arch. Environ. Contam. Toxicol. 14:111-129.

Schoeny, R., T. Cody, M. Radike, J. Caruso, J. Rogers, B. Smiddy, M. Trentman, and D. Warshawsky. 1984. Metabolism, growth effects and mutagenicity of plant metabolites of benzo(a)pyrene. Pages 1197-1211 *in* M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: mechanisms, methods and metabolism. Battelle Press, Columbus, Ohio.

Schoor, W.P. 1984. Benzo(a)pyrene metabolism in marine fish and some analytical aspects of its metabolites. Pages 391-396 *in* K.L. Hoover (ed.). Use of small fish in carcinogenicity testing. Natl. Cancer Inst. Mono. 65. Bethesda, Maryland.

Schoor, W.P., and M. Srivastava, 1984. Position-specific induction of benzo(a)pyrene metabolism by 3-methylcholanthrene and phenobarbital in mullet (*Mugil cephalus*), a marine fish. Comp. Biochem. Physiol. 73C:391-396.

Schultz, M.E., and J.R. Schultz. 1982. Induction of hepatic tumors with 7,12-dimethylbenz(a)anthracene in two species of viviparous fishes (genus *Poeciliopsis*). Environ. Res. 271:337-351.

Schwen, R.J., and G.J. Mannering. 1982a. Hepatic cytochrome P-450-dependent monooxygenase systems of the trout, frog and snake - II. Monooxygenase activities. Comp. Biochem. Physiol. 71B:437-443.

Schwen, R.J., and G.J. Mannering. 1982b. Hepatic cytochrome P-450-dependent monooxygenase systems of the trout, frog and snake - III. Induction. Comp. Biochem. Physiol. 71B:445-453.

Shiraishi, H., N.H. Pilkington, A. Otuski, and K. Fuwa. 1985. Occurrence of chlorinated polynuclear aromatic hydrocarbons in tap water. Environ. Sci. Technol. 19:585-590.

Sims, P., and P.L. Grover. 1981. Involvement of dihydrodiols and diol epoxides in the metabolic activation of polycyclic hydrocarbons other than benzo(a)pyrene. Pages 117-181 *in* H.V. Gelboin and P.O. Ts'o (eds.). Polycyclic hydrocarbons and cancer. Vol. 3. Academic Press, New York.

Sims, R.C., and R. Overcash. 1983 Fate of polynuclear aromatic compounds (PNAs) in soil-plant systems. Residue Rev. 88:1-68

Sirota, G.R., and J.F. Uthe. 1981. Polynuclear aromatic hydrocarbon contamination in marine shellfish. Pages 329-341 *in* M. Cooke and A.J. Dennis (eds.). Chemical analysis and biological fire: polynuclear aromatic hydrocarbons. Fifth international symposium. Battelle Press, Columbus, Ohio.

Sirota, G.R., J.F. Uthe, A. Sreedharan, R. Matheson, C.J. Musial, and K. Hamilton. 1983. Polynuclear aromatic hydrocarbons in lobster (*Homarus americanus*) and sediments in the vicinity of a coking facility. Pages 1123-1136 *in* M. Cooke and N.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio.

Slaga, T.J., W.M. Bracken, A. Viaje, D.L. Berry, S.M. Fischer, D.R. Miller, W. Levin, A.H. Conney, H. Yagi, and D.M. Jerina. 1978. Tumor initiating and promoting activities of various benzo(a)pyrene metabolites in mouse skin. Pages 371-382 *in* P.W. Jones and R.I. Freudenthal (eds.). Carcinogenesis a comprehensive survey. Vol. 3. Polynuclear aromatic hydrocarbons: second international symposium on analysis, chemistry, and biology. Raven Press, New York.

Smith, J.D., J. Bagg, and B.M. Bycroft. 1984. Polycyclic aromatic hydrocarbons in the clam *Tridacna maxima* from the Great Barrier Reef, Australia. Environ. Sci. Technol. 18:353-358.

Smith, J.D., J.Y. Hauser, and J. Bagg. 1985. Polycyclic aromatic hydrocarbons in sediments of the Great Barrier Reef region, Australia. Mar. Pollut. Bull. 16:110-114.

Solbakken, J.E., K. Ingebrigtsen, and K.H. Palmork. 1984. Comparative study on the fate of the polychlorinated biphenyl 2, 4, 5, 2', 4', 5' - hexachlorobiphenyl and the polycyclic aromatic hydrocarbon phenanthrene in flounder (*Platichthys flesus*), determined by liquid scintillation counting and autoradiography. Mar. Biol. 83:239-246.

Southworth, G.R. 1979. Transport and transformation of anthracene in natural waters. Pages 359-380 *in* L.L Marking and R.A. Kimerle (eds.). Aquatic toxicology. ASTM STP-667. American Society for Testing and Materials, Philadelphia, Pennsylvania.

Southworth, G.R., J.J. Beauchamp, and P.K. Schmeider. 1978. Bioaccumulation potential of polycyclic aromatic hydrocarbons in *Daphnia pulex*. Water Res. 12:973-977.

Srivastava, V.K., P.K. Srivastava, and U.K. Misra. 1985. Polycyclic aromatic hydrocarbons of coal fly ash: analysis by gas-liquid chromatography using nematic liquid crystals. J. Toxicol. Environ. Health 15:333-337.

Statham, C.N., M.J. Melancon, Jr., and J.J. Lech. 1976. Bioconcentration of xenobiotics in trout bile: a proposed monitoring aid for some waterborne chemicals. Science 193:680-681.

Stegeman, J. 1981. Polynuclear aromatic hydrocarbons and their metabolism in the marine environment. Pages 1-60 *in* H.V. Gelboin and P.O. Ts'o (eds.). Polycyclic hydrocarbons and cancer. Vol. 3. Academic Press, New York.

Stegeman, J.J., T.R. Skopek, and W.G. Thilly. 1982. Bioactivation of polynuclear aromatic hydrocarbons to cytotoxic and mutagenic products by marine fish. Pages 201-211 *in* N.L. Richards and B.L. Jackson (eds.). Symposium: carcinogenic polynuclear aromatic hydrocarbons in the marine environment. U.S. Environ. Protection Agency Rep. 600/9-82-013.

Stoker, P.W., M.R. Plasterer, R.L. McDowell, R. Campbell, S. Fields, R. Price, C. Muehle, W.R. West, G.M. Both, J.R. Larsen, and M.L. Lee. 1984. Effects of coal-derived tars on selected aquatic and mammalian organisms. Pages 1239-1257 *in* M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: mechanisms, methods and metabolism. Battelle Press, Columbus, Ohio.

Strand, J.W., and A.W. Andren. 1980. Polyaromatic hydrocarbons in aerosols over Lake Michigan, fluxes to the Lake. Pages 127-137 *in* A. Bjorseth and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: chemistry and biological effects. Battelle Press, Columbus, Ohio.

Suess, M.J. 1976. The environmental load and cycle of polycyclic aromatic hydrocarbons. Sci. Total-Environ. 6:239-250.

Sugimura, T. 1986. Studies on environmental chemical carcinogenesis in Japan. Science 233:312-318.

Sullivan, T.J., and M.C. Mix. 1985. Persistence and fate of polynuclear aromatic hydrocarbons deposited on slash burn sites in the Cascade Mountains and coast range of Oregon. Arch. Environ. Contam. Toxicol. 14:187-192.

Szentpaly, L.V. 1984. Carcinogenesis by polycyclic aromatic hydrocarbons: a multilinear regression on new type PMO indices. J. Am. Chem. Soc. 106:6021-6028.

Thomas, W., A. Ruhling, and H Simon. 1984. Accumulation of airborne pollutants (PAH, chlorinated hydrocarbons, heavy metals) in various plant species and humus. Environ. Pollut. 36A:295-310.

Tsang, W-S., and G.W. Griffin. 1979. Metabolic activation of polynuclear aromatic hydrocarbons. Pergamon Press, Oxford, England. 125 pp.

Valerio, F., P. Bottino, D. Ugolini, M.R. Cimberle, G.A. Tozzi, and A. Frigerio. 1984. Chemical and photochemical degradation of polycyclic aromatic hydrocarbons in the atmosphere. Sci. Total Environ. 40:169-188.

van Noort, P.C.M., and E. Wondergem. 1985. Scavenging of airborne polycyclic aromatic hydrocarbons by rain. Environ. Sci. Technol. 19:1044-1048.

Varanasi, U., and D.J. Gmur. 1980. Metabolic activation and covalent binding of benzo(a)pyrene to deoxyribonucleic acid catalyzed by liver enzymes of marine fish. Biochem. Pharmacol. 29:753-762.

Varanasi, U., and D.J Gmur. 1981. In vivo metabolism of naphthalene and benzo(a)pyrene by flatfish. Pages 367-376 *in* M. Cooke and A.J. Dennis (eds.). Chemical analysis and biological fate: polynuclear aromatic hydrocarbons. Fifth international symposium. Battelle Press, Columbus, Ohio.

Varanasi, U., D.J. Gmur, and M.M. Krahn. 1980. Metabolism and subsequent binding of benzo(a)pyrene to DNA in pleuronectid and salmonid fish. Pages 455-470 *in* A. Bjorseth and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: chemistry and biological effects. Battelle Press, Columbus, Ohio.

Varanasi, U., M. Nishimoto, and J. Stover. 1984. Analyses of biliary conjugates and hepatic DNA binding in benzo(a)pyrene-exposed English sole. Pages 1315-1328 *in* M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: mechanisms, methods and metabolism. Battelle Press, Columbus, Ohio.

Varanasi, U., W.L. Reichert, J.E. Stein, D.W. Brown, and H.R. Sanborn. 1985. Bioavailability and biotransformation of aromatic hydrocarbons in benthic organisms exposed to sediment from an urban estuary. Environ. Sci. Technol. 19:836-841.

von Hofe, E., and H.W. Puffer. 1986. In vitro metabolism and in vivo binding of benzo(a)pyrene in the California killifish (*Fundulus parvipinnis*) and speckled sanddab (*Citharichthys stigmaeus*). Arch. Environ. Contam. Toxicol. 15:251-256.

Wang, D.T., and O. Meresz. 1982. Occurrence and potential uptake of polynuclear aromatic hydrocarbons of highway traffic origin by proximally grown food crops. Pages 885-896 *in* M. Cooke, A.J. Dennis, and G.L. Fisher (eds.). Polynuclear aromatic hydrocarbons: physical and biological chemistry. Battelle Press, Columbus, Ohio.

Ward, E.C., M.J. Murray, and J.H. Dean. 1985. Immunotoxicity of nonhalogenated polycyclic aromatic hydrocarbons. Pages 291-313 *in* J.H. Dean, M.I. Luster, A.E. Munson, and H. Amos (eds.). Immunotoxicology and imunopharamacology. Raven Press, Nev York.

Warshawsky, D., T. Cody, M. Radike, B.A. Smiddy, and B. Nagel. 1983. Toxicity and metabolism of benzo(a)pyrene in the green alga *Selenastrum capricornutum*. Pages 1235-1245 *in* M. Cooke and A.J. Dennis.(eds.). Polynuclear aromatic hydrocarbons: formation, metabolism and measurement. Battelle Press, Columbus, Ohio.

West, W.R., P.A. Smith, G.M. Booth, S.A. Wise, and M.L. Lee. 1986. Determination of genotoxic polycyclic aromatic hydrocarbons in a sediment from the Black River (Ohio). Arch. Environ. Contam. Toxicol. 15:241-249.

West, W.R., P.A. Smith, P.W. Stoker, G.M. Booth, T. Smith-Oliver, B.E. Butterworth, and M.L. Lee. 1984. Analysis and genotoxicity of a PAC-polluted river sediment. Paces 1395-1411 in M. Cooke and A.J. Dennis (eds.). Polynuclear aromatic hydrocarbons: mechanisms, methods and metabolism. Battelle Press, Columbus, Ohio.

Whitehouse, B. 1985. The effects of dissolved organic matter on the aqueous partitioning of polynuclear aromatic hydrocarbons. Estuar. Coastal Shelf Sci. 20:393-402.

Williams, U.P., J.W. Kiceniuk, and J.R. Botta. 1985. Polycyclic aromatic hydrocarbon accumulation and sensory evaluation of lobsters (*Homarus americanus*) exposed to diesel oil at Arnold's Cove, Newfoundland. Canada Tech. Rep. Fish. Aquatic Sci. 1402. 13 pp.

Yan, L.S. 1985. Study of the carcinogenic mechanism for polycyclic aromatic hydrocarbons - extended bay region theory and its quantitative model. Carcinogenesis 6:1-6.

Yoshikawa, T., L.P. Ruhr, W. Flory, D. Giamalva, D.F. Church, and W.A. Pryor. 1985. Toxicity of polycyclic aromatic hydrocarbons. I. Effect of phenanthrene, pyrene, and their ozonized products on blood chemistry in rats. Toxicol. Appl. Phamacol. 79:218-226.

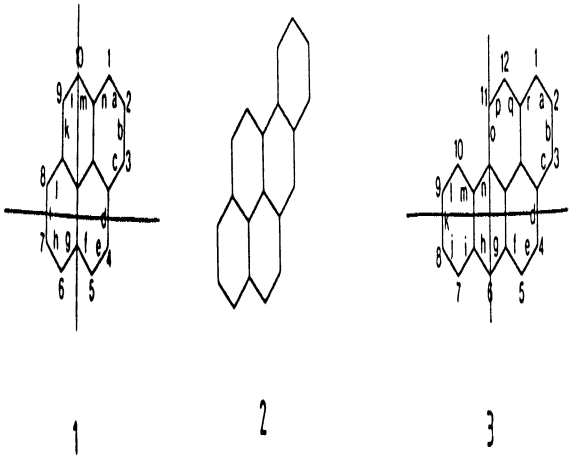


Figure 1. Nomenclature of PAHs (modified from Lee and Grant, and Grimmer 1983). The PAH formula is oriented so that the greatest number of rings are in a horizontal row and a maximum number of rings are above and to the right of the horizontal row. The first carbon atom that belongs to the uppermost ring and is not engaged in ring fusion with another ring is given the number C-1; numbering continues in a clockwise direction omitting those carbon atoms which do not carry a hydrogen atom. The bond between C-1 and C-2 is designated as side “a”; other peripheral sides continue in clockwise direction in alphabetical order. Examples are: (1) pyrene (correctly oriented, numbered, and lettered), (2) benzo(a)pyrene (not oriented correctly), (3) benzo(a)pyrene (correctly oriented, numbered, and lettered).

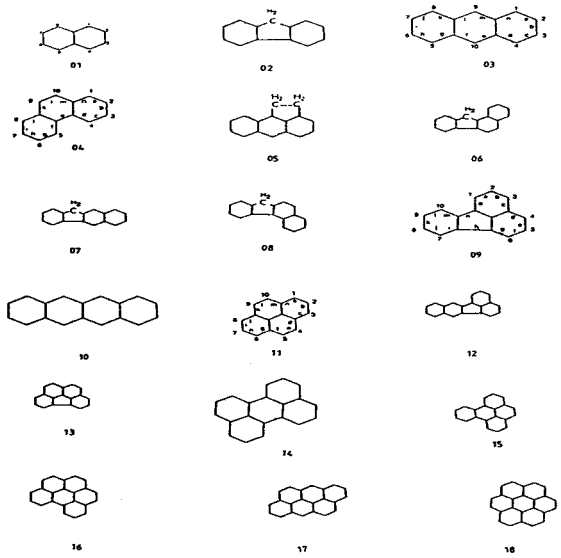


Figure 2. Ring structures of representative noncarcinogenic PAHs (modified from Lee and Grant 1981, and Neff 1985). The numbering and lettering system for several PAHs is also given. Compounds are: (1) naphthalene, (2) fluorene, (3) anthracene, (4) phenanthrene, (5) aceanthrylene, (6) benzo(a)fluorene, (7) benzo(a)fluorene, (8) benzo(a)fluorene, (9) fluoranthene, (10) napthacene, (11) pyrene, (12) benzo(a)fluoranthene, (13) benzo(g, h, i)fluoranthene, (14) perylene, (15) benzo(e)pyrene, (16) benzo(g, h, i)perylene, (17) anthanthrene, (18) coronene.

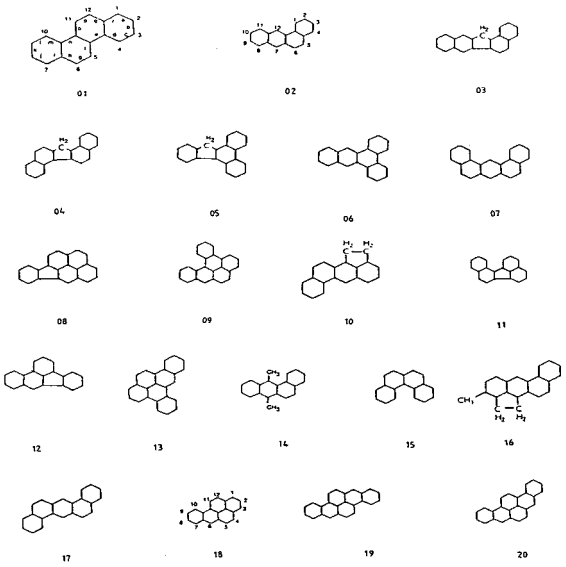


Figure 3. Ring structures of representative tumorogenic, cocarcinogenic, and carcinogenic PAHs (modified from Lee and Grant 1981). The numbering and lettering system for several PAHs is also given. Compounds are: (1) chrysene, (2) benz(a)anthracene, (3) dibenzo(a,h)fluorene, (4) dibenzo(a,g)fluorene, (5) dibenzo(a,c)fluorene, (6) dibenz(a,c)anthracene, (7) dibenz(a,j)anthracene, (8) indeno (1,2,3-cd) pyrene, (9) dibenzo(a,1)pyrene, (10) cholanthrene, (11) benzo(j)fluoranthene, (12) benzo(b)fluoranthene, (13) dibenzo(a,e)pyrene, (14) dimethylbenz(a)anthracene, (15) benzo(c)phenanthrene, (16) 3-methylcholanthrene, (17) dibenz(a,h)anthracene, (18) benzo(a)pyrene, (19) dibenzo(a,h)pyrene, (20) dibenzo(a,i)pyrene. Compounds 1 to 9 are weakly carcinogenic, cocarcinogenic, or tumorogenic; compounds 10 to 13 are carcinogenic; compounds 14 to 20 are strongly carcinogenic.

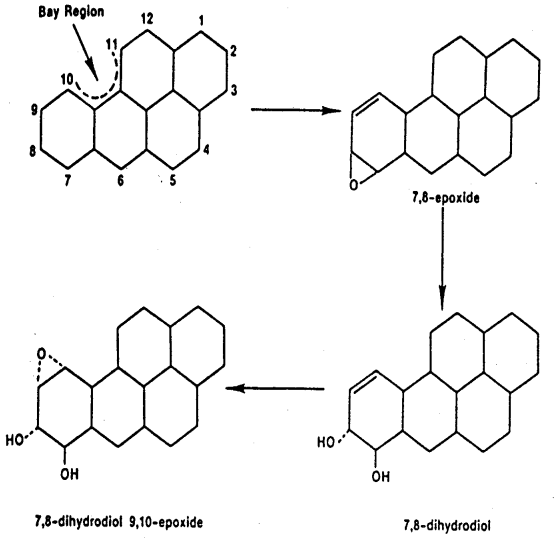


Figure 4. The bay region dihydrodiol epoxide route of benzo(a)pyrene (modified from Dipple 1985).

Biological Report 85(1.12)
January 1988

Contaminant Hazard Reviews
Report No. 12

ARSENIC HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

Arsenic (As) is a relatively common element that occurs in air, water, soil, and all living tissues. It ranks 20th in abundance in the earth's crust, 14th in seawater, and 12th in the human body.

Arsenic is a teratogen and carcinogen that can traverse placental barriers and produce fetal death and malformations in many species of mammals. Although it is carcinogenic in humans, evidence for arsenic-induced carcinogenicity in other mammals is scarce. Paradoxically, evidence is accumulating that arsenic is nutritionally essential or beneficial. Arsenic deficiency effects, such as poor growth, reduced survival, and inhibited reproduction, have been recorded in mammals fed diets containing <0.05 mg As/kg, but not in those fed diets with 0.35 mg As/kg. At comparatively low doses, arsenic stimulates growth and development in various species of plants and animals.

Most arsenic produced domestically is used in the manufacture of agricultural products such as insecticides, herbicides, fungicides, algicides, wood preservatives, and growth stimulants for plants and animals. Living resources are exposed to arsenic by way of atmospheric emissions from smelters, coal-fired power plants, and arsenical herbicide sprays; from water contaminated by mine tailings, smelter wastes, and natural mineralization; and from diet, especially from consumption of marine biota. Arsenic concentrations are usually low (<1.0 mg/kg fresh weight) in most living organisms but are elevated in marine biota (in which arsenic occurs as arsenobetaine and poses little risk to organisms or their consumer) and in plants and animals from areas that are naturally arseniferous or are near industrial manufacturers and agricultural users of arsenicals. Arsenic is bioconcentrated by organisms, but is not biomagnified in the food chain.

Arsenic exists in four oxidation states, as inorganic or organic forms. Its bioavailability and toxic properties are significantly modified by numerous biological and abiotic factors that include the physical and chemical forms of arsenic tested, the route of administration, the dose, and the species of animal. In general, inorganic arsenic compounds are more toxic than organic compounds, and trivalent species are more toxic than pentavalent species. Arsenic may be absorbed by ingestion, inhalation, or through permeation of skin or mucous membranes; cells take up arsenic through an active transport system normally used in phosphate transport. The mechanisms of arsenic toxicity differ greatly among chemical species, although all appear to cause similar signs of poisoning. Biomethylation is the preferred detoxification mechanism for absorbed inorganic arsenicals; methylated arsenicals usually clear from tissues within a few days.

Episodes of arsenic poisoning are ether acute or subacute; chronic cases of arsenosis are seldom encountered in any species except man. Single oral doses of arsenicals fatal to 50% of sensitive species tested ranged from 17 to 48 mg/kg body weight (BW) in birds and from 2.5 to 33 mg/kg BW in mammals. Susceptible species of mammals were adversely affected at chronic doses of 1 to 10 mg As/kg BW, or 50 mg As/kg diet. Sensitive aquatic species were damaged at water concentrations of 19 to 48 ug As/l (the U.S. Environmental Protection Agency drinking water criterion for human health protection is 50 ug/l), 120 mg As/kg diet, or (in the case of freshwater fish) tissue residues >1.3 mg/kg fresh weight. Adverse effects to crops and vegetation were recorded at 3 to 28 mg of water soluble As/l (equivalent to about 25 to 85 mg total As/kg soil) and at atmospheric concentrations >3.9 ug As/m^3.

Numerous and disparate arsenic criteria have been proposed for the protection of sensitive natural resources; however, the general consensus is that many of these criteria are inadequate and that additional information is needed in at least five categories: (1) developing standardized procedures to permit correlation of biologically observable effects with suitable chemical forms of arsenic; (2) conducting studies under controlled conditions with appropriate aquatic and terrestrial indicator organisms to determine the effects of chronic exposure to low doses of inorganic and organic arsenicals on reproduction, genetic makeup, adaptation, disease resistance, growth, and other variables (3) measuring interaction effects of arsenic with other common environmental contaminants, including carcinogens, cocarcinogens, and promoting agents; (4) monitoring the incidence of cancer and other abnormalities in natural resources from areas with relatively high arsenic levels, and correlating these with the possible carcinogenicity of arsenic compounds; and (5) developing appropriate models of arsenic cycling and budgets in natural ecosystems.

DISCLAIMER

Mention of trade names or commercial products does not constitute U.S. Government endorsement or recommendation for use.

Suggested citation for this report:

Eisler, R. 1988. Arsenic hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.12).

TABLES

ACKNOWLEDGMENTS

I thank Nancy A. Bushby, Lynda J. Garrett, and Joyce E. Haber for literature search and retrieval; Julia L. Armstrong for secretarial help; Matthew C. Perry, Charles J. Stafford, Donald H. White, and Laverne Cleveland for technical and scientific review; and Paul H. Eschmeyer and James R. Zuboy for editorial services.

INTRODUCTION

Anxiety over arsenic (As) is understandable, and frequently justifiable. Arsenic compounds were the preferred homicidal and suicidal agents during the Middle Ages, and arsenicals have been regarded largely in terms of their poisonous characteristics in the nonscientific literature (NAS 1977). Data collected on animals, including man, indicate that inorganic arsenic can cross the placenta and produce mutagenic, teratogenic, and carcinogenic effects in offspring (Nagymajtenyi et al. 1985). Correlations between elevated atmospheric arsenic levels and mortalities from cancer, bronchitis, and pneumonia were established in an epidemiological study in England and Wales, where deaths from respiratory cancer were increased at air concentrations >3 ug As/m^3 (NRCC 1978). Chronic arsenical poisoning, including skin cancer and a gangrenous condition of the hand and feet called Blackfoot's disease, has occurred in people from several communities in Europe, South America, and Taiwan that were exposed to elevated concentrations of arsenic in drinking water (EPA 1980). More recently, about 12,000 Japanese infants were poisoned (128 deaths) after consuming dry milk containing 15 to 24 mg inorganic As/kg, which originated from contaminated sodium phosphate used as a milk stabilizer. Fifteen years after exposure, the survivors sustained an elevated frequency of severe hearing loss and brain wave abnormalities Pershagen and Vahter 1979).

Many reviews on ecotoxicological aspects of arsenic in the environment are available; particularly useful are those by Woolson (1975), NAS (1977), NRCC (1978), Pershagen and Vahter (1979), EPA (1980, 1985), Hood (1985), and Andreas (1986). These authorities agree on six points. 1. Arsenic is a relatively common element, and is present in air, water, soil, plants, and in all living tissues. 2. Arsenicals have been used in medicine as chemotherapeutics since 400 BC, and organoarsenicals were used extensively for this purpose until about 1945, with no serious effects when judiciously administered. 3. Large quantities of arsenicals are released into the environment as a result of industrial and especially agricultural activities, and these may pose potent ecological dangers. 4. Exposure of humans and wildlife to arsenic may occur through air (emissions from smelters, coal-fired power plants, herbicide sprays), water (mine tailings runoff, smelter wastes, natural mineralization), and food (especially seafoods). 5. Chronic exposure to arsenicals by way of the air, diet, and other routes have been associated with liver, kidney, and heart damage hearing loss; brain wave abnormalities; and impaired resistance to viral infections. And 6. Exposure to arsenic has been associated with different types of human cancers such as respiratory cancers and epidermoid carcinomas of the skin, as well as precancerous dermal keratosis. Only recently (Deknudt et al. 1986) has the epidemiological evidence of human carcinogenicity been confirmed by carcinogenesis in experimental animals.

This report was prepared in response to requests for information from environmental contaminant specialists of the U. S. Fish and Wildlife Service. It is part of a continuing series of reviews on chemical pollutants and natural resources.

SOURCES, FATE, AND USES

Global production of arsenic is estimated to be 75,000 to 100,000 tons annually, of which the United States produces about 21,000 tons and uses about 44,000 tons; major quantities are imported from Sweden, the world's leading producer (NAS 1977; EPA 1980). Almost all (97%) of the arsenic made worldwide enters end-product manufacture in the form of arsenic trioxide (As_2O_3), and the rest is used as additives in producing special lead and copper alloys (NAS 1977). More than 80% of the As_2O_3 is used to manufacture products with agricultural application, such as insecticides, herbicides, fungicides, algicides, sheep dips, wood preservatives, dyestuffs, and the medicines for eradication of tapeworm in sheep and cattle (NAS 1977). The sole producer and refiner of As_2O_3 in the United States is a copper smelter in Tacoma, Washington (NAS 1977).

Arsenic naturally occurs as sulfides and as complex sulfides of iron, nickel, and cobalt (Woolson 1975). In one form or another, arsenic is present in rocks, soils, water, and living organisms at concentrations of parts per billion to parts per million (NAS 1977). Soil arsenic levels are normally elevated near arseniferous deposits, and in mineralized zones containing gold, silver, and sulfides of lead and zinc (Dudas 1984). Secondary iron oxides formed from the weathering of pyrite act as scavengers of arsenic (Dudas 1984). Pyrite is a known carrier of arsenic and may contain up to 5,600 mg/kg; for example, total arsenic is 10X above normal background levels in soils derived from pyritic shale (Dudas 1984). Natural weathering of rocks and soils adds about 40,000 tons of arsenic to the oceans yearly, accounting for <0.01 mg/l input to water on a global basis (NRCC 1978). Many species of marine plants and animals often contain naturally high concentrations of arsenic (NAS 1977), but it is

usually present in a harmless organic form (Woolson 1975). Anthropogenic input of arsenic to the environment is substantial, and exceeds that contributed by natural weathering processes by a factor of about 3X (NRCC 1978).

The most important concept with respect to arsenic cycling in the environment is constant change. Arsenic is ubiquitous in living tissue and is constantly being oxidized, reduced, or otherwise metabolized. In soils, insoluble or slightly soluble arsenic compounds are constantly being resolubilized, and the arsenic is being presented for plant uptake or reduction by organisms and chemical processes. Man reportedly has modified the arsenic cycle only by causing localized high concentrations (NAS 1977). The speciation of arsenic in the environment. is affected partly by indiscriminate biological uptake, which consumes about 20% of the dissolved arsenate pool and results in measurable concentrations of reduced and methylated arsenic species. The overall arsenic cycle is similar to the phosphate cycle; however, regeneration time for arsenic is much slower--on the order of several months (Sanders 1980). The ubiquity of arsenic in the environment is evidence of the redistribution processes that have been operating since early geologic time (Woolson 1975). A prehuman steady state solution to the global arsenic cycle (Austin and Millward 1984) indicates that major reservoirs of arsenic (in kilotons) are magma (50 billion), sediments (25 billion), oceanic deep waters (1.56 million), land (1.4 million), and ocean mixed layers (270,000); minor amounts occur in ocean particulates (100), and in continental (2.5) and marine tropospheres (0.069). Arsenic is significantly mobilized from the land to the troposphere by both natural and anthropogenic processes. Industrial emissions account for about 30% of the present day burden of arsenic in the troposphere (Austin and Millward 1984). Agronomic ecosystems, for example, may receive arsenic from agricultural sources such as organic herbicides, irrigation waters, and fertilizers, and from such nonagricultural sources as fossil fuels and industrial and municipal wastes (Woolson 1975). Arsenic is mobile and nonaccumulative in air, pant, and water phases of agronomic ecosystems; arsenicals sometimes accumulate in soils, but redistribution mechanisms usually preclude hazardous accumulations (Woolson 1975).

Arsenic compounds have been used in medicine since the time of Hippocrates, ca. 400 BC (Woolson 1975). Inorganic arsenicals have been used for centuries, and organoarsenicals for at least a century in the treatment of syphylis, yaws, amoebic dysentery, and trypanosomiasis (NAS 1977). During the period 1200 to 1650, however, arsenic was used extensively in homicides (NRCC 1978). In 1815, the first accidental death was reported from arsine (AsH_3) poisoning, and in 1900-1903 accidental poisonings from consumption of arsenic-contaminated beer were widely reported (NRCC 1978). In 1938, it was established that arsenic can counteract selenium toxicity (NRCC 1978). The introduction of arsphenamine, an organoarsenical, to control venereal disease earlier this century gave rise to intensive research by organic chemists, which resulted in the synthesis of at least 32,000 arsenic compounds. But the advent of penicillin and other newer drugs nearly eliminated the use of organic arsenicals as human therapeutic agents (EPA 1980). Arsenical drugs are still used in treating certain tropical diseases, such as African sleeping sickness and amoebic dysentery, and are used in veterinary medicine to treat parasitic diseases, including filariasis in dogs (*Canis familiaris*) and blackhead in turkeys (*Meleagris gallopavo*) and chickens, *Gallus* spp. (NAS 1977). Today, abnormal sources of arsenic that can enter the food chain from plants or animals include arsenical pesticides such as lead arsenate; arsenic acid, $HAsO_3$; sodium arsenite, $NaAsO_2$; sodium arsenate, Na_2AsO_4; and cacodylic acid, $(CH_3)_2$ As(OH) (NAS 1977).

The major uses of arsenic are in the production of herbicides, insecticides, desiccants, wood preservatives, and growth stimulants for plants and animals. Much smaller amounts are used in the manufacture of glass (nearly all of which contains 0.2% to 1.0% arsenic as an additive--primarily as a decolorizing agent) and textiles, and in medical and veterinary applications (NAS 1977; EPA 1980). Arsenic is also an ingredient in lewisite, a blistering poison gas developed (but not used) during World War I, and in various police riot control agents (NAS 1977). The availability of arsenic in certain local areas has been increased by various human activities: smelting and refining of gold, silver, copper, zinc, uranium, and lead ores; combustion of fossil fuels, such as coal and gasoline; burning of vegetation from cotton gins treated with arsenical pesticides; careless or extensive use of arsenical herbicides, pesticides, and defoliants; dumping of land wastes and sewage sludge (1.1 mg/l) in areas that allow leaching into groundwater; use of domestic detergents in wash water (2.5 to 1,000 mg As/1); manufacture of glass; and by the sinking of drinking water wells into naturally arseniferous rock (NRCC 1978; EPA 1980). There are several major anthropogenic sources of environmental arsenic contamination: industrial smelters--the effluent from a copper smelter in Tacoma, Washington, contained up to 70 tons of arsenic discharged yearly into nearby Puget Sound (NRCC 1978); coal-fired power plants, which collectively emit about

3,000 tons of arsenic annually in the United States (EPA 1980); and production and use of arsenical pesticides, coupled with careless disposal of used pesticide containers (NAS 1977). Elevated levels of arsenic have been reported in soils near smelters, in acid mine spoils, and in orchards receiving heavy applications of lead arsenate (NAS 1977; Dudas 1984). Air concentrations of arsenic are elevated near metal smelters, near sources of coal burning, and wherever arsenical pesticides are applied (NAS 1977). Atmospheric deposition of arsenic has steadily increased for at least 30 years, as judged by sedimentary evidence from lakes in upstate New York (Smith et al. 1987). Arsenic is introduced into the aquatic environment through atmospheric deposition of combustion products and through runoff from fly-ash storage areas near power plants and nonferrous smelters (Smith et al. 1987). Elevated arsenic concentrations in water were recorded near mining operations, and from mineral springs and other natural waters--usually alkaline and with high sodium and bicarbonate contents (NAS 1977). In the United States, the most widespread and frequent increases in dissolved arsenic concentrations in river waters were in the northern Midwest; all evidence suggests that increased atmospheric deposition of fossil fuel combustion products was the predominant cause of the trend (Smith et al. 1987).

Agricultural applications provide the largest anthropogenic source of arsenic in the environment (Woolson 1975). Inorganic arsenicals (arsenic trioxide; arsenic acid; arsenates of calcium, copper, lead, and sodium; and arsenites of sodium and potassium) have been used widely for centuries as insecticides, herbicides, algicides, and desiccants. Paris green (cuprous arsenite) was successfully used in 1867 to control the Colorado potato beetle (*Leptinotarsa decemlineata*) in the eastern United States. Arsenic trioxide has been applied widely as a soil sterilant. Sodium arsenite has been used for aquatic weed control, as a defoliant to kill potato vines before tuber harvest, as a weed killer along roadsides and railroad rights-of-way, and for control of crabgrass (*Digitaria sanguinalis*). Calcium arsenates have been applied to cotton and tobacco fields to protect against the boll weevil (*Anthonomus grandis*) and other insects, Lead arsenate has been used to control insect pests of fruit trees, and for many years was the only insecticide that controlled the codling moth (*Carpocapsa pomonella*) in apple orchards and the horn worm larva (Sphyngidae) on tobacco. Much smaller quantities of lead arsenate are now used in orchards because fruit growers rely primarily on carbamate and organophosphorus compounds to control insect pests; however, lead arsenate is still being used by some growers to protect orchards from certain chewing insects. The use of inorganic arsenicals has decreased in recent years due to the banning of sodium arsenite and some other arsenicals for most purposes, although they continue to be used on golf greens and fairways in certain areas to control annual bluegrass (*Poa annua*). In recent decades, inorganic arsenicals have been replaced by organoarsenicals for herbicidal application, and by carbamate and organophosphorus compounds for insect control (Woolson 1975). By the mid-1950's, organoarsenicals were used extensively as desiccants, defoliants, and herbicides (NRCC 1978). Organoarsenicals marketed in agriculture today, which are used primarily for herbicidal application, include cacodylic acid (also known as dimethylarsinic acid) and its salts--monosodium and disodium methanearsonate (Woolson 1975; NAS 1977). Organoarsenicals are used as selective herbicides for weedy grasses in turf, and around cotton and noncrop areas for weed control; at least 1.8 million ha (4.4 million acres) have been treated with more than 8,000 tons of organoarsenicals (NAS 1977). In 1945, it was discovered that one organoarsenical (3-nitro-4 hydroxyphenyl arsonic acid) controlled coccidiosis and promoted growth in domestic chicken (Woolson 1975). Since that time, other substituted phenylarsonic acids have been shown to have both therapeutic and growth promoting properties as feed additives for poultry and swine (*Sus* spp.), and are used for this purpose today under existing regulations (Woolson 1975; NAS 1977)--although the use of arsenicals in poultry food was banned in France in 1959 (NRCC 1978).

CHEMICAL AND BIOCHEMICAL PROPERTIES

Elemental arsenic is a gray, crystalline material characterized by atomic number 33, atomic weight of 74.92, density of 5.727, melting point of 817 °C, sublimation at 613 °C, and chemical properties similar to those of phosphorus (Woolson 1975; NAS 1977; NRCC 1978; EPA 1980; 1985). Arsenic has four valence states: -3, 0, +3, and +5. Arsines and methylarsines, which are characteristic of arsenic in the -3 oxidation state, are generally unstable in air. Elemental arsenic, As° is formed by the reduction of arsenic oxides. Arsenic trioxide (As+3) is a product of smelting operations and is the material used in synthesizing most arsenicals. It is oxidized catalytically or by bacteria to arsenic pentoxide (As+5) or orthoarsenic acid (H_3AsO_4). Arsenic in nature is rarely in its free state. Usually, it is a component of sulfidic ores, occurring as arsenide; and arsenates, along with arsenic trioxide, which is a weathering product of arsenides. Most arsenicals degrade or weather to form arsenate, although arsenite may form under anaerobic conditions. Biotransformations may occur, resulting in volatile arsenicals that normally are returned to the land where soil adsorption, plant uptake, erosion,

leaching, reduction to arsines, and other processes occur. This natural arsenic cycle reflects a constant shifting of arsenic between environmental compartments.

Arsenic species in flooded soils and water are subject to chemically and microbiologically mediated oxidation or reduction and methylation reactions. At high Eh values (i.e., high oxidation-reduction potential) typical of those encountered in oxygenated waters, pentavalent As+5 tends to exist as H_3AsO_4 H_2AsO_4, $HAsO_2$, and AsO_4^{-3}. At lower Eh, the corresponding trivalent arsenic species can be present, as well as AsS_2, (Thanabalasingam and Pickering 1986). In aerobic soils, the dominant arsenic, species was As+5, and small quantities of arsenite and monomethylarsonic acid were present in mineralized areas; in anaerobic soils, As+3 was the major soluble species (Haswell et al. 1985). Inorganic arsenic is more mobile than organic arsenic, and thus poses greater problems by leaching into surface waters and groundwater (NRCC 1978). The trivalent arsenic species are generally considered to be more toxic, more soluble, and more mobile than As+5 species (Thanabalasingam and Pickering 1986). Soil microorganisms metabolize arsenic into volatile arsine derivatives. Depending on conditions, 17% to 60% of the total arsenic present in soil may be volatilized (NRCC 1978) Estimates of the half-life of arsenic in soil varied from 6.5 years for arsenic trioxide to 16 years for lead arsenate (NRCC 1978).

In water, arsenic occurs in both inorganic and organic forms, and in dissolved and gaseous states (EPA 1980). The form of arsenic in water depends on Eh, pH, organic content, suspended solids, dissolved oxygen, and other variables (EPA 1985). Arsenic in water exists primarily as a dissolved ionic species; particulates account for less than 1% of the total measurable arsenic (Maher 1985a). Arsenic is rarely found in water in the elemental state (0), and is found in the -3 state only at extremely low Eh values (Lima et al. 1984). Common forms of arsenic encountered in water are arsenate, arsenite, methanearsonic acid, and dimethylarsinic acid (EPA 1985). The formation of inorganic pentavalent arsenic, the most common species in water, is favored under conditions of high dissolved oxygen, basic pH, high Eh, and reduced content of organic material; reverse conditions usually favor the formation of arsenites and arsenic sulfides (NRCC 1978; Pershagen and Vahter 1979; EPA 1980), although some arsenite is attributed to biological activity (Maher 1985a). Water temperature seems to affect arsenic species composition in the estuary of the River Beaulieu in the United Kingdom, where reduced and methylated species predominate during warmer months and inorganic As during colder months; the appearance of methylated arsenicals during the warmer months is attributed both to bacterial and abiotic release from decaying plankton and to grazing by zooplankton (Howard et al. 1984). Also contributing to higher water or mobile levels are the natural levels of polyvalent anions, especially phosphate species. Phosphate, for example, displaces arsenic held by humic acids and sorbs strongly on the hydrous oxides of arsenates (Thanabalasingam nd Pickering 1986).

Physical processes play a key role in governing arsenic bioavailability in aquatic environments. For example, arsenates are readily sorbed by colloidal humic material under conditions of high organic content, low pH, low phosphate, and low mineral content (EPA 1980; Thanabalasingam and Pickering 1986). Arsenates also coprecipitate with, or adsorb on, hydrous iron oxides and form insoluble precipitates with calcium, sulfur, aluminum, and barium compounds (EPA 1980). Removal of arsenic from seawater by iron hydroxide scavenging seems to be a predominant factor in certain estuaries. The process involves both As^{+3} and As^{+5} and results in a measurable increase in arsenic levels in particulate matter, especially at low salinities (Sloot et al. 1985). Arsenic sulfides are comparatively insoluble under conditions prevalent in anaerobic aqueous and sedimentary media containing hydrogen sulfide; accordingly, these compounds may accumulate as precipitates and thus remove arsenic from the aqueous environment. In the absence of hydrogen sulfide, these sulfides decompose within several days to form arsenic oxides, sulfur, and hydrogen sulfide (NAS 1977).

In reduced environments, such as sediments, arsenate is reduced to arsenite and methylated to methylarsinic acid or dimethylarsenic acids: these compounds may be further methylated to trimethylarsine or reduced to dimethylarsine, and may volatilize to the atmosphere where oxidation reactions result in the formation of dimethylarsinic acid (Woolson 1975). Arsenates are more strongly adsorbed to sediments than are other arsenic forms, the adsorption processes depending strongly on arsenic concentration, sediment characteristics, pH, and ionic concentration of other compounds (EPA 1980). An important mechanism of arsenic adsorption onto lake sediments involves the interaction of anionic arsenates and hydrous iron oxides. Current evidence suggests that arsenic is incorporated into sediments at the time of hydrous oxide formation, rather than by adsorption onto existing surfaces (Aggett and Roberts 1986). Arsenic concentrations in lake

sediments are also correlated with manganese; hydrous manganese oxides--positively charged for the adsorption of Mn^{+2} ions--play a significant role in arsenic adsorption onto the surface of lake sediments (Takamatsu et al. 1985). The mobility of arsenic in lake sediments and its release to the overlying water is related partly to seasonal changes. In areas that become stratified in summer, arsenic released from sediments accumulates in the hypolimnion until turnover, when it is mixed with epilimnetic waters; this mixing may result in a 10 to 20% increase in arsenic concentration (Aggett and O'Brien 1985). Microorganisms (including four species of fungi) in lake sediments oxidized inorganic As^{+3} to As^{+5} and reduced inorganic As^{+5} to As^{+3} under aerobic conditions; under anaerobic conditions, only reduction was observed (Freeman et al. 1986). Inorganic arsenic can be converted to organic alkyl arsenic acids and methylated arsines under anaerobic conditions by fungi, yeasts, and bacteria--although biomethylation may also occur under aerobic conditions (EPA 1980).

Most arsenic investigators now agree on the following points: (1) arsenic may be absorbed by ingestion, inhalation, or through permeation of the skin or mucous membranes; (2) cells accumulate arsenic by using an active transport system normally used in phosphate transport; (3) arsenicals are readily absorbed after ingestion, most being rapidly excreted in the urine during the first few days, or at most a week (the effects seen after long-term exposure are probably a result of continuous daily exposure, rather than of accumulation); (4) the toxicity of arsenicals conforms to the following order, from greatest to least toxicity: arsines > inorganic arsenites > organic trivalent compounds (arsenoxides) > inorganic arsenates > organic pentavalent compounds > arsonium compounds > elemental arsenic; (5) solubility in water and body fluids appears to be directly related to toxicity (the low toxicity of elemental arsenic is attributed to its virtual insolubility in water and body fluids, whereas the highly toxic arsenic trioxide, for example, is soluble in water to 12.0 g/l at 0 C, 21.0 g/l at 25 C, and 56.0 g/l at 75 C); and (6) the mechanisms of arsenical toxicity differ considerably among arsenic species, although signs of poisoning appear similar for all arsenicals (Woolson 1975; NRCC 1978; Pershagen aid Vahter 1979).

The primary toxicity mode of inorganic As+3 is through reaction with sulfhydryl groups of proteins and subsequent enzyme inhibition; inorganic pentavalent arsenate does not react as readily as As+3 with sulfhydryl groups, but may uncouple oxidative phosphorylation (Howard et al. 1984; EPA 1985). Inorganic As+3 interrupts oxidative metabolic pathways and sometimes causes morphological changes in liver mitochondria. Arsenite in vitro reacts with protein-SH groups to inactivate enzymes such as dihydrolipoyl dehydrogenase and thiolase, producing inhibited oxidation of pyruvate and beta-oxidation of fatty acids (Belton et al. 1985). Inorganic As+5 may also exert toxic effects by the reaction of arsenous acid (HAsO) with the sulfhydryl (SH) groups of enzymes. In the first reaction, arsenous acid is reduced to arsonous acid ($AsOH_2$), which then condenses to either monothiols or dithiols to yield dithioesters of arsonous acid. Arsonous acid may then condense with enzyme SH groups to form a binary complex (Knowles and Benson 1984a,b).

Methylation to methylarsonic acid ($(CH3)_2AsO_3H_2$) and dimethylarsinic acid ($(CH3)_2AsO_2H$) is usually the major detoxification mechanism for inorganic pentavalent arsenates and trivalent arsenites in mammals. Methylated arsenicals rapidly clear from all tissues except perhaps the thyroid (Marafante et al. 1985; Vahter and Marafante 1985; Yamauchi et al. 1986) Methylated arsenicals are probably common in nature. Methylation of arsenic (unlike methylation of mercury) greatly reduces toxicity and is a true detoxification process (Woolson 1975). Before methylation (which occurs largely in the liver), As+5 is reduced to As+3-- the kidney being an important site for this transformation (Belton et al. 1985). Arsenate reduction and, subsequent methylation is rapid: both. arsenite and dimethylarsinate were present in hamster (*Cricetus* sp.) plasma only 12 minutes postinjection of inorganic As+5 (Hanlon and Ferm 1986c). Demethylation of methylated arsenicals formed in vivo has not yet been reported (EPA 1980).

Toxic effects of organoarsenicals are exerted by initial metabolism to the trivalent arsonoxide form, and then by reaction with sulfhydryl groups of tissue proteins and enzymes to form an arylbis (organylthio) arsine (NAS 1977). This form, in turn, inhibits oxidative degradation of carbohydrates and decreases cellular ATP, the energy storage molecule of the cell (NRCC 1978). Among the organoarsenicals, those physiologically most injurious are methylarsonous acid ($CH3As(OH)_2$) and dimethylarsinous acid ($(CH3)_2AsOH$) (Knowles and Benson 1984b). The enzyme inhibitory forms of organoarsenicals (arsonous acid) are formed from arsenous acid and the corresponding arsonic acids by a wide variety of enzymes and subcellular particles (Knowles and Benson 1984a). Organoarsenicals used as growth promoters and drugs are converted to more easily excretable

(and sometimes more toxic) substances, although most organoarsenicals are eliminated without being converted to inorganic arsenic or to demethylarsinic acids (Pershagen and Vahter 1979).

ESSENTIALITY, SYNERGISM, AND ANTAGONISM

Limited data are available on the beneficial, protective, and essential properties of arsenic, and on its interactions with other chemicals.

Arsenic apparently behaves more like an environmental contaminant than as a nutritionally essential mineral (NAS 1977). Nevertheless, low doses (<2 ug/daily) of arsenic stimulated growth and metamorphosis in tadpoles, and increased viability and cocoon yield in silkworm caterpillars (NAS 1977). Arsenic deficiency has been observed in rats: signs include rough haircoat, low growth rate, decreased hematocrit, increased fragility of red cells, and enlarged spleen (NAS 1977). Similar results have been documented in goats and pigs fed diets containing less than 0.05 mg As/kg (NAS 1977). In these animals, reproductive performance was impaired, neonatal mortality was increased, birth weight was lower, and weight gains in second-generation animals were decreased; these effects were not evident in animals fed diets containing 0.35 mg As/kg (NAS 1977).

The use of phenylarsonic feed additives to promote growth in poultry and swine and to treat specific diseases does not seem to constitute a hazard to the animal or to its consumers. Animal deaths and elevated tissue arsenic residues occur only when the arsenicals are fed at excessive dosages for long periods (NAS 1977). Arsenic can be detected at low levels in tissues of animals fed organoarsenicals, but it is rapidly eliminated when the arsenicals are removed from the feed for the required 5-day period before marketing (Woolson 1975).

Selenium and arsenic are antagonists in several animal species. In rats, dogs, swine, cattle, and poultry, the arsenic protects against selenium poisoning if arsenic is administered in the drinking water and selenium through the diet (NAS 1977; NRCC 1978; Pershagen and Vahter 1979). Inorganic arsenic compounds decrease the toxicity of inorganic selenium compounds by increasing biliary excretion (NRCC 1978). However, in contrast to antagonism shown by inorganic arsenic-inorganic selenium mixtures, the toxic effects of naturally methylated selenium compounds (trimethylselenomium chloride and dimethyl selenide) are markedly enhanced by inorganic arsenicals (NRCC 1978).

Toxic effects of arsenic can be counteracted with saline purgatives, with various demulcents that coat irritated gastrointestinal mucous membranes, and by sodium thiosulfate (NAS 1977), and by mono- and dithiol-containing compounds and 2,3-dimercaptopropanol (Pershagen and Vahter 1979). Arsenic uptake in rabbit intestine is inhibited by phosphate, casein, and various metal chelating agents (EPA 1980). Mice and rabbits are significantly protected against sodium arsenite intoxication *by* N-(2,3-dimercaptopropyl)phthalamidic acid (Stine et al. 1984). Conversely, the toxic effects of arsenite are potentiated by excess dithiols, cadmium, and lead, as evidenced by reduced food efficiency and disrupted blood chemistry in rodents (Pershagen and Vahter 1979).

Arsenic effectively controls filariasis in cattle; new protective uses are under investigation. The control of parasitic nematodes (*Parafilaria bovicola*) in cattle was successful after 30 weekly treatments in plungement dips containing 1,600 mg As_2O_3/l; however, the muscle of treated cattle contained up to 1.3 mg As/kg, or 12X the amount in controls (Nevill 1985). Existing anionic organic arsenicals used to control tropical nematode infections in humans have sporadic and unacceptable lethal side effects. Cationic derivatives have been synthesized in an attempt to avoid the side effects and have been examined for effects on adult nematodes (*Brugia pahangi*) in gerbils (*Meriones unguiculatus*). All arsenicals were potent filaricides; the most effective-compounds tested killed 95% of adult *B. pahangi* after five daily subcutaneous injections of 3.1 mg As/kg body weight (Denham et al. 1986).

Animals previously exposed to sublethal levels of arsenic may develop tolerance to arsenic on reexposure. Although the mechanism of this process is not fully understood, it probably includes the efficiency of in vivo methylation processes (EPA 1980). For example, resistance to toxic doses of As+3 or As+5 increases in mouse fibroblast cells pretreated with a low As+3 concentration (Fischer et al. 1985). Also, growth is better in arsenic-conditioned mouse cells in the presence of arsenic than in previously unexposed cells, and inorganic arsenic is more efficiently methylated. In vivo biotransformation and excretion of inorganic arsenic as monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) has been demonstrated in a number of mammalian species,

including man. It seems that cells may adapt to arsenic by increasing the biotransformation rate of the element to methylated forms, such as MMA and DMA (Fischer et al. 1985). Pretreatment of ovary cells of Chinese hamster (*Cricetus* spp.) ovary cells with sodium arsenite provided partial protection against adverse effects of methyl methanesulfonate (MMS), and may even benefit the MMS-treated cells; however, posttreatment dramatically increases the cytotoxic, clastogenic, and mitotic effects induced by MMS (Lee et al. 1986b).

Although arsenic is not an essential plant nutrient, small yield increases have sometimes been observed at low soil arsenic levels, especially for tolerant crops such as potatoes, corn, rye, and wheat (Woolson 1975). Arsenic phytotoxicity of soils is reduced with increasing lime, organic matter, iron, zinc, and phosphates (NRCC 1978). In most soil systems, the chemistry of As becomes the chemistry of arsenate; the estimated half-time of arsenic in soils is about 6.5 years, although losses of 60% in 3 years and 67% in 7 years have been reported (Woolson 1975). Additional research is warranted on the role of arsenic in crop production, and in nutrition, with special reference to essentiality for aquatic and terrestrial wildlife.

BACKGROUND CONCENTRATIONS

GENERAL

In abundance of elements, arsenic ranks 20th in the earth's crust (1.5 to 2 mg/kg) 14th in seawater, and 12th in the human body (Woolson 1975). It occurs in various forms, including inorganic and organic compounds and trivalent and pentavalent states (Pershagen and Vahter 1979). In aquatic environments, higher arsenic concentrations are reported in hot springs, in groundwaters from areas of thermal activity or in areas containing rocks with high arsenic content, and in some waters with high dissolved salt content (NAS 1977). Most of the other elevated values reported in lakes, rivers, and sediments are probably due to anthropogenic sources, which include smelting and mining operations; combustion of fossil fuel; arsenical grasshopper baits; synthetic detergent and sewage sludge wastes; and arsenical defoliants, herbicides, and pesticides (NAS 1977). Most living organisms normally contain measurable concentrations of arsenic, but except for marine biota, these are usually less than 1 mg/kg fresh weight. Marine organisms, especially crustaceans, may contain more than 100 mg As/kg dry weight, usually as arsenobetaine, a water soluble organoarsenical that poses little risk to the organism or its consumer. Plants and animals collected from naturally arseniferous areas or near anthropogenic sources may contain significantly elevated tissue residues of arsenic. Additional and more detailed information on background concentrations of arsenic in abiotic and living resources was given by NAS (1977), Hall et al. (1978), NRCC (1978), EPA (1980), Jenkins (1980), and Eisler (1981).

NONBIOLOGICAL SAMPLES

Arsenic is a major constituent of at least 245 mineral species, of which arsenopyrite is the most common (NAS 1977). In general, background concentrations of arsenic are 0.2 to 15 mg/kg in the lithosphere, 0.005 to 0.1 ug/m in air, <10 ug/l in water, and <15 mg/kg in soil (NRCC 1978). The commercial use and production of arsenic compounds have raised local concentrations in the environment far above the natural background concentrations (Table 1).

Weathering of rocks and soils adds about 45,000 tons of arsenic to the oceans annually, accounting for less than 0.01 mg/l on a global basis (NRCC 1978). However, arsenic inputs to oceans increased during the past century both from natural sources and as a result of industrial use, agricultural and deforestation activities, emissions from coal and oil combustion, and loss during mining of metal ores. If present activities continue, arsenic concentrations in oceanic surface waters may increase overall by about 2% *by* the year 2000, with most of the increased burden in estuaries and coastal oceans--e.g., Puget Sound, Washington; the Tamar, England; and the Tejo, Portugal (Sanders 1985). Estimates of the residence times of arsenic are 60,000 years in the ocean and 45 years in a freshwater lake (NRCC 1978). In the hydrosphere, inorganic arsenic occurs predominantly as As+5 in surface waters, and significantly as As+3 in groundwaters containing high levels of total arsenic. The main organic species in freshwater are methylarsonic acid and dimethylarsinic acid, and these are usually present in lower concentrations than inorganic arsenites and arsenates (Pershagen and Vahter 1979). Total arsenic concentrations in both surface and groundwaters are usually < 10 ug/l; in certain areas, however, levels above 1 mg/l have been recorded (Pershagen and Vahter 1979).

In air, most arsenic particulates consist of inorganic arsenic compounds, often as As+3. Burning of coal and arsenic-treated wood, and smelting of metals are major sources of atmospheric arsenic contamination (i.e., >1

ug/m^3); in general, atmospheric arsenic levels are higher in winter, due to increased use of coal for heating (Pershagen and Vahter 1979).

The main carrier of arsenic in rocks and in most types of mineral deposits is iron pyrite (FeS_2) which may contain >2,000 mg/kg of arsenic (NRCC 1978). In localized areas, soils are contaminated by arsenic oxide fallout from smelting ores (especially sulfide ores) and combustion of arsenic-rich coal (Woolson 1975).

Arsenic in lacustrine sediment columns is subject to control by diagenetic processes and adsorption mechanisms, as well as anthropogenic influences (Farmer and Lovell 1986). For example, elevated levels of arsenic in surface or near surface sediments may be due to several causes (Farmer and Lovell 1986): natural processes (Loch Lomond, Scotland); or to human activities such as smelters (Lake Washington, Washington; Kelly Lake, Ontario, Canada), manufacture of arsenical herbicides (Brown's Lake, Wisconsin), and mining operations (Northwest Territories, Canada). Elevated levels of arsenic in sediments of the Wailoa River, Hawaii, are caused by As_2O_3 applied as an anti-termite agent between 1932 and 1963, and are mostly in anaerobic sediment regions where the chemical has been relatively undisturbed by biological activity; low levels of arsenic in the biota of that estuary suggest that arsenic is trapped in the anaerobic sediment layers (Hallacher et al. 1985).

Arsenic geochemistry in Chesapeake Bay, Maryland, depends on anthropogenic inputs and phytoplankton species composition (Sanders 1985). Inputs of anthropogenic arsenic into Chesapeake Bay are estimated at 100 kg daily, or 39 tons/year--probably from sources such as unreported industrial discharges, use of arsenical herbicides, and from wood preservatives (Sanders 1985). The chemical form of the arsenic in solution varies both seasonally and along the axis of the Bay. Arsenic is present only as arsenate in winter, but substantial quantities of reduced and methylated forms are present in summer in different areas. The forms and distribution patterns of arsenic during the summer suggest that separate formation processes exist. Arsenite, present in low salinity regions, may have been formed by chemical reduction in anoxic, subsurface waters and then mixed into the surface layer. Methylated arsenicals are highly correlated with ;landing crops of algae. One particular form, methylarsonate, is significantly correlated with the dominant alga *Chroomonas*. Since both arsenic reactivity and toxicity are altered by transformation of chemical form, the observed variations in arsenic speciation have considerable geochemical and ecological significance (Sanders 1985).

BIOLOGICAL SAMPLES

Background arsenic concentrations in living organisms are usually <1 mg/kg fresh weight in terrestrial flora and fauna, birds, and freshwater biota. These levels are higher, sometimes markedly so, in biota collected from mine waste sites, arsenic-treated areas, near smelters and mining areas, near areas with high geothermal activity, and near manufacturers of arsenical defoliants and pesticides (Table 2). Marine organisms, however, normally contain arsenic residues of several to more than 100 mg/kg dry weight (Lunde 1977); as discussed later, however, these concentrations present little hazard to the organism or to its consumers.

Shorebirds (seven species) wintering in the Corpus Christi, Texas, area contained an average of only 0.3 mg As/kg fresh weight in livers (maximum of 1.5 mg/kg), despite the presence of smelters and the heavy use of arsenical herbicides and defoliants; these values probably reflect normal background concentrations (White et al. 1980). Similar arsenic levels are reported in livers of brown pelicans (*Pelecanus occidentalis*) collected from South Carolina (Blus et al. 1977). The highest arsenic concentration recorded in seemingly unstressed coastal birds was 13.2 mg/kg fresh weight lipids (Table 2). This tends to corroborate the findings of others who demonstrated that arsenic concentrates in lipid fractions of marine plants, invertebrates, and higher organisms. An abnormal concentration of 16.7 mg As/kg fresh weight was recorded in liver of an osprey (*Pandion haliaetus*) from the Chesapeake Bay region (Wiemeyer et al. 1980). This bird was alive but weak, with serious histopathology including the absence of subcutaneous fat, and the presence of serous fluid in the pericardial sac and disorders of the lung and kidney. It died shortly after collection. Arsenic concentrations in liver from other ospreys collected in the same area usually were <1.5 mg As/kg fresh weight.

Arsenic concentrations in tissues of marine biota show a wide range of values, being highest in lipids, liver, and muscle tissues, and varying with the age of the organism, geographic locale, and proximity to anthropogenic activities (Table 2). In general, tissues with high lipid content contained high levels of arsenic. Crustacean tissues sold for human consumption and collected in U.S. coastal waters usually contained 3 to 10

mg As/kg fresh weight (Hall et al. 1978), or 1 to 100 mg/kg dry weight (Fowler and Unlu 1978), and were somewhat higher than those reported for finfish and molluscan tissues. Marine finfish tissues usually contained 2 to 5 mg As/kg fresh weight (Table 2). However, postmortem reduction of As+5 to As+3 occurs rapidly in fish tissues (Reinke et al. 1975), suggesting a need for additional research in this area. Maximum arsenic values recorded in elasmobranchs (mg/kg fresh weight) were 30 in muscle of a shark, *Mustelus antarcticus*, and 16.2 in muscle of a ray, *Raja* sp. (Eisler 1981). The highest arsenic concentration recorded in marine mammals, 2.8 mg As/kg fresh weight lipid, was from a cetacean captured by Norwegian whalers (Eisler 1981).

Arsenic appears to be elevated in marine biota because of their ability to accumulate arsenic from seawater or food sources, and not due to localized pollution (Maher 1985b). The great majority of the arsenic in marine organisms exists as water-soluble and lipid-soluble organoarsenicals that include arsenolipids, arsenosugars, arsenocholine, arsenobetaine ($(CH3)_3AsCH_2COOH$), monomethylarsonate ($CH3AsO(OH)_2$), and demethylarsinate ($(CH3)_2AsO(OH)$), as well as other forms. There is no convincing hypothesis to account for the existence of all the various forms of organoarsenicals found in marine organisms. One suggested hypothesis is that each form involves a single anabolic/catabolic pathway concerned with the synthesis and turnover of phosphatidylcholine (Phillips and Depledge 1986). Arsenosugars (arsenobetaine precursors) are the dominant arsenic species in brown kelp (*Ecklonia radiata*), giant clam (*Tridacna maxima*), shrimp (*Pandalus borealis*), and ivory shell (*Buccinum striatissimum*) (Shiomi et al. 1984a,b; Francesconi et al. 1985; Matsuto et al. 1986; Phillips and Depledge 1986). For most marine species, however, there is general agreement that arsenic exists primarily as arsenobetaine, a water soluble organoarsenical that has been identified in tissues of western rock lobster (*Panulirus cygnus*), American lobster (*Homarus americanus*), octopus (*Paroctopus* sp.), sea cucumber (*Stichopus japonicus*), blue shark (*Prionace glauca*), sole (*Limanda* sp.), squid (*Sepioteuthis australis*), prawn (*Penaeus latisulcatus*), scallop (*Pecten alba*), and many other species including teleosts, molluscs, tunicates, and crustaceans (Shiomi et al. 1984b; Francesconi et al. 1985; Hanaoka and Tagawa 1985a,b; Maher 1985b; Norin et al. 1985; Matsuto et al. 1986). The potential risks associated with consumption of seafoods containing arsenobetaine seem to be minor. The chemical was not mutagenic in the bacterial *Salmonella typhimurium* assay (Ames test), had no effect on metabolic inhibition of Chinese hamster ovary cells at 10,000 mg/l, and showed no synergism or antagonism on the action of other contaminants (Jongen et al. 1985). Arsenobetaine was not toxic to mice at oral doses of 10,000 mg/kg body weight during a 7-day observation period, and was rapidly absorbed from the gastrointestinal tract and rapidly excreted in urine without metabolism, owing to its high polar and hydrophilic characteristics (Kaise et al. 1985).

LETHAL AND SUBLETHAL EFFECTS

GENERAL

As discussed later, most authorities agree on 10 points: (1) inorganic arsenicals are more toxic than organic arsenicals, and trivalent forms are more toxic than pentavalent forms; (2) episodes of arsenic poisoning are either acute or subacute--cases of chronic arsenosis are rarely encountered, except in humans; (3) early developmental stages are the most sensitive to arsenic; (4) inorganic arsenic can traverse placental barriers--as little as 1.7 mg As+5/kg body weight at critical stages of hamster embryogenesis, for example, can produce fetal death and malformation; (5) biomethylation is the preferred detoxification mechanism for inorganic arsenicals; (6) arsenic is bioconcentrated by organisms, but not biomagnified in the food chain; (7) depressed crop yields were recorded at 3 to 28 mg of water soluble soil As/l, or about 25 to 85 mg total As/kg soil--adverse effects on vegetation were recorded at concentrations in air >3.9 ug As/m^3; (8) some aquatic species were adversely affected at water concentrations of 19 to 48 ug As/l, or 120 mg As/kg in the diet, or tissue residue of 1.3 to 5 mg As/kg fresh weight; (9) sensitive species of birds died following single oral doses of 17.4 to 47.6 mg As/kg body weight; and (10) adverse effects were noted in mammals at single oral doses of 2.5 to 33 mg As/kg body weight, at chronic oral doses of 1 to 10 mg As/kg body weight, and at feeding levels of 50 mg, sometimes only 5 mg, As/kg in the diet.

It is emphasized in the literature that arsenic metabolism and toxicity vary greatly between species, and that effects are significantly altered by numerous physical, chemical, and biological modifiers. Adverse health effects, for example, may involve respiratory, gastrointestinal, cardiovascular, and hematopoietic systems, and may range from reversible effects to cancer and death, depending partly on the physical and chemical forms of arsenic tested, the route of administration, and dose.

CARCINOGENESIS, MUTAGENESIS, AND TERATOGENESIS

Epidemiological studies show that increased risk of cancers in skin, lung, liver, lymph, and hematopoietic systems of humans is associated with exposure to inorganic arsenicals. These increased cancer risks are especially prevalent among smelter workers and in those engaged in the production and use of arsenical pesticides where atmospheric levels exceed 54.6 ug As/m^3 (NRCC 1978; Belton et al. 1985; Pershagen and Bjorklund 1985). Skin tumors, mainly of low malignancy, have been reported after consumption of arsenic-rich drinking waters; a total dose of several grams, probably as As+3 is usually required for the development of skin tumors (Pershagen and Vahter 1979). High incidences of skin cancer and hyperpigmentation were noted among several population groups, especially Taiwanese and Chileans, consuming water containing more than 0.6 mg As/l; the frequency of cancer was highest among people over age 60 who demonstrated symptoms of chronic arsenic poisoning (NRCC 1978).

Arsenic reportedly inhibits cancer formation in species having a high incidence of spontaneous cancers (NRCC 1978). In fact, arsenic may be the only chemical for which there is sufficient evidence for carcinogenicity in humans but not in other animals (Woolson 1975; Belton et al. 1985; Lee et al. 1985). In general, animal carcinogenicity tests with inorganic and organic arsenicals have been negative (Hood 1985), even when the chemicals were administered at or near the highest tolerated dosages for long periods (NAS 1977). Most studies of arsenic carcinogenesis in animals were presumably of insufficient duration to simulate conditions in long-lived species such as humans (NRCC 1978). However, mice developed leukemia and lymphoma after 20 subcutaneous injections of 0.5 mg As+5/kg body weight: 46% of the experimental group developed these signs vs. none in controls (NRCC 1978). Recently, pulmonary tumorogenicity has been demonstrated in hamsters administered calcium arsenate intratracheally (Pershagen and Bjorklund 1985). Cacodylic acid and other organoarsenicals are not carcinogenic, but may be mutagenic at very high doses (Hood 1985).

Several inorganic arsenic compounds are weak inducers of chromosomal aberrations, sister chromatid exchange, and in vitro transformation of mammalian cells; however, there is no conclusive evidence that arsenic causes point mutations in any cellular system (Pershagen and Vahter 1979; Belton et al. 1985; Lee et al. 1985; Deknudt et al. 1986). Studies with bacteria suggest that arsenite is a comutagen, or may inhibit DNA repair (Belton et al. 1985).

Arsenic is a known teratogen in several classes of vertebrates, and has been implicated as a cause of birth defects in humans. Specific developmental malformations have been produced experimentally in mammals using inorganic As+3 or As+5 either through a single dose or a continuous dose during embryogenesis (Hanlon and Ferm 1986b). Teratogenic effects are initiated no later than 4 hours postadministration of As; fetal abnormalities are primarily neural tube defects (Hanlon and Ferm 1985c), but may also include protruding eyes, incomplete development of the skull, abnormally small jaws and other skeletal anomalies (NRCC 1978). Inorganic As+3 and As+5, but not organoarsenicals, cross placental barriers in many species of mammals, and result in fetal deaths and malformations (NRCC 1978; EPA 1980). Recent studies with hamsters, for example, showed that sodium arsenite can induce chromatid breaks and chromatid exchanges in Chinese hamster ovary cells in a dose dependent manner (Lee et al. 1986b). In an earlier study (Lee et al. 1985), As+3 was about 10X more potent than As+5 in effecting transformations, The birth defects were most pronounced in golden hamsters exposed to As+5 during the 24-hour period of critical embryogenesis--i.e., day 8 of gestation (Ferm and Hanlon 1985)--when 1.7 mg As+5/kg body weight induced neural tube defects in about 90% of the fetuses. Hanlon and Ferm (1986a) showed that hamsters exposed to As+5 and heat stress (39 °C for 50 minutes) on day 8 of gestation produced a greater percentage of malformed offspring (18 to 39%) than did hamsters exposed to As+5 alone (4% to 8%).

TERRESTRIAL PLANTS AND INVERTEBRATES

In general, arsenic availability to plants is highest in coarse-textured soils having little colloidal material and little ion exchange capacity, and lowest in fine-textured soils high in clay, organic material, iron, calcium, and phosphate (NRCC 1978). To be absorbed by plants, arsenic compounds must be in a mobile form in the soil solution. Except for locations where arsenic content is high, e.g., around smelters, the accumulated arsenic is distributed throughout the plant body in nontoxic amounts (NAS 1977). For most plants, a significant depression in crop yields was evident at soil-As concentrations of 3 to 28 mg/l of water soluble arsenic and 25 to 85 mg/kg of total arsenic (NRCC 1978). Yields of peas (*Pisum sativum*), a sensitive species, were decreased at 1 mg/l of water soluble arsenic or 25 mg/kg of total soil As; rice (*Oryza sativum*) yields were decreased 75% at 50 mg/l of

disodium methylarsonate in silty loam; and soybeans (*Glycine max*) grew poorly when residues exceeded 1 mg As/kg (Table 3; NRCC 1978). Forage plants grown in soils contaminated with up to 80 mg total As/kg from arsenical orchard sprays contained up to 5.8 mg As/kg dry weight; however, these plants were considered nonhazardous to grazing ruminants (Merry et al. 1986).

Attention was focused on inorganic arsenical pesticides after accumulations of arsenic in soils eventually became toxic to several agricultural crops, especially on former orchards and cotton fields. Once toxicity is observed, it persists for several years even if no additional arsenic treatment is made (Woolson 1975). Poor crop growth was associated with bioavailability of arsenic in soils. For example, alfalfa (*Medicago sativa*) and barley (*Hordeum vulgare*) grew poorly in soils containing only 3.4 to 9.5 mg As/kg, provided the soils ware acidic, lightly textured, low in phosphorus and aluminum, high in iron and calcium, and contained excess moisture (Woolson 1975). Use of inorganic arsenical herbicides, such as calcium arsenate, to golf course turfs for control of fungal blight sometimes exacerbates the disease. The use of arsenicals on Kentucky bluegrass (*Poa pratensis*) is discouraged under conditions of high moisture and root stress induced by previous arsenical applications (Smiley et al. 1985).

Methylated arsenicals, whether herbicides or defoliants, are sprayed on plant surfaces. They can reach the soil during application or can be washed from the plants. Additional arsenic enters soils by exchange from the roots or when dead plant materials decay (Hood 1985). Cacodylic acid and sodium cacodylate are nonselective herbicides used in at least 82 products to eliminate weeds and grasses around trees and shrubs, and to eradicate vegetation from rights-of-ways and other noncrop areas (Hood 1985). Normal application rates of various organoarsenicals for crop and noncrop purposes rarely exceed 5 kg/ha (Woolson 1975). Under recommended treatment levels, organoarsenical soil residues were not toxic to crops, and those tested (soybean, beet, wheat) were more resistant to organoarsenicals than to comparable levels of inorganic arsenicals (Woolson 1975).

Air concentrations up to 3.9 ug As/m^3 near gold mining operations were associated with adverse effects on vegetation; higher concentrations of 19 to 69 ug As/m^3, near a coal fired power plant in Czechoslovakia, produced measurable contamination in soils and vegetation in a 6-km radius (NRCC 1978).

The phytotoxic actions of inorganic and organic arsenicals are different and each is significantly modified by physical processes. The primary mode of action of arsenite in plants is inhibition of light activation, probably through interference with the pentose phosphate pathway (Marques and Anderson 1986). Arsenites penetrate the plant cuticle to a greater degree than arsenates (NAS 1977). One of the first indications of plant injury by sodium arsenite is wilting caused by loss of turgor, whereas stress due to sodium arsenate does not involve rapid loss of turgor (NAS 1977). Organoarsenicals, such as cacodylic acid, enter plants mostly by absorption of sprays; uptake from the soil contributes only a minor fraction (Hood 1985). The phytotoxicity of organoarsenical herbicides is characterized by chlorosis, cessation of growth, gradual browning, dehydration, and death (NAS 1977). In general, plants cease to grow and develop after the roots have absorbed much arsenic (NRCC 1978). Plants can absorb arsenic through the roots and foliage, although translocation is species dependent. Concentrations of arsenic in plants correlate highly and consistently with water extractable soil arsenic, and usually poorly with total soil arsenic (NRCC 1978). For example, concentrations of arsenic in corn (*Zea mays*) grown in calcareous soils for 25 days were significantly correlated with the soil water extractable arsenic fraction, but not other fractions; extractable phosphorus was correlated positively to both arsenic in corn and to the water soluble arsenic fraction (Sadiq 1986). In the moss *Hylocomium splendens*, arsenate accumulation from solution was through living shoots, optimum uptake being between pH 3 and 5 (Wells and Richardson 1985). Some plants, such as beets (*Beta vulgaris*) accumulated arsenic more readily at elevated temperatures, but the addition of phosphate fertilizers markedly depressed uptake (Merry et al. 1986).

Soils amended with arsenic-contaminated plant tissues were not measurably affected in CO_2 evolution and nitrification, suggesting that the effects of adding arsenic to soils does not influence the decomposition rate of plant tissues by soil microorganisms (Wang et al. 1984). The half-life of cacodylic acid is about 20 days in untreated soils and 31 days in arsenic-amended soils (Hood 1985). Estimates of the half-life of inorganic arsenicals in soils are much longer, ranging from 6.5 years for arsenic trioxide to 16 years for lead arsenate (NRCC 1978).

Data on arsenic effects to soil biota and insects are limited. In general, soil microorganisms are capable of tolerating and metabolizing relatively high concentrations of arsenic (Wang et al. 1984). This adaptation seems usually to be due to decreased permeability of the microorganism to arsenic (NAS 1977). Tolerant soil microbiota can withstand concentrations up to 1,600 mg/kg; however, growth and metabolism were reduced in sensitive species at 375 mg As/kg and, at 150 to 165 mg As/kg, soils were devoid of earthworms and showed diminished quantities of bacteria and protozoans (NRCC 1978). Honeybees (*Apis mellifera*) that were killed accidentally by As+3 spray dusting contained 4 to 5 ug As per bee (NAS 1977)--equivalent to 21 to 31 mg/kg body weight (Table 3). Larvae of the western spruce budworm (*Choristoneura occidentalis*) continued to feed on As+3 -contaminated vegetation until a threshold level of about 2,300 to 3,300 mg As/kg dry weight whole larvae was reached; death then sometimes occurred (Table 3; Robertson and McLean 1985). Larvae that had accumulated sufficient energy reserves completed the first stage of metamorphosis, but developed into pupae of subnormal weight; larvae containing <2,600 mg As+3/kg ultimately developed into adults of less than normal weight, and some containing >2,600 mg/kg dry weight died as pupae (Robertson and McLean 1985).

AQUATIC BIOTA

Adverse effects of arsenicals on aquatic organisms have been reported at concentrations of 19 to 48 ug/l in water, 120 mg/kg in diets, and 1.3 to 5 mg/kg fresh weight in tissues (Table 4). The most sensitive aquatic species tested showing adverse effects were three species of marine algae, which showed reduced growth in the range of 19 to 22 ug As+3/l; developing embryos of the narrow-mouthed toad (*Gastrophryne carolinensis*), of which 50% were dead or malformed in 7 days at 40 ug As+3/l; and a freshwater alga (*Scenedesmus obliquus*), in which growth was inhibited 50% in 14 days at 48 ug As+5/l (Table 4). Chronic studies with mass cultures of natural phytoplankton communities exposed to low levels of arsenate (1.0 to 15.2 ug/l) showed that As+5 differentially inhibits certain plants, causing a marked change in species composition, succession, and predator-prey relations; the significance of these changes on carbon transfer between trophic levels is unknown (Sanders and Cibik 1985; Sanders 1986). Adverse biological effects have also been documented at water concentrations of 75 to 100 ug As/l. At 75 ug As+5/l, growth and biomass in freshwater and marine algae was reduced; at 85 to 88 ug/l of As+5 or various methylated arsenicals, mortality was 10% to 32% in amphipods (*Gammarus pseudolimnaeus*) in 28 days; at 95 ug As+3/l, marine red alga failed to reproduce sexually; and at 100 ug As+5/l, marine copepods died and goldfish behavior was impaired (Table 4). Rainbow trout (*Salmo gairdneri*) fed diets containing up to 90 mg As+5 kg were only slightly affected, but those given diets containing 120 mg As/kg (as As+3 or As+5), and higher, grew poorly, avoided food, and failed to metabolize food efficiently; no toxic effects were reported over 8 weeks of exposure to diets containing 1,600 mg/kg, as methylated arsenicals (Table 4). In bluegills (*Lepomis macrochirus*), tissue residues of 1.35 mg As/kg fresh weight in juveniles and 5 mg/kg in adults are considered elevated and potentially hazardous (NRCC 1978).

Toxic and other effects of arsenicals to aquatic life are significantly modified by numerous biological and abiotic factors (Woolson 1975; NAS 1977; NRCC 1978; EPA 1980, 1985; Howard et al. 1984; Michnowicz and Weaks 1984; Bryant et al. 1985; Sanders 1986). The LC-50 values, for example, are markedly affected by water temperature, pH, Eh, organic content, phosphate concentration, suspended solids, and presence of other substances and toxicants, as well as arsenic speciation, and duration of exposure. In general, inorganic arsenicals are more toxic than organoarsenicals to aquatic biota, and trivalent species are more toxic than pentavalent species. Early life stages are most sensitive, and large interspecies differences are recorded, even among those closely related taxonomically.

Arsenic is accumulated from the water by a variety of organisms; however, there is no evidence of magnification along the aquatic food chain (Woolson 1975; NAS 1977; NRCC 1978; Hallacher et al. 1985; Hood 1985). In a marine ecosystem based on the alga *Fucus vesiculosus*, arsenate (7.5 ug As+5/l) was accumulated by all biota. After 3 months, arsenic was concentrated most efficiently by *Fucus* (120 mg/kg dry weight in apical fronds) and filamentous algal species 30 mg/kg dry weight); little or no bioaccumulation occurred in invertebrates, although arsenic seemed to be retained by gastropods and mussels (Rosemarin et al. 1985). In a freshwater food chain composed of algae, daphnids, and fish, water concentrations of 0.1 mg cacodylic acid/l produced residues (mg As/kg dry weight), after 48 hours of 4.5 in algae and 3.9 in daphnids, but only 0.09 in fish (NAS 1977). Microcosms of a Delaware Cordgrass (*Spartina alterniflora*) salt marsh exposed to elevated levels of As showed that virtually all arsenic was incorporated into plant tissue or strongly sorbed to cell surfaces (Sanders and Osman 1985). Studies with radioarsenic and mussels (*Mytilus galloprovincialis*) showed that accumulation varied with nominal arsenic concentrations, tissues, age of the mussel, and temperature and

salinity of the medium (Unlu and Fowler 1979). Arsenate uptake increased with increasing arsenic concentration in the medium, but the response was not linear, accumulation being suppressed at higher external arsenic concentrations. Smaller mussels took up more arsenic than larger ones. In both size groups, arsenic was concentrated in the byssus and digestive gland. In general, arsenic uptake and loss increased at increasing temperatures. Uptake was significantly higher at 19 o/oo salinity than at 38 o/oo, but loss rate was about the same at both salinities. Radioarsenic loss followed a biphasic pattern; biological half-life was 3 and 32 days for the fast and slow compartments, respectively; secretion of the byssal thread played a key role in elimination (Unlu and Fowler 1979). Factors known to modify rates of arsenic accumulation and retention in a marine shrimp (*Lysmata seticaudata*) include water temperature and salinity, arsenic concentration, age, and especially frequency of molting (Fowler and Unlu 1978).

Bioconcentration factors (BCF) experimentally determined for arsenic in aquatic organisms are, except for algae, relatively low. The BCF values for inorganic As+3 in most aquatic invertebrates and fish exposed for 21 to 30 days did not exceed 17X; the maximum was 6X for As+5, and 9X for organoarsenicals (EPA 1980, 1985). Significantly higher BCF values were recorded in other aquatic organisms (NRCC 1978), but they were based on mean arsenic concentrations in natural waters that seemed artificially high. A BCF of 350X was reported for the American oyster (*Crassostrea virginica*) held in 5 ug As+3/l for 112 days (Zaroogian and Hoffman 1982). There was no relation between oyster body burdens of arsenic and exposure concentrations; however, diet seemed to contribute more to arsenic uptake than did seawater concentrations (Zaroogian and Hoffman 1982). An arsenic-tolerant strain of freshwater alga (*Chlorella vulgarus*) from an arsenic-polluted environment showed increasing growth up to 2,000 mg As+5/l, and could survive at 10,000 mg As+5/l (Maeda et al. 1985). Accumulations up to 50,000 mg As/kg dry weight were recorded (Maeda et al. 1985)--suggesting a need for additional research on the extent of this phenomenon and its implications on food web dynamics.

Some investigators have suggested that arsenic in the form of arsenite is preferentially utilized by marine algae and bacteria (Johnson 1972; Bottino et al. 1978; Johnson and Burke 1978). Arsenate reduction to arsenite in seawater depends on phosphorus in solution and available algal biomass (Johnson and Burke 1978). During algal growth, as phosphate is depleted and the P+5/As+5 ratio drops, the rate of As+5 reduction increases. The resultant As+3, after an initial peak, is rapidly oxidized to As+5, indicating the possibility of biological catalysis of oxidation as well as mediation of As+5 reduction. It is generally accepted that As+3 is more toxic than arsenates to higher organisms; however, As+5 had a more profound effect on growth and morphology of marine algae than did As+3. Possibly marine algae erect a barrier against the absorption of As+3, but not of As+5. Within the cell, As+5 can then be reduced to the possibly more toxic As+3. For example, the culture of two species of marine algae (*Tetraselmis chui, Hymenomonas carterae*) in media containing various concentrations of As+5 or As+3 showed that arsenic effects varied with oxidation state, ration, and light intensity. Arsenate was incorporated and later partly released by both species. Differences between rates of uptake and release suggest that As+5 undergoes chemical changes after incorporation into algal cells (Bottino et al. 1978). When bacterial cultures from the Sargasso Sea and from marine waters of Rhode Island were grown in As+3-enriched media, the bacteria reduced all available As+5 and utilized As+3 during the log growth phase--presumably as an essential trace nutrient. The arsenate reduction rate per cell was estimated to be 75×10^{-11} mg As/minute (Johnson 1972).

The ability of marine phytoplankton to accumulate high concentrations of inorganic arsenicals and transform them to methylated arsenicals that are later efficiently transferred in the food chain is well documented (Irgolic et al. 1977; Benson 1984; Matsuto et al. 1984; Freeman 1985; Froelich et al. 1985; Maeda et al. 1985; Norin et al. 1985; Sanders 1985; Yamaoka and Takimura 1986). Algae constitute an important source of organoarsenic compounds in marine food webs. In the food chain composed of the alga *Dunaliella marina*, the grazing shrimp *Artemia salina*, and the carnivorous shrimp *Lysmata seticaudata*, organic forms of arsenic were derived from in vivo synthesis by *Dunaliella* and efficiently transferred, without magnification, along the food chain (Wrench et al. 1979). Laboratory studies with five species of euryhaline algae grown in freshwater, or seawater, showed that all species synthesized fat soluble and water soluble arseno-organic compounds from inorganic As +3 and As+5. The BCF values in the five species examined ranged from 200X to about 3,000X--accumulations being highest in lipid phases (Lunde 1973). In Charlotte Harbor, Florida, a region that has become phosphate-enriched due to agricultural activity, virtually all of the arsenic taken up by phytoplankters was biomethylated and returned to the estuary, usually as monomethylarsonic and dimethylarsenic acids (Froelich et al. 1985). The ability of marine phytoplankton to methylate arsenic and release the products to a surrounding environment

varies between species and even within a particular species in relation to their possession of necessary methylating enzymes (Sanders 1985). The processes involved in detoxifying arsenate after its absorption by phytoplankton are not firmly established, but seem to be nearly identical in all plants, suggesting a similar evolutionary development. Like phosphates and sulphates, arsenate may be fixed with ADP, reduced to the arsonous level, and successfully methylated and adenosylated--ultimately producing the 5-dimethylarsenosoribosyl derivatives accumulating in algae (Benson 1984).

Sodium arsenite has been used extensively as an herbicide for control of mixed submerged aquatic vegetation in freshwater ponds and lakes; concentrations of 1.5 to 3.8 mg As+3/l have usually been effective and are considered safe for fish (NAS 1977). Recent data, however, have indicated that As+3 concentrations considered effective for aquatic weed control may be harmful to several species of freshwater teleosts, including bluegills, flagfish, fathead minnows, and rainbow trout (Table 4). Finfishes exposed to 1 to 2 mg total As/l for 2 to 3 days may show one or more of several signs: hemorrhagic spheres on gills; fatty infiltration of liver; and necrosis of heart, liver, and ovarian tissues (NRCC 1978). In green sunfish (*Lepomis cyanellus*), hepatocyte changes parallel arsenic accumulations in the liver (Sorensen et al. 1985). Organoarsenicals are usually eliminated rapidly by fish and other aquatic fauna. Rainbow trout, for example, fed a marine diet containing 15 mg organic arsenic/kg had only negligible tissue residues 6 to 10 days later, although some enrichment was noted in eyes, throat, gills, and pyloric caeca (Pershagen and Vahter 1979). Oral administration of sodium arsenate to estuary catfish (*Cnidoglanis macrocephalus*) and school whiting (*Sillago bassensis*) resulted in tissue accumulations of trimethylarsine oxide. Arsenobetaine levels, which occur naturally in these teleosts, were not affected by As+5 dosing. The toxicity of trimethylarsine oxide is unknown, but the ease with which it can be reduced to the highly toxic trimethylarsine is cause for concern (Edmonds and Francesconi 1987).

BIRDS

Signs of inorganic trivalent arsenite poisoning in birds (muscular incoordination, debility, slowness, jerkiness, falling hyperactivity, fluffed feathers, drooped eyelid, huddled position, unkempt appearance, loss of righting reflex, immobility, seizures) were similar to those induced by many other toxicants and did not seem to be specific for arsenosis. Signs occurred within 1 hour and deaths within 1 to 6 days postadministration; remission took up to 1 month (Hudson et al. 1984). Internal examination suggested that lethal effects of acute inorganic arsenic poisoning were due to the destruction of blood vessels lining the gut, which resulted in decreased blood pressure and subsequent shock (Nystrom 1984). Coturnix (*Coturnix coturnix*), for example, exposed to acute oral doses of As+3 showed hepatocyte damage, i.e., swelling of granular endoplasmic reticulum; these effects were attributed to osmotic imbalance, possibly induced by direct inhibition of the sodium pump by arsenic (Nystrom 1984)

Western grasshoppers (*Melanophus* spp.) poisoned by arsenic trioxide were fed, with essentially no deleterious effects, to nestling northern bobwhites (*Colinus virginianus*), mockingbirds (*Mimus polyglottos*), American robins, (*Turdus migratorius*), and other songbirds (NAS 977). Up to 134 poisoned grasshoppers, containing a total of about 40 mg As, were fed to individual nestlings without any apparent toxic effect. The species tested that were most sensitive to various arsenicals were brown-headed cowbird (*Molothrus ater*) with an LD-50 (11-day) value of 99.8 mg of copper acetoarsenite/kg diet; California quail (*Callipepla californica*) with an LD-50 single oral dose value of 47.6 mg of sodium arsenite/kg body weight; and chicken with 33 and turkey with 17.4 mg/kg body weight of 3-nitro-4-hydroxy phenylarsonic acid as a single oral dose (Table 5).

Chickens rapidly excrete arsenicals; only 2% of dietary sodium arsenite remained after 60 hours (NAS 1977), and arsanilic acid was excreted largely unchanged (Woolson 1975). Excretion of arsanilic acid by chickens was affected by uptake route: excretion was more rapid if administration was by intramuscular injection than if it was oral (NRCC 1978). Studies with inorganic As+5 and chickens indicated that arsenates rapidly penetrated mucosal and serosal surfaces of epithelial membranes; that As+5 intestinal absorption was essentially complete within 1 hour at 370 mg As+5/kg BW but only 50% complete at 3,700 mg/kg BW; that Vitamin D_3 was effective in enhancing duodenal As+5 absorption in rachitic chicks; and that As+5 and phosphate did not appear to share a common transport pathway in the avian duodenum (Fullmer and Wasserman 1986).

MAMMALS

Mammals are exposed to arsenic primarily by the ingestion of naturally contaminated vegetation and water, or through human activity. In addition, feed additives containing arsonic acid derivatives are often fed to domestic livestock to promote growth and retard disease. Some commercial pet foods contain up to 2.3 mg As/kg dry weight (NRCC 1978). Uptake may occur by ingestion (the most likely route), inhalation, and absorption through skin and mucous membranes. Soluble arsenicals are absorbed more rapidly and completely than are the sparingly soluble arsenicals, regardless of the route of administration (NRCC 1978).

Acute episodes of poisoning in warm-blooded organisms by inorganic and organic arsenicals are usually characterized by high mortality and morbidity over a period of 2 to 3 days (NAS 1977; Selby et al. 1977). General signs of arsenic toxicosis include intense abdominal pain, staggering gait, extreme weakness, trembling, salivation, vomiting, diarrhea, fast and feeble pulse, prostration, collapse, and death. Gross necropsy shows a reddening of gastric mucosa and intestinal mucosa, a soft yellow liver, and red edematous lungs. Histopathological findings show edema of gastrointestinal mucosa and submucosa; necrosis and sloughing of mucosal epithelium; renal tubular degeneration; hepatic fatty changes and necrosis; and capillary degeneration in gastrointestinal tract, vascular beds, skin, and other organs. In subacute episodes, where animals live for several days, signs of arsenosis include depression, anorexia, increased urination, dehydration, thirst, partial paralysis of rear limbs, trembling, stupor, coldness of extremities, and subnormal body temperatures (NAS 1977; Selby et al. 1977). In cases involving cutaneous exposure to arsenicals, a dry, cracked, leathery, and peeling skin may be a prominent feature (Selby et al. 1977). Nasal discharges and eye irritation were documented in rodents exposed to organoarsenicals in inhalation toxicity tests (Hood 1985). Subacute effects in humans and laboratory animals include peripheral nervous disturbances, melanosis, anemia, leukopenia, cardiac abnormalities, and liver changes. Most adverse signs rapidly disappeared after exposure ceased (Pershagen and Vahter 1979).

Arsenic poisoning in most animals is usually manifested by acute or subacute signs; chronic poisoning is infrequently seen (NAS 1977). The probability of chronic arsenic poisoning from continuous ingestion of small doses is rare, because detoxication and excretion are rapid (Woolson 1975). Chronic toxicity of inorganic arsenicals is associated with weakness, paralysis, conjunctivitis, dermatitis, decreased growth, and liver damage (NRCC 1978). Arsenosis, produced as a result of chronic exposure to organic arsenicals, was associated with demyelination of optic and sciatic nerves, depressed growth, and decreased resistance to infection (NRCC 1978).

The technical literature on arsenic (Table 6) shows general agreement on eight points: (1) Arsenic metabolism and effects are significantly influenced by the organism tested, the route of administration, the physical and chemical form of the arsenical, and the dose. (2) Inorganic arsenic compounds are more toxic than organic arsenic compounds and trivalent species more so than pentavalent. (3) Inorganic arsenicals can cross the placenta in most species of mammals. (4) Early developmental stages are the most sensitive, and man appears to be one of the most susceptible species. (5) Animal tissues usually contain low levels (<0.3 mg As/kg fresh weight) of arsenic; after the administration of arsenicals these levels are elevated, especially in liver, kidney, spleen, and lung; several weeks later, arsenic is translocated to ectodermal tissues (hair, nails) because of the high concentration of sulfur-containing proteins in these tissues. (6) Inorganic arsenicals are oxidized in vivo, biomethylated, and usually excreted rapidly in the urine, but organoarsenicals are usually not subject to similar transformations. (7) Acute or subacute arsenic exposure can lead to elevated tissue residues, appetite loss, reduced growth, loss of hearing, dermatitis, blindness, degenerative changes in liver and kidney, cancer, chromosomal damage, birth defects, and death. (8) Death or malformations have been documented at single oral doses of 2.5 to 33 mg As/kg body weight, at chronic doses of 1 to 10 mg As/kg body weight, and at dietary levels >5 and <50 mg As/kg diet.

Episodes of wildlife poisoning by arsenic are infrequent. White-tailed deer (*Odocoileus virginianus*) consumed, by licking, fatal amounts of sodium arsenite used to debark trees. The practice of debarking trees with arsenicals for commercial use has been almost completely replaced by mechanical debarking equipment (NAS 1977). Snowshoe hares (*Lepus* sp.) appear to be especially sensitive to methylated arsenicals; hares died after consuming plants heavily contaminated with monosodium methanearsonate as a result of careless silviculture practices (Hood 1985).

Unlike wildlife, reports of arsenosis in domestic animals are common in ovines and felines, less common in ovines and equines, and rare in porcines and poultry (NAS 1977). In practice, the most dangerous arsenic preparations are dips, herbicides, and defoliants in which the arsenical is in a highly soluble trivalent form, usually as trioxide or arsenite (Selby et al. 1977). Accidental poisoning of cattle with arsenicals, for example, is well documented. In one instance, more than 100 cattle died after accidental overdosing with arsenic trioxide applied topically to control lice. On necropsy, there were subcutaneous edematous swellings and petechial hemorrhages in the area of application, and histopathology of intestine, mucosa, kidney, and epidermis (Robertson et al. 1984). In Bangladesh, poisoned cattle showed depression, trembling, bloody diarrhea, restlessness, unsteady gait, stumbling, convulsions, groaning, shallow labored breathing, teeth grinding, and salivation (Samad and Chowdhury 1984). Cattle usually died 12 to 36 hours after the onset of signs; necropsy showed extensive submucosal hemorrhages of the gastrointestinal tract (Samad and Chowdhury 1984), and tissue residues >10 mg/kg fresh weight in liver and kidney (Thatcher et al. 1985). It sometimes appears that animals, especially cattle, develop an increased preference for weeds sprayed with an arsenic weed killer, not because of a change in the palatability of the plant, but probably because arsenic compounds are salty, and thus attractive to animals (Selby et al. 1977).

When extrapolating animal data from one species to another, the species tested must be considered. For example, the metabolism of arsenic in the rat (*Rattus* sp.) is unique, and very different from that in man and other animals. Rats store arsenic in blood hemoglobin, excreting it very slowly--unlike most mammals which rapidly excrete ingested inorganic arsenic in the urine as methylated derivatives (NAS 1977). Blood arsenic, whether given as As+3 or As+5, rapidly clears from humans, mice, rabbits, dogs, and primates, with a half-life of 6 hours for the fast phase and about 60 hours for the slow phase (EPA 1980). In rat, however, blood arsenic is mostly retained in erythrocytes, and clears slowly, with a Tb 1/2 of 60 to 90 days (EPA 1980). In rats, the excretion of arsenic into bile is 40X faster than in rabbits and up to 800X faster than in dogs (Pershagen and Vahter 1979). There is now general and widespread agreement that the rat is unsatisfactory for use in arsenic research (NAS 1977; NRCC 1978; Pershagen and Vahter 1979; EPA 1980; Webb et al. 1986).

Dimethylarsinic acid is the major metabolite of orally administered arsenic trioxide, and is excreted rapidly in the urine (Yamauchi and Yamamura 1985). The methylation process is true detoxification, since methanearsonates and cacodylates are about 200X less toxic than sodium arsenite (NAS 1977). The marmoset monkey (*Callithrix jacchus*), unlike all other animal species studied to date, was not able (for unknown reasons) to metabolize administered As+5 to demethylarsinic acid. Most was reduced to As+3. Only 20% the total dose was excreted in urine as unchanged As+5, another 20% as As+3, and the rest was bound to tissues giving distribution patterns similar to arsenite (Vahter and Marafante 1985). Accordingly, the marmoset--like the rat--may be unsuitable for research with arsenicals.

Arsenicals were ineffective in controlling certain bacterial and viral infections. Mice experimentally infected with bacteria (*Klebsiella pneumonias*) or viruses (pseudorabies, encephalitis, encephalomyocarditis) showed a significant increase in mortality when treated with large doses of arsenicals compared to nonarsenic-treated groups (NAS 1977; Aranyi et al. 1985).

It has been suggested, but not yet verified, that many small mammals avoid arsenic-treated feeds and consume other foods if given the choice (NAS 1977); also, that cacodylic acid, which has negligible effects on wildlife, reduces species diversity due to selective destruction of vegetation (Hood 1985). Both topics merit more research.

CURRENT RECOMMENDATIONS

Numerous criteria for arsenic have been proposed to protect natural resources and human health (Table 7). But many authorities recognize that these criteria are not sufficient for adequate or (in some cases) reasonable protection, and that many additional data are required if meaningful standards are to be promulgated (NAS 1977); NRCC 1978; Pershagen and Vahter 1979; EPA 1980, 1985). Specifically, data are needed on the following subjects: cancer incidence and other abnormalities in natural resources from areas with elevated arsenic levels, and the relation to potential carcinogenicity of arsenic compounds; interaction effects of arsenic with other carcinogens, cocarcinogens, promoting agents, inhibitors, and common environmental contaminants; controlled studies with aquatic and terrestrial indicator organisms on physiological and biochemical effects of long-term, low-dose exposures to inorganic and organic arsenicals--including effects on reproduction and genetic makeup; methodologies for establishing maximum permissible tissue concentrations for arsenic; effects

of arsenic in combination with infectious agents; mechanisms of arsenical growth-promoting agents; role of arsenic in nutrition; extent of animal adaptation to arsenicals, and the mechanisms of action, and physicochemical processes influencing arsenic cycling. In addition, techniques should be developed and procedures implemented in three fields: (1) development of more sophisticated measurements of chemical forms of arsenic in plant and animal tissues; (2) correlations of biologically observable effects with appropriate chemical forms of arsenic; and (3) management of arsenical wastes that will accommodate recycling, reuse, and long term storage.

Some proposed, arsenic criteria merit additional comment, such as those on aquatic life protection, levels in seafoods and drinking water, and use in food-producing animals as growth stimulants or for disease prevention and treatment.

For saltwater life protection, the current water quality criterion of 36 ug As+3/l (EPA 1985; Table 7) seems to offer a reasonable degree of safety; only a few species of algae show adverse effects at <36 ug/1--e.g., reduced growth at 19 to 22 ug/l. In 1980, this criterion was 508 ug/l (EPA 1980), or about 14X higher; the current downward modification seems to be indicative of the increasingly stringent arsenic criteria formulated by regulatory agencies. But the current criterion for freshwater life protection of 190 ug As+3/1 (EPA 1985; Table 7), which is down from 440 ug As+3/1 in 1980 (EPA 1980), is unsatisfactory. Many species of freshwater biota are adversely affected at <190 ug/l of As+3, As+5, or various organoarsenicals (Table 4). These adverse effects include death and malformations of toad embryos at 40 ug/l, growth inhibition of algae at 48 to 75 ug/l, mortality of amphipods and gastropods at 85 to 88 ug/l, and behavioral impairment of goldfish (*Carassius auratus*) at 100 ug/l. It seems that some downward adjustment in the current freshwater aquatic life protection criterion is warranted.

Current permissible concentrations of arsenic in seafood in Hong Kong destined for human consumption range from 6 to 10 mg/kg fresh weight (Table 7); however, these values are routinely exceeded in 22% of finfish, 20% of bivalve molluscs, 67% of gastropods, 29% of crabs, 21% of shrimp and prawns, and 100% of lobsters (Phillips et al. 1982). The highest arsenic recorded in Hong Kong seafood products was in gastropods (*Hemifusus* spp.), in which the concentrations of 152 to 176 mg/kg FW were among the highest recorded in any species to date (Phillips et al. 1982). Probably most of the arsenic in seafood products is present as arsenobetaine or in other comparatively harmless forms. In effect, arsenic criteria for seafoods are neither enforced nor enforceable. Most toxicologists from the U.S. Food and Drug Administration believe that the average daily intake of arsenic in the different food commodities does not pose a hazard to the consumer (Jelinek and Corneliussen 1977).

For maximum protection of human health from the potential carcinogenic effects due to exposure of arsenic through drinking water or contaminated aquatic organisms, the ambient water concentration should be zero, based on the nonthreshold assumption for arsenic. But zero level may not be attainable. Accordingly, the levels that may result in an incremental increase of cancer risk over a lifetime are estimated at 10^{-5} , or one additional case per 100,000 population. These values are estimated at 0.022 ug As/l for drinking water, and 0.175 ug As/l for water containing edible aquatic resources (EPA 1980; Table 7).

Various phenylarsonic acids--especially arsanilic acid, sodium arsanilate, and 3-nitro-4-hydroxy-phenylarsonic acid--have been used as feed additives for disease control and for improvement of weight gain in swine and poultry for almost 40 years (NAS 1977). The arsenic is present as As+5 and is rapidly excreted; present regulations require withdrawal of arsenical feed additives 5 days before slaughter for satisfactory depuration (NAS 1977). Under these conditions, total arsenic residues in edible tissues do not exceed the maximum permissible limit of 2 mg/kg fresh weight (Jelinek and Corneliussen 1977). It now seems that organoarsenicals will continue to be used as feed additives unless evidence indicates otherwise.

LITERATURE CITED

Aggett, J., and G. A. O'Brien. 1985. Detailed model for the mobility of arsenic in lacustrine sediments based on measurements in Lake Ohakuri. Environ. Sci. Technol. 19:231-238.

Aggett, J., and L. S. Roberts. 1986. Insight into the mechanism of accumulation of arsenate and phosphate in hydro lake sediments by measuring the rate of dissolution with ethylenediaminetetracetic acid. Environ. Sci. Technol. 20:183-186.

Andreas, M. 0. 1986. Organoarsenic compounds in the environment. Pages 198-228 *in* P. J. Craig (ed.). Organometallic compounds in the environment. Principles and reactions. John Wiley, New York.

Aranyi, C., J. N. Bradof, W. J. O'Shea, J. A. Graham, and F. J. Miller. 1985. Effects of arsenic trioxide inhalation exposure on pulmonary antibacterial defenses in mice. J. Toxicol. Environ. Health 15:163-172.

Austin, L. S., and G. E. Millward. 1984. Modelling temporal variations in the global tropospheric arsenic burden. Atmosph. Environ. 18:1909-1919.

Belton, J. C., N. C. Benson, M. L. Hanna, and R. T. Taylor. 1985. Growth inhibitory and cytotoxic effects of three arsenic compounds on cultured Chinese hamster ovary cells. J. Environ. Sci. Health 20A:37-72.

Benson, A. A. 1984. Phytoplankton solved the arsenate - phosphate problem. Pages 55-59 *in* 0. Holm-Hansen, L. Bolis, and R. Gilles (eds.). Lecture notes on coastal and estuarine ecology. 8. Marine phytoplankton and productivity. Springer-Verlag, Berlin.

Blus, L. J., B. S. Neely, Jr., T. G. Lamont, and B. Mulhern. 1977. Residues of organochlorines and heavy metals in tissues and eggs of brown pelicans 1969-73. Pestic. Monitor. J. 11:40-53.

Bottino, N. R., R. D. Newman, E. R. Cox, R. Stockton, M. Hoban, R. A. Zingaro, and K. J. Irgolic. 1978. The effects of arsenate and arsenite on the growth and morphology of the marine unicellular algae *Tetraselmis chui* (Chlorophyta) and *Hymenomonas carterae* (Chrysophyta). J. Exp. Mar. Biol. Ecol. 33:153-168.

Bryant, V., D. M. Newbery, D. S. McLusky, and R. Campbell. 1985. Effect of temperature and salinity on the toxicity of arsenic to three estuarine invertebrates (*Corophium volutator*, *Macoma balthica*, *Tubifex costatus*). Mar. Ecol. Prog. Ser. 24:129-137.

Charbonneau, S. M., K. Spencer, F Bryce, and E. Sandi. 1978. Arsenic excretion by monkeys dosed with arsenic-containing fish or with inorganic arsenic. Bull. Environ. Contam. Toxicol. 20:470-477.

Cockell, K. A., and J. W. Hilton. 1985. Chronic toxicity of dietary inorganic and organic arsenicals to rainbow trout (*Salmo gairdneri* R.). Fed. Proc. 44(4):938.

Deknudt, G., A. Leonard, J. Arany, G. J. Du Buisson, and E. Delavignette. 1986. *In vivo* studies in male mice on the mutagenic effects of inorganic arsenic. Mutagenesis 1:33-34.

Denham, D. A., S. L. Oxenham, I. Midwinter, and E. A. H. Friedheim. 1986. The antifilarial activity of a novel group of organic arsenicals upon *Brugia pahangi*. J. Helminthol. 60:169-172.

Dudas, M. J. 1984. Enriched levels of arsenic in post-active acid sulfate soils in Alberta. Soil Sci. Soc. Am. J. 48:1451-1452.

Edmonds, J. S., and K. A. Francesconi. 1987. Trimethylarsine oxide in estuary catfish (*Cnidoglanis macrocephalus*) and school whiting (*Sillago bassensis*) after oral administration of sodium arsenate; and as a natural component of estuary catfish. Sci. Total Environ. 64: 317-323.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

EPA. 1980. Ambient water quality criteria for arsenic. U.S. Environ. Protection Agency Rep. 440/5-80-021. 205 pp.

EPA. 1985. Ambient water quality criteria for arsenic - 1984. U.S. Environ. Protection Agency Rep. 440/5-84-033. 66 pp.

Farmer, J. G., and M. A. Lovell. 1986. Natural enrichment of arsenic in Loch Lomond sediments. Geochim. Cosmochim. Acta 50:2059-2067.

Ferm, V. H., and D. P. Hanlon. 1985. Constant rate exposure of pregnant hamsters to arsenate during early gestation. Environ. Res. 37:425-432.

Ferm, V. H., and D. P. Hanlon. 1986. Arsenate-induced neural tube defects not influenced by constant rate administration of folic acid. Pediatric Res. 20:761-762.

Fischer, A. B., J. P. Buchet, and R. R. Lauwerys. 1985. Arsenic uptake, cytotoxicity and detoxification studied in mammalian cells in culture. Arch. Toxicol. 57:168-172.

Fowler, S. W., and M. Y. Unlu. 1978. Factors affecting bioaccumulation and elimination of arsenic in the shrimp *Lysmata seticaudata*. Chemosphere 9:711-720.

Francesconi, K. A., P. Micks, R. A. Stockton, and K. J. Irgolic. 1985. Quantitative determination of arsenobetaine, the major water-soluble arsenical in three species of crab, using high pressure liquid chromatography and an inductively coupled argon plasma emission spectrometer as the arsenic-specific detector. Chemosphere 14:1443-1453.

Freeman, M. C. 1985. The reduction of arsenate to arsenite by an *Anabaena* bacteria assemblage isolated from the Waikato River. N.Z. J. Mar. Freshwater Res. 19:277-282.

Freeman, M. C., J. Aggett, and G. O'Brien. 1986. Microbial transformations of arsenic in Lake Ohakuri, New Zealand. Water Res. 20:283-294.

Froelich, P. N., L. W. Kaul, J. T. Byrd, M. O. Andreas, and K. K. Roe. 1985. Arsenic, barium, germanium, tin, dimethylsulfide and nutrient biogeochemistry in Charlotte Harbor, Florida, a phosphorus-enriched estuary. Estuar. Coastal Shelf Sci. 20:239-264.

Fullmer, C. S., and R. H. Wasserman. 1985. Intestinal absorption of arsenate in the chick. Environ. Res. 36:;06-217.

Goede, A. A. 1985. Mercury, selenium, arsenic and zinc in waders from the Dutch Wadden Sea. Environ. Pollut. 37A:287-309.

Hall, R. A., E. G. Zook, and G. M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resources. U. S. Dep. Commerce NOAA Tech. Rep. NMFS SSRF-721. 313 pp.

Hall, R. J. 1980. Effects of environmental contaminants on reptiles: a review. U.S. Fish Wildl. Serv. Spec. Sci. Rep.-Wildl. 228. 12 pp.

Hallacher, L. E., E. B. Kho, N. D. Bernard, A. M. Orcutt, W. C. Dudley, Jr., and T. M. Hammond. 1985. Distribution of arsenic in the sediments and biota of Hilo Bay, Hawaii. Pac. Sci. 39:266-273.

Hanaoka, K., and S. Tagawa. 1985a. Isolation and identification of arsenobetaine as a major water soluble arsenic compound from muscle of blue pointer *Isurus oxyrhynchus* and whitetip shark *Carcharhinus longimanus*. Bull. Jpn. Soc. Sci. Fish. 51:681.-685.

Hanaoka, K., and S. Tagawa. 1985b. Identification of arsenobetaine in muscle of roundnose flounder *Eopsetta grigorjewi* Bull. Jpn. Soc Sci. Fish. 51:1203.

Hanlon, D. P., and V. H. Ferm. 1986a. Teratogen concentration changes as the basis of the heat stress enhancement of arsenate teratogenesis in hamsters. Teratology 34:189-193.

Hanlon, D. P., and V. H. Ferm. 1986b. Concentration and chemical status of arsenic in the blood of pregnant hamsters during critical embryogenesis. 1. Subchronic exposure to arsenate using constant rate administration. Environ. Res. 40:372-379.

Hanlon, D. P., and V. H. Ferm. 1986c. Concentration and chemical status of arsenic in the blood of pregnant hamsters during critical embryogenesis. 2. Acute exposure. Environ. Res. 40:380-390.

Haswell, S. J., P. O'Neill, and K. C Bancroft. 1985. Arsenic speciation in soil-pore waters from mineralized and unmineralized areas of south-west England. Talanta 32:69-72.

Hood, R. D. 1985. Cacodylic acid: agricultural uses, biologic effects, and environmental fate. VA Monograph. 171 pp. Avail. from Sup. Documents, U.S. Govt. Printing Off., Washington D.C. 20402.

Hood, R. D., G. C. Vedel-Macrander, M. J. Zaworotko, F. M. Tatum, and R. G. Meeks. 1987. Distribution, metabolism, and fetal uptake of pentavalent arsenic in pregnant mice following oral or intraperitoneal administration. Teratology 35:19-25.

Howard, A. G., M. H. Arbab-Zavar, and S. Apte. 1984. The behaviour of dissolved arsenic in the estuary of the River Beaulieu. Estuarine Coastal Shelf Sci. 19:493-504.

Hudson, R. H., R. K. Tucker, and M A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 PP

Irgolic, K. J., E. A. Woolson, R. A. Stockton, R. D. Newman, N. R. Bottino, R. A. Zingaro, P. C. Kearney, R. A. Pyles, S. Maeda, W. J. McShane, and E. R. Cox. 1977. Characterization of arsenic compounds formed by *Daphnia magna* and *Tetraselmis chui* from inorganic arsenate. Environ. Health Perspec. 19:61-66.

Jauge, P., and L. M. Del-Razo. 1985 Uric acid levels in plasma and urine in rats chronically exposed to inorganic AS(III) and As(V). Toxicol. Lett. 26:31-35.

Jelinek, C. F., and P. E. Corneliussen. 1977. Levels of arsenic in the United States food supply. Environ. Health Perspec. 19:83-87.

Jenkins, D. W. 1980. Biological monitoring of toxic trace metals. Vol. 2. Toxic trace metals in plants and animals of the world. Part 1. U.S. Environ. Protection Agency Rep. 600/3-80-090:30-138.

Johnson, D. L. 1972. Bacterial reduction of arsenate in seawater. Nature (Lond.) 240:44-45.

Johnson, D. L., and R. M. Burke. 1978. Biological mediation of chemical speciation. II. Arsenate reduction during marine phytoplankton blooms. Chemosphere 8:645-648.

Johnson, W. W., and M. T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Jongen, W. M. F., J. M. Cardinaals, and P. M. J. Bos. 1985. Genotoxicity testing of arsenobetaine, the predominant form of arsenic in marine fishery products. Food Chem. Toxicol. 23:669-673.

Kaise, T., S. Watanabe, and K. Itoh. 1985. The acute toxicity of arsenobetaine. Chemosphere 14:1327-1332.

Knowles, F. C., and A. A. Benson. 1984a. The mode of action of arsenical herbicides and drugs. Z. gesampte Hyg. (Berlin) 30:407-408.

Knowles, F. C., and A. A. Benson. 1984b. The enzyme inhibitory form of inorganic arsenic. Z. ges. Hyg. (Berlin) 30:625-626.

Lee, T. C., K. C. C. Lee, C. Chang, and W. L. Jwo. 1986a. Cell-cycle dependence of the cytotoxicity and clastogenicity of sodium arsenate in Chinese hamster ovary cells. Bull. Inst. Zool. Acad. Sinica 25:91-97.

Lee, T. C., M. Oshimura, and J. C. Barrett. 1985. Comparison of arsenic-induced cell transformation, cytotoxicity, mutation and cytogenetic effects in Syrian hamster embryo cells in culture. Carcinogenesis 6:1421-1426.

Lee, T. C., S. Wang-Wuu, R. Y. Huang, K. C. C. Lee, and K. Y. Jan. 1986b. Differential effects of pre- and posttreatment of sodium arsenite on the genotoxicity of methyl methanesulfonate in Chinese hamster ovary cells. Cancer Res. 46:1854-1857.

Lima, A. R., C. Curtis, D. E. Hammermeister, T. P. Markee, C. E. Northcott, and L. T. Brooke. 1984. Acute and chronic toxicities of arsenic (III) to fathead minnows, flagfish, daphnids, and an amphipod. Arch. Environ. Contam. Toxicol. 13:595-601.

Lunde, G. 1973. The synthesis of fat and water soluble arseno organic compounds in marine and limnetic algae. Acta Chem. Scand. 27:1586-1594.

Lunde, G. 1977. Occurrence and transformation of arsenic in the marine environment. Environ. Health Perspec. 19:47-52.

Maeda, S., S. Nakashima, T. Takeshita, and S. Higashi. 1985. Bioaccumulation of arsenic by freshwater algae and the application to the removal of inorganic arsenic from an aqueous phase. Part II. By *Chlorella vulgaris* isolated from arsenic-polluted environment. Separation Sci. Technol. 20:153-161.

Maher, W. A. 1985a. Arsenic in coastal waters of South Australia. Water Res. 19:933-934.

Maher, W. A. 1985b. The presence of arsenobetaine in marine animals. Biochem. Physiol. 80C:199-201.

Mankovska, B. 1986. Accumulation of As, Sb, S, and Pb in soil and pine forest. Ekologia (CSSR) 5:71-79.

Marafante, E., M. Vahter, and J. Envall. 1985. The role of the methylation in the detoxication of arsenate in the rabbit. Chem.-Biol. Interact. 56:225-238.

Marques, I. A., and L. E. Anderson. 1986. Effects of arsenite, sulfite, and sulfate on photosynthetic carbon metabolism in isolated pea (*Pisum sativum* L., cv Little Marvel) chloroplasts. Plant Physiol. 82:488-493.

Matsuto, S., H. Kasuga, H. Okumoto, and A. Takahashi. 1984. Accumulation of arsenic in blue-green alga, *Phormidium* sp. Comp. Biochem. Physiol. 78C:377-382.

Matsuto, S., R. A. Stockton, and K. J. Irgolic. 1986. Arsenobetaine in the red crab, *Chionoecetes opilio*. Sci. Total Environ. 48:133-140.

Merry, R. H., K. G. Tiller, and A. M. Alston. 1986. The effects of contamination of soil with copper, lead and arsenic on the growth and composition of plants. I. Effects of season, genotype, soil temperature and fertilizers. Plant Soil 91:115-128.

Michnowicz, C. J., and T. E. Weaks. 1984. Effects of pH on toxicity of As, Cr, Cu, Ni, and Zn to *Selenastrum capricornutum* Printz. Hydrobiologia 118:299-305.

Nagymajtenyi, L., A. Selypes, and G. Berencsi. 1985. Chromosomal aberrations and fetotoxic effects of atmospheric arsenic exposure in mice. J. Appl. Toxicol. 5:61-63.

NAS. 1977. Arsenic. Natl. Acad. Sci., Washington, D.C. 332 pp.

Nevill, E. M. 1985. The effect of arsenical dips on *Parafilaria bovicola* in artificially infected cattle in South Africa. Onderstepoort J. Vet. Res. 52:221-225.

Norin, H., M. Vahter, A. Christakopoulos, and M. Sandstrom. 1985. Concentration of inorganic and total arsenic in fish from industrially polluted water. Chemosphere 14:1125-334.

NRCC. 1978. Effects of arsenic in the Canadian environment. Natl. Res. Coun. Canada Publ. No. NRCC 15391. 349 pp.

Nystrom, R. R. 1984. Cytological changes occurring in the liver of coturnix quail with an acute arsenic exposure. Drug Chem. Toxicol. 7:587-594.

Passino, D. R. M., and A. J. Novak. 1984. Toxicity of arsenate and DDT to the cladoceran *Bosmina longirostris*. Bull. Environ. Contam. Toxicol. 33:325-329.

Pershagen, G., and N. E. Bjorklund. 1985. On the pulmonary tumorogenicity of arsenic trisulfide and calcium arsenate in hamsters. Cancer Lett. 27:99-104.

Pershagen, G., and M. Vahter. 1979. Arsenic--a toxicological and epidemiological appraisal. Naturvardsverket Rapp. SNV PM 1128, Liber Tryck, Stockholm. 265 pp.

Phillips, D. J. H., and M. H. Depledge. 1986. Chemical forms of arsenic in marine organisms, with emphasis on *Hemifusus* species. Water Sci. Technol. 18:213-222.

Phillips, D. J. H., G. B. Thompson, K. M. Gabuji, and C. T. Ho. 1982. Trace metals of toxicological significance to man in Hong Kong seafood. Environ. Pollut. 3B:27-45.

Reinke, J., J. F. Uthe, H. C. Freeman, and J. R. Johnston. 1975. The determination of arsenite and arsenate ions in fish and shellfish by selective extraction and polarography. Environ. Lett. 8:371-380.

Robertson, I. D., W. E. Harms, and P. J. Ketterer. 1984. Accidental arsenical toxicity of cattle. Aust. Veterin. J. 61:366-367.

Robertson, J. L., and J. A. McLean. 1985. Correspondence of the LC 50 for arsenic trioxide in a diet-incorporation experiment with the quantity of arsenic ingested as measured by X-ray, energy-dispersive spectrometry. J. Econ. Entomol. 78:1035-1036.

Rosemarin, A., M. Notini, and K. Holmgren. 1985. The fate of arsenic in the Baltic Sea *Fucus vesiculosus* ecosystem. Ambio 14:342-345.

Sadiq, M. 1986. Solubility relationships of arsenic in calcareous soils and its uptake by corn. Plant Soil 91 241-248.

Samad, M. A., and A. Chowdhury. 1984 Clinical cases of arsenic poisoning in cattle. Indian J. Vet. Med. 4:107 108.

Sanders, J. G. 1980. Arsenic cycling in marine systems. Mar. Environ. Res. 3:257-266.

Sanders, J. G. 1985. Arsenic geochemistry in Chesapeake Bay: dependence upon anthropogenic inputs and phytoplankton species composition. Mar. Chem. 17:329-340.

Sanders, J. G. 1986. Direct and indirect effects of arsenic on the survival and fecundity of estuarine zooplankton. Can. J. Fish. Aquat. Sci. 43:694-699.

Sanders, J. G., and S. J. Cibik. 1985. Adaptive behavior of euryhaline phytoplankton communities to arsenic stress. Mar. Ecol. Prog. Ser. 22:199-205.

Sanders, J. G., and R. W. Osman. 1985. Arsenic incorporation in a salt marsh ecosystem. Estuarine Coastal Shelf Sci. 20:387-392.

Selby, L. A., A. A. Case, G. D. Osweiler, and H. M. Hages, Jr. 1977. Epidemiology and toxicology of arsenic poisoning in domestic animals. Environ. Health Perspec. 19:183-189.

Sheppard, M. I., D. H. Thibault, and S. C. Sheppard. 1985. Concentrations and concentration ratios of U, As and Co in Scots Pine grown in a waste-site soil and an experimentally contaminated soil. Water Air Soil Pollut. 26:85-94.

Shiomi, K., A. Shinagawa, K. Hirota, H. Yamanaka, and T. Kikuchi. 1984a. Identification of arsenobetaine as a major arsenic compound in the ivory shell *Buccinum striatissimum*. Agric. Biol. Chem. 48:2863-2864.

Shiomi, K., A. Shinagawa, T. Igarashi, H. Yamanaka, and T. Kikuchi. 1984b. Evidence for the presence of arsenobetaine as a major arsenic compound in the shrimp *Sergestes lucens*. Experientia 40:1247-1248.

Sloot, H. A. van der, D. Hoede, J. Wijkstra, J. C. Duinker, and R. F. Nolting. 1985. Anionic species of V, As, Se, Mo, Sb, Te and W in the Scheldt and Rhine estuaries and the southern bight (North Sea). Estuarine Coastal Shelf Sci. 21:633-651.

Smiley, R. W., M. C. Fowler, and R. C. O'Knefski. 1985. Arsenate herbicide stress and incidence of summer patch on Kentucky bluegrass turfs. Plant Dis. 69:44-48.

Smith, R. A., R. B. Alexander, and M. G. Wolman. 1987. Water-quality trends in the Nation's rivers. Science 235:1607-1615.

Sorensen, E. M. B., R. R. Mitchell, A. Pradzynski, T. L. Bayer, and L. L. Wenz. 1985. Stereological analyses of hepatocyte changes parallel arsenic accumulation in the livers of green sunfish. J. Environ. Pathol. Toxicol. Oncol. 6:195-210.

Spehar, R. L., J. T. Fiandt, R. L. Anderson, and D. L. DeFoe. 1980. Comparative toxicity of arsenic compounds and their accumulation in invertebrates and fish. Arch. Environ. Contam. Toxicol. 9:53-63.

Stine, E. R., C. A. Hsu, T. D. Hoovers, H. V. Aposhian, and D. E. Carter. 1984. N-(2,3-dimercaptopropyl) phthalamidic acid: protection, *in vivo* and *in vitro*, against arsenic intoxication. Toxicol. Appl. Pharmacol. 75:329-336.

Takamatsu, T., M. Kawashima, and M. Koyama. 1985. The role of Mn^{2+} - rich hydrous manganese oxide in the accumulation of arsenic in lake sediments. Water Res. 19:1029-1032.

Taylor, D., B. G. Maddock, and G. Mance. 1985. The acute toxicity of nine 'grey list' metals (arsenic, boron, chromium, copper, lead, nickel, tin, vanadium and zinc) to two marine fish species: dab (*Limanda limanda*) and grey mullet (*Chelon labrosus*). Aquatic Toxicol. 7:135-144.

Thanabalasingam, P., and W. F. Pickering. 1986. Arsenic sorption by humic acids. Environ. Pollut. 12B:233-246.

Thatcher, C. D., J. B. Meldrum, S. E. Wikse, and W. D. Whittier. 1985. Arsenic toxicosis and suspected chromium toxicosis in a herd of cattle. J. Am. Vet. Med. Assoc. 187:179-182.

Thursby, G. B., and R. L. Steele. 1984. Toxicity of arsenite and arsenate to the marine macroalgae *Champia parvula* (Rhodophyta). Environ. Toxicol. Chem. 3:391-397.

Unlu, M. Y., and S. W. Fowler. 1979. Factors affecting the flux of arsenic through the mussel *Mytilus galloprovincialis*. Mar. Biol. 51:209-219.

Vahter, M., and E. Marafante. 1985. Reduction and binding of arsenate in marmoset monkeys. Arch. Toxicol. 57:119-124.

Veen, N. G. van der, and K. Vreman. 1985. Transfer of cadmium, lead, mercury and arsenic from feed into various organs and tissues of fattening lambs. Neth. J. Agric. Sci. 34:145-153.

Vos, G., and J. P. C. Hovens. 1986. Chromium, nickel, copper, zinc, arsenic, selenium, cadmium, mercury and lead in Dutch fishery products 1977-1984. Sci. Total Environ. 52:25-40.

Vreman, K., N. G. van der Veen, E. J. van der Molen, and W. G. de Ruig. 1986. Transfer of cadmium, lead, mercury and arsenic from feed into milk and various tissues of dairy cows: chemical and pathological data. Neth. J. Agric. Sci. 34:129-144.

Wang, D. S., R. W. Weaver, and J. R. Melton. 1984. Microbial decomposition of plant tissue contaminated with arsenic and mercury. Environ. Pollut. 34A:275-282.

Webb, D. R., S. E. Wilson, and D. E. Carter. 1986. Comparative pulmonary toxicity of gallium arsenide, gallium (III) oxide, or arsenic (III) oxide intratracheally instilled into rats. Toxicol. Appl. Pharmacol. 82:405-416.

Wells, J. M., and D. H. S. Richardson. 1985. Anion accumulation by the moss *Hylocomium splendens*: uptake and competition studies involving arsenate, selenate, selenite, phosphate, sulphate and sulphite. New Phytol. 101:571-583.

White, D. H., K. A. King, and F. M. Prouty. 1980. Significance of organochlorine and heavy metal residues in wintering shorebirds at Corpus Christi, Texas, 1976-77. Pestic. Monitor. J. 14:58-63.

Wiemeyer, S. N., T. G. Lamont, and L. N. Locke. 1980. Residues of environmental pollutants and necropsy data for eastern United States ospreys, 1964-1973. Estuaries 3:55-167.

Wiener, J. G., G. A. Jackson, T. W. May, and B. P. Cole. 1984. Longitudinal distribution of trace elements (As, Cd, Cr, Hg, Pb, and Se) in fishes and sediments in the upper Mississippi River. Pages 139-170 *in* J. G. Wiener, R. V. Anderson and D. R. McConville (eds.). Contaminants in upper Mississippi River. Butterworth Publ., Stoneham, Massachusetts.

Windom, H., R. Stickney, R. Smith, D. White, and F. Taylor. 1973. Arsenic, cadmium, copper, mercury, and zinc in some species of North Atlantic finfish. J. Fish. Res. Board Can 30:275-279.

Woolson, E. A. (ed.). 1975. Arsenical pesticides. Am. Chem. Soc. Symp. Ser. 7. 176 pp.

Wrench, J., S. W. Fowler, and M. Y. Unlu. 1979. Arsenic metabolism in a marine food chain. Mar. Pollut. Bull. 10:18-20.

Yamaoka, Y., and O. Takimura. 1986. Marine algae resistant to inorganic arsenic. Agric. Biol. Chem. 50:185-186.

Yamauchi, H., K. Takahashi, and Y. Yamamura. 1986. Metabolism and excretion of orally and intraperitoneally administered gallium arsenide in the hamster. Toxicology 40:237-246.

Yamauchi, H., and Y. Yamamura. 1985. Metabolism and excretion of orally administered arsenic trioxide in the hamster. Toxicology 34:113-121.

Zaroogian, G. E., and G. L. Hoffman. 1982. Arsenic uptake and loss in the. American oyster, *Crassostrea virginica.* Environ. Monitor. Assess. 1:345-358.

Table 1. Total arsenic concentrations in selected nonbiological materials.

Material and units (in parentheses)	Concentration[a]	Reference[b]
Air (ug/m^3)		
Remote areas	<0.02	1
Urban areas	(0.0-0.16)	
Near smelters		
U.S.S.R.	(0.5-1.9)	2
Texas	Max. 1.4	2
Tacoma, Washington	Max. 1.5	2
Romania	Max. 1.6	2
Germany	(0.9-1.5)	2
Coal-fired power plant, Czechoslovakia	(19 to 69)	3
Orchard spraying of Pb arsenate	Max. 260,000	3
Near U.S. cotton gin burning vegetation treated with arsenic	Max. 400	3
Drinking water (g/L)		
Nationwide, U.S.A.	2.4 (0.5-214)	4
Fairbanks, Alaska	224 (1-2,450)	4
Bakersfield, California	(6-393)	4
Nevada, 3 communities	(51-123)	4
Mexico, from plant producing As_2O_3	(4,000-6,000)	2
Japan, near factory producing arsenic sulfide	3,000	2
Ghana, near gold mine	1,400	2
Minnesota, contaminated by residual arsenical grasshopper bait	(11,800-21,000)	1
Methylated arsenicals, U.S.A.	usually <0.3 (0.01-1)	5
Dust (mg/kg)		
Tacoma, Washington		
Near smelter	1,300	1
Remote from smelter	70	1
Fossil fuels (mg/kg)		
Coal		
Canada	4 (0.3-100)	3
USA	5	2

Czechoslovakia	Max. 1,500	2
Worldwide	13 (0.0-2,000)	1
Coal ash	(<20-8,000)	3
Flyash	(2.8-200)	3
Petroleum	0.2	3
Petroleum ash	Max. 100,000	3
Automobile particulates	298	3
Groundwater (ug/L)		
Near polymetallic sulfide		
deposits	Max. 400,000	3
Near gold mining activities	>50	2
USA	Usually <10	2
USA	17.9 (0.01-800)	3
Lake water (ug/L)		
Dissolved solids		
<2,000 mg/L	(0.0-100)	6
>2,000 mg/L	(0.1-2,000)	6
Lake Superior	(0.1-1.6)	6
Japan, various	(0.2-1.9)	6
Germany, Elbe River	(20-25)	6
Searles Lake, California	(198,000-243,000)	1,4
California, other lakes	(0.0-100)	1,4
Michigan	Max. 2.4	1,4
Wisconsin	(4-117)	1,4
Florida	Max. 3.6	1,4
Lake Chatauqua, New York	(3.5-35.6)	1.4
Lake Ohakuri, New Zealand	(30-60)	7
Finfeather Lake, Texas	Max. 240,000	8
Thermal waters, worldwide	(20-3,800)	
	Max. 276,000	1,2,3,9
Rain (ug/L)		
Canada	(0.01-5)	3
Rhode Island	0.8	1
Seattle, Washington	17	1
River water (ug/L)		
Polluted, USA	Max. 6,000	4
Nonpolluted, USA	Usually <5	4
Nationwide, USA, 1974-1981		
25th percentile	<1	10
50th percentile	1	10
75th percentile	3	10
Rock (mg/kg)		
Limestones	1.7 (0.1-20)	1

Sandstones	2 (0.6-120)	1
Shales and clays	14.5 (0.3-490)	1
Phosphates	22.6 (0.4-188)	1
Igneous, various	1.5-3 (0.06-113)	1
Seawater (ug/L)		
Worldwide	2 (0.15-6)	6
Pacific Ocean	(1.4-1.8)	11
Atlantic Ocean	(1.0-1.5)	11
South Australia		
Total dissolved As	1.3 (1.1-1.6)	12
As^{+5}	1.29	12
As^{+3}	0.03	12
Particulate As	<0.0006	12
U.K., Beaulieu estuary		
Water temperature <12° C		
Inorganic arsenic	(0.4-0.9)	13
Suspended arsenic	(0.02-0.24)	13
Organoarsenicals	(0.19-0.75)	13
Water temperature >12° C		
Inorganic arsenic	(0.6-1.1)	13
Suspended arsenic	(0.2-0.6)	13
Organoarsenicals	ND	13
Sediments (mg/kg dry weight)		
Near sewer outfall	35	3
From areas contaminated by smelteries, arsenical herbicides, or mine tailings		
Surface	(198-3,500)	1,7,9,14,15
Subsurface	(12-25)	1,7,9,14,15
Upper Mississippi River	2.6 (0.6-6.2)	16
Lake Michigan	(5-30)	1
Naturally elevated	>500	1,9
Oceanic	33.7 (<0.4-455)	3
Lacustrine	(5-26.9) Max. 13,000	3
Snow (mg/kg)		
Near smelter	>1,000	3
Soil pore waters (ug/L)		
Mineralized areas		
Arsenate	(79-210)	17
Arsenite	(2-11)	17
Monomethyl arsonic acid (MMAA)	(4-22)	17
Total arsenic	(93-240)	17

Unmineralized areas		
Arsenate	(18-49)	17
Arsenite	(1-7)	17
MMAA	<1	17
Total arsenic	(13-59)	17
Soils (mg/kg dry weight)		
USA, uncontaminated	7.4	18
Worldwide, uncontaminated	7.2	18
Canada		
Near Gold mine		
Air levels 3.9 mg As/m^3	21,213	3
80 km distant	(10-25)	3
Near smelter		
Japan	Max. 2,470	2
Tacoma, Washington	Max. 380	2
Treated with arsenical pesticides		
USA	165 (1-2,554)	6
Canada	121	6
Synthetic detergents (mg/kg)		

[a]Concentrations are listed as mean, minimum-maximum (in parentheses), and maximum (Max.).

[b]References: 1, NAS 1977; 2, Pershagen and Vahter 1979; 3, NRCC 1978; 4, EPA 1980; 5, Hood 1985; 6, Woolson 1975; 7, Freeman et al. 1986; 8, Sorensen et al. 1985; 9, Farmer and Lovell 1986; 10, Smith et al. 1987; 11, Sanders 1980; 12, Maher 1985a; 13, Howard et al. 1984; 14, Hallacher et al. 1985; 15, Takamatsu 1985; 16, Wiener et al. 1984; 17, Haswell et al. 1985; 18, Dudas 1984.

Table 2. Arsenic concentrations in field collections of selected species of flora and fauna. Values listed are in mg As/kg fresh weight (FW), or dry weight (DW).

Ecosystem, species, and other variables	Concentration in mg/kg[a]	Reference[b]
Terrestrial Plants		
Colonial bentgrass, *Agrostis tenuis*		
On mine waste site	1,480, Max. 3,470 DW	1
On low arsenic soil	(0.3-3) DW	1
Scotch heather, *Calluna vulgaris*		
On mine waste site	1,260 DW	1
On low arsenic soil	0.3 DW	1
Coontail, *Ceratophyllum demersum*		
From geothermal area, New Zealand	(20-1,060) DW	1
Cereal grains		
From arsenic treated areas	Usually <3 DW, Max. 252 DW	2
Nontreated areas	Usually <0.5 DW, Max. 5 DW	2
Grasses		
From arsenic treated areas	(0.5-60,000) DW	2
Nontreated areas	(0.1-0.9) DW	2
Apple, *Malus sylvestris*		
Fruit	<0.1 FW; <1.8 DW	1
Alfalfa, *Medicago sativa*		
USA	1.6 FW	1
Montana, smelter area	(0.4-5.7) FW	1
White spruce, *Picea alba*		
Arsenic-contaminated soil		
Branch	(2.8-14.3) DW	1
Leaf	(2.1-9.5)	1
Trunk	(0.3-55) DW	1
Root	(45-130) DW	1
Control site		
All samples	<2.4 DW	1
Pine, *Pinus silvestris*, needles		
Near U.S.S.R. metals smelter; soil levels 120.0 mg As/kg	22 FW	3
Trees		
Nontreated areas	Usually <1 DW	2
Lowbush blueberry, *Vaccinium angustifolium*		

Maine, leaf		
Arsenic-treated soil	(6.8-15) DW	1
Control	0.8 DW	1
Various species		
From uncontaminated soils	(<0.01-5) DW	2
From arsenic-impacted (80 mg/kg) soils	1.2 (<0.2-5.8) DW	4
Vegetables		
From arsenic-treated areas	Usually <3 DW, Max. 145 DW	2
Nontreated areas	Usually <1 DW, Max. 8 DW	2
Vegetation		
Near gold mine, Canada, Air levels up to 3.9 mg As/m^3	Max. 11,438 DW	5
80 km distant	(12-20) DW	5
Freshwater Flora		
Aquatic Plants		
Arsenic-treated areas	(20-1,450) DW	2
Untreated areas	(1.4-13) DW	2
Irish moss, *Chondrus crispus*		
Whole	(5-12) DW	1
Pondweeds, *Potamogeton* spp.		
Whole		
Near geothermal area	(11-436) DW	1
Control site	<6 DW	
Freshwater Fauna		
Alewife, *Alosa pseudoharengus*		
Whole, Michigan	0.02 FW	1
Muscle, Wisconsin	0 FW	1
White sucker, *Catostomus commersoni*		
Muscle	(0.03-0.13) FW	1
Whole	(0.05-0.16) FW	1
Common carp, *Cyprinus carpio*		
Upper Mississippi River, 1979		
Whole	0.4 (0.2-0.6) DW	6
Liver	0.4 (0.3-1) DW	6
Nationwide		
Whole	0.05 FW	1
Muscle	(0.0-0.2) FW	1
Northern pike, *Esox lucius*		
Muscle		
Canada	(0.05-0.09) FW	1

Great Lakes	<0.05 FW	1
Sweden	0.03 FW	1
New York	<0.1 FW	1
Wisconsin	<0.01 FW	1
Fish, various species		
Whole	Max. 1.9 FW	2
Whole	(0.04-0.2) FW	7
Netherlands, 1977-1984		
Muscle	(0.04-0.15) FW	8
Nationwide, USA		
Whole, 1976-1977	(0.05-2.9) FW	9
Near smelter (water arsenic 2.3-2.9 mg/L)		
Muscle, 3 species		
Total arsenic	0.05-0.24) FW	10
Inorganic arsenic	(0.01-0.02) FW	10
Liver, 2 species		
Total arsenic	0.15 FW	10
Inorganic arsenic	0.01 FW	10
Control location (water arsenic <0.5 mg/L)		
Muscle		
Total arsenic	(0.06-0.09) FW	10
Inorganic arsenic	<0.03 FW	10
Liver		
Total arsenic	0.09 FW	10
Inorganic arsenic	<0.01 FW	10
Channel catfish, *Ictalurus punctatus*		
Muscle		
Native	(0.0-0.3) FW	1
Cultured	(0.2-3.1) FW	1
Whole, nationwide	(<0.05-0.3) FW	1
Green sunfish, *Lepomis cyanellus*, liver		
Polluted waters (from manufacturer of arsenical defoliants and pesticides), Texas. Mean water concentration 13.5 mg As/L; sediment content of 4,700 mg/kg		
Age 1 to 2	(19.7-64.2) DW	11
Age 3	15 DW	11

Age 4	(6.1-11.5) DW	11
Bluegill, *Lepomis macrochirus*		
From pools treated with arsenic		
Muscle	1.3 FW	1
Skin and scales	2.4 FW	1
Gills and GI tract	17.6 FW	1
Liver	11.6 FW	1
Kidney	5.9 FW	1
Ovary	8.4 FW	1
Control locations		
All tissues	<0.2 FW	1
Whole		
Nationwide	(<0.05-0.15) FW	1
Upper Mississippi River, 1979	0.3 (0.2-0.4) DW	6
Smallmouth bass, *Micropterus dolomieui*		
Muscle		
Wisconsin	<0.13 FW	1
Lake Erie	0.22 FW	1
New York	(0.03-0.51) FW	1
Whole, nationwide	(<0.05-0.28) FW	1
Largemouth bass, *Micropterus salmoides*		
Whole, nationwide	(<0.05-0.22) FW	1
Muscle		
Wisconsin	(0.0-0.12) FW	1
New York	(0.03-0.16) FW	1
Striped bass, *Morone saxatilis*		
Muscle	(0.2-0.7) FW	1
Coho salmon, *Oncorhynchus kisutch*		
Muscle		
Wisconsin	<0.15 FW	1
Lake Erie	(0.07-0.17) FW	1
New York	<0.5 FW	1
USA	0.09 FW	1
Yellow perch, *Perca flavescens*		
All tissues	<0.16 FW	1
Rainbow trout, *Salmo gairdneri*		
All tissues	<0.4 FW	1
Atlantic salmon, *Salmo salar*		
Oil		

Liver	6.7 FW	1
Muscle	(0.8-3.1) FW	1
Lake trout, *Salvelinus namaycush*		
Whole, nationwide	(0.06-0.68) FW	1
Marine Flora		
Algae		
Green	(0.5-5) DW	2
Brown	Max. 30 DW	2
11 species	(2-58) DW	12
Various species	(10-100) DW	13
Seaweed, *Chondrus crispus*		
Alga, *Fucus* spp.		
Oil	(6-27) FW	2
Fatty acid	(5-6) FW	2
Brown alga, *Fucus vesiculosus*		
Whole	(35.2-80) DW	1
Brown alga, *Laminaria digitata*		
Whole	94 DW	2
Whole	(42-50) DW	1
Oil	(155-221) DW	2
Fatty acid	(8-36) DW	2
Alga, *Laminaria hyperborea*		
Total arsenic	142 DW	12
Organic arsenic	139 DW	12
Sargassum weed, *Sargassum fluitans*		
Total arsenic	19.5 FW	7
As^{+3}	1.8 FW	7
As^{+5}	17.7 FW	7
Organoarsenicals	0.2 FW	7
Seaweed, *Sargassum* sp.		
Total arsenic	(4.1-8.7) FW	5
As+3	(0.14-0.35) FW	5
As+5	(1.9-7.3) FW	5
Organoarsenicals	Max. 0.1 FW	5
Seaweeds		
Whole	(3.8-93.8) DW	2
Whole	(10-109) DW	12
Oil fraction	(5.7-221) FW	12
Marine Molluscs		
Ivory shell, *Buccinum striatissimum*		
Muscle		
Total arsenic	38 FW	14

Arsenobetaine	24.2 FW	14
Midgut gland		
Total arsenic	18 FW	14
Arsenobetaine	10.8 FW	14
Oysters, *Crassostrea* spp.		
Soft parts	(1.3-10) DW, (0.3-3.4) FW	12
American oyster, *Crassostrea virginica*		
Soft parts	2.9 FW	1
Soft parts	10.3 DW	15
Spindle shells, *Hemifusus* spp.		
Hong Kong 1984, Muscle		
Total arsenic	Max. 500 FW	16
Inorganic arsenic	<0.5 FW	16
Limpet, *Littorina littorea*		
Soft parts		
Near arsenic source	11.5 DW	12
Offshore	4 DW	12
Squid, *Loligo vulgaris*		
Soft parts	(0.8-7.5) FW	1
Hardshell clam, *Mercenaria mercenaria*		
Soft parts		
Age 3 years	3.8 DW	12
Age 4 years	4.7 DW	12
Age 10 years	9.3 DW	12
Age 15 years	8.4 DW	12
Molluscs, edible tissues		
Hong Kong, 1976-1978		
Bivalves	(3.2-39.6) FW	17
Gastropods	(19-176) FW	17
Cephalopods	(0.7-5.5)	17
USA		
6 species	(2-3) FW	18
8 species	(3-4) FW	18
3 species	(4-5) FW	18
4 species	(7-20) FW	18
Mussel, *Mytilus edulis*		
Soft parts	2.5 (1.4-4.6) FW	8
Soft parts	(1.6-16) DW	12
Scallop, *Placopecten magellanicus*		
Soft parts	1.6 (1.3-2.4) FW	1

Marine Crustaceans		
Blue crab, *Callinectes sapidus*		
Florida, whole	7.7 FW	1
Maryland, soft parts	(0.5-1.8) FW	1
Dungeness crab, *Cancer magister*		
Muscle	6.5 (2.2-37.8) FW	1
Muscle	4 FW	19
Alaskan snow crab, *Chinocetes bairdii*		
Muscle	7.4 FW	19
Copepods, whole	(2-8.2) DW	12
	(0.4-1.3) FW	12
Shrimp, *Crangon crangon*		
Netherlands, 1977-1984		
Muscle	3 (2-6.8) FW	8
Crustaceans, edible tissues		
Hong Kong, 1976-1978		
Crabs	(5.4-19.1) FW	17
Lobsters	(26.7-52.8) FW	17
Prawns and shrimps	(1.2-44) FW	17
USA		
6 species	(3-5) FW	18
3 species	(5-10) FW	18
4 species	(10-20) FW	18
2 species	(20-30) FW	18
1 species	(40-50) FW	18
American lobster, *Homarus americanus*		
Muscle	(3.8-7.6) DW,	
	Max. 40.5 FW	1
Hepatopancreas	22.5 FW	1
Whole	(3.8-16) DW,	12
	(1-3) FW	12
Stone crab, *Menippe mercenaria,* whole	(9-11.8)FW	1
Deep seaprawn, *Pandalus borealis*		
Head and shell	68.3 DW	1
Muscle	61.6 DW	1
Oil	42 DW, 10.1 FW	1
Egg	3.7-14 FW	1
Prawns, *Pandalus* spp.		
Whole	(7.3-11.5) FW	12
Alaskan king crab, *Paralithodes camtschatika*		
Muscle	8.6 FW	19

Brown shrimp, *Penaeus aztecus*		
Muscle	(3.1-5.2) FW	1
Whole	0.6 DW	1
White shrimp, *Penaeus setiferus*		
Muscle		
Mississippi	(1.7-4.4) FW	1
Florida	(2.8-7.7) FW	1
Shrimp, *Sergestes lucens*		
Muscle		
Total arsenic	5.5 FW	20
Arsenobetaine	4.5 FW	20
Shrimps		
Exoskeleton	15.3 FW	7
Muscle, 2 species	(18.8-41.6) FW, (3.8-128) DW	2
Marine Fishes		
Whitetip shark, *Carcharhinus longimanus*		
Muscle	3.1 FW	21
Black sea bass, *Centropristis striata*		
Muscle	6.4 DW	1
Elasmobranchs		
Muscle		
Sharks	Max. 30 FW	12
Rays	Max. 16.2 FW	12
Roundnose flounder, *Eopsetta grigorjewi*		
Muscle	20.1 FW	22
Finfishes		
Near metal smelter, water concentration 2.3-2.9 mg As/L		
Muscle, 6 species		
Total arsenic	(0.2-2.6) FW	10
Inorganic arsenic	(0.02-0.1) FW	10
Liver, 4 species		
Total arsenic	(0.4-1.8) FW	10
Inorganic arsenic	(0.02-0.07) FW	10
Control location, water concentration <2.0 mg As/L		
Muscle, 5 species		
Total arsenic	(0.1-1.2) FW	10
Inorganic arsenic	(0.02-0.15) FW	10
Liver, 4 species		
Total arsenic	(0.2-1.5) FW	10

Inorganic arsenic	(0.02-0.05) FW	10
Finfish, Hong Kong, 1976-1978		
Edible tissues	Max. 21.1 FW	17
Finfish, Netherlands, 1977-1984		
Muscle, 4 species	(2.8-10.9) FW	8
Finfish, North America		
Liver		
49 species	(0.7-5) FW	18
26 species	(5-20) FW	18
6 species	(20-50) FW	18
Muscle		
91 species	(0.6-4) FW	18
41 species	(4-8) FW	18
27 species	(8-30) FW	18
4 species		
Total arsenic	(1.4-10) FW	23
Inorganic arsenic	<0.5 FW	23
Whole		
16 species	(1-8) FW	18
Finfish, worldwide		
Various tissues		
Total arsenic	(ND-142) FW	2
Inorganic arsenic	(0.7-3.2) FW	2
Organic arsenic	(3.4-139) FW	2
Atlantic cod, *Gadus morhua*		
Muscle	2.2 FW	2
Liver	9.8 FW	2
Blue pointer, *Isurus oxyrhinchus*		
Muscle	9.5 FW	21
Striped bass, *Morone saxatilis*		
Muscle	(0.3-0.5) FW, 1.8 DW	12
Liver	0.7 FW	12
Striped mullet, *Mugil cephalus*		
Viscera	Max. 1.3 FW	24
English sole, *Parophrys vetulus*		
Muscle	1.1 (0.6-11.5) FW	1
Skate, *Raja* sp.		
Muscle	16.2 FW	1
Windowpane flounder, *Scopthalmus aquosus*		
Muscle	(1.4-2.8) FW	1

Spiny dogfish, *Squalus acanthias*		
Muscle	10 DW	25
Liver	5.7 DW	25
Spleen	9.8 DW	25
Yolk sac	9.1 DW	25
Embryo	2.6 DW	25
Amphibians and Reptiles		
Alligator, *Alligator mississippiensis*		
Egg	(0.05-0.2) FW	1
Crocodile, *Crocodylus acutus*		
Egg	0.2 FW	26
Frogs, *Rana* spp.		
All tissues	<0.4 FW	1
Toads, 2 species		
All tissues	<0.05 FW	
Birds		
American black duck, *Anas rubripes*		
Egg	0.2 FW	12
Ducks, *Anas* spp.		
All tissues	<0.4 FW	1
Scaup, *Aythya* spp.		
All tissues	<0.4 FW	1
Gulls, 3 species		
Oil	(0.6-13.2) FW	12
Osprey, *Pandion haliaetus*		
Liver	Max. 16.7 FW	27
Brown pelican, *Pelecanus occidentalis*		
Egg		
South Carolina, 1971-72	0.3 (0.08-0.8) FW	28
Florida, 1969-70	0.1 (0.07-0.2) FW	28
Liver, 1972-72,		
GA, FL, SC		
Found dead	(0.2-1) FW	28
Shot	(0.3-0.9) FW	28
Shorebirds		
Corpus Cristi, Texas, 1976-1977		
Liver, 7 species	(0.05-1.5) FW	29
New Zealand, 5 species		
Feather	<1 FW	12
Liver	Max. 2.6 FW	12
Starling, *Sturnus vulgaris*		
Whole, nationwide, USA, 1971	(<0.01-0.21) FW	2
Icelandic redshank, *Tringa totanus robusta*		

Netherlands, 1979-1982		
Feather		
Juveniles	Max. 0.8 FW	30
Adults	(0.5-3.2) FW	30
Mammals		
Fin whale,		
Balaenoptera physalis		
Blubber oil	1.8 FW	1
Cow, *Bos bovis*		
Downwind from copper smelter		
16-21 km		
Hair	8.9 FW	1
Milk	0.013 FW	1
Blood	0.026 FW	1
60 km		
Hair	0.46 FW	1
Milk	0.002 FW	1
Blood	0.009 FW	1
Controls		
Milk	<0.001 FW	31
Muscle	0.005 FW	31
Liver	(0.008-0.012) FW	31
Kidney	(0.017-0.053) FW	31
Domestic animals		
All tissues	<0.3 FW	2
Livestock		
All tissues	<0.6 FW	2
Marine mammals		
Pinnipeds		
All tissues	Max. 1.7 FW	12
Cetaceans		
Muscle	0.4 DW	12
Oil	(0.6-2.8) FW	12
White-tailed deer,		
Odocoileus virginianus		
Tennessee, killed from		
arsenic herbicide		
Liver	19 FW	1
Kidney	17.8 FW	1
Rumen contents	22.5 FW	1
Harbor seal,		
Phoca vitulina		
UK, all tissues	<0.3 FW	1

Fox, *Vulpes* sp.		
All tissues	<0.7 FW	1
Wildlife		

[a]Concentrations are listed as mean, minimum-maximum (in parentheses), and maximum (Max.).

[b]References: 1, Jenkins 1980; 2, NAS 1977; 3, Mankovska 1986; 4, Merry et al. 1986; 5, NRCC 1978; 6, Wiener et al. 1984; 7, Woolson 1975; 8, Vos and Hovens 1986; 9, Lima et al. 1984; 10, Norin et al. 1985; 11, Sorensen et al. 1985; 12, Eisler 1981; 13, Pershagen and Vahter 1979; 14, Shiomi et al. 1984a; 15, Zaroogian and Hoffman 1982; 16, Phillips and Depledge 1986; 17, Phillips et al. 1982; 18, Hall et al. 1978; 19, Francesconi et al. 1985; 20, Shiomi et al. 1984b; 21 Hanaoka and Tagawa 1985a; 22, Hanaoka and Tagawa 1985b; 23, Reinke et al. 1975; 24, Hallacher et al. 1985; 25, Windom et al. 1973; 26, Hall 1980; 27, Wiemeyer et al. 1980; 28, Blus et al. 1977; 29, White et al. 1980; 30, Goede 1985; 31, Vreman et al. 1986.

Table 3. Toxic and sublethal effects of various arsenic compounds on selected species of terrestrial plants and invertebrates.

Ecosystem, species, and other variables	Arsenic concentration and effects	Reference[a]
Terrestrial Plants		
Crops		
Total water soluble As in soils	Depressed crop yields at 3 to 28 mg/L	1
Total soil As concentrations	Depressed crop yields at 25 to 85 mg/kg	1
Common bermudagrass, *Cynodon dactylon*		
Arsenite	Plants grown on As- amended soils (up to 90 mg As^{+3}/kg) contained up to 17 mg As/kg dry weight in stems, 20 in leaves, and 304 in roots	2
Fruit orchards		
Inorganic arsenites and arsenates	Soils contain 31 to 94 mg/kg dry weight (vs. 2.4 in untreated orchards); whole rodents contain <0.002 mg As/kg fresh weight (vs. nondetectable in untreated orchards)	3
Soybean, *Glycine max*		
Total As	Toxic signs at plant residues >1 mg total As/kg	1
Grasslands		
Cacodylic acid	Kill of 75% to 90% of all species at 17 kg/ha; recovery modest	3
Rice, *Oryza sativum*		
Disodium methylarsonate	75% decrease in yield at soil (silty loam) concentrations of 50 mg/kg	1

Scots pine, *Pinus sylvestris*		
Inorganic As^{+5}	Seedlings die when soil (sandy) concentrations exceed 250 mg/kg dry weight. Maximum BCF factors low: 0.6 for roots; 0.1 for shoots. Residues >62 mg As/kg DW in shoots are toxic, and 3,300 mg/kg DW usually fatal	4
Pea, *Pisum sativum*		
Sodium arsenite	15 mg/L inhibits light activation and photosynthetic CO_2 fixation in chloroplasts	5
Sandhill plant communities		
Cacodylic acid	No lasting effect at 2.25 kg/ha. Some species defoliated st 6.8 kg/ha. Significant effect, including 75% defoliation of oaks and death of all pine trees, at 34 kg/ha	3
Cowpea, *Vigna* sp.		
Total water soluble As in soils	Decreased yields at 1 mg/L	1
Total soil As concentrations (loamy sand)	Toxic at 25 mg/kg	1
Yeast		
Arsenate	At 75 mg/L, 60% reduction in phosphate transport and glucose metabolism in 30 min; at 375 mg/L, 100% reduction	1
Terrestrial Invertebrates		
Honeybee, *Apis mellifera*		
Inorganic arsenite	Following arsenic spray dusting, dead bees contained 20.8 to 31.2 mg/kg FW (adults) or 5 to 13 mg/kg FW (larvae)	6
Beetles		
Cacodylic acid	Dietary levels of 100 to 1,000 mg/kg fatal to certain pestiferous species	3
Western spruce budworm, *Christoneura occidentalis*, sixth instar stage		
Arsenic trioxide	Dietary levels of 99.5 mg/kg FW killed 10%, 2,250 mg/kg killed 50%, and 65,300 mg/kg was fatal to 90%. Newly molted pupae and adults of As-exposed larvae had reduced weight. Regardless of dietary levels, concentrations of As ranged up to 2,640 mg/kg DW in dead pupae, and 1,708 mg/kg DW in adults	7

[a]References: 1, NRCC 1978; 2, Wang et al. 1984; 3, Hood 1985 4, Sheppard et al. 1985; 5, Marques and

Anderson 1986; 6, Jenkins 1980; 7, Robertson and McLean 1985.

Table 4. Lethal and sublethal effects of various arsenic compounds on selected species of aquatic biota.

Ecosystem, species, arsenic compound, and other variables	Arsenic concentration	Effect	Reference[b]
Freshwater Plants			
Algae, various species			
As^{+3}	1.7 mg/L	Toxic	1
As^{+3}	4 mg/L	Decomposition	1
As^{+3}	2.3 mg/L	95% to 100% kill in 2 to 4 weeks of 4 species	2,3
As^{+5}	0.075 mg/L	Decreased growth	3
Alga, *Ankistrodesmus falcatus*			
As^{+5}	0.26 mg/L	EC-50 (14 days)	3
Alga, *Scenedesmus obliquus*			
As^{+5}	0.048 mg/L	EC-50 (14 days)	3
Alga, *Selenastrum capricornutum*			
As^{+5}	0.69 mg/L	EC-50 (4 days)	3
Freshwater Invertebrates			
Cladoceran, *Bosmina longirostris*			
As^{+5}	0.85 mg/L	50% immobilization in 96 h	4
Cladoceran, *Daphnia magna*			
As^{+3}	0.63 to 1.32 mg/L	MATC[c]	3
As^{+3}	0.96 mg/L	LC-5 (28 days)	5
As^{+3}			
Starved	1.5 mg/L	50% immobilization (96 h)	6
Fed	4.3 mg/L	50% immobilization (96 h)	6
As^{+5}	0.52 mg/L	Reproductive impairment of 16% in 3 weeks	3
As^{+5}	0.93 mg/L	LC-5 (28 days); maximum bioconcentration factor (BCF) of 219X	5
As^{+5}	7.4 mg/L	LC-50 (96 h)	2

DSMA	0.83 mg/L	LC-0 (28 days)	5
SDMA	1.1 mg/L	LC-0 (28 days)	5
Total As	1 mg/L	18% decrease in body weight in 3 weeks	1
Total As	1.4 mg/L	50% reproductive impairment in 3 weeks	1
Total As	2.8 mg/L	LC-50 (21 days)	1
Total As	4.3 to 7.5 mg/L	Immobilization (21 days)	1
Cladoceran, *Daphnia pulex*			
As^{+5}	49.6 mg/L	50% immobilization (48 h)	4
As^{+3}	1.3 mg/L	LC-50 (96 h)	2,3
As^{+3}	3 mg/L	EC-50 (48 h)	7
Amphipod, *Gammarus pseudolimnaeus*			
As^{+3}	0.87 mg/L	50% immobilization (96 h)	6
As^{+3}	0.088 mg/L	LC-20 (28 days)	5
As^{+3}	0.96 mg/L	LC-100 (28 days)	5
As^{+5}	0.97 mg/L	LC-20 (28 days); no accumulations	5
DSMA	0.086 mg/L	LC-10 (28 days)	5
DSMA	0.97 mg/L	LC-40 (28 days)	5
SDMA	0.85 mg/L	LC-0 (28 days)	5
Snail, *Helisoma campanulata*			
As^{+3}	0.96 mg/L	LC-10 (28 days)	5
As^{+5}	0.97 mg/L	LC-0 (28 days); maximum BCF of 99X	5
DSMA	0.97 mg/L	LC-0 (28 days)	5
SDMA	0.085 mg/L	LC-0 (28 days)	5
SDMA	0.085 mg/L	LC-32 (28 days)	5
Stonefly, *Pteronarcys californica*			
As^{+3}	38 mg/L	LC-50 (96 h)	7
Stonefly, *Pteronarcys dorsata*			
As^{+3}	0.96 mg/L	LC-0 (28 days)	5
As^{+5}	0.97 mg/L	LC-20 (28 days); maximum BCF of 131X	5

DSMA	0.97 mg/L	LC-0 (28 days)	5
SDMA	0.85 mg/L	LC-0 (28 days)	5
Cladoceran, *Simocephalus serrulatus*			
As^{+3}	0.81 mg/L	LC-50 (96 h)	3
Zooplankton			
As^{+3}	0.4 mg/L	No effect	1
As^{+3}	1.2 mg/L	Population reduction	1
Freshwater Vertebrates			
Marbled salamander, *Ambystoma opacum*			
As^{+3}	4.5 mg/L	EC-50 (8 days) concentration producing death and malformations in developing embryos	3
Goldfish, *Carassius auratus*			
As^{+5}	0.1 mg/L	15% behavioral impairment in 24 h; 30% impairment in 48 h	1
As^{+5}	24.6 to 41.6 mg/L	LC-50 (7 days)	1
As^{+3}	0.49 mg/L	EC-50 (7 days)	3
MSMA	5 mg/L	LC-50 (96 h)	3
Narrow-mouthed toad, *Gastrophryne carolinensis*			
As^{+3}	0.04 mg/L	50% death or mal-formations noted in developing embryos in 7 days	3
Channel catfish, *Ictalurus punctatus*			
As^{+3}	25.9 mg/L	LC-50 (96 h)	8
Flagfish, *Jordanella floridae*			
As^{+3}	14.4 mg/L	LC50 (96 h)	6
As^{+3}	2.1 to 4.1 mg/L	MATC[c]	3
Bluegill, *Lepomis macrochirus*			
As^{+3}			
Juveniles	0.69 mg/L	Reduced survival 16 weeks after a single treatment	2,3
Adults	0.69 mg/L	Histopathology after 16 weekly treatments	2

As^{+3}	4 mg/L	Population reduction of 42% after several monthly applications	8
As^{+3}	30 to 35 mg/L	LC-50 (96 h)	7,8
MSMA	1.9 mg/L	LC-50 (96 h)	3
Total As	Tissue residues of 1.35 mg/kg fresh weight (juveniles) and 5 mg/kg (adults)	Threshold acute toxic value	1
Spottail shiner, *Notropis hudsonius*			
As^{+3}	45 mg/L	LC-50 (25 h)	8
As^{+3}	29 mg/L	LC-50 (48 h); survivors with fin and scale damage	8
Chum salmon, *Oncorhynchus keta*			
As^{+3}	11 mg/L	LC-50 (48 h)	8
Minnow, *Phoxinus phoxinus*			
As^{+3}	20 mg/L	Equilibrium loss in 36 h	8
As^{+5}	234 to 250 mg/L	Lethal	8
Fathead minnow, *Pimephales promelas*			
As^{+3}	14.1 mg/L	LC-50 (96 h)	6
As^{+3}	2.1 to 4.8 mg/L	MATC[c]	6
As^{+5}	25.6 mg/L	LC-50 (96 h)	3
As^{+5}	0.53 to 1.50 mg/L	MATC[c]	3
Rainbow trout, *Salmo gairdneri*			
As^{+3}	0.13 mg/L	Ec-10 (28 days)	3
As^{+3}			
Embryos	0.54 mg/L	LC-50 (28 days)	2
Adults	23 to 26.6 mg/L	LC-50 (96 h)	5
As^{+3}	0.96 mg/L	LC-50 (28 days)	7,8
As^{+3} or As^{+5}	Fed diets containing 120 to 1,600 mg As/kg for 8 weeks	Growth depression, food avoidance, and impaired feed efficiency at all levels	9
As^{+5}	Fed diets containing 10 to	No effect level at about 10 mg/kg diet.	

	90 mg As/kg for 16 weeks	Some adaptation to dietary As observed in trout fed 90 mg/kg diet, as initial negative growth gave way to slow positive growth over time	9
As^{+5}	0.97 mg/L	LC-0 (28 days); no accumulations	5
DSMA	0.97 mg/L	LC-0 (28 days)	5
SDMA	0.85 mg/L	LC-0 (28 days)	5
SC	1,000 mg/L	LC-0 (28 days)	14
DMA or ABA	Fed diet containing 120 to 1,600 mg/kg for 8 weeks	No toxic response at any level tested	9
Brook trout, *Salvelinus fontinalis*			
As^{+3}	15 mg/L	LC-50 (96 h)	3
Marine Plants			
Algae, 2 spp.			
As^{+3} or As^{+5}	1 mg/L	No effect	10
As^{+5}	1,000 mg/L	No deaths	10
Algae, 3 spp.			
As^{+3}	0.019 to 0.022 mg/L	Reduced growth	3
Red alga, *Champia parvula*			
As^{+3}	0.065 mg/L	Normal sexual reproduction	10
As^{+3}	0.095 mg/L	No sexual reproduction	10
As^{+3}	0.30 mg/L	Death	10
As^{+5}	10 mg/L	Normal growth, but no sexual reproduction	10
Phytoplankton			
As^{+5}	0.075 mg/L	Reduced biomass of populations in 4 days	3
Red alga, *Plumaria elegans*			
As^{+3}	0.58 mg/L	Arrested sporeling development 7 days posttreatment after exposure for 18 h	12

Alga, *Skeletonema costatum*			
As^{+5}	0.13 mg/L	Growth inhibition	3
Alga, *Thalassiosira aestivalis*			
As^{+5}	0.075 mg/L	Reduced chlorophyll a	3
Marine Invertebrates			
Copepod, *Acartia clausi*			
As^{+3}	0.51 mg/L	LC-50 (96 h)	3
Dungeness crab, *Cancer magister*			
As^{+3}	0.23 mg/L	LC-50 (96 h) for zoea	3
Amphipod, *Corophium volutator*			
As^{+5}			
Water temperature, °C			
5	8 mg/L	LC-50 (230 h)	11
10	8 mg/L	LC-50 (150 h)	11
15	8 mg/L	LC-50(74 h)	11
15	4 mg/L	LC-50 (140 h)	11
15	2 mg/L	LC-50 (192 h)	11
Pacific oyster, *Crassostrea gigas*			
As^{+3}	0.33 mg/L	LC-50 (96 h) for embryos	3
American oyster, *Crassostrea virginica*			
As^{+3} (eggs)	7.5 mg/L	LC-50 (48 h)	8
Copepod, *Eurytemora affinis*			
As^{+5}	0.025 mg/L	No effect	12
As^{+5}	0.1 mg/L	Reduced juvenile survival	12
As^{+5}	1 mg/L	Reduced adult survival	12
Clam, *Macoma balthica*			
As^{+5}			
Water temperature, °C			
5	220 mg/L	LC-50 (192 h)	11
10	60 mg/L	LC-50 (192 h)	11
15	15 mg/L	LC-50 (192 h)	11
Mysid, *Mysidopsis bahia*			
As^{+3}	0.63 to 1.27 mg/L	MATC[c]	3
As^{+5}	2.3 mg/L	LC-50 (96 h)	3
Blue mussel, *Mytilus edulis*			
As^{+3}	16 mg/L	Lethal in 3 to 16 days	8
Mud snail, *Nassarius obsoletus*			
As^{+3}	2 mg/L	Depressed oxygen	

		consumption in 72 h	8
Oligochaete annelid, *Tubifex costatus*			
As^{+5}			
Water temperature, °C			
5	500 mg/L	LC-50 (130 h)	11
10	500 mg/L	LC-50 (115 h)	11
15	500 mg/L	LC-50 (85 h)	11
Marine Vertebrates			
Grey mullet, *Chelon labrosus*			
As^{+3}	27.3 mg/L	LC-50 (96 h); some skin discoloration	13
Dab, *Limanda limanda*			
As^{+3}	28.5 mg/L	LC-50 (96 h); respiratory problems	13
Pink salmon, *Oncorhynchus gorbuscha*			
As^{+3}	2.5 mg/L	LC-0 (10 days)	8
As^{+3}	3.8 mg/L	LC-54 (10 days)	3
As^{+3}	7.2 mg/L	LC-100 (7 days)	3
Teleosts, 3 spp.			

---

[a]As^{+3}, inorganic trivalent arsenite; As^{+5}, inorganic pentavalent arsenate; DMA, dimethylarsinic acid; ABA, p-aminobenzenearsonic acid; DMSA, disodium methylarsenate ($CH_3AsO(ONa)_2$); SDMA, sodium dimethylarsenate ($(CH_3)_2AsO(ONa)$); MSMA, monosodium methanearsonate; SC, sodium cacodylate.

[b]References: 1, NRCC 1978; 2, EPA 1980; 3, EPA 1985; 4, Passino and Novak 1984; 5, Spehar et al. 1980; 6, Lima et al. 1984; 7, Johnson and Finley 1980; 8, NAS 1977; 9, Cockell and Hilton 1985; 10, Thursby and Steele 1984; 11, Bryant et al. 1985; 12, Sanders 1986; 13, Taylor et al. 1985; 14, Hood 1985.

[c]Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Table 5. Lethal and sublethal effects of various arsenicals on selected species of birds.

Species and arsenic compound	Effect	Reference[a]
Chukar, *Alectoris chukar*		
Silvisar-510 (mixture of cacodylic acid and tri-ethanolamine cacodylate)	Single oral LD-50 dose of ~2,000 mg/kg body weight (BW); signs of poisoning evident within 10 min and mortalities within 1 to 2 days postadminis-tration. Remission took up to 1 month	1
Mallard, *Anas platyrhynchos*		
Sodium arsenite	323 mg/kg BW is LD-50 acute oral value	1,2,3
Sodium arsenite	500 mg/kg diet is fatal to 50% in 32 days; 1,000 mg/kg diet fatal to 50% in 6 days	2
Sodium cacodylate	1,740 to 5,000 mg/kg diet fatal to 50% in 5 days	4
Silvisar 510	Single oral LD-50 >2,400 mg/kg BW; regur-gitation and excessive drinking noted	1
Lead arsenate	5,000 mg/kg diet not fatal in 11 days	2
Copper acetoarsenite	5,000 mg/kg diet fatal to 20% in 11 days	2
California quail, *Callipepla californica*		
Sodium arsenite	LD-50 single oral dose of 47.6 mg/kg BW	1
Northern bobwhite, *Colinus virginianus*		
Copper acetoarsenite	480 mg/kg in diet fatal to 50% in 11 days	2
Sodium cacodylate	1,740 mg/kg in diet for 5 days produced no effect on behavior, no signs of intoxication, and negative necropsy	4

Monosodium methanearsonate, CH_4AsNaO_3	Single oral LD-50 dose of 3,300 mg/kg BW	4
Chicken, *Gallus gallus*		
Inorganic trivalent arsenite	Up to 34% dead embryos at dose range of 0.01-1 mg As^{+3}/embryo; threshold for malformations at dose range 0.03-0.3 mg/embryo	3
Inorganic pentavalent arsenate	Up to 8% dead at dose range 0.01-1 mg As^{+5}/embryo; threshold for malformations at dose range 0.3-3 mg/embryo	3
Disodium methyl arsenate	Teratogenic to embryos when injected at 1 to 2 mg/egg	3,4
Sodium cacodylate	Developmental abnormal-ities at embryonic injected doses of 1 to 2 mg/egg	4
Dodecylamine p-chlorophenylarsonate	At dietary levels of 23.3 mg/kg, liver residues were 2.9 mg/kg FW at 9 weeks. No ill effects noted	5
3-Nitro-4-hydroxy phenylarsonic acid	At 18.7 mg/kg diet for 9 weeks, liver residues of 2.4 mg/kg FW. Those fed diets containing 187 mg/kg for 9 weeks had no ill effects; liver content of 7.5 mg/kg FW	5
3-Nitro-4-hydroxy phenylarsonic acid	LC-50 dose of 33 mg/kg BW (single oral) or 9.7 mg/kg BW (intraperitoneal injection)	2
Arsanilic acid	Fed diets containing 45 mg/kg for 9 weeks; no effect except slightly elevated liver content of 1.2 mg/kg fresh weight. At dietary levels of 455 kg/mg, liver residues were 6.4 mg/kg FW after 9 weeks; no other effects evident	5
Cacodylic acid	Dosed orally without effect at 100 mg/kg BW daily for 10 days	4

Chickens, *Gallus* spp.		
Arsanilic acid	50% excreted in 36 to 38 h	3
Arsenate	50% excreted in 60 to 63 h	3
Turkey, *Meleagris gallopavo*		
3-Nitro-4-hydroxy phenylarsonic acid	Single oral LD-50 dose of 17.4 mg/kg BW	2
Brown-headed cowbird, *Molothrus ater*		
Copper acetoarsenite	All survived 11 mg/kg diet for 6 months; maximum whole body residue of 1.7 mg As/kg dry weight	2
Copper acetoarsenite	All survived 33 mg/kg diet for 6 months (whole body content of 6.6 mg As/kg dry weight) or 7 months (8.6 DW)	2
Copper acetoarsenite	99.8 mg/kg in diet fatal to 50% in 11 days	2
Copper acetoarsenite	100 mg/kg in diet for 3 months fatal to 100%; tissue residues of 6.1 dry weight in brain, 40.6 in liver	2
Gray partridge, *Perdix perdix*		
Lead arsenate	300 mg/kg BW fatal in 52 h	2
Ring-necked pheasant, *Phasianus colchicus*		
Sodium arsenite	Single oral dose of 386 mg/kg BW is LD-50 value	1
Copper acetoarsenite	Single oral dose of 1.403 mg/kg BW is LD-50 value	3

[a]References: 1, Hudson et al. 1984; 2, NAS 1977; 3, NRCC 1978; 4, Hood 1985; 5, Woolson 1975.

Table 6. Lethal and sublethal effects of various arsenicals on selected species of mammals.

Organism and arsenical	Effect	Reference[a]
Cow, *Bos bovis*		
Arsenate	Cows fed 33 mg As^{+5} daily per animal for 3 months had slightly elevated levels in muscle (0.02 mg/kg fresh weight vs. 0.05 in controls) and liver (0.03 vs. 0.012), but normal levels in milk and kidney	1
Arsenite	Cows fed 33 mg As^{+3} daily per animal for 15 to 28 months had tissue levels, in mg/kg fresh weight, of 0.002 for milk (vs. <0.001 for controls), 0.03 for muscle (vs. 0.005), 0.1 for liver (vs. 0.012), and 0.16 for kidney (vs. 0.053)	1
Cattle, *Bos* spp.		
Arsenic pentoxide (wood ashes treated with As preservative)	Several deaths after eating wood ashes (780 mg/kg dry weight); tissue residues, in mg As/kg fresh weight, of 13.9 in liver, 23.7 in kidney, and 25.8 in rumen contents (vs. normal values of <0.5)	2
Arsenic trioxide	Single oral dose of 15 to 45 grams/animal fatal	3
Arsenic trioxide	Toxic dose is 33 to 55 mg/kg body weight (BW), or 13.2 to 22 grams for a 400-kg animal. Animals accidentally poisoned topically contained up to 15 mg As/kg fresh weight liver, 23 in kidney, and 45 in urine (vs. <1 for all normal tissues)	4
Cacodylic acid, $(CH_3)_2AsO(OH)$	Calves were anorexic in 3 to 6 days when fed diets containing 4,700 mg/kg.	
	Adult oral dosages of 10 mg/kg BW daily for 3 weeks followed by 20 mg/kg BW daily for 5 to 6 weeks was lethal. Adverse effects at 25 mg/kg BW daily for 10 days	5
Methanearsonic acid,	Calves were anorexic in 3 to 6 days	

$CH_3AsO(OH)_2$	when fed diets containing 4,000 mg/kg	5
Monosodium methanearsonate	10 mg/kg BW daily for 10 days fatal	3
Sodium arsenite	Single oral dose of 1 to 4 grams fatal	3
Dog, *Canis familiaris*		
Cacodylic acid	Single oral LD-50 value of 1,000 mg/kg BW. Fed diets containing 30 mg/kg for 90 days with no ill effects	5
Methanearsonic acid	Fed diets containing 30 mg/kg for 90 days with no ill effects	5
Sodium arsenite	50 to 150 mg fatal	3
Domestic goat, *Capra* sp.		
Arsenic acid	Single oral dose of 2.5 to 7.5 mg/kg BW (50 to 150 mg) was acutely toxic	3
Guinea pig, *Cavia* sp.		
Arsenic acid	Dietary levels of 350 mg/kg resulted in blindness and optic disc atrophy in 25 to 30 days	6
Arsenic trioxide	Fed diets containing 50 mg/kg for 21 days; elevated As residues, in mg/kg fresh weight, of 4 in blood, 15 in heart (vs. <1 for all control tissues)	7
Sodium arsanilate	Subcutaneous injection of 70 mg/kg BW caused degeneration of sensory walls of inner ear; elevated As residues in cochlea	6
Sodium arsenate	Intraperitoneal injection of 0.2 mg/kg BW at age 2 months causes deafness	6
Hamster, *Cricetus* sp.		
Arsenate	Maternal dose of 5 mg As^{+5}/kg BW caused some fetal mortality, but no malformations; higher dose of 20 mg/kg BW caused 54% fetal deaths and malformations	3
Calcium arsenate	Pulmonary tumorigenicity demonstrated 70 weeks after 15 intratracheal weekly injections of 3 mg/kg BW	8
Dimethylarsinate	50% growth reduction in Chinese hamster ovary cells (CHOC) at 90 to 112 mg/L	9
Gallium arsenide	Single oral dose of 100 mg/kg BW mostly (85%) eliminated in 5 days, usually in	

	form of organoarsenicals; all tissue levels <0.25 mg/kg	10
Sodium arsenate	Dosed intravenously on day 8 of gestation: 2 mg/kg BW had no measurable effect; 8 mg/kg produced increased incidence of malformation and resorption; 16 mg/kg BW killed all embryos	6
Sodium arsenate	50% growth reduction in CHOC at 2.25 mg/L	9
Sodium arsenite	Chinese hamster ovary cells (CHOC) show 50% growth reduction at 0.3 mg/L	9
Sodium cacodylate	Single intraperitoneal injection of 900 to 1,000 mg/kg during midgestation results in some maternal deaths, and increased incidences of fetal malformations	5
Horse, *Equus caballus*		
Sodium arsenite	Daily doses of 2 to 6 mg/kg BW (1 to 3 grams) for 14 weeks is fatal	3
Cat, *Felis domesticus*		
Inorganic arsenate or arsenite	Chronic oral toxicity at 1.5 mg/kg BW	6
Human, *Homo sapiens*		
Arsenic trioxide	Fatal at 70 to 189 mg, equivalent to about 1 to 2.6 mg As/kg BW	6
Arsenic trioxide	LD-50 dose of 7 mg/kg BW	3
Cacodylic acid	LD-50 of 1,350 mg/kg BW	3
Lead arsenate	Some deaths at 7 mg/kg BW	3
Total arsenic	Accumulations of 1 mg/kg BW daily for 3 months in children, or 80 mg/kg BW daily for 3 years produced symptoms of chronic arsenic poisoning	3
Total arsenic, daily oral dose	Prolonged dosages of 3 to 4 mg daily produced clinical symptoms of chronic arsenic intoxication	3
Total arsenic in drinking and cooking water	Prolonged use produced symptoms of chronic arsenic intoxication (0.6 mg/L) or skin cancer (0.29 mg/L)	3
Total arsenic, probably as arsenate	12,000 Japanese infants poisoned (128 deaths) from consumption of dry milk contaminated with arsenic; average exposure of 3.5 mg As daily for one month. Severe hearing loss, brain wave abnormalities, and other central nervous system disturbances noted 15 years postexposure	6

Total inorganic arsenic	Daily dose of 3 mg for 2 weeks may cause severe poisoning in infants, and symptoms of toxicity in adults	6
Cynmolgus monkey, *Macaca* sp.		
Fish arsenic meal (witch flounder, *Glyptocephalus cynoglossus*) containing 77 mg total As/kg	Given a single meal at 1 mg/kg BW; tissue residues normal after 14 days	11
As above, except arsenic trioxide substituted for total As	As above	11
Mammals, many species		
Calcium arsenate	Single oral LD-50 range of 35 to 100 mg/kg BW	3
Lead arsenate	Single oral LD-50 range of 10 to 50 mg/kg BW	3
Mammals, most species		
Arsenic trioxide	3 to 250 mg/kg BW lethal	12
Sodium arsenite	1 to 25 mg/kg BW lethal	12
Mouse, *Mus* spp.		
Arsenate	Maternal dose of 10 mg As^{+5}/kg BW results in some fetal deaths and malformations	3
Arsenic trioxide	Single oral LD-50 (96 h) value of 39.4 mg/kg BW; LD-0 (96 h) of 10.4 mg/kg BW	12
Arsenic trioxide	"Adapted" group (50 mg As/L in drinking water for 3 months) had subcutaneous LD-50 value of 14 mg/kg BW vs. 11 for nonadapted group	12
Arsenic trioxide	Air concentrations of 28.5 mg/m^3 for 4 h daily on days 9 to 12 of gestation caused fetotoxic effects and chromosomal damage to liver cells by day 18; effects included reduced survival, impaired growth, retarded limb ossification, and bone abnormalities. At 2.9 mg/m^3, a 9.9% decrease in fetal weight was recorded; at 0.26 mg/m^3, a 3.1% decrease was measured	13
Cacodylic acid	Oral dosages of 400 to 600 mg/kg BW on days 7 to 16 of gestation produces fetal malformations (cleft palate), delayed	

	skeletal ossification, and fetal weight reduction	5
Sodium arsenate	Maximum tolerated doses in terms of abortion or maternal death over 24 h in 18-day pregnant mice were 20 mg As^{+5}/kg BW, intraperitoneal route, and 50 mg/kg BW when administered orally. Residue half-life was about 10 h regardless of route of administration	14
Sodium arsenite	Fed 5 mg/kg diet for three generations: reduced litter size, but outwardly normal	6
Sodium arsenite	LD-50 of 9.6 mg/kg BW, subcutaneous route; LD-90 (7 days postadministration) of 11.3 mg/kg BW, subcutaneous route	15
Sodium arsenite	LD-50 of 12 mg/kg BW intraperitoneal route. At 10 mg/kg BW, damage to bone marrow and sperm	16
Sodium cacodylate	Single intraperitoneal injection of 1,200 mg/kg BW during midgestation results in increased rates of fetal skeletal malformations	5
Mule deer, *Odocoileus hemionus hemionus*		
Silvisar-510 (mixture of cacodylic acid and tri-ethanolamine cacodylate)	Single oral LD-50 dose >320 mg/kg BW; appetite loss	17
White-tailed deer, *Odocoileus virginianus*		
Sodium arsenite (used to debark trees)	Lethal dose of 923 to 2,770 mg equivalent to about 34 mg/kg BW; liver residues of 40 mg/kg fresh weight	12
Arsenic acid (herbicide to control Johnson grass)	23 deer killed from apparent misuse. Arsenic levels, in mg/kg fresh weight, in deer found dead were 19 in liver, 18 in kidney, and 22.5 in rumen contents. Soils from area contained ~2.4 mg As/kg, and water 0.42 mg As/L	12
Domestic sheep, *Ovis aries*		
Arsanilic acid	One-year-old castrates fed diets with 273 mg As/kg for 28 days had 0.54 mg As/L in blood, 29 mg/kg dry weight in liver, 24 in kidney,	

	and 1.2 in muscle (vs. <0.01 in all control tissues). After 6 days on an As-free diet, liver residues were <5 mg/kg DW. Maximum tissue levels in sheep fed diets containing 27 mg As/kg for 28 days were 3.2 mg/kg DW kidney; for a 144 mg/kg DW diet, the maximum tissue level was 27 mg/kg DW liver	7
Sodium arsenite	Single oral dose of 5 to 12 mg/kg BW (0.2 to 0.5 grams) was acutely toxic	3
Soluble arsenic	Lambs fed supplemental arsenic for 3 months at 2 mg As/kg dry weight diet contained maximum concentrations of 2 mg/kg fresh weight brain (vs. 1 in controls), 14 in muscle (2), 24 in liver (4), and 57 in kidney (10)	18
Total arsenic	Sheep fed on diets containing lakeweed, *Lagarosiphon major* (288 mg As/kg DW) at 58 mg total As/kg diet for 3 weeks without ill effect. Tissue residues increased during feeding, but rapidly declined when lakeweed was removed from diet	7
Rat, *Rattus* spp.		
Arsanilic acid	No teratogenesis observed in 7 generations at dietary level of 17.5 mg/kg; positive effect on litter size and survival	6
Arsenate	Fed diets containing 50 mg/kg for 10 weeks with no effect on serum uric acid levels	19
Arsenic trioxide	Single oral LD-50 (96 h) value of 15.1 mg/kg BW	12
Arsenic trioxide	Single dose of 17 mg/kg BW administered intratracheally is maximally tolerated nonlethal dose; 2 weeks later, blood As elevated (36 mg/L) and lung histopathology evident	20
Arsenic trioxide	After 21 days on diet containing 50 mg/kg, tissue arsenic levels were elevated in blood (125 mg/L vs. 15 in controls), heart (43 mg/kg FW vs. 3.3), spleen (60 vs. <0.7) and kidney (25 vs. 1.5)	7

Arsenite	Oral administration of 1.2 mg/kg BW daily for 6 weeks reduced uric acid levels in plasma by 67%	19
Arsenite	Oral administration of 1.2 mg/kg BW daily for 6 weeks reduced uric acid levels in plasma by 67%	19
Cacodylic acid	Fetal and maternal deaths noted when pregnant rats dosed by gavage at 50 to 60 mg/kg BW daily during gestation days 6 to 13. Fetal abnormalities observed when dams given oral dosages of 40 to 60 mg/kg BW on days 7 to 16 of gestation	5
3-Nitro-4-hydroxy-phenylarsonic acid	Single oral LD-50 value of 44 mg/kg BW	12
Sodium arsenate	LD-75 (48 h) value of 14 to 18 mg/kg BW (intraperitoneal route)	12
Sodium arsenate	Single intraperitoneal injection of 5 to 12 mg/kg on days 7 to 12 of gestation produced eye defects, exencephaly, and faulty development of kidney and gonads	6
Sodium arsenite	LD-75 (48 h) value of 4.5 mg/kg BW (intraperitoneal injection	12
Rodents, various species		
Cacodylic acid	LD-50 (various routes) values range from 470 to 830 mg/kg BW	5
Sodium cacodylate	LD-50 (various routes) values range from 600 to 2,600 mg/kg BW	5
Pig, *Sus* sp.		
Sodium arsenite	Drinking water containing 500 mg/L lethal at 100 to 200 mg/kg BW	12
3-Nitro-4-hydroxy-phenylarsonic acid	Arsenosis documented after 2 months on diets containing 100 mg/kg, or after 3 to 10 days on diets containing 250 mg/kg	12
Rabbit, *Sylvilagus* sp.		
Cacodylic acid	Adverse effects at dermal dosages equivalent to 4 to 6 grams/kg BW	5
Calcium arsenate	Single oral dose of 23 mg/kg BW fatal in 3 days	12
Copper acetoarsenite	Single oral dose of 10.5 mg/kg BW fatal in 50 h	12
Inorganic arsenate	Single oral LD-50 value of 8 mg/kg BW	3

[a]References: 1, Vreman et al. 1986; 2, Thatcher et al. 1985; 3, NRCC 1978; 4, Robertson et al. 1884; 5, Hood 1985; 6, Pershagen and Vahter 1979; 7, Woolson 1975; 8, Pershagen and Bjorklund 1985; 9, Belton et al. 1985; 10, Yamauchi et al. 1986; 11, Charbonneau et al. 1978; 12, NAS 1977; 13, Nagymajtenyi et al. 1985; 14, Hood et al. 1987; 15, Stine et al. 1984; 16, Deknudt et al. 1986; 17, Hudson et al. 1984; 18, Veen and Vreman 1986; 19, Jauge and Del-Razo 1985; 20, Webb et al. 1986.

Table 7. Proposed arsenic criteria for protection of selected natural resources and human health.

Resource, criterion, and other variables	Criterion or effective arsenic concentration (reference)
Aquatic Life	
Freshwater biota: medium concentrations	Four-day mean water concentration not to exceed 190 ug total recoverable inorganic As^{+3}/L more than once every 3 years; 1-h mean not to exceed 360 ug inorganic As^{+3}/L more than once every 3 years. Insufficient data for criteria formulation for inorganic As^{+5}, or for any organoarsenical (EPA 1985)
Freshwater biota: tissue residues	Diminished growth and survival reported in immature bluegills (*Lepomis macrochirus*) when total arsenic residues in muscle >1.3 mg/kg fresh weight (FW) or >5 mg/kg in adults (NRCC 1978)
Saltwater biota: medium concentrations	Four-day average water concentration not to exceed 36 ug As^{+3}/L more than once every 3 years; 1-h mean not to exceed 69 ug As^{+3}/L more than once every 3 years. Insufficient data for criteria formulation for inorganic As^{+5}, or for any organoarsenical (EPA 1985)
Saltwater biota: tissue residues	Depending on chemical form of arsenic, certain marine teleosts may be unaffected at muscle total arsenic residues of 40 mg/kg FW (NRCC 1978)
Birds	
Tissue residues	Residues, in mg total As/kg FW, liver or kidney in 2 to 10 range are considered elevated; residues >10 mg/kg are indicative of arsenic poisoning (Goede 1985)
Turkey, *Meleagris gallopavo*	
Arsanilic acid in diet	Maximum dietary concentration for turkeys less than 28 days old is 300 to 400 mg/kg feed (NAS 1977)
Phenylarsonic feed additives for disease control and improvement of weight gain in domestic poultry; safe dietary levels	Maximum levels in diets, in mg/kg feed, are 50 to 100 for arsanilic acid, 25 to 188 for 3-nitro-4-hydroxy-phenylarsonic acid (for chickens and turkeys, not recommended for ducks and geese), and 180 to 370 for others (NAS 1977)
Domestic Livestock	
Prescribed limits for arsenic in feedstuffs	
Straight feedstuffs, except	<2 mg total As/kg FW (Vreman et al. 1986)

those listed below	
Meals from grass, dried	<4 mg total As/kg FW (Vreman et al. 1986)
lucerne, or dried clover	
Phosphate mealstuffs	<10 mg total As/kg FW (Vreman et al. 1986)
Fish meals	<10 mg total As/kg FW (Vreman et al. 1986)
Tissue residues	
Poisoned	
Liver, kidney	5 to >10 total As/kg FW (Thatcher et al. 1985; Vreman et al. 1986)
Normal, muscle	<0.3 mg total As/kg FW (Veen and Vreman 1986)
Vegetation	
No observable effects	<1 mg total water soluble soil As/L; <25 mg total As/kg soil; <3.9 ug As/m^3 air (NRCC 1978)
Human Health	
Diet	
Permissible levels	
Total diet	<0.5 mg As/kg dry weight diet (Sorensen et al. 1985)
Fruits, vegetables	The tolerance for arsenic residues as As_2O_3, resulting from pesticidal use of copper, magnesium, and sodium arsenates is 3.5 mg/kg (Jelinek and Corneliussen 1977)
Muscle of poultry and swine, eggs, swine edible byproducts	< 0.5 mg total As/kg FW (Jelinek and Corneliussen 1977)
Edible byproducts of chickens and turkey, liver and kidney of swine	<2 mg total As/kg FW (Jelinek and Corneliussen 1977)
Seafood products	In Hong Kong, limited to 6 mg total As/kg FW for edible tissues of finfish, and 10 mg/kg for molluscs and crustaceans (Phillips et al. 1982)
Adverse effects	
Consumption of aquatic organisms living in As-contaminated waters	
Cancer risk of	
10^{-5}	0.175 ug As/L (EPA 1980)
10^{-6}	0.0175 ug As/L (EPA 1980)
10^{-7}	0.00175 ug As/L (EPA 1980)
Drinking water	
Allowable concentrations	
Total arsenic	<10 ug/L (NAS 1977)
Total arsenic	<50 ug/L (Pershagen and Vahter 1979; EPA 1980; Norin et al. 1985)
Adverse effects	
Cancer risk of	

10^{-5}	0.022 ug As/L (EPA 1980)
10^{-6}	0.0022 ug As/L (EPA 1980)
10^{-7}	0.00022 ug As/L (EPA 1980)
Symptoms of arsenic toxicity observed	9% incidence at 50 ug As/L, 16% at 50 to 100 ug/L, and 44% at >100 ug As/L (NRCC 1978)
Harmful after prolonged consumption	
"Cancer"	In Chile, cancer rate estimated at 0.01% at 82 ug As/L, 0.17% at 600 ug As/L (NRCC 1978)
Skin cancer	0.26% frequency at 290 ug/L and 2.14% at 600 ug/L (EPA 1980)
Total intake	
No observable effect	
North America	0.007 to 0.06 mg As daily (Pershagen and Vahter 1979)
Japan	0.07 to 0.17 mg As daily (Pershagen and Vahter 1979)
USA	
1960's	0.05 to 0.1 mg As daily (Pershagen and Vahter 1979)
1974	0.015 mg As daily (Pershagen and Vahter 1979)
Canada	0.03 mg As daily (NRCC 1978)
Netherlands	
Acceptable	2 ug total inorganic As/kg body weight (BW) (about 0.14 mg daily for 70 kg adult); 0.094 mg daily through fishery products (Vos and Hovens 1986)
Adverse effects (Prolonged exposure)	
Subclinical symptoms	0.15 to 0.6 mg As daily (NRCC 1978)
Intoxication	3 to 4 mg As daily (NRCC 1978)
Blackfoot disease	Total dose of 20 grams over several years increases prevalence of disease by 3% (Pershagen and Vahter 1979)
Mild chronic poisoning	0.15 mg As daily or about 2 ug/kg BW daily (NRCC 1978)
Chronic arsenicism	Lifetime cumulative absorption of 1 gram As, or intake of 0.7 to 2.6 grams/year for several years (in medications) can produce symptoms after latent period of 4 to 24 years (NRCC 1978)
Tissue residues	
No observed effect levels	
Urine	<0.05 mg As/L (NRCC 1978)
Liver, kidney	<0.5 mg As/L (NRCC 1978)
Blood	<0.7 As/kg (NRCC 1978)
Hair	<2 mg As/kg (NRCC 1978)
Fingernail	<5 mg As/kg (NRCC 1978)

Arsenic-poisoned	
Liver, kidney	2 to 100 mg As/kg FW; confirmatory tests >10 mg As/kg FW; residues in survivors several days later 2 to 4 mg/kg FW (NAS 1977)
Whole body	In child, symptoms of chronic arsenicism evident at 1 mg As/kg BW, equivalent to intake of about 10 mg/month for 3 months; for adults, these values were 80 mg/kg BW, equivalent to about 2 grams/year for 3 years (NRCC 1978)
Air	
Allowable concentrations	
Arsine	<200 ug/m^3 for USA industrial workers; proposed mean arsine limit of <4 ug/m^3 in 8 h period and <10 ug/m^3 maximum in 15 min (NAS 1977)
Arsine	<4 ug/m^3 (NRCC 1978)
Total As	<3 ug/m^3 in USSR and Czechoslovakia, <500 µg/m^3 for USA industrial workers (NAS 1977)
Total As (threshold limit value-time weighted average: 8 h/day, 40-h work week)	Proposed limit of <50 ug/m^3, maximum of 2 µg/m^3 in 15 min, <10 ug airborne inorganic As/m^3 (EPA 1980)
Arsenic trioxide	<0.3 ug/m^3 in USSR, <0.1 ug/m^3 in USA (Nagymajtenyi et al. 1985)
Adverse effects	
Increased mortality	Associated with daily time-weighted average As exposure of >3 ug/m^3 for 1 year (NRCC 1978)
Respiratory cancer (increased risk)	Associated with chronic exposure >3 ug As/m^3, or occupational exposure (lifetime) of >54.6 ug As/m^3 (NRCC 1978)
Respiratory cancer (increased risk)	Exposure to 50 ug As/m^3 for more than 25 years associated with 3X increase (Pershagen and Vahter 1979)
Skin diseases	Associated with ambient air concentrations of 60 to 13,000 ug As/m^3 (NRCC 1978)

Biological Report
March 1988

Contaminant Hazard Reviews
Report No. 13

CHLORPYRIFOS HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

By

Edward W. Odenkirchen

Department of Biology
The American University
Washington, DC 20016

And

Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

Chlorpyrifos (phosphorothioic acid O, O,-diethyl 0-(3,5,6,-trichloro-2-pyridinyl) ester), an organophosphorus compound with an anticholinesterase mode of action, is used extensively in a variety of formulations to control a broad spectrum of agricultural and other pestiferous insects. Domestic use of chlorpyrifos in 1982 was about 3.6 million kg; the compound is used mostly in agriculture, but also to control mosquitos in wetlands (0.15 million kg applied to about 600,000 ha) and turf-destroying insects on golf courses (0.04 million kg).

Accidental or careless applications of chlorpyrifos have resulted in the death of many species of nontarget organisms such as fish, aquatic invertebrates, birds, and humans. Applications at recommended rates of 0.028 to 0.056 kg/surface ha for mosquito control have produced mortality, bioaccumulation, and deleterious sublethal effects in aquatic plants, zooplankton, insects, rotifers, crustaceans, waterfowl, and fish; adverse effects were also noted in bordering invertebrate populations.

Degradation rate of chloropyrifos in abiotic substrates varies, ranging from about 1 week in seawater (50% degradation) to more than 24 weeks in soils under conditions of dryness, low temperatures, reduced microbial activity, and low organic content; intermediate degradation rates reported have been 3.4 weeks for sediments and 7.6 weeks for distilled water. In biological samples, degradation time is comparatively short--usually less than 9 hours in fishes, and probably the same in birds and invertebrates.

Chlorpyrifos is acutely toxic to some species of aquatic invertebrates and teleosts at nominal water concentrations ranging between 0.035 and 1.1 ug/l. Acute single-dose oral LD-50 values of chlorpyrifos to susceptible avian species ranged from 5 to 13 mg/kg body weight. Mammals were comparatively tolerant of chlorpyrifos: acute oral LD-50's were reported to be 151 mg/kg body weight, and higher. Lethal dietary concentrations for sensitive species of birds ranged from 30 to 50 mg chlorpyrifos/kg food. Sublethal effects were recorded in all species of organisms examined at concentrations below those causing mortality. These effects included bioconcentration from the medium by teleosts (410X to 1,000X); cholinesterase activity reduction in brain and hematopoietic tissues; reduced growth; impaired reproduction, including sterility and developmental abnormalities; motor incoordination; convulsions; and depressed population densities of aquatic invertebrates.

Three courses of action are recommended. (1) Restrict the use of chlorpyrifos for mosquito control in wetlands, estuaries, and waterfowl breeding areas because recommended treatment levels are demonstrably harmful to nontarget resident biota. (2) Curtail agricultural use in watershed areas pending acquisition of additional data on chlorpyrifos toxicokinetics. (3) Develop suitable replacements for chlorpyrifos in mosquito control programs; specifically, pesticides with more specificity to target organisms, and lower toxicity to nontarget biota.

DISCLAIMER

Mention of trade names or commercial products does not constitute U.S. Government endorsement or recommendation for use.

Suggested citation for this report:

Odenkirchen, E. W., and R. Eisler. 1988. Chlorpyrifos hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.13).

TABLES

ACKNOWLEDGMENTS

We thank Julia L. Armstrong for secretarial assistance; Nancy A. Bushby, Joyce E. Haber, and Lynda J. Garrett for information retrieval; Robert J. Chinnis, Stephen C. Grebe, Matthew C. Perry, Joseph B. Hunn, and Lowell C. McEwen for reviewing the manuscript; and Paul H. Eschmeyer and James R. Zuboy for editorial services.

INTRODUCTION

Chlorpyrifos (phosphorothioic acid 0, 0-diethyl O-(3,5,6-trichloro-2-pyridinyl) ester), also known commonly as Dursban and Lorsban, was first registered as a broad spectrum insecticide in 1965, and subsequently was used widely to control a variety of pests such as fire ants, turf and ornamental plant insects, cockroaches, mosquitos, termites, hornflies, lice, and fleas (EPA 1986). In 1982, total agricultural use of chlorpyrifos was estimated at 2.2 to 3.2 million kg, and industrial uses ranged between 0.68 and 1.04 million kg (EPA 1982). In 1984, about 0.15 million kg (0.33 million pounds) of chlorpyrifos was applied to about 600,000 ha (1.48 million acres) of wetlands in the United States for mosquito control (Odenkirchen 1987). Treatment programs in which chlorpyrifos concentrations suitable for mosquito control and other insect pests were used have been shown to be detrimental to nontarget species, including aquatic organisms, waterfowl, and terrestrial organisms from surrounding ecosystems (Linn 1968; Hurlbert et al. 1970, 1972; Atkins 1972; Streu and Cruz 1972; Nelson and Evans 1973; Butcher et al. 1977; Thirugnanam and Forgash 1977; Tagatz et al. 1982;.Goodman et al. 1985a; McEwen et al. 1986; Mayer 1987; Odenkirchen 1987; Smith 1987). Domestic use of chlorpyrifos has resulted in the death of an 11-day-old infant (CDC 1980) and the poisoning of office workers (Hodgson et al. 1986). Prophylactic use of chlorpyrifos on farm animals has caused reproductive impairment of livestock (Everett 1982). Chlorpyrifos-resistant strains of insects have been detected recently; they include the German cockroach (*Blattella germanica*) in Florida and Nebraska (Milio et al. 1987) and the sawtoothed grain beetle (*Oryzaephilus surinamensis*) in Australia (Collins 1985).

This report was prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service. It is part of a continuing series of brief reviews on chemical contaminants and natural resources.

ENVIRONMENTAL CHEMISTRY

Formulations of chlorpyrifos include emulsifiable concentrates, wettable powders, granules, pellets, microencapsulates and impregnated materials. Suggested diluents for concentrates include water and petroleum distillates, such as kerosene and diesel oil. Carrier compounds include synthetic clays with alkyl/aryl sulfonates as wetting agents (Table 1). Little information is available to assess the influence of various use formulations on toxicity, dispersal, decomposition, and bioavailability. Chemical and other properties of chlorpyrifos are summarized in Table 2.

The degradation half-life time (Tb 1/2) of chlorpyrifos is 7.1 days in seawater (Schimmel et al. 1983), and 53 days in distilled water (Freed et al. 1979). Degradation is usually through hydrolysis to produce 3,5,6-trichloro-2-pyridinol, and phosphorothioics acid (Brust 1966; Smith 1966, 1968; Marshall and Roberts 1978). Temperature, pH, radiation, and metal cations all significantly affect chlorpyrifos Tb 1/2 in water: half-life is decreased with increasing water pH, temperature, sunlight, and metal cation concentrations (Brust 1966; Mortland and Raman 1967; Smith 1968; Schaefer and Dupras 1969, 1970; Meikle and Youngson 1970).

In soil, Tb1/2 values for chlorpyrifos range from less than 1 week to more than 24 weeks, depending on soil moisture, microbial activity, clay and organic content, and temperature. In 411 soils studied, increasing temperature resulted in decreased Tb 1/2 values (Miles et al. 1983). Degradation was more rapid in sandy loam than in organic muck soils, more rapid in moist than in dry soils, and more rapid in clay than in other soil types (Getzin 1981; Miles et al 1983, 1984). The major routes of chlorpyrifos loss from soils are chemical hydrolysis in moist soils, clay-catalyzed hydrolysis in dry soils, and microbial degradation and volatilization (Marshall and Roberts 1978).

The half-life of chlorpyrifos in sediments is comparatively long; it was 24 days in a sediment-water slurry Schimmel et al. 1983). In a pond treated with chlorpyrifos, total waterborne residues decreased by a factor of more than 10X, while total sediment residues rose by about 3X (Hurlbert et al. 1970). Similar results were noted in an artificial lake treated with chlorpyrifos: lake water concentrations peaked 1 day after treatment at 0.9 ug/l and plateaued near 0.2 ug/l after 3 weeks (Mulla et al. 1973).

Table 1. Selected chlorpyrifos formulations and carriers (modified from Marshall and Roberts 1978).

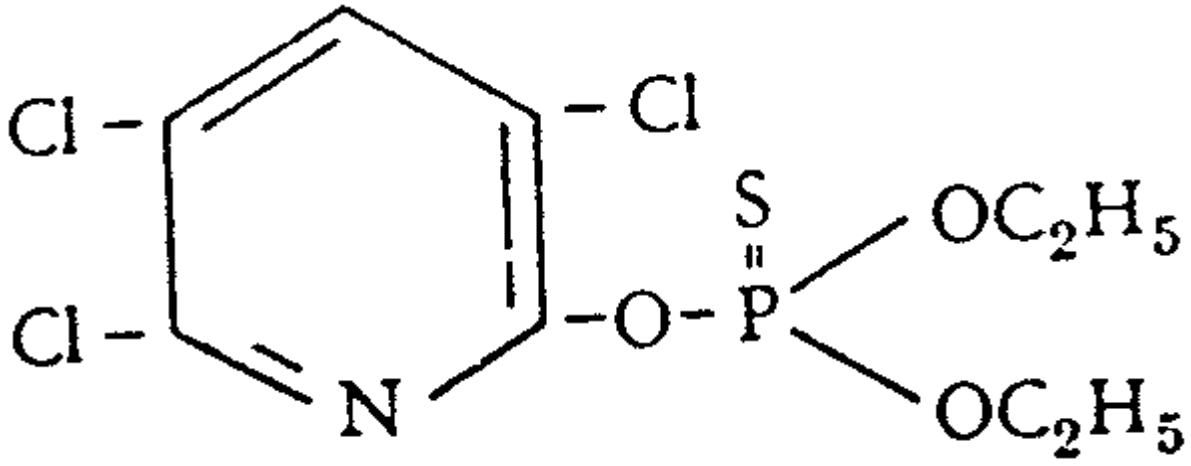
Compound[a]	Formulation	Carrier
Dursban 2E	Emulsifiable concentrate of 0.285 kg/L (2.4 lb/gal)	Solution in aromatic distillate with anionic/ nonionic emulsifier blend and residual chlorinated solvent
Dursban M	Emulsifiable concentrate of 0.57 kg/L (4.8 lb/gal)	As above
Dursban 6	Solution of 0.855 kg/L (7.2 lb/gal)	Solution in an aromatic distillate
Dursban 2½G	Granular, 2.5%	Absorbed onto stabilized clay with release agents added
Lorsban 4C	Emulsifiable concentrate of 0.479 kg/L (4.0 lb/gal)	Solution in aromatic naphtha with emulsifiers
Lorsban 25W	Wettable powder, 25%	Dispersion on blended clays with alkyl/aryl sulfonates as wetting agents

[a]Dursban and Lorsban are registered trademarks of the Dow Chemical Company.

Table 2. Chemical and other properties of chlorpyrifos (from Brust 1966; Rigterink and Kenaga 1966; Kenaga 1971; Windholz 1976).

Variable	Datum
Chemical name	Phosphorothioic acid 0, 0-diethyl 0-(3,5,6 -trichloro-2-pyridinyl) ester
Alternate names	CAS 2921-88-2; Dursban; Lorsban; Dowco 179; ENT 27311; Trichlorpyrphos; Brodan; Eradex; Killmaster; Pyrinex; Chlorpyriphos-ethyl
Primary uses	Insecticide, acaricide
Producers	Dow Chemical Company; Makhteshim-Agan (Israel); All India Medical Corp.; Planters Products, Inc.
Empirical formula	$C_9H_{11}Cl_3NO_3PS$

Structural formula



Molecular weight	350.57
Physical state at 25 C	White granular crystalline solid
Melting point	41.5 to 43.5 C
Vapor pressure	
25 °C	1.87×10^{-5} mm Hg
35 °C	8.87×10^{-5} mm Hg
Heat of sublimation	26,800 cal/mol
Percent by weight	
Carbon	30.83
Hydrogen	3.16
Chlorine	30.34
Nitrogen	4.00
Oxygen	13.69
Phosphorus	8.83
Sulfur	9.15
Solubility	
Water, 23 to 25 °C	0.4–2.0 mg/L
Isooctane, 23 °C	790.0 g/kg
Methanol, 23 °C	450.0 g/kg
Log n-octanol/water partition coefficient	5.2
Soil organic carbon/ water partition coefficient	13,600

LABORATORY INVESTIGATIONS

AQUATIC ORGANISMS

During 96-hour toxicity tests, several species of freshwater and marine invertebrates and fishes died at chlorpyrifos concentrations between 0.035 and 0.58 ug/l. LC-50 (96-hour) values, in ug chlorpyrifos/l, for sensitive species tested were 0.035 for mysid shrimp *Mysidopsis bahia*; 0.11 for amphipod, *Gammarus lacustris*; 0.13 for fathead minnow, *Pimephales promelas*; 0.38 for stonefly, *Pteronarcella badia*; and 0.58 for striped bass, *Morone saxatilis*; (Mayer and Ellersieck 1936; Table 3). Toxicity was usually greater at elevated temperatures and at increasing pH levels (Johnson and Finley 1980). In general, arthropods were the most sensitive group assayed and molluscs the most tolerant (Borthwick and Walsh 1981; Table 3). The bullfrog (*Rana catesbeiana*) also appears to be comparatively tolerant to chlorpyrifos, as judged by a single oral LD-50 value of >400 mg/kg body weight (Hudson et al. 1984).

Sublethal effects of chlorpyrifos exposure have been documented for many species of freshwater and marine fauna; they include inhibition of cholinesterase (ChE) activity levels in brain and hematopoietic organs, sluggishness, motor incoordination, delayed maturation and growth, reproductive impairment, and reduced feed intake (Rongsriyam et al. 1968; Thirugnanam and Forgash 1977; Marshall and Roberts 1978; Tagatz et al. 1982; Jarvinen et al. 1983; EPA 1985, 1986; Goodman et al. 1985b; Norberg and Mount 1985; Hansen et al. 1986). Reproductive impairment, for example, was observed in *Daphnia magna* at 0.08 ug chlorpyrifos/1 (EPA 1985). Reduction in setting rate was shown in oyster larvae after exposure to 0.1 ug/l for 8 days (Tagatz et al. 1982). In fathead minnows exposed to 0.12 ug chlorpyrifos/1 for 200 days, ChE activity was significantly reduced, fecundity was reduced, maturation delayed and, in second generation fish, growth and maturation were reduced (Jarvinen et al. 1983). Equilibrium loss was documented in 50% of brown shrimp (*Penaeus aztecus*) after exposure to 0.32 ug chlorpyrifos/1 for 24 hours (Marshall and Roberts 1978). Growth of the California grunion (*Leuresthes tenuis*) was reduced 20% in an early life stage during immersion in 0.5 ug chlorpyrifos/1 for 35 days and 26% in fry after exposure to 1.0 ug/l for 26 days (Goodman et al. 1985b). Additional and more comprehensive data on sublethal effects of chlorpyrifos to aquatic biota are listed elsewhere (EPA 1986).

Table 3. Acute toxicities of chlorpyrifos to selected species of aquatic invertebrates and fishes. Values are in µg chlorpyrifos per liter of medium fatal to 50 percent in 96 hours.

Organism and other variables	LC-50, in µg/L	Reference[a]
Invertebrates		
Mysid, *Mysidopsis bahia*	0.035	1
Dragonfly (naiad), *Pseudagrion* spp.	0.10[b]	2
Amphipod, *Gammarus lacustris*	0.11	3
Stonefly, *Pteronarcella badia*	0.38	4
Stonefly, *Claassenia sabulosa*	0.57	4
Cladoceran, *Daphnia magna*	1.0[c]	5
Grass shrimp, *Palaemonetes pugio*	1.5[d]	5
Crayfish, *Orconectes immunis*	6.0	6
Dragonfly (naiad), *Crocothemis erythryaea*	6.0[b]	2
Stonefly, (larva), *Pteronarcys californica*	10.0	4
Red crayfish, *Procambarus clarki*	41.0[e]	7
Ram's horn snail, *Helisoma trivolvis*	>2,000[f]	8
Snail, *Lanistes carinatus*	2,710[b]	2

Fish		
Fathead minnow, *Pimephales promelas*	0.13	9
Striped bass, *Morone saxatilis*	0.58	10
Tidewater silverside, *Menidia peninsula*		
Flow-through test	0.7	11
Static test	3.0	11
California grunion, *Leuresthes tenuis*		
Flow-through test	1.1	11
Static test	3.1	11
Atlantic silverside, *Menidia menidia*		
Flow-through test	1.4	11
Static test	3.4	11
Bluegill, *Lepomis macrochirus*		
13 °C	5.1	12
29 °C	1.1	12
Longnose killifish, *Fundulus similis*	4.1	1
Inland silverside, *Menidia beryllina*	4.2	13
Striped mullet, *Mugil cephalus*	5.4	1
Rainbow trout, *Salmo gairdneri*		
17.3 °C	9.0	6
12.7 °C	7.1	14
7.2 °C	15.0	14
1.6 °C	51.0	14
Cutthroat trout, *Salmo clarki*	18.0	12
Lake trout, *Salvelinus namaycush*	98	12
Sheepshead minnow, *Cyprinodon variegatus*	136	13
Channel catfish, *Ictalurus punctatus*	280	12
Mosquitofish, *Gambusia affinis*	340[b]	2
Gulf toadfish, *Opsanus beta*	520	13

---

[a]References: 1, Shimmel et al. 1983; 2, Karim et al. 1985; 3, Sanders 1969; 4, Sanders and Cope 1968; 5, Marshall and Roberts 1978; 6, Phipps and Holcombe 1985; 7, Chang and Lange 1967; 8, Kenaga et al. 1965; 9, Jarvinen and Tanner 1982; 10, Korn and Earnest 1974; 11, Borthwick et al. 1985; 12, Johnson and Finley 1980; 13, Clark et al. 1985; 14, Macek et al. 1969.

[b]24-hour LC-50.

[c]6.6-hour LC-50.

[d]48-hour LC-50.

[e]36-hour LC-50.

[f]72-hour LC-50.

Bioconcentration of chlorpyrifos from the medium varied substantially among five species of fishes, but generally paralleled ambient levels of chlorpyrifos (Table 4). Increases in bioconcentration factors (BCF) in chlorpyrifos-exposed teleosts may be associated with three variables: increased metabolic rate, as indicated by hyperventilation, hyperactivity, and decreased growth; increased bioavailability of chlorpyrifos as a result of solvent-induced supersaturation or increased food availability; and decreased depuration rates due to possible physiological dysfunction (Goodman et al. 1985a,.b; Hansen et al. 1986). At high BCFs, adverse effects on growth and survival were observed in sheepshead minnow (*Cyprinodon variegatus)* by Cripe et al. (1986) and in Gulf toadfish (*Opsanus beta*) by Hansen et al. (1986). Chlorpyrifos is excreted rapidly from fish; the estimated Tb 1/2 is 8.7 hours, and equilibration occurs with them surrounding medium in 24 to 72 hours (Smith et al. 1966; Blau and Neely 1975; Marshall and Roberts 1978). No detectable chlorpyrifos residues were found after 12 days in 10 species of estuarine invertebrates--including oligochaete annelids, molluscs, and crustaceans--after treatment with 0.046 kg chlorpyrifos/ha (Marganian and Wall 1972).

BIRDS AND MAMMALS

Signs of chlorpyrifos intoxication, as summarized by Hudson et al. (1984), include excessive blinking, hypoactivity, hyperexcitability, excessive drinking, muscular incoordination, rapid breathing, muscular weakness, tremors, piloerection (mammals) or fluffed feathers (birds), salivation, lacrimation, diarrhea, excessive urination, prostration, loss of righting reflex, spasms, tetany, coma, and convulsions. Death usually occurs between 1 hour and 9 days after exposure, Chlorpyrifos oxon (

0,0-diethyl-0-(3,5,6-trichloro-2-pyridyl) phosphate) is the active oxygen analog of chlorpyrifos and is probably responsible for most of the anticholinesterase mode of action of chlorpyrifos; the oxon is extensively and rapidly detoxified in mammalian liver via enzymatic hydrolysis by at least two microsomal esterases (Sultatos and Murphy 1983). Significant accumulations of chlorpyrifos were not detected in domestic turkeys (*Meleagris gallopavo*) and chickens. In birds kept in pens on soil treated with 4.5 to 9.0 kg active ingredients chlorpyrifos/ha, tissue residues were 0.16 mg/kg after 1 week; these decreased thereafter, although birds remained on the treated soil (Kenaga 1974).

LD-50 values, based on a single oral dose, ranged from 5 to 157 mg chlorpyrifos/kg body weight (BW) in birds, and from 151 to 1,000 in mammals; however, 7 of 14 avian species had reported LD-50 values of <25.0 mg/kg BW (Table 5). Many species of birds that survived chlorpyrifos poisoning showed gross pathological changes (Tucker and Crabtree 1970); furthermore, the slope of the acute dose-response curve was low (Hudson et al. 1984). These findings suggested that decreasing dosage levels did not produce proportional decreases in response, and indicated a reduced safety margin for chlorpyrifos owing to mortalities that occur frequently at levels much lower than the calculated LD-50 values (Hudson et al. 1984); however, more research is needed to verify this trend.

Table 4. Chorpyrifos bioconcentration factors (BCF) by selected species of fishes (Goodman et al. 1985a, b; Hanesen et al. 1986).

Species	Exposure duration, in days	Mean concentration in medium, µg/L	Approximate BCF[a]
Gulf toadfish,	49	1.4	100
Opsanus beta	49	3.7	260
	49	8.2	270
	49	9.7	480
	49	24.0	620
	49	46.0	650
California grunion,	35	0.14	1,000
Leuresthes tenuis	35	0.30	700
	35	0.63	620

	26	0.13	<1
	26	0.28	58
	26	0.62	66
	26	1.3	450
Inland silverside,	28	0.08	<1
Menidia beryllina	28	0.18	105
	28	0.36	200
	28	0.75	130
	28	1.8	440
Atlantic silverside	28	0.08–1.1	<1
Menidia menidia			
Tidewater silverside,	28	0.09	410
Menidia peninsulae	28	0.19	400
	28	0.38	580

[a]Bioconcentration factor: concentration in whole organism (µg/kg fresh weight) divided by concentration in medium (µg/L).

Reduction in cholinesterase activity levels of various tissues (blood, brain) is one of the earliest signs of chlorpyrifos intoxication. Cholinesterase reductions have been demonstrated in turkeys fed diets containing 50 mg chlorpyrifos/kg (estimated daily dose of 0.7 mg/kg BW) for 20 days (Schlinke et al. 1969), in chickens fed diets of 25 mg/kg (estimated daily dose of 0.94 mg/kg BW) for 20 days (Schlinke 1970), and in mallard (*Anas platyrhynchos*) ducklings fed 75 mg chlorpyrifos/kg diet for 14 days (Herin et al. 1978). Low temperatures (27.5 C Vs. 35°C) potentiated dose-related ChE depression in juvenile northern bobwhite (*Colinus virginianus)*, suggesting a need for more research on cold stress interactions between acute oral chlorpyrifos exposure (Maguire and Williams 1987).

Dietary concentrations of 30 to 100 mg chlorpyrifos/kg feed produce some deaths in birds, and 136 to about 500 mg/kg feed usually kills at least 50% (Table 6). In chickens fed diets of 100 mg chlorpyrifos/kg--equivalent to an estimated daily dose of 6.8 mg/kg BW--egg fertility was reduced by 15% and hatchability by 17% (Schom et al. 1973). Dietary levels lethal to mallard ducklings were 136 to 180 mg/kg feed, equivalent to 10 mg/kg BW fed daily for 5 days (Kenaga 1974). In adult mallards given diets containing 80 mg chlorpyrifos/kg for 60 to 84 days, body weight, food consumption, brain cholinesterase activity levels, and egg production were all reduced; moreover, egg weight and eggshell thickness were reduced, the resultant ducklings weighed less than controls, and survival was comparatively poor at age 7 days. No effect on any variable was observed at diets of 8 mg/kg (Gile and Meyers 1986; Meyers and Gile 1986).

Dermal application routes are also toxic. Some deaths were recorded in turkeys from dermal treatments of 15 to 20 mg chlorpyrifos/kg BW (Schlinke et al. 1969). Higher levels applied to feathers killed turkeys within 8 hours (Marshall and Roberts 1978). Newborn piglets (*Sus* spp.) were especially more sensitive than those 30-36 hours old to cutaneous applications of chlorpyrifos; newborns showed clinical signs consistent with organophosphorus toxicosis after a 2.5% aerosol preparation (dosage unknown) was applied to the tail and umbilicus (Long et al. 1986). Accidental poisoning of cattle (*Bos* spp.) by chlorpyrifos through dermal application to control ticks resulted in some deaths; among bulls that survived, sperm production was reduced 43% in seriously affected animals and 12% in those with no outward signs of poisoning (Everett 1982).

Chlorpyrifos is not mutagenic, as judged by mitotic recombination assays (Poole et al. 1976), and did not increase sister chromatid exchange above background in tests with chick (*Gallus* spp.) embryos and Chinese hamster (*Cricetus* spp.) ovary cells (Muscarella et al. 1984).

Table 5. Chlorpyrifos toxicity to a variety of birds and mammals via single oral dose route of administration. Values are in mg chlorpyrifos/kg body weight lethal to 50% within 14 days.

Organism, and other variables	LD-50, in mg/kg body weight	Reference[a]
Birds		
European starling, *Sturnus vulgaris*	5	1
Ring-necked pheasant, *Phasianus colchicus*		
Male	8.4	2
Female	17.7	3
Red-winged blackbird, *Agelaius phoeniceus*	13	1
Common grackle, *Quiscalus quiscula*	13	1
House sparrow, *Passer domesticus*	10 to 21	1,3
Japanese quail, *Coturnix japonica*	15.9	2
Sandhill crane, *Grus canadensis*	25 to 50	3
Rock dove, *Columba livia*	26.9	2
Crow, *Corvus brachyrhynchos*	>32	1
Canada goose, *Branta canadensis*	40 to 80	4
Chukar, *Alectoris chukar*		
Male	61.1	3
Female	60.7	2
Northern bobwhite, *Colinus virginianus*		
Technical grade	32	5
Lorsban 15G	108	5
Mallard, *Anas platyrhynchos*		
Age 36 h	14.5	6
Age 7 days	29.4	6
Age 30 days	50.4	6
Age 6 months	83.3	6
Ringed turtle dove, *Streptopelia risoria*	157	5
Mammals		
Albino rat, *Rattus norvegicus*	151	4
Guinea pig, *Cavia porcellus*	500	7
Domestic goat, *Capra hircus*	500 to 1,000	4
White rabbit, *Oryctolagus cuniculus*	1,000 to 2,000	7

[a]References: 1, Schafer 1972; 2, Tucker and Haegele 1971; 3, Tucker and Crabtree 1970; 4, Hudson et al. 1984; 5, Hill and Camardese 1984; 6, Hudson et al. 1972; 7, Smith 1987.

Table 6. Dietary toxicity of chlorpyrifos to selected species of birds.

Species, and age (in days)	Duration of dietary exposure, in days	Minimum lethal concentration, in mg/kg diet	LD-50, in mg/kg diet	Reference[a]
Mallard, *Anas platyrhynchos*				
(1 to 5)	5	30	136	1
(5 to 7)	5	30 to 90	180	1
(10)	5 plus 3 untreated	-	940	2
Pekin duck, *Anas* sp.				
(5)	21	-	>1,000	1
Northern bobwhite,*Colinus virginianus*				
(1 to 5)	5	50 to 100	505	1
Turkey, *Meleagris gallopavo*				
(84)	28	>100	>100	1
Japanese quail, *Coturnix japonica*				
(14)	5 plus 3 untreated	-	299	2
(14)	5 plus 3 untreated	-	492	3
Chicken, *Gallus* sp.				
(10 to 12)	14	<200	400	1
(28)	28	50 to 100	> 100	1
(Adults)	365	-	>200	1
Ring-necked pheasant, *Phasianus colchicus*				
(10)	5 plus 3 untreated	-	553	2
Coturnix quail, *Coturnix risoria*				
(14 to 21)	5	-	299	1
(Adults)	28	300	500	1

[a]References: 1, Kenaga, 1974; 2, Hill et al. 1975; 3, Hill and Camardese 1986.

Chlorpyrifos-impregnated ear tags are under development to control horn flies (*Haematobia irritans*) in U.S. cattle (Byford et al. 1986). Cattle fitted with ear tags (0.96 g chlorpyrifos per tag/365 kg animal, or about 2.6 mg chlorpyrifos/kg BW) had slightly elevated tissue residues (0.13 mg/kg fat) after 12 weeks, but residues were well within current acceptable tolerance levels of 2.0 mg chlorpyrifos/kg fresh weight cattle fat, meat, or meat by-products (Byford et al. 1986). In dogs (*Canis familiaris)*, chlorpyrifos-impregnated collars provided effective control of adult fleas (*Ctenocephalides* spp.) for up to 11 months, with no significant adverse reactions regardless of canine coat length, size, or age (Higgins and Jarvis 1986).

FIELD INVESTIGATIONS

There have been many accidental spills of chlorpyrifos, but little quantitative assessment of the environmental effects. One exception is a spill in April 1985 in England (Boreham and Birch 1987). In that instance, a truck overturned, spilling 205 liters of chlorpyrifos into an adjacent stream that drained into the Roding River. A resulting sharp decrease in the number and type of macroinvertebrate benthic organisms in affected parts of the river, compared to unaffected areas, lasted 6 months. In addition, certain chlorpyrifos-resistant benthic organisms were unusually abundant.

Chlorpyrifos controls mosquito larvae at applied dosages between 0.028 and 0.056 kg/ha, equivalent to 9 to 18 ug chlorpyrifos/1 in 152 mm (6 inches) of water (Marshall and Roberts 1977; Eaton et al. 1985); in 1984 alone, chlorpyrifos was used for this purpose on about 600,000 ha (Odenkirchen 1987). No obvious deleterious effects of chlorpyrifos have yet been noted in mammals, amphibians, or reptiles under field conditions of current use (Table 7). However, at recommended dosage application rates for control of mosquitos and other pestiferous insects (usually 0.028 to 0.056 kg/ha), adverse effects have been documented on survival, reproduction, metabolism, and species diversity of a variety of fishes, terrestrial and aquatic invertebrates, freshwater flora, waterfowl, and horned larks (*Eremophila alpestris)*, and on the marketability of various crops (Mulla et al. 1971, 1973; Hurlbert et al. 1972; Macek et al. 1972; Nelson and Evans 1973; Hoy and Shea 1981; Table 7).

We emphasize that the effectiveness of chlorpyrifos under field conditions, like that of other organophosphorus pesticides, is significantly modified by numerous variables such as formulation, route of administration, pond substrate, dose, and water temperature (Macek et al. 1969; Bailey et al. 1970; Rawn et al. 1978; Odenkirchen 1987).

Table 7. Chlorpyrifos effects on selected ecosystems.

Ecosytstem, and other information	Application rate and other variables	Effects and reference
Aquatic		
Lake	0.004 kg/ha, emulsifiable concentrate, oil diluent single application	After 24 h, aquatic insect populations reduced 14% to 40% and snails reduced 10% (Moore and Breeland 1967)
Freshwater lake	0.014 kg/ha (equivalent to about 1.2 µg/L), single application	Freshwater algae (*Ankistrodesmus* sp., *Tetraedron* sp.) reduced 30% to 90% 7 days posttreatment; reduced population growth evident one year postapplication (Brown et al. 1976)
Flooded rice field	Individual applications of 0.014 to 0.019 kg/ha, emulsifiable concentrate, oil diluent, 3 applications at 5-week intervals	Mortality after 72 h, 32% in caged bluegills (*Lepomis macrochirus*), 50% to 70% in mayfly nymphs (*Siphlonurus* sp.), and

		32% in predatory diving beetles (Washino et al. 1972)
Freshwater ponds, (8 m x 17 m x 0.3 m deep)	Individual applications of 0.011, 0.056, 0.11, or 1.11 kg/ha; 4 applications at 2-week intervals	Initial population inhibition of mosquitofish (*Gambusia* sp.), but reproduction resumed except for 1.11 kg/ha group. Fish whole body residues in 0.056 kg/ha group, in mg/kg body weight, were 2.8 at 4 h 1.7 at 24 h, and 0.1 after 2 weeks. Insect and zooplankton populations reduced >92%; little recovery was evident after third treatment. The 0.056 kg/ha treatment regimen, at 4 h, resulted in residues of 10 µg/L in water, 375 µg/kg in vegetation, and nondetectable levels in mud; at 14 days, all residues were nondetectable (Hurlbert et al. 1970)
Artificial lake	0.02 kg/ha, granular formulation, single application	Chironomid larvae population remained >90% depressed for 5 months (Mulla et al. 1971)
Salt marsh	0.028 kg/ha (0.025 lbs/acre), single aerial application, mosquito larvicide granules	No observable effects on caged blue crabs (*Callinectes sapidus*), penaeid shrimp, or fishes; some fiddler crabs (*Uca* sp.) dead (FWS 1968)
Salt marsh	Individual applications of 0.028 kg/ha, 4 applications at 2-week intervals	In killifish (*Fundulus heteroclitus*), convulsions, ChE depression, and deaths noted. ChE remained depressed for

		about 10 weeks after final application (Thirugnanam and Forgash 1977)
Artificial streams, each 520 m long, 0.14 ha of surface area, with pools 30.5 m long x 3.6 m wide x 81 cm deep	Continuous treatment stream recieved 0.22 µg chlorpyrifos/L for days 1 to 41, and 1.0 µg/L from days 41 to 100. Intermittent treatment stream received dosage 14x higher than continuous treatment stream, but dosage was confined to 24 h every 14 days. Chlorpyrifos administered as emulsifiable concentrate in petroleum derivative solvent	When compared to control stream, no effect on total abundance of benthic organisms. However, in both treated streams, species diversity decreased by equal amounts and was still decreasing at day 100. Adverse sublethal effects were noted in fathead minnow, *Pimephales promelas* (spinal deformities) and bluegills (ChE inhibition, signs of organophosphorus poisoning) only in the pulse-dosed stream. In all streams, however, fish survived, grew, and reproduced equally well (Eaton et al. 1985)
Shallow pond, mean depth 0.25 m, surface area 0.11 ha, high vegetation	Individual applications of 0.056 kg/ha technical grade, 2 applications at 34-day interval	After 63 days, 46% to 55% mortality in centrarchid populations, and 75% reduction in insect populations of caddisflies, mayflies, and midges (Macek et al. 1972)
Shallow ponds	0.056 kg/ha, emulsifiable concentrate, oil diluent single application	All caged green sunfish (*Lepomis cyanellus*) died (Linn 1968)
Woodland pools	Single application of 0.056 kg/ha, granular formulation	Increased algal growth on leaf litter observed months after treatment, attributed to reduction in grazing stress by

		mosquito larvae (Hagmann and Porteus 1972)
Woodland pools	0.056 kg/ha, granular formulation, single application	Isopod populations reduced 90% to 95% (Cooney and Pickard 1974)
Freshwater ponds	Single dose of chlorpyrifos, equivalent at 4, 10, or 1,000 µg/L	Increased algal bloom duration in treated ponds, possibly due to loss of grazing fauna (Butcher et al. 1977)
Salt marsh, 202 ha (500 acres),	0.56 kg/ha (0.5 lbs/acre), single application applied as aerial spray, to kill mosquito larvae	Killed significant numbers of fishes and crustaceans (FWS 1968)
Salt marsh, 78 ha plot	0.56 kg/ha, emulsifiable concentrate, once, aerially	After 48 h, mortality was 35% in caged fish and 84% in caged shrimp; no other adverse effects were noted during the next 27 days (Wall and Marganian 1971)
Salt marsh estuary, Bay St. Louis, Mississippi, 408 ha site (1,008 acres)	0.56 kg/ha (0.5 lbs/acre), granular, single aerial application, for mosquito control	After spraying, all caged fiddler crabs died, white shrimp (*Penaeus setiferus*) populations were reduced, and large numbers of blue crabs were found dead. No observable effects on terrestrial organisms, including insects. One month after spraying, shrimp and blue crab populations seemed normal, although fiddler crabs were absent (FWS 1967)
Freshwater pond	Single application of pelletized 10.6% chlorpyrifos to obtain theoretical water concentrations of 250 µg/L and higher	Species diversity of diatoms reduced >50% in 6 weeks, vs. 12% increase in controls (Nelson et al. ı .

Terrestrial

Temporary woodland pool	Average maximum water concentration of 1.6 µg chlorpyrifos/L	No obvious adverse effects on wildlife, i.e., 3 spp. of rodents, one sp. frog, one sp. turtle (Nelson and Evans 1973)
Freshwater ponds (8 m x 17 m x 0.3 m deep)	Individual applications of 0.011, 0.056, 0.11 and 1.11 kg/ha; 4 applications at 2-week intervals	High mortality (>42%) of mallard (*Anas platyrhynchos*) ducklings on all treated ponds, vs. none dead on control ponds (Hurlbert et al. 1970)
Salt marsh	0.025 kg/ha, single application	No gross effects on wildlife (Ludwig et al. 1968)
Rice field area	0.029 kg/ha, single application	All honeybees (*Apis* sp.) within 0.4 km downwind of spray area were dead; 95% were dead at 0.8 km and 89% at 1.2 km (Atkins 1972)
New Mexico ranchlands	Dust formulations of 0.48 and 1.97 kg/ha, to control wildlife flea populations	No observable deleterious effects in rodents and rabbits 3 to 4 weeks posttreatment (Miller et al. 1970)
Wheat fields	0.56 and kg/ha, to control pale western cutworm (*Agrotis orthogonia*)	Horned larks (*Eremophila alpestris*) had brain ChE activity levels depressed 22% at 3 days posttreatment, and 8% at 16 days. No sick or dead birds found; however, no systematic searches were made for the small lark carcasses, nor were specific observations for toxic signs conducted (McEwen et al. 1986)
Iraqi date palm (*Phoenix* sp.) orchards	Emulsifiable concentrate applied once after fruiting and infesta-	Chlrorpyrifos residues in dates decreased from 1.28 mg/kg fresh weight

	tion with high pressure ground sprayers at 0.98 kg/ha to control insect pests	at day one postapplication to 0.2 mg/kg on day 15, to 0.05 on day 29, and to nondetectable concentrations on day 71. Concentrations of the chlorpyrifos oxygen analog, however, after reaching a peak of 0.5 mg/kg on day 15, were still detectable (0.1 mg/kg) at day 85, suggesting that dates should be harvested at least 8 weeks after chlorpyrifos treatment (Mansour 1985)
Turf	1.12 kg/ha, emulsifiable concentrate, single application, to control chinch bug (*Blissus leucopterus listus*)	Most arthropods in turf killed immediately after application. Target pest populations remained depressed for one year posttreatment, but other insect populations recovered to levels greater than controls after 3.5 months (Streu and Cruz 1972)

RECOMMENDATIONS

Current water quality criteria formulated for chlorpyrifos by the U.S. Environmental Protection Agency (EPA 1986) for aquatic life protection seem to afford a reasonable degree of safety, at least during short-term exposure. Specifically, the proposed criteria for freshwater are 0.041 ug/l (4-day average concentration) and 0.083 ug/l (1-hour average concentration), neither of which should be exceeded more than once every 3 years; for saltwater, the criteria are 0.0056 ug/l and 0.011 ug/l, respectively.

The acceptable tolerance level of chlorpyrifos in meat and meat by-products destined for human consumption is 2.0 mg/kg fresh weight (Byford et al. 1986). The significance of this concentration to animal health, or to consumers other than man, is unknown. More research is needed to establish maximum tolerable chlorpyrifos limits in tissues of sensitive fish and wildlife.

Information is lacking on the effectiveness of chlorpyrifos in large-scale (>40 ha) coldwater ecosystems, typical of those found in Alaska or northern tier States; accordingly, we recommend initiation of long-term studies in these potential problem areas.

As judged by our analysis of available literature, three courses of action now seem warranted: (1) Restrict the use of chlorpyrifos for mosquito control in wetlands, estuaries, and waterfowl breeding areas because recommended treatment levels are demonstrably harmful to nontarget species, including mallard ducklings. The unsuitability of chlorpyrifos for mosquito control is further supported by the finding that certain mosquito populations in California are showing signs of chlorpyrifos resistance, and thus may require more aggressive future treatment programs (tarsalis populations (Reisen et al. 1984). (2) Curtail agricultural use of chlorpyrifos in watershed areas pending acquisition of additional data on its transport, fate, and effects, including data on chlorpyrifos flux rates from oils and sediments and its resultant bioavailability. (3) Develop suitable replacements for chlorpyrifos in mosquito control programs. These replacement compounds should exhibit a relatively long half-life in aquatic environments while avoiding the broad spectrum toxicity typical of chlorpyrifos to large numbers of nontarget organisms.

LITERATURE CITED

Atkins, E. L. 1972. Rice field mosquito control studies with low volume Dursban sprays in Colusa County, California. V. Effects on honey bees. Mosq. News 32:538-541.

Bailey, D. L., G. C. Labrecque, and T. L. Whitfield. 1970. Slow-release and emulsifiable formulations of Dursban and Abate for controlling larvae of *Culex pipiens quinquefasciatus*. Mosq. News 30:465-467.

Blau, G. E., and W. B. Neely. 1975. Mathematical model building with an application to determine the distribution of Dursban insecticide added to a simulated ecosystem. Adv. Ecol. Res. 9:133-162.

Boreham, S., and P. Birch. 1987. The use of indicator organisms to assess aquatic pollution following a motorway insecticide spill. Sci. Total Environ. 59:477-480.

Borthwick, P. W., J. M. Patrick, Jr., and D. P. Middaugh. 1985. Comparative acute sensitivities of early life stages of atherinid fishes to chlorpyrifos and thiobencarb. Arch. Environ. Contam. Toxicol. 14:465-473.

Borthwick, P. W., and G. E. Walsh. 1931. Initial toxicological assessment of Ambush, Bolero, Bux, Dursban, Fentrifanil, Larvin, and Pydrin: static acute toxicity tests with selected estuarine algae, invertebrates, and fish. U.S. Environ. Protection Agency Rep. 60014-81-076. 20 pp

Brown, J. R., L. Y. Chow, and C. B. Deng. 1976. The effects of Dursban upon fresh water phytoplankton. Bull. Environ. Contam. Toxicol. 15:437-441.

Brust, H. F. 1966. A summary of chemical and physical properties of Dursban. Down to Earth 22:21-22.

Butcher, J. E., M. G. Boyer, and C. D. Fowle. 1977. Some changes in pond chemistry and photosynthetic activity following treatment with increasing concentrations of chlorpyrifos. Bull. Environ. Contam. Toxicol. 17:752-758.

Byford, R. L., J. A. Lockwood, S. M. Smith, C. W. Harmon, C. C. Johnson, D. G. Luther, H. F. Morris, Jr., and A. J. Penny. 1986. Insecticide residues in cattle treated with a cypermethrin, chlorpyrifos, piperonyl butoxide-impregnated ear tag. Bull. Environ. Contam. Toxicol. 37:692-697.

CDC. 1980. Pesticide poisoning in an infant. Center for Disease Control, Mortal. Morbid. 29:254-255.

Chang, V. C. S., and W. H. Lange. 1967. Laboratory and field evaluation of selected pesticides for control of red crayfish in California rice fields. J. Econ. Entomol. 60:473-477.

Clark, J. R., J. M. Patrick, Jr., D. P. Middaugh, and J. C. Moore. 1985. Relative sensitivity of six estuarine fishes to carbophenothion, chlorpyrifos, and fenvalerate. Ecotoxicol. Environ. Safety 10:382-390.

Collins, P. J. 1985. Resistance to grain protectants in field populations of the sawtoothed grain beetle in southern Queensland. Aust. J. Exp. Agric, 25:683-686.

Cooney, J. C., and E. Pickard. 1974. Field tests with Abate and Dursban insecticides for control of flood water mosquitos in the Tennessee Valley region. Mosq. News 34:12-22.

Cripe, G. M., D. J. Hansen, S. F. Macauley, and J. Forester. 1986. Effects of diet quantity on sheepshead minnows (*Cyprinodon variegatus*) during early life-stage exposures to chlorpyrifos. Pages 450-460 *in* T. M. Poston and R. Purdy (eds.). Aquatic toxicology and environmental fate: ninth symposium. ASTM Spec. Tech. Publ. 921, American Society for Testing and Materials, Philadelphia, Pennsylvania.

Eaton, J., J. Arthur, R. Hermanutz, R. Kiefer, L. Mueller, R. Anderson, R. Erickson, B. Nordlung, J. Rogers, and H. Pritchard. 1985. Biological effects of continuous and intermittent dosing of outdoor experimental streams with chlorpyrifos. Pales 85-118 *in* R. C. Bahner and D. J. Hansen (eds.). Aquatic toxicology and hazard assessment: eighth symposium. ASTM Spec. Tech. Publ. 891, American Society for Testing and Materials, Philadelphia, Pennsylvania.

EPA. 1982. Preliminary quantitative use analysis. Available from U.S. Environ. Protection Agency, Economics Analysis Branch, 401 M St. S.W., Washington D.C., 20460. 10 pp.

EPA. 1985. Disciplinary review ecological effects profile. Available from U.S. Environ. Protection Agency, Office of Pesticide Programs, 401 M St. S.W., Washington D.C. 20460. 10 pp.

EPA. 1986. Ambient water quality criteria for chlorpyrifos - 1986. U.S. Environ. Protection Agency Rep. 440/5-86-005. 64 pp.

Everett, R. W. 1982. Effects of Dursban 44 on semen output of Holstein bulls. Dairy Sci. 65:1781-1791.

Freed, V. H., C. T. Chiou, and D. W. Schmedding. 1979. Degradation of selected organophosphate pesticides in water and soil. J. Agric. Food Chem. 27:706.

FWS. 1967. Effects of granular application of Dursban on some estuary and salt marsh organisms. U.S. Fish. Wildl. Serv. Spec. Rep., Pesticide Surveillance Program, Atlanta, Georgia. Mimeo. 34 pp.

FWS. 1968. Field appraisal of tests to control salt marsh mosquito with Dursban applied as a larvicide and adulticide in Florida. U.S. Fish Wildl. Serv. Spec. Rep., Pesticide Field Appraisal Program, Atlanta, Georgia. Mimeo. 25 pp.

Getzin, L. W. 1981. Dissipation of chlorpyrifos from dry soil surfaces. J. Econ. Entomol. 74:707-713.

Getzin, L. W., and I. Rosenfield. 1968. Organophosphorus insecticide degradation by heat-labile substances in soil. J. Agric. Food Chem. 16: 598-601.

Gile, J. D., and S. M. Meyers. 1986. Effects of adult mallard age on avian reproductive tests. Arch. Environ. Contam. Toxicol. 15:751-756.

Goodman, L. R., D. J. Hansen, D. P. Middaugh, G. M. Cripe, and J. C. Moore. 1985a. Method for early life-stage toxicity tests using three atherinid fishes and results with chlorpyrifos. Pages 145-154 *in* R. D. Cardwell, R. Purdy and R. C. Bahner (eds.). Aquatic toxicology and hazard assessment: seventh symposium. ASTM Spec. Tech. Publ. 854, American Society for Testing and Materials, Philadelphia, Pennsylvania.

Goodman, L. R., D. J. Hansen, G. M. Cripe, D. P. Middaugh, and J. C. Moore. 1985b. A new early life-stage toxicity test using the California grunion (*Leuresthes tenuis*) and results with chlorpyrifos. Ecotoxicol. Environ. Safety 10:12-21.

Hagmann, L. E., and D. J. Porteus. 1972. Pre-hatch treatments with Dursban IG granular insecticide for control of mosquito larvae. Down to Earth 28:21-24.

Hansen, D. J., L. R. Goodman, G. M. Cripe, and S. F. Macauley. 1986. Early life-stage toxicity test methods for Gulf toadfish (*Opsanus beta*) and results using chlorpyrifos. Ecotoxicol. Environ. Safety 11:15-22.

Harris, C. R., H. J. Svec, and P. Martel. 1975. Laboratory and field studies on the effectiveness of post planting insecticide treatments in controlling the darksided and redbacked cutworms attacking tobacco. Proc. Entomol. Soc. Ont. 104:59-64.

Herin, R. A., J. E. Sluggs, E. M. Loves, L. T. Heiderscheit, J. D. Farmer, and D. Prather. 1978. Correlation of salt gland function with levels of chlorpyrifos in the feed of mallard ducklings. Pestic. Biochem. Physiol. 9:157-164.

Higgins, P. C., and R. A. Jarvis. 1986. Chlorpyrifos - the latest advance in controlling fleas in dogs and cats. Aust. Vet. Pract. 16:103.

Hill, E. F., and M. B. Camardese. 1984. Toxicity of anticholinesterase insecticides to birds: technical grade versus granular formulations. Ecotoxicol. Environ. Safety 8:551-563.-

Hill, E. F., and M. B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to coturnix. U.S. Fish Wildl. Serv., Fish Wildl. Tech. Rep. 2. 147 pp.

Hill, E. F., R. G. Heath, J. W. Spann, and J. D. Williams. 1975. Lethal dietary toxicities of environmental pollutants to birds. U.S. Fish Wildl. Serv. Spec. Sci. Rep. -- Wildl. No. 191. 61 pp.

Hodgson, M. J., G. D. Block, and D. K. Parkinson. 1986. Organophosphate poisoning in office workers. J. Occup. Med. 28:434-437.

Hoy, J. B., and P. J. Shea. 1981. Effects of lindane, chlorpyrifos, and carbaryl on a California pine forest soil arthropod community. Environ. Entomol. 10:732-740.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1972. Effects of age on sensitivity: acute oral toxicity of 14 pesticides to mallard ducks of several ages. Toxicol. Appl. Pharmacol. 22:556-561.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp

Hurlbert, S.H., M.S. Mulla, J.O. Keith, W.E. Westlake, and M. E. Dusch. 1970. Biological effects and persistence of Dursban® in freshwater ponds. J. Econ. Entomol. 63:43-52.

Hurlbert, S. H., M. S. Mulla, and H. R. Willson. 1972. Effects of an organophosphorus insecticide on the phytoplankton, zooplankton, and insect populations of fresh-water ponds. Ecol. Monogr. 42:269-299.

Jarvinen, A. W., B. R. Nordling, and M. E. Henry. 1983. Chronic toxicity of Dursban® (chlorpyrifos) to the fathead minnow (*Pimephales promelas)* and the resultant acetylcholinesterase inhibition. Ecotoxicol. Environ. Safety 7:423-434.

Jarvinen, A. W., and D. K. Tanner. 1982. Toxicity of selected controlled released and corresponding unformulated technical grade pesticides to the fathead minnow (*Pimephales promelas)*. Environ. Pollut. 27A:179-195.

Johnson, W. W., and M. T. Finley- 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Karim, A.A.R.A., A.A.M. Haridi, And E.A.E. Rayah. 1985. The environmental impacts of four insecticides on non-target organisms in the Gezira irrigation scheme canals of Sudan. J. Trop. Med. Hyg. 88:161-168.

Kenaga, E. E. 1971. Some physical, chemical and insecticidal properties of some 0-0-dialkyl O-(3,5,6-trichloro-2-pyridyl) phosphates and phosphorothioates. Bull. World Health Org. 44:225-228.

Kenaga, E. E. 1974. Evaluation of the safety of chlorpyrifos to birds in areas treated for insect control. Residue Rev. 50:1-41.

Kenaga, E. E., W. K. Whitney, J. L. Hardy, and A. E. Doty. 1965. Laboratory tests with Dursban® insecticide. J. Econ. Entomol. 58:1043-1650.

Korn, S., and R. Earnest. 1974. Acute toxicity of 20 insecticides to striped bass (*Morone saxtilis*). Calif. Fish Game 60:128-131.

Linn, J. D. 1968. effects of low volume spraying of Dursban and Fenthion on fish. Down to Earth-24:28-30.

Long, G. G., A. B. Scheidt, R. J. Everson, and F. W. Oehme. 1986. Age related susceptibility of newborn pigs to the cutaneous application of chlorpyrifos. Vet. Hum. Toxicol. 28:297-299.

Ludwig, P.D., H.J. Dishburger, J.C. McNeill, W.D. Miller and J.R. Rice. 1968. Biological effects and persistence of Dursban® insecticide in a salt-marsh habitat. J. Econ. Entomol. 61:626-633.

Macek, K. J., C. Hutchinson, and 0. B. Cope. 1969. The effects of temperature on the susceptibility of bluegills and rainbow trout to selected pesticides. Bull. Environ. Contam. Toxicol. 4:174-183.

Macek, K. J., D. F. Walsh, J. W. Hogan, and D. D. Holz. 1972. Toxicity of the insecticide Dursban® to fish and aquatic invertebrates in ponds. Trans. Am. Fish. Soc. 101:420-427.

Maguire, C. C., and B. A. Williams. 1987. Cold stress and acute organophosphorus exposure: interaction effects on juvenile northern bobwhite. Arch. Environ. Contam. Toxicol. 16:477-481.

Mansour, S. A. 1985. Determination of residues of chlorpyrifos and its oxygen analog in dates. J. Pestic. Sci. 10:677-680.

Marganian, V. M., and W. J. Wall, Jr. 1972. Dursban® and diazinon residues in biota following treatment of intertidal plots on Cape Cod -- 1967-69. Pestic. Monit. J. 6:160-165.

Marshall, W. F., and J. R. Roberts. 1978. Ecotoxicology of chlorpyrifos. Natl. Res. Counc. Canada, Assoc. Comm. Sci. Crit. Environ. Qual., Publ. 16059, Ottawa, Ontario, Canada. 314 pp.

Mayer, F. L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U.S. Environ. Protection Agency Rep. 600/8-87/017. 274 pp.

Mayer, F. L., Jr., and M. R. Ellersieck. 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals. U.S. Fish Wildl. Serv. Resour. Publ. 160. 579 pp.

McEwen, L. C., L. R. DeWeese, and P. Schladweiler. 1986. Bird predation on cutworms (Lepidoptera : Noctuidae) in wheat fields and chlorpyrifos effects on brain cholinesterase activity. Environ. Entomol. 15:147-151.

Meikle, B. W., and C. R. Youngson. 1970. Hydrolysis rate of Dowco 179 in water. Dow Chemical Company. Agric. Res. Rep. GS-1154. 6 pp. Walnut Grove Creek, California.

Meyers, S. M., and J. D. Gile. 1986. Mallard reproductive testing in a pond environment: a preliminary study. Arch. Environ. Contam. Toxicol. 15: 757-761.

Miles, J. R. W., C.R. Harris, and C.M. Tu. 1983. Influence of temperature on the persistence of chlorpyrifos and chlorfenvinphos in sterile and natural mineral and organic soils. J. Environ. Sci. Health B18:705-712.

Miles, J. R. W., C.R. Harris, and C.M. Tu. 1984. Influence of moisture in the persistence of chlorpyrifos and chlorfenvinphos in sterile and natural mineral and organic soils. J. Environ. Sci. Health B19:237-243.

Milio, J. F., P. G. Koehler, and R. S. Patterson. 1987. Evaluation of three methods for detecting chlorpyrifos resistance in German cockroach (Orthoptera: Blattellidae) populations. J. Econ. Entomol. 30:44-46.

Miller, B.E., D.L. Forcum, K.W. Week, J.R. Wheeler, and C.D. Rail. 1970. An evaluation of insecticides for flea control on wild animals. J. Med. Entomol. 7:697-702.

Moore, J. B., and S. G. Breeland. 1967. Field evaluation of two mosquito larvicides, Abate and Dursban against *Anopheles quadrimaculatus* and associated *Culex* species. Mosq. News 27:105-111.

Mortland, M. M., and K. U. Raman. 1967. Catalytic hydrolysis of some organic phosphate pesticides by copper (II). Agric. Food Chem. 15:163-167.

Mulla, M. S., R. L. Norland, and D. M. Fanuva. 1971. Control of chironomid midges in recreational lakes. J. Econ. Entomol. 64:300-307.

Mulla, M. S., R. L. Norland, W. E. Westlake, B. Dell, and J. S. Amant. 1973. Aquatic midge larvicides: their efficacy and residues in water, soil, and fish in a warm water lake. Environ. Entomol. 2:58-65.

Muscarella, D. E., J. F. Keown, and S. E. Bloom. 1984. Evaluation of the genotoxic and embryotoxic potential of chlorpyrifos and its metabolites in vivo and in vitro. Environ. Mut. 6:13-23.

Nelson, J. H., and E. S. Evans, Jr. 1973. Field evaluations of the larvicidal effectiveness. Effects on non-target species and environmental residues of a slow-release polymer formulation of chlorpyrifos. U.S. Army Environ. Hygiene Agency Rep. No. 44-022-73/75. Aberdeen Proving Ground, Maryland. 15 pp.

Nelson, J. H., D. L. Stoneburner, E. S. Evans, Jr., N. E. Pennington, and M. V. Meisch. 1976. Diatom diversity as a function of insecticidal treatment with a controlled-release formulation of chlorpyrifos. Bull. Environ. Contam. Toxicol. 15:630-634.

Norberg, T. J., and D. I. Mount. 1985. A new fathead minnow (*Pimephales promelas*) subchronic toxicity test. Environ. Toxicol. Chem. 4:711-718.

Odenkirchen, E. W. 1987. Hazards of chlorpyrifos, an organophosphorus pesticide, to natural resources: a review. M.A. Thesis. The American University, Washington, D.C. 63 pp.

Phipps, G. L., and G.W. Holcombe. 1985. A method for aquatic multiple species toxicant testing: acute toxicity of 10 chemicals to 5 vertebrates and 2 invertebrates. Environ. Pollut. 38A:1,41-157.

Poole, D.C., V.F. Simmon, and G.W. Newell. 1976. In vitro mutagenic activity of fourteen pesticides. Toxicol. Appl. Pharmacol. 41:196.

Rawn, G. P., G. R. B. Webster, and G. M. Findlay. 1978. Effect of pool bottom substrate on residues and bioactivity of chlorpyrifos, against larvae of Culex tarsalis (Diptera: Culicidae). Can. Entomol. 110:1269-1276.

Reisen, W.K., G. Yoshimura, W.C. Reeves, M.M. Milby, and R.P. Meyer. 1984. The impact of aerial applications of ultra-low volume adulticides on *Culex tarsalis* populations (Diptera: Culicidae) in Kern County, California, USA, 1982. J. Med. Entomol. 21:573-585.

Rigterink, R. H., and E. E. Kenaga. 1966. Synthesis and insecticidal activity of some 0,0-dialkyl 0-3,5,6-trichloro-2-pyridyl phosphates and phosphorothioates. J. Agric. Food Chem. 14:304-306.

Rongsriyam, Y., S. Prownebon, and S. Hirakoso. 1968. Effects of insecticides on the feeding activity of the guppy, a mosquito eating fish, in Thailand. Bull. World Health Org. 39:977-980.

Sanders, H. 0. 1969. Toxicity of pesticides to the crustacean *Gammarus lacustris*. U.S. Fish Wildl. Serv. Tech. Paper 25. 14 pp.

Sanders, H. O., and 0. B. Cope. 1968. The relative toxicity of several pesticides to naiads of three species of stoneflies. Limnol. Oceanog. 13: 112-117.

Schaefer, C.H., and E.F. Dupras, Jr. 1969. The effects of water quality, temperature and light on the stability of organophosphorus larvicide used for mosquito control. Proc. Pap. Annu. Conf. Calif. Mosq. Control Assoc. 37:67-75.

Schaefer, C. H., and E. F. Dupras, Jr. 1970. Factors affecting the stability of Dursban in polluted waters. J. Econ. Entomol. 63:701-705.

Schafer, E. W. 1972. The acute oral toxicity of 369 pesticidal, pharmaceutical and other chemicals to wild birds. Toxicol. Appl. Pharmacol. 21:315-330.

Schimmel, S.C., R.L. Garnes, J.M. Patrick, Jr., and J.C. Moore. 1983. Acute toxicity, bioconcentration, and persistence of AC 222, 705, benthiocarb, chlorpyrifos, fenvalerate, methyl parathion, and permethrin in the estuarine environment. J. Agric. Food Chem. 31:104-113.

Schlinke, J.C. 1970. Chronic toxicity of Dursban in chickens, 1969. J. Econ. Entomol. 63:319.

Schlinke, J. C., J. S. Palmer, and L. Hunt. 1969. Preliminary toxicologic study of a phosphorothioate insecticidal compound in turkeys. Am. J. Vet. Res. 30:1705-1709.

Schom, C. B., U. K. Abbott, and N. Walker. 1973. Organophosphorus pesticide effects on domestic and game bird species. Dursban. Poult. Sci. 52:2083.

Smith, G. J. 1987. Pesticide use and toxicology in relation to wildlife: organophosphorus and carbamate compounds. U.S. Fish Wildl. Serv. Resour. Publ. 170. 171 pp.

Smith, G. N. 1966. Basic studies on Dursban insecticide. Down to Earth 22: 3-7.

Smith, G. N. 1968. Ultraviolet light decomposition studies with Dursban and 3,5,6-trichloro-2-pyridinol. J. Econ. Entomol. 61:793-799.

Smith G. N., B. S. Watson, and F. S. Fischer. 1966. The metabolism of (C^{14})0,0-diethyl O-(3,5,6-trichloro-2-pyridyl) phosphorothioate (Dursban) in fish. J. Econ. Entomol. 59:1464-1475.

Streu, H. T., and C. Cruz. 1972. Control of the hairy chinch bug in turfgrass in the northeast with Dursban insecticide. Down to Earth 28:1-4.

Sultatos, L.G., and S.D. Murphy. 1983. Hepatic microsomal detoxification of the organophosphates paraoxon and chlorpyrifos oxon in the mouse. Drug Metabol. Dispos. 11:232-238.

Tagatz, M.E., N.R. Gregory, and G.R. Plaia. 1982. Effects of chlorpyrifos on field- and laboratory-developed estuarine benthic communities. J. Toxicol. Environ. Health 10:411-421.

Thirugnanam, M., and A. J. Forgash. 1977. Environmental impact of mosquito pesticides: toxicity and anticholinesterase activity of chlorpyrifos to fish in a salt marsh habitat. Arch. Environ. Contam. Toxicol. 5:415-425.

Tucker, R.K., and D.G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 84:56-57.

Tucker, R. K., and M. A. Haegele. 1971. Comparative acute oral toxicity of pesticides to six species of birds. Toxicol. Appl. Pharmacol. 20:57-65.

Wall, W.J., Jr., and V.M. Marganian. 1971. Control of *Culicoides melleus* (coq.) (Diptera: Cercetopogonidae) with granular organophosphorus pesticides and the direct effect on other fauna. Mosq. News 31:209-214.

Wall, W. J., Jr., and V. M. Marganian. 1973. Control of salt-marsh culicoids and tabanus larvae in small plots with granular organophosphorus pesticides. Mosq. News 33:88-93.

Washino, R. K., W. Ahmed, J. D. Linn, and K. G. Whitesell. 1972. Rice field mosquito control studies with low volume Dursban® sprays in Colusa County, California. IV. Effects upon aquatic nontarget organisms. Mosq. News 32:531-537.

Windholz, M. (ed.). Rahway, New Jersey. 1976. The Merck Index, ninth edition. Merck and Co.,

BIOLOGICAL REPORT 85(1.14)
APRIL 1988

Contaminant Hazard Reviews
REPORT NO. 14

LEAD HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by

Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

Lead (Pb) and its compounds have been known to man for about 7,000 years, and Pb poisoning has been recognized for at least 2,500 years. All credible evidence indicates that Pb is neither essential nor beneficial to living organisms, and that all measured effects are adverse--including those on survival, growth, reproduction, development, behavior, learning, and metabolism.

Various living resources are at increased risk from Pb: migratory waterfowl that frequent hunted areas and ingest shot; avian predators that eat game wounded by hunters; domestic livestock near smelters, refineries, and Pb battery recycling plants; captive zoo animals and domestic livestock held in enclosures coated with Pb-based paints; wildlife that forage extensively near heavily traveled roads; aquatic life in proximity to mining activities, areas where Pb arsenate pesticides are used, metal finishing industries, organolead industries, and areas of Pb aerosol fallout; and crops and invertebrates growing or living in Pb-contaminated soils.

Adverse effects on aquatic biota reported at waterborne Pb concentrations of 1.0 to 5.1 ug/l included reduced survival, impaired reproduction, reduced growth, and high bioconcentration from the medium. Among sensitive species of birds, survival was reduced at doses of 50 to 75 mg Pb^{2+}/kg body weight (BW) or 28 mg organolead/kg BW, reproduction was impaired at dietary levels of 50 mg Pb /kg, and signs of poisoning were evident at doses as low as 2.8 mg organolead/kg BW. In general, forms of Pb other than shot (or ingestible Pb objects), or routes of administration other than ingestion, are unlikely to cause clinical signs of Pb poisoning in birds. Data for toxic and sublethal effects of Pb on mammalian wildlife are missing. For sensitive species of domestic and laboratory animals, survival was reduced at acute oral Pb doses of 5 mg/kg BW (rat), at chronic oral doses of 5 mg/kg BW (dog), and at dietary levels of 1.7 mg/kg BW (horse). Sublethal effects were documented in monkeys exposed to doses as low as 0.1 mg Pb/kg BW daily (impaired learning at 2 years postadministration) or fed diets containing 0.5 mg Pb/kg (abnormal social behavior). Signs of Pb exposure were recorded in rabbits given 0.005 mg Pb/kg BW and in mice given 0.05 mg Pb/kg BW. Tissue Pb levels were elevated in mice given doses of 0.03 mg Pb/kg BW, and in sheep given 0.05 mg Pb/kg BW. In general, organolead compounds were more toxic than inorganic Pb compounds, food chain biomagnification of Pb vas negligible, and younger organisms were most susceptible. More research seems merited on organolead toxicokinetics (including effects on behavior and learning), and on mammalian wildlife sensitivity to Pb and its compounds.

Recent legislation limiting the content of Pb in paints, reducing the Pb content in gasoline, and eliminating the use of Pb shot nationwide (Pb shot phaseout program/schedule starting in 1986, and fully implemented by 1991) in waterfowl hunting areas will substantially reduce environmental burdens of Pb and may directly benefit sensitive fishery and wildlife resources. Continued nationwide monitoring of Pb in living resources is necessary in order to correlate reduced emission sources with reduced tissue Pb concentrations.

DISCLAIMER

Mention of trade names or commercial products does not constitute endorsement or recommendation for use by the U.S. Government.

Suggested citation for this report:

Eisler, R. 1988. Lead hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.14).

TABLES

ACKNOWLEDGMENTS

I thank Nancy A. Bushby, Lynda J. Garrett, and Joyce E. Haber for technical services; Julia Armstrong and Jean Higgis for secretarial help; Louis N. Locke, Jerry R. Longcore, Keith A. Morehouse, Oliver H. Pattee, Matthew C. Perry, and Christopher J, Schmitt for reviewing the manuscript; and Paul H. Eschmeyer and James R. Zuboy for editorial services.

INTRODUCTION

Lead (Pb) has been known for centuries to be a cumulative metabolic poison; however, acute exposure is lessening. Of greater concern is the possibility that continuous exposure to low concentrations of the metal as a result of widespread environmental contamination may result in adverse health effects (Nriagu 1978b). Environmental pollution from Pb is now so high that body burdens in the general human population are closer than the burdens of any other toxic chemical to those that produce clinical poisoning (Hejtmancik et al. 1982). Further, Pb is a mutagen and teratogen when absorbed in excessive amounts, has carcinogenic or cocarcinogenic properties, impairs reproduction and liver and thyroid functions, and interferes with resistance to infectious diseases (EPA 1979).

Ecological and toxicological aspects of lead and its compounds in the environment have been extensively reviewed. (Wetmore (1919); Bellrose (1959), Aronson (1971), Barth et al. (1973), NRCC (1973), Holl and Hampp (1975), Boggess (1977), Rolfe and Reinbold (1977), Forbes and Sanderson (1978), Nriagu (1978a, 1978b), Wong et al. (1978), CEP (1979), EPA. (1979, 1980, 1985), Levander (1979), Tsuchiya (1979), Branica and Konrad (1980), Jenkins (1980) NAS (1980), Eisler (1981), Harrison and Laxen (1981), Demayo et al. (1982), Mudge (1983), De Michele (1984), Feierabend and Myers (1984), Walsh and Tilson (1984), Lumeij (1985), Feierabend and Russell (1986), FWS (1986a), Kania and Nash (1986), Lansdown and Yule (1986), McDonald (1986), Sanderson and Bellrose (1986), Pain (1987). There is agreement by all authorities on five points. First, Pb is ubiquitous and is a characteristic trace constituent in rocks, soils, water, plants, animals, and air. Second, more than 4 million metric tons of Pb are produced worldwide each year, mostly for the manufacture of storage batteries, gasoline additives, pigments, alloys, and ammunition. The widespread broadcasting of Pb through anthropogenic activities, especially during the past 40 years, has resulted in an increase in Pb residues throughout the environment--an increase that has dislocated the equilibrium of the biogeochemical cycle of Pb. Third, Pb is neither essential nor beneficial to living organisms; all existing data show that its metabolic effects are adverse. Fourth, Pb is toxic in most of its chemical forms and can be incorporated into the body by inhalation, ingestion, dermal absorption, and placental transfer to the fetus. Fifth, Pb is an accumulative metabolic poison that affects behavior, as well as the hematopoietic, vascular, nervous, renal, and reproductive systems. In humans, Pb causes stillbirths, miscarriages, inhibited development of fetuses, decreased male fertility, and abnormal sperm. Severe damage to the central nervous system from exposure to large amounts of Pb may result in stupor, convulsions, coma, and death. Children that survive Pb poisoning are often permanently retarded or have permanent neurological handicaps. At subclinical injury levels, Pb causes slight, but irreversible, damage to the brain development of growing children.

Natural resources are also affected by environmental Pb contamination, and some wildlife species numbers may be reduced as a result. For example, waterfowl deaths resulting from the ingestion of spent Pb shot pellets from shotgun shells were discovered more than 100 years ago in Italy and in the United States; since then Pb poisoning of waterfowl has occurred in 15 countries (Street 1983). In North America alone, approximately 3,000 tons of Pb shot are expended annually into lakes, marshes, and estuaries by several million waterfowl hunters (FWS 1986, 1987). Spent pellets are eaten by waterfowl and other birds, either in mistake for seeds or as pieces of grit. These pellets may be retained in the gizzard for weeks, where they are reduced chemically and mechanically, form soluble toxic salts, and cause characteristic signs of Pb intoxication--especially lethargy and emaciation (Street 1983). At least 2% of all North American waterfowl--or about 2 million ducks and geese (Lumeij 1985)--die each year as a direct result of ingestion of Pb shot (Bellrose 195!). These deaths contribute to the decline of some species, such as the canvasback, *Aythya valisineria* (Dieter 1979), pintail, *Anas acuta* (White and Stendell 1977), and black duck, *Anas rubripes* (Pain and Rattner 1988). Up to 7X more waterfowl died from Pb toxicosis as a result of ingesting spent pellets than from wounding by hunters (Zwank et al. 1985). In addition, Pb-poisoned waterfowl show delayed mortality from Pb-induced starvation, are readily captured by predators, are susceptible to disease, and reproduce poorly (Dieter 1979). Susceptibility is markedly influenced by species, by the number and size of shot ingested, and by the types of foods eaten (White and Stendell 1977). Swans are among the more vulnerable waterfowl. In England, Pb poisoning through the ingestion of discarded Pb fishing sinkers is the major cause of death in the mute swan, *Cygnus olor* (Birkhead 1983); for all species of swans in England, about half died as a direct result of Pb poisoning (Demayo et al. 1982). In Washington State, 30% of the endangered trumpeter swans (*Cygnus buccinator*) found dead had died of Pb poisoning from ingestion of Pb shot (Kendall and Driver 1982). Lead toxicosis caused by ingestion of spent shot and other Pb objects has also been reported for sandhill crane, *Grus canadensis* (Windingstad et al. 1984); Canada goose, *Branta canadensis* (Szymczak and Adrian 1978); mourning dove, *Zenaidura macroura* (Locke and Bagley

1967); and wild turkey, *Meleagris gallopavo* (Stone and Butkas 1978). Secondary poisoning has been documented in at least five species of raptors that ate food containing Pb shot (especially hunter-wounded animals): Andean condor, *Vultur gryphus* (Locke et al. 1969); bald eagle, *Haliaeetus leucocephalus* (Pattee and Hennes 1983); honey buzzard, *Pernis apivorus* (Lumeij et al. 1985); king vulture, *Sarcorhampus papa* (Decker et al 1979); and California condor *Gymnogyps californianus* (Janssen et al. 1986).

The availability of Pb-based paints, discarded oil filters, used crankcase oil, Pb storage batteries, or pastures contaminated by industrial lead operations make Pb one of the most common causes of accidental poisoning in domestic animals (Demayo et al. 1982). Cattle and horses in the vicinity of a Pb smelter in California developed signs of Pb poisoning, and many died between 1880, when the smelter opened, and 1971, when the smelter closed (Burrows 1981). Of the mules used in the early mining of Pb, all died during their first year of service (Burrows 1981). Lead toxicosis has been reported in buffalos and cattle in India after they ate green fodder near a factory that recycled Pb from old batteries (Kwatra et al. 1986). Total milk yield declined sharply, and stillbirths and abortions increased significantly in cattle that ingested Pb-contaminated hay; the field from which the hay had been cut had a history of use for clay pigeon shoots and contained an estimated 3.6 tons of Pb shot pellets (Frape and Pringle 1984). In sheep grazing in areas near Pb mines, the frequency of abortions was high, and the learning behavior of the lambs was impaired (Demayo et al. 1982). Many species of zoo animals, including monkeys, fruit-eating bats, and parrots, have been fatally poisoned from ingestion of flaking Pb-based paint on the walls and bars of their cages (NRC 1973). Ingestion of Pb-based paint chips was one cause of epizootic mortality of fledgling Laysan albatross, *Diomedea immutabilis*, at Midway Atoll in 1983 (Sileo and Fefer 1987). At present, there is no known dietary requirement for Pb in domestic animals, nor has it been shown unequivocally that Pb plays any beneficial role (NRCC 1973). On the contrary, Pb demonstrably and adversely affects weight, survival, behavior, litter size, and skeletal development (Tsuchiya 1979), and induces teratogenic and carcinogenic responses in some species of experimental animals (NRCC 1973; EPA 1980).

Lead is not essential for plants, and excessive amounts can cause growth inhibition, as well as reduced photosynthesis, mitosis, and water absorption (Demayo et al. 1982). The decline of some European spruce forests has been attributed to excessive concentrations of atmospheric Pb (Backhaus and Backhaus 1986).

Lead is toxic to all phyla of aquatic biota, though effects are modified significantly by various biological and abiotic variables (Wong et al. 1978). Wastes from Pb mining activities have severely reduced or eliminated populations of fish and aquatic invertebrates, either directly through lethal toxicity or indirectly through toxicity to prey species (Demayo et al. 1982). Health advisories warning anglers against eating Pb-contaminated fish have been posted in Missouri (Schmitt and Finger 1987). The significant increases in Pb concentration shown by marine corals between 1954 and 1980 were representative of the increases noted in other biota as a direct result of increased global Pb availability during that period (Dodge and Gilbert 1984).

In this report, I summarize available data on lead in the environment, with emphasis on fishery and wildlife resources, and review current recommendations for the protection of sensitive species. This account is part of a continuing series of brief, reviews prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service.

SOURCES AND USES

Lead is a comparatively rare metal, with an average abundance in the earth's crust of 16 mg/kg (EPA 1980); it is also a major constituent of more than 200 identified minerals, of which only 3 are sufficiently abundant to form mineral deposits (EPA 1980): galena (PbS), angelesite ($PbSO_4$), and cerusite ($PbCO_3$). Galena, the primary form of Pb in the natural state, is often associated with sphalerite (ZnS), pyrite (FeS_2), chalcopyrite ($CuFeS_2$), and other sulfur salts (May and McKinney 1981). Most (88 %) of the domestic primary Pb production originates from stratabound deposits in southeastern Missouri, another 8% from Idaho's Couer D'Alene district, and the rest from deposits in Colorado and Utah. Primary Pb is smelted and refined at plants in Texas, Montana, Nebraska, Missouri, and Idaho. Scrap Pb, or secondary Pb, accounted for about half the domestic consumption in 1978; by 1980, more Pb was produced from secondary sources than from domestic ores (May and McKinney 1981).

About 4 million tons of Pb are refined annually worldwide (Table 1) Domestic Pb consumption is 1.3 million tons annually, of which about half is used in storage battery manufacture and, until recently, about 20% in the manufacture of gasoline antiknock additives such as tetramethyllead (TML) and tetraethyllead (TEL) (Table 2). Pigments and ceramics account for about 6% of consumption, and metallic Pb products, Pb-containing alloys, paint, solder, and ammunition constitute other minor use categories (EPA 1980). Lead enters the atmosphere mainly through smelter emissions, primarily as $PbSO_4$ and PbO- $PbSO_4$, and through vehicle emissions, which include unburned Pb, TEL, TML, and various Pb halides, sulfates, phosphates, and oxides (Harrison and Laxen 1981).

Lead and its compounds have been known to man for about 7,000 years, and Pb poisoning has occurred for at least 2,500 years (Barth et al. 1973). In Egypt, between 5,000 and 7,000 BC, Pb was used for glazing pottery, solder, ornaments, net sinker, anchors, caulking, coins, weights, aqueducts, piping, and cooking utensils (Nriagu 1978a). The biocidal properties of Pb were familiar to the ancient Egyptians, and Pb salts were sometimes used by them for homicidal purposes (De Michele 1984). Lead encephalopathy (inflammation of the brain) has been recognized since 400 BC among workers in the Pb trades; initial symptoms are dullness, irritability, ataxia, headaches, memory loss, and restlessness. These symptoms often progressed to delirium, mania, coma, convulsions, and sometimes death. The same general effects were described in young children and infants, among which mortality was sometimes 40% (EPA 1980). Extensive use of Pb by the Romans, circa 500, in pipes for water transport, in cosmetics, and as a wine sweetener (Harrison and Laxen 1981), is estimated to have increased environmental Pb levels to about 5X the existing background levels (Eisenreich et al. 1986). The decline of the Roman Empire may have been hastened by endemic lead poisoning--a theory supported by residue data showing high Pb concentrations in bones and remains of Roman aristocrats (Nriagu 1978a)--perhaps through ingestion of excessive amounts of wine laced with Pb (De Michele 1984). After the fall of the Romans, the use of Pb declined sharply. In the 14th century, gunpowder was introduced into Europe and was the impetus for the development of a weapon that fired a malleable metal pellet: a lead shot (EPA 1979). Otherwise, the metal's resistance to corrosion led to its use as lead sheets applied as roofing for cathedrals and as protective encasement of underground pillars. In 1721, the first Pb mine was established in the New World by English settlers at Falling Creek, Virginia, primarily to supply bullets and shot (EPA 1979). By 1750, European and British Pb smelting operations were flourishing (Nriagu 1978a). In 1763, Pb deposits in southeastern Missouri were permanently opened (EPA 1979). The 18th century's Industrial Revolution produced an estimated 10-fold increase in existing Pb background levels (Eisenreich et al. 1986). In the late 1700's, symptoms of acute Pb poisoning recorded among industrial workers were called "Mill Reek" or "Devonshire Colic" (NRCC 1973). Lead poisoning was frequently recorded among U.S. lead miners in 1870-1900, especially in Utah, Colorado, and New Mexico. By 1880, the United States had surpassed Germany and Spain in the mining and refining of Pb, and has continued as the leader in the output of refined Pb (EPA 1979). Air pollution from combustion of leaded gasoline containing TEL rose in the 1920's (NRCC 1973). In the mid-1940's, atmospheric Pb concentrations increased sharply due to massive increases in Pb emissions from automobiles; since then, increased Pb emissions to the atmosphere have matched trends in gasoline Pb content and consumption (Eisenreich et al. 1986; Smith et al. 1987). In 1957, the United States was overtaken by Australia and the USSR in domestic mine production of Pb; however, in 1967, the opening of the "New Lead Belt" in Missouri revived mining in the United States, and subsequently Pb was produced at the annual rate of 450,000 to 550,000 metric tons (EPA 1979). In 1975, the United States was again the leading Pb producer from mine sources, accounting for 16% of the world total; at that time, about 70% of the world Pb production came from the USA, the USSR, Australia, Canada, Peru, Mexico, China, Yugoslavia, and Bulgaria (Tsuchiya 1979,). In 1986, world mine production of lead was 2,352,000 tons of which USA mine production was 353,000 tons, or 15% of the world total, and production in Missouri was 308,000 tons, or 87% of the USA total (personal communication, R. L. Amistadi, Doe Run Company, St. Louis, Missouri).

Table 1. World Pb production, consumption, and principal end uses (modified from Harrison and Laxen 1981; Demayo et al. 1982).

Production consumption, and use	Metric tons, in thousands
Production, 1978	
Mined Pb	3,625
Refined Pb	4,202
Consumption	
1977	2,995
1980	3,801
Principal end uses of refined Pb	
1977	
Storage batteries	1,478
Pigments and chemicals	369
Tetraalkyllead	292
Cable covering	216
Pipe and sheeting	160
Other	480
1980	
Storage batteries	1,330
Tetraethyllead	380
Cable covering	380
Solder	380
Litharge	190
Building construction	190
Caulking	190
Other	760

Table 2. Use patterns for Pb in selected countries (from EPA 1979).

	Thousands of metric tons (percent)					
Use	USA		Europe[a]		Japan	
Storage batteries	613	(47)	392	(34)	93	(40)
Cable sheathing	14	(1)	145	(13)	16	(7)
Pigments and chemicals	303	(23)	294	(26)	62	(27)
Alloys	75	(6)	50	(4)	15	(7)
Ammunition	66	(5)	b	(-)	b	(-)
Other	226	(18)	267	(23)	44	(19)
Total	1,297		1,148		230	

[a] France, West Germany, Italy, UK

[b] Not reported.

CHEMICAL PROPERTIES

Elemental Pb is a bluish-gray, soft metal of atomic weight 207.19 and atomic number 82; it melts at 327.5 C, boils at 1,749 C, and has a density of 11.34 g/cm^3 at 25^{o}C. Metallic Pb is sparingly soluble in hard, basic waters to 30 ug/l, and up to 500 ug/l in soft, acidic waters. Lead has four stable isotopes: Pb-204 (1.5%), Pb-206 (23.6%), Pb-207 (22.6%), and Pb-208 (52.3%). Of its 24 radioactive isotopes, two (Pb-210, Tb 1/2 of 22 years; Pb-212, Tb ½ of 10 hours) have been used in tracer experiments. Lead occurs in four valence states: elemental (Pb^o), monovalent (Pb^+), divalent (Pb^{2+}), and tetravalent (Pb^{4+}); all forms are environmentally important, except possibly Pb^+. In nature, lead occurs mainly as Pb^{2+}; it is oxidized to Pb^{4+} only under strong oxidizing conditions, and few simple compounds of Pb^{4+} other than PbO_2 are stable. Some Pb salts are comparatively soluble in water (lead acetate, 443 g/l; lead nitrate, 565 g/l; lead chloride, 9.9 g/1), whereas others are only sparingly soluble (lead sulfate, 42.5 mg/l; lead oxide, 17 mg/l; lead sulfide, 0.86 mg/1); solubility is greatest at elevated temperatures in the range 0 to 40° C. Of the organoleads, tetraethyllead (TEL) and tetramethyllead (TML) are the most stable and the most important because of their widespread use as antiknock fuel additives. Both are clear, colorless, volatile liquids, highly soluble in many organic solvents; however, solubility in water is only 0.18 mg/l for TEL, and 18.0 mg/l for TML. Boiling points are 199^o C for TEL and 110 C for TML; both undergo photochemical degradation in the atmosphere to elemental Pb and free organic radicals, although the fate of automotive organoleads has yet to be fully evaluated. Additional information on the general chemistry of lead and its compounds was reviewed by NRCC (1973), Boggess (1977), Nriagu (1978a), EPA (1979, 1980), Tsuchiya (1979), Harrison and Laxen (1981), and Demayo et al. (1982).

Lead chemistry is complex. In water, for example, Pb is most soluble and bioavailable under conditions of low pH, low organic content, low concentrations of suspended sediments, and low concentrations of the salts of calcium, iron, manganese, zinc, and cadmium. Accordingly, solubility of lead is low in water, except in areas of local point source discharges (Harrison and Laxen 1981; Scoullos 1986). Lead and its compounds tend to concentrate in the water surface microlayer (i.e., the upper 0.3 mm), especially when surface organic materials are present in thin films (Demayo et al. 1982). Organolead compounds are generally of anthropogenic origin and are found mostly in the aquatic environment as contaminants; however, some organolead complexes form naturally, and their rate of formation may be affected by man-made organoleads (Nriagu 1978a). In surface waters, Pb exists in three forms: dissolved labile (e.g., Pb^{2+}, $PbOH^+$, $PBCO_3$), dissolved bound (e.g., colloids or strong complexes), or as a particulate (Benes et al. 1985). The labile forms represent a significant part of the Pb input from washout of atmospheric deposits, whereas particulate and bound forms were common in urban runoff and ore-mining effluents (Benes et al. 1985). The solubility of Pb compounds in water is pH dependent, and ranges from about 10 g Pb/1 at pH 5.5, to less than 1 ug Pb/1 at pH 9.0 (EPA 1980); little detectable Pb remains in solution at pH >8.0 (Prause et al. 1985). At pH 6.5 and water alkalinity of 25 mg $CaCO_3$/1, elemental Pb is soluble to 330 ug/l; however, Pb under the same conditions is soluble to 1,000 ug/l (Demayo et al. 1982). In acidic waters, the common forms of dissolved Pb are salts of $PbSO_4$ and $PbCl_4$, ionic Pb, cationic forms of lead hydroxide, and (to a lesser extent) the ordinary hydroxide $Pb(OH)_2$. In alkaline waters, common species include the anionic forms of Pb carbonate and hydroxide, and the hydroxide species present in acidic waters (NRCC 1973). Unfortunately, the little direct information available about the speciation of Pb in natural aqueous solutions has seriously limited our understanding of Pb transport and removal mechanisms (Nriagu 1978a).

Most Pb entering natural waters is precipitated to the sediment bed as carbonates or hydroxides (May and McKinney 1981). Lead is readily precipitated by many common anions; desorption and replacement by other cations is extremely slow (Boggess 1977). In some acidic lakes, the deposition of particulate Pb was strongly correlated with the deposition of aluminum and carbon, especially during periods of increasing pH (White and Driscoll 1985). Precipitation of sparingly soluble Pb compounds is not a primary factor controlling the concentration of dissolved Pb in stream waters. Migration and speciation of Pb was strongly affected by water flow rate, increasing flow rate resulting in increased concentrations of particulate and labile Pb and a decrease in bound forms. At low stream flow, Pb was rapidly removed from the water column by sedimentation (Benes et al. 1985).

In the sediments, Pb is mobilized and released when the pH decreases suddenly or ionic composition changes (Demayo et al. 1982). However, there was no significant release of Pb from dredge spoils suspended in estuarine waters of different salinities for 4 weeks (Prause et al. 1985). Some Pb^{2+} in sediments may be transformed to tetraalkyllead compounds, including TML, through chemical and microbial processes. There is also the possibility of methylation of ionic Pb in vivo by fish and other aquatic biota, but the mechanisms are unclear (May and McKinney 1981). Methylation of Pb in sediments was positively related to increasing temperatures, reduced pH, and microbial activity, but seemed to be independent of Pb concentration (Demayo et al. 1982). In general, the concentration of tetraalkylleads in sediments is low, representing less than 10% of total Pb (Chau et al. 1980).

MODE OF ACTION

Lead modifies the function and structure of kidney, bone, the central nervous system, and the hematopoietic system and produces adverse biochemical, histopathological, neuropsychological, fetotoxic, teratogenic, and reproductive effects (Boggess 1977; Nriagu 1978b; De Michele 1984). Inorganic Pb absorbed into the mammalian body enters the bloodstream initially and attaches to the red blood cell. There is a further rapid distribution of the Pb between blood extracellular fluid and other storage sites that is so rapid that only about half the freshly absorbed Pb remains in the blood after a few minutes. The storage sites for Pb are uncertain, although they are probably in soft tissues as well as bone; the half-time residence life (Tb 1/2) of inorganic Pb is estimated to be 20 days in blood, 28 days in whole body, and 600 to 3,000 days in bone (Harrison and Laxen 1981). Inorganic Pb in the environment can be biologically methylated to produce alkyllead compounds (Walsh and Tilson 1984). Bile is an important route of excretion; ingested Pb probably proceeds sequentially from gut, to blood, to bone and soft tissue, and by way of the bile to small intestine and fecal excretion (De Michele 1984).

Tetraalkyllead mode of action differs from that of inorganic Pb. Although initial entry is still into the bloodstream, the Pb is evenly distributed between blood plasma and the red blood cells. Tetraalkylleads are lost rapidly from the bloodstream, although some reappear in 5 to 10 hours associated exclusively with the red blood cells, probably as trialkyllead, though a fraction may be converted to inorganic Pb. The organoleads concentrate in liver, and it is there that tetraalkyllead is probably converted to trialkyllead. Otherwise, the Pb is widely dispersed throughout the body with Tb 1/2 values of 200 to 350 days (Harrison and Laxen 1981). Tetraethyllead, by virtue of its liposolubility, is rapidly accumulated in nonbony tissues, particularly the brain, where the onset of signs of poisoning is rapid (Nriagu 1978b). Short-term repeated exposures of rats (*Rattus* spp.) to TEL results in a neurotoxic syndrome consisting of altered reactivity to noxious stimulation through disruption of forebrain-area function (Hong et al 1983). Several fish species metabolize tetraalkylleads to trialkyllead compounds by way of their mixed function oxidase system (Wong et al. 1981). The trialkyllead derivatives are considered responsible for the toxicity of the parent compound (Walsh and Tilson 1984). Trialkylleads and dialkylleads rapidly traverse biological membranes in bird eggs and accumulate in the yolk and developing embryo (Forsyth et al. 1985). At present, the organolead mode of action is poorly understood, but organolead compounds are known to inhibit amino acid transport, uncouple oxidative phosphorylation, and inhibit cerebral glucose metabolism (Hong et al. 1983).

Biochemically, Pb exerts deleterious effects on hematopoiesis through derangement of hemoglobin synthesis, resulting in a shortened life span of circulating erythrocytes, often resulting in anemia. Two essential enzymes in heme formation that are extremely sensitive to Pb are delta aminolevulinic acid dehydratase (ALAD), which catalyzes the dehydration of delta amino levulinic acid (ALA) to form porphobilinogen (PBG), and ferrochelatase (= heme synthetase), which catalyzes the insertion of Fe^{2+} into protoporphyrin IX (PP). This second reaction requires the presence of glutathione and ascorbic acid. Some of the intermediates in heme follow sequentially: ALA, PBG, uroporphyrinogen III, coproporphyrinogen III, protoporphyrinogen IX, and PP. It is now well established that ALAD and ferrochelatase are the most sensitive biochemical indicators of Pb exposure, the net result being lowered ALAD activity and elevated PP activity (Barth et al. 1973; Nriagu 1978b; EPA 1979, 1980; Tsuchiya 1979; Harrison and Laxen 1981; Hoffman et al. 1981; De Michele 1984; Schmitt et al. 1984; Lumeij 1985).

Inhibition of blood ALAD activity after exposure to Pb has been documented in many species of freshwater and marine teleosts (Hodson 1976; Hodson et al. 1977, 1980; Johansson-Sjobeck and Larsson 1979; Krajnovic-Ozretic and Ozretic 1980; Demayo et al. 1982; Schmitt et al. 1984; Haux et al. 1986), in the freshwater cladoceran, *Daphnia magna* (Berglind et al. 1985), in ducks, quail, doves, swallows, raptors, and songbirds

(Finley et al. 1976.; Dieter and Finley 1978; Dieter 1979; Hoffman et al. 1981; Franson and Custer 1982; Kendall et al. 1982; Kendall and Scanlon 1982; Eastin et al. 1983; Franson et al. 1983; Hoffman et al. 1985a, 1985b; Beyer et al. 1988), and in humans, sheep, mice, rats, rabbits, and calves (Barth et al. 1973; Boggess 1977; Nriagu 1978b; Tsuchiya 1979; Hejtmancik et al. 1982; Hayashi 1983; Peter and Strunc 1983; Schlick et al. 1983; Gietzen and Wooley 1984; Zmudzki et al. 1984). Lead-induced ALAD inhibition has been recorded not only in blood, but also in brain, spleen, liver, kidney, and bone marrow (Johansson-Sjobeck and Larsson 1979; Hoffman et al. 1981, 1985a, 1985b; Schlick et al. 1983; Friend 1985). Time for ALAD recovery to normal levels is dose dependent, organ specific, and usually directly correlated with blood Pb concentrations (Finley et al. 1976; Hodson et al. 1977; Dieter 1979; Hayashi 1983; Friend 1985). ALAD activity levels in Pb-stressed teleosts were normal 3 to 11.7 weeks postadministration (Hodson et al. 1977; Johansson-Sjobeck and Larsson 1979; Krajnovic-Ozretic and Ozretic 1980; Demayo et al. 1982); this range was 2 to 14 weeks in birds (Dieter and Finley 1978; Kendall et al. 1982; Kendall and Scanlon 1982; Friend 1985), and 3 to 12 weeks in mammals (Barth et al. 1973; Schlick et al. 1983). The physiological significance of depressed blood ALAD activity levels, except perhaps as an early indicator of Pb exposure, is debatable. Aside from a few instances of moderate anemia in workers at lead smelters, other abnormalities noted were not regarded as serious (Barth et al. 1973 Lead-induced depression in ALAD activity in mallard (*Anas platyrhynchos* ducklings and ring-necked pheasant (*Phasianus colchicus*) chicks was not associated with signs of overt toxicity (Eastin et a . 1983); a similar case is made for Pb-stressed domestic chickens (*Gallus* sp.) showing 98% reduction in ALAD activity (Franson and Custer 1982), and for American kestrel (*Falco sparverius*) showing an 80% reduction (Franson et al. 1983). Birds may be more sensitive than mammals to Pb-induced depressions in blood ALAD activity (Dieter et al. 1976). In ducks, for example, inhibition of ALAD would be more harmful than a comparable depression in mammals, for three reasons (Dieter et al. 1976). First, metabolic activity is greater in nucleated duck erythrocytes than in human erythrocytes. Second, ducks require porphyrin synthesis not only for hemoglobin production (as in humans), but also for production of respiratory heme-containing enzymes. Finally, the half-life of erythrocytes is shorter in ducks than in humans: 40 days vs. 120 days.

Elevated blood protoporphyrin IX activity resulting from Pb-inhibition of heme synthetase has been documented for humans and small mammals (Peter and Strunc 1983) and for many species of birds (Anders et al. 1982; Carlson and Nielsen 1985; Friend 1985; Franson et al. 1986; Beyer et al. 1988); recovery to normal levels occurs in a Pb-free environment in 2 to 7 weeks. Franson et al. (1986) endorsed the blood protoporphyrin IX technique instead of ALAD as a means of measuring Pb stress because of its comparative simplicity and lower cost.

Other chemical changes that have been observed as a result of Pb exposure include increased serum creatinine and serum alanine aminotransferase in birds, suggestive of kidney and liver alterations (Hoffman et al. 1981); changes in potassium, chloride, and glucose metabolism in rainbow trout, *Salmo gairdneri* (Haux and Larsson 1982); and a decrease in brain acetylcholinesterase activity in rats (Gietzen and Wooley 1984).

In kidney, Pb tends to accumulate in the proximal convoluted tubule cells of the renal cortex, producing morphological changes such as interstitial fibrosis, edema, and acid-fast intranuclear inclusion bodies, as well as biochemical changes (Locke et al. 1966; Boggess 1977; Nriagu 1978b; EPA 1980; De Michele 1984). Renal intranuclear inclusion bodies occurred in 83% of mallards experimentally poisoned by dietary Pb acetate or Pb shot (Beyer et al. 1988); similar results have been reported in other species of birds (Clemens et al. 1975; Anders et al. 1982) and in primates, cattle, and bats (Zook et al. 1972; Osweiler and Van Gelder 1978; Colle et al. 1980; Tachon et al. 1983).

In the cladoceran *Daphnia magna,* about 90% of the total body Pb burden is adsorbed to the exoskeleton (Berglind et al. 1985). In animals with a vertebral column, total amounts of Pb tend to increase with age; by far the most Pb is bound to the skeleton, especially in areas of active bone formation (Barth et al. 1973; Tsuchiya 1979; EPA 1980; Hejtmancik et al. 1982; Mykkanen et al. 1982; Peter and Strunc 1983; De Michele 1984; Eisler 1984; Berglind et al. 1985; Marcus 1985). The retention of Pb stored in bone pools poses a number of difficulties for the usual multicompartmental loss-rate models. Some Pb in bones of high medullary content, such as the femur and sternum, have relatively long retention times--i.e., Tb 1/2 of >20 years in humans--whereas Pb stored in bones of low medullary content have Tb 1/2 values of 20 to 200 days, similar to the values for Pb in soft tissues and blood (Tsuchiya 1979; Marcus 1985). In birds, medullary bone undergoes sequences of bone formation and destruction associated with the storage and liberation of calcium during eggshell formation, indicating that sex and physiological condition primarily influence Pb kinetics in avian bone (Finley

and Dieter 1978). Marcus (1985) endorsed the use of diffusion models based on the exchange of Pb between blood in canaliculi and the crystalline bone of the osteon to account for retention and bioavailability. More research is needed on the role of bone in Pb kinetics.

Lead damages nerve cells and ganglia, and alters cell structure and enzyme function. Axonal degenerative changes, especially in neuronal cell bodies, were recorded in Pb-poisoned freshwater snails (*Viviparous ater*), leading to altered protein synthesis (Fantin et al. 1985). Mallards dosed orally with Pb shot developed demyelinating lesions in vagal, branchial, and sciatic nerves, and showed vascular damage in the cerebellum; lesions were similar to those in Pb-intoxicated guinea pigs (*Cavia* sp.), rats, and guinea hens, *Gallus* sp. (Hunter and Wobeser 1980). Crop stasis in birds, which is characterized by paralysis of the alimentary tract, impaction of food in the gizzard and proventriculus, and regurgitation of crop fluid, has been produced by Pb shot or Pb acetate solutions. Lead induces crop dysfunction by acting either directly on the smooth muscle or on associated nerve plexuses of crop tissue, depending on the route of administration (Clemens et al. 1975; Boyer et al. 1985; Boyer and Di Stefano 1985). Mammals, including humans, undergo similar alimentary distress following intakes of lead (Boyer et al. 1985).

Effects of Pb on the nervous system are both structural and functional, involving the cerebellum, spinal cord, and motor and sensory nerves; the result may be deterioration of intellectual, sensory, neuromuscular, and psychological functions (Nraigu 1978b). The pathogenesis of Pb-induced injury to the nervous system is poorly understood, but may be mediated through vascular damage, the direct action of Pb on neurons, or alterations in porphyrin metabolism (Hunter and Wobeser 1980). Retarded brain growth in prenatal guinea pigs has been recorded at subclinical levels of Pb (i.e., at concentrations producing no elevation in blood Pb and no change in body weight), and this effect is potentiated at temperatures of 42^{o} C (Edwards and Beatson 1984). Lead may cause a transient disturbance in the blood-brain barrier during early postnatal growth of rats. This effect is associated with the presence of hemorrhagic lesions, suggesting focal damage to the vessels as an important event in the pathogenesis of Pb encephalopathy to suckling rats (Sundstrom et al. 1985). Brain histopathology has been recorded in Pb-poisoned chickens (Narbaitz et al. 1985) and cattle (Osweiler and Van Gelder 1978). Brain Pb concentrations are usually among the lowest in body organs, but the brain is one of the main sites of action. During chronic Pb poisoning, distribution of Pb in the brain is positively related to both dose and duration of exposure; preferential accumulation is in the hippocampus area of the brain. Significant amounts of Pb persisted in rat brain tissue up to 4 weeks after the withdrawal of Pb treatment (Collins et al. 1982). The role of organolead compounds in hippocampal function is largely unknown (Czech and Hoium 1984).

Absorption and retention of Pb from the gastrointestinal tract, the major pathway of intake, varies widely because of the age, sex, and diet of the organism. Diet is the major modifier of Pb absorption and of toxic effects in many species of domestic and laboratory animals, waterfowl, and aquatic organisms. In fact, the lack of certain major minerals in the diet often affected toxicity and storage of Pb in tissue more than did doubling the dosages of Pb in the diet (Levander 1979). Dietary deficiencies in calcium, zinc, iron, vitamin E, copper, thiamin, phosphorus, magnesium, fat, protein, minerals, and ascorbic acid increased Pb absorption and its toxic effects (Longcore et al. 1974b; Forbes and Sanderson 1978; Levander 1979; Sleet and Soares 1979; Colle et al. 1980; EPA 1980; Hodson et al. 1980; De Michele 1984; Stone and Fox 1984; Zmudzki et al. 1983, 1984; Carlson and Nielsen 1985; Gilmartin et al. 1985). Toxic effects of Pb-stressed fauna also were exacerbated when animals were fed diets containing excess cadmium, lactose, ethylenediaminetetraacetic acid, zinc, fat, protein, sodium citrate, ascorbate, amino acids, vitamin D, copper, mercury, fiber content, and nitrilotriacetic acid (Clemens et al. 1975; Forbes and Sanderson 1978; Nriagu 1978b; Levander 1979; EPA 1980; Krajnovic-Ozretic and Ozretic 1980; Burrows and Borchard 1982; Hamir et al. 1982; Zmudzki et al. 1983, 1984; De Michele 1984; Carlson and Nielson 1985). Protection against various toxic effects of ingested Pb was provided by measured dietary supplements of calcium, iron, zinc, ascorbic acid, and vitamin E (Krajnovic-Ozretic and Ozretic 1980; Gilmartin et al. 1985). Many other conditions affect Pb absorption, including size of Pb particle (EPA 1980; Hamir et al. 1982), type of Pb compound ingested (EPA 1980), presence of other compounds that act synergistically (Barth et al. 1973) or antagonistically (Luoma and Bryan 1978), and dosage (Finley and and Dieter 1978). For example, smaller Pb particles, <180 um in diameter, were absorbed from the intestinal tract up to 7 times more rapidly than larger particles of 180 to 250 um (EPA 1980). However, when large pieces of Pb are ingested, such as lead shot, these may lodge in the gastrointestinal tract, dissolve slowly, and cause Pb poisoning (Nriagu 1978b). Also, lead phthalates were absorbed more rapidly than carbonates, acetates,

sulfides, and naphthanates, in that sequence (EPA 1980). It is evident that all of these variables, as well as diet, need to be considered in risk assessment of Pb.

BACKGROUND CONCENTRATIONS

GENERAL

Lead concentrations were usually highest in ecosystems nearest Pb mining, smelting, and refining activities; Pb storage battery recycling plants; areas of high vehicular traffic; urban and industrialized areas; sewage and spoil disposal areas; dredging sites; and areas of heavy hunting pressure. In general, Pb does not biomagnify in food chains. Older organisms usually contain the greatest body burdens, and Pb accumulations are greatest in bony tissues. It seems that resources that are now at high risk (i.e., increased mortality, reduced growth, or impaired reproduction) from Pb include the following: migratory waterfowl that congregate at heavily-hunted areas; raptors that eat hunter-wounded game; domestic livestock near smelters, refineries, and recycling plants; wildlife that forage extensively near heavily traveled roads; aquatic life in proximity to mining activities, Pb arsenate pesticides, metal finishing industries, lead alkyl production, and Pb aerosol fallout; and crops and invertebrates growing or living in Pb-contaminated soils. Data on background concentrations in nonbiological and living resources are cited extensively in Bernhard and Zattera (1975), Nriagu (1978a,b), Wong et al. (1978), Branica and Konrad (1980), Jenkins (1980), Eisler (1981), Harrison and Laxen (1981), and Demayo et al. (1982).

NONBIOLOGICAL SAMPLES

Average Pb concentrations in nonbiological materials worldwide were much higher in sediments (47,000 ug/kg), soils (16,000), and sediment interstitial waters (36) than in atmospheric and other hydrospheric compartments (Table 3). Most of the lead discharged into surface waters is rapidly incorporated into suspended and bottom sediments, and most will ultimately be found in marine sediments (Harrison and Laxen 1981). Sediments now constitute the largest global reservoir of Pb; sediment interstitial waters and soils constitute secondary reservoirs (Table 3).

Lead concentrations were elevated in certain nonbiological materials as a result of nonhunting human activities and natural processes (Table 4). In sediments, Pb concentrations ranged from 3 mg/kg in carbonate marls off the Florida coast to more than 11,000 mg/kg at Sorfjord, Norway, the site of massive discharges of Pb-containing industrial and domestic wastes (Nriagu 1978a). Lead contaminates sediments from sources as diverse as steelworks, shipyards, crude oil refineries, cement and ceramic factories, Pb storage battery recycling plants, and heavy traffic (Scoullos 1986). Mining activities are also important. High concentrations of Pb were measured in sediments (up to 2,200 mg/kg) and detritus (up to 7,000 mg/kg) of the Big River in southeastern Missouri (Czarneski 1985). The Big River drains what was once the largest Pb-mining district in the world; commercial mining was extensive between the early 1700's and 1972. During this period more than 200 metric tons of tailings accumulated within the Big River watershed as a result of seepage from tailings ponds, from erosion of tailings piles on the banks, and through accidental discharges (Niethammer et al. 1985).

Table 3. Amounts of lead in global reservoirs (modified from Nriagu 1978a).

Reservoir	Concentration (µg/kg)	Total Pb in pool (millions of metric tons)
Atmosphere	0.0035	0.018
Lithosphere		
Soils	16,000	4,800
Sediments	47,000	48,000,000
Hydrosphere		
Oceans	0.02	27.4
Sediment interstitial waters	36	12,000
Lakes and rivers	2	0.061
Glaciers	0.003	0.061
Groundwater	20	0.082
Biosphere		
Land biota		
Living	100	0.083
Dead	3,000	2.1
Marine biota		
Living	500	0.0008
Dead	2,500	2.5
Freshwater biota		
All	2,500	0.825

Table 4. Lead concentrations in selected nonbiological materials.

Material (units)	Concentration[a]	Reference[b]
Air (µg/m^3)		
Nonurban areas	0.1	EPA 1980
Urban areas	(0.3–2.5)	NRCC 1973
Metropolitan areas	(2–10)	EPA 1980
Rural roads	6	NRCC 1973
Heavy traffic	40	
Near industrial sources	May exceed 1,000	EPA 1980
Rain (µg/L)		
Minnesota		
1979		
Rural	6	Eisenreich
Urban	29	et al. 1986

1983		
Rural	2	
Urban	4	
Atmospheric deposition (g/ha)		
New Jersey Pine Barrens		
1971–79	350	Turner et al. 1985
1980–82	140	
Ice (µg/L)		
Greenland		
800 BC	0.001	NRCC 1973
1750	0.01	
1940	0.07	
1973	>0.2	
Soils (mg/kg dry weight)		
Near Pb smelter		
Missouri	128	Burrows 1981
British Columbia	>1,000	
Distance from highway		
2 m	500	Krishnayya and
20 m	312	Bedi 1986
40 m	112	
60 m	46	
Near metal smelter	(1,200–2,700)	Beyer et al. 1985
Control site	(99–490)	
Near factory	(210–485)	Edwards and Clay 1977
Reference site (1,000 m distant)	(10–30)	
Worldwide	10 (2–200)	Demayo et al. 1982
USA	20 (10–700)	
Forest litter (g/ha)		
Vermont	20,000	Friedland and Johnson 1985
New Jersey	7,600	Turner et al. 1985
Water (µg/L)		
Egypt, Nile River		
Industrialized area	9.5	Fayed and Abd-El-Shafy 1985
Sweden		
Polluted lake		
Shallow water	3.3 (1.5–4.5)	Haux et al. 1986
Deep water	(8–41)	
Reference lake	0.1	
Greece, seawater		
Industrialized area	(2–5.5)	Scoullos 1986
USA		
Maine		

Pre-snowmobile	4.1	Adams 1975
Ice-out	135	
Nationwide		
Rivers	5 (0.6–120)	Demayo et al. 1982
Streams	23	
England		
Coastal sea water	Max. 2.3	
Offshore	(0.02–0.03)	
Solids entering surface waters (mg/kg dry weight)		
Street dust		
Urban	(1,000–4,000)	Harrison and
Rural	440	Laxen 1981
Highway runoff		
Suspended sediments	(3,100–5,800)	
Settleable solids	16,000	
Sewage sludge	(100–1,400)	
Suspended sediments in mineralized areas	(1,000–8,000)	
Integrated study (µg/kg		
Tennessee stream		
Water	(0.01–0.019)	Demayo et al. 1982
Dissolved solids	(30–84)	
Coarse particles	(124–653)	
Colloidal particles	(62–2,820)	
Sediments (mg/kg dry weight)		
Egypt, Nile River		
Industrialized area	Max. 1,800	Fayed and Abd-El-Shafy 1985
Greece		
Near major industries	(500–600)	Scoullos 1986
Several km distant	40	
Preindustrial levels	10	
Norway		
Sorfjord	Max. 11,000	Nriagu 1978a
Sweden		
Polluted lake	(2,000–2,500)	Haux et al. 1986
Reference lake	110	
USA		
Chesapeake Bay, 1979–81	(1–134)	Di Giulio and Scanlon 1985
Upper Mississippi River	13 (0.4–86)	Wiener et al. 1984
Southeastern Missouri, Big River, 1979–1981		
Sediments	(1,400–2,200)	Czarneski 1985

Organic detritus	(800–7,000)	
Florida	3	Nriagu 1978a
Oceanic		
Near shore	20	Demayo et al. 1982
Deep sea	45	
Clay	9	
Carbonate	80	

[a]Concentrations are shown as mean, minimum and maximum (in parentheses), and maximum (Max.).

[b]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

In soils, Pb concentrates in organic-rich surface horizons (NRCC 1973). In one instance, only 17 mg of soluble Pb/kg was found in soils 3 days after the addition of 2,784 mg of Pb (as lead nitrate)/kg (NRCC 1973). The estimated residence time of Pb in soils is about 20 years; complete turnover in topsoil is expected every few decades (Nriagu 1978a). In forest litter, however, the mean residence time of Pb is lengthy; estimates range from 220 years (Turner et al. 1985) to more than 500 years (Friedland and Johnson 1985).

Lead deposited on roadways is removed in drainage water, and later accumulated in roadside soils (Harrison et al. 1985). Amounts of Pb in roadside soils are increased as a direct result of the combustion of gasoline containing organolead additives. In general, the amounts of Pb were greatest along roads with the highest density of vehicular traffic, and amounts decreased rapidly with increasing distance from the roadway (Harrison and Dyer 1974; Boggess 1977; Chmiel and Harrison 1981; Way and Schroder 1982; Table 4). Elevated levels of Pb in soils also were recorded from the vicinity of storage battery reclamation plants, smelting activities, and mining and milling operations (Boggess 1977; Burrows 1981; Kisseberth et al. 1984). Fly ash from coal burned in homes or privately hauled from power plants, which contains 100 to 450 mg Pb/kg and is frequently used to reclaim land for the growth of forage and pasture crops and as an alkaline amendment in the reclamation of strip mined areas (Nriagu 1978a), is considered another source of soil Pb. Two additional sources of Pb in soils are municipal sewage sludge and lead-arsenate pesticides (Nriagu 1978a). Sewage sludge, which contains up to 100 mg Pb/kg and is applied as a fertilizer and soil conditioner at the rate of 50 million tons annually, may increase top soil levels by as much as 25 mg Pb/kg. Lead arsenate, a pesticide used to reduce bird hazards near airport runways by controlling earthworm abundance, and also to control pests in fruit orchards, represents another local source of lead contamination to soils.

Lead reaches the aquatic environment through industrial and municipal discharges, in atmospheric deposition, from weathering processes in areas of natural Pb mineralization, and in highway runoff (EPA 1980; Harrison and Laxen 1981; Birdsall et al. 1986). Industrial Pb input to aquatic environments is estimated at 10X that introduced by natural weathering processes (Scoullos 1986); sewage and aerosols are major sources (Harrison and Laxen 1981). Snowmobile exhausts are considered a major source of lead in some locations; concentrations up to 135 ug Pb/l have been recorded in surface waters at the time of ice breakup (Adams 1975). On the other hand, Pb content in water (and sediments) of a fly ash settling pond of a coal-fired power plant did not increase as a result of plant operations (White et al. 1986).

Anthropogenic activities leading to increased air Pb levels include primary and secondary lead smelting, the burning of gasoline containing lead antiknock agents, coal combustion, storage battery manufacture, and pigment production (NRCC 1973). It is generally agreed that combustion of leaded gasoline is the primary source of atmospheric Pb. Atmospheric Pb is usually attached to aerosols <0.2 um in diameter, is efficiently scavenged by precipitation, has a short atmospheric residence time that is usually measured in days but may range up to 14 weeks depending on meteorological conditions, and may be transported long distances (i.e., hundreds or thousands of kilometers) from emitting sources (NRCC 1973; Harrison and Laxen 1981; Harrison et al. 1985; Eisenreich et al. 1986). Along roadways, more than 90% of Pb emissions are dispersed by the atmosphere away from the immediate vicinity of the road; air Pb levels stabilize at low levels about 30 m from the road as a result of rapid settling of particles >5 um in diameter, and from the downwind traverse of particles entrained in the turbulent atmosphere (Boggess 1977; Harrison et al 1985). Since 1970, the lead content in

gasoline has decreased; profiles of Pb in dated sediment cores and Pb in atmospheric aerosols suggest that the environment is responding to decreasing use of leaded gasoline, and that atmospheric Pb concentrations and fluxes will continue to decrease susbstantially if use of Pb in gasoline is further decreased (Eisenreich et al. 1986).

FUNGI, MOSSES, LICHENS

Concentrations of Pb were highest in specimens collected near metal smelters, lead mines, industrial areas, and urban locations (Table 5). Lead concentrations were 9 to 13X greater in a lichen (*Parmelia baltimorensis*) collected in Washington, DC, in 1970 than in the same lichen collected 34 years earlier (Jenkins 1980).

TERRESTRIAL PLANTS

Elevated Pb contents were recorded in various species of plants from the vicinity of metal smelters, roadsides, soils heavily contaminated with Pb, natural ore deposits, and Pb recycling factories (Table 5). Bioavailability of Pb in soils to plants is limited, but is enhanced by reduced soil pH, reduced content of organic matter and inorganic colloids, reduced iron oxide and phosphorus content, and increased amounts of Pb in soils (NRCC 1973; Boggess 1977). Lead, when available, becomes associated with plants by way of active transport through roots and by absorption of Pb that adheres to foliage (Boggess 1977). Lead concentrations were always higher in the older parts of plants than in shoots or flowers (Bunzl and Kracke 1984; Table 5).

Table 5. Lead concentrations in field collections of selected species of flora and fauna. Values shown are in mg Pb/kg (ppm) fresh weight (FW), or dry weight (DW).

Taxonomic group, organism, tissue, and other variables	Concentration[a]	Reference[b]
Fungi, Mosses, and Lichens		
Fungi, 4 species		
Near metal smelter	4 DW	Beyer et al. 1985
Control site	2 DW	
Moss, *Brachythecium rivulare*		
Near lead mines	(1,330–8,206) DW	McLean and Jones 1975
Moss, *Hypnum cupressiforme*		
Sweden, museum specimens		
Year of collection		
1860	(18–27)DW	Ruhling and
1880	(20–37) DW	Tyler 1968
1900	(40–70) DW	
1920	(22–90) DW	
1940	(15–70) DW	
1960	(65–75) DW	
1968	(70–90) DW	
Vicinity urban industry	Max. 11,611 DW	Goodman and Roberts 1971
Lichen, *Parmelia baltimorensis*		
Washington, DC		
1938	106 DW	Jenkins 1980
1958	270 DW	
1970	(950–1,371) DW	

Connecticut, 1971	198 DW	
Algae and Macrophytes		
Acorns and berries, 4 species		
Near metal smelter	4 DW	Beyer et al. 1985
Control site	3 DW	
Aquatic macrophytes, whole		
Nile River, Egypt		
Industrialized area	Max. 22 DW	Fayed and
Abd-El-Shafy 1985		
Aquatic plants, 7 species		
From lead shot seeded area		
Roots	19 DW	Behan et al. 1979
Shoots	3 DW	
Control area		
Roots	5 DW	
Shoots	1 DW	
Swiss chard, *Beta vulgaris cicla*		
Leaf		
15 m from highway	220 DW	Jenkins 1980
20 m from highway	154 DW	
Control area	<3 DW	
Alga, *Blidingia minima*		
Whole, Raritan Bay, New Jersey		
Water Pb content		
0.002 mg/L	12 DW	Seeliger and
0.01 mg/L	172 DW	Edwards 1977
Brome grass, *Bromus* spp.		
Grown in soil with 680 mg Pb/kg	34 DW	Jenkins 1980
Control	7 DW	
Weed, *Cassia* sp., India		
Distance from highway (meters)		
2	(208–303) DW	Krishnayya and
20	(90–97) DW	Bedi 1986
40	(55–68) DW	
60	(20–22) DW	
Green alga, *Cladophora* sp.		
Missouri, tailings pond	11,300 DW	
1.6–4.0 km downstream	(200–4,600) DW	
6.1–9.6 km downstream	(100–2,600) DW	
Alga, *Enteromorpha llinza*		
Whole, Raritan Bay, New Jersey		
Water Pb content		
0.002 mg/L	18 DW	Seeliger and

0.01 mg/L	68 DW	Edwards 1977
Red fescue grass, *Festuca rubra*		
Leaf, Wales, UK		
Distance downwind from smelter		
1.5 km	814 DW	Goodman and
8 km	30 DW	Roberts 1971
25 km	14 DW	
>25 km	(5–12) DW	
Foliage, 8 species		
Near metal smelter	21 DW	Beyer et al. 1985
Control site	10 DW	
Alga, *Fucus distichus*		
Distance from Pb deposit		
1 km	1 DW	Bohn 1979
2 km	0.6 DW	
Alga, *Fucus vesiculosus*		
Whole, Raritan Bay, New Jersey		
Water Pb content		
0.002 mg/L	8 DW	Seeliger and
0.01 mg/L	38 DW	Edwards 1977
Lettuce, *Lactuca satvia*		
Pb-contaminated areas	71 FW	Demayo et al. 1982
Uncontaminated areas	0.5 FW	
Mule deer forage, Colorado,		
Roadside		
1978	59 DW	Harrison and
1979	42 DW	Dyer 1984
Rice, *Oryza sativa*		
Grown 10 m from highway		
Grain	0.2 DW	Ter Haar 1970
Straw	5.8 DW	
Grown 230 m from highway		
Grain	0.2 DW	
Straw	2.1 DW	
Spruce, *Picea abies*, Germany, 1984		
Declining spruce forest		
Litter	416 DW	Backhaus and
Needles	13 DW	Backhaus 1986
Nondeclining stand		
Litter	213 DW	
Needles	2 DW	
Shortleaf pine, *Pinus echinata*		
Missouri, leaf		

Distance from smelter, km		
0.8	3,546 (420–11,750) DW	Bolter et al. 1973
0.8–1.6	497 (101–1,475) DW	
1.6–2.4	274 (52–1,050) DW	
2.4–3.2	142 (62–412) DW	
3.2	123 (22–661) DW	
Pondweed, *Potamogeton* sp.		
Missouri, tailings pond	11,300 DW	Jenkins 1980
1.6 km downstream	3,500 DW	
8.1 km downstream	100 DW	
Black cherry, *Prunus serotina*		
Leaves, 1978		
Near roadway	(9–14) DW	Beyer and Moore 1980
>30 m distant	(2–6) DW	
Potato, *Solanum tuberosum*		
Pb-contaminated areas	13 FW	Demayo et al. 1982
Uncontaminated areas	1 FW	
Submerged aquatic vegetation, 1979–81		
Chesapeake Bay, 5 species	7.4 (0.5–30) DW	Di Giulio and Scanlon 1985
Alga, *Ulva* sp.		
Whole, Raritan Bay, New Jersey		
Water Pb content		
0.002 mg/L	20 DW	Seeliger and
0.01 mg/L	76 DW	Edwards 1977
Blueberry, *Vaccinium pallidum*		
Leaf, Missouri		
Distance from smelter		
1.6–3.2 km	495 (141–874) DW	Jenkins 1980
3.2–4.8 km	203 DW	
4.8–6.5 km	76 DW	
6.5–8.1 km	68 DW	
8.1–9.7 km	64 DW	
9.7–11.3 km	41 (29–101) DW	
Vegetation		
Vermont forest		
Root bark	33 DW	Friedland and
Twigs	28 DW	Johnson 1985
Bark	23 DW	
Root wood	10 DW	
Foliage	3 DW	
Wood	3 DW	
New Jersey Pine Barrens		

Roots	18 DW	Turner et al. 1985
Bark	15 DW	
Foliage	4 DW	
Wood	0.5 DW	
Near roadway, UK 1979		
Grass	63 DW	Chmiel and
Grass seeds	99 DW	Harrsion 1981
Hawthorn, *Crataegus* spp.		
Leaves	146 DW	
Fruit	4 DW	
Control site, UK 1979		
Grass	2 DW	
Grass seeds	4 DW	
Hawthorn		
Leaves	4 DW	
Fruit	2 DW	
Grass		
Near factory	(830–1,840) DW	Edwards and
1,000 m distant		Clay 1977
Growing	(120–1,200) DW	
Dead and litter	(370–1,570) DW	
1,700 m distant		
Growing	(240–420) DW	
Dead and litter	(170–1,970) DW	
Near Pb smelter, forage		
Missouri	979 FW	Burrows 1981
British Columbia	(100–200) FW	
Kansas, vegetation		
Near highway	11 DW	Robel et al. 1981
Distant site	3 DW	
Invertebrates		
Limpet, *Acmaea digitalis*		
California		
Near bridges		
Soft parts	931 DW	Graham 1972
Shell	108 DW	
Pb-free area		
Soft parts	8 DW	
Shell	9 DW	
Bee, *Apis* sp.		
Honey		
Pb-contaminated area	(1–8) FW	Demayo et al. 1982
Uncontaminated area	<0.5 FW	

Sea urchin, *Arbacia lixula*		
Soft parts, Italy		
Unpolluted	21 DW	Sheppard and
Polluted	58 DW	Bellamy 1974
Beetles, *Coleoptera*, UK 1979		
Near roadway	32 DW	Chmiel and
Control site	1 DW	Harrison 1981
Bivalve molluscs, 3 species, soft parts, Chesapeake Bay, 1979–81	5 (0.6–27) DW	Di Giulio and Scanlon 1985
Crawfish, *Cambarus* sp.		
Whole, Missouri		
At tailings pond	500 DW	Gale et al. 1976
1 km downstream	400 DW	
25 km downstream	2 DW	
Dung beetles, whole		
Near roadway	13 DW	Robel et al. 1981
Distant site	6 DW	
Earthworms, whole		
Blacksburg, VA, 1974		
From high traffic density area (21,000 vehicles/day)		
6 m from highway	51 DW	Goldsmith and
18 m distant	32 DW	Scanlon 1977
From low traffic density area (1,100 vehicles/day)		
18 m distant	12 DW	
Near highway	(38–331) DW	Beyer and Moore 1980
Earthworm, *Eisenia rosea*		
Whole, Illinois		
Control areas	32 DW	Jenkins 1980
From areas receiving sludge at 1600 kg Pb/hectare	624 DW; Max. 981 DW	
Earthworm, *Eisenoides carolinensis*		
Whole, uncontaminated area	2,100 DW	Beyer and Cromartie 1987
Insects, various species		
Distance from highway		
0–7 meters		
Sucking	16 DW	Anderson 1977
Chewing	27 DW	
Predatory	31 DW	
13–20 meters		
Sucking	9 DW	

Chewing	10 DW	
Predatory	20 DW	
>20 meters		
Sucking	5 DW	
Chewing	5 DW	
Predatory	6 DW	
Kansas, 1978		
Near roadway	50 DW	Udevitz et al. 1980
Control site	15 DW	
Lepidopteran larvae, UK, 1979		
Near roadway	118 DW	Chmiel and
Control site	<1 DW	Harrison 1981
Earthworm, *Lumbricus terrestris*		
Whole, Maryland		
Distance from highway, meters		
3.0	269 DW	Gish and
6.1	113 DW	Christensen 1973
12.2	80 DW	
24.4	43 DW	
48.8	52 DW	
Eastern tent caterpillar, *Malacosoma americanum*		
Whole, 1978		
Near roadway	7 DW	Beyer and Moore 1980
>10 m distant	<5.3 DW	
Millipedes, Diplopoda		
UK 1979		
Near roadway	162 DW	Chmiel and
Control site	34 DW	Harrison 1981
USA		
Near highway	(43–82) DW	Beyer and Moore 1980
Coral, *Montastrea annularis*		
Virgin Islands, 1980, skeleton		
Polluted reef (Sewage, dredging)	0.4 FW	Dodge and
Pristine reef	0.09 FW	Gilbert 1984
Blue mussel, *Mytilus edulis*		
Soft parts		
Germany	(2–6) DW	Jenkins 1980
New Zealand	12 (<3–25) DW	
Norway	(2–3,100) DW	
England	9 DW; (0.5–3) FW	
Australia	(0.7–10) FW	
Spain	(2–15) DW	
Greenland	(2–21) FW	

Beetle, *Nicrophorus tomentosus* whole		
Near metal smelter	3 DW	Beyer et al. 1985
Control site	2 DW	
Grass shrimp, *Palaemonetes pugio*		
Whole, Virginia		
Natural marsh	0.2 DW	Drifmeyer and
Spoil disposal area	11 DW	Odum 1975
Shrimp, *Pandalus montagui*		
Soft parts		
Sewage dump area	31 DW	Mackay et al. 1972
Control area	24 DW	
Sea urchin, *Paracentrotus lividus*		
Soft parts, Italy		
Unpolluted	20 DW	Sheppard and
Polluted	42 DW	Bellamy 1974
Caterpillar, *Porethetria dispar* Whole		
Near metal smelter	9 DW	Beyer et al. 1985
Control site	3 DW	
Blackfly, *Simulium* sp.		
Larva		
Missouri		
Tailings pond	14,233 DW	Gale et al. 1976
Illinois	24 DW	Anderson 1977
Slugs, Gastropoda, UK, 1979		
Near roadway	141 DW	Chmiel and
Control site	27 DW	Harrison 1981
Spiders, Aranea, UK, 1979		
Near roadway	560 DW	
Control site	<1 DW	
Tubificid worms		
Rural streams	16 DW	Boggess 1977
Urban streams	367 DW	
Woodlice, Isopoda		
UK, 1979		
Near roadway	152 DW	Chmiel and
Control site	19 DW	Harrison 1981
USA		
Near highway	(380–682) DW	Beyer and Moore 1980
Fish		
Spotted wolffish, *Anarhichas minor*		
Near Pb mine, Greenland		
Liver	Max. 1.8 FW	Bollingberg and
Muscle	Max. 0.12 FW	Johansen 1979

Coastal marine fishes, USA		
Liver		
5 species	(<0.1–0.2) FW	Hall et al. 1978
20 species	(0.2–0.4) FW	
33 species	(0.4–0.6) FW	
13 species	(0.6–0.8) FW	
6 species	(0.8–1) FW	
5 species	(1–3) FW	
Muscle		
5 species	(0.1–0.3) FW	
92 species	(0.3–0.5) FW	
51 species	(0.5–0.7) FW	
7 species	(0.7–1) FW	
4 species	(1–3) FW	
Whitefish, *Coregonus* spp., Sweden		
Liver		
Polluted lake	(6–7) DW	Haux et al. 1986
Reference lake	<1 DW	
Fish		
Upper Mississippi River (Minnesota-Iowa), 1979		
Common carp, *Cyprinus carpio*		
Whole	3(1–12) DW	Wiener et al. 1984
Liver	9 (2–32) DW	
Bluegill, *Lepomis macrochirus*		
Whole	0.4 (0.2–1.1) DW	
Fish, whole		
Nationwide		
1971	Max. 1.4 FW	Walsh et al. 1977
1972	0.4 (Max. 5.2) FW	
1973	Max. 1.4 FW	
1976–77	0.3 FW	May and McKinney 1981
1978–79	0.2 (0.1–6.7) FW	Lowe et al. 1984
1980–81	0.2 (0.1–1.9) FW	
Southeastern Missouri, Big River		
Upstream from mine site		
Catostomids, 3 species	<0.1 FW	Schmitt et al. 1984
Other species	<0.3 FW	
Downstream		
Catostomids	0.4–0.8 FW	
Longear sunfish, *Lepomis megalotis*	18 FW	
Black redhorse, *Moxostoma duquesnei*	15 FW	
Smallmouth bass, *Micropterus dolomieui*	9 FW	

Bluegill, whole		
Missouri, mine tailings pond,		
At pond	128 DW	Gale et al. 1976
1 km downstream	23 DW	
65 km downstream	5 DW	
Plaice, *Platichthys flesus*, whole		
Polluted area, UK		
Age 2+	20 DW	Hardisty et al. 1974
Age 3+	24 DW	
Age 4+	26 DW	
Age 5+	28 DW	
Uncontaminated area, UK		
Age 2+	14 DW	
Age 3+	16 DW	
Age 4+	18 DW	
Age 5+	19 DW	
Integrated studies		
Great Lakes, Lake Ontario		
Plankton	4 DW	Demayo et al. 1982
Zooplankton	(1–5) DW	
Fish	(0.1–0.13) FW	
Marine food chain, Central Pacific		
Seawater	0.006 FW	Flegal 1985
Phytoplankton	0.05 FW	
Zooplankton	0.04 FW	
Carnivores, muscle		
Intermediate (anchovy)	0.02 FW	
Top (tuna)	0.0003 FW	
Oklahoma pond		
Water0.013 FW	Demayo et al. 1982	
Sediments		
Surface	529 DW	
12 cm depth	206 DW	
Plantkton	281 DW	
Benthos	37 DW	
Mosquitofish, *Gambusia* sp.	11 DW	
Amphibians and reptiles		
Amphibians, whole		
Near metal smelter	No species found	Beyer et al. 1985
Control site, 5 species	12 DW	
Frog, *Rana* sp., tadpole, whole		
Missouri, tailings pond	4,139 DW	Gale et al. 1976
Distance downstream		

from tailings pond		
1 km	552 DW	
25 km	37 DW	
Southeastern Missouri, 1981–82, Big River		
Bullfrog, *Rana catesbeiana*, carcass		
Upstream from mine site	1 (Max. 6) FW	Niethammer et al.
Downstream	33 (Max. 300) FW	1985
Northern water snake, *Nerodia sipedon*, carcass		
Upstream	0.2 (Max. 0.6) FW	
Downstream	7 (Max. 14) FW	
Common box turtle, *Terrapene carolina* (Age 15 years)		
Near lead smelter, Missouri		
Humerus	51 FW	Beresford et al.
Femur	64 FW	1981
Liver	21 FW	
Kidney	24 FW	
Blood	6 FW	
Skin	0.4 FW	
Near Morgantown WV, Control site (Age 17 years)		
Humerus	4 FW	
Femur	4 FW	
Liver	1 FW	
Kidney	2 FW	
Blood	0.1 FW	
Skin	0.1 FW	
Toad, *Xenopus laevis*		
Fed worms from Pb-contaminated soils		
Bone	24 FW	Ireland 1977
Skin	3 FW	
Muscle	1 FW	
Kidney	15 FW	
Liver	7 FW	
Fed uncontaminated worms		
Bone	5 FW	
Skin	0.8 FW	
Muscle	0.6 FW	
Kidney	3 FW	
Liver	1 FW	
Birds		

Canvasback, *Aythya valisineria*		
Blood		
Chesapeake Bay, 1974		
Normal	(0.059–0.064) FW	Dieter et al. 1976
Abnormal (17%)	0.263 FW	
Wingbone		
La Crosse, Wisconsin		
1976		
Males	18 (6–56) DW	Fleming 1981
Females	5 (1–20) DW	
Immatures		
Males	0.8 (0.1–4) DW	
Females	1 (0–21) DW	
1977		
Males	11 (9–12) DW	
Females	8 (1–48) DW	
Immatures		
Males	0.8 (<0.1–7) DW	
Females	<0.5 DW	
Keokuk, Iowa		
1976		
Males	6 (4–10) DW	
Females	5 (1–20) DW	
Immatures		
Males	0.5 (0.1–2) DW	
Females	1 (0.1–22) DW	
1977		
Males	2 (0.2–19) DW	
Females	4 (1–19) DW	
Birds		
Galveston Bay, Texas, 1980–81, 3 species, liver	(0.1–0.5) FW	King and Cromartie 1986
Texas		
Probers with Pb shot in gizzards		
Bone	11 FW	Hall and Fisher 1985
Feather	4 FW	
Liver	0.3 FW	
Probers without Pb shot in gizzards		
Bone	6 FW	
Feather	5 FW	
Liver	<0.1 FW	
Non-probers		
Bone	6 FW	

Feather	2 FW	
Liver	<0.1 FW	
Ruffed grouse, *Bonasa umbellus*		
Virginia, rural areas		
Liver	2.3 DW	Kendall et al. 1984
Bone	2.8 (0.4–9) DW	
Knot, *Calidris canutus*		
Feather		
Juvenile	2 DW	Goede and
Adult	7 DW	de Voogt 1985
Rock dove, *Columba livia*		
UK		
Urban area		
Kidney		
Female	204 DW; (9–30) FW	Johnson et al. 1982
Male	122 DW	
Bone		
Female	338 DW	
Male	126 DW	
Rural area		
Kidney		
Female	6 DW; (1.2–1.9) FW	
Male	8 DW	
Bone		
Female	16 DW	
Male	19 DW	
Tokyo, Japan		
Femur		
Urban areas	(16–31) FW	Ohi et al. 1974
Suburban areas	(2–3) FW	
Kidney		
Urban areas	(2–3) FW	
Suburban areas	<1 FW	
Mute swan, *Cygnus olor*		
Denmark, 1982		
Blood		
Adults	0.25 (0.13–0.54) FW	Eskildsen and Grandjean 1984
Juveniles	0.11 (0.07–0.39) FW	
Peregrine falcon, *Falco peregrinus*		
Baltimore, Maryland, Age 7+		
Liver	0.8 FW	De Ment et al. 1986
Kidney	1.4 FW	
Prey organism		

Rock dove		
Urban		
Blood	1 (0.3–17) FW	
Liver	3 FW	
Kidney	9 FW	
Whole	5 FW	
Rural		
Blood	<0.1 FW	
Liver	0.4 FW	
Kidney	0.5 FW	
Whole	0.3 FW	
Common loon, *Gavia immer*, Pb poisoned		
Liver	(21–39) FW	Locke et al. 1982
Bald eagle, *Haliaeetus leucocephalus*		
Nationwide, 1978–81, found dead, suspected Pb poisoning		
Liver	28 (11–61) FW	Reichel et al. 1984
Liver		
Control	0.6 FW	Bagley and Locke 1967
Pb-poisoned	21 FW	Mulhern et al. 1970
Barn swallow, *Hirundo rustica*		
Near Baltimore-Washington Parkway, 1979		
Feather		
Male	67 (55–82) DW	Grue et al. 1984
Female	54 (43–68) DW	
Nestling	2 (2–3) DW	
Carcass		
Male	5 (4–6) DW	
Female	9 (6–12) DW	
Nestling	2 (1–2) DW	
Stomach contents		
Male	5 DW	
Female	7 DW	
Nestling	3 DW	
Reference colony, 1979		
Feather		
Male	24 (21–28) DW	
Female	19 (16–22) DW	
Nestling	2 (2–3) DW	
Carcass		
Male	4 (3–5) DW	
Female	5 (3–7) DW	
Nestling	1 DW	

Stomach contents		
Male	0.2 DW	
Female	2 DW	
Nestling	2 DW	
House sparrow, *Passer domesticus*		
Illinois		
Urban areas		
Feather	158 DW	Getz et al. 1977a
Intestine	26 DW	
Liver	12 DW	
Lung	7 DW	
Kidney	34 DW	
Femur	130 DW	
Muscle	2 DW	
Rural areas		
Feather	27 DW	
Intestine	2 DW	
Liver	0.6 DW	
Lung	0.9 DW	
Kidney	3 DW	
Femur	17 DW	
Muscle	0.9 DW	
Brown pelican, *Pelecanus occidentalis*		
Egg		
South Carolina 1971–72	0.03 (0.01–0.11) FW	Blus et al. 1977
Florida, 1969–70	0.03 (0.01–0.05) FW	
Liver		
Found dead		
1972		
Georgia	0.1 FW	
Florida	0.1 FW	
1973		
South Carolina	0.3 FW	
Florida	0.2 FW	
Shot, 1970		
Florida	0.1 FW	
South Carolina	0.1 FW	
Sora rail, *Porzana carolina*		
Maryland		
Lead shot in gizzard		
Liver	(0.1–17) FW	Stendell et al. 1980
Bone	(1–127) DW	
No lead shot in gizzard		

Liver	(<0.01–0.08) FW	
Bone	(<0.4–42) DW	
Songbirds, carcass		
Near metal smelter, 10 species	56 (9–240) DW	Beyer et al. 1985
Control site, 9 species	15 (6–25) DW	
Southeastern Missouri,		
1981–82, Big River		
Green backed heron, *Butorides striatus*		
Liver		
Upstream from mine site	0.1 (Max. 0.3 FW	Niethammer
Downstream	0.5 (Max. 1.5) FW	et al. 1985
Northern rough–winged swallow, *Stelgidopteryx serripennis*		
Carcass		
Upstream from mine site	0.5 (Max. 5) FW	
Downstream	1 (Max. 15) FW	
European starling, *Sturnus vulgaris*		
Nesting near highway, Maryland		
Carcass	(4–10) DW	Grue et al. 1986
Feathers	(7–52) DW	
Stomach contents	(84–94) DW	
Control site		
Carcass	(1–3) DW	
Feathers	(3–14) DW	
Stomach contents	(6–7) DW	
Nationwide, whole less beaks, skins, wings and feet		
1971	1.3 (0.1–6.6) FW	Martin and
Chicago, Ill.	5.0 FW	Nickerson 1973
Indiana, urban	3.4 FW	
Quincy, MA	6.6 FW	
Jamestown, NY	5.1 FW	
1973	0.9 (<0.1–3.2) FW	White et al. 1977
Urban	1.1 (<0.1–3.2) FW	
Rural	0.7 (<0.1–2.4) FW	
Robin, *Turdus migratorius*		
Illinois		
Urban areas		
Feather	79 DW	Getz et al. 1977a
Intestine	24 DW	
Liver	10 DW	
Lung	10 DW	
Kidney	25 DW	
Femur	133 DW	
Muscle	1 DW	

Rural areas		
Feather	25 DW	
Intestine	3 DW	
Liver	2 DW	
Lung	2 DW	
Kidney	7 DW	
Femur	41 DW	
Muscle	1 DW	
Waterfowl, nationwide, 7 species		
Wingbones, 1972–73	(<0.5–361) DW	Stendell et al. 1979
Mallard, *Anas platyrhynchos*		
Adult	12 DW	
Immature	10 DW	
Pacific flyaway		
Alaska	6 DW	
Washington		
Eastern	8 DW	
Western	24 DW	
Oregon		
Columbia River	45 DW	
Other	15 DW	
California		
Merced	15 DW	
Sacramento	38 DW	
Other	25 DW	
Northern pintail, *Anas acuta*		
Adult	7 DW	
Immature	6 DW	
Mottled duck, *Anas fulvigula*		
Adult	48 DW	
Immature	40 DW	
Canvasback		
Adult	17 DW	
Immature	8 DW	
Redhead, *Aythya americana*		
Adult	26 DW	
Immature	24 DW	
Lesser scaup, *Aythya affinis*		
Adult	3 DW	
Immature	2 DW	
Black duck, *Anas rubripes*		
Adult	8 DW	
Mammals		

Field mouse, *Apodemus sylvaticus*		
Near abandoned Pb mine		
Whole body	(9–14) DW	Roberts et al. 1978
Kidney	(39–46) DW	
Liver	(12–13) DW	
Bone	(189–352) DW	
Brain	(6–13) DW	
Muscle	(7–10) DW	
Control area		
Whole body	1 DW	
Kidney	(9–13) DW	
Liver	(5–8) DW	
Bone	(11–21) DW	
Brain	(3–4) DW	
Muscle	(5–6) DW	
Short-tailed shrew, *Blarina brevicauda*		
Carcass		
Near metal smelter	109 DW	Beyer et al. 1985
Control site	18 DW	
From area of high traffic levels (>12,000 vehicles/day)		
Total body	18 DW	Getz et al. 1977c
Gut	24 DW	
Spleen	4 DW	
Liver	5 DW	
Lung	17 DW	
Kidney	12 DW	
Femur	67 DW	
Muscle	10 DW	
From area of low traffic levels (<400 vehicles/day)		
Total body	6 DW	
Gut	3 DW	
Spleen	2 DW	
Liver	1 DW	
Lung	8 DW	
Kidney	4 DW	
Femur	12 DW	
Muscle	5 DW	
Cow, *Bos bovis*		
Missouri, hair		
Near Pb smelter		
Fall	94 DW	Dorn et al. 1974

Winter	87 DW	
Spring	96 DW	
Summer	66 DW	
Control area		
Fall	2 DW	
Winter	4 DW	
Spring	2 DW	
Summer	1 DW	
Dung		
Near roadway	10 DW	Robel et al. 1981
Distant site	8 DW	
Dog, *Canis familiaris*		
Blood		
Healthy	(0.01–0.05) FW	NRCC 1973
Pb-poisoned	(0.06–0.15) FW	
Big brown bat, *Eptesicus fuscus*		
Whole, minus GI tract and large embryos		
Males47 (20–90) FW	Clark 1979	
Females	32 (20–56) FW	
Guano	61 DW	
Stomach contents	4 DW	
Horse, *Equus caballus*		
Near smelter, British Columbia		
Liver	18 FW	Burrows 1981
Kidney	16 FW	
Bone	88 FW	
Near Pb smelter (some deaths), California		
Liver	(15–222) FW	Knight and
Kidney	(14–80) FW	Burau 1973
Blood	(0.4–0.5) FW	
Control areas		
Blood	(0.1–0.3) FW	Jenkins 1980
Bank vole, *Clethrionomys glareolus*		
Whole body		
Near abandoned Pb mine	(16–21) DW	Roberts et al. 1978
Control area	(2–3) DW	
Chipmunk, *Eutamias townsendii*		
Hair		
Roadside location	235 DW	Raymond and
Control area	6 DW	Forbes 1975
Prairie vole, *Microtus ochrogaster*		
Illinois, whole body		

Near heavy traffic	8 DW	Getz et al. 1977b
Control area	3 DW	
Little brown bat, *Myotis lucifugus*		
Whole	17 (11–29) FW	Clark 1979
Guano	65 DW	
Stomach contents	26 FW	
Bats, *Myotis* spp., Florida 1981–83		
Guano	(3–6) DW	Clark et al. 1986
White-tailed deer, *Odocoileus virginianus*		
Near zinc smelter, Pennsylvania		
Feces	16 (6–37) DW	Sileo and Beyer 1985
Bone	9 (4–17) DW	
Teeth	6 (3–11) DW	
Kidney	2 (1–3) DW	
Liver	<2 DW	
Control area, 100 km from smelter		
Feces	8 (4–16) DW	
Bone	6 (3–11) DW	
Teeth	2 (1–4) DW	
Kidney	0.8 (0.5–1) DW	
Liver	<0.4 DW	
Muskrat, *Ondatra zibethicus*		
Liver		
Upstream from mine site	0.2 (Max. 0.3) FW	Niethammer
Downstream	0.7 (Max. 1.6) FW	et al. 1985
Sheep, *Ovis aries*		
Meat	<0.2 FW	Bunzl and
Liver	<1.5 FW	Kracke 1984
Kidney	<1.1 FW	
Sheep forage		
Grass		
Green	<12 FW	
Old	<33 FW	
Other	<24 FW	
White-footed mouse, *Peromyscus leucopus*		
Carcass		
Near metal smelter	17 DW	Beyer et al. 1985
Control site	7 DW	
Deer mice, *Peromyscus maniculatus*		
From high bone density traffic area		
Bone	52 DW	Mierau and
Kidney	9 DW	Favara 1975
Liver	3 DW	

Brain	1 DW	
Feces	154 DW	
From low density traffic area		
Bone	5 DW	
Kidney	3 DW	
Liver	1 DW	
Brain	0.1 DW	
Feces	7 DW	
Roadside locations		
Brain	(0.6–0.8) DW	Jenkins 1980
Liver	(0.9–3) DW	
Kidney	(2–8) DW	
Bone	(14–52) DW	
Hair	235 DW	
Control areas		
Brain	0.1 DW	
Liver	1 DW	
Kidney	3 DW	
Bone	5 DW	
Hair	6 DW	
Illinois, 1982		
Distance from lead battery reclamation plant		
100 m		
Liver	4 FW	Kisseberth
Kidney	13 FW	et al. 1984
Bone	79 FW	
1,000 m		
Liver	1 FW	
Kidney	3 FW	
Bone	2 FW	
Whole, 1978–79		
Near Cu-Zn mine		
Juveniles	4 FW	Smith and
Adults	5 FW	Rongstad 1982
Control site		
Juveniles	0.5 FW	
Adults	0.7 FW	
Raccoon, *Procyon lotor*		
Connecticut, Pb-intoxicated		
Liver, kidney	>35 FW	Diters and Nielsen 1978
Commensal rat, *Rattus norvegicus*		
Houston, Texas, 1978–79		
Urban		

Bone	125 FW	Way and
Kidney	9 FW	Schroder 1982
Stomach contents	31 FW	
Feces	72 FW	
Rural		
Bone	8 FW	
Kidney	3 FW	
Stomach contents	3 FW	
Feces	8 FW	
Roadside mammals, 1976		
Whole, minus GI tract and large embryos		
Short-tailed shrew		
Near highway	26 (6–130) FW	Clark 1979
Distant site	2 FW	
Meadow vole, *Microtus pennsylvanicus*		
Near highway	2 (0.2–5) FW	
Distant site	<1.4 FW	
White-footed mouse		
Near highway	5 (0.4–41) FW	
Distant site	1 (0.3–13) FW	
Common shrew, *Sorex araneus*, UK, 1979		
Near roadway		
Liver	17 DW	Chmiel and
Kidney	46 DW	Harrison 1981
Bone	193 DW	
Pelt	10 DW	
Control site		
Liver	<1 DW	
Kidney	9 DW	
Bone	41 DW	
Pelt	3 DW	

[a]Concentrations are listed as mean, (minimum-maximum), and maximum (Max.).

[b]Each reference applies to data in the same row and in the rows that immediately follow for which no reference is indicated.

Damage to plants with elevated Pb contents is usually negligible, but varies widely among species. Atmospheric Pb may have contributed to the decline of European spruce forests. The mean Pb content of needles and litter was significantly higher where tree decline was most pronounced than in areas where forests were unaffected (Backhaus and Backhaus 1986). Lead can have deleterious effects on plant growth processes at current Pb levels in urban areas and may similarly affect plants in rural areas in the future (Rolfe and Reinbold 1977). A reduction in yield of corn or soybeans is expected in low-binding capacity soils with Pb levels greater than 200 mg/kg (Rolfe and Reinbold 1977). Hay grown near roadsides may be toxic to horses and cattle (Rolfe and Reinbold 1977). In extreme cases, reforestation has been initiated in areas where forage is so heavily contaminated with Pb that it has become necessary to slaughter domestic livestock because the

amounts of Pb in their livers and kidneys became unacceptably high (Edwards and Clay 1977). Typical area reforestation includes removal of contaminated forage by cutting, bailing, and burying native grasses; burning of stubble and litter; and adding of agricultural lime at the rate of 2,244 kg/ha (2,000 pounds/acre) to all soils within 1,525 m (5,000 feet) of sites where Pb levels exceed 175 mg/kg (Edwards and Clay 1977).

TERRESTRIAL INVERTEBRATES

In earthworms, lead levels were highest in those closest to highways and in areas with high volumes of traffic (Goldsmith and Scanlon 1977; Table 5). Various species of insects and soil invertebrates from roadsides, from areas receiving sewage sludge, and from metal smelter environs also contain high amounts of Pb (Table 5). Amounts of Pb in whole body were higher in earthworms, millipedes, and woodlice collected from soil and plant litter near highways than away from highways; soil and litter seem to be major reservoirs of Pb in roadside communities (*Malacosoma americanum*) and their host plant (Beyer and Moore 1980). In contrast, Pb concentrations in the eastern tent caterpillar (*Malacosoma americanum*) were lower than those reported for roadside soil and litter invertebrates, and were about 76% of that in leaves of its host, the black cherry *Prunus serotina* (Beyer and Moore 1980).

The use of terrestrial invertebrates as sentinel organisms has been suggested for monitoring Pb. The spider *Araneus umbricatus*, for example, contained Pb body burdens that correlated with that in a lichen (*Lecanora conizaeoides*) that is currently used to monitor atmospheric Pb (Clausen 1984). Similarly, the woodlouse (*Porcellio scaber*) seems to reflect Pb concentrations in adjacent soil or leaf litter (Hopkin et al. 1986).

AQUATIC BIOTA

Freshwater algae, invertebrates, and fish had comparatively elevated Pb concentrations when collected near industrialized areas, ponds with high numbers of Pb shot, urban areas, Pb mines, and tailings ponds (Table 5). For marine biota, Pb residues were highest where Pb concentrations were high in the water--near bridges, near industrial disposal areas, near sewage and disposal areas, near dredging sites, and at mining sites (Table 5). Among aquatic biota, Pb concentrations were usually highest in algae and benthic organisms, and lowest in upper trophic level predators. No significant biomagnification of Pb occurs in aquatic food chains (Boggess 1977; Rolfe and Reinbold 1977; Branica and Konrad 1980; Demayo et al. 1982; Flegal 1985; Table 5). Lead concentrations in cartilaginous and bony fishes--and also birds and mammals--were usually highest in areas of high human and vehicular density, and near lead mines and ore concentration plants. Lead concentrations in aquatic (and terrestrial) vertebrates tend to increase with increasing age of the organism, and to localize in hard tissues such as bone and teeth (Eisler 1981, 1984).

In stream sediments, Pb was highest in urban streams and lowest in the rural streams, reflecting Pb inputs from storm runoff; species diversity was greater in the rural streams, due partly to lowered contaminant loadings, including Pb (Rolfe and Reinbold 1977).

Nationwide monitoring of freshwater fishes conducted periodically by the U.S. Fish and Wildlife Service (National Biocontaminant Monitoring Program) showed that whole body Pb burdens were highest for Atlantic coast streams, the Great Lakes drainage, the Mississippi River system, the Columbia River system, and in certain Hawaiian streams (May and McKinney 1981). Major sources of Pb in Atlantic coast streams included wastes from metal finishing industries, brass manufacturing, lead alkyl production, primary and secondary Pb smelting, coal combustion, and manufacture of lead oxide. For the Great Lakes, especially for the Lake St. Clair collection site, industrial sources and urban Pb aerosol fallout from the Detroit area were major sources. In the Mississippi River system, naturally occurring deposits of Pb ores, and effluents from zinc producers and industrial dischargers were prevalent. The Columbia River system was characterized by Pb inputs from natural geologic deposits, industrial effluents, and the mining and smelting of Pb. Hawaiian streams received most of their Pb from urban runoff, vehicle sources, and agricultural and residential use of Pb arsenate (May and McKinney 1981).

Fish collected in 1979-1981 in the Big River, Missouri, near a ruptured tailings pond dam where Pb concentrations in tailings approached 4,000 mg/kg, contained greatly elevated whole body Pb burdens of 9 to 18 mg/kg fresh weight (Schmitt et al. 1984). By comparison, the highest Pb concentration recorded to date in the National Biocontaminant Monitoring Program is 6.7 mg/kg fresh weight in whole Mozambique tilapia (*Tilapia*

mossambica) from Honolulu in 1979 (Lowe et al. 1985). Catostomids from contaminated portions of the Big River contained elevated blood Pb levels, depressed blood ALAD activity levels, and Pb concentrations in edible tissues exceeding 0.3 mg/kg fresh weight--a level considered hazardous to human health (Schmitt et al. 1984). The Missouri Department of Health later issued an advisory against eating castostomids caught in a 65-km section of the Big River (Czarneski 1985).

Whitefish, *Coregonus* spp., from Pb-contaminated Swedish lakes, showed depressed blood ALAD and blood chemistry derangement when compared to fish from a reference lake--suggesting that Pb affects natural populations of fish in a manner similar to that observed in laboratory studies (Haux et al. 1986).

The significance of organolead residues in aquatic life is unknown, and merits additional research. In Ontario, Canada, about 16% of all fish sampled contained tetraalkyllead compounds, although none were recorded in water, vegetation, or sediments from the collection sites (Chau et al. 1980). Tetramethyllead reportedly was produced from biological and chemical methylation of several inorganic and organic Pb compounds in the aquatic environment, and has been detected at low concentrations in marine mussels, lobsters, and bony fishes (Wong et al. 1981).

AMPHIBIANS AND REPTILES

Tadpoles of bullfrogs (*Rana catesbeiana*) and green frogs (*R. clamitans*) from drainages along highways with different daily average traffic volumes (4,272 to 108,800 vehicles per day) contained elevated amounts of Pb (up to 270 mg/kg dry weight), which were positively correlated with Pb in sediments and with average daily traffic volume. Lead in tadpoles living near highways may contribute to the Pb levels reported in wildlife that eat tadpoles. Diets with amounts of Pb similar to those in tadpoles collected near heavily traveled highways have caused adverse physiological and reproductive effects in some species of birds and mammals (Birdsall et al. 1986). Elevated Pb sconcentrations also were recorded in various species of amphibians and reptiles collected near Pb smelters and mines (Table 5).

BIRDS

In general, Pb concentrations were highest in birds from urban locations (perhaps reflecting greater exposure to automotive and industrial contamination) and in birds near Pb mining and smelting facilities. Lead residues also are greatest in older birds (especially in bone, because of accumulation over time), in sexually mature females, and in waterfowl that have ingested Pb shot pellets (Table 5).

Continued deposition of Pb shot by hunters into wetlands habitats exposes birds to lead. Lead shot is a substantial localized source of contamination, especially in prime waterfowl habitat (Bellrose 1951, 1959; NRCC 1973; White and Stendell 1977; Stendell et al. 1979; Wobeser 1981; Clausen et al. 1982; Longcore et al. 1982; Mudge 1983; Driver and Kendall 1984; Hall and Fisher 1985). Several million hunters are estimated to deposit more than 6,000 metric tons of Pb shot annually into lakes, marshes, and estuaries; this represents about 6,440 pellets per bird bagged. Shot densities as great as 860,000 pellets/ha (2,124,000/acre) have been estimated in some locations (Wobeser 1981), although concentrations of 34,000 to 140,000/ha are more common (Longcore et al. 1982; Driver and Kendall 1984). For example, Pb shot in bottom sediments from Merrymeeting Bay, Maine, a prime waterfowl staging area, averaged 99,932 shot/ha (274,000/acre), and ranged from 59,541 to 140,324/ha; shot were significantly more numerous in silt than in sand sediments. In general, shot sink more rapidly in soft than in firm substrates, and there is only slight carryover of shot from one season to the next in areas with silt or peat bottoms (Wobeser 1981).

Waterfowl and other birds ingest spent shot during feeding and retain them as grit in the gizzard; the pellets are eroded and soluble Pb is absorbed from the digestive tract. In many species, the ingestion of a single pellet is often fatal. Most deaths, however, go unnoticed and unrecorded. Species such as the mallard and pintail that feed in shallow water by sifting through bottom mud are more likely to encounter shot than are species that feed on submerged vegetation or at the surface (Wobeser 1981). Ingested Pb shot was recorded in 6 of 10 duck species; the frequency was 8.1% in American black ducks sampled in Maine during the hunting seasons of 1976 through 1980 (Longcore et al. 1982). In dry seasons, species that probe for food deep in the sediment are especially susceptible (Hall and Fisher 1985). In England, ingested pellets occurred in 3.2% of the total waterfowl in 16 species examined. Incidences of shot were relatively high (7.1% to 11.8%) in four species (Mudge 1983): greylag goose (*Anser anser*), gadwall (*Anas strepera*). pochard (*Aythya ferina*), and tufted duck

(*Aythya fuligula*). At least 8,000 mallards in Britain die each winter of Pb toxicosis from ingestion of spent shot (Mudge 1983). It is estimated that about 2.4 million ducks die worldwide of Pb shot poisoning each year--and this estimate does not include population losses resulting from the sublethal effects of Pb (Wobeser 1981). Among larger species of waterfowl, outbreaks of Pb poisoning have been documented in Canada geese, whistling swans (*Cygnus columbianus*), trumpeter swans, and mute swans (Eskildsen and Grandjean 1984). Lead-poisoned waterfowl tend to seek seclusion and often die in areas of heavy cover; these carcasses are rapidly removed by predators and scavengers, and may result in secondary Pb poisoning, especially among raptors such as the bald eagle (Feierabend and Myers 1984; Reichel et al. 1984). Of 293 bald eagles found dead nationwide between 1978 and 1981, 17 (5.8%) probably died of Pb poisoning after ingesting hunter-killed or hunter-crippled waterfowl containing Pb pellets (Reichel et al. 1984).

The relation between embedded shot and lead toxicosis is unclear. The incidence of embedded shot in various species of waterfowl ranged from 11% to 43% in adults, and 2% to 11% in immatures (Perry and Artmann 1979; Perry and Geissler 1980). Many birds that were struck by shotgun pellets but survived may have died prematurely or been eaten by predators. In one study, the bodies of 23% of adult Atlantic brant (*Branta bernicla hrota*) that died from starvation in New Jersey in 1977 contained embedded lead shot (Kirby et al. 1983). The effects on survival and fecundity of receiving and carrying relatively high frequencies of embedded shot might be significant, and during years of low adult numbers might have substantial population consequences (Kirby et al. 1983).

Lead in seeds and invertebrates within rights-of-way of major highways probably is not a hazard to adult ground-foraging songbirds, as judged from experiments with the European starling (*Sturnus vulgaris*). However, the effects of Pb on survival of fledglings are unknown, although Pb causes reductions in blood hemoglobin, hematocrit, ALAD activity, and brain weight (Grue et al. 1986). In another study, Pb concentrations in feather, carcass, and stomach contents of adult and nestling barn swallows (*Hirundo rustica*) were greater near a major U.S. highway than in a rural area; however, the number of eggs and nestlings, the body weight of nestlings at 17 days of age, and body weights of adults were similar in the two colonies, suggesting that contamination of roadsides with Pb from automobile emissions is not a major hazard to birds that feed on flying invertebrates (Grue et al. 1984).

Signs of Pb poisoning, i.e., depressed blood ALAD activity or elevated blood Pb levels, were reported for birds near a metal smelter (Beyer et al. 1985), in 17% of canvasbacks from Chesapeake Bay in 1974 (Dieter et al. 1976), and in three species of waders from the Dutch Wadden Sea living in an urban postnuptial moulting area (Goede and de Voogt 1985). The decline in submerged aquatic vegetation in Chesapeake Bay and the later shift in diet of some waterfowl species of Chesapeake Bay from the vegetation (Pb content 2.2 to 18.9 mg/kg dry weight), to the softshell clam *Mya arenaria* (1.3 to 7.6 mg Pb/kg dry weight), or to other bivalve molluscs (0.8 to 20.4 mg Pb/kg dry weight), probably did not increase dietary Pb burdens in these species (Di Guilio and Scanlon 1985).

The significance of trace amounts of organolead residues in birds is unknown. Trialkyllead seems to concentrate in avian kidney, but contributes less than 5% of the total amount of Pb in kidneys (Johnson et al. 1982).

MAMMALS

The highest body burdens of Pb reported in mammals were near urban areas of dense vehicular traffic, near metal mines and smelters, or near plants that reclaimed storage batteries; concentrations were higher in older organisms, especially in bone and hematopoietic tissues (Table 5; Goldsmith and Scanlon 1977; Way and Schroder 1982). A similar pattern of Pb occurrence and distribution was evident for human populations (Barth et al. 1973).

Diet provides the major pathway for Pb exposure, and amounts in bone are indicative of estimated Pb exposure and metabolism (Chmiel and Harrison 1981). Amounts of whole body Pb and feeding habits of roadside rodents were correlated: body burdens were highest in insectivores such as shrews; intermediate in herbivores, and lowest in granivores (Boggess 1977; Getz et al. 1977c). Food chain biomagnification of Pb, although uncommon in terrestrial communities, may be important for carnivorous marine mammals, such as the California sea lion (*Zalophus californianus*); accumulations were 52 highest in hard tissues, such as bone and teeth, and lowest in soft tissues, such as fat and muscle (Braham 1973). A similar pattern was observed in the

harbor seal, *Phoca vitulina* (Roberts et al. 1976).

The most sensitive index of Pb intoxication in populations of deer mice was the formation of acid-fast-staining intranuclear inclusion bodies within proximal convoluted tubule cells of kidney; secondary indicators included decreased body weight, renal edema, reticulocytosis, increased urinary ALA excretion, and decreased hematocrit (Mierau and Favara 1975). Mierau and Favara (1975) concluded that Pb pollution from automobile exhausts has had little impact on deer mice, and that severe Pb poisoning is unlikely at traffic densities below 200,000 vehicles per day. Others, however, believe that Pb emissions from automotive exhausts may pose unnecessary risks to various species of bats, rodents, and mule deer (*Odocoileus hemionus*). Estimated doses of Pb ingested by the little brown bat (*Myotis lucifugus*) and highway populations of shrews and voles equaled or exceeded dosages that have caused death or reproductive impairment in domestic animals; further, mean Pb concentrations in bats and shrews near highways exceed those reported for small rodents with Pb-induced renal abnormalities collected from abandoned Pb-mining sites (Clark 1979). Mule deer from the Rocky Mountain National Park, Colorado, that graze on (heavily contaminated) roadside forage must consume 1.4% of their daily intake from roadsides before harmful amounts of Pb (3 mg Pb/day) are obtained (Harrison and Dyer 1984); however, this value needs to be verified.

Cows (*Bos bovis*) adjacent to a Pb battery reclamation plant showed signs of Pb toxicosis, including muscle tremors, blindness, dribbling urine, and drooling. Mice trapped within 400 m of the plant had acid-fast-staining intranuclear inclusions in renal tubular epithelial cells--a useful diagnostic indicator of Pb poisoning. A faulty air pollution control system at the plant caused deposition of particulate Pb on the cornfield used for cattle forage, and was the probable source of the Pb toxicosis in the animals (Kisseberth et al. 1984). Industrial airborne Pb pollution is responsible for contamination of cattle and horses (*Equus caballus*) within 1,000 m of the source, resulting in elevated blood Pb levels in both species, stillbirths and abortions in cattle, and some deaths in horses (Edwards and Clay 1977).

Proximity to the smokestacks of metal smelters is positively associated with increased levels of Pb in the hair (manes) of horses and in tissues of small mammals, and is consistent with the results of soil and vegetation analyses (EPA 1972). Lead concentrations were comparatively high in the hair of older or chronically impaired horses (EPA 1972). However, tissues of white-tailed deer (*Odocoileus virginianus*) collected near a zinc smelter did not contain elevated levels of Pb (Sileo and Beyer 1985). Among small mammals near a metal smelter, blood ALAD activity was reduced in the white-footed mouse but normal in others, e.g., the short-tailed shrew (Beyer et al. 1985). The interaction effects of Pb components in smelter emissions with other components, such as zinc, cadmium, and arsenic, are unresolved (EPA 1972), and warrant additional research.

LETHAL AND SUBLETHAL EFFECTS

GENERAL

Lead adversely affects survival, growth, reproduction, development, and metabolism of most species under controlled conditions, but its effects are substantially modified by numerous physical, chemical, and biological variables. In general, organolead compounds are more toxic than inorganic Pb compounds, food chain biomagnification of Pb is negligible, and the younger, immature organisms are most susceptible. Uptake of Pb by terrestrial plants is limited by the low bioavailability of Pb from soils; adverse effects seem to occur only at total concentrations of several hundred mg Pb/kg soil.

In aquatic environments, waterborne Pb was the most toxic form. Adverse effects were noted on daphnid reproduction at 1.0 ug Pb^{2+} /1, on rainbow trout survival at 3.5 ug tetraethyllead/l, and on growth of marine algae at 5.1 ug Pb $^{2+}$/1. High bioconcentration factors were recorded for filter-feeding bivalve molluscs and freshwater algae at 5.0 ug Pb $^{2+}$/1.

Ingestion of spent lead shot by migratory waterfowl and other birds is a significant cause of mortality in these species, and also in raptors that eat the waterfowl killed or wounded by hunters. Forms of Pb other than shot are unlikely to cause clinical signs of Pb poisoning in birds, except for certain alkyllead compounds that bioconcentrate in aquatic food items. Among sensitive species of birds, survival was reduced at doses of 75 to 150 mg Pb^{2+} /kg BW or 28 mg alkyllead/kg BW, reproduction was impaired at dietary levels of 50 mg Pb^{2+} /kg, and signs of poisoning were evident at doses as low as 2.8 mg alkyllead/kg BW.

The veterinary medical literature on Pb toxicosis is abundant for domestic livestock and small laboratory animals, but notably lacking for feral mammals. Among sensitive species of mammals, survival was reduced at acute oral doses as low as 5 mg/kg BW in the rat, at chronic oral doses of 0.3 mg/kg BW in the dog, and at dietary levels of 1.7 mg Pb/kg BW in the horse. Sublethal effects were documented in monkeys given doses as low as 0.1 mg Pb/kg BW daily (impaired learning 2 years postadministration), or fed diets containing 0.5 mg Pb/kg (abnormal social behavior). Reduction in ALAD activity was recorded in blood of rabbits given 0.005 mg Pb/kg BW, and in mice given 0.05 mg Pb/kg BW. Tissue residues increased in mice given 0.03 mg Pb/kg BW, and in sheep given 0.05 mg Pb/kg BW.

TERRESTRIAL PLANTS AND INVERTEBRATES

Fruits and vegetables acquire Pb by surface deposition from rainfall, dust, and soil, and by biological uptake through the root system (EPA 1980). Foliar absorption of Pb and transport to the root could account for a significant portion of the Pb in root tissues; however, this transport process varies widely among species. Dollard (1986) showed that this pathway accounted for 35% of the root Pb content in the radish (*Raphanus sativus*), but for <3% in carrots (*Daucus carota*) and beans (*Phaseolus vulgaris*). Corn (*Zea mays*) contained 30 mg Pb/kg dry weight when grown in soils containing Pb concentrations of 924 mg/kg, but only 17 mg/kg when grown in soils containing 786 mg Pb/kg. Sadiq (1985) concluded that contamination of soils with up to 800 mg Pb/kg probably does not elevate concentrations of Pb in corn plants. Within any plant species, however, there are Pb-resistant and Pb-sensitive breeds; some genetically fixed resistant species grow in soils containing up to 10,000 mg Pb/kg (Holl and Hampp 1975).

Plants readily accumulate Pb from soils of low pH or low organic content; however, uptake is significantly reduced after the application of lime or phosphate, which converts Pb to hydroxides, carbonates, or phosphates of relatively low solubility (Demayo et al. 1982). Lead persists for lengthy periods in forest litter; the estimated Tb 1/2 is 220 years (Turner et al. 1985). Lead seems to be tightly bound by most soils, and substantial amounts must accumulate before it affects the growth of higher plants (Boggess 1977). Although Pb is preferentially bound in soils by organics and oxides, interaction kinetics of Pb with other metals are complex and largely unknown (Bjerre and Schierup 1985). For example, uptake of Pb from soils by oat seeds (*Avena sativa*) was inhibited by cadmium salts, and reduced in loamy or organic soils; further, Pb in soils interfered with manganese uptake, and also increased the availability of cadmium and other heavy metals (Bjerre and Schierup 1985).

Lead inhibits plant growth, reduces photosynthesis, and reduces mitosis and water absorption (Demayo et al. 1982). Inhibition of photosynthesis is attributed to the blocking of protein sulfhydryl groups and to changes in phosphate levels in living cells (Holl and Hampp 1975). For two species of roadside weeds (*Cassia* spp.), pollen germination was reduced by 90% and seed germination by 87% at Pb levels of about 500 mg/kg dry weight in soil and about 300 mg/kg dry weight in foliage (Krishnayya and Bedi 1986). Normal germination rates were recorded at Pb levels of 46 mg/kg in soil and 22 mg/kg dry weight in foliage; however, some adverse effects were evident at Pb levels of 12 to 312 mg/kg in soil, and 55 to 97 mg/kg dry weight in foliage (Krishnayya and Bedi 1986). Tetraethyllead from automobile exhaust fumes is known to react in the light to produce the highly phytotoxic triethyllead cation (Backhaus and Backhaus 1986), which can freely permeate the plasma membranes of plant cells (Stournaras et al. 1984). Growth of cultures of soybean (*Glycine max*) cells exposed to 207 ug Pb/1 (as triethyllead salts) was inhibited before the cells died (Stournaras et al. 1984). There is no 56 evidence for biomagnification of Pb in the food chain of vegetation, to cattle, to dung, to the dung beetle (Robel et al. 1981), nor is there convincing evidence that any terrestrial vegetation is important in food chain biomagnification of Pb (EPA 1980).

Concentrations of Pb in soil litter ranged from 3,200 mg/kg in locations near a zinc smelter in Palmerton, Pennsylvania, to 150 mg/kg at sites 105 km distant; relative concentrations of cadmium, zinc, and copper were similar (Beyer et al. 1984). In woodlice (*Porcellio scaber*) fed litter from these locales for 8 weeks, survival decreased as metal content in the litter increased, but the major cause of death was zinc poisoning and not Pb poisoning (Beyer et al. 1984). Woodlouse (*Oniscus asellus*) hepatopancreas that were collected 3 km downwind of a metal smelter contained large amounts of zinc, copper, cadmium and Pb. Centipedes (*Lithobius variegatus*) that ate woodlice hepatopancreas did not assimilate Pb even though the food contained concentrations that were many times greater than normally encountered (Hopkin and Martin 1984). However, survival and reproduction were reduced in woodlice (*P. scaber*) fed soil litter treated with 12,800 mg Pb/kg, as lead oxide, for 64 weeks, or two generations (Beyer and Anderson 1985). This amount of Pb is similar to the

amounts reportedly associated with reductions in natural populations of decomposers, such as fungi, earthworms, and arthropods. The poisoning of decomposers may disrupt nutrient cycling, reduce the number of invertebrates available to other wildlife for food, and contribute to food chain contamination (Beyer and Anderson 1985). The effects of Pb on soil microbial populations is unknown (Boggess 1977).

Herbivorous land snails (*Helix* spp.) are important in Pb cycling through contaminated ecosystems (Dallinger and Wieser 1984; Beeby 1985). *Helix pomatia* fed lettuce enriched with Pb (about 1,000 mg Pb/kg dry weight lettuce) for 32 days contained 1,301 mg Pb/kg dry weight in the mid-gut gland (vs. 52 in controls), and much lower amounts (<30 mg/kg) in other tissues. After the snail had fed on uncontaminated lettuce for 50 days, Pb remained elevated at 1,203 mg,/kg in the mid-gut gland, which contained more than 90% of the total body burden (Dallinger and Wieser 1984).

AQUATIC BIOTA

In general, the responses of aquatic species to Pb insult differed markedly (Table 6). Among sensitive species, however, several trends were evident: (1) dissolved waterborne Pb was more toxic than total Pb; (2) organic lead compounds were more toxic than inorganic forms; (3) adverse effects on daphnid reproduction were evident at 1.0 ug Pb^{2+} /l; (4) high bioconcentrations were measured in oysters at 1.0 ug Pb /1 and in freshwater algae at 5.0 ug Pb^{2+} /l; (5) tetramethyllead was acutely toxic to rainbow trout at 3.5 ug/l; (6) growth inhibition of a marine alga was reported at 5.1 ug Pb^{2+} /1; and (7) for all species, effects were most pronounced at elevated water temperatures and reduced pH, in comparatively soft waters, in younger life stages, and after long exposures (Table 6).

Table 6. Lethal and sublethal effects of lead[a] to selected species of aquatic organisms.

Ecosystem, taxonomic group, species, and other variables	Concentration (µg Pb/L medium)	Exposure duration	Effect[b]	Reference[c]
Freshwater				
Algae and macrophytes				
Alga, *Selenastrum capricornutum*	5	28 days	BCF 92,000	1
Alga, *S. capricornutum*	50	28 days	BCF 26,000	1
Alga, *Chlamydomonas reinhardii*	207	3 h	BCF 26; some inhibition of photosynthesis	2
Alga, *C. reinhardii*	1,000	3 h	BCF 20; 50% inhibition of photosynthesis	2
Alga, *C. reinhardii*	4,140	24 h	Lethal	2
Alga, *Microcystis aeruginosa*	450	8 days	Immobilization	3
Invertebrates				
Daphnid, *Daphnia magna*	1	19 days	Reproductive impairment, 10%	4
Daphnid, *D. magna*	10	19 days	Reproductive impairment, 50%	4
Daphnid, *D. magna*	30	21 days	Reproductive impairment, 16%	3, 5
Water hardness (mg $CaCO_3$/L)				
52	9–16.7	Lifetime	MATC	3
102	78–181	Lifetime	MATC	3
151	85–193	Lifetime	MATC	3
54	612	96 h	LC-50	3

110	952	96 h	LC-50	3
152	1,910	96 h	LC-50	3
45	300	21 days	LC-50	6, 7
45	450	48 h	Immobilization, 50%	3, 7
Snail, *Lymnaea palustris*	12–54	Lifetime	MATC	3
Snail, *L. palustris*	3.8	Lifetime	No deaths	8
Snail, *L. palustris*	19	Lifetime	Significant mortality	8
Snail, *L. palustris*	36	Lifetime	Reduction in biomass, 50%	8
Snail, *L. palustris*	48	Lifetime	Reduction in biomass, 100%	8
Snail, *L. palustris*	54	Lifetime	Hatching success reduced; survivors dead by age 80 days	8
Protozoan, *Entosiphon sulcatum*	20	72 h	Immobilization	3
Amphipod, *Gammarus pseudolimnaeus* LC-50	5	28.4	60 days	
Amphipod *G. pseudolimnaeus*	124	96 h	LC-50	9
Aquatic invertebrates	32	28 days	BCF 1,000 to 9,000	5
Protozoan, *Uronema* sp.	70	20 h	Immobilization	3
Midge, *Tanytarsus dissimilis*	258	10 days	LC-50	3
Isopod, *Asellus meridianus*				
Nontolerant strain	280	48 h	LC-50	5
From Pb-contaminated river	3,500	48 h	LC-50	5
Daphnid, *Daphnia hyalina*	600	48 h	LC-50	6
Snail, *Viviparus ater*	1,000	7 days	Neuronal cytolysis	10
Snail, *V. ater*	117,000	96 h	LC-50	10
Aquatic insects, 5 species	3,500 to 64,000	7 to 14 days	LC-50	5
Isopod, *Asellus aquaticus*				
Nontolerant strain				
Pretreated for 5 days to 100 mg Pb/L	794,000	48 h	LC-50	11
No pretreatment	330,000	48 h	LC-50	11
Fish				
Rainbow trout, *Salmo gairdneri*				
Tetramethyl Pb				
Weight 1 gram	3.5	72 h	LC-50	12
Weight 1 gram	3.5	7 days	BCF 726 for whole trout	12
Weight 1 gram	3.5	14 days	LC-50	12
Weight 20 grams	24	8 to 14 days	Some deaths at day 8; BCF 17,300 for intestinal lipids at day 10 and 12,540 at day 14	

Pb^{2+}	13	32 weeks	Anemia; reduced blood ALAD activity	3
Pb^{2+}	14	14 days	Reduced stamina	3
Pb^{2+}	10	30 days	ALAD depression, 21%	13
Pb^{2+}	75	30 days	ALAD depression, 74%	13
Pb^{2+}	300	30 days + 7 weeks post-exposure	ALAD depression, 86%; anemia; basophilic stippling of erythrocytes	13
Pb^{2+}	13	4 weeks	Erythrocyte ALAD inhibition	6
Eyed eggs	10,000	56 h	LC-50	14
Eyed eggs	20,000	20 h	LC-50	14
Water hardness (mg $CaCO_3$/L)				
28				
Total Pb	7.2–14.6	Lifetime	MATC	15
Dissolved	4.1–7.6	Lifetime	MATC	15
Dissolved Pb	1,200	96 h	LC-50	5
35	71–146	Lifetime	MATC	3
353				
Total Pb	506,500	96 h	LC-50	15
Dissolved Pb	1395	96 h	LC-50	15
Dissolved Pb	120–360	Lifetime	MATC	15
Dissolved Pb	18.2–31.7	Lifetime	MATC	15
28				
Pre-hatch fry	4–7.6	Lifetime	MATC	5
Post-hatch fry	7.6–14.6	Lifetime	MATC	5
28	14.6	19 months	Vertebral deformities; caudal fin erosion	6
353	31	19 months	As above	6
28	7.2	19 months	No harmful effects	6
353	18.2	19 months	As above	6
Lake trout, *Salvelinus namaycush*				
Water hardness 33	48–83	Lifetime	MATC	16
Zebrafish, *Brachydanio rerio*				
Egg	50	24 h	Pigmentation patterns of fry irreversibly altered	17
Egg	72	24 h	Hatching inhibited	17
Brook trout, *Salvelinus fontinalis*				
Water hardness 44				
Total Pb	58–119	3 generations	MATC	3, 5, 18
Dissolved Pb	39–84	3 generations	MATC	5,18
Total Pb	4,100	96 h	LC-50	18

Dissolved Pb	3,362	96 h	LC-50	18
Total Pb	134	21 days	Growth reduction	6
Total Pb	119	3 generations	First generation: BCF 571 for liver and 1,806 for kidney. Second generation: BCF 420 for liver, 1,504 for kidney; severe spinal deformities in 34%. Third generation: spinal deformities in 21%, reduction in body weight	18
Total Pb	235	2 generations	All with spinal deformities	18
Bluegill, *Lepomis macrochirus*				
Water hardness 41	70–120	Lifetime	MATC	16
Channel catfish, *Ictalurus punctatus*				
Water hardness 36	75–136	Lifetime	MATC	16
White sucker, *Catostomus commersoni*				
Water hardness 34	119–253	Lifetime	MATC	5
Cyprinid, *Puntius conchonius*	127	4 months	Gonadal pathology	19
Cyprinid, *P. conchonius*	379	96 h	LC-50	19
Goldfish, *Carassius auratus*	200	4–5 days	ALAD inhibition	6
Northern pike, *Esox lucius*				
Water hardness 34 (mg $CaCO_3$/L)	253–483	Lifetime	MATC	5
Threespine stickleback, *Gasterosteus aculeatus*	300	96 h	LC-100	6
Smallmouth bass, *Micropterus dolomieui*				
Water hardness 152 (mg $CaCO_3$/L)				
Fingerlings	405	90 days	No effect on growth, behavior, blood chemistry	20
Swim-up fry	2,800	96 h	LC-50	20
Fingerlings	29,000	96 h	LC-50	20
Egg and sac-fry	>15,900	96 h	LC-50	20
Fathead minnow, *Pimephales promelas*				
Water hardness (mg $CaCO_3$/L)				
20	6,500	96 h	LC-50	7
360	460,000	96 h	LC-50	7

Marine				
Algae and macrophytes				
Diatom, *Skeletonema costatum*	0.05	12 days	No effect on growth	21
Diatom, *S. costatum*	5.1	12 days	Growth inhibition, 50%	3
Diatom, *S. costatum*	10	12 days	Growth inhibition, 100%	21
Alga, *Phaeodactylum tricornutum*				
Pb^{2+}	20	<1 h	BCF 582,000	22
Pb^{2+}	>5,000	96 h	LC-50	23
Tetramethyl Pb1	1,300	96 h	LC-50	23
Trimethyl Pb	800	96 h	LC-50	23
Triethyl Pb	100	96 h	LC-50	23
Tetraethyl Pb	100	96 h	LC-50	23
Phytoplankton, mixed populations	21	4 days	Reduced biomass	3
Alga, *Dunaliella tertiolecta*				
Tetraethyl Pb	150	96 h	Growth inhibition	3
Tetramethyl Pb	1,650	96 h	Growth inhibition	3
Invertebrates				
American oyster, *Crassostrea virginica*, soft parts	1.0	140 days	BCF 6,600	24
American oyster, soft parts	3.3	140 days	BCF 3,454	24
Blue mussel, *Mytilus edulis*				
Pb^{2+}, adults	>500,000	96 h	LC-50	23
Pb^{2+}, larvae	476	96 h	LC-50	3
Triethyl Pb	1,100	96 h	LC-50; BCF 10	23
Trimethyl Pb	500	96 h	LC-50; BCF 23	23
Tetramethyl Pb	270	96 h	LC-50; BCF 170	23
Tetraethyl Pb	100	96 h	LC-50; BCF 120	23
Pb^{2+}	10	63 days	BCF 12,580 for kidney and 1,580 for soft parts	25
Pb^{2+}	500	150 days	BCF 25,670 for soft parts	26
Softshell clam, *Mya arenaria*				
Soft parts				
Temperature, °C				
0–10	14	42 days	BCF 158	27
0–10	70	42 days	BCF 180	27
16–22	14	14 days	BCF 351	27
16–22	70	7 days	BCF 237	27
Mysid, *Mysidopsis bahia*	17–37	Lifetime	MATC	3
Sandworm, *Neanthes arenaceodentata*				

Salinity, o/oo				
15	20	23 days	Inhibited reproduction	28
20	3,100	28 days	Inhibited reproduction	28
Temperature, °C				
15	10,700	96 h	LC-50	28
20	7,700	96 h	LC-50	28
Shrimp, *Crangon crangon*				
Pb^{2+}	375,000	96 h	LC-50	23
Trimethyl Pb	8,800	96 h	LC-50; BCF 1	23
Triethyl Pb	5,800	96 h	LC-50; BCF 2	23
Tetramethyl Pb	110	96 h	LC-50; BCF 20	23
Tetraethyl Pb	20	96 h	LC-50; BCF 650	23
American lobster, *Homarus americanus*	50	30 days	Reduced ALAD activity	3
American lobster	50	30 days	Biochemical alterations in antennal gland; BCF 2,760 for antennal gland, and 58 for gill	29
Protozoan, *Cristigera* sp.	150	12 h	Reduced growth	3
Amphipod, *Ampelisca abdita*	547	96 h	LC-50	3
Dungeness crab, *Cancer magister*	575	96 h	LC-50	38
Sea urchin, *Anthocidaris crassispina* (embryos)	1,100	48 h	No effect on development	30
Sea urchin (embryos)	2,200	48 h	Development inhibited	30
Fish				
Plaice, *Pleuronectes platessa*				
Tetramethyl Pb	50	96 h	LC-50; BCF 60	23
Tetraethyl Pb	230	96 h	LC-50; BCF 130	23
Triethyl Pb	1,700	96 h	LC-50; BCF 2	23
Trimethyl Pb	24,600	96 h	LC-50; BCF 1	23
Diethyl Pb	75,000	96 h	LC-50	23
Pb^{2+}	180,000	96 h	LC-50	23
Dimethyl Pb	300,000	96 h	LC-50	23
Mummichog, *Fundulus heteroclitus*	315	96 h	LC-50	3

[a]As total Pb, unless indicated otherwise.

[b]BCF = bioconcentration factor; MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolic upset during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

[c]References: 1, Vighi 1981; 2, Irmer et al. 1986; 3, EPA 1985; 4, Berglind et al. 1985; 5, Demayo et al. 1982; 6, Wong et al. 1978; 7, NRCC 1973; 8, Borgmann et al. 1978; 9, Spehar et al. 1978; 10, Fantin et al. 1985; 11, Fraser 1980; 12, Wong et al. 1981; 13, Johansson-Sjobeck and Larsson 1979; 14, Rombaugh 1985; 15, Davies et al. 1976; 16, EPA 1980; 17, Ozoh 1980; 18, Holcombe et al. 1976; 19, Kumar and Pant 1984; 20, Coughlan et al. 1986; 21, Rivkin 1979; 22, Schulz-Baldes and Lewin 1976; 23, Maddock and Taylor 1980; 24, Zaroogian et al. 1979; 25, Schulz-Baldes 1974; 26, Schulz-Baldes 1972; 27, Eisler 1977; 28, Reish and Gerlinger 1984; 29, Gould and Grieg 1983; 30, Kobayashi 1971.

Lead is toxic to all phyla of aquatic biota, but its toxic action is modified by species and physiological state, and by physical and chemical variables. Wong et al. (1978) stated that only soluble waterborne Pb is toxic to aquatic biota, and that free cationic forms are more toxic than complexed forms. The biocidal properties of soluble Pb are also modified significantly by water hardness: as hardness increased, Pb becomes less bioavailable because of precipitation increases (NRCC 1973). In salmonids, for example, the toxicity and fate of Pb are influenced by the calcium status of the organism, and this relation may account for the reduced effects of Pb in hard or estuarine waters. In coho salmon (*Oncorhynchus kisutch*), an increase in waterborne or dietary calcium reduced uptake and retention of Pb in skin and skeleton (Varanasi and Gmur 1978).

Organolead compounds are, in general, more toxic than inorganic Pb compounds to aquatic organisms. Ethyl derivatives were more toxic than methyl derivatives, and toxicity increased with increasing degree of alkylation, tetralkyllead being the most toxic (Chau et al. 1980). Tetraethyllead was about 10X more effective than tetramethyllead in reducing oxygen consumption by coastal marine bacteria, and was 1.5 to 4X more toxic than tetramethyllead to marine teleosts (Marchetti 1978). Tetramethyllead chloride was 20X as toxic as $Pb(NO_3)_2$ to freshwater algae, and 2X as toxic as trimethyllead acetate (Wong et al. 1978). In seawater, the release of tetraalkyllead compounds is more likely than accumulation to result in acutely toxic effects; however, alkyllead compounds degrade rapidly to trialkyllead chlorides, which are only 0.1 to 0.01 as toxic as TEL compounds (Haddock and Taylor 1980). Alkyllead compounds are accumulated more readily by freshwater teleosts than are inorganic Pb compounds. The BCF values for tetramethyllead and rainbow trout, for example, ranged from 124 in lipids after exposure for 1 day, to 934 after 7 days (Demayo et al. 1982). Depuration of tetramethyllead is rapid; the estimated Tb 1/2 values range from 30 hours for intestinal lipids to 45 hours for skin and cephalic fat deposits (Wong et al. 1981). Some microorganisms in lake sediments transform certain inorganic and organic Pb compounds into the more toxic tetramethyllead, but the pathways are not well understood (Wong et al. 1978).

Lethal solutions of Pb (as well as of many other heavy metals) cause increased mucous formation in fishes. The excess coagulates over the entire body and is particularly prominent over the gills, interfering with respiratory function and resulting in death by anoxia (Aronson 1971; NRCC 1973). Increasing waterborne concentrations of Pb over 10 ug/l are expected to provide increasingly severe long-term effects on fish and fisheries (Demayo et al. 1982). Fish that are continuously exposed to toxic concentrations of waterborne Pb show various signs of Pb poisoning: spinal curvature, usually as lordosis; anemia; darkening of the dorsal tail region, producing a black-tail effect due to selective destruction of chromatophores but not of melanophores; degeneration of the caudal fin; destruction of spinal neurons; ALAD inhibition in erythrocytes, spleen, liver, and renal tissues; reduced ability to swim against a current; destruction of the respiratory epithelium; basophilic stippling of erythrocytes; elevated Pb concentrations in blood, bone, gill, liver, and kidney; muscular atrophy; paralysis; renal pathology; growth inhibition; retardation of sexual maturity; altered blood chemistry; testicular and ovarian histopathology; and death (Aronson 1971; NRCC 1973; Adams 1975; Davies et al. 1976; Holcombe et al. 1976; Hodson et al. 1977, 1980, 1982; Johansson-Sjobeck and Larsson 1979; Reichert et al. 1979; Ozoh 1980; Demayo et al 1982; Kumar and Pant 1984; Rai and Qayyum 1984; Hodson and Spry 1985; Haux et al. 1986). The prevalence of signs is closely correlated with duration of exposure to Pb and to its uptake (Hodson et al 1982). Toxic effects of Pb uptake in fishes are increased under conditions favoring their rapid growth. Hodson et al. (1982) have shown that the rate of intoxication by Pb--as judged by uptake rates into tissues and incidence and prevalence of black tail--did not increase with fish size, but rather with growth rate.

Rooted aquatic plants, such as wild rice (*Zizania aquatica*), can accumulate up to 67 mg Pb/kg dry weight when cultured in tanks contaminated with high concentrations of powdered Pb (equivalent to 7,400 kg Pb/ha);

however, this level is not considered hazardous to waterfowl feeding on wild rice (Behan et al. 1979). Lead content in plants collected from heavily hunted areas near refuges did not differ from those collected in the protected areas (Behan et al. 1979), which suggests that Pb bioavailability to rooted aquatics is substantially lower from shot than from powdered Pb. In another study with rooted macrophytes, *Navicula* sp. and *Elodea canadensis* rapidly accumulated Pb from solutions containing 1.0 mg Pb^{2+} /l, i.e., 70 mg Pb/kg dry weight per minute; the process was overwhelmingly passive (Everard and Denny 1985). Depuration was rapid; 90% of the Pb sorbed during the first hour by shoots of *Elodea* was released within 14 days after transfer to clean water, though 10% seemed to be irreversibly bound (Everard and Denny 1985).

High accumulations of Pb from ambient seawater by marine plants is well documented; concentration factors vary from 13,000 to 82,000 for algae from Raritan Bay, New Jersey (Seeliger and Edwards 1977), and from 1,200 to 26,000 for algae from Sorfjorden, Norway (Melhuus et al. 1978). Studies on the kinetics of lead uptake and retention in two species of marine algae (*Phaeodactylum tricornutum*, *Platymonas subcordiformes*) showed that both species accumulated Pb from the medium at ambient concentrations of 20 ug/l, and higher (Schulz-Baldes and Lewin 1976). In the first phase, usually completed within minutes after addition of Pb, cells of *Phaeodactylum* became saturated when the Pb reached a remarkable 11,640 mg/kg dry weight. In the second phase, the lead content of *Platymonas* continued to rise slowly, but that of *Phaeodactylum* declined after 2 or 3 days. In both species the content of bound Pb increased with increasing exposure time, suggesting that during prolonged exposure Pb is initially adsorbed to the cell surface, then translocated into the cell wall, the plasma membrane, and eventually the cytoplasm (Schulz-Baldes and Lewin 1976).

Sediments are not only sinks for Pb but may act as a source of Pb to aquatic biota after contamination from the original source has subsided (Knowlton et al. 1983). The uptake of Pb from artificially contaminated pond sediments was recorded in roots and foliage of submersed aquatic macrophytes (*Potamogeton foliosus*, *Najus guadalupensis*) and in the exoskeleton of crayfish (*Orconectes nais*). Accumulation of Pb in crayfish primarily was through adsorption; most was lost through molting, though some internal uptake and elimination occurred without molting (Knowlton et al. 1983). Crustacean molts represent 15% of the Pb body burden and are probably more significant than fecal pellets in Pb cycling processes (Fowler 1977).

Median BCF values in aquatic biota exposed to various concentrations of Pb^{2+} for 14 to 140 days varied from about 42 in fish to 2,570 in mussels; intermediate values were 536 for oysters, 500 for insects, 725 for algae, and 1,700 for snails (EPA 1985). There are several notable exceptions to this array: significantly higher values have been reported in crustacean hepatopancreas (Heyraud and Cherry 1979), in various species of freshwater invertebrates (Spehar et al. 1978), in fish bone (Demayo et al. 1982) and liver (Haux and Larsson 1982), and in whole oysters (Zaroogian et al. 1979). In oysters, for example, BCF values varied from 3,450 to 6,600 after exposure to solutions containing 1.0 to 3.3 ug Pb^{2+} /1 for 140 days, but oysters and their progeny were apparently unaffected at whole body burdens (less shell) up to 11.4 mg Pb/kg dry weight (Zaroogian et al. 1979). Many species of aquatic biota contain Pb in amounts >1,000 mg/kg fresh weight (>10,000 mg/kg dry weight) including some marine seaweeds, freshwater macrophytes and algae, annelids, crustaceans, echinoderms, molluscs, and teleosts (Wong et al. 1978); presumably, the Pb was sorbed passively and little, if any, was incorporated biologically. Variations in Pb concentrations in aquatic biota probably reflect the ability of individual species to adsorb waterborne Pb, and may be a direct function of the ratio of surface to body weight (Demayo et al. 1982). The residence time of Pb in aquatic biota seems to be related to the route of administration: Tb 1/2 values were 9 days by waterborne routes and 40 days by diet (Vighi 1981).

Although Pb is concentrated by biota from water, there is no convincing evidence that it is transferred through food chains (Branica and Konrad 1980; Settle and Patterson 1980). Lead concentrations tended to decrease markedly with increasing trophic level in both detritus-based and grazing aquatic food chains (Wong et al. 1978). In the marine food chain of seawater (<0.08 ug Pb/1), to a brown alga (*Egregia laevigata*), to the red abalone (*Haliotis rufescens*), Pb concentrations in the alga and abalone were both <0.04 mg Pb/kg fresh weight after 6 months, indicating negligible biomagnification (Stewart and Schulz-Baldes 1976). When seawater contained 1,000 ug Pb/l, young abalones that fed on *Egregia* for 6 months contained up to 21 mg Pb/kg fresh weight, but neither growth nor activity was affected; Pb selectively accumulated in the digestive gland (38 mg/kg), and was lowest in muscle (<l mg/kg)--the part normally consumed by humans (Stewart and Schulz-Baldes 1976). In the freshwater food chain of an alga (*Selenastrum capricornutum*), to a daphnid (*Daphnia magna*), to the guppy (*Poecilia reticulata*), Pb accumulation progressively decreased from the alga to the guppy.

Thus, in organisms held for 28 days in solutions containing 5 ug Pb/l, Pb content was 460 mg/kg dry weight in the alga, 23 mg/kg in the grazing daphnids, and 4 to 16 mg/kg in the guppies that fed on the daphnids (Vighi 1981). Concentrations of Pb in the freshwater snail, *Lymnaea peregra*, collected near an abandoned Pb mine were positively correlated with the Pb content in its diet; the digestive glands contained up to 5,600 mg/kg dry weight (Everard and Denny 1984). The gut contents of eels (*Anguilla anguilla*) grazing on contaminated snails contained up to 4,350 mg Pb/kg, but the Pb was rapidly released; feces from both snails and eels return the Pb to the ecosystem as particulates and detritus (Everard and Denny 1984).

As discussed earlier, Pb clearly inhibits the formation of heme at several points, adversely affects blood chemistry, and accumulates in hematopoietic organs of aquatic organisms. In addition, Pb interferes with chlorophyll formation in plants by inhibiting the conversion of coproporphyrinogen to proporphyrinogen by competing with iron, inhibits allantoise formation in annelids, inhibits alpha-glycerophosphate dehydrogenase activity in trout, increases glutamic oxalacetate transaminase activity in *Daphnia*, affects neural and hormonal systems that control activity and metabolic rates in fish, interacts with polar sites of glycoproteins in epidermal mucous of fish, and may inhibit vitamin C and tryptophan metabolism (Wong et al. 1978).

Some populations of freshwater isopods are tolerant to Pb. Inasmuch as nontolerant isopods from an unpolluted site can be made tolerant by exposure to low levels, it is suggested that naturally occurring tolerance may be achieved by acclimatization (Fraser 1980). Research is needed on Pb transformation mechanisms, on toxic forms of Pb and interaction effects with other compounds, and on effects of Pb-contaminated sediments on benthos (Wong et al. 1978).

AMPHIBIANS AND REPTILES

Lead poisoning in adult leopard frogs (*Rana pipiens*) is indicated by a series of signs: sloughing of integument; sluggishness; decreased muscle tone; decreases in red blood cells, white blood cells, neutrophils, and monocytes; erosion of the gastric mucosa; and (before death) excitement, salivation, and muscular twitching. The 30-day LC-50 value for *R. pipiens* was 105 mg Pb/l, but some deaths and elevated liver residues were noted at water concentrations as low as 25 mg/l (Kaplan et al. 1967). In soft water (99 mg $CaCO_3$/1) some marbled salamanders (*Ambystoma opacum*) exposed to 1.4 mg Pb/1 died in 8 days (EPA 1985). At about 1.0 mg/l, Pb blocked synaptic transmission by competitive inhibition of calcium in the bullfrog, *Rana catesbeiana* (Kober and Cooper 1976). At 0.5 mg Pb/l, tadpoles of *Rana utricularia* required additional time to metamorphose; and at 1.5 mg Pb/l, thyroid histopathology was recorded and the delay in metamorphosis was more pronounced (Yeung 1978).

No data were available on toxic or sublethal effects of Pb to reptiles under controlled conditions.

BIRDS

Lead poisoning resulting from the ingestion of Pb shotgun pellets has been recognized as a cause of waterfowl deaths since the late 1800's (Wetmore 1919; Bellrose 1959). More than a million ducks--especially mallards--and geese die annually from Pb shot poisoning (Clemens et al. 1975). The principal cause is the ingestion of spent shot by migrating birds feeding in heavily hunted areas. The pellets are retrieved from the marshy bottoms of shallow and deep water by waterfowl in search of feed and grit. Shot retained in the gizzard is solubilized by a combination of the powerful muscular grinding action and the low pH (2.0 to 3.5) of gizzard contents. The released Pb is available for absorption, producing weakened birds whose reproductive abilities are reduced and that may starve or fall prey to predators (Clemens et al. 1975). Absorbed lead causes a variety of effects leading to death, including damage to the nervous system, muscular paralysis, inhibition of heme synthesis, and damage to kidneys and liver (Mudge 1983). Lead poisoning in waterfowl is a debilitating disease in which death follows exposure by an average of 2 to 3 weeks (Friend 1985). During this time, affected birds lose mobility, tend to avoid other birds, and become increasingly susceptible to predation and other causes of mortality. Accordingly, acute large-scale die-offs of Pb-poisoned waterfowl are uncommon (Friend 1985).

The relation between incidence of Pb shot in waterfowl gizzards and biological effects varies widely, and is probably a function of shot availability caused by differences in shooting intensity, size of pellets, availability of

grit, firmness of soil and sediments, and depth of surface water (Street 1983). Also, Pb accumulations and the frequency of avian Pb toxicosis following ingestion of Pb shot are modified by the age and sex of the bird, geographic location, habitat, and time of year (Finley and Dieter 1978; Mudge 1983; Srebocan and Rattner 1988).

The effect of diet on vulnerability to Pb makes interpretation of published information on experimental Pb poisoning in waterfowl extremely difficult (Chasko et al. 1984). For example, many mallards on a diet of corn die within 10 to 14 days after ingesting a single Pb shot, whereas similar birds on a balanced commercial duck ration appear outwardly normal after ingesting as many as 32 pellets of the same size (Wobeser 1981). Also, multiple nutritional deficiencies may have additional effects in potentiating the toxicity of Pb in mallards (Carlson and Nielsen 1985).

Birds of prey may ingest Pb in the form of shot from dead or crippled game animals, or as biologically incorporated Pb from Pb-poisoned waterfowl, small roadside mammals, and invertebrates (Stendell 1980; Pattee 1984). Lead poisoning in carnivorous birds has been reported in various species of eagles, condors, vultures, and falcons, and most--if not all--cases seem to result from ingestion of Pb shot in food items (Custer et al. 1984). Some raptors ingest many shot in a short time. For example, the stomach of a bald eagle suspected of dying from Pb poisoning contained 75 shot (Jacobson et al. 1977). Results of experimental Pb shot poisoning of bald eagles (Table 7) confirmed results of nationwide monitoring showing that 5.4% of all dead eagles found in 1974-1975 died of Pb poisoning, as evidenced by liver Pb levels of 23 to 38 mg/kg fresh weight (Pattee et al. 1981). Ingestion of food containing biologically incorporated Pb, although contributing to the Pb burden of carnivorous birds, is unlikely in itself to cause clinical Pb poisoning (Custer et al. 1984). A similar case is made for powdered Pb (Franson et al. 1983), and forms of Pb other than shot (Table 7); the strong indication is that the form in which Pb is ingested is crucial.

Signs of Pb poisoning in birds have been extensively documented (Bellrose 1951, 1959; Jordan and Bellrose 1951; Clemens et al. 1975; Forbes and Sanderson 1978; Hunter and Wobeser 1980; Pattee et al. 1981; Wobeser 1981; Franson and Custer 1982; Johnson et al. 1982; Eastin et al. 1983; Kendall and Scanlon 1983; Street 1983; Di Giulio and Scanlon 1984; Fimreite 1984; Gjerstad and Hanssen 1984; Hudson et al. 1984; Anderson and Havera 1985; Burger and Gochfeld 1985; Carlson and Nielsen 1985; Friend 1985; Hoffman et al. 1985a; Lumeij 1985; Beyer et al. 1988). Outwardly, Pb-poisoned birds show the following signs: loss of appetite, lethargy, weakness, emaciation, tremors, drooped wings, green liquid feces, and impaired locomotion, balance, and depth perception. Internally, Pb-poisoned birds show microscopic lesions of the proventricular epithelium, pectoral muscles, brain, proximal tubular epithelium of the kidney, and bone medullary osteocytes; an enlarged bile-filled gall bladder; anemia; elevated protoporphyrin IX levels in blood; decreased ALAD activity levels in blood, brain, and liver; reduced brain weight; abnormal skeletal development; cephalic edema; and esophageal impaction. Postmortem examination of Pb-poisoned birds may show edematous lungs; serous fluid in the pleural cavity; bile regurgitation; abnormal gizzard lining; a usually pale, emaciated, and dehydrated carcass; and elevated Pb levels in liver (>2 mg/kg fresh weight, >10 mg/kg dry weight), kidney (>6 mg/kg dry weight), and blood (> 0.2 mg/1).

Toxic and sublethal effects of Pb and its compounds on birds held under controlled conditions vary widely with species, with age and sex, and with form and dose of administered Pb (Table 7). Several generalizations are possible: decreased blood ALAD and increased protoporphyrin IX activity levels are useful early indicators of Pb exposure; Pb shot and certain organolead compounds are the most toxic forms of Pb; nestlings are more sensitive than older stages; and tissue Pb concentrations and pathology both increase in birds given multiple doses over extended periods (Table 7).

Table 7. Lethal and sublethal effects of lead to selected species of birds.

Species, route of administration, dose, and other variables	Effects	Reference[a]
Northern pintail, *Anas acuta*		
Single oral dose of 2 No. 5 pellets	No difference from control group in band recovery rate from hunter kills	1
Mallard, *Anas platyrhynchos*		
Single oral dose of 1 No. 4 shot (1.4 g)	Some deaths. Residues (mg/kg fresh weight) >3 in brain, >10 in clotted heart blood, >6 in kidney, and up to 20 in liver	2
Single oral dose		
1 No. 6 shot (1.0 g)	Mortality 9% in 20 days	3
1 No. 4 shot (1.6 g)	Mortality 19% in 20 days	3
2 No. 6 shot (2.0 g)	Mortality 23% in 20 days	3
4 No. 6 shot (4.0 g)	Mortality 36% in 20 days	3
6 No. 6 shot (6.0 g)	Mortality 50% in 20 days	3
8 No. 6 shot (8.0 g)	Mortality 100% in 20 days	3
Single oral dose of 1 No. 4 shot (205 mg), equal to 151 mg/kg body weight (BW)	Some deaths; blood ALAD activity depressed 30% after 3 months, 15% after 4 months	4
Single oral dose of 1 No. 4 Pb shot (200 mg)	Residues (mg/kg dry weight femur) 488 in laying hen, 114 in nonlaying hen, and 9 in drake	5
Single oral dose of 1 shot (200 mg)	After 30 days, residues (mg/kg fresh weight) 1.0 in blood, 2.5 in liver, and 0.5 in brain. Decrease in ALAD activity in blood and cerebellum	6
Single oral dose of shot	Dosed birds recaptured in significantly greater numbers than controls	7
Single oral dose of tetraethyllead	LD-50 of 107 mg/kg BW. Signs of intoxication included	

	excessive drinking, regurgitation, hypoactivity, muscular incoordination, fluffed feathers, eyelid drooping, tremors, and loss of appetite. Regurgitation within 7 min, other signs as soon as 20 min, and death usually between 1 and 4 days posttreatment. Remission took up to 8 days	7a
Fed diets containing 25 mg Pb/kg, as lead nitrate, for 12 weeks	No deaths; no pathology; no significant accumulations of Pb in liver, kidney, or bone; no changes in hemoglobin or hematocrit; decrease in blood ALAD activity, and increase in blood Pb levels--both returned to normal diet within 3 weeks on Pb-free diet	8
Fed diets containing 100 mg Pb^{2+}/kg	Elevated levels in bone (9.6 mg/kg fresh weight vs. 0.7 in controls) and egg (1.3 vs. 0.9 in controls)	9
Fed diets containing metallic Pb for 42 days		
100 mg/kg diet dry weight	Elevated Pb levels (mg/kg dry weight) in kidney (23), liver (7), and bone (5)	10
10 mg/kg diet	Residues (mg/kg dry weight) of 4 in kidney (vs. <0.5 in controls), 0.7 in liver (vs. <0.5 in controls), and 0.8 in bone (vs. 0.9 in controls)	10
Ducks, *Anas* spp.		
Single oral dose of 2 shot (254 mg) or 5 shot (635 mg)	Weight loss, emaciation, elevated Pb concentrations in bone, some deaths. American black duck, *Anas rubripes*, more sensitive than mallards	11
Birds		
Dietary route, 11 species,	All had inclusions in proximal	

diagnosed as Pb-poisoned	convoluted tubules of kidney; liver Pb residues ranged from 3.1 to 15 mg/kg fresh weight	12
Lethal dietary administration of lead acetate, 6 species	Before death, birds were emaciated and showed increases in blood protoporphyrin and decreases in ALAD; renal intra-nuclear inclusion bodies were present in 83% of all birds that died from Pb poisoning. Median Pb concentrations (mg/kg fresh weight) ranged in the liver from 20 in male red-winged blackbirds (*Agelaius phoeniceus*) to 111 in female northern bobwhites (*Colinus virginianus*), and in the kidney from 22 mg/kg in the blackbird to 190 in the bobwhite	13
Rock dove, *Columba livia*		
Intragastric administration of 6.25 mg Pb (as lead acetate)/kg BW daily for 64 weeks	Anemia, elevation of erythrocyte porphyrin, kidney pathology; residues (mg/kg fresh weight) of 603 in kidney, 501 in bone, 8 in liver, 2 in brain, 4.4 in blood, 0.8 in sciatic nerve, and 0.1 in crop	14
Intubation of 6.25 mg Pb (as lead acetate)/kg BW, chronic exposure	Interfered with four-step learning sequence; elevated blood Pb levels remained for 5 weeks after Pb exposure	15
Japanese quail, *Coturnix japonica*		
Single oral dose of tetraethyllead	LD-50 of 24.6 mg/kg BW	7a
Fed diets containing different forms of Pb for 5 days		
5,000 mg metallic Pb/kg	No effect on survival or food consumption	16
5,000 mg Pb (as lead nitrate)/kg	No overt signs of toxicity	16
5,000 mg Pb (as lead subacetate $C_4H_{10}O_8Pb_3$)/kg	No overt signs of toxicity	16
2,761/mg Pb (as	LD-50	16

lead arsenate)/kg		
Prairie falcon, *Falco mexicanus*		
Fed shotgun-killed pheasants and ducks	Death, preceded by vomiting, ataxia, blindness, and convulsions. Lead shot recovered from stomach; residues (mg/kg dry weight) of 57 in liver and 78 in kidney	17
American kestrel, *Falco sparverius*		
Fed mallard homogenate containing 16 to 87 (biologically incorporated) mg Pb/kg fresh weight for 60 days	Residues of 0.4 mg/kg fresh weight in liver and 7.6 mg/kg dry weight in bone	18
Oral administration of 1 No. 9 shot daily for 60 days	Residues (mg/kg fresh weight) of 0.4 in liver and 28.7 in bone	18
Fed control diet containing 0.4 mg Pb^{2+}/kg fresh weight	Residues of 0.1 mb/kg fresh weight in liver and 4.2 mg/ kg dry weight in bone	18
Fed diets containing 50 mg metallic Pb powder/kg for at least 5 months	Blood ALAD reduced 80%; liver residues of 1.3 to 2.4 mg/kg dry weight; no effects on blood chemistry	19
As above, except diet contained 10 mg/kg	No measurable effects	19
Fed diets containing metallic Pb powder for 6 months		
50 mg Pb/kg diet	No adverse effects on survival, egg laying, fertility, or egshell thickness. Elevated residues (mg/kg dry weight) in humerus (13), tibia (62), and liver (2)	20
10 mg Pb/kg diet	Elevated Pb in bone (4 to 9 mg/kg dry weight vs. <0.8 in controls) and in liver (3 vs. <0.5 in controls)	20
Nestlings dosed orally		

with metallic Pb powder daily for 10 days		
625 mg/kg BW	Mortality (40% in 6 days); reduced growth; reduced kidney and liver weight; abnormal skeletal development; ALAD depression in all tissues examined; elevated burdens (mg/kg fresh weight) in kidney (15), liver (6), and brain (3)	21
125 mg/kg BW	Reduced growth, reduced brain weight, abnormal skeletal development, ALAD depressions in hematopoietic tissues, elevated burdens (mg/kg fresh weight) in kidney (7), and liver (4)	21
25 mg/kg BW	ALAD depression in all tissues examined; burdens (mg/kg fresh weight) elevated in kidney (3) and in liver 1.4)	21
Fed 60 days with homogenized cockerels (*Gallus* sp.) containing up to 448 mg (biologically incorporated) Pb/kg dry weight	No effect on survival, growth, hemoglobin, hematocrit, and erythrocyte number. Elevated burdens in kidney, liver, femur, brain, and blood	22
Chicken, *Gallus* sp.		
Fed diets containing 1,850 mg Pb/kg, as lead acetate, for 4 weeks	No deaths or severe clinical hematological effects; growth rate suppressed 47%, blood Pb residues 3.2 to 8.3 mg/L	23
Bald eagle, *Haliaeetus leucocephalus*		
Oral administration of 10 No. 4 shot (2,000 mg)		
Eagles dying 10 to 133 days posttreatment	Residue levels (mg/kg dry weight) 0.9 in muscle, 1.4 in brain, 6 in kidney, 10 in tibia, 10.3 in humerus, 10.4 in femur, and 16.6 in liver. Loss in body weight 16% to 23%	

	at death	24
Eagle sacrificed at day 133 posttreatment (bird went blind)	Residue levels (mg/kg dry weight) <0.1 in muscle, 2.1 in brain, 3.2 in kidney, 3.4 in liver, and 12.2 to 13.8 in bone	24
Controls	Residue levels (mg/kg dry weight) <0.1 muscle, 0.1 in brain, 0.4 in liver, 0.5 in kidney, and 4.5 to 6.6 in bone	24
Willow ptarmigan, *Lagopus lagopus*		
Single oral dose		
1 No. 6 shot (100 mg)	Weight loss of 12% in 15 days; residues of 3.3 mg/kg fresh weight in liver, 56 mg/kg dry weight in tibia	25, 26
3 No. 6 shot (300 mg)	Some deaths between days 8 and 15 posttreatment, reduced food intake, weight loss, lethargy, diarrhea; residues of 7.3 mg/kg fresh weight liver, 139 dry weight tibia	25, 26
6 No. 6 shot (600 mg)	If shot retained in gizzard, death resulted; residues (mg/kg) 72 fresh weight in liver, 154 dry weight in tibia	25, 26
Controls	Residues (mg/kg) 0.1 fresh weight in liver, 5 dry weight in tibia	25, 26
Raptors, 4 spp.		
Fed rock doves (*Columba livia*) and brown hares (*Lepus europaeus*) containing Pb shot for 3 weeks to 6 months	Death preceded by weight loss, convulsions, and inability to fly. Residues (mg/kg dry weight) at death ranged from 57 to 175 in liver, and 34 to 221 in kidney	27
Common tern, *Sterna hirundo*		
Single injection of 200 mg Pb^{2+}	Adverse effects on behavior (locomotion, balance, righting response, feeding tasks, behavioral thermo-regulation); most apparent	

	within 5 days postinjection	28
Ringed turtle-dove, *Streptopelia risoria*		
Single oral dose of 2 pellets (220 mg)	Blood Pb (mg/L) 4.69 at 24 h, and 0.14 at 14 days (vs. control values of 0.004 to 0.012 mg/L); blood ALAD depressed from 24 h through 14 days	29
Single oral dose of 4 shot (440 mg)	Mortality 71% at 6 C in 7 days; nil at 21 C in 9 days--but some with seizures and kidney histopathology. No spermatozoa in seminiferous tubules. Lead residues elevated in bone, liver, and brain in both groups, but more elevated in cold-stressed group	30, 31
Single oral dose of 4 shot (440 mg)	Testicular damage in adults held at 6 C or 21 °C; mortality higher in cold-stressed group	32
Single oral dose of 4 shot (488 mg)	Some deaths. Intranuclear inclusion bodies in cells of kidney proximal convoluted tubules	12
Single oral dose of 75 mg Pb/kg BW, as lead acetate	Some deaths; kidney damage	12
Intubation with 75 mg Pb (as lead acetate)/kg BW daily for 7 days	Residues, (mg/kg dry weight) 457 in kidney, 29 in liver, and 12.4 in brain; seizures; depressed blood ALAD activity; blood Pb concentration 311 mg/L	33
Controls	Concentrations (mg/kg dry weight) 8.2 in kidney, 3.0 in brain, 1.2 in liver; blood Pb concentration 18 mg/L	33
Drinking water with 100 µg Pb^{2+}/L for 2 weeks before pairing, and throughout a breeding cycle	Reduction in testes weight and speratozoa number. No effect on egg production or fertility. Bone Pb levels higher than controls especially in females. Significantly higher Pb	

	concentrations in bone, liver, and feather in progeny of Pb-treated parents than in controls	34
European starling, *Sturnus vulgaris*		
Oral administration (capsule) of triethyllead chloride at 2,000 ug daily (28 mg/kg BW) for 11 days, or until death	Mortality 100% by day 6. Dying birds showed decreased respiration, squatting, fluffed feathers, and abnormal head posture. Average residues (mg/kg fresh weight) 6.0 in bone, 7.3 in brain 19.9 in kidney, 20.0 in muscle, and 40.2 in liver.	35
As above, but dose was 200 ug daily (2.8 mg/kg BW)	No deaths, reduced food consumption. All tissue residues <2.0 mg/kg fresh weight (vs. <0.1 in controls).	35
Oral administration (capsule) of trimethyllead chloride at 2,000 ug daily (28 mg/kg BW) for 11 days, or until death	Mortality 100% by day 6. Signs included impaired balance, tremors, fluffed feathers, uncoordinated feeding movements, weight loss, inability to fly. Residues (mg/kg fresh weight) averaged 4.3 in bone, 11.0 in muscle, 16.7 in brain, 30.2 in kidney, and 82.4 in liver	35
As above, but dose was 200 µg daily (2.8 mg/kg BW)	No deaths, survivors hyperactive. Average tissue residues (mg/kg fresh weight) 0.4 in bone, 3.1 in muscle, 3.5 in brain, 3.7 in liver, and 5.4 in kidney	35
Mourning dove, *Zenaida macroura*		
Single oral dose		
1 No. 8 shot (72 mg)	Mortality 24% in 4 weeks; normal courtship and reproductive activities, but egg hatching significantly reduced; Pb residues elevated in kidney, liver, and bone	36
2 No. 8 shot (144 mg)	Mortality 60% in 4 weeks	36

4 No. 8 shot (288 mg)	Mortality 52% in 4 weeks	36
Single oral dose of		
4 No. 8 shot		
4 days posttreatment	Residues (mg/kg dry weight)	
	345 to 639 in kidney and	
	58 to 215 in liver (vs. <12 in	
	controls)	37
8 days posttreatment	Residues (mg/kg dry weight)	
	1,279 to 1,901 in kidney and	
	179 to 267 in liver	37

[a]References: 1, Deuel 1985; 2, Longcore et al. 1974a; 3, Longcore et al. 1974b; 4, Dieter and Finley 1978; 5, Finley and Dieter 1978; 6, Dieter and Finley 1979; 7, Bellrose 1951; 7a, Hudson et al. 1984; 8, Finley et al. 1976; 9, Haegele et al. 1974; 10, Di Giulio and Scanlon 1984; 11, Chasko et al. 1984; 12, Kendall and Scanlon 1985; 13, Beyer et al. 1988; 14, Anders et al. 1982; 15, Dietz et al. 1979; 16, Hill and Camardese 1986; 17, Redig et al. 1980; 18, Stendell 1980; 19, Franson et al. 1983; 20, Pattee 1984; 21, Hoffman et al. 1984a,b; 22, Custer et al. 1984; 23, Franson and Custer 1982; 24, Pattee et al. 1981; 25, Gjerstad and Hanssen 1984; 26, Fimreite 1984; 27, Macdonald et al. 1983; 28, Burger and Gochfeld 1985; 29, Kendall et al. 1982; 30, Kendall and Scanlon 1981; 31, Kendall and Scanlon 1984; 32, Veit et al. 1983; 33, Kendall and Scanlon 1982; 34, Kendall and Scanlon 1981; 35, Osborn et al. 1983; 36, Buerger et al. 1986; 37, Kendall and Scanlon 1983.

Trialkyllead salts are 10 to 100X more toxic to birds than are inorganic Pb salts; they tend to accumulate in lipophilic soft tissues in the yolk and developing embryo, and have high potential as neurotoxicants (Forsyth et al. 1985); accordingly more research is needed on alkyllead toxicokinetics. Some alkyllead compounds have been implicated in bird kills. In autumn 1979, about 2,400 birds of many species were found dead or disabled on the Mersey estuary, England, an important waterfowl and marsh bird wintering area; smaller kills were observed in 1980 and 1981 (Bull et al. 1983). Affected birds contained elevated Pb concentrations in liver (>7.5 mg/kg fresh weight), mostly as organolead. Bull et al. (1983) suggested that trialkyllead compounds were discharged from a petrochemical factory producing alkylleads, into the estuary where they were accumulated (up to 1.0 mg/kg fresh weight) by clams (*Macoma balthica*) and other invertebrates on which the birds could feed. Birds dosed experimentally with trialkyllead compounds died with the same behavioral and internal signs found in Mersey casualties; tissue levels of trialkyllead were similar in the two groups of birds (Osborn et al. 1983). Sublethal effects that might influence survival in the wild were found in both sublethally dosed and apparently healthy wild birds when tissue levels of trialkyllead compounds were matched in the two groups of birds. It was concluded that trialkyllead compounds were the main cause of the observed mortalities and that many apparently healthy birds were still at risk (Osborn et al. 1983).

Nestlings of altricial species (those confined to the nest for some time after hatch) may be considerably more sensitive to Pb exposure than adults, and also more sensitive than hatchlings of many precocial species (Hoffman et al. 1985a). Hatchlings of precocial species, including chickens, Japanese quail (*Coturnix coturnix*), mallards, and pheasants, are relatively tolerant to moderate Pb exposure, i.e., there was no effect on growth at dietary levels of 500 mg Pb/kg, or survival at 2,000 mg Pb/kg (Hoffman et al. 1985a,b).

Some species of domestic birds are resistant to Pb toxicosis. for example, blood Pb levels of 3.2 to 3.8 mg/l in Pb-stressed cockerels (*Gallus* sp.) were much higher than residues considered diagnostic for Pb poisoning in most domestic mammals, except swine--which tolerated up to 143 mg Pb/1 blood (Franson and Custer 1982).

MAMMALS

Three stages of recognizable Pb poisoning, or plumbism, have been reported in humans (NRCC 1973): (1) mild or severe dysfunction of the alimentary tract as shown by loss of appetite, constipation, abdominal cramps, headaches, general weakness, and fatigue; (2) atrophy of forearm extensor muscles., or paralysis of these muscles and more striking atrophy; and (3) lead encephalopathy, which occurs frequently in Pb-poisoned infants

and young children, but only rarely in industrial workers. In general, people with hepatitis, anemia, and nervous disorders were more susceptible to Pb poisoning (Barth et al. 1973). The transfer of Pb across the human placenta and its potential threat to the fetus have been recognized for more than 100 years; women occupationally exposed to Pb showed a comparatively high abortion rate (Tachon et al. 1983). Sensitivity of the brain to the toxic effects of Pb is considerably greater in the fetus than in the infant or young child (EPA 1980). Lead is not considered carcinogenic to humans (Tsuchiya 1979). However, reports of chromosomal aberrations in human blood lymphocytes (Barth et al. 1973) suggested that Pb is a probable mutagen.

Signs of plumbism in domestic and laboratory animals (data on feral mammals are noticeably lacking), which are similar to those in humans, have been well documented (Barth et al. 1973; NRCC 1973; Mierau and Favara 1975; Davies et al. 1976; Roberts et al. 1976; Forbes and Sanderson 1978; Nriagu 1978b; Osweiler and Van Gelder 1978; Tsuchiya 1979; Ward and Brooks 1979; EPA 1980; Mahaffey et al. 1980; Hamir 1981; Harrison and Laxen 1981; Burrows and Borchard 1982; Demayo et al. 1982; Hamir et al. 1982; Mykkanen et al. 1982; Tachon et al. 1983; Gietzen and Wooley 1984; Berglind et al. 1985; Table 8). There is general agreement on several details: significant differences occur between species in response to Pb insult; effects of lead are more pronounced with organolead than inorganic lead compounds; younger developmental stages are the most sensitive; and the effects are exacerbated by elevated temperatures, and by diets deficient in minerals, fats, and proteins. Tetramethyllead, for example, is about 7X more toxic than tetraethyllead to animals, and both compounds showed toxic effects earlier than did inorganic Pb compounds. In severe cases, death is usually preceded by impairment of normal functions of the central nervous system, the gastrointestinal tract, and the muscular and hematopoietic systems. Signs include vomiting, lassitude, loss of appetite, uncoordinated body movements, convulsions, stupor, and coma. In nonfatal cases, signs may include depression, anorexia, colic, disturbed sleep patterns, diarrhea, anemia, visual impairment, blindness, susceptibility to bacterial infections, excessive salivation, eye blinking, renal malfunction, peripheral nerve diseases affecting the motor nerves of the extremities, reduced growth, reduced life span, abnormal social behavior, and learning impairment. Lead crosses the placenta and is passed in milk, producing early intoxication of the fetus during pregnancy and the newborn during lactation. High Pb doses in mammals induce abortion, reduce or terminate pregnancy, or can result in stillbirths or an increase in skeletal malformations. These signs, together with Pb levels in blood and tissues and histopathological examination, are used to diagnose Pb poisoning.

Lead adversely affected the survival of sensitive mammals tested at different concentrations (Table 8): 5 to 108 mg Pb/kg BW in rats (acute oral),0.32 mg Pb/kg BW daily in dogs (chronic oral), and 1.7 mg Pb/kg diet in horses (chronic dietary). Adverse sublethal effects (Table 8) were noted in monkeys given 0.1 mg Pb/kg BW daily (impaired learning 2 years postadministration) or fed diets containing 0.5 mg Pb/kg (abnormal social behavior); in rabbits given 0.005 mg Pb/kg BW (reduced blood ALAD activity) or 0.03 mg Pb/kg BW (elevated blood Pb levels); in mice at 0.05 mg Pb/kg BW (reduced ALAD activity); or in sheep at 0.05 mg Pb/kg BW (tissue accumulations).

Table 8. Lethal and sublethal effects of lead to selected species of mammals.

Species, dose, and other variables	Effects	Reference[a]
Cattle, cows, *Bos* spp.		
Tissue Pb (mg/kg fresh weight)	Signs of clinical Pb toxicosis	
0.81 in blood, 26.4 in liver, 50.3 in kidney, and 400 in rumen contents	observed	1
Calves given 2.7 mg Pb/kg body weight (BW), as Pb acetate, for 20 days; milk diet	Death	2
Calves given 3.0 to 3.5 mg Pb/kg BW daily for 3 months;	No effect	2

grain and hay diet		
Calves given 5 mg Pb/kg BW, as Pb acetate, for 7 days; grain and hay diet	Appeared normal	3
Calves given 5 mg Pb/kg BW, as Pb acetate, for 7 days; milk diet	Signes of Pb poisoning; some deaths	3,4
Calves given 5 mg Pb/kg BW daily for 10 to 20 days	Blindness, 16% mortality	4
Calves given forage containing 5 to 6 mg Pb/kg	Fatal in 2 months	1
Calves given 5 to 6 mg Pb/kg BW daily for 3 years	Chronic toxicity	2
Adults given 6 mg Pb/kg BW daily for 3 years	No deaths	5
Calves given 6 to 7 mg Pb/kg BW daily for 2 months	Fatal	2
Fed 6 to 7 mg Pb (as Pb acetate)/kg BW daily	Intoxication within 8 weeks; most dead at day 105	6
Consumed vegetation (17 to 20 mg Pb/kg fresh weight) near Pb battery recycling plant	Some deaths, mostly younger animals; neurological signs. Lead levels, in mg/kg fresh weight, were 13.8 to 35.8 in blood, 6.9 to 96.5 in feces, 97 in liver, and 138 in kidney. Histopathology of liver and kidney	7
Calves given 20 mg Pb/kg BW daily	Fatal in 8 to 22 days	2
Accidentally exposed for 10 days to toxic levels of Pb, as Pb shot, through corn silage. Silage storage area received shot from a nearby trap shooting range. Silage contained 32 mg Pb/kg	1.5% dead (2/70), 27% with signs of poisoning (kidney pathology, hemorrhaging). Tissue Pb concentrations of 16 mg/kg fresh weight in liver, >32 in kidney, and up to 0.8 in blood	6
Calves, single oral dose of 220 to 400 mg Pb/kg BW, as Pb acetate	LD-50	2
Total dose of 50 to 100 grams	Toxic	6
Dog, *Canis familiaris*		
Fed 0.32 mg Pb/kg BW daily	Chronic toxic level	4
Fed 3 mg Pb/kg BW daily, as	Anorexia and convulsions	

lead carbonate	at 180 days	8
Fed low calcium/phosphorus diet containing 100 mg Pb/kg, equivalent to about 3.5 mg Pb/kg BW	At 12 weeks, anemia, weight loss, and renal necrosis Tissue Pb levels (mg/kg fresh weight) 1.2 in brain, 1.7 in blood, 15.7 in spleen, 23.4 in liver, 32.2 in kidney, and 735 in bone	9
Total dose of 10 to 25 grams	Toxic	6
Goat, *Capra* sp.		
Total dose of 20 to 25 grams	Toxic	6
Guinea pig, *Cavia cobaya*		
Single intraperitoneal injection of 25 mg/kg BW, as Pb acetate	Reduced brain weight of newborn pigs. Effect synergized when dams were exposed to elevated (42 C) temperatures for 24 h: 88% with microencephaly vs. 5% in group given 25 mg/kg without hyperthermia	10
Horse, *Equus caballus*		
Tissue Pb levels, in mg/kg fresh weight, of 0.39 in blood, 18 in liver, and 16 in kidney	Signs of clinical Pb toxicosis observed	1
Ate forage containing 1.7 mg Pb/kg	Fatal in several months	1
Consumed 2.4 mg Pb/kg BW daily	Lethal	4
Fed 6.25 mg Pb/kg BW daily for 105 days, as Pb acetate	No deaths; blood Pb levels of 350 to 380 µg/L at day 105	6
Fed hay collected near Idaho smelter containing 423 mg Pb/kg, equivalent to about 7.4 mg Pb/kg BW daily	All dead in 84 to 100 days. Total Pb ingested ranged from 136 to 154 grams	11
Fed 9.8 mg Pb/kg BW daily for 105 days, as Pb acetate	No deaths; blood Pb levels of 530 to 650 µg/L at day 105	6
Fed noncontaminated hay plus 10 mg Pg/kg BW daily, as Pb acetate	All dead in 113 to 304 days. Total Pb ingested ranged from 190 to 544 grams	11
Total dose of 500 to	Toxic	6

700 grams		
Cat, *Felis domesticus*		
Fed pine voles (*Pitymys pinetorium*) from orchard sprayed with Pb arsenate. Concentrations (mg Pb/kg dry weight) were 60.3 in whole voles, 5.7 in cat diet containing voles, and 3.2 in control cat diet	After 86 days, tissue residues elevated in cat kidney (1.3 mg Pb/kg dry weight vs. 0.2 for controls), liver (0.5 vs. 0.1), and bone (5.0 vs. 0.9)	12
Rabbit, *Lepus* sp.		
Given 0.9, 0.03, 0.06, 0.15, 0.3, or 3 mg Pb/kg BW for 6 days	Blood Pb levels (µg/L) generally increased from 170 (control) to 910 (0.03), 530 (0.06), 1,430 (0.15), 1,930 (0.3), and 5,160 (3.0)	13
Exposed to 2.46 µg Pb/m^3 air for life	No effect	13
>5 µg Pg/kg BW daily	Reduced blood ALAD activity	13
Mouse, *Mus* sp.		
0.05 to 0.1 mg Pb/kg BW daily	Irreversible inhibition of ALAD activity in bone marrow and red blood cells	14
Tissue concentrations of 0.78 mg/kg femur bone marrow, 3.7 mg/L blood, 15.8 mg/kg brain, or 43 mg/kg liver	Inhibition of ALAD activity 50% within 10 min	14
1.5 mg Pb/kg BW daily, as tetraethyllead chloride	Reduction in success of implanted ova	8
2.2 mg/kg BW or 3 mg/kg BW daily, as tetraethyllead	Frequency of pregnancy reduced when dose given 3 to 5 days after mating	8
Pregnant females given single intrauterine injection of 20 mg Pb/kg BW on day 8 of gestation	Smaller litters, increased fetal deaths	15
800 mg Pb/L, as lead acetate, in drinking water for 11 weeks	Decrease in litter size, decreased survival of pups, and decrease birth weight	16
1,000 mg Pb/L in drinking water for 9 months	No effect on survival or fertility	4

Sheep, *Ovis aries*		
Lambs fed 50 µg Pb/kg daily (~ 3 mg)	Tissue accumulations	5
Lambs exposed to low levels (350 µg Pb/L blood) *in utero*	Impaired visual discrimination and learning behavior	17
1.0 mg Pb/kg BW daily, as Pb acetate, for 3 months	Of 10 ewes, 3 aborted, 6 delivered normally, and 1 died; placental transfer of Pb established	5
Pregnant ewes given 3 mg Pb/kg BW daily	No effect	4
4.2 mg Pb/kg BW in diet for 4 weeks before gestation, and throughout gestation and lactation	Lambs showed impaired learning	18
Fed 5 mg Pb/kg BW first 45 days of pregnancy	Bore normal full-term lambs	9
Given 5 mg Pb/kg BW daily for one year	No adverse effects	5
Pregnant ewes given 5.7 mg Pb/kg BW daily	Fatal	4
Nonpregnant ewes given 6 mg Pb/kg BW daily	Toxic threshold	4
8 mg Pb/kg BW daily for 220 days	Mortality	5
Fed 9 mg Pb/kg BW throughout pregnancy	Aborted and died	9
Fed diet containing 138 mg/kg dry weight for 124 days	Elevated residues in bone (22 mg/kg vs. 2.6 in controls) and kidney (8.3 vs. 1.0)	4
Lambs fed diets containing 400 mg Pb/kg, but deficient in calcium and sulphate	Dead within 5 weeks	4
Lambs fed diets containing 400 mg Pb/kg, diet adequate in minerals	Some weight loss in 10 months, but normal otherwise	4
Single oral dose of 600 mg Pb/kg BW	Fatal	9
Total dose of 20 to 25 grams	Toxic	6
Primates, various species		
Cynmolgus monkey, *Macaca iris*		
Intramuscular injection of 1.0 mg Pb/kg BW daily during pregnancy or lactation	Fetus exposed to lead through placenta or maternal milk	19

1.5 mg Pb/L in drinking water as lead acetate, for 9 months (equivalent to 0.5 mg Pb/kg BW daily), or 6 mg/L (2 mg/kg BW), or 15 mg/L (5 mg/kg BW)	Increasing blood Pb levels from third month, according to dose; kidney pathology. Effects more severe in animals on low calcium diets	20
Intramuscular administration of 5 mg Pb^{2+}/kg BW daily during pregnancy or lactation	Abortions and death in pregnant monkeys; cerebral pathology in newborns	19
Cynmolgus monkey, *Macaca fascicularis*		
Dosed orally from birth to age 200 days with 100 µg Pb (as Pb acetate)/kg BW, 5x weekly, milk substitute diet	Blood Pb concentration of 254 µg/L; declined to 131 µg/L over next 100 to 150 days. At age 3 years, impaired ability to perform motor discrimination reversal tasks	21
As above, except dose is 50 µg Pb/kg BW	Blood Pb levels of 154 µg/L (vs. 35 µg/L in controls), declining to 109 µg/L at day 150 post-administration. At age 3 years, group showed impaired color discrimination. No overt signs of toxicity, normal blood chemistry (except Pb), normal growth and development skills	21
Rhesus monkey, *Macaca mulatta*		
Infants given 0.5 mg Pg/kg diet for 4 weeks	Hyperactivity, insomnia, abnormal social behavior	18
Adults given 20 mg Pb/L in drinking water for 4 weeks	No effect	18
Baboon, *Papio anubis*		
Intratracheal injection of lead carbonate at doses of 50 to 135 mg Pb/kg BW for 29 to 362 days	73% dead (11/15) on receiving total dose of 1,250 to 7,800 mg Pb. Before death, some animals lost weight, became increasingly aggressive, had hepatic centrilobular necrosis, were uncoordinated and weak, and experienced convulsions; the blood contained up to 62 mg Pb/L	22
Single injection of 105 mg Pb/kg BW	Blood Pb concentrations rose from 117 µg/L at start to 3,100 µg/L at day 4 postadministration;	

	blood Pb remained >1,000 µg/L for at least 24 days	22
Rat, *Rattus* spp.		
Exposed to 10 µg Pb/m^3 air for one year	Elevated tissue residues in blood, soft tissues, and bone	13
Exposed to 21.5 µg Pb/m^3 air for one year	Blood Pb increased, but stabilized after 4 months; Pb levels remained elevated in bone, kidney, and liver after 6 months	13
1.5 mg Pb/L in drinking water for several days	Disturbed sleep patterns	18
Weanling females given 0.0, 0.5, 5, 25, 50, or 250 mg Pb (as Pb acetate)/L drinking water for 6 to 7 weeks, then mated and exposed continuously through gestation and lactation	At 25 mg/L and higher, growth retardation and delayed vaginal opening observed; some maternal deaths occurred and were associate with blood Pb concentrations >200 µg/L. Some pup malformations and deaths in all groups. The 5 mg/L group had elevated blood Pb levels	23
Single intravenous injection (mg Pb/kg BW in parentheses)		
Tetramethyllead (80)	LD-50	24
Tetraethyllead (10)	LD-50	24
Trimethyllead (20 to 25)	LD-50	24
Triethyllead (8)	LD-50	24
Single oral dose (mg Pb/kg BW)		
Tetramethyllead (108)	LD-50	24
Tetraethyllead (12)	LD-50	24
Single intraperitoneal injection (mg Pb/kg BW)		
Tetramethyllead (70 to 100)	LD-50	24
Tetraethyllead (10)	LD-50	24
Trimethyllead (17)	LD-50	24
Triethyllead (5)	LD-50	24
5 mg Pb/L drinking water, lifetime exposure	Lowered survival and reduced longevity	4
Single intraperitoneal injection of 7 mg Pb/kg BW, as tetraethyllead	Depressed food intake, and hyperactivity	25
Male weanlings exposed to age	At day 86: behavioral deficits;	

50 days to drinking water containing 25 mg Pg/L, as Pb acetate	blood Pb concentrations of 150 to 200 µg/L; brain Pb levels (µg/kg) 70 in treated group vs. 28 in controls	26
25 mg Pb/kg diet for 3 weeks	Increased locomotor activity	18
21-day-old rats exposed to 50, 100, or 500 mg Pb/L drinking water, as Pb acetate, for 335 days	Impaired behavior during first 4 months at 50 mg/L, but not thereafter. At 100 mg Pb/L and higher, behavior was impaired for at least 100 days postadministration. Brain and blood Pb levels reflected exposure concentration and duration	27
Neonatal rats given 50 mg Pb/kg BW intragastrically as Pb acetate, on days 6 to 18 postpartum	Impaired transfer of maze learning acquired during food deprivation	28
100 mg/kg BW daily, as lead nitrate	Some deaths of progeny in 3 weeks	8
Lead acetate in drinking water at 100, and 300 mg Pb/L from age 21 to 55 days	Impaired motor skills	29
200 mg/kg BW daily	50% of progeny dead in 3 weeks	8
4,000 mg Pb/L in drinking water for 130 days	Serum testosterone levels depressed, Leydig cell lesions; no effect at lower concentration tested (2,000 mg/L)	30
Nursing rats given diets containing zero, 2,000, 4,000, or 10,000 mg Pb/kg as metallic Pb powder	Lead-treated rats showed dose-related response to noise stimuli. Blood Pb levels (µg/L) in pups were 40 for controls, 250 for the 2,000 mg/kg group, 360 for the 4,000 mg/kg group, and 550 for the 10,000 mg/kg group	31
Swine, *Sus* sp.		
Oral doses of 64 mg Pb/kg BW, as Pb acetate, 6x weekly for 13 weeks	No deaths, reduced blood ALAD activity, blood Pb concentration (a remarkable) 143 mg/L	32
As above, except doses administered intraperitoneally	All died	32
Total dose of 10 to 25 grams	Toxic	6

[a] References: 1, Osweiler and Van Gelder 1983; 2, Zmudzki et al. 1983; 3, Zmudzki et al. 1984; 4, Demayo et al. 1982; 5, NRCC 1973; 6, Dollahite et al. 1978; 7, Kwatra et al. 1986; 8, Clark 1979; 9, Forbes and Sanderson 1978; 10, Edwards and Beatson 1984; 11, Burrows and Borchard 1982; 12, Gilmartin et al. 1985; 13, Barth et al. 1973; 14, Schlick et al. 1983; 15, Wide 1985; 16, Sharma and Kanwar 1985; 17, EPA 1980; 18, Nriagu 1978b; 19, Tachon et al. 1983; 20, Colle et al. 1980; 21, Rice 1985; 22, Hopkins 1970; 23, Kimmel et al. 1980; 24, Branica and Konrad 1980; 25, Czech and Hoium 1984; 26, Cory-Slechta et al. 1985; 27, Cory-Slechta et al. 1983; 28, Massaro et al. 1986; 29, Cory-Slechta et al. 1981; 30, Zirkin et al. 1985; 31, Barrett and Livesey 1985; 32, Lassen and Buck 1979.

Although Pb is undeniably toxic at high levels of exposure, the implications of lower levels of exposure are poorly defined (Nriagu 1978b). Behavioral effects such as hyperactivity, distractability, and decreased learning ability, as well as certain peripheral neuropathies, have been ascribed to subclinical Pb exposure (Hejtmancik et al. 1982). Impaired learning ability of Pb-stressed animals showing no obvious signs of Pb intoxication has been documented for rats (Cory-Slechta et al. 1981, 1983, 1985; Angell and Weiss 1982; Nation et al. 1982; Geist et al. 1985; Massaro et al. 1986), sheep (Nriagu 1978b; EPA 1980), and primates (Rice 1985)--although variability was great in all studies. Some learning deficits may be reversible and may not persist beyond a period of rehabilitation (Geist et al. 1985), and some may be induced only at relatively high exposure levels (Hastings et al. 1984). Abnormal social behavior (usually aggression) has been reported in baboons and monkeys (Hopkins 1970; Nriagu 1978b), although mice showed inhibited development of isolation-induced aggression (Ogilvie and Martin 1982). Altered parent-child relationships were suggested when suckling rats were used as surrogates. In that study, pregnant rats fed diets containing powdered Pb nursed for longer periods than normal, and the resultant offspring were slower to explore their environment (Barrett and Livesey 1983). Lead-exposed pups, with blood Pb levels as low as 200 ug/l (considered elevated but within the "normal" range) at weaning, showed an altered dam-pup interaction that resulted in the dam spending longer periods in the nest than usual. Retarded development of Pb-treated pups may account for the longer bouts of nesting by Pb-stressed dams, and the delay in age at which pups explore and learn. Barrett and Livesey (1983) concluded that maternal behavior was related to delays in pup development, and that the functional isolation of pups from their environment may be the antecedent to altered behavior later in maturity.

No data are currently available on effects of Pb-induced altered parent-offspring relationships, impaired learning ability, or abnormal social behavior for any population of free-ranging wildlife.

Ingestion of Pb-containing paint from bars or walls is a significant cause of death among captive wild animals--including many species of apes, monkeys, bears, ferrets, pinnipeds, foxes, panthers, bats, raccoons, and armadillos--and is probably underreported (Hopkins 1970; Zook et al. 1972; Fowler 1975; Forbes and Sanderson 1978). A similar situation exists for domestic animals--including dogs, cats, goats, horses, swine, cattle, and sheep (Dollahite et al. 1978; Forbes and Sanderson 1978; Osweiler and Van Gelder 1978; Hamir 1981). Passage of laws regulating the amount of Pb in paint has decreased the frequency of Pb poisoning, but many animals are still at risk from this source. Lead also occurs in used motor oils, gasoline, batteries, shot, putty, golf balls, linoleum, and printers ink--all of which are considered sources of Pb poisoning to domestic animals (Dollahite et al. 1978).

Although the use of lead arsenate as an insecticide in orchards is diminishing, residues of Pb still remain in the upper soil surface and will continue to remain bioavailable almost indefinitely (Gilmartin et al. 1985).

Naturally occurring radiolead-210, which has a half-life of 22 years, is a significant contributor to the natural radiation dose in man; comparatively high levels have been reported in certain grasses and lichens, and their consumers, such as reindeer, caribou, and ptarmigan, as well as in lanternfishes (Nriagu 1978b). The implications of this finding to wildlife health are unknown.

CURRENT RECOMMENDATIONS

Proposed Pb criteria for the protection of natural resources and human health are numerous and disparate (Table 9). Some of the criteria do not provide adequate protection. The most recent criteria for aquatic life protection, for example, range from 1.3 to 7.7 ug total waterborne Pb/1 (Table 9; EPA 1985); however, within this range high accumulations and adverse effects on growth and reproduction were recorded among sensitive species. Moreover, certain organolead compounds were lethal to some species of aquatic biota within this

range, but no criteria have been formulated yet for this highly toxic group of chemicals. Nor have any criteria been proposed for Pb in tissues of aquatic biota connoting elevated or hazardous levels to the organism. It is noteworthy that health effects to man through ingestion of Pb-contaminated seafood (and probably other fishery products) are considered negligible. Total Pb concentrations observed in highly polluted areas in the 1970's were usually about one-tenth those showing effects on marine organisms (Branica and Konrad 1980).

Organolead compounds are more toxic than ionic forms. Since methylation of ionic Pb in vivo or in stored tissues is possible, and since some liver enzyme systems are capable of converting tetraethyllead to the more toxic triethyllead species, it would appear that the current Canadian permissible concentration limit of 10 mg Pb/kg fresh weight in fishery products should be reevaluated downwards (Sirota and lithe 1977). Downward evaluation has also been recommended for the standard of 2 mg/kg in the UK, where new guidelines have been recommended for total Pb and for tetralkyllead compounds in fishery products (Wong et al. 1981). Increasing use of organolead compounds as wood preservatives, as biocides, and as catalysts in the manufacture of plastics, polyurethanes, and polyvinyl chlorides (Walsh and Tilson 1984) may adversely affect survival, sensory reponsiveness, and behavioral reactivity in aquatic organisms (Chau et al. 1980; Maddock and Taylor 1980; Wong et al. 1981; Demayo et al. 1982) and avian wildlife (Bull et al. 1983; Osborn et al. 1983; Forsyth et al. 1985). It seems that additional research is needed on organolead toxicokinetics, with special reference to fishery and wildlife resources.

Table 9. Proposed lead criteria for the protection of natural resources and human health.

Resource, (units), and other variables	Criterion	Reference[a]
Crops		
Irrigation water (mg/L)		
USA		
Neutral and alkaline soils	<10	Demayo et
Acidic soils	<5	al. 1982
Chronic use	<5	Abbasi and
Short-term use	<20	Soni 1986
Canada		
Continuous use	<5	Demayo et
Intermittent use	<10	al. 1982
Australia		
Aquatic life		
Freshwater (µg total Pb/L)		
USA		
Water hardness, in mg $CaCO_3$/L		
50	1.3[b], 34[c]	EPA 1985
100	3.2[b], 82[c]	
200	7.7[b], 200[c]	
Great Lakes		
Superior	<100	Harrison and
Huron	<200	Laxen 1981
Others	<250	
England	<400	

Seawater (µg total Pb/L)	5.6[b], 140[c]	EPA 1985
Water (µg/L)		
Tetraalkyllead	<1	Maddock and
Trialkyllead	<100	Taylor 190
Sewage effluent limits (µg/L)		
California	<4,000	Harrison and
Industrial discharge limits		Laxen 1981
to surface waters (µg/L)		
Illinois	<100	
USA	<500	
Canada	<2,000	
Switzerland	<5,000	
Birds		
Canvasback, *Aythya valisineria*		
Elevated		
Wingbones, immatures		
(mg/kg dry weight)	>20	Fleming 1981
Blood (mg/L)	>0.2	Dieter et al. 1976
American kestrel, *Falco sparverius*		
Nestlings (mg/kg fresh weight)		
Elevated		
Liver	>2	Hoffman et al.
Kidney	>6	1985a
Poisoned		
Liver	>5	
Kidney	>15	
Bald eagle,		
Haliaeetus leucocephalus		
Elevated (mg/kg dry weight)		
Kidney	>6	Pattee et al.
Liver	>10	1981
Waterfowl		
Elevated (mg/kg dry weight)		
Liver	>2	Friend 1985
Blood	>0.2	
Poisoned (mg/kg fresh weight)		
Liver		
Total Pb	>8	
Trimethyllead	>0.5	Osborn et al. 1983
Blood	>0.4	Birkhead 1983
Mammals		
Cattle, *Bos* spp.		

Poisoned (mg/kg fresh weight)		
Blood	>1	Kwatra et al.
Liver	>20	1986
Kidney	>40	
Feces	>35	
Domestic livestock		
Drinking water (µg/L)		
USA	<100	Demayo et al.
Australia	<250	1982
Canada		
Horse	<500	
Others	<1,000	
Forage (mg/kg fresh weight)		
Horse	<80	Edwards and
Cattle	<200	Clay 1977
Tissue residues		
Unstressed (mg/kg fresh weight)		
Blood	<0.2	Osweiler and
Liver	<1.1	Van Gelder 1978
Kidney	<1.2	
Mouse, *Mus* sp.		
Elevated (mg/kg body weight daily)		
Total intake	>0.05	Schlick et al. 1983
Mule deer, *Odocoileus hemionus*		
Excessive (mg/day)		
Total intake	>3	Harrison and Dyer 1984
Raccoon, *Procyon lotor*		
Elevated (mg/kg fresh weight)		
Liver	>10	Diters and Nielsen 1978
Human health		
Drinking water (µg/L)		
USA		
1975	<500	Harrison and
1977	<250	Laxen 1981
1980	<50	EPA 1980; NAS 1980
South Africa	<500	Harrison and Laxen 1981
Canada, Australia	<50	Demayo et al. 1982
USSR, Japan	<100	Abbasi and
India	10 to <100	Soni 1986

World Health Organization	<100	
Food (mg/kg fresh weight)		
Citrus	<1	NAS 1980
Raw fruits and vegetables	<7	
Fishery products		
Canada	<10	Sirota and Uthe 1977
USA	<0.3	Schmitt et al.
UK		1984
Fish	<2 (~14 dry weight)	Maddock and Taylor 1980
Shellfish	<5 (~35 dry weight)	
Meat, except liver	<0.3	Bunzl and
Liver	<0.8	Kracke 1984
Total diet	<0.3	Czarneski 1985
Daily intake, all sources (mg)		
Unacceptable	>2.3	Nriagu 1978b
Average		
Adult	<0.3	EPA 1980
Child	<0.21	
Urinary Pb levels (µg/L)		
Normal	<80	Nriagu 1978b
Acceptable	80 to 120	
Excessive	120 to 220	
Dangerous	>200	
Blood (µg Pb/L)[g]		
Acceptable (ALAD inhibition, protoporphyrin elevation)	100 to 300	Barth et al. 1973; Nriagu
Anemia, neurobehavioral effects, some poisoning in children	>400	1978b; EPA 1980; Harrison and Laxen 1981
Central nervous system deficits, peripheral neuropathy, intellectual deficits	500 to 700	
Brain structure alterations, encephalopathy	>800	
Life-threatening	>1,000	
Target	<150, maximum 300	
Air (µg Pb/m^3)		
Safe, USA	<1.5 (3-month arithmetic mean)	NAS 1980
Occupational, USA	<50[f]	EPA 1979;

		NAS 1980
Proposed, worldwide	<2	Barrett and Howells 1984
Hazardous	2,220	Barth et al. 1973
House paints (mg/L)	<600	EPA 1979
Gasoline (mg/L)		
USA		
Recent	473 to 658[d]	EPA 1979
Proposed	131[e]	
UK		
1972	840	Harrison and
1978	450	Laxen 1981
1981	400	Barrett and
Proposed	150	Howells 1984
West Germany	150	Harrison and Laxen 1981

[a]Each reference applies to the values in the same row, and in the rows that follow for which no other reference is indicated.

[b]Four-day average, not to be exceeded more than once every 3 years.

[c]One-hour average, not to be exceeded more than once every 3 years.

[d]Equals 1.8 to 2.5 g/gallon.

[e]Equals 0.5 g/gallon.

[f]Average 8-hour period.

[g]Blood Pb levels, usually expressed as µg/deciliter, have been converted to µg/L, for uniformity, in the present work.

The evidence implicating ingestion of spent lead shot as a major cause of mortality in waterfowl and other birds is overwhelming. Moreover, forms of inorganic lead--besides Pb shot or other ingestible-sized Pb objects--are not known to produce subclinical signs of Pb toxicosis in avian populations. Accordingly, in the 1986 advent of the Pb shot phaseout, steel shot nontoxic zones were established for the protection of bald eagles and waterfowl in 44 States. Possession of shotshells containing Pb shot by hunters of waterfowl in a steel shot zone is now considered a violation of Federal regulations (FWS 1986, 1986a, 1987). By 1991-1992, and thereafter, all uses of Pb shot for hunting waterfowl and coots are to be eliminated nationwide, including Alaska. The conversion to a nontoxic shot zone may be deferred until--but not beyond--the 1991-1992 hunting season in States that demonstrate, through monitoring, compliance with the following criteria: minimum of 100 birds sampled; less than 5% of birds examined having one or more Pb shot in the gizzard; and less than 5% of the birds collected having >2 mg Pb/kg fresh weight in liver, or with >0.2 mg Pb/1 in blood, or with blood protoporphyrin concentrations >0.4 mg/l. In addition, the occurrence of three or more individual specimens confirmed as lead-poisoned during the monitoring year will disqualify the area for deferral (FWS 1986, 1986a, 1987). States may elect to forego monitoring and convert to nontoxic shot zones on a countywide or statewide scheduled or accelerated basis (FWS 1986, 1987).

The level of human exposure in Pb-using industries has been reduced considerably in recent years; associated with this observation is the reduction in Pb content of gasolines, the removal of Pb-based paints for interior household use, and the reduction in Pb content of outside paints (Table 9; Boggess 1977). These actions will undoubtedly prove beneficial in reducing the elevated Pb concentrations now observed in communities of flora and fauna along heavily traveled roads, and in providing additional protection to captive zoo animals and other animals held in enclosures with Pb-painted bars and walls. The decreased use of leaded

gasoline has resulted in a significant decline in Pb concentrations in streams (Smith et al. 1987), and in whole body burdens of Pb in starlings collected nationwide, among which the decline was most pronounced in birds from urban areas (White et al. 1977). Continued nationwide monitoring of Pb in fish and wildlife is necessary to determine if this is a continuing downward trend, and also to identify areas of high or potential Pb contamination.

Data for Pb effects on mammalian wildlife are conspicuously absent. In view of the large interspecies differences in Pb responses reported for domestic livestock and laboratory populations of small animals (Table 9), more research is needed to determine if Pb criteria for these groups are applicable to sensitive species of mammalian wildlife.

One of the more insidious effects documented for Pb in warm-blooded organisms is neurobehavioral deficits (including learning impairments) at dose levels producing no overt signs of toxicity, i.e., apparently normal growth and developmental skills, and sometimes, nonelevated blood Pb levels (EPA 1980, 1985; Rice 1985). Behavioral deficits have been reported for young rats when blood Pb levels exceeded 0.1 mg/l, and in children with blood Pb concentrations of 0.4 to 0.5 mg/l (EPA 1980; Rice 1985), and in birds when Pb was administered early in development (Burger and Gochfeld 1985). Recently, behavioral impairment was recorded in 3-year-old monkeys that received 50 or 100 ug Pb/kg BW from birth to age 200 days. Blood Pb levels immediately after exposure, and at time of testing, were 0.15 to 0.25 mg/l (age 200 days), and 0.11 to 0.13 mg/l (age 3 years); this is the first report of behavioral impairment in a primate species at blood Pb concentrations that are considered to be well within the bounds of safety for children (Rice 1985). This subject appears to constitute a high priority research need for wildlife species of concern.

LITERATURE CITED

Abbasi, S.A., and R. Soni. 1986. An examination of environmentally safe levels of zinc (II), cadmium (II) and lead (II) with reference to impact on channelfish *Nuria denricus*. Environ. Pollut. 40A:37-51.

Adams, E.S. 1975. Effects of lead and hydrocarbons from snowmobile exhaust on brook trout (*Salvelinus fontinalis*). Trans. Am. Fish. Soc. 104:363-373.

Anders, E., D.D. Dietz, C.R. Bagnell, Jr., J. Gaynor, M R. Krigman, D.W. Ross, J.D. Leander, and P. Mushak. 1982. Morphological, pharmacokinetic, and hematological studies of lead-exposed pigeons. Environ. Res. 28:344-363.

Anderson, R.V. 1977. Concentrations of cadmium, copper, lead and zinc in thirty-five genera of freshwater macroinvertebrates from the Fox River, Illinois and Wisconsin. Bull. Environ. Contam. Toxicol. 18:345-349.

Anderson, W.L., and S.P. Havera. 1985. Blood lead, protoporphyrin, and ingested shot for detecting lead poisoning in waterfowl. Wildl. Soc. Bull. 13:26-31.

Angell, N.F., and B. Weiss. 1982. Operant behavior of rats exposed to lead before or after weaning. Toxicol. Appl. Pharmacol. 63:62-71.

Aronson, A.L. 1971. Biologic effects of lead in fish. J. Wash. Acad. Sci. 61:124-128.

Backhaus, B., and R. Backhaus. 1986. Is atmospheric lead contributing to mid-European forest decline? Sci. Total Environ. 50:223-225.

Bagley, G.E., and L.N. Locke. 1967. The occurrence of lead in tissues of wild birds. Bull. Environ. Contam. Toxicol. 2:297-305.

Barrett, B., and R. Howells. 1984. Legal control of standards: lead in petrol. Sci. Total Environ. 33:1-13.

Barrett, J., and P.J. Livesey. 1983. Lead induced alterations in maternal behavior and offspring development in the rat. Neurobehav. Toxicol. Teratol. 5:557-563.

Barrett, J., and P.J. Livesey. 1985. Low level lead effects on activity under varying stress conditions in the developing rat. Pharmacol. Biochem. Behav. 22:107-118.

Barth, D., A. Berlin, R. Engel, P. Recht, and J. Smeets (eds.). 1973. Proceedings international symposium. Environmental health aspects of lead. Comis. European Commun., Luxembourg. 1,168 pp.

Beeby, A. 1985. The role of *Helix aspersa* as a major herbivore in the transfer of lead through a polluted ecosystem. J. Appl. Ecology 22: 267-275.

Behan, M.J., T.B. Kinraide, and W.I. Selser. 1979. Lead accumulation in aquatic plants from metallic sources including shot. J. Wildl. Manage. 43:240-244.

Bellrose, F.C. 1951. Effects of ingested lead shot upon waterfowl populations. Trans. North Am. Wildl. Conf. 16:125-135.

Bellrose, F.C. 1959. Lead poisoning as a mortality factor in waterfowl populations. Illinois Nat. Hist. Surv. Bull. 27:235-288.

Benes, P., M. Cejchanova, and B. Havlik. 1985. Migration and speciation of lead in a river system heavily polluted from a smelter. Water Res. 19:1-6.

Beresford, W.A., M.P. Donovan, J.M. Henninger, and M.P. Waalkes. 1981. Lead in the bone and soft tissues of box turtles caught near smelters. Bull. Environ. Contam. Toxicol. 27:349-352.

Berglind, R., G. Dave, and M.L. Sjobeck. 1985. The effects of lead on aminolevulinic acid dehydratase activity, growth, hemoglobin content, and reproduction in *Daphnia magna*. Ecotoxicol. Environ. Safety 9: 216-229.

Bernhard, M., and A. Zattera. 1975. Major pollutants in the marine environment. Pages 195-300 *in* E.A. Pearson and E.D. Frangipane (eds.). Marine pollution and marine waste disposal. Pergamon Press, New York.

Beyer, W.N., and A. Anderson. 1985. Toxicity to woodlice of zinc and lead oxides added to soil litter. Ambio 14:173-174.

Beyer, W. N., and E. J. Cromartie. 1987. A survey of Pb, Cu, Zn, Cd, Cr, As and Se in earthworms and soil from diverse sites. Environ. Monitor. Assess. 8:27-36.

Beyer, W. N., G. W. Miller, and E. J. Cromartie. 1984. Contamination of the 02 soil horizon by zinc smelting and its effect on woodlouse survival. J. Environ. Qual. 18: 247-251.

Beyer, W.N., and J. Moore. 1980. Lead residues in eastern tent caterpillars (*Malacosoma americanum*) and their host plant (*Prunus serotina*) close to a major highway. Environ. Entomol. 9:10-12.

Beyer, W.N., O.H. Pattee, L. Sileo, D.J. Hoffman, and B.M. Mulhern. 1985. Metal contamination in wildlife living near two zinc smelters. Environ. Pollut. 38A:63-86.

Beyer, W.N., J.W. Spann, L. Sileo, and J.C. Franson. 1988. Lead poisoning in six captive avian species. Arch. Environ. Contam. Toxicol. 17:121-130.

Birdsall, C.W., C.E. Grue, and A. Anderson. 1986. Lead concentrations in bullfrog *Rana catesbeiana* and green frog *R. clamitans* tadpoles inhabiting highway drainages. Environ. Pollut. 4OA:233-247.

Birkhead, M. 1983. Lead levels in the blood of mute swans *Cygnus olor* on the River Thames. J. Zool. (Lond.) 199:59-73

Bjerre, G.K., and H.H. Schierup. 1985. Uptake of six heavy metals by oat as influenced by soil type and additions of cadmium, lead, zinc and copper. Plant Soil 88:57-69.

Blus, L.J., B.S. Neely, Jr., T.G. Lamont, and B. Mulhern. 1977. Residues of organochlorines and heavy metals in tissues and eggs of brown pelicans, 1969-73. Pestic. Monitor. J. 11:40-53.

Boggess, W.R. (ed.). 1977. Lead in the environment. Natl. Sci. Found. Rep.NSF/RA-770214. 272 pp. Avail. from U.S. Gov. Printing Office, Washington,D.C. 20402.

Bohn, A. 1979. Trace metals in fucoid algae and purple sea urchins near a high Arctic lead/zinc ore deposit. Mar. Pollut. Bull. 10:325-327.

Bollingberg, H., and P. Johansen. 1979. Lead in spotted wolffish, *Anarhichas minor*, near a zinc-lead mine in Greenland. J. Fish. Res. Board Can. 36:1023-1028.

Bolter, E., D. Hemphill, B. Wixson, D. Butherus, and R. Chen. 1973. Geochemical and vegetation studies of trace substances from lead smelting. Pages 79-86 *in* D.D. Hemphill (ed.). Trace substances in environmental health. Vol. VT-. Univ. Missouri, Columbia.

Borgmann, U., O. Kramar, and C. Loveridge. 1978. Rates of mortality, growth, and biomass production of *Lymnaea palustris* during chronic exposure to lead. J. Fish. Res. Board Can. 35:1109-1115.

Boyer, I.J., and V. Di Stefano. 1985. An investigation of the mechanism of lead-induced relaxation of pigeon crop smooth muscle. J. Pharmacol. Exp. Ther. 234:616-623.

Boyer, I.J., D.A. Cory-Slechta, and V. Di Stefano. 1985. Lead induction of crop dysfunction in pigeons through a direct action on neural or smooth muscle components of crop tissue. J. Pharmacol. Exp. Ther. 234:607-615.

Braham, H.W. 1973. Lead in the California sea lion (*Zalophus californianus*). Environ. Pollut. 5:253-258.

Branica, M., and Z. Konrad (eds.). 1980. Lead in the marine environment. Pergamon Press, Oxford, England. 353 pp.

Buerger, T.T., R.E. Mirarchi, and M.E. Lisano. 1986. Effects of lead shot ingestion on captive mourning dove survivability and reproduction. J. Wildl. Manage. 50:1-8.

Bull, K.R., W.J. Avery, P. Freestone, J.R. Hall, D. Osborn, A.S. Cooke, and T. Stowe. 1983. Alkyl lead pollution and bird mortalities on the Mersey estuary, UK, 1979-1981. Environ. Pollut. 31A:239-259.

Bunzl, K., and W. Kracke. 1984. Distribution of ^{210}Pb, ^{210}Po, stable lead and fallout ^{137}Cs in soil, plants and moorland sheep of a heath. Sci. Total Environ. 39:143-159.

Burger, J., and M. Gochfeld. 1985. Early postnatal lead exposure: behavioral effects in common tern chicks (*Sterna hirundo*). J. Toxicol. Environ. Health 16:869-886.

Burrows, G.E. 1981. Lead toxicosis in domestic animals: a review of the role of lead mining and primary lead smelters in the United States. Vet. Human Toxicol. 23:337-343.

Burrows, G.E., and R.E. Borchard. 1982. Experimental lead toxicosis in ponies: comparison of the effects of smelter effluent-contaminated hay and lead acetate. Am. J. Vet. Res. 43:2129-2133.

Carlson, B.L., and S.W. Nielsen. 1985. Influence of dietary calcium on lead poisoning in mallard ducks (*Anas platyrhynchos*). Am. J. Vet. Res. 46:276-282.

CEP. 1979. International conference. Management and control of heavy metals in the environment. CEP Consultants, Edinburgh, UK. 664 pp.

Chasko, G.G., T.R. Hoehn, and P. Howell-Heller. 1984. Toxicity of lead shot to wild black ducks and mallards fed natural foods. Bull Environ. Contam. Toxicol. 32:417-428.

Chau, Y.K., P.T.S. Wong, O. Kramer, G.A. Bengert, R.B. Cruz, J.O. Kinrade, J. Lye, and J.C. Van Loon. 1980. Occurrence of tetraalkyllead compounds in the aquatic environment. Bull. Environ. Contam. Toxicol. 24:265-269.

Chmiel, K.M., and R.M. Harrison. 1981. Lead content of small mammals at a roadside site in relation to the pathways of exposure. Sci. Total Environ. 17:145-154.

Clark, D.R., Jr. 1979. Lead concentrations: bats vs. terrestrial small mammals collected near a major highway. Environ. Sci. Technol. 13:338-341.

Clark, D.R., Jr., A.S. Wenner, and J.F. Moore. 1986. Metal residues in bat colonies, Jackson County, Florida, 1981-1983. Florida Field Natur. 14:38-45.

Clausen, B., K. Elvestad, and 0. Karlog. 1982. Lead burden in mute swans from Denmark. Nord. Vet.-Med. 34:83-91.

Clausen, I.H.S. 1984. Lead (Pb) in spiders: a possible measure of atmospheric Pb pollution. Environ. Pollut. 8B:217-230.

Clemens, E.T., L. Krook, A.L. Aronson, and C.E. Stevens. 1975. Pathogenesis of lead shot poisoning in the mallard duck. Cornell Vet. 65:248-285.

Colle, A., J.A. Grimaud, M. Boucherat, and Y. Manvel. 1980. Lead poisoning in monkeys: functional and histopathological alterations of the kidneys. Toxicology 18:145-158.

Collins, M.F., P.D. Hrdina, E. Whittle, and R.L. Singhal. 1982. Lead in blood and brain regions of rats chronically exposed to low doses of the metal. Toxicol. Appl. Pharmacol. 65:314-322.

Cory-Slechta, D.A., S.T. Bissen, A.M. Young, and T. Thompson. 1981. Chronic postweaning lead exposure and response duration performance. Toxicol. Appl. Pharmacol. 60:78-84.

Cory-Slechta, D.A., B. Weiss, and C. Cox. 1983 Delayed behaviorial toxicity of lead with increasing exposure concentration. Toxicol. Appl. Pharmacol. 71:342-352.

Cory-Slechta, D.A., B. Weiss, and C. Cox. 1985. Performance and exposure indices of rats exposed to low concentrations of lead. Toxicol. Appl. Pharmacol. 78:291-299.

Coughlan, D.J., S.P. Gloss, and J. Kubota. 1986 Acute and sub-chronic toxicity of lead to the early life stages of smallmouth bass (*Micropterus dolomieui*). Water, Air, Soil Pollut. 28:265-275.

Custer, T.W., J.C. Franson, and O.H. Pattee. 1984. Tissue lead distribution and hematologic effects in American kestrels (*Falco sparverius* L.) fed biologically incorporated lead. J. Wildl. Dis. 20:39-43.

Czarneski, J.M. 1985. Accumulation of lead in fish from Missouri streams impacted by lead mining. Bull. Environ. Contam. Toxicol. 34:736-745.

Czech, D.A., and E. Hoium. 1984. Some aspects of feeding and locomotor activity in adult rats exposed to tetraethyl lead. Neurobehav. Toxicol. Teratology 6:357-361.

Dallinger, R., and W. Wieser. 1984. Patterns of accumulation, distribution and liberation of Zn, Cu, Cd and Pb in different organs of the land snail *Helix pomatia* L. Comp. Biochem. Physiol. 79C:117-124.

Davies, P.H., J.P. Goettl, Jr., J.R. Sinley, and N.F. Smith. 1976. Acute and chronic toxicity of lead to rainbow trout *Salmo gairdneri*, in hard and soft water. Water Res. 10:199-206.

Decker, R.A., and A.M. McDermid, and J.W. Prideaux. 1979. Lead poisoning in two captive king vultures. J. Am. Vet. Med. Assoc. 175:1009.

Demayo, A., M.C. Taylor, K.W. Taylor, and P.V. Hodson. 1982. Toxic effects of lead and lead compounds on human health, aquatic life, wildlife plants, and livestock. CRC Crit. Rev. Environ. Control 12:257-305.

De Ment, S.H., J.J. Chisolm, Jr., J.C. Barker, and J.D. Strandberg. 1986. Lead exposure in an "urban" peregrine falcon and its avian prey. J. Wildl. Dis. 22:238-244.

De Michele, S.J. 1984. Nutrition of lead. Comp. Biochem. Physiol. 78A:401-408.

Deuel, B. 1985. Experimental dosing of northern pintails in California. Calif. Fish Game 71:125-128.

Dieter, M.P. 1979. Blood delta-aminolevulinic acid dehydratase (ALAD) to monitor lead contamination in canvasback ducks (*Aythya valisineria*). Pages 177-191 *in* National Academy of Sciences. Animals as monitors of environmental pollutants. Washington, D.C.

Dieter, M.P., and M.T. Finley. 1978. Erythrocyte -aminolevulinic acid dehydratase activity in mallard ducks: duration of inhibition after lead shot dosage. J. Wildl. Manage. 42:621-625.

Dieter, M.P., and M.T. Finley. 1979. Delta aminolevulinic acid dehydratase enzyme activity in blood, brain, and liver of lead-dosed ducks. Environ. Res. 19:127-135.

Dieter, M.P., M.C. Perry, and B.M. Mulhern. 1976. Lead and PCB's in canvasback ducks: relationship between enzyme levels and residues in blood. Arch. Environ. Contam. Toxicol. 5:1-13.

Dietz, D.D., D.E. McMilland, and P. Mushak. 1979. Effects of chronic lead administration on acquisition and performance of serial position sequences by pigeons. Toxicol. Appl. Pharmacol. 47:377-384.

Di Giulio, R.T., and P.F. Scanlon. 1984. Effects of cadmium and lead ingestion on tissue concentrations of cadmium, lead, copper, and zinc in mallard ducks. Sci. Total Environ. 39:103-110.

Di Giulio, R.T., and P.F. Scanlon. 1985. Heavy metals in aquatic plants, clams, and sediments from the Chesapeake Bay, U.S.A. Implications for waterfowl. Sci. Total Environ. 41:259-274.

Diters, R.W., and S.W. Nielsen. 1978. Lead poisoning of raccoons in Connecticut. J. Wildl. Dis. 14:187-192.

Dodge, R.E., and T.R. Gilbert. 1984. Chronology of lead pollution contained in banded coral skeletons. Mar. Biol. 82:9-13.

Dollahite, J.W., R.L. Younger, H.R. Crookshank, L.P. Jones, and H.D. Petersen. 1978. Chronic lead poisoning in horses. Am. J. Vet. Res. 39:961-964.

Dollard, G.J. 1986. Glasshouse experiments on the uptake of foliar applied lead. Environ. Pollut. 4OA:109-119.

Dorn, C.R., P.E. Phillips, J.O. Pierce, and G.R. Chase. 1974. Cadmium, copper, lead and zinc in bovine hair in the lead belt of Missouri. Bull. Environ. Contam. Toxicol. 11:626-630.

Drifmeyer, J.E., and W.E. Odum. 1975. Lead, zinc and manganese in dredgespoil pond ecosystems. Environ. Conserv. 2:39-43.

Driver, C.J., and R.J. Kendall. 1984. Lead shot ingestion in waterfowl in Washington State, 1978-1979. Northwest Sci. 58:103-107.

Eastin, W.C., Jr., D.J. Hoffman, and C.T. O'Leary. 1983. Lead accumulation and depression of -aminolevulinic acid dehydratase (ALAD) in young birds fed automotive waste oil. Arch. Environ. Contam. Toxicol. 12:31-35.

Edwards, M.J., and J. Beatson. 1984. Effects of lead and hyperthermia on prenatal growth of guinea pigs. Teratology 30-:413-421.

Edwards, W.C., and B.R. Clay. 1977. Reclamation of rangeland following a lead poisoning incident in livestock from industrial airborne contamination of forage. Vet. Human. Toxicol. 19:247-249.

Eisenreich, S.J., N.A. Metzer, N.R. Urban, and J.A. Robbins. 1986. Response of atmospheric lead to decreased use of lead in gasoline. Environ. Sci. Technol. 20:171-174.

Eisler, R. 1977. Toxicity evaluation of a complex metal mixture to the softshell clam *Mya arenaria*. Mar. Biol. 43:265-276.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. Biol. Trace Elem. Res. 6:165-180.

EPA. 1972. Helena Valley, Montana, area environmental pollution study. U.S. Environ. Protection Agency Rep. AP-91. 179 pp. Avail. from U.S. Environ. Protection Agency, Office of Air Programs, Research Triangle Park, North Carolina 27711.

EPA. 1979. The health and environmental impacts of lead and an assessment of a need for limitations. U.S. Environ. Protection Agency Rep. 560/2-79-001. 494 pp.

EPA. 1980. Ambient water quality criteria for lead. U.S. Environ. Protection Agency Rep. 440/5-80-057. 151 pp. Avail. from Natl. Tech. Infor. Serv., 5285 Port Royal Road, Springfield, Virginia 22161.

EPA. 1985. Ambient water quality criteria for lead - 1984. U.S. Environ. Protection Agency Rep. 440/5-84-027. 81 pp. Avail. from Natl. Tech. Infor. Serv., 5285 Port Royal Road, Springfield, Virginia 22161.

Eskildsen, J., and P. Grandjean. 1984. Lead exposure from lead pellets: age-related accumulation in mute swans. Toxicol. Lett. 21:225-229.

Everard, M., and P. Denny. 1984. The transfer of lead by freshwater snails in Ullswater, Cumbria. Environ. Pollut. 35A:299-314.

Everard, M., and P. Denny. 1985. Flux of lead in submerged plants and its relevance to a freshwater system. Aquatic Bot. 21:181-193.

Fantin, A.M.B., A. Franchini, E. Ottaviani, and L. Benedetti. 1985. Effect of pollution on some freshwater species. II. Bioaccumulation and toxic effects of experimental lead pollution on the ganglia in *Viviparus ater* (Mollusca, Gastropoda). Basic Appl. Histochem. 29:377-387.

Fayed, S.I., and H.I. Abd-El-Shafy. 1985. Accumulation of Cu, Zn, Cd, and Pb by aquatic macrophytes. Environ. Int. 11:77-87.

Feierabend, J.S., and 0. Myers. 1984. A national summary of lead poisoning in bald eagles and waterfowl. 90 pp. Avail. from National Wildlife Federation, 1412 Sixteenth St. NW, Washington, D.C. 20036.

Feierabend, J.S., and A.B. Russell (eds.). 1986. Lead poisoning in wild waterfowl - a workshop. National Wildlife Federation, 1412 Sixteenth St. NW, Washington, D.C. 139 pp.

Fimreite, N. 1984. Effects of lead shot ingestion in willow grouse. Bull. Environ. Contam. Toxicol. 33:121-126.

Finley, M.T., and M.P. Dieter. 1978. Influence of laying on lead accumulation in bone of mallard ducks. J. Toxicol. Environ. Health 4:123-129.

Finley, M.T., M.P. Dieter, and L.N. Locke. 1976. Sublethal effects of chronic lead ingestion in mallard ducks. J. Toxicol. Environ. Health 1:929-937.

Flegal, A.R. 1985. Lead in a pelagic food chain. Pages 83-90 *in* J. Salanki (ed.). Heavy metals in water organisms. Symposia Biologica Hungarica, Vol. 29. Akademiai Kiado, Budapest, Hungary.

Fleming, W.J. 1981. Environmental metal residues in tissues of canvasbacks. J. Wildl. Manage. 45:508-511.

Forbes, R.M., and G.C. Sanderson. 1978. Lead toxicity in domestic animals and wildlife. Pages 225-227 *in* J.O. Nriagu (ed.). The biogeochemistry of lead in the environment. Part B. Biological effects. Elsevier/NorthHolland Biomedical Press, Amsterdam.

Forsyth, D.S., W.D. Marshall, and M.C. Collette. 1985. Interaction of alkyllead salts with avian eggs. J. Environ. Sci. Health 2OA:177-191.

Fowler, M.E. 1975. Toxicities in exotic and zoo animals. Vet. Clinics North Amer. 5:685-698.

Fowler, S.W. 1977. Trace elements in zooplankton particulate products. Nature (Lond.) 269:51-53..

Franson, J.C., and T.W. Custer. 1982. Toxicity of dietary lead in young cockerels. Vet. Human Toxicol. 24:421-423.

Franson, J.C., G.M. Haramis, M.C. Perry, and J.F. Moore. 1986. Blood protoporphyrin for detecting lead exposure in canvasbacks. Pages 32-37 *in* J.S. Feierabend and A.B. Russell (eds.). Lead poisoning in wild waterfowl - a workshop. National Wildlife Federation, 1412 Sixteenth St. NW, Washington, D.C.

Franson, J.C., L. Sileo, O.H. Pattee, and J.F. Moore. 1983. Effects of chronic dietary lead in American kestrels (*Falco sparverius*). J. Wildl. Dis. 19:110-113.

Frape, D.L., and J.D. Pringle. 1984. Toxic manifestations in a dairy herd consuming haylage contaminated by lead. Vet. Rec. 114:615-616.

Fraser, J. 1980. Acclimation to lead in the freshwater isopod *Asellus aquaticus*. Oecologia 45:419-420.

Friedland, A.J., and A.H. Johnson. 1985. Lead distribution and fluxes in a high-elevation forest in northern Vermont. J. Environ. Qual. 14:332-336.

Friend, M. 1985. Interpretation of criteria commonly used to determine lead poisoning problem areas. U.S. Fish Wildl. Serv., Fish Wildl. Leafl. 2. 4 PP-

FWS. 1986. Migratory bird hunting; availability of a final supplemental environmental impact statement (SEIS) on the use of lead shot for hunting migratory birds in United States. Federal Register 51(124):23443-23447.

FWS. 1986a. Use of lead shot for hunting migratory birds in the United States. Final supplemental environmental impact statement. 535 + xx pp. Avail. from U.S. Fish Wildlife Service, Office of Migratory Bird Management, Washington, D.C. 20240.

FWS. 1987. Migratory bird hunting; zones in which lead shot will be prohibited for the taking of waterfowl, coots and certain other species in the 1987-88 hunting season. Federal Register 52(139):27352-27368.

Gale, N. L., E. Bolter, and B.G. Wixson. 1976. Investigation of Clearwater Lake as a potential sink for heavy metals from lead mining in southeast Missouri. Pages 95-106 *in* D.D. Hemphill (ed.). Trace substances in environmental health. Vol. X. Univ. Missouri, Columbia.

Geist, C.R., S.W. Balko, M.E. Morgan, and R. Angiak. 1985. Behavioral effects following rehabilitation from postnatal exposure to lead acetate. Percep. Motor Skills 60:527-536.

Getz, L.L., L.B. Best, and M. Prather. 1977a. Lead in urban and rural song birds. Environ. Pollut. 12:235-239.

Getz, L.L., L. Verner, and M. Prather. 1977b. Lead concentrations in small mammals living near highways. Environ. Pollut. 13:151-157.

Getz, L.L., A.W. Haney, R.W. Larimore, J.W. McNurney, H.V. Leland, P.W. Price, G.L. Rolfe, R.L. Wortman, J.L. Hudson, R.L. Solomon, and K.A. Reinbold. 1977c. Transport and distribution in a watershed ecosystem. Pages 105-134 *in* W.R. Boggess, (ed.). Lead in the environment. Natl. Sci. Found. Rep. NSF/RA-770214. Avail. from U.S. Govt. Printing Office, Washington, D.C. 20402.

Gietzen, D.W., and D.E. Wooley. 1984. Acetylcholinesterase activity in the brain of rat pups and dams after exposure to lead via the maternal water supply. Neurotoxicology 5:235-246.

Gilmartin, J.E., D.K. Alo, M.E. Richmond, C.A. Bache, and D.J. Lisk. 1985. Lead in tissues of cats fed pine voles from lead-arsenate treated orchards. Bull. Environ. Contam. Toxicol. 34:291-294.

Gish, C.D., and R.E. Christensen. 1973. Cadmium, nickel, lead and zinc in earthworms from roadside soil. Environ. Sci. Technol. 7:1060-1072.

Gjerstad, K.O., and I. Hanssen. 1984. Experimental lead poisoning in willow ptarmigan. J. Wildl. Manage. 48:1018-1022.

Goede, A.A., and P. de Voogt. 1985. Lead and cadmium in waders from the Dutch Wadden Sea. Environ. Pollut. 37A:311-322.

Goldsmith, C.D., and P.F. Scanlon. 1977. Lead levels in small mammals and selected invertebrates associated with highways of different traffic densities. Bull. Environ. Contam. Toxicol. 17:311-316.

Goodman, G.T., and T.M. Roberts. 1971. Plants and soils as indicators of metals in the air. Nature (Lond). 231:287-292.

Gould, E., and R.A. Greig. 1983. Short-term low-salinity response in lead-exposed lobsters, *Homarus americanus* (Milne Edwards). J. Exp. Mar. Biol. Ecol. 69:283-295.

Graham, D.L. 1972. Trace metal levels in intertidal mollusks of California. Veliger 14:365-372.

Grue, C.E., D.J. Hoffman, W.N. Beyer, and L.P. Franson. 1986. Lead concentrations and reproductive success in European starlings *Sturnus vulgaris* nesting within highway roadside verges. Environ. Pollut. 42A:157-182.

Grue, C.E., T.J. O'Shea, and D.J. Hoffman. 1984. Lead concentrations and reproduction in highway-nesting barn swallows. Condor 86:383-389.

Haegele, M.A., R.K. Tucker, and R.H. Hudson. 1974. Effects of dietary mercury and lead on eggshell thickness in mallards. Bull. Environ. Contam. Toxicol. 8:5-11.

Hall, R.A., E.G. Zook, and G.M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resource. U.S. Dep. Commerce, NOAA Tech. Rep. NMFS SSRF-721. 313 pp.

Hall, S.L., and F.M. Fisher, Jr. 1985. Lead concentrations in tissues of marsh birds: relationship of feeding habits and grit preference to spent shot ingestion. Bull. Environ. Contam. Toxicol. 35:1-8.

Hamir, A.N. 1981. Lead poisoning of dogs in Australia. Veety Rec. 108:438-439.

Hamir, A.N., N.D. Sullivan, and P.D. Handson. 1982. The effects of age and diet on the absorption of lead from the gastrointestinal tract of dogs. Aust. Vet. J. 58:266-268.

Hardisty, M.W., S. Kartar, and M. Sainsbury. 1974. Dietary habits and heavy metal concentrations in fish from the Severn Estuary and Bristol Channel. Mar. Pollut. Bull. 5:61-63.

Harrison, P.D., and M.I. Dyer. 1984. Lead in mule deer forage in Rocky Mountain National Park, Colorado. J. Wildl. Manage. 48:510-517.

Harrison, R.M., W.R. Johnston, J.C. Ralph, and S.J. Wilson. 1985. The budget of lead, copper and cadmium for a major highway. Sci. Total Environ. 46:137-145.

Harrison, R.M., and D.P.H. Laxen. 1981. Lead pollution. Causes and control. Chapman and Hall, New York. 168 pp.

Hastings, L., H. Zenick, P. Succop, T.J. Sun, and R. Sekeres. 1984. Relationship between hematopoietic parameters and behaviorial measures in lead-exposed rats. Toxicol. Appl. Pharmacol. 73:416-422.

Haux, C., and A. Larrson. 1982. Influence of inorganic lead on the biochemical blood composition in the rainbow trout, *Salmo gairdneri*. Ecotoxicol. Environ. Saf. 6:28-34.

Haux, C., A. Larsson, G. Lithner, and M.L. Sjobeck. 1986. A field study of physiological effects on fish in lead-contaminated lakes. Environ. Toxicol. Chem. 5:283-288.

Hayashi, M. 1983. Lead toxicity in the pregnant rat. I. The effect of high-level lead on -aminolevulinic acid dehydratase activity in maternal and fetal blood or tissues. Environ. Res. 30:152-160.

Hejtmancik, M.R., Jr., E.B. Dawson, and B.J. Williams. 1982. Tissue distribution of lead in rat pups nourished by lead-poisoned mothers. J. Toxicol. Environ. Health 9:77-86.

Heyraud, M., and R.D. Cherry. 1979. Polonium-210 and lead-210 in marine food chains. Mar. Biol. 52:227-236.

Hill, E.F., and M.B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to Coturnix. U.S. Fish Wildl. Serv., Fish Wildl. Tech. Rep. 2. 147 pp.

Hodson, P.V. 1976. -amino levulinic acid dehydratase activity of fish blood as an indicator of a harmful exposure to lead. J. Fish. Res. Board Can. 33:268-271.

Hodson, P.V., B.R. Blunt, D.J. Spry, and K. Austen. 1977. Evaluation of erythrocyte -amino levulinic acid dehydratase activity as a short-term indicator in fish of a harmful exposure to lead. J. Fish. Res. Board Can. 34:501-508.

Hodson, P.V., D.G. Dixon, D.J. Spry, D.M. Whittle, and J.B. Sprague. 1982. Effect of growth rate and size of fish on rate of intoxication by waterborne lead. Can. J. Fish. Aquat. Sci. 39:1243-1251.

Hodson, P.V., J.W. Hilton, B.R. Blunt, and S.J. Slinger. 1980. Effects of dietary ascorbic acid on chronic lead toxicity to young rainbow trout (*Salmo gairdneri*). Can. J. Fish. Aquat. Sci. 37:170-176.

Hodson, P.V., and D.J. Spry. 1985. Effect of sulfite dechlorination on the accumulation of waterborne lead by rainbow trout (*Salmo gairdneri*). Can. J. Fish. Aquat. Sci. 42:841-844.

Hoffman, D.J., J.C. Franson, O.H. Pattee, C.M. Bunck, and A. Anderson. 1985a. Survival, growth, and accumulation of ingested lead in nestling American kestrels (*Falco sparverius*). Arch. Environ. Contam. Toxicol. 14:89-94.

Hoffman, D.J., J.C. Franson, O.H. Pattee, C.M. Bunck, and H.C. Murray. 1985b. Biochemical and hematological effects of lead ingestion in nestling American kestrels (*Falco sparverius*). Comp. Biochem. Physiol. 80C:431-439.

Hoffman, D.J., O.H. Pattee, S.N. Wiemeyer, and B. Mulhern. 1981. Effects of lead shot ingestion on -aminolevulinic acid dehydratase activity, hemoglobin concentration, and serum chemistry in bald eagles. J. Wildl. Dis. 17:423-431.

Holcombe, G.W., D.A. Benoit, E.N. Leonard, and J.M. McKim. 1976. Long-term effects of lead exposure on three generations of brook trout (*Salvelinus fontinalis*). J. Fish. Res. Board Can. 33:1731-1741.

Holl, W., and R. Hampp. 1975. Lead and plants. Residue Rev. 54:79-111.

Hong, J.S., H.A. Tilson, P. Hudson, S.F. Ali, W.E. Wilson, and V. Hunter. 1983. Correlation of neurochemical and behaviorial effects of triethyl lead chloride in rats. Toxicol. Appl. Pharmacol. 69:471-479.

Hopkin, S.P., G.N. Hardisty, and M.H. Martin. 1986. The woodlouse *Porcellio scaber* as a 'biological indicator' of zinc, cadmium, lead and copper pollution. Environ. Pollut. 11B:271-290.

Hopkin, S.P., and M.H. Martin. 1984. Assimilation of zinc, cadmium, lead and copper by the centipede *Lithobius variegatus* (Chilopoda). J. Appl. Ecol. 21:535-546.

Hopkins, A. 1970. Experimental lead poisoning in the baboon. Brit. J. Indust. Med. 27:130-140.

Howard, D.R., and R.A. Braum. 1980. Lead poisoning in a dairy herd. Annu. Proc. Am. Assoc. Vet. Lab. Diag. 23:53-58.

Hudson, R.H., R. K. Tucker, and M.A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp.

Hunter, B., and G. Wobeser. 1980. Encephalopathy and peripheral neuropathy in lead-poisoned mallard ducks. Avian Dis. 24:169-178.

Ireland, M.P. 1977. Lead retention in toads *Xenopus laevis* fed increasing levels of lead in contaminated earthworms. Environ. Pollut. 12:85-92.

Irmer, U., I. Wachholz, H. Schafer, and D.W. Lorch. 1986. Influence of lead on *Chlamydomonas reinhardii* Danegard (Volvocales, Chlorophyta): accumulation, toxicity and ultrastructural changes. Environ. Exper. Bot. 26:97-105.

Jacobson, E., J. W. Carpenter, and M. Novilla. 1977. Suspected lead toxicosis in a bald eagle. J. Am. Vet. Med. Assoc. 171:952-954.

Janssen, D.L., J.E. Oosterhuis, J.L. Allen, M.P. Anderson, D.G. Kelts, and S.N. Wiemeyer. 1986. Lead poisoning in free-ranging California condors. J. Am. Vet. Med. Assoc. 189:1115-1117.

Jenkins, D.W. 1980. Biological monitoring of trace metals. Vol. 2. Toxic trace metals in plants and animals of the world. Part II. U.S. Environ. Protection Agency Rep. 600/3-80-091:619-778.

Johansson-Sjobeck, M.J., and A. Larsson. 1979. Effects of inorganic lead on delta-aminolevulinic acid dehydratase activity and hematological variables in the rainbow trout, *Salmo gairdneri*. Arch. Environ. Contam. Toxicol. 8:419-431.

Johnson, M.S., H. Pluck, M. Hutton, and G. Moore. 1982. Accumulation and renal effects of lead in urban populations of feral pigeons, *Columba livia*. Arch. Environ. Contam. Toxicol. 11:761-767.

Jordan, J. S., and F. C. Bellrose. 1951. Lead poisoning in wild waterfowl. Illinois Nat. Hist. Surv. Div., Biol. Notes 26. 27 pp.

Kania, D. M., and T. Nash. 1986. Impact of lead on migratory birds in Missouri. Unpubl. rep. 41 pp. Available from U.S. Fish Wildl. Serv.,P.O. Box 1506, Columbia, Missouri 65205.

Kaplan, H.M., T.J. Anrholt, and J.E. Payne. 1967. Toxicity of lead nitrate solutions for frogs (*Rana pipiens*). Lab. Animal Care 17:240-246.

Kendall, R.J. and C.J. Driver. 1982. Lead poisoning in swans in Washington State. J. Wildl. Dis. 18:385-387.

Kendall, R.J., G.W. Norman, and P.F. Scanlon. 1984. Lead concentrations in ruffed grouse collected from southwestern Virginia. Northwest Sci. 58:14-17.

Kendall, R.J., and P.F. Scanlon. 1981. Effects of chronic lead ingestion on reproductive characteristics of ringed turtle doves *Streptopelia risoria* and on tissue lead concentrations of adults and their progeny. Environ. Pollut. 26A:203-213.

Kendall, R.J., and P.F. Scanlon. 1982. The toxicology of ingested lead acetate in ringed turtle doves *Streptopelia risoria*. Environ. Pollut. 27A:255-262.

Kendall, R.J., and P.F. Scanlon. 1083. Histologic and ultrastructural lesions of mourning doves (*Zenaida macroura*) poisoned by lead shot. Poult. Sci. 62:952-956.

Kendall, R.J., and P.F. Scanlon. 1984. The toxicology of lead shot ingestion in ringed turtle doves under conditions of cold exposure. J. Environ. Pathol. Toxicol. 5:183-192.

Kendall, R.J., and P.F. Scanlon. 1981. Histology and ultrastructure of kidney tissue from ringed turtle doves that ingested lead. J. Environ. Pathol. Toxicol. Oncol. 6:85-96.

Kendall, R.J., P.F. Scanlon, and R.T. Di Giulio. 1982. Toxicology of ingested lead shot in ringed turtle doves. Arch. Environ. Contam. Toxicol. 11:259-263.

Kendall, R.J., H.P. Veit, and P.F. Scanlon. 1981. Histological effects and lead concentrations in tissues of adult male ringed turtle doves that ingested lead shot. J. Toxicol . Environ. Health 8:649-658.

Kimmel, C.A., L.D. Grant, C.S. Sloan, and B.C. Gladen. 1980. Chronic low-level lead toxicity in the rat. 1. Maternal toxicity and perinatal effects. Toxicol. Appl. Phamacol. 56:28-41.

King, K.A., and E. Cromartie. 186. Mercury, cadmium, lead, and selenium in three waterbird species nesting in Galveston Bay, Texas, USA. Colon. Waterbirds 9:90-94.

Kirby, R.E., H.H. Obrecht III, and M.C. Perry. 1983. Body shot in Atlantic brant. J. Wildl. Manage. 47: 27-530.

Kisseberth, W.C., J.P. Sundberg, .W. Nyboer, J.D. Reynolds, S.C. Kasten, and V.R. Beasley. 1984. Industrial lead contamination of an Illinois wildlife refuge and indigenous small mammals. J. Am. Vet. Med. Assn. 185:1309-1313.

Knight, H.D., and R.G. Burau 19 3. Chronic lead poisoning in horses. J. Am. Vet. Med. Assoc. 162:781-786.

Knowlton, M.F., T.P. Boyle, and J.R. Jones. 1983. Uptake of lead from aquatic sediment by submersed macrophytes and crayfish. Arch. Environ. Contam. Toxicol. 12:535-541.

Kobayashi, N. 1971. Fertilized sea urchin eggs as an indicatory material for marine pollution bioassay, preliminary experiments. Publ. Seto Mar. Biol. Lab. (Japan) 18:379-406.

Kober, T.E., and G.P. Cooper. 1976. Lead competitively inhibits calcium-dependent synoptic transmission in the bullfrog sympathetic ganglion. Nature (Lond). 262:704-705.

Krishnayya, N.S.R., and S.J. Bedi., 1986. Effect of automobile lead pollution in *Cassia tora* L. and *Cassia occidentalis* L. Environ. Pollut. 4OA:2 1-226.

Krajnovic-Ozretic, M., and B. Ozretic. 1980. The ALA-D activity test in lead exposed grey mullet *Mugil auratus*. Mar. Ecol. Prog. Ser. 3:187-191.

Kumar, S., and S.C. Pant. 1984.. Comparative effects of the sublethal poisoning of zinc, copper and lead on the gonads of the teleost *Puntius conchonius* Ham. Toxicol. Lett. 23:189-194.

Kwatra, M.S., B.S. Gill, R. Singh,, and M. Singh. 1986. Lead toxicosis in buffaloes and cattle in Punjab. Indian J. Anim. Sci. 56:412-413.

Lansdown, R., and W. Yule (eds.). 1986. Lead toxicity. History and environmental impact. Johns Hopkins Univ. Press, Baltimore, Maryland. 286 pp.

Lassen, E.D., and W.B. Buck. 1979. Experimental lead toxicosis in swine. Am. J. Vet. Res. 40:1359-1364.

Levander, O.A. 1979. Lead toxicity and nutritional deficiencies. Environ. Health Perspec. 29:115-125.

Locke, L. N., and G. E. Bagley. 1967. Lead poisoning in a sample of Maryland mourning doves. J. Wildl. Manage. 31:515-518.

Locke, L. N., G. E. Bagley, D. N. Frickie, and L. T. Young. 1969. Lead poisoning and aspergillosis in an Andean condor. J. Am. Vet. Med. Assoc. 155:1052-1056.

Locke, L. N., G. E. Bagley, and H. D. Irby. 1966. Acid-fast intranuclear inclusion bodies in the kidneys of mallards fed lead shot. Bull. Wildl. Dis. Assoc. 2:127-131.

Locke, L.N., S.M. Kerr, and D. Zoromski. 1982. Case report - lead poisoning in common loons (*Gavia immer*). Avian Dis. 26:392-396.

Longcore, J.R., L.N. Locke, G.E. Bagley, and R. Andrews. 1974a. Significance of lead residues in mallard tissues. U.S. Fish Wildl- Serv. Spec. Sci. Rep. - Wildl. 182. 24 pp.

Longcore, J.R., R. Andrews, L.N. Locke, G.E. Bagley, and L.T. Young. 1974b. Toxicity of lead and proposed substitute shot to mallards. U.S. Fish Wildl. Serv. Spec. Sci. Rep.- Wildl. 183. 23 pp.

Longcore, J.R., P.O. Corr, and H.E. Spencer, Jr. 1982. Lead shot incidence in sediments and waterfowl gizzards from Merrymeeting Bay, Maine. Wildl. Soc. Bull. 10:3-10.

Lowe, T.P., T.W. May, W.G. Brumbaugh, and D.A. Kane. 1985. National Contaminant Biomonitoring Program: concentrations of seven elements in freshwater fish, 1978-1981. Arch. Environ. Contam. Toxicol. 14:363-388.

Lumeij, J.T. 1985. Clinicopathologic: aspects of lead poisoning in birds: a review. Vet. Q. 7:133-138.

Lumeij, J.T., W.T.C. Wolvekamp, G.M. Bron-Dietz, and A.J.H Schotman. 1985. An unusual case of lead poisoning in a honey buzzard (*Pernis apivorus*).Vet. Q. 7:165-168.

Luoma, S.N., and G.W. Bryan. 1978. Factors controlling the availability of sediment-bound lead to the estuarine bivalve *Scrobicularia plana*. J. Mar. Biol. Assoc. U.K. 58:793-802.

Macdonald, J.W., C.J. Randall, H.M. Ross, G.M. Moon, and A.D. Ruthven. 1983. Lead poisoning in captive birds of prey. Vet. Rec. 113:65-66.

Mackay, D.W., W. Halcrow, and I. Thornton. 1972. Sludge dumping in the Firth of Clyde. Mar. Pollut. Bull. 3:7-10.

Maddock, B.G., and D. Taylor. 1980. The acute toxicity and bioaccumulation of some lead alkyl compounds in marine animals. Pages 233-261 *in* M. Branica and Z. Konrad (eds.). Lead in the marine environment. Pergamon Press, Oxford, England.

Mahaffey, K.R., J.I. Rader, J.M. Schaefer, and S.N. Kramer. 1980. Comparative toxicity to rats of lead acetate from food or water. Bull. Environ. Contam. Toxicol. 25:541-546.

Marchetti, R. 1978. Acute toxicity of alkyl leads to some marine organisms. Mar. Pollut. Bull. 9:206-20.

Marcus, A.H. 1985. Multicompartment kinetic models for lead. I. Bone diffusion models for long-term retention. Environ. Res. 36:441-458.

Martin, W.E., and P.R. Nickerson. 1973. Mercury, lead, cadmium, and arsenic residues in starlings - 1971. Pestic. Monitor. J. 7:67-72.

Massaro, T.F., G.D. Miller, and, E.J. Massaro. 1986. Low-level lead exposure affects latent learning in the rat. Neurobehav. Toxicol. Teratol. 8:109-113.

May, T.W., and G.L. McKinney. 1981. Cadmium, lead, mercury, arsenic, and selenium concentrations in freshwater fish, 1976-77 - National Pesticide Monitoring Program. Pestic. Monitor. J. 15:14-38.

McDonald, L.J. 1986. Suspected lead poisoning in an Amazon parrot. Can. Vet. J. 27:131-134.

McLean, R.O., and A.K. Jones. 1975. Studies of tolerance to heavy metals in the flora of the rivers Ystwyth and Clarach, Wales. Freshwater Biol. 5:431-444.

Melhuus, A., K.L. Seip, H.M. Seip, and S. Mykelstad. 1978. A preliminary study of the use of benthic algae as biological indicators of heavy metal pollution in Sorfjorden, Norway. Environ. Pollut. 15:101-107.

Mierau, G.W., and B.E. Favara. 1975. Lead poisoning in roadside populations of deer mice. Environ. Pollut. 8:55-64.

Mudge, G.P. 1983. The incidence and significance of ingested lead pellet poisoning in British wildfowl. Biol. Conserve 27:333-372.

Mulhern, B.M., W.L. Reichel, L.N. Locke, T.G. Lamont, A. Belisle, E. Cromartie, G.E. Bagley, and R.M. Prouty. 1970. Organochlorine residues and autopsy data from bald eagles 1966-68. Pestic. Monitor. J. 4:141-144.

Mykkanen, H.M., M.C. Lancaster, J. W. T. Dickerson. 1982. Concentrations of lead in the soft tissues of male rats during a long-term dietary exposure. Environ. Res. 28:147-153.

Narbaitz, R., 1. Marino, and K. Sarkar. 1985. Lead-induced early lesions in the brain of the chick embryo. Teratology 32:389-396.

NAS. 1980. Lead in the human environment. National Academy of Sciences; Washington, D.C. 525 pp.

Nation, J.R., D.E. Clark, A.E. Bourgeois, and J.K. Rogers. 1982. Conditioned suppression in the adult rat following chronic exposure to lead. Toxicol. Lett. 14:63-67.

Niethammer, K.R., R.D. Atkinson, T.S. Baskett, and F.B. Samson. 1985. Metals in riparian wildlife of the lead mining district of southeastern Missouri. Arch. Environ. Contam. Toxicol. 14:213-223.

NRCC. 1973. Lead in the Canadian environment. Natl. Res. Coun. Canada Publ. BY73-7 (ES). 116 pp. Avail. from Publications, NRCC/CNRC, Ottawa, Canada KIA OR6.

Nriagu, J.O. (ed.). 1978a. The biogeochemistry of lead in the environment. Part A. Ecological cycles. Elsevier/North Holland Biomedical Press, Amsterdam. 422 pp.

Nriagu, J.O. (ed.). 1978b. The biogeochemistry of lead in the environment. Part B. Biological effects. Elsevier/North Holland Biomedical Press, Amsterdam. 397 pp.

Ogilvie, D.M., and A.H. Martin 1982. Aggression and open-field activity of lead-exposed mice. Arch. Environ. Contam. Toxicol. 11:249-252.

Ohi, G., H. Seki, K. Akiyama, and H. Yagyu. 1974. The pigeon, a sensor of lead pollution. Bull. Environ. Contam . Toxicol. 12:92-98.

Osborn, D., W.J. Eney, and K.R Bull 1983. The toxicity of trialkyl lead compounds to birds. Environ. Pollut. 31A:261-275.

Osweiler, G.D., and G.A. Van Gelder. 1978. Epidemiology of lead poisoning in animals. Pages 143-177 *in* F.W. Oehme (ed.). Toxicity of heavy metals in the environment. Part 1. Marcel Dekker, New York.

Ozoh, P.T.E. 1980. Effect of lead on pigment pattern formation in zebrafish (*Brachydanio rerio*). Bull. Environ. Contam. Toxicol. 24:276-282.

Pain, D. J. 1987. Lead poisoning in waterfowl: an investigation of sources and screening techniques. Ph.D. thesis, Oxford University, England. 335 pp.

Pain, D. J., and B. A. Rattner. 1988. Mortality and hematology associated with the ingestion of one number four lead shot in black ducks, *Anas rubripes*. Bull. Environ. Contam. Toxicol. 40:159-164.

Pattee, O.H. 1984. Eggshell thickness and reproduction in American kestrels exposed to chronic dietary lead. Arch. Environ. Contam. Toxicol. 13:29-34.

Pattee, O.H., and S.K. Hennes 1983. Bald eagles and waterfowl: the lead shot connection. Trans. N. Am. Wildl. Nat. Resour. Conf. 48:230-237.

Pattee, O.H., S.N. Wiemeyer, B.M. Mulhern, L. Sileo, and J.W. Carpenter. 1981. Experimental lead-shot poisoning in bald eagles. J. Wildl. Manage. 45:806-810.

Perry, M. C., and J. W. Artmann. 1979. Incidence of embedded and ingested shot in oiled ruddy ducks. J. Wildl. Manage. 43:266-269.

Perry, M. C., and P. H. Geissler. 1980. Incidence of embedded shot in canvasbacks. J. Wildl. Manage. 44:888-894.

Peter, F., and G. Strunc. 1983. Effect of ingested lead on concentration of blood and tissue lead in rabbits. Clin. Biochem. 16:202-205.

Prause, B., E. Rehm, and M. Schulz-Baldes. 1985. The remobilization of Pb and Cd from contaminated edge spoil after dumping in the marine environment. Environ. Technol. Lett. 6:261-266.

Rai, R., and M.A. Qayyum. 1984. Haematological responses in a freshwater fish to lead poisoning. J . Environ. Biol. 5:53-56.

Raymond, R.B., and R.B. Forbes. 11975. Lead in hair of urban and rural small mammals. Bull. Environ. Contam. Toxicol. 13:551-553.

Redig, P.T., C.M. Stowe, D.M. Barnes, and T.D. Arent. 1980. Lead toxicosis in raptors. J. Am. Vet. Med . Assoc. 177:941.

Reichel, W.L., S.K. Schmeling, E. Cromartie, T.E. Kaiser, A.J. Krynitsky, T.G. Lamont, B.M. Mulhern, R.M. Prouty, C.J. Stafford, and D.M. Swineford. 1984. Pesticide, PCB, and lead residues and necropsy data for bald eagles from 32 states - 1978-81. Environ. Monitor. Assess. 4:395-403.

Reichert, W.L., D.A. Federighi, and D.C. Malins. 1979. Uptake and metabolism of lead and cadmium in coho salmon (*Oncorhynchus kisutch*). Comp. Biochem. Physiol. 63C:229-234.

Reish, D.J., and T.V. Gerlinger. 1964. The effects of cadmium, lead, and zinc on survival and reproduction in the polychaetous annelid *Neanthes arenaceodentata* (F. Nereididae). Pages 383-389 *in* P.A. Hutchings (ed.) Proceedings of the first international polychaete conference. Sydney. Linnean Soc. N.S.W., Australia.

Rice, D.C. 1985. Chronic low-lead exposure from birth produces deficits in discrimination reversal in monkeys. Toxicol. Appl. Pharmacol. 77:201-210.

Rivkin, R.B. 1979. Effects of lead on the growth of the marine diatom *Skeletonema costatum*. Mar. Biol. 50:239-247.

Robel, R.J., C.A. Howard, M.S. Udevitz, and B. Curnutte, Jr. 1981. Lead contamination in vegetation, cattle dung, and dung beetles near an interstate highway, Kansas. Environ. Entomol. 10:262-263.

Roberts, R.D., M.S. Johnson, and M. Hutton. 1978. Lead contamination of small mammals from abandoned metalliferous mines. Environ. Pollut. 15:61-69.

Roberts, T.M., P.B. Heppleston, and R.D. Roberts. 1976. Distribution of heavy metals in tissues of the common seal. Mar. Pollut. Bull. 7:194-196.

Rolfe, G.L., and K.A. Reinbold. 1977. Environmental contamination by lead and other heavy metals. Volume I: introduction and summary. Univ. Illinois, Inst. Environ. Studies, Urbana-Champaign. 120 pp.

Rombaugh, P.J. 1985. The influence of the zona radiata on the toxicities of zinc, lead, mercury, copper and silver ions to embryos of steelhead trout *Salmo gairdneri*. Comp. Biochem. Physiol. 82C:115-117.

Ruhling, A., and G. Tyler. 1968 An ecological approach to the lead problem. Bot. Notiser. 121:321 342.

Sadiq, M. 1985. Uptake of cadmium, lead and nickel by corn grown in contaminated soils. Water Air Soil Pollut. 26:185-190.

Sanderson, G.C., and F.C. Bellrose. 1986. A review of the problem of lead poisoning in waterfowl. Illinois Nat. Hist. Surv., Spec. Publ. 4. 34 pp.

Schlick, E., K. Mengel, and K.D. Friedberg. 1983. The effect of low lead doses in vitro and in vivo on the *d* -ala- *d* activity of erythrocytes, bone marrow cells, liver and brain of the mouse. Arch. Toxicol. 53:193-205.

Schmitt, C.J., F.J. Dwyer, and S.E. Finger. 1984. Bioavailability of Pb and Zn from mine tailings as indicated by erythrocyte -aminolevulinic acid dehydratase (ALA-D) activity in suckers (Pisces: Catostomidae). Can. J. Fish. Aquat. Sci. 41:1030-104).

Schmitt, C. J., and S. E. Finger. 1987. The effects of sample preparation on measured concentrations of eight elements in edible tissues of fish from streams contaminated by lead mining. Arch. Environ. Contam. Toxicol. 16:185-207.

Schulz-Baldes, M. 1972. Toxicity and accumulation of lead in the common mussel *Mytilus edulis* in laboratory experiment. Mar. Biol. 16:226-229.

Schulz-Baldes, M. 1974. Lead uptake from sea water and food, and lead loss in the common mussel, *Mytilus edulis*. Mar. Biol. 25:177-193.

Schulz-Baldes, M., and R.A. Lewin. 1976. Lead uptake in two marine phytoplankton organisms. Biol. Bull. 150:118-127.

Scoullos, M.J. 1986. Lead in coastal sediments: the case of the Elefsis Gulf, Greece. Sci. Total Environ. 49:199-219.

Seeliger, U., and P. Edwards. 1977. Correlation coefficients and concentration factors of copper and lead in seawater and benthic algae. Mar. Pollut. Bull. 8:16-19.

Settle, D. M., and C. C. Patterson. 1980. Lead in albacore: guide to lead pollution in Americans. Science 207:1167-1176.

Sharma, S., and K.C. Kanwar. 1985. Reproductive performance in mice following lead administration. Res. Bull. Panjab Univ. 36:389-394.

Sheppard, C.R.C., and D.J. Bellamy. 1974. Pollution of the Mediterranean around Naples. Mar. Pollut. Bull. 5:42-44.

Sileo, L., and W.N. Beyer. 1985. Heavy metals in white-tailed deer living near a zinc smelter in Pennsylvania. J. Wildl. Dis. 21:289-296.

Sileo, L., and S. I. Fefer. 1987. Paint chip poisoning of Laysan albatross at Midway Atoll. J. Wildl. Dis. 23:432-437.

Sirota, G.R., and J.F. Uthe. 1977. Determination of tetraalkyl lead compounds in biological materials. Anal. Chem. 49:823-825.

Sleet, R.B., and J.H. Soares, Jr. 1979. Some effects of Vitamin E deficiency on hepatic xanthine dehydrogenase activity, lead, and ~ tocopherol concentrations in tissues of lead-dosed mallard ducks. Toxicol. Appl. Pharmacol. 47:71-78.

Smith, G.J., and O.J. Rongstad. 1982. Small mammal heavy metal concentrations from mined and control sites. Environ. Pollut. 28A:121-134.

Smith, R. A., R. B. Alexander, and P. G. Wolman. 1987. Water-quality trends in the Nation's rivers. Science 235:1607-1615.

Spehar, R.L., R.L. Anderson, and J.T. Fiandt. 1978. Toxicity and bioaccumulation of cadmium and lead in aquatic invertebrates. Environ. Pollut. 15:195-208.

Srebocan, E., and B. A. Rattner. 1988. Heat exposure and the toxicity of one number four lead shot in mallards, *Anas platyrhynchos*. Bull. Environ. Contam. Toxicol. 40:165-169.

Stendell, R.C. 1980. Dietary exposure of kestrels to lead. J. Wildl. Manage. 44:527-530.

Stendell, R.C., J.W. Artmann, and E. Martin. 1980. Lead residues in sora rails from Maryland. J. Wildl. Manage. 44:525-527.

Stendell, R.C., R.I. Smith, K.P. Burnham, and R.E. Christensen. 1979. Exposure of waterfowl to lead: a nationwide survey of residues in wing bones of seven species, 1972-73. U.S. Fish Wildl. Serv. Spec. Sci. Rep. -Wildl. 223. 12 pp.

Stewart, J., and M. Schulz-Baldes. 1976. Long-term lead accumulation in abalone (*Haliotis* spp.) fed on lead-treated brown algae (*Egregia laevigata*). Mar. Biol. 36:19-24.

Stone, C.L., and M.R.S. Fox. 1984. Effects of low levels of dietary lead and iron on hepatic RNA, protein, and minerals in young Japanese quail. Environ. Res. 33:322-332.

Stone, W.B., and S.A. Butkas. 1978. Lead poisoning in a wild turkey. N.Y. Fish Game J. 25:169.

Stournaras, C., G. Weber, H. P. Zimmermann, K.H. Doenges, and H. Faulstich. 1984. High cytotoxicity and membrane permeability of Et_3Pb^+ in mammalian and plant cells. Cell Biochem. Func. 2:213-216.

Street, M. 1983. The assessment of mortality resulting from the ingestion of spent lead shot by mallard wintering in South East England. Congr. Int. Fauna Cinegetica y Silvestre 15 (1981):161-167.

Sundstrom, R., K. Muntzing, H. Kalimo, and P. Sourander. 1985. Changes in the integrity of the blood-brain barrier in suckling rats with low dose lead encephalopathy. Acta Neuropathol. 68:1-9.

Szymczak, M.R., and W.J. Adrian. 1978. Lead poisoning in Canada geese in southeast Colorado. J. Wildl. Manage. 42:299-306.

Tachon, P., A. Laschi, J.P. Briffaux, and G. Brain. 1983. Lead poisoning in monkeys during pregnancy and lactation. Sci. Total Environ. 30:221-229.

Ter Haar, G.I. 1970. Air as a source of lead in edible crops. Environ. Sci. Technol. 4:226-229.

Tsuchiya, K. 1979. Lead. Pages 451-484 *in* L. Friberg, G.E. Nordberg, and V.B. Vouk (eds.). Handbook on the toxicology of metals. Elsevier/NorthHolland Biomedical Press, Amsterdam.

Turner, R.S., A.H. Johnson, and D. Wang. 1985. Biogeochemistry of lead in McDonalds Branch watershed, New Jersey Pine Barrens. J. Environ. Qual. 14:305-314.

Udevitz, M.S., C.A. Howard, R.J. Robel, and B. Curnutte, Jr. 1980. Lead contamination in insects and birds near an interstate highway, Kansas. Environ. Entomol. 9:35-36.

Varanasi, U., and D.J. Gmur. 1978. Influence of water-borne and dietary calcium on uptake and retention of lead by coho salmon (*Oncorhynchus kisutch*). Toxicol. Appl. Pharmacol. 46:65-75.

Veit, H.P., R.J. Kendall, and P.F. Scanlon. 1983. The effect of lead shot ingestion on the testes of adult ringed turtle doves (*Streptopelia risoria*). Avian Dis. 27:442-452.

Vighi, M. 1981. Lead uptake and release in an experimental trophic chain.Ecotoxicol. Environ. Safety 5:177-193.

Walsh, D.F., B.L. Berger, and J.R. Bean. 1977. Mercury, arsenic, lead, cadmium, and selenium residues in fish, 1971-73 - National PesticideMonitoring Program. Pestic. Monitor. J. 11:5-34.

Walsh, T.J., and H.A. Tilson. 1984. Neurobehaviorial toxicology of the organoleads. Neurotoxicology 5:67-86.

Ward, N.I., and R.R. Brooks. 1979. Lead levels in wool as an indication of lead in blood of sheep exposed to automotive emissions. Bull. Environ. Contam. Toxicol. 21:403-408.

Way, C.A., and G.D. Schroder. 1982. Accumulation of lead and cadmium in wild populations of the commensal rat *Rattus norvegicus*. Arch. Environ. Contam. Toxicol. 11:407-417.

Wetmore, A. 1919. Lead poisoning in waterfowl. U.S. Dep. Agricul. Bull. 793. 12 pp.

White, D.H., J.R. Bean, and J.R. Longcore. 1977. Nationwide residues of mercury, lead, cadmium, arsenic, and selenium in starlings, 1973. Pestic. Monitor. J. 11:35-39.

White, D.H., K.A. King, C.A. Mitchell, and B.M. Mulhern. 1986. Trace elements in sediments, water, and American coots (*Fulica americana*) at a coal-fired power plant in Texas, 1979-1982. Bull. Environ. Contam. Toxicol. 36:376-383.

White, D.H., and R.C. Stendell. 1977. Waterfowl exposure to lead and steel shot on selected hunting areas. J. Wildl. Manage. 41:469-475.

White, J.R., and C.T. Driscoll. 1985. Lead cycling in an acidic Adirondack lake. Environ. Sci. Technol. 19:1182-1187.

Wide, M. 1985. Lead exposure on critical days of fetal life affects fertility in the female mouse. Teratology 32:375-380.

Wiener, J.G., G.A. Jackson, T.W. May, and B.A. Cole. 1984. Longitudinal distribution of trace elements (As, Cd, Cr, Hg, Pb, and Se) in fishes and sediments in the upper Mississippi River. Pages 139-170 *in* J.G. Wiener, R.V. Anderson, and D.R. McConville (eds.). Contaminants in the upper Mississippi River. Butterworth Publ., Stoneham, Massachusetts.

Windingstad, R.M., S.M. Kerr, L.P. Locke, and J.J. Hurt. 1984. Lead poisoning of sandhill cranes (*Grus canadensis*). Prairie Nat. 16:21-24.

Wobeser, G.A. 1981. Diseases of wild waterfowl. Plenum Press, New York. 300 pp.

Wong, P.T.S., Y.K. Chau, O. Kramar, and G.A. Bengert. 1981. Accumulation and depuration of tetramethyllead by rainbow trout. Water Res. 15:621-625.

Wong, P.T.S., B.A. Silverberg, Y.K. Chau, and P.V. Hodson. 1978. Lead and the aquatic biota. Pages 279-342 *in* J.O. Nriagu (ed.). The biogeochemistry of lead in the environment. Part B. Biological effects. Elsevier/North Holland Biomedical Press, Amsterdam.

Yeung, G.L. 1978. The influence of lead, an environmental pollutant on metamorphosis of *Rana utricularia* (Amphibia: Ranidae). Arkansas Acad. Sci. Proc. 32:83-86.

Zaroogian, G.E., G. Morrison, and J.F. Heltshe. 1979. *Crassostrea virginica* as an indicator of lead pollution. Mar. Biol. 52:189-196.

Zirkin, B.R., R. Gross, and L.L. Ewing. 1985. Effects of lead acetate on male rate reproduction. Pages 13 - 145 *in* F. Hamburger and A.M. Goldberg (eds.). Concepts in toxicology. Vol. 3. In vitro embryotoxicity and teratogenicity tests. Karger, Basel, Switzerland.

Zmudzki, J., G.R. Bratton, C. Womac, and L. Rowe. 1983. Lead poisoning in cattle: reassessment of the minimum toxic oral dose. Bull. Environ. Contam. Toxicol. 30:435-441.

Zmudzki, J., G.R. Bratton, C. Womac, and L.D. Rowe. 1984. The influence of milk diet, grain diet, and method of dosing on lead toxicity in young calves. Toxicol. Appl. Pharmacol. 76:490-497.

Zook, B.C., R.M. Sauer, and F.,M. Garner. 1972. Lead poisoning in captive wild animals. J. Wildl. Dis. 8:264-272.

Zwank, P.J., V.L. Wright, P.M. Shealy, and J.D. Newsom. 1985. Lead toxicosis in waterfowl on two major wintering areas in Louisiana. Wildl. Soc. Bull. 13:17-26.

BIOLOGICAL REPORT 85(1.15)
JANUARY 1989

Contaminant Hazard Reviews
REPORT NO. 15

TIN HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by

Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

Tin (Sn) has influenced our life style for the past 5,000 years. Today we are exposed to tin on a daily basis; including tinplated baby food cans; alloys such as pewter, bronze, brass, and solder; and toothpaste containing stannous flouride. These inorganic tin compounds are not highly toxic due to their low solubility, poor absorption, low accumulation, and rapid excretion. Synthetic organotin compounds, however, first manufactured commercially in the 1960's, may present a variety of problems to animals, including impaired behavior and reduced growth, survival, and reproduction. Some triorganotins--for example, in antifouling marine paints, in molluscicides, and in agricultural pesticides--can be harmful to sensitive species of nontarget biota at recommended application protocols.

Background concentrations of organotin compounds are frequently elevated--occasionally to dangerous levels--in aquatic organisms collected near marinas and other locales where organotin-based antifouling paints are extensively used. But more information is needed on background concentrations of organotins, especially those from terrestrial ecosystems.

Tributyltin compounds are especially toxic to aquatic organisms. Adverse effects were noted at concentrations of 0.001 to 0.06 ug/l on molluscs and at 0.1 to 1.0 ug/l on algae, fish, and crustaceans. In general, bioconcentration of organotins from seawater was high, especially by algae, but degradation was sufficiently rapid to preclude food chain biomagnification. In contrast, current environmental concentrations of some organotins are not likely to be directly toxic to birds and mammals. Birds seem to be relatively resistant to organotins, although data are scarce. Preliminary studies of 75 days duration suggest that diets containing 50 mg tin as trimethyltin chloride/kg were fatal to ducklings; 5 mg/kg killed 40%, and 0.5 mg/kg was not lethal. Trimethyltin compounds were lethal to other species of birds tested at doses of 1 to 3 mg/kg body weight. Other tests with ducklings and eleven other mono-, di-, tri-, and tetraalkyltin compounds at dietary levels equivalent to about 50 mg Sn/kg showed no adverse effects on survival. Small laboratory mammals were adversely affected by trimethyltin compounds at doses as low as 0.15 mg/l in drinking water (learning deficits), 0.63 mg/kg body weight (diet aversion), and 1.25 mg/kg body weight (death); neurotoxicological effects of trimethyltins were usually not reversible. Triethyltins were also toxic to small mammals, but effects--which were similar to those of trimethyltins--were usually reversible after cessation of exposure.

All evidence to date indicates that organotin compounds are not carcinogenic.

Methodologies and data necessary for the promulgation of effective criteria and standards to protect natural resources seem to be deficient in eight key areas: (1) routine analytical chemical methodologies for extraction, separation, and identification of inorganic and organic tin compounds and their chemical speciation products in biological and other samples; (2) mechanisms of toxicity for organotin compounds; (3) rates of uptake, retention, and translocation of organotins in biota; (4) persistence and mobility rates of organotins in nonbiological materials; (5) rates of tin methylation and biotransformation in biological and abiotic samples; (6) organotin interactions with other toxic chemicals; (7) quantitative structure activity relation for use in evaluating organotin toxicity; and (8) long-term environmental monitoring studies in terrestrial and aquatic ecosystems for establishment of baseline concentrations.

DISCLAIMER

Suggested citation for this report:

Eisler, R. 1989. Tin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.15).

TABLES

ACKNOWLEDGMENTS

I thank Lynda J. Garrett, Joyce E. Haber, Christine Holden, and Nancy A. Bushby for technical services; Julia L. Armstrong for secretarial assistance; Denny R. Buckler, W. James Fleming, Roy B. Laughlin, Jr., and T. Peter Lowe for constructively reviewing the manuscript; and Nancy M. Wells and James R. Zuboy for editorial services.

INTRODUCTION

Interest in the toxicity of tin compounds dates to the early 1800's when investigators demonstrated that inorganic tin compounds produced muscular weakness, loss of pain sensation, and immobility in dogs (Reiter and Ruppert 1984; Idemudia and McMillan 1986b). In man, organotins can be assimilated by inhalation, absorption through the skin, and from food and drinking water (Zuckerman et al. 1978). The first documented case of organotin poisoning of humans was in 1880 when workers complained of headaches, general weakness, nausea, and diarrhea after exposure to triethyltin acetate vapors (Reiter and Ruppert 1984). Renewed interest in the toxicity of organotin compounds resulted from a medical tragedy in France in 1954. "Stalinon," a proprietary compound of diethyltin diiodide plus linoic acid used to treat furuncles and other skin infections, caused 217 poisonings and 111 deaths (Piver 1973; Duncan 1980; Idemudia and McMillan 1986b). The identified toxic components in Stalinon were triethyltin contaminants; victims received a total dose of 3 grams over a 6- to 8-week period. Symptoms included constant severe headache, rapid weight loss, vomiting, urine retention, vertigo, hypothermia, abdominal pain, and visual and psychic disturbances. Some of the more severely affected patients had convulsions. Death usually occurred in coma or from respiratory or cardiac failure. In survivors, headaches and diminished visual acuity remained for at least 4 years.

Recent world production of organotin compounds is about 30,000 tons, although relatively few organotin compounds, perhaps only 25, are presently produced and used to any great extent (Laughlin and Linden 1985). Diorganotins are used in the manufacture of antioxidants, whereas triorganotins are used as general biocides against microbial and invertebrate pests and in marine antifouling paints (Laughlin and Linden 1985). The first antifouling paints incorporating an organotin compound as a biocide were developed in 1961. Because of their effectiveness and availability in a variety of colors, tributyltin antifouling paints are now the most commonly used type, replacing copper-, mercury-, and lead-based paints (Stebbing 1985). Worldwide synthesis of tributyltin compounds is about 900 metric tons annually for all applications (Laughlin et al. 1986a). Tributyltins are highly toxic to aquatic plants and animals, readily accumulate in fish and molluscs from contaminated localities, and are present in some harbors where their release from antifouling paints--found usually on small boats and recreational craft--is the putative source (Walsh et al. 1985; EPA 1986; Laughlin et al. 1986a). Tributyltin is a contributory factor and probably a major cause for the reproductive failure of the European flat oyster (*Ostrea edulis*) in recent years in some locations (Thain and Waldock 1986). in fact, tributyltins are capable of causing adverse biological effects at levels far below that of any previously reported marine pollutant (Lawler and Aldrich 1987).

The widespread agricultural applications of trialkyltin biocidal agents have greatly increased the relative exposure risks to workers handling these materials (Rosenberg et al. 1985). Internationally, tin was recognized as a potential environmental contaminant at the Paris and Helsinki conventions in 1974; in later conventions, organotin compounds were moved to the "black list" (Vrijhof 1985). Due to the increasing use of organotin compounds as a class, the Canadian government, in 1979, placed organotins on Canada's Category III Contaminant List. Category III indicates that additional data are needed on the occurrence, persistence, and toxicity of organotins for preparation of informed environmental and human health risk assessments (Chau et al. 1984).

Many reviews and bibliographies are available on the environmental impacts of inorganic and organic tin compounds.[1] These authorities agree that inorganic tin compounds are comparatively harmless and that many organotin compounds are potentially very hazardous to natural resources--especially tributyltin compounds to aquatic biota. One rare exception to this generalization involved 113 cases of acute gastrointestinal illness in Washington and Oregon in 1969 associated with ingestion of canned tomato juice contaminated by inorganic tin; detinning in many cans resulted in tin levels as high as 477 mg inorganic tin per liter of juice. It seems that excessive use of nitrate fertilizer on one tomato crop was the ultimate cause of the detinning (Barker and Runte 1972).

This report summarizes selected data on ecological and toxicological aspects of organic and inorganic tin compounds, with emphasis on fishery and wildlife resources. It is part of a continuing series of reports on chemical contaminants prepared in response to informational requests from environmental specialists of the U.S. Fish and Wildlife Service.

[1] Barnes and Stoner (1959); Piver (1973); Kimbrough (1976); CEC (1978); Zuckerman et al. (1978); Duncan (1980); Watanabe (1980); WHO (1980); Blunden and Chapman (1982); Blunden et al. (1984, 1985); Krigman and Silverman (1984); Reiter and Ruppert (1984); Reuhl and Cranmer (1984); Wilkinson (1984); Hall and Pinkney (1985); Laughlin and Linden (1985); McMillan and Wenger (1985); Thompson et al (1985); Blunden and Chapman (1986); Cardwell and Sheldon (1986); Chang (1986); Maton (1986); Sylph (1986a, b); EPA (1987); Snoeij et al. (1987).

CHEMICAL AND BIOCHEMICAL PROPERTIES

GENERAL

The chemical, physical, and biochemical properties of inorganic tin compounds differ dramatically from those of representative organotin compounds. There is general agreement that inorganic tins are not highly toxic due to their poor absorption and rapid turnover rate in tissues and to their being essential for growth in at least one species (rat). Of the 260 known organotin compounds, all but a few are manufactured, and 36 are listed as toxic (Watanabe 1980). Most authorities agree on several points regarding organotin compounds: information concerning the mechanism of toxic action is incomplete; there is no evidence of carcinogenicity; trialkyltin compounds are the most toxic; and there are large differences in resistance between and within species.

INORGANIC TIN

Elemental tin has an atomic number of 50, an atomic mass of 118.69, and exists in three allotropic forms: white tin at room temperature, nonmetallic grey tin at <13.3 C, and brittle tin at >161 C. White tin is a stable silver-white, lustrous, soft metal with a density of 7.27, a melting point of 231.9 C, and a boiling point of 2,507 C. Tin has 10 stable isotopes (Sn-112, -114, -115, -116, -117, -118, -119, -120, -122, and -124), the most for any element. Inorganic tin compounds exist in the +2 (stannous) and +4 (stannic) oxidation states. Stannous compounds are generally more polar than stannic compounds, are unstable in dilute aqueous solutions, are easily oxidized, and normally contain some Sn+4. Stannic oxide occurs naturally as the mineral cassiterite, has a melting point of 1,127 C, and has wide application in industry. Additional information on inorganic tin chemistry is listed in Zuckerman et al. (1978), WHO (1980), and Davies and Smith (1982).

Signs of inorganic tin poisoning in mammals include local effects such as vomiting, diarrhea, and eye and nose irritation; however, these vary considerably among species (WHO 1980). The major systemic effects include ataxia, twitching of limbs, weakness of limbs, paralysis, growth retardation, decreased hemoglobin levels, and--at extremely high doses--testicular degeneration, pancreatic atrophy, formation of spongy brain white matter, and kidney necrosis. In humans, symptoms of inorganic tin intoxication include nausea, vomiting, diarrhea, stomach ache, fatigue, and headache. The lowest concentration producing outbreaks was about 250 mg Sn per liter in canned orange and apple juice. Ingestion of 50 mg of tin through eating canned peaches that contained Sn concentrations of about 450 mg/kg caused acute symptoms in 2 of 7 human volunteers (WHO 1980). Inhalation of SnO_2 dust is a hazard in the deep-mining of tin; deposits in lungs are easily detectable as "stannosis" (Krigman and Silverman 1984).

Inorganic tin and its salts are not highly toxic due to their poor absorption, relative insolubility of their oxides, and rapid tissue turnover (WHO 1980; Hassett et al. 1984; Krigman and Silverman 1984; Blunden and Chapman 1986). The absorption of ingested inorganic tin is usually less than 5%, although up to 20% has been reported. Stannous compounds are more readily absorbed from the gastrointestinal tract than stannic compounds, but absorbed tin leaves the vascular system rapidly. Bone is the main site of tin deposition, followed by lung, liver, and kidney. Penetration of the blood-brain and placental barriers by inorganic tin seems to be very slight. Except for lung, inorganic tin does not accumulate in organs with increasing age. Absorbed inorganic tin is excreted mainly in the urine, although excretion through the bile may account for up to 15% of the total. Tin and its inorganic compounds do not produce significant dermatitis or allergic reactions to skin epithelium, and results of all long-term studies of carcinogenicity, teratogenicity, and mutagenicity have been negative to date (WHO 1980).

The half-time (Tb 1/2) of inorganic tins in animals was reviewed by WHO (1980). Studies with Sn+2 in mouse, rat, monkey, and dog show that in all species elimination is a four-compartment process regardless of the route of administration (i.e., intraperitoneal or intravenous). The Tb 1/2 for the longest-lived Sn component

was >3 months. In studies with rats, for example, radiotin-113 in skeleton following intramuscular administration had a Tb1/2 of 3 to 4 months, but for oral administration of Sn+2 and Sn+4 it was only 28 to 40 days in bone and 10 to 20 days in liver and kidney.

Inorganic tin can be biomethylated by microorganisms in the aquatic environment and subsequently mobilized in the ecosystem (Tugrul et al. 1983; Yemenicioglu et al. 1987). The process is slow and usually does not proceed beyond the monomethyltin stage (Zuckerman et al. 1978), although dimethyltin formation by *Pseudomonas* bacteria has been reported (Smith 1978b).

Tin is an essential nutrient for growth in the rat, and a tin-deficient diet leads to reduced growth (WHO 1980; Krigman and Silverman 1984). The mechanism of action is unclear, but involves increasing metabolic activity of liver lysosomes and liver hydrolytic enzymes during regeneration (Dwivedi et al. 1985a,b).

ORGANOTINS

Organotins are compounds with at least one tin-carbon bond. In most organotin compounds, tin is in the tetravalent oxidation state. Four series of organotin compounds are known: R_4Sn, R_3SnX, R_2SnX_2, and $RSnX_3$ wherein R is usually a butyl, octyl, or phenyl group, and X is commonly chloride, fluoride, oxide, hydroxide, carboxylate, or thiolate (CEC 1978). The possible molecular composition and structure of the R groups are virtually unlimited (Laughlin et al. 1985). At least 260 organotin compounds presently are known, of which 36 are listed as toxic chemicals (Watanabe 1980). Except for some methyltin compounds, all organotins are manufactured (Laughlin et al. 1985). Most commercially used organotins are characterized by low mobility in the environment because of low aqueous solubility, low vapor pressure, and high affinity for soils and organic sediments (Blunden and Chapman 1986). Solubility data for organotin compounds are incomplete. In general, their solubility in water is limited to about 5 to 50 mg/l, but they are very soluble in many common organic solvents (WHO 1980). The presence of chloride in seawater reduces the solubility of tributyltin and triphenyltin compounds, probably by association with the hydrated cation to form the covalent organotin chloride (Blunden et al. 1985). Organotin compounds are analyzed in aqueous media by spectrophotometric, fluorometric, and electrochemical techniques. However, if picomole per liter concentrations are required, additional techniques must be used. More work needs to be done on analytical detection methods of organotins in sediments and biota (Thompson et al. 1985).

Methylation of inorganic and methyltin compounds has been reported with the formation of mono-, di-, tri-, and tetramethyltin compounds. In addition, tributylmethyltin and dibutylmethyltin species have been found in harbor sediments, which suggests that some butyltin compounds may be methylated in aquatic systems (Guard et al. 1981; Thompson et al. 1985; Donard et al. 1987).

Abiotic and biological degradation of organotins generally occurs through sequential dealkylation or dearylation (Zuckerman et al. 1978; WHO 1980; Smith 1981b; Chau et al. 1984; Blunden et al. 1985). Organotin compounds undergo successive cleavage of tin-carbon bonds to ultimately produce inorganic tin as follows: $R_4Sn \xrightarrow{k4} R_3SnX \xrightarrow{k3} R_2SnX_2 \xrightarrow{k2} RSnX_3 \xrightarrow{k1} SnX_4$. The reaction rate, k, usually proceeds as k4 > k3 > k2 = k1. The breaking of a Sn-C bond can occur by a number of different processes, including ultraviolet irradiation (UV), biological cleavage, chemical cleavage, gamma irradiation, and thermal cleavage (WHO 1980; Blunden and Chapman 1982, 1986; Blunden et al. 1985; Thompson et al. 1985). In general, UV and biological cleavage are the most important processes. The main abiotic factors that seem to limit organotin persistence in the environment are elevated temperatures, increased intensity of sunlight, and aerobic conditions (Table 1). A probable environmental degradation scheme for tributyltin and triphenyltin compounds is shown in Figure 1.

The tendency of an organotin compound to be concentrated by an organism depends on its partition behavior between lipid and aqueous phases. In general, compounds highly soluble in octanol and only slightly soluble in water have high Kow values. Kow values of organotins increase with number and molecular weight of organic groups attached to the tin atom, with significant bioaccumulation potential for organotins with R groups of butyl and larger (Thompson et al. 1985). Kow values for tributyltins in seawater vary from 5,500 to 7,000, but can be significantly modified by salinity and speciation products (Laughlin et al. 1986b). Thus, organotins would be expected to accumulate in lipid-rich surface microlayers of natural waters (Cardwell and Sheldon 1986) and

in biota (as discussed later). However, the ability of microorganisms, algae, and higher organisms to reduce various organotins into less toxic metabolites that can be rapidly excreted seems to preclude food chain biomagnification and to lessen the potential hazards to natural resources from consumption of organisms with elevated organotin residues (Table 1; Cardwell and Sheldon 1986).

Most authorities now agree on five points: (1) information concerning the mechanism of the toxic action of organotin compounds is inadequate; (2) results of all studies with various organotins for possible carcinogenicity are negative; (3) triorganotin compounds are the most toxic group of organotins; (4) large inter- and intraspecies differences exist in resistance to organotin compounds; and (5) organotins can alter enzyme activity levels in many organs and tissues including brain, liver, and kidney (Piver 1973; Duncan 1980; WHO 1980; Davies and Smith 1982; Maguire et al. 1982; Arakawa and Wada 1984; Dwivedi et al. 1985b; Blunden and Chapman 1986).

The monoorganotin compounds, $RSnX_3$ have a generally low toxicity and do not seem to have any important biological action in mammals (Duncan 1980; Davies and Smith 1982; Krigman and Silverman 1984; Blunden and Chapman 1986).

Dialkylorganotins, R_2SnX_2, are associated with hepatotoxicity (ethyl, propyl, butyl, and pentyltins), immunotoxic effects to T-cells (butyl and octyltins), and skin and eye irritation (methyl, ethyl, propyl, butyl, and octyltins; Watanabe 1980; Krigman and Silverman 1984). The diorganotins combine with coenzymes or enzymes possessing dithiol groups and exert their toxic action by inhibiting alpha-keto acid oxidation and blocking mitochondrial respiration (Duncan 1980; WHO 1980; Davies and Smith 1982). Resistance to diorganotin toxicity varies widely among species. For example, dibutyltins and dioctyltins--unlike other organotins tested--were toxic to rat thymocytes, but did not induce similar effects on lymphoid atrophy in mice, guinea pigs, or Japanese quail (Seinen et al. 1977b). Selected dibutyltins are effective as antihelminthics and are used to kill parasitic worms in chickens and turkeys without harm to host birds (Davies and Smith 1982).

Table 1. Biological and abiotic degradation times of selected organotins.

Degradation route, organism or compartment, and tin compound	Time for 50% degradation and other variables (reference)
Biological	
Microorganisms	
Tributyltin	1 to 2 weeks in aerated medium in dark, 6 to 13 weeks in aerated medium in light, <1 year in anaerobic medium (Cardwell and Sheldon 1986)
Triphenyltin	60 to 140 days under aerobic, light conditions (Smith 1981b)
Algae, *Ankistrodesmus falcatus*	
Tributyltin	25 days (Maguire et al. 1984)
Bivalve molluscs, 3 species	
Tributyltin	10 to 14 days (Cardwell and Sheldon 1986; Laughlin et al. 1986a)
Sheepshead minnow, *Cyprinodon variegatus*	
Tributyltin	14 to 28 days (Cardwell and Sheldon 1986)
Abiotic	
Distilled water	
Tributyltin	>89 days at initial concentration of 0.7 mg Sn/L, 18 days at 2.0 to 4.0 mg Sn/L (Walsh et al. 1986a)
Freshwater	

Tributylin	3 to 89 days (Duncan 1980; Smith 1981b; Ward et al. 1981; Maguire and Tkacz 1985; Walsh et al. 1985)
Triphenyltin	8 months at 1.0 to 2.5 mg/L, 100 days at 0.5 mg/L (Duncan 1980)
Diphenyltin	2 to 3 days (Soderquist and Crosby 1980)
Seawater	
Tributyltin	6 to 19 days; most rapid at low initial concentrations under high illumination (Seligman et al. 1986)
Triphenyltin	About 140 days (Duncan 1980)
Sediments	
Trimethyltin	About 80 days at 16 C to form the more volatile $(CH_3)_4Sn$ (Guard et al. 1981)
Tributyltin	At least 10 months at 20 ºC (Maguire and Tkacz 1985)

In any member of the organotin series R_nSnX_{4-n}, progressive substitution of organic groups at tin produces a maximum biological activity for the triorganotin derivatives, R_3SnX (Davies and Smith 1982). Among triorganotin compounds, trimethyltins are highly toxic to insects, birds, and mammals; triethyltins to mammals; tripropyltins to gram-negative bacteria; tributyltins to fish, molluscs, fungi, and gram-positive bacteria; triphenyltins to fish, fungi, and molluscs; and tricyclohexyltins to mites (Duncan 1980; Davies and Smith 1982; Maguire et al. 1982; Blunden and Chapman 1986). In mammals, the lower triorganotin homologues (trimethyltins, triethyltins) are essentially neurotoxic, the intermediate trialkyltins and triphenyltins are primarily immunotoxic, and the higher homologues are only slightly toxic or not toxic (Krigman and Silverman 1984; Snoeij et al. 1985). The toxicity of triorganotin compounds is probably due to their ability to bind to proteins and to inhibit mitochondrial oxidative phosphorylation (Smith 1978b; Duncan 1980; WHO 1980; Davies and Smith 1982; Blunden and Chapman 1986). Triorganotins also interfere with phagocytosis and exocytosis and other pathways where sulfhydryl groups play a pivotal role (Elferink et al. 1986), and inhibit uptake of gamma-aminobutyric acid and Na^+-K^+-ATPase in brain (Costa 1985). Impairment of phagocytosis and related activities of polymorphonuclear leukocytes may enhance susceptibility for infection (Elferink et al. 1986).

Trimethyltins are the most toxic trialkyltins to mammals, regardless of the nature of the substituent (X group) according to Smith (1978b). They induce pathological lesions in brain and overt neurological and behavioral changes in rodents (Chang 1986). Trimethyltins are neurotoxins that damage the limbic system, cerebral cortex, and brain stem and can traverse the placenta and accumulate in the fetus (Reuhl aid Cranmer 1984). Trimethyltins (but not inorganic, monomethyl, or dimethyltins) inhibit brain protein synthesis by 47% and can cause a decrease of 4.2 °C in body temperature of mice within 1 hour postadministration of 3.0 mg/kg body weight (Costa and Sulaiman 1986). Raising the ambient temperature to 35 °C prevented hypothermia in treated mice and resulted in only a 20% inhibition in protein synthesis. More research is needed on the role of protein synthesis in organotin-induced neurotoxicity.

Triethyltins modify phosphorylation processes in subcellular fractions of rat brain proteins (Piver 1973; Neumann and Taketa 1987). Signs of triethyltin poisoning in rodents include weakness of hindlimbs, dyspnea, and peripheral vasodilation (Watanabe 1980). Internally, acute triethyltin intoxication is characterized by a transient edema of the central and peripheral nervous systems manifested by extensive intramyelinic vacuolation due to splitting of myelin lamellae; changes are reversible (Watanabe 1980; Reuhl and Cranmer 1984). Neuronal death is reported following triethyltin intoxication during the neonatal period, possibly as a result of elevated intracranial pressure (Reuhl and Cranmer 1984). In rabbit brain, triethyltins alter activity of pyruvate dehydrogenase (Neumann and Taketa 1987).

Studies on tributyltin uptake and depuration from food or water by rats, crabs, oysters, and fish showed that in all species it was accumulated and metabolized, at least partly, within 48 hours to dibutyltins, monobutyltins, and more polar metabolites; however, oysters (*Crassostrea virginica)* metabolized significantly less tributlytin than did other species tested (Lee 1985). The accumulation of tributyltin compounds in different tissues

correlated well with lipid content nd supports a partitioning mode of uptake (Laughlin et al. 1986a). The mixed function oxygenase system from hepatic tissues was able to metabolize tributyltins by forming hydroxylated metabolites (Lee 1985). Tributyltins are also potent cytotoxicants in rabbit erythrocyte and skin cultures (Gray et al. 1985).

The potential of tricyclohexyltins to modify the inducibility of cytochrome P-450 by various substances, such as 3-methylcholanthrene, is of considerable toxicological importance (Rosenberg et al. 1985). Significant metabolic interactions can result from a combination of environmental chemicals and drugs that produce alterations in heme and mixed function oxygenase activity (Rosenberg et al. 1985), suggesting that more research is needed on interaction effects of organotins with other environmental substances or contaminants.

The biological effects of the tetraorganotin compounds, R_4Sn, seem to be caused entirely by the R_3SnX derivative that is produced by their rapid in vivo dealkylation (Duncan 1980; Davies and Smith 1982; Blunden and Chapman 1986). Increasing toxicity of tetra- and triorganotins in mammals has been shown to be associated with decreasing length of their ligands, as reflected by solubility in biological fluids (Arakawa et al. 1981). It is not known if damage is produced by the metal or by its alkyl derivative, but the presence of trialkyl groups seems to enhance the toxicity of tin--probably by increasing its partition into lipids, thus aiding the absorption of the metal and speeding its distribution to the site of action (Arakawa et al. 1981).

SOURCES AND USES

Metallic tin is derived mainly from the mineral cassiterite (SnO_2) and to a lesser extent from the sulphide ore stannite Cu_2S-FeS-SnS_2, although it can be derived from rarer minerals such as malayaite, $CaSnSiO_5$. (Blunden et al. 1985). Tin is one of the earliest metals known and has influenced our life style through the ages. Tin alloy artifacts dating from about 5,000 years ago have been unearthed at Ur, the site of ancient Babylonia (Zuckerman et al. 1978). Today we are exposed to tin on a daily basis through the use of tinplated food cans; of alloys such as pewter, bronze, brass, and solder; and from toothpaste containing stannous flouride (Zuckerman et al. 1978). Inorganic tin compounds are also used in a variety of industrial processes such as the strengthening of glass, as a base for colors, as catalysts in various chemical reactions, as stabilizers in perfumes and soaps, and as dental anticariogenic agents (WHO 1980). Organotin use is increasing rapidly in antifouling marine paints, in molluscicides, and in agriculture, which often causes serious adverse effects on nontarget biota.

In 1975, the total world tin production was 236,000 tons, of which 72% was produced by China (10%), Indonesia (8%), Malaysia (35%), Thailand (7%), and 6% each by the UK and USSR (WHO 1980). The world production of recycled tin was about 20,000 tons, of which France produced about half (WHO 1980). The production and consumption of tin chemicals, especially organotins, has increased markedly in the past several decades (Table 2).

The United States is the major consumer of tin and organotin compounds, followed by Japan, the UK, Germany, and France (WHO 1980). In 1976, for example, the United States consumed 11,000 tons of organotins, or about 39% of the world organotin production (Chau et al. 1984). The projected total demand for primary tin up to the year 2000 is estimated at 7.5 million tons. Total reserves currently are about 6.5 million tons; however, it is likely that new discoveries and increases in known reserves will result in sufficient new tin to meet the demand for this period (WHO 1980).

The uses of inorganic and organotin compounds are numerous and increasing (Table 3). Industrial consumption of organotins, for example, rose from about 5,000 tons in 1965 to about 35,000 tons in 1980. At present, the uses of nontoxic organotin compounds (R_2SnX_2 and $RSnX_3$ types) account for about 67% of the total world production, although use of R_3SnX types as selective biocides has increased disproportionately in recent years (Davies and Smith 1982). Tin now has more of its organometallic derivatives in commercial use than any other element (Blunden et al. 1985).

Table 2. Annual tin production and consumption.

Chemical group and other variables	Amount, in metric tons	Reference[a]
Organotins		
Production Worldwide		
Total		
1950	<5,000	1
1955	~5,000	2
1976	24,000 to 28,000	3, 4, 5, 6
1986	30,000	2
Triorganotins	8,000	2
Tributyltins	900	7
Di- and monoorganotins	27,000	2
USA		
1965	2,300	8
1976	10,400	8
1986	25,000	8
Consumption		
Worldwide		
Total		
1965	5,000	9
1967	8,000	10
1975	25,000	10
1980	30,000 to 35,000	9
Biocidal applications		
1975	10,000	10
Total tin, Production, worldwide,		
1975, Total	236,000	4
1975, Primary tin	217,000	4
1976, Total	180,000 to 200,000	2, 3, 5
1976, Total	155,000	1
Tinplate	52,700	1
Solder	48,100	1
Chemicals	20,000	1
Other uses	34,200	1
1976, Total	225,000	4
Ores	157,500	4
Scrap metal	67,500	4

[a]References: 1, Blunden et al. 1985; 2, Blunden and Chapman 1986; 3, Zuckerman et al. 1978; 4, WHO 1980; 5, Chau et al. 1984; 6, Guard et al. 1981; 7, Laughlin et al. 1986a; 8, Walsh et al. 1985; 9, Davies and Smith 1982; 10, CEC 1978.

Table 3. Major uses of inorganic and organic tin compounds.

Compounds, uses, and references (in parentheses)
INORGANIC TIN COMPOUNDS: Tin plate, solder, brass, bronze, and other alloys; heat stabilizers for polyvinyl chloride manufacture; tin and tin alloy electroplating baths; catalysts for silicone and polyurethane foam production; in glass manufacture; flame retardants for woolen fabrics; in toothpastes and dentifrices; for control of parasitic worms in sheep; radiopharmaceuticals; in ceramic glazes and pigments; in fluorescent phosphors, in weighting and dying of silk; stone polishing; corrosion inhibitors; color and perfume stabilizers in soaps (WHO 1980; Blunden et al. 1985).
MONOORGANOTINS: Polyvinyl chloride stabilizers, catalysts, SnO_2 precursors (CEC 1978; WHO 1980; Chau et al. 1984; Blunden et al. 1985, Blunden and Chapman 1986).
DIORGANOTINS: Catalysts for silicones, polyurethane foams; polyvinyl chloride stabilizers; precursor for forming SnO_2 films on glass; antihelminthics for poultry; lubricating oil additives (Piver 1973; CEC 1978; WHO 1980; Chau et al. 1984; Blunden et al. 1985; Blunden and Chapman 1986).
TRIORGANOTINS: Agrochemical fungicides, herbicides, miticides, insecticides, nematocides, acaricides, antifeedants; biocide in marine paints; slimicide in paper pulp mills and cooling towers; rodent repellant; molluscicides; wood preservative fungicides; disinfectants; stone preservation; textile and leather protection (Piver 1973; Hunter 1976; Kumpulainen and Koivistoinen 1977; CEC 1978; WHO 1980; Davies and Smith 1982; Chau et al. 1984; Subramanian 1984; Wilkinson 1984; Blunden et al. 1985; Maguire and Tkacz 1985; Thompson et al. 1985; Blunden and Chapman 1986),
TETRAORGANOTINS: Used in manufacture of R_nSnX_{4-n} compounds from $SnCl_4$; catalysts for olefin polymers; stabilizers for transformer oils; corrosion inhibitor in lubricating oils (CEC 1978; WHO 1980; Davies and Smith 1982)

Biocidal applications of organotins to control marine fouling communities, agricultural pests, and as selective molluscicides merit brief additional comment. The use of antifoulants on ships is necessitated by the damage some organisms can cause to wooden structures and by the reduced fuel efficiency and speed due to drag when vessels become heavily fouled (Laughlin et al. 1984). Until recently, the most widely used antifouling paint contained a copper base that is biocidally active when copper leaches as an ion from the paint (Hall et al. 1987). However, short effective lifetimes and high costs have limited the usefulness of copper-based paints. Organocompounds of arsenic, mercury, or lead have also been used in antifouling paints, but these paints have been removed from the commercial market due to the toxicological risks during preparation and application and to their hazards to the environment (Blunden et al. 1985; Hall et al. 1987). Organotin coatings are currently promoted because of their excellent antifouling action, long lifetime (up to 4 years), and lack of corrosion (Messiha and Ikladious 1986). Oganotin coatings, especially tributyltins, present potential environmental problems to nontarget aquatic biota due to their extreme toxicity.

Use of organotin antifouling paints on recreational and commercial water craft has increased markedly in recent years. In Maryland, for example, 50% to 75% of the recreational boats used in Chesapeake Bay are covered with organotin paints (Hall et al. 198). The organotin biocide released by hydrolysis from the surface of the paint film into seawater provides the antifoulant action. In consequence, the depleted outer layer of paint film, containing hydrophilic carboxylate groups, is easily eroded by moving seawater exposing a fresh surface layer of organotin acrylate polymer. In continuing tests by the U.S. Navy, ablative organotin fouling coatings have demonstrated more than 48 months of protection (Blunden et al. 1985). As discussed later, the use of organotin compounds in antifouling paints has been severely curtailed. Several organotins have been used extensively as agricultural pesticides, especially tricyclohexyltin and triphenyltin compounds (Hunter 1976;

Kumpulainen and Koivistoinen 1977; Blunden et al. 1985). In general, these compounds showed low phytotoxicity, low toxicity to nontarget organisms, no evidence of development of resistant insect strains, and degradation to form harmless tin residues. It is probable that agricultural uses of organotins will increase. The toxicity of triorganotin compounds to aquatic invertebrates, especially slow release formulations of tributyltins, is usually high, and this property has been used advantageously to eradicate certain species of freshwater snails that are intermediate vectors of schistosomiasis, i.e., *Biomphalaria* spp., *Bulinus* spp. (Chliamovitch and Kuhn 1977; CEC 1978; Duncan 1980; Seinen et al. 1981). Unfortunately, nontarget biota, including some sensitive species of fishes, are killed at recommended application levels (EPA 1987).

Organotins enter air, soil, and water primarily as a result of routine agricultural, industrial, municipal, and biocidal operations (Table 4). Deposition rates of organotins from air into soils and water are unknown at present, but may be significant around urban and industrialized areas. Total tin concentrations--primarily inorganic tin--in the atmosphere of the northern hemisphere are significantly higher than those in the southern hemisphere and are dominated by anthropogenic sources (Table 5). The most important of these sources seems to be the incineration of municipal wastes, which accounts for most of the tin flux to the atmosphere (Byrd and Andreae 1986a). Riverine fluxes of tin to the oceans vary between 36 and 71 million kg annually, almost all of it in particulate fractions (Byrd and Andreae 1986b).

Table 4. Possible modes of entry of organotins into air, soil, and water (Blunden et al. 1985).

Environmental compartment and organotin group	Sources
Air	
R_3SnX	Agricultural spraying, volatilization from biocidal treatments, antifouling paint sprays
R_3SnX, R_2SnX_2, $RSnX_3$	Incineration of organotin-treated or -stabilized waste materials
R_2SnX_2, $RSnX_3$	Glass coating operations to produce SnO_2 films
Soil	
R_3SnX	Agricultural applications, wood preservation
R_3SnX, R_2SnX_2, $RSnX_3$	Burial of waste materials containing organotins
Water R_3SnX	Antifouling coatings, molluscicides, overspray from agricultural operations, land runoff from agricultural use, industrial processes (i.e., slimicides in paper manufacture)
R_2SnX_2, $RSnX_3$	Leaching from organotin stabilized polyvinyl chloride

Table 5. Total tin flux to the atmosphere and hydrosphere (modified from Byrd and Andreae 1986a, b).

Environmental compartment and other variables	Annual flux, in millions of kilograms
Atmosphere	
Northern hemisphere	
Anthropogenic	16.6
Natural	1.2
Total	17.8

Southern hemisphere	
Anthropogenic	1.6
Natural	0.7
Total	2.3
Hydrosphere	
Riverine flux to oceans	
Dissolved fraction	0.09
Particulate fraction	35.6–71.2

BACKGROUND CONCENTRATIONS

GENERAL

In aquatic environments, organotin concentrations were elevated in sediments, biota, and surface water microlayers collected near marinas, aquaculture rearing pens, and other facilities where organotin-based antifouling paints were used. In some cases, organotin concentrations in the water column were sufficiently high to pose a substantial risk to sensitive species. Data are now extremely limited on background concentrations of organotins in all environmental samples, especially in terrestrial ecosystems, and this may be attributed, in part, to limitations in routine chemical analytical capabilities.

NONBIOLOGICAL

Tin concentrations in water, air, soils, sediments, and other nonbiological materials are documented but information is scarce except for aquatic systems (Table 6). In aquatic systems, several trends were evident. First, tin and organotin compounds tend to concentrate in surface microlayers by factors up to 10,000X relative to subsurface water; in the case of organotins, this may be due to partitioning into the film of petroleum hydrocarbons commonly present on water surfaces (Maguire et al. 1982; Cleary and Stebbing 1987; Hall et al. 1987). Second, organotin concentrations, especially tributyltins, were highest in the vicinity of marinas and harbors, and this is consistent with its use as an antifouling agent in some paints for boats, ships, and docks (Chau et al. 1984; Maguire et al. 1986; Randall et al. 1986; Valkirs et al. 1986). Peak tributyltin concentrations occurred in late spring and early summer in association with postwinter launching of freshly painted boats (Hall et al. 1987). Third, organotin levels throughout the water column of marinas in numerous freshwater and marine locations were sufficiently elevated to cause chronic toxic effects in sensitive organisms including algae, copepods, oysters, mussel larvae, and fish (Maguire et al. 1982, 1986; Waldock and Thain 1983; Chau et al. 1984; Maguire and Tkacz 1985; Beaumont and Newman 1986; Cardwell and Sheldon 1986; Thain and Waldock 1986; Cleary and Stebbing 1987; Hall et al. 1987; Stromgren and Bongard 1987). Fourth, methyltin species were infrequently detected. Their occurrence was positively correlated with the presence of relatively high concentrations of inorganic tin and was due primarily to biotic and abiotic methylation of both organotin and inorganic tin compounds (Chau et al. 1984; Maguire et al. 1986). Finally, butyltin species were detected in harbor sediments at concentrations that were toxicologically hazardous to benthic fauna (Waldock and Thain 1983; Chau et al. 1984; Maguire et al. 1986). Tributyltin species can be accumulated from the sediments by oligochaetes (*Tubifex tubifex, Limnodrilus hoffmeisteri*), thus making it potentially available to bottom-feeding fish; oligochaetes can also degrade tributyltins by a sequential debutylation, with Tb1/2 estimates of 5 months in water and 4 months in water-sediment mixtures (Maguire and Tkacz 1985).

Table 6. Tin concentrations in nonbiological materials.

Sample (units), tin species, and other variables	Concentration[a]	Reference[b]
Saline waters (µg/L)		
Total tin		
Chesapeake Bay	Max. 0.46	1

San Diego Bay	Max. 0.07	1
Southwest UK, 1984	Max. 3.2	2
France, Arcachon Bay		
1982	5.05	3
1983	2.20	3
1985	1.00	3
Northeastern Mediterranean	Max. 0.32	4
Total organotin		
England		
Subsurface		
Southwest	Max. 0.29	1
Southeast	Max. 0.06	1
Surface microlayer		
Southwest	Max. 1.1	1
Southeast	Max. 0.06	1
France, Arcachon Bay		
1982	0.20	3
1983	<0.15	3
1985	<0.15	3
Inorganic tin		
San Diego Bay, California	Max. 0.009	5
Northeastern Mediterranean	Max. 0.24	6
Methyltin		
Western Florida	<0.009	7
Gulf of Mexico	<0.015	7
Dimethyltin		
Western Florida	<0.005	7
Gulf of Mexico	<0.007	7
Baltimore Harbor, Maryland	Max. 0.1	7
Trimethyltin		
Western Florida	<0.0005	7
Gulf of Mexico	<0.001	7
Baltimore Harbor, Maryland	Max. 0.02	7
Tetramethyltin		
Baltimore Harbor, Maryland	Max. 0.3	7
Butyltin		
Tejo estuary, Portugal	0.0011	7
Baltimore Harbor	Max. 0.3	7
San Diego Bay	Max. 0.05	5
Dibutyltin		
San Diego Bay	Max. 0.46	5
San Diego Bay	Max. 0.13	8
Chesapeake Bay, 1985–86		

Surface microlayer	Max. 1.16	8
Water column		
Marinas	(0.02–0.15)	8
Other locations	<0.04	8
Tributyltin		
Coastal waters, UK	Max. 0.43	7
Marinas, UK	Max. 2.3	7
San Diego Bay, California	Max. 0.93	5
Main channel	Max. 0.06	7
Boat basin	Max. 0.55	7
Surface microlayer	(0.06–0.25)	8
Water column	(0.01–0.18)	8
Chesapeake Bay, 1985–86		
Surface microlayer	Max. 1.2	8
Water column		
Marinas	(0.05–1.0)	8
Other locations	0.02	8
Southwest UK, 1984	Max. 0.88	2
Maryland		
Baltimore Harbor		
Surface microlayer	Max. 4.57	8
Annapolis, water column	0.07	8
Tetrabutyltin		
Chesapeake Bay	ND	8
Freshwater (µg/L)		
Total tin		
Drinking water	Usually <1.0, Max. 30.0	9
Great Lakes		
Subsurface	Max. 1.2	1
Surface microlayer	Max. 24.9	1
Inorganic tin		
Canadian marinas, 1982–84		
Lake St. Clair	6.7	10
Whitby	37.2	10
Port Hope	9.9	10
Methyltin		
Canada		
Marina	1.2	11
Harbors, lakes, rivers	(0.06–1.0)	7
USA rivers	<0.002	7
German rivers	<0.08	7
Florida lakes, ponds, rivers	<0.012	7
Dimethyltin		

Canadian marina	Max. 0.4	11
USA rivers	0.004	7
German rivers	Max. 0.26	7
Florida lakes, ponds, rivers	<0.008	7
Trimethyltin		
Canadian marina	Max. 0.05	11
Lake Superior	0.05	7
USA rivers	0.002	7
German rivers	0.002	7
Florida lakes, ponds, rivers	<0.008	7
Butyltin		
Canada		
Marinas		
Whitby	0.62	10
Port Hope	0.42	10
Lake St. Clair	8.5	11
Hamilton Harbor, Canada	0.02	7
Subsurface waters		
33 locations	detectable	12
188 locations	ND	12
Dibutyltin		
Canada		
Marinas		
Whitby	1.46	10
Port Hope	0.08	10
Lake St. Clair		
Subsurface	7.3	11
Surface microlayer	107.0	11
Harbor areas, lakes, rivers	(0.01–0.3)	7
Surface microlayer	(0.7–2,600)	7
Subsurface waters		
27 locations	detectable	12
194 locations	ND	12
Surface waters	(0.01–7.3)	8
Tributyltin		
Canada		
Marinas		
Lake St. Clair		
Subsurface	0.18	10
Surface microlayer	50.9	11
Whitby	4.2	10
Port Hope	5.7	10
Harbor areas, lakes, rivers	(0.01–1.0)	7

Surface microlayer	(0.2–60.0)	7
Subsurface waters		
1 location	2.34	12
7 locations	(0.4–1.8)	12
13 locations	(0.07–0.4)	12
22 locations	detectable	12
178 stations	ND	12
Surface waters	(0.01–2.9)	8
Air (µg/m^3)		
USA cities	Usually <0.01 (0.003–0.3); Max. 0.8 (Boston)	9
Japan		
Near furnaces	(10–640)	9
700 m distant	(3.8–4.4)	9
Soils (mg/kg)		
In mineral soils containing tin	>1,000	9
In unmineralized soils	(2.0–<200)	9
Sediments (mg/kg)		
Inorganic tin		
Toronto Harbor	Max. 0.62	13
Sault St. Marie	15.5	10
Lake Superior	0.7	10
Wabigoon River	(0.3–1.2)	10
Turkey	(0.5–1.1)	14
Northeast Mediterranean	Max. 2.3	6
Great Bay, New Hampshire	(0.40–0.63)	15
Methyltin		
Lake Superior	ND	10
Wabigoon River	0.1	10
Turkey	0.3	14
Northeast Mediterranean	Max. 0.01	6
Great Bay, New Hampshire	Max. 0.08	15
San Diego Bay	Max. 0.003	7
Chesapeake Bay	Max. 0.0008	7
Dimethyltin		
Turkey	Max. 0.01	14
Great Bay, New Hampshire	Max. 0.05	15
San Diego Bay	Max. 0.003	7
Trimethyltin		
Turkey	Max. 0.02	14
Great Bay, New Hampshire	ND	15
San Diego Bay	Max. 0.0002	7

Butyltin		
Toronto Harbor	Max. 0.08	13
Sault St. Marie	0.15	10
Wabigoon River	(0.04–0.11)	10
Great Bay, New Hampshire	(0.003–0.03)	15
Canada		
Marinas	0.02	7
Other locations	(0.014–0.58)	7
San Diego Bay	Max. 0.007	7
Mission Bay, California	Max. 0.011	7
Dibutyltin		
Toronto Harbor	Max. 0.26	13
Great Bay, New Hampshire	(0.001–0.015)	15
Canada		
Marinas	0.074	7
Harbors, lakes, rivers	(0.05–0.35)	7
Tributyltin		
Toronto Harbor	Max. 1.28	13
Great Bay, New Hampshire	(0.012–0.044)	15
Lake St. Clair, marina	0.125	7
Canadian harbors, lakes, and rivers	(0.11–0.54)	7
Minerals (mg/kg)		
Total tin		
Shale	4.1	16
Igneous rock	2.5	16
Oceanic clay	2.4	16
Oceanic carbonate	0.4	16
Sandstone	0.12	16

[a]Concentrations are expressed as mean, (minimum-maximum), maximum (Max.), and nondetectable (ND).

[b]References: 1, Cleary and Stebbing 1987; 2, Cleary and Stebbing 1985; 3, Alzieu et al. 1986; 4, Salihoglu et al. 1987; 5, Valkirs et al. 1986; 6, Yemenicioglu et al. 1987; 7, Hall and Pinkney 1985; 8, Hall et al. 1987; 9, WHO 1980; 10, Chau et al. 1984; 11, Maguire et al. 1982; 12, Maguire et al. 1986; 13, Maguire and Tkacz 1985; 14, Tugrul et al. 1983; 15, Randall et al. 1986; 16, Thompson et al. 1985.

BIOLOGICAL

Information on background concentrations of total tin in tissues of field populations of animals and plants was abundant, but few data were available on organotin species (Table 7).

Tin concentrations in marine algae and macrophytes varied between 0.5 and 101 mg total Sn/kg dry weight and clearly demonstrated that most species of aquatic flora bioconcentrate tin from seawater (Table 7). Marine plants are also important in the cycling of tin. Living algae are effective in immobilizing tin from seawater and regulating the formation and degradation of toxic methyltin compounds (Donard et al. 1987). Dead and decaying algae accumulate inorganic and organotin compounds, release them, and ultimately remove tin from the estuary to the atmosphere by formation of tetramethyltins (Donard et al. 1987).

Organotin content in fish tissues is quite variable, ranging from a low of 3% to 6% of the total tin body burden (Tugrul et al. 1983) to 18% for goatfish (*Upeneus moluccensis)* to 5% for *Mullus barbatus*, another species of goatfish (Salihoglu et al. 1987). By contrast, the limpet (*Patella caerulea*) contains 35% to 75% of its total tin body burden as organotin (Tugrul et al. 1983).

In January 1982, France banned organotin compounds for use in antifouling paints. By 1985, tin and organotin concentrations in seawater and Pacific oysters (*Crassostrea gigas*) were 5 to 10X lower than those found in 1982 (Alzieu et al. 1986). In Arcachon Bay, France, a decrease in the incidence and extent of anomalies in oyster calcification mechanisms was noted that seemed to be correlated with decreases in tin contamination (Alzieu et al. 1986). Crassostreid oysters can accumulate radiotin (Sn-113) to a higher degree than other species of bivalve molluscs, a characteristic that may be useful as a bioindicator in the event of contamination due to this isotope (Patel and Ganguly 1973).

Antifouling paints containing tributyltin compounds are used widely on netting panels of sea cages at fish and shellfish aquaculture units to minimize the obstruction of water exchange through the cages (Davies et al. 1987). Under these conditions, tributyltin paints were detrimental to the growth and survival of juvenile scallops and to calcium metabolism and growth of adult oysters (Paul and Davies 1986) and resulted in elevated concentrations of tributyltin in salmon tissues (Short and Thrower 1986; Davies and McKie 1987). Scallops (*Pecten maximus)* reared in sea pens for 31 weeks on nets coated with tributyltin oxide contained 2.5 mg total Sn/kg fresh weight soft parts (1.9 mg tributyltin/kg), but lost up to 40% during a 10-week depuration period. Scallop adductor muscle contained 0.53 mg tributyltin/kg, suggesting that this tissue--the one consumed by humans--is a probable tin storage site (Davies et al. 1986). Pacific oysters (*Crassostrea gigas*) reared for 31 weeks on tributyltin-exposed nets contained a maximum of 1.4 mg tributyltin/kg FW at week 16 (controls 0.12 mg/kg), but lost 90% during a 10-week depuration period (Davies et al. 1986). Atlantic salmon (*Salmo salar)* held for 3 months during summer in cages with tributyltin-treated net panels contained 0.75 to 1.5 mg tributyltin/kg fresh weight muscle vs. 0.28 mg/kg at start (Davies and McKie 1987). Based on laboratory studies, it is probable that Atlantic salmon were exposed to approximately 1.0 ug tributyltin/l during this interval (Davies and McKie 1987). Chinook salmon (*Oncorhynchus tshawytscha)*, reared in sea pens treated with tributyltin paints, contained <0.013 mg tributyltin/kg muscle fresh weight when introduced into the pens. Concentrations were 0.3 mg/kg after 3 months, 0.8 mg/kg at 13 months, and 0.9 mg/kg at 19 months. Cooking did not destroy or remove organotins from salmon muscle tissues (Short and Thrower 1986).

Table 7. Tin concentrations in field collections of living flora and fauna. Unless indicated otherwise, all values are in mg total Sn/kg fresh weight (FW) or dry weight (DW) tissue.

Taxonomic group, organism, and other variables	Concentration, in ppm[a]	Reference[b]
Algae and higher plants		
Algae, marine		
Whole, 10 species	(11–49) DW	1
Whole, 2 species	(96–101) DW	1
Swiss chard, whole,		
Beta vulgaris cicla		
Grown in soil at pH		
5.5	(12–51) DW	2
6.0	8 DW	2
6.5	<0.5 DW	2
Mangrove, *Bruguiera*		

caryophylloides, leaf		
Controls	1.3 DW	2
On Sn drainage	9.4 DW	2
Green alga, *Enteromorpha* spp.		
Inorganic tin	0.4 FW; 4.4 DW	3
Monomethyltins	0.5 FW	3
Dimethyltins	0.5 FW	3
Trimethyltins	<0.001 FW	3
Tetramethyltins	ND	3
Monbutyltins	0.006 FW; 0.4 DW	3
Tributyltins	0.05 FW; 0.6 DW	3
Seaweeds, whole, 5 species		
May	(0.5–1.8) DW	1
June	(0.5–2.2) DW	1
June	(0.1–0.5) FW	1
Wheat, *Triticum vulgare*		
Japan	0.5 FW	2
USA	(5.6–7.9) FW	2
Elm, *Ulmus americana*		
Wood, Vermont		
40 years old	1.7 FW; 1.8 DW	2
80 years old	1.4 FW; 1.5 DW	2
Vegetation		
Near tin smelter	(338–2,165) DW	2
Corn, *Zea mays*	0.1 FW	2
Invertebrates		
Pacific oyster, *Crassostrea gigas*		
Soft parts		
Arcachon Bay, France, July		
1982		
Total tin	Max. 7.0 DW	4
Organotin	Max. 1.6 DW	4
1983		
Total tin	Max. 4.0 DW	4
Organotin	Max. 0.8 DW	4
1985		
Total tin	Max. 0.9 DW	4
Organotin	Max. 0.4 DW	4
Soft parts		
Controls	0.1 FW	5
Reared in sea cages painted with tributyltin for 16 weeks		

Total tin	1.4 FW	5
Tributyltin	0.9 FW	5
American oyster, *Crassostrea virginica*		
Shell	<0.1 DW	2
Soft parts	1.4 FW	2
Crustaceans, marine		
Edible tissues		
5 species	(0.6–0.7) FW	6
8 species	(0.7–0.9) FW	6
3 species	(0.9–2.0) FW	6
American lobster, *Homarus americanus*		
Muscle	0.6 FW	2
Molluscs, marine		
Edible tissues		
3 species	(0.3–0.5) FW	6
7 species	(0.5–0.7) FW	6
4 species	(0.7–0.9) FW	6
4 species	(0.9–2.0) FW	6
Mussel, *Mytilus edulis*		
Soft parts	(1.3–7.1) DW	7
Hepatopancreas		
San Diego harbor	(1.9–3.5) DW	8
Offshore	(<0.7–2.0) DW	8
Common dogwhelk, *Nucellus lapillus*		
Soft parts, uncontaminated		
Total tin	Max. 0.3 FW	9
Total tin	(0.1–0.2) DW	10
Tributyltin	(0.1–0.2) DW	10
Dibutyltin	(0.01–0.05) DW	10
European oyster, *Ostrea edulis*		
Uncontaminated area		
All tissues	<0.1 FW	11
River Crouch, UK		
Flesh	(0.27–0.33) FW	11
Eggs	0.33 FW	11
Larvae	0.30 FW	11
Limpet, *Patella caerulea*		
N.E. Mediterranean, 1980		
Shell		
Total tin	0.013 DW	12
Methyltin	0.0004 DW	12

Dimethyltin	0.0002 DW	12
Trimethyltin	0.0009 DW	12
Soft parts		
Total tin	0.075 DW	12
Methyltin	0.001 DW	12
Dimethyltin	0.009 DW	12
Trimethyltin	0.026 DW	12
Scallop, *Pecten maximus*		
Reared in sea pens with tributyltin-coated netting for 3 weeks		
Total tin		
Gonad	0.6 FW	5
Adductor muscle	0.6 FW	5
Gills	0.6 FW	5
Digestive gland	1.0 FW	5
Tributyltin		
Gonad	0.4 FW	5
Digestive gland	0.5 FW	5
Adductor muscle	0.5 FW	5
Gills	0.6 FW	5
Fish		
Pacific herring, *Clupea harengus pallasi*		
Whole, Vancouver, Canada 1984		
Inorganic tin	0.04 FW	13
Butyltin	0.06 FW	13
Dibutyltin	0.05 FW	13
Tributyltin	0.24 FW	13
Lake whitefish, *Coregonus clupeaformis*, muscle	(0.8–3.6) FW	2
Northern pike, *Esox lucius,* muscle		
Manitoba, Canada	(0.7–5.4) FW	2
Lake Erie	0.5 FW	
Fish, marine		
Liver		
27 species	(<0.1–0.4) FW	6
45 species	(0.4–0.8) FW	6
10 species	(0.8–2.0) FW	6
Muscle		
8 species	(0.2–0.4) FW	6
110 species	(0.4–0.6) FW	6
34 species	(0.6–0.8) FW	6
7 species	(0.8–2.0) FW	6
Whole		

2 species	(0.3–0.6) FW	6
12 species	(0.8–2.0) FW	6
3 species	(2.0–9.0) FW	6
Atlantic cod,		
Gadus morhua, muscle	(0.5–3.7) FW	2
Atlantic halibut,		
Hippoglossus hippoglossus, muscle	1.2 FW	2
Rainbow smelt,		
Osmerus mordax, muscle	1.2 FW	2
Yellow perch, *Perca flavescens,* muscle	0.6 FW	2
Winter flounder,		
Pseudopleuronectes americanus, muscle	3.2 FW	2
Atlantic salmon, *Salmo salar*		
Muscle	0.07 FW	14
Gonad	0.15 FW	14
Gill	0.03 FW	14
Kidney	0.06 FW	14
Liver	0.04 FW	14
Lake trout, *Salvelinus namaycush*		
Whole, Canada, 1982–84		
Methyltin	(0.2–0.9) FW	15
Dimethyltin	(ND–0.2) FW	15
Trimethyltin	ND	15
Inorganic tin	(0.2–0.3) FW	15
Inorganic tin	Max. 0.9 FW	13
Spiny dogfish, *Squalus acanthias*		
Muscle	2.0 DW	2
Birds		
Ruffed grouse,		
Bonasa umbellus, liver	0.5 FW	2
Chicken, *Gallus gallus*		
Muscle	1.7 FW	2
Egg	0.9 FW	2
Mammals		
Cow, *Bos bovis*		
Muscle	Max. 2.8 FW	2
MilkMax. 0.9 FW	2	
Beaver, *Castor canadensis,* heart	7.3 FW	2
Woodchuck, *Marmota monax*, liver	1.8 FW	2
White-tailed deer,		
Odocoileus virginianus		
Liver	0.8 FW	2
Kidney	Max. 2.2 FW	2

Heart	ND	2
Muskrat, *Ondatra zibethicus,* liver	0.3 FW	2
Sheep, *Ovis aries*		
Liver	0.3 FW	2
Muscle	1.4 FW	2
Harbor seal, *Phoca vitulina*		
All tissues	<0.1 FW	2
Fox, *Vulpes* sp., liver	3.5 FW	2

[a]Concentrations are expressed as mean, (minimum-maximum), maximum (Max.), and nondetectable (ND).

[b]References: 1, Eisler 1981; 2, Jenkins 1980; 3, Donard et al. 1987; 4, Alzieu et al. 1986; 5, Davies et al. 1986; 6, Hall et al. 1978; 7, Karbe et al. 1977; 8, Young et al. 1979; 9, Davies et al. 1987; 10, Bryan et al. 1986; 11, Thain and Waldock 1986; 12, Tugrul et al. 1983; 13, Maguire et al. 1986; 14, Davies and McKie 1987; 15, Chau et al. 1984.

LETHAL AND SUBLETHAL EFFECTS

GENERAL

Inorganic tin compounds are of low toxicologic risk due largely to their low solubility, poor absorption, low accumulations in tissues, and rapid excretion. By contrast, some organotin compounds--especially trialkyltins--produce a variety of harmful effects resulting in impaired behavior and lowered growth, survival, and reproduction. Among aquatic organisms, tributyltin compounds were especially potent. Adverse effects were noted in molluscs at water concentrations of 0.001 to 0.06 ug/l and in algae, fish, and other species of invertebrates at 0.1 to 1.0 ug/l. Bioconcentration of organotins was high, but degradation was sufficiently rapid to preclude food chain biomagnification. Birds seem to be relatively resistant to organotins, although data are extremely scarce. Preliminary data suggest that diets containing 50 mg of tin as trimethyltin chloride/kg are fatal to all mallard ducklings in 75 days; however, no deaths occurred in 75 days at 50 mg/kg of eleven other mono-, di-, tri-, and tetraalkyltin compounds. Trimethyltin was lethal to other species of birds tested at doses of 1 to 3 mg/kg body weight. Trimethyltins and triethyltins were the most toxic organotin compounds tested on small laboratory mammals. Neurotoxicological effects of trimethyltins were usually not reversible, while those caused by triethyltins were reversible after exposure. Adverse effects of trimethyltins were produced at concentrations as low as 0.15 mg/l in drinking water (learning deficits), 0.625 mg/kg BW (diet aversion), and 1.25 mg/kg BW (death).

AQUATIC ORGANISMS

Results of acute toxicity tests with several organotin compounds and *Daphnia magna* indicated several distinct trends: toxicity increased with length of alkyl group from methyl to butyl; the anion substituents are relatively unimportant; and bioavailability is correlated with increasing solubility in lipids, which is a direct function of Kow, the n-octanol/water partition coefficient (Vighi and Calamari 1985). Structure-activity relations seem to have high predictive capacity in hazard assessment, and those for organotins seem particularly promising (Vighi and Calamari 1985). For example, studies on the biocidal properties of structurally distinct diorganotins (R_2SnX_2) and triorganotins (R_3SnX) to zoeae of a marine crab show, within a homologous series, that diorganotins are less toxic than the corresponding triorganotins (Table 8). It was concluded that the toxicity of organotins to crab zoeae seems to be a function of the hydrophobic characteristics conferred by the number and structure of the organic ligands (Laughlin et al. 1985).

Table 8. Toxicity of selected diorganotin and triorganotin compounds to zoeae of the marine mud crab (*Rithropanopeus harrisii*) exposed from hatching to age 14 days (modified from Laughlin et al. 1985).

Compound tested and formula	Lowest concentrations tested, in mg/L, producing Some deaths, but <50%		At least 50% mortality	
	Total product	Tin only	Total product	Tin only
Diorganotins				
Deimthyltin dichloride, $(CH_3)_2SnCl_2$	10.0	5.4	20.0	10.8
Diethyltin dichloride, $(C_2H_5)_2SnCl_2$	2.5	1.2	5.0	2.4
Dipropyltin dichloride, $(C_3H_7)_2SnCl_2$	2.5	1.1	5.0	2.2
Dibutyltin dichloride, $(C_4H_9)_2SnCl_2$	0.25	0.097	2.0	0.78
Dephenyltin dichloride, $(C_5H_{11})_2SnCl_2$	0.5	0.18	0.75	0.27
Dicyclohexyltin dichloride, $(C_6H_{13})_2SnCl_2$	0.125	0.041	0.25	0.082
Triorganotins				
Trimethyltin hydroxide, $(CH_3)_3SnOH$	0.075	0.05	0.1	0.067
Triethyltin hydroxide, $(C_2H_5)_3SnOH$	0.075	0.04	0.1	0.053
Tripropyltin oxide, $(C_3H_7)_3Sn)_2O$	0.025	0.015	0.05	0.03
Tributyltin oxide, $((C_4H_9)_3Sn)_2O$	0.01	0.005	0.02	0.011
Triphenyltin hydroxide, $(C_5H_{11})_3SnOH$	0.01	0.003	0.02	0.007
Tricyclohexyltin bromide, $(C_6H_{13})_3SnBr$	0.006	0.0016	0.009	0.0023

Signs of tributyltin poisoning in rainbow trout and other freshwater teleosts include sluggishness; loss of appetite; altered body pigmentation; air gulping; loss of positive rheotaxis; increased rate of opercular movements; damaged gills, cornea, and epithelial cells of bile duct; and increases in blood hemoglobin, erythrocyte number, and hematocrit (Chliamovitch and Kuhn 1977; Thompson et al. 1985). These changes were consistent with the known inhibitory effects on mitochondrial and oxidative phosphorylation of triorganotin compounds. Suppression of regeneration in echinoderms, and presumably other aquatic groups, may be due

primarily to neurotoxicological action of orginotins, or secondarily by direct action on tissue at the breakage point (Walsh et al. 1986b).

Studies on lethal and sublethal effects of tin compounds to representative species of aquatic organisms demonstrate that organotin compounds are more toxic than inorganic tin compounds; triorganotin compounds are more toxic than mono-, di-, or tetraorgano forms; and tributyltin compounds are the most toxic triorganotin compounds tested (Table 9). Adverse effects of tributyltins were noted at water concentrations of 0.001 to 0.06 ug/l in marine gastropod and bivalve molluscs and at 0.1 to 1 ug/l in algae, echinoderms, fish, crustaceans and coelenterates (Table 9). In order of toxicity, tributyltins were followed by tripropyltins (harmful effects recorded at 0.001 to 10 ug/l to gastropods, fish, and algae), triphenyltins (0.6 to 1 ug/l to diatoms and annelids), triethyltins (3.8 to 10 ug/l to fish and algae), trimethyltins (20 ug/l to algae and crustaceans), and tripentyltins (50 to 100 ug/l to gastropods). Because many organotin compounds are slow-acting poisons, short-term toxicity tests seriously underestimate the toxicity of these compounds (Laughlin and Linden 1985).

Biological factors known to modify lethal and sublethal effects of organotins include age of the organism, inherent interspecies resistance, and tissue specificity. Abiotic modifiers include exposure route, and physicochemical regimen. Early developmental stages were more sensitive to organotins than later developmental stages in marine annelids (Walsh et al. 1986a), mysid shrimp (Hall and Pinkney 1985), and rainbow trout (Thompson et al. 1985). Mortality of zoeae of fiddler crabs (*Uca pugilator*) to trimethyltins was greatest at elevated temperatures and low salinities (Thompson et al. 1985). Mussels exposed through a diet of algae showed slow accumulation of organotins when compared to exposure from the medium; the reverse was observed for crabs (Evans and Laughlin 1984; Hall and Pinkney 1985; Laughlin et al. 1986a). A marine diatom (*Thalassiosira pseudonana*) showed no adaptation or resistance to triphenyltins or tributyltins (Walsh et al. 1985), but another diatom (*Amphora coffeaeformis*) was extremely resistant (Thomas and Robinson 1986, 1987). Finally, mortality was substantially higher when organisms were exposed simultaneously to organotins through water and sediments; in the case of grass shrimp (*Palaemonetes pugio*), the addition of contaminated sediments increased mortality by up to 1,000X (Clark et al. 1987).

Table 9. Lethal and sublethal effects of inorganic and organic tin compounds in ambient medium to selected species of aquatic organisms.

Compound and organism	Concentration (µg/L)	Effect	Reference[a]
Inorganic tins			
Dab (fish), *Limanda limanda*	35	No deaths in 96 h	1
Marine diatoms, 2 species	316 to 325	50% growth inhibition in 72 h	2
Monmethyltins			
Marine diatom, *Skeletonema costatum*	78	50% growth inhibition in 72 h	2
Dimethyltins			
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
Trimethyltins			
Alga, *Scenedesmus quadricauda*	20	LC-87 (30 days)	3
Alga, *Chlorella vulgaris*	20	LC-100 (30 days)	3
Alga, *Asteromonas gracilis*	20	LC-100 (12 days)	3
Cladoceran, *Daphnia magna*	20	LC-61 (30 days)	3
Marine diatoms, 2 species	214	50% growth inhibition in 72 h	2
Tetramethyltins			
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
Diethyltins			

Snail, *Biomphalaria glabrata*	50 to 100	LC-50 (24 h)	4
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
Triethyltins			
Marine diatom, *Thalassiosira pseudonana*	3.8	LC-50 (72 h)	2
Sevyuga sturgeon, *Accipenser stellatus*, larvae	10	LC-100 (48 h)	3
Common carp, *Cyprinus carpio*	10	BCF's after 45 days ranged between 5x in muscle and 88x in blood	3
Marine diatom, *Skeletonema costatum*	40.2	LC-50 (72 h)	2
Tetraethyltins			
Marine diatoms, 2 species	127 to 142	50% growth inhibition in 72 h	2
Tripropyltins			
Snail, *Lymnaea stagnalis*	0.001 to 1.0	Fecundity reduced after exposure for 3 months	3
Sheep sturgeon, *Accipenser nudiventris*	0.001	Larvae die when exposed from fertilization	3
A. nudiventris	0.01	Prolarvae die when exposed continuously from fertilization	3
Loach (fish), *Misgurnis fossilis*, larvae	<1	Normal development	3
M. fossilis	10	No development	3
Algae, Lake Ontario	4	50% reduction in primary productivity in 4 h	3
Alga, *Ankistrodesmus falcatus*	14	50% growth reduction in 8 days	3
Snail, *B. glabrata*	40 to 280	LC-50 (24 h)	4
Monobutyltins			
Golden orfe (fish), *Leuciscus idus melanotus*	>45,000	LC-50 (48 h)	5
Dibutyltins			
Duck mussel, *Anodonta anatina*	15	After 7 months, tin localized exclusively in epithelial cells of kidney, accompanied by significant decrease in cellular glycogen content	6, 29
Marine diatom, *S. costatum*	35 to 56	50% growth inhibition in 72 h	2
Golden orfe	1,000	LC-50 (48 h)	5
Tributyltins			
Dogwhelk, *Nucella lapillus*	0.001 to 13%	Development of male 0.02 characteristics in	

		of female snails after 31 days, 27% in 91 days and 41% in 120 days. Whole body BCF values about 19,000x in 31 days, 36,000x in 91 days,78,000x in 120 days	7
Snail, *B. glabrata*	0.001	Reduction in egg deposition on continuous exposure from hatching	8
B. glabrata	0.1	Exposure for 34 days followed by 50-day recovery period produced 60% mortality, 80% reduction in egg deposition, and reduced growth	3
B. glabrata	0.4	LC-99 (30 days)	9
B. glabrata	1.0	50% reduction in egg laying after exposure for 2 to 3 weeks	3
B. glabrata	3	BCF of 48x in muscle after 120 h	3
B. glabrata	7	LC-100 (20 days)	9
B. glabrata	15	LC-100 (5 days)	9
B. glabrata	75	LC-100 (24 h)	4
Pacific oyster, *Crassostrea gigas*	0.01 to 0.02	Spat show reduced growth and hypoxia compensation after 2 weeks	10
C. gigas	0.15	Reduced growth and shell thickening after 8 weeks	11
C. gigas	0.2	BCF of ~ 6,000x in adult soft tissues in 21 days, 11,400x in whole spat in 56 days	3
C. gigas, larvae	1.0	LC-100 (12 days)	8
C. gigas, larvae	1.6	LC-100 (48 h)	12
C. gigas	1.6	No growth. BCF after 8 weeks varied from 2,300x to 3,100x	11
Copepod, *Eurytemora affinis*	0.0125	No adverse effects in 13 days	34
E. affinis	0.1	LC-74 (13 days)	34
E. affinis	0.5	Reduction in brood size in 48 h	34
E. affinis	0.6	LC-50 (72 h)	34
E. affinis	2.2	LC-50 (48 h)	34
Bay mussel, *Mytilus edulis*	0.05	Some larval deaths in 96 h	13
M. edulis, larvae	0.1	LC-50 (15 days)	14
M. edulis, larvae	0.24	Growth reduction after 45 days	12, 14
M. edulis	0.31	No shell growth in 66 days	14
M. edulis	0.4	Reduction in shell growth rate in 7days	15
M. edulis, adults	0.97	LC-50 (66 days)	14, 16
M. edulis, larvae	0.5	LC-100 (96 h)	13
European oyster, *Ostrea edulis*	0.06	Reduced growth rate in 10 days	14
O. edulis	0.24	No larval release after	

		exposure for 74 days; BCF of 875x	17
O. edulis	2.6	Reduced growth in 74 days; BCF of 397x	17
O. edulis, larvae	3.4	LC-50 (48 h)	17
Marine algae, 3 species	0.1	Reduced growth rate in 48 h	18
Brittle star, *Ophioderma brevispina*	0.1	Arm regeneration inhibited	19
Sheepshead minnow, *Cyprinodon variegatus*	0.18 to 1.0	Maximum BCF's after 167 days were 1,600x in muscle, 3,900x in viscera, 52,000x in liver; no adverse effects on growth or reproduction	20
C. variegatus	0.96	LC-50 (21 days)	8
C. variegatus	1.6	Maximum BCF's after 58 days were 1,810x in muscle, 2,120x in head, 4,580x in viscera, and 2,600x in whole fish. Loss after 28 days depuration ranged from 64% to 80%	20
C. variegatus	3.2	LC-100 (21 days)	20
C. variegatus	5 to 8	LC-50 (96 h)	3
C. variegatus	18	LC-50 (7 days)	8
Oysters, several species	0.2	LC-70 (113 days)	8
Rainbow trout, *Salmo gairdneri*	0.2 to 1.0	Exposure of yolk-sac fry for 110 days produced liver disfunction, reduced growth, and altered blood chemistry; no deaths	8, 21
S. gairdneri	5	Kidney degeneration in 12 days, some deaths	21
S. gairdneri	11. to 20	LC-50 (96 h)	5, 22
S. gairdneri	11.7	Bile duct pathology after 5 days; destruction of corneal epithelium after 7 days	3
S. gairdneri	21	LC-50 (48 h)	9
S. gairdneri	28	LC-50 (24 h)	23
Baltic amphipod, *Gammarus oceanicus,* larvae	0.3	Reduced survival after 5 weeks	24
G. oceanicus	3	LC-100 (16 days)	3
Alga, *Skeletonema costatum*	0.33 to 0.36	50% growth inhibition in 72 h	2
Copepod, *Acartia tonsa*	0.4	50% immobilization in 144 h	25
A. tonsa	0.55	LC-50 (6 days)	8
A. tonsa	1.0	LC-50 (96 h)	25
Fiddler crab, *Uca pugilator*	0.5	Limbs regenerated during	

		19 days showed a variety of deformities and retardation of regenerative growth	26, 35
U. pugilator	0.5 to 50	Non-dose dependent reduction in burrowing activity in 15 to 60 min; hyperactivity in 1 to 3 weeks	36
Mysid shrimp, *Metamysidopsis elongata,* juveniles	0.5 to 1.0	LC-50 (96 h)	3
American oyster, *Crassostrea virginica*	0.73 to 1.9	Reduced larval growth in 66 days	16
C. virginica, larvae	0.9	50% immobilization in 48 h	12
Hydroid, *Campanularia flexuosa*	1.0	100% growth inhibition in 11 days	3
Cladoceran, *D. magna*	1.0	Reduced survival and impaired reproduction in 15 days	14
D. magna	1.7	LC-50 (48 h)	12
D. magna	3	LC-50 (24 h)	23
American lobster, *Homarus americanus*	1.0	No effect on larval metamorphosis in 6 days	8
H. americanus, larvae	5	LC-100 (6 days)	25
H. americanus, larvae	20	LC-100 (24 h)	3
Shrimp, *Crangon crangon*, larvae	1.5	LC-50 (96 h)	12
C. crangon, adults	41	LC-50 (96 h)	12
Copepod, *Nitroca spinipes*	2	LC-50 (96 h)	25
Round Crucian carp, *Carassius carassius grandoculis*	2	BCF after 7 days of about 500x in vertebra, 630x in muscle, 3,160x in kidney, and 5,020x in liver	27
Sole, *Solea solea*, larvae	2	LC-50 (96 h)	3
Lugworm, *Arenicola cristata*	2	LC-0 (168 h)	28
A. cristata, larvae	4	LC-100 (96 h)	23
Algae, various species	3 to 16	50% reduction in primary productivity in 4 h to 8 days	3
Barnacle, *Balanus amphitrite*	4	LC-50 (24 h) nauplii	3
Freshwater clam, *Anodonta anatina*	5	LC-100 (6 weeks)	29
Mud snail, *Nassarius obsoletus*	5 to 6	Induced male characteristics in females in 64 days	3
N. obsoletus	8	LC-50 (61 days)	3
Tubifex worm, *Tubifex tubifex*	6	LC-50 (48 h)	9
Amphipod, *Orchestia traskiana*	6	LC-47 (9 days)	3
O. traskiana	10	LC-80 (9 days)	3
O. traskiana	15	LC-93 (9 days)	3
Mud crab, *Rithropanopeus harrisii*	6	BCFs after 4 days were 650x in muscle,	

		4,400x in hepatopancreas, and 1,300x in gill	37
R. harrisii	15	Weight loss after 15 days	3, 37
Bluegill, *Lepomis macrochirus*	7.6	LC-50 (96 h)	12
L. macrochirus	33	LC-50 (48 h)	8
Mysid shrimp, *Mysidopsis bahia*	8	LC-50 (96 h)	30
Mummichog (fish), *Fundulus heteroclitus*	9	Avoidance	3
F. heteroclitus	24	LC-50 (96 h)	12
Crab, *Carcinus maenus*	10	LC-50 (96 h)	3
Amphioxus, *Branchiostoma caribaeum*	10	LC-100 (96 h)	30
Snail, *Neritina* sp.	10	LC-100 (6 days)	3
Snails, *Biomphalaria* spp.	10 to 30	LC-50 (24 h)	8
Channel catfish, *Ictalurus punctatus*	12	LC-50 (96 h)	8
Marine diatom, *S. costatum*	14.7	LC-50 (72 h)	2
Snail, *Lymnaea* sp.	15	LC-100 (~5 days)	3
Atlantic menhaden, *Brevoortia tyrannus*	15	Avoidance by juveniles	3
Speckled sanddab, *Citharichthys stigmaeus*	20	LC-50 (96 h)	3
Grass shrimp, *Palaemonetes pugio*	20	LC-50 (96 h)	30
Green alga, *Ankistrodesmus falcatus*	20	BCF of ~ 30,000x at day 7	23
A. falcatus	40	BCF of 8,600x at day 7	23
Guppy, *Poecilia reticulata*	21 to 30	LC-50 (96 h)	8
P. reticulata	26 to 34	LC-50 (48 h)	5
Mozambique tilapia, *Tilapia mossambica*	28	LC-50 (24 h)	8
Duckweed, *Lemna media*	30	Reduced growth in 10 days	31
Snail, *Australorbis glabratus*	30	LC-100 (5 days)	31
European frog, *Rana temporaria*, tadpole	30	LC-50 (5 days)	32
R. temporaria, tadpole	75	LC-100 (24 h)	9
Harlequin fish, *Rasbora heteromorpha*	42	LC-50 (48 h)	8
Jewelfish, *Hemichromus bimaculatus*	45	LC-70 (48 h)	8
Fathead minnow, *Pimephales promelas*	45	LC-50 (96 h)	8
Golden orfe	50	LC-50 (48 h)	5
Cladoceran, *Daphnia longispina*	60	LC-100 (72 h)	31
Bleak (fish), *Alburnus alburnus*	70 to 400	LC-50 (96 h)	5
Goldfish, *Carassius auratus*	75	LC-100 (24 h)	31
Duckweed, *Lemna media*	500	LC-100 (10 days)	31
Tetrabutyltins			
Golden orfe	10,000	LC-50 (48 h)	5

Tripentyltins			
Snail, *B. glabrata*	50 to 100	LC-50 (24 h)	4
Triphenyltins			
Marine diatoms, 2 species	0.6 to 1.1	50% growth inhibition in 72 h	2
Lugworm, *A. cristata*	0.75–1.0	Abnormal larval development	28
A. cristata, larvae	1.5 to 2.5	LC-0 (168 h)	28
A. cristata, larvae	4 to 10	LC-100 (96 h)	23
Algae, various species	2 to 20	50% growth inhibition in 4 h to 8 days	3
Marine diatom, *S. costatum*	4.3 to 13.8	LC-50 (72 h)	2
Copepod, *Nitroca spinipes*	8	LC-50 (96 h)	3
Snail, *B. glabrata*	10 to 1,000	LC-50 (24 h)	4
Rainbow trout	15	LC-50 (96 h)	30
Snail, *Biomphalaria sudanica*	17	LC-50 (24 h)	3
Cladoceran, *D. magna*	20	LC-100 (30 days)	3
Cladoceran, *D. longispina*	50	LC-100 (48 h)	33
Snail, *Australorbis glabratus*	50	LC-100 (7 days)	33
A. glabratus	200	LC-100 (72 h)	33

[a]References: 1, Taylor et al. 1985; 2, Walsh et al. 1985; 3, Hall and Pinkney 1985; 4, Duncan 1980; 5, Blunden and Chapman 1986; 6, Herwig and Holwerda 1986; 7, Bryan et al. 1986; 8, Thompson et al. 1985; 9, Chliamovitch and Kuhn 1977; 10, Lawler and Aldrich 1987; 11, Waldock and Thain 1983; 12, Champ 1986; 13, Dixon and Prosser 1986; 14, Cardwell and Sheldon 1986; 15, Stromgren and Bongard 1987; 16, Valkirs et al. 1987; 17, Thain and Waldock 1986; 18, Beaumont and Newman 1986; 19, Walsh et al. 1986b; 20, Ward et al. 1981; 21, Seinen et al. 1981; 22, Douglas et al. 1986; 23, Maguire et al. 1984; 24, Laughlin et al. 1984; 25, U'ren 1983; 26 Weis et al. 1987; 27, Tsuda et al. 1986; 28, Walsh et al. 1986a; 29, Holwerda and Herwig 1986; 30, Clark et al. 1987; 31, Floch et al. 1964; 32, Laughlin and Linden 1982; 33, Floch and Deschiens 1962; 34, Hall et al. 1988; 35, Weis and Kim 1988; 36, Weis and Perlmutter 1987; 37, Evans and Laughlin 1984.

Aside from direct toxic effects that antifouling paint residues may have on marine life, there is no evidence of any risk from cytogenetic damage. Tributyltins, for example, were not genotoxic to larvae of the mussel (*Mytilus edulis*) based on results of sister chromatid exchange and analysis of chromosomal aberrations (Dixon and Prosser 1986). Teratogenic effects, however, were detected in larvae of the lugworm (*Arenicola cristata*) at sublethal concentrations of tributyltins (Walsh et al. 1986a), and algae (*Nitzschia liebethrutti*) exposed to 15 mg inorganic Sn/l for 14 days had frustule abnormalities (Saboski 1977).

Bioconcentration of inorganic and organic tin compounds from the medium is considerable. Bioconcentration factors (BCF's) for inorganic tin and marine algae were about 1,900X; moreover, tin-resistant bacteria contained a remarkable 3.7 to 7.7 grams Sn/kg dry weight (Maguire et al. 1984). BCF's for organotin compounds varied from about 400X to 30,000X among various species of molluscs, algae, and crustaceans and were highest when ambient tin concentrations were <1.0 ug/l, when exposure times were comparatively lengthy, and when organism lipid content was elevated (Thompson et al. 1985;Champ 1986; Laughlin et al. 1986a; Thain and Waldock 1986). Sheepshead minnows (*Cyprinodon variegatus*) were unable to reach equilibrium with a medium containing 1.61 ug tributyltin/l after 58 days of exposure and maximum BCF values recorded were 2,600X in whole fish, 1,810X in muscle, 4,580X in viscera, and 2,120X in the remainder of the carcass; however, whole body loss was 52% after depuration for 7 days and 74% after 28 days (Ward et al. 1981). Sheepshead minnows were able to metabolize tributyltins into lower alkyl moieties, which were less toxic. Thus, even though significant bioconcentration occurred, the chronic toxicity of tributyltins to sheepshead minnow was not significantly greater than its acute toxicity (Ward et al. 1981).

Benthic fauna are probably capable of transferring organotins from sediments to bottom-feeding teleosts. For example, sediments spiked with 0.98 mg Sn/kg dry weight, as tributyltin, resulted in concentrations of 4.41 mg/kg whole body dry weight in oligochaete annelid worms after 22 weeks, up from 0.38 at the start (Maguire and Tkacz 1985).

Imposex--the superimposition of male characteristics onto a functionally normal female reproductive anatomy--is a phenomenon documented in populations of marine gastropod molluscs in the vicinity of yacht basins and marinas and is a sensitive indictor of tributyltin contamination. A female with imposex displays one or more male characteristics such as a penis, a vas deferens, or convolution of the normally straight gonadal oviduct. It is measured by frequency of occurrence in the adult females and by the intensity of expression of all male characteristics in bearer females. Imposex is prevalent in mud snails (*Nassarius obsoletus*) near estuarine marinas and has been induced experimentally in that species by exposure for 60 days to three tributyltin compounds at concentrations of 4.5 to 5.5 ug/l (Smith 1981a,b). Imposex has been documented extensively in declining populations of the common dogwhelk (*Nucella lapillus*), especially in southwestern England (Bryan et al. 1986, 1987; Gibbs and Bryan 1986; Davies et al. 1987; Gibbs et al. 1987). These authorities agree on six points: (1) dogwhelk populations near centers of boating and shipping activity show the highest degrees of imposex, coinciding with the introduction and increasing use of antifouling paints containing tributyltin compounds; (2) imposex is not correlated with tissue burdens of arsenic, cadmium, copper, lead, silver, or zinc, but is correlated with increasing concentrations of tributyltin and dibutyltin fractions; (3) transplantation of dogwhelks from a locality with little boating activity to a site near a heavily used marina causes a marked increase in the degree of imposex and in tissue accumulations of tributyltins; (4) imposex can be induced in female dogwhelks by exposure to 0.02 ug Sn/l leached from a tributyltin antifouling paint; after exposure for 120 days, 41% of the females had male characters and whole body residues of 1.65 mg Sn/kg dry weight soft parts (vs. 0.1 in controls), of which almost all was tributyltin (1.64 vs. 0.08 mg/kg in controls). Concentrations as low as 0.0015 ug tributyltin/l can initiate imposex in immature females; (5) declining dogwhelk populations studied were characterized by a moderate to high degree of imposex, relatively fewer functional females, few juveniles, and a general scarcity of laid egg capsules. Many females in late imposex contained aborted capsules as a result of oviduct blockage, resulting in sterility and premature death; and (6) there was no evidence that loss of tin leads to any remission of imposex; in fact, all evidence indicates that gross morphological changes that occur in late imposex are irreversible. It is clear that additional research is needed on the imposex phenomenon in molluscs and on its implications to vertebrates and other taxonomic groups.

BIRDS

Information is scarce on the effects of tin and organotin compounds on birds. However, limited data suggest that triorganotin compounds, especially trimethyltins--and to a lesser extent triethyltins--are the most toxic (Table 10).

Dr. W. James Fleming of the Patuxent Wildlife Research Center has recently concluded a 75-day feeding study with mallard ducklings (*Anas platyrhynchos*) and 12 organotin compounds. Preliminary results indicated that trimethyltin was the most toxic compound tested. A dietary level of 50 mg of Sn as trimethyltin chloride/kg food was fatal to all ducklings; 5 mg/kg killed 40%, but all survived at 0.5 mg/kg diet. Death was preceded by mild to severe tremors, progressing to ataxia and lethargy. Large neurons of the pons, medulla oblongata, gray matter of the spinal cord, and cells of the cerebral cortex exhibited degeneration and necrosis. All ducklings survived exposure to 50 mg/kg ration of tetraethyltin, tetrabutyltin, tetraphenyltin, triethyltin chloride, tripropyltin chloride, tributyltin chloride, tributyltin oxide, triphenyltin chloride, tricyclohexyltin chloride, dimethyltin chloride, and dibutyltin chloride (Fleming, personal communication). Sublethal effects were recorded at 50 mg triethyltin chloride/kg (low body weight, vacuolization of spinal cord and brain white matter), at 50 mg tributyltin chloride/kg (enlarged liver), and at 50 mg tetrabutyltin/kg (elevated kidney weight). Residue and other analyses are now in progress.

Table 10. Lethal and sublethal effects of selected organotin compounds to birds.

Compound and organism	Effect (reference)
Dialkyltins	
Japanese quail, *Coturnix japonica*	No measurable effect at dietary levels of 150 mg/kg for 2 weeks (Seinen et al. 1977b)
Trialkyltins	
Mallard, *Anas platyrhynchos*	Ducklings fed diets containing 50 mg trimethyltin chloride/kg died within 60 days (personal communication, Dr. W. James Fleming, Patuxent Wildlife Research Center)
Pigeon, *Columba* sp.	Trimethyltin injections (3 intra-muscular injections, 2 weeks apart) at 1.0 mg/kg body weight interfered with ability to perform motor tasks; no evidence of cumulative effects (Idemudia and McMillan 1986b)
Domestic chicken, *Gallus* sp.	Single oral dose of 3 mg trimethyltin/kg body weight produced tremors, convulsions, and death within 24 h (Stoner et al. 1955)
Pigeon	Triethyltin injections (4 intramuscular injections, 2 weeks apart) at 1.75 mg/kg body weight resulted in total suppression of pecking behavior for 3 h; recovery underway by 27 h post-injection (Idemudia and McMillan 1986a)
Domestic chicken	Single oral dose of 3 mg triethyltin sulfate/kg body weight resulted in immediate collapse, salivation, convulsions, and death in a few min; at 2 mg/kg, bird was unconscious for 1 to 1.5 h postadministration, with recovery beginning in 1 day (Stoner et al. 1955)
Domestic chicken	Feeding of 160 mg triethyltin hydroxide/kg diet for 15 weeks was not fatal, but caused muscular weakness and some diet avoidance (Stoner et al.1955)
Japanese quail	Acute oral LD-50 of tricyclohexyltin hydroxide varies between 255 and 390 mg/kg body weight; dietary levels of 20 mg/kg had no measurable effect on growth, survival, or reproduction (Zuckerman et al. 1978)
Domestic chicken	Acute oral LD-50 of 654 mg of tricyclohexyltin hydroxide (Smith 978a)
Tetraalkyltins	
Domestic chicken	Daily doses >0.0001 mg tetraethyltin/ kg body weight produced Adverse effects on blood chemistry and CNS (Duncan 1980)

MAMMALS

Inorganic tin compounds and some heterocyclic organic tin compounds are of low toxicologic risk to mammals (Table 11), due largely to their low solubility, poor absorption, low tissue accumulations, and rapid tissue excretion (Hiles 1974; Kimbrough 1976). Inorganic tin compounds accumulate mostly in liver and kidney, rarely in brain, in proportion to dose and regardless of the exposure route (Hassett et al. 1984). Noncyclic organotin compounds, by contrast, have produced adverse effects on the skin, eyes, gastrointestinal tract, liver, bile duct, kidney, hematopoietic system, central nervous system, reproduction, growth, and chromosomes of small laboratory animals (Table 11). Effects of diorganotin compounds can be distinguished from those of tri- and tetraorganotin compounds. The chief toxicological difference is that some trialkyltins have a specific effect on the central nervous system resulting in cerebral edema, whereas diorganotins do not produce this effect but are potent irritants that induce inflammatory reactions. The tetraorganotins resemble triorganotins, which are usually more toxic than either mono- and diorganotins (WHO 1980; Table 11).

Diorganotin compounds cause cerebral edema and inhibit mitochondrial respiration by preventing the oxidation of keto acids, presumably through inhibition of alpha-keto oxidase activity (Piver 1973; WHO 1980). Large interspecies variability exists in the capacity of diorganotins to induce lymphoid atrophy. For example, dioctyltins and dibutyltins were selectively cytotoxic to rat thymocytes after dietary exposures of 50 to 150 mg/kg diet for 2 weeks; in contrast, no lymphoid atrophy occurred in mice, guinea pig, or Japanese quail given similar dosages and exposures (Seinen et al. 1977a,b). Route of exposure can also modify effects of diorganotins. Oral exposure to dibutyltin compounds, for example, produces inflammatory changes in bile duct of rat and necrotic changes in liver of mice and rats; dermal exposure causes bile duct injury in rats and rabbits; and intravenous administration produces pulmonary edema in rats (WHO 1980). Intratesticular administration of high doses of some dibutyltins produced marked degeneration in rat testes within 7 days, including atrophy of seminiferous tubules and complete arrest of spermatogenesis; however, similar results have been reported for cadmium, zinc, and copper salts (Saxena et al. 1985).

Table 11. Effects of tin compounds on selected species of animals.

Tin compound, organism	Dose	Effect (reference)[a]
Inorganic tins		
Rat, *Rattus* sp.	6.7 mg/kg body weight (BW)	Single intraperitoneal (ip) injection caused deficits in auditory startle habituation tests (1)
Dog, *Canis familiaris*	54 mg/kg BW	LD-100, single oral dose (2)
Rat	20 to 30 mg/kg BW, or 1.0 g/kg diet	No observed effect level after 13 weeks (3)
Rat	188 mg/kg BW	LD-50, single oral dose of tin fluoride (4)
Rat	700 mg/kg BW	LD-50, single oral dose of tin chloride (4)
Rat	2,275 mg/kg BW	LD-50, single oral dose of Sn^{+2} (3)
Rat	10 g/kg diet	Normal growth after 4 weeks (3)
Rat	>10 g/kg BW	LD-50, single oral dose of SnO (4)
Mouse, *Mus* sp.	Radiotin-113	50% clearance after 29 days following ip injection (5)
Methyltins		
Rat	120 mg/L drinking water	Impaired learning of pups when dam consumed Sn-laced water throughout 21-day gestation (6)
Rat	575 to 1,370 mg/kg BW	LD-50, single oral dose (7, 8)

Rat	600 mg/L	LC-50, aerosol dose for 1 h (7)
Ethyltins		
Rat	200 mg/kg BW	LD-50, single oral dose (7)
Butyltins		
Mouse	1,400 to >6,000 mg/kg BW	LD-50, single oral dose (3)
Rat	2,220 to 2,300 mg/kg BW	LD-50, single oral dose (7)
Octyltins		
Rat	2,400 to 3,800 mg/kg BW	LD-50, single oral dose (7)
Mouse	4,600 mg/kg BW	LD-50, single oral dose (3)
Dimethyltins		
Rat	74 to 237 mg/kg BW	LD-50, single oral dose (7)
Rat	1,070 mg/L	LC-50, aerosol dose for 1 h (7)
Diethyltins		
Rat	40 to 100 mg/kg BW	LD-50, single oral dose (9)
Dibutyltins		
Rat	0.1 and 1.0 mg/kg BW	Kidney damage after 12-month dietary exposure (3)
Mouse	1 to 10 mg/L drinking water	Reduction in tumor growth rates (10)
Rat	2 mg/kg BW daily or 40 mg/kg diet	No observable effect level after 90 days (9)
Rat, mouse	10 mg/kg BW	Dermal application daily for 10 days causes severe effect on skin and bile duct (3)
Mouse	35 to 112 mg/kg BW	LD-50, single oral exposure (9)
Rat	80 mg/kg diet	Slight reduction in growth rate and food intake; mild anemia after 90 days (9)
Rat	100 to 520 mg/kg BW	LD-50, single oral dose (8)
Dioctyltins		
Rat	50 or 150 mg/kg diet	After 6 weeks altered immune function as evidenced by inhibition of T-lymphocyte activity (11)
Guinea pig, *Cavia* sp.; mouse	50 or 150 mg/kg diet	No evidence of altered immune function (11)
Rat	945 to 7,000 mg/kg BW	LD-50, single oral exposure (7, 8, 9)
Mouse	1,140 to 4,000 mg/kg BW	LD-50, single oral exposure (9)
Trimethyltins		
Rat	0.15 to 1.0 mg/L in drinking water	Dams consuming contaminated water throughout 21-day gestation pro-

		duced pups with decreased learning ability at age 11 days (6)
Rat	0.625 mg/kg BW	3 ip doses resulted in flavor aversion (12)
Cynomolgus monkey, *Macaca fascicularis*	0.75 mg/kg BW	Single intravenous (iv) injection produced reduced appetite 7 days postexposure (13)
Cynomolgus monkey	1.1 mg/kg BW	Single iv injection resulted in tremors, hyperactivity, ataxia, stupor, unconsciousness (13)
Cynomolgus monkey	1.25 mg/kg BW	Single iv injection is fatal within 4 days (13)
Cynomolgus monkey	1.5 mg/kg BW	Single iv injection is fatal within 2 days (13)
Cynomolgus monkey	3.0 mg/kg BW	Single iv injection is fatal within 24 h (13)
Hamster, *Cricetus* sp.	About 3.0 mg/kg BW	LD-100, single oral dose (14, 15)
Rat	3.0 mg/kg BW	Loss in body weight and disrupted diurnal pattern of drinking and in rearing young after single oral dose, 2-week observation period (16)
Mouse	3.0 mg/kg BW	Single ip dose produced hypoactivity and impaired motor activity (12)
Marmoset, *Callithrix jacchus*	About 3.0 mg/kg BW	LD-50, single oral dose (14, 15)
Gerbil, *Gerbillus* sp.	About 3.0 mg/kg BW	LD-50, single oral dose (14, 15)
Man, *Homo sapiens*	About 3.0 mg/kg BW	LD-50, single oral dose (14, 15)
Rat	<4 mg/kg BW	No effect following stomach gavage route of administration (1)
Rat	5 mg/kg BW	Single oral dose produces hyperactivity (12)
Rat	6 mg/kg BW	No significant effect on behavior (17)
Rat	7 mg/kg BW	Significantly altered behavior (17)
Rat	>8 mg/kg BW	Lethal within 4 days after stomach gavage (1)
Rat	9.1 to 30 mg/kg BW	LD-50, single oral dose (9, 18)
Rat	15 mg/kg diet	Neuronal degradation in 2 weeks (19)
Rat	16 mg/kg BW	LD-50, single ip dose (2)
Rat	30 mg/kg BW	LD-100, single oral dose (7)
Triethyltins		
Rat	0.25 mg/kg BW	Impaired response to pain after 14 subcutaneous (sc) injections (12)
Rat	0.38 mg/kg BW	Flavor aversion after 2 ip doses (12)
Rat	1.0 mg/kg BW	Reduced amplitude startle response after 3 oral doses (12)
Rat	1.5 mg/kg BW	Hypoactivity, single sc injection (12)
Mouse	2.0 mg/kg BW	Hypoactivity, 27 days after single ip injection (12)
Rat	4.0 to 9.0 mg/kg BW	LD-50, single oral dose (8)

Guinea pig	5 to 10 mg/kg BW	LD-50, single oral dose (9)
Rat	5 mg/L in drinking water for 15 days followed by 10 mg/L for 15 days	Brain edema (20)
Rat	10 mg/kg BW	LD-50, single ip dose (2)
Rat	10 mg/kg BW	LD-100, single oral dose (7)
Rabbit, *Lepus* sp.	10 mg/kg BW	LD-50, single ip dose (2)
Rabbit	10 mg/kg BW	LD-50, single oral dose (8)
Rabbit, rat, guinea pig	10 mg/kg BW	LD-100, single oral dose (21)
Rat	15 mg/kg diet	Cerebral edema in 2 weeks (19)
Rat	20 mg/kg diet	After 7 days, decreased food intake; after 3 to 4 weeks, hind limb weakness and some deaths; on return to normal diet, signs of poisoning gone in 7 days with normal weight in 4 weeks (21)
Rabbit	40 mg/kg diet	Muscular weakness after chronic exposure (21)
Tripropyltins		
Rat	44 to 120 mg/kg BW	LD-50, single oral dose (4, 8)
Tributyltins		
Rabbit	0.04 mg/kg BW	After 16 weeks, central nervous system dysfunction (20)
Guinea pig	0.2 mg/L air	Ocular and nasal irritation, asphyxic convulsions, death within 1 h (20)
Mouse	0.2 mg/kg BW	Reduces mammary tumor growth rate; adversely affects thymus gland growth (22)
Rat	0.36 to 0.95 mg/kg BW	Single dermal application causes skin irritation (3)
Rat	10 mg/kg BW	LD-50, single ip dose (2)
Rabbit	12 mg/kg BW	Daily doses for 6 months were not fatal; signs of intoxication disappeared within a few weeks after withdrawal (20)
Guinea pig	20 mg/kg BW	LD-50, single oral dose (9)
Rat	32 mg/kg diet	Impaired growth after 30 days (20)
Mouse	46 to 230 mg/kg BW	LD-50, single oral dose. LD-50 values were lowest for tributyltin acetate (46 mg/kg BW) followed by benzoate

		(108), chloride (117), laurate (180), and oleate (230) (9)
Rat	50 to 380 mg/kg BW	LD-50, single oral dose (7, 8, 9)
Rabbit	60 mg/kg BW	LD-50, single oral dose (9)
Rat	150 mg/kg diet	61% reduction in thymus weight after 2 weeks (19)
Rat	320 mg/kg diet	Some deaths in 30 days (20)
Triphenyltins		
Rat	0.6 mg/kg BW daily	After 6 weeks, diminished exploratory behavior in maze and significantly more errors in maze learning (23)
Guinea pig	3.7 mg/kg BW	LD-50, single ip dose (2)
Guinea pig	10 to 24 mg/kg BW	LD-50, single oral dose (2, 9)
Guinea pig	25 to 50 mg/kg diet	At 25 mg/kg, 83% dead in 77 days; at 50 mg/kg, all dead by day 29 (7)
Rat	25 to 300 mg/kg diet	No measurable effect at 25 mg/kg in 170 days; some lesions at 50 mg/kg in 105 days; impaired growth at 200 mg/kg in 70 days; weight loss and some deaths at 300 mg/kg in 117 days (7)
Rat	34 mg/kg BW	LD-50, single ip dose (23)
Mouse	81 to 245 mg/kg BW	LD-50, single oral dose (3)
Rat	118 to 268 mg/kg BW	LD-50, single oral dose (7, 8)
Trihexyltins		
Rat	1,000 mg/kg BW	LD-50, single oral dose (8)
Tricyclohexyltins		
Dogs, rats	6 to 12 mg/kg diet	Some weight loss in 2 years, but no other toxic effects (20)
Rat	13 mg/kg BW	LD-50, single ip dose (2)
Sheep, *Ovis* sp.	15 to 150 mg/kg BW	No observed effect at injected dose of 15 mg/kg BW; adverse effects at 25 to 50 mg/kg; death at 150 mg/kg (8)
Rat	25 mg/kg BW	Gastroenteritis after 19 days (3)
Rat	235 to 650 mg/kg BW	LD-50, single oral dose (20)
Rabbit	500 to 1,000 mg/kg BW	LD-50, single oral dose (7)
White-footed mice, *Peromyscus leucopus*	710 mg/kg BW	LD-50, single oral dose (3)
Guinea pig	780 mg/kg BW	LD-50, single oral dose (7)
Dogs, monkeys, cats (*Felis domesticus*)	>800 mg/kg BW	LD-50, single oral dose (8)
Mouse	1,070 mg/kg BW	LD-50, single oral dose (3)
Trioctyltins		
Rat	29,200 mg/kg BW	LD-50, single oral dose (7)

Tetramethyltins		
Rat	195 to 331 mg/kg BW	LD-50, single oral dose (7)
Tetraethyltins		
Rabbit	7 mg/kg BW	LD-50, single oral dose (8)
Rat	9 to 16 mg/kg BW	LD-50, single oral dose (8)
Mouse	40 mg/kg BW	LD-50, single oral dose (3)
Guinea pig	40 mg/kg BW	LD-50, single oral dose (3)
Tetrabutyltins		
Rat	6,000 mg/kg BW	LD-50, single oral dose (7)

[a]References: 1, Hassett et al. 1984; 2, Kimbrough 1976; 3, WHO 1980; 4, Blunden et al. 1985; 5, Brown et a. 1977; 6, Noland et al. 1982; 7, Smith et al. 1978a; 8, Zuckerman et al. 1978; 9, Piver 1973; 10, Cardarelli et al. 1984a; 11, Seinen et al. 1977a; 12, Reiter and Rupert 1984; 13, Reuhl et al. 1985; 14, Aldridge et al. 1981; 15, Brown et al. 1984; 16, Bushnell and Evans 1985; 17, McMillan and Wenger 1985; 18, Watanabe 1980; 19, Snoeij et al. 1985; 20, Duncan 1980; 21, Stoner et al. 1955; 22, Cardarelli et al. 1984b; 23, Lehotzky et al. 1982.

Trimethyltin, triethyltin, and tributyltin compounds are highly toxic to animals and man. Trimethyltin and triethyltin compounds are more toxic to mammals than are the higher triorganotin homologues, probably because of poorer absorption of higher trialkyltin compounds from the gastrointestinal tract (Kimbrough 1976; WHO 1980). Trimethyltin and triethyltin compounds are potent inhibitors of oxidative phosphorylation in the mitochondria for which these compounds have a high binding affinity (WHO 1980). Different triorganotin compounds cause different neuronal patterns of toxicity in adult animals (Reiter and Rupert 1984). Trimethyltins, for example, produce largely irreversible behavioral impairments, such as hyperactivity and impaired learning and performance, and these are consistent with reported neuronal cell death in limbic system structures. Triethyltins, with their direct effect on muscle--consistent with reports of myelin vacuolation and cerebral edema--produce largely reversible effects (Reiter and Ruppert 1984). Differences in chronic toxicity between triethyltins and trimethyltins have resulted in different strategies in assessment of hazard. Evaluations of triethyltin have focused on repeated testing throughout dosing, followed by a recovery period. But evaluations of trimethyltin-induced behavioral impairments have generally focused on testing weeks to months after exposure (Reiter and Rupert 1984).

Symptoms of trimethyltin intoxication in man include irritability, headache, depression, aggressiveness, disorientation, appetite loss, memory deficits, and decreased libido; changes were largely reversible following cessation of exposure (Reiter and Ruppert 1984; Reuhl et al. 1985). At high doses, trimethyltins cause death in primates and humans, preceded by seizures, anorexia, and emotional lability (Brown et al. 1984). Trimethyltin produced adverse effects in laboratory animals over an unusually narrow dose range, with differences of 10X or less between doses producing no observable effects and those producing 100% mortality in all species tested (McMillan and Wenger 1985). Trimethyltin effects in small laboratory animals are usually not reversible. Signs of trimethyltin poisoning include tremors, hyperexcitability, aggressive behavior, weight loss, neuronal destruction in hippocampus and other portions of the brain, seizures, learning and memory impairment, self-mutilation, altered sensitivity to stimuli, and disrupted patterns of drinking and eating (Aldridge et al. 1981; Brown et al. 1984; Hassett et al. 1984; Reiter and Ruppert 1984; Bushnell and Evans 1985; McMillan and Wenger 1985; Reuhl et al. 1985). Trimethyltin-induced behavioral disruptions usually peak 3 to 5 days after exposure, but effects persist for extended periods and seem to be irreversible (Reiter and Ruppert 1984; McMillan and Wenger 1985). Rats sometimes survive the trimethyltin behavior syndrome and appear outwardly normal, although later neuropathological examination shows extensive bilateral damage, including hippocampus shrinkage and cell loss (Aldridge et al. 1981).

Triethyltins were the most potent organotins tested on mammals, although other organotins produced similar signs of poisoning (Table 11). Mammals poisoned by triethyltin compounds showed muscle weakness within hours of dosing; after a short period of recovery, tremors developed, leading to convulsions and death 2 to 5 days after dosing. Although toxicity produced by triethyltins becomes more pronounced with continued exposure, reversal of behavioral deficits occurs within weeks after dosing is terminated (Reiter and Ruppert 1984). Initial reaction to triethyltin exposure in rats was fluid accumulation in white matter of the central nervous

system, which persisted for as long as the compound was administered; after administration the effects reversed (Piver 1973). There is general agreement that triethyltin-induced behavioral changes are accompanied by cerebral edema, neurodegenerative disorders, interference with oxidative phosphorylation, and disrupted metabolism of glucose and enzyme activity (Kimbrough 1976; Hassett et al. 1984; Reiter and Ruppert 1984; McMillan and Wenger 1985; Reuhl et al. 1985; Linee and Hennon 1986).

Triphenyltins are skin and eye irritants to rats and rabbits (WHO 1980). They do not accumulate in rats, dogs, and guinea pigs although some triphenyltin acetate was partly absorbed by cattle and sheep--with most excreted in 6 to 8 weeks (Duncan 1980). Thymus atrophy was associated with a lymphocyte depletion in the thymic cortex and is the predominant effect of the intermediate trialkyltins. Intermediate trialkyltin homologues caused a dose-related reduction of thymus weight in male rats after 2 weeks on diets containing 150 mg organotin/kg; decreases were 19% for triphenyltin, 47% for tripropyltin, and 61% for tributyltin (Snoeij et al. 1985). Tributyltins and other organotins induce chromosomal aberrations in mammals, although this was not observed in tests with aquatic invertebrates (Dixon and Prosser 1986).

Tetraorganotin compounds produce muscular weakness, paralysis, respiratory failure, tremors, and hyperexcitability as acute effects in mice and dogs; latent effects are similar to those seen in triorganotin poisoning (WHO 1980). Tetramethyltin, for example, produces the same toxic syndrome as trimethyltin in rats because it is rapidly dealkylated in vitro to the latter compound (Aldridge et al. 1981). Signs of triorganotin poisoning in rabbits were evident shortly after administration of tetraorganotin compounds, suggesting that triorganotins were soon distributed to the site of action in amounts sufficient to produce signs of poisoning (Arakawa et al. 1981). The dealkylation and distribution of tetraorganotins are related to alkyl chain length and to their accumulations in tissues, including brain. In 3-hour studies with rabbits, at intravenous dosage rates of 2 to 3 mg/kg BW, tetraethyltin was quickly distributed to liver, but tetrapropyltin and tetrabutyltin were slowly distributed (Arakawa et al. 1981). Tetraethyltin was more readily converted into the corresponding trialkyltin than was tetrapropyltin. About 20% of the tetraethyltin, 4% of the tetrapropyltin, and 1% of the tetrabutyltin were converted to their corresponding trialkyltins. Thus, the extent of formation of triorganotins decreased as the size and stability of the ligand increased. There was poor distribution of tetraorganotins to brain, but the amounts of triorganotin metabolites found in brain increased over time. Particularly, the transfer of triethyltin to the brain was significant and compatible with the appearance of signs of toxicity. It was concluded that the extent of the dealkylation and the toxicity of organotin compounds depends on the length of their alkyl group, which was associated with their rate of absorption and ultimate distribution (Arakawa et al. 1981).

Organotin compounds are not mutagenic, teratogenic, or carcinogenic, as judged by largely negative but incomplete evidence (Duncan 1980; WHO 1980; Cardarelli et al. 1984b). It has been suggested that some organotins retard the onset and growth of cancer in laboratory animals and that the anticarcinogenic action is mediated through the thymus gland (Cardarelli et al. 1984b). The absence of tin in tissues may also be associated with tumor development (Cardarelli et al. 1984)). In one study, mice with cancer-prone mammary glands and transplanted mammary tumors had significantly reduced tumor growth rates after oral dosing with tributyltin fluoride (Cardarelli et al. 1984b). In another study, tumor growth rates were significantly reduced in mice continuously exposed to various diorganotin compounds in drinking water at I and 10 mg/l (Cardarelli et al. 1984a). It is hypothesized that the unknown thymic organotins are antagonistic to cancers in mice and possibly man (Cardarelli et al. 1984a, b). Additional research on potential anticarcinogenic properties of organotins is clearly indicated.

TERRESTRIAL INVERTEBRATES

Resistance to organotin acaricides has been reported in several populations of spider mites. After cyhexatin and fenbutatin oxide were used for 10 to 17 years on pears and apples to control mites, populations of McDaniel spider mite (*Tetranychus mcdanieli*), two-spotted spider mite (*T. urticae*), and European red mite *Panonychus ulmi*) slowly began to develop strains that were resistant to these chemicals (Croft et al. 1987).

CURRENT RECOMMENDATIONS

Proposed organotin criteria for the protection of aquatic life, domestic animals, and human health, vary substantially (Table 12). The most stringent criteria now proposed are for triorganotins and aquatic life; these vary from 0.002 to 0.008 ug/l (Table 12). But even these comparatively low concentrations will not protect certain species of gastropod molluscs or larvae of the sheep sturgeon (*Accipenser nudiventris*) from tributyltin

impacts, as discussed earlier. No criteria are currently proposed for protection of mammals against trimethyltins and triethyltins, the most toxic organotins tested in this group. Trimethyltins, for example, produce nonreversible neurotoxicological effects to certain species of small laboratory animals at concentrations as low as 0.15 mg/l drinking water or 0.625 mg/kg BW and are fatal at 1.25 mg/kg BW.

Hazard evaluation posed by organotin compounds to natural resources is predicated partly on their chemical composition, partly on their concentration and persistence in abiotic materials and diet items, and partly on their availability from these materials to organisms. In each of these areas, key data are missing for promulgation of effective regulations. It seems that additional research is needed in eight areas to acquire these data: (1) the development of sensitive and rapid analytical schemes for the extraction and separation of inorganic tin and organic tin compounds and their chemical speciation products from water, sediments, and biological materials (WHO 1980; Reuhl and Cranmer 1984; Hall and Pinkney 1985; Laughlin and Linden 1985; Thompson et al. 1985; Blunden and Chapman 1986); (2) elucidation of mechanisms and modes of toxicity for organotin compounds, especially those involving sublethal chronic exposures and cellular and subcellular impacts (WHO 1980; Reuhl and Cranmer 1984; Hall and Pinkney 1985; Thompson et al. 1985; Vrijhof 1985); (3) acquisition of data on organotin toxicokinetics, including data on routes of exposure, uptake, retention, and translocation. Studies should emphasize whole organisms, to determine if food chain biomagnification is a potential problem; reproductive organs, in which organotin burdens may affect proliferation; and edible tissue , especially muscle and liver, which are selectively consumed by humans and various animal species (WHO 1980; Reuhl and Cranmer 1984; Wilkinson 1984; Hall and Pinkney 1985; Thompson et al. 1985); (4)determination of the persistence and mobility of organotin compounds-- especially in aquatic abiotic materials, such as sediments, sediment interstitial waters, suspended particulates, and the water column--and on the partitioning of these compounds between the surface microlayer and subsurface waters (Wilkinson 1984; Thompson et al. 1985); (5) determination of the extent of tin methylation and the biotransformation and pharmacodynamics of organotins (WHO 1980); (6) measurement of biological interaction effects of organotins with other toxic chemicals under stressful environmental conditions of temperature, oxygen, and other variables (Thompson et al. 1985); (7) development of quantitative structure activity relations for use in evaluating toxicity of organotin compounds (Hall and Pinkney 1985; Laughlin and Linden 1985; Laughlin et al. 1985; Laughlin 1987); and (8) initiation of long-term environmental monitoring studies in terrestrial and aquatic ecosystems to establish appropriate baseline concentrations and to separate these from contaminant effects (Kumpulainen and Koivistoinen 1977; WHO 1980; Hall and Pinkney 1985; Thompson et al. 1985).

Table 12. Proposed organotin criteria for protection of natural resources and human health.

Resource, organotin compound	Criterion or effective tin concentration	Reference[a]
Aquatic life		
Freshwater		
Triorganotins		
North Carolina	<0.008 µg/L	1
Triethyltins		
Max. permissible concentration	<100 µg/L	2
Tributyltins		
Acute value	<0.97 µg/L	3
Chronic value	<0.30 µg/L	3
Safe level	0.12 to <0.27 µg/L	2
Saltwater		
Triorganotins		
North Carolina	<0.002 µg/L	1, 4

Safe level, USA	<0.05 µg/L	5
Tributyltins		
4-day average	<0.017 µg/L (not to be exceeded more than once in 3 years)	6
Chronic value	<0.064 µg/L	3
Acute value	<0.22 µg/L	3
1-h average	<0.43 µg/L (not to be exceeded more than once in 3 years)	6
Safe level, UK	<0.02 µg/L	4
Water		
Dibutyltins		
Dibutyltin dichloride, USSR	<2,000 µg/L	7
Dibutyltin disulfide, USSR	<20,000 µg/L	7
Tributyltins		
USA, Canada	<0.2 µg/L	8
In schistosomiasis control	<0.1 µg/L	9
Tetraethyltin, USSR	<200 µg/L	7
Marine antifouling paints		
Organotins	<4 grams/L	4
Sediments		
Freshwater		
Tributyltins		
4-day average	<30 µg/kg	3
1-h average	<48 µg/kg	3
Saltwater		
Tributyltins		
4-day average	<7 µg/kg	3
1-h average	<1 µg/kg	3
No effect level on annelids, mysids, clams	<610 µg/kg	3
Domestic and laboratory animals		
Diet		
Dibutyltins		
Rat, age 3 months	<40 mg/kg diet	10
Rat, age 6 months	<20 mg/kg diet	10
Triphenyltins		
Guinea pig,		

daily intake	<0.1 mg/kg body weight (BW)	10
Tricyclohexyltins		
Rat, daily	<3 mg/kg BW	10
Dog, daily	<0.75 mg/kg BW	10
Intrarumenal dose		
Tricyclohexyltins		
Sheep, single dose	<15 mg/kg BW	10
Drinking water		
Tributyltins		
Rat	<0.007 µg/L	11
Human health		
Air		
Organotins	<100 µg/m^3	7, 12
Organotins, daily	<200 µg/kg BW	7
Triethyltins, occupational exposure	<100 µg/m^3	13
Tricyclohexyltins	<1,200 µg/m^3	7
Diet		
Total tin		
Daily intake	0.2 to 8.8 mg	7
Daily intake		
From fresh foods	1 to 4 mg	10
From water	<0.03 mg	10
Daily intake, adult	0.003 to <0.13 mg/kg BW	7
Daily intake, adult	0.2 to 17 mg/kg BW	10
Composition of diet		
Inorganic tin	~1 mg/kg	10
Organic tin	<2 mg/kg	10
Tricyclohexyltins		
Peaches	<4 mg/kg	8
Apples, pears	<2 mg/kg	7
Meat	<0.2 mg/kg	7
Milk	<0.05 mg/L	7
Total daily intake	<0.0075 mg/kg BW	7, 14

[a]References: 1, Anon. 1985; 2, Duncan 1980; 3, Cardwell and Sheldon 1986; 4, Side 1987; 5, USN 1984; 6, Hall et al. 1987; 7, Zuckerman et al. 1978; 8, Thompson et al. 1985; 9, Chliamovitch and Kuhn 1977; 10, WHO 1980; 11, Simmonds 1986; 12, Blunden and Chapman 1986; 13, Watanabe 1980; 14, CEC 1978.

Antifouling paints containing organotin compounds have been associated with a number of adverse effects to marine biota, including contamination of salmon farmed in sea cages with treated net panels (Side 1987) and reduced growth of oysters (Cleary and Stebbing 1985). The United States Navy, however, proposes to implement fleetwide use of organotin antifouling paints that contain tributyltin as a biocide. This procedure will

result in a 15% fuel consumption reduction, increase the interval between cleaning ship hulls from 2 years (with cuprous oxide-based antifouling paints) to about 7 years, and increase ship speed up to 40% as a direct result of reduced drag (USN 1984). Since naval vessels rarely remain moored for extended periods in coastal areas, hazard effects to the environment are minimal--despite the size of the vessel--when compared to boating practices at local marinas (USN 1984). Accordingly, civilian use of marine paints containing organotin compounds has been severely restricted in recent years. France banned tributyltin compounds in antifouling paints in January 1982 for use on vessels under 25 m (82 feet) length (Waldock and Thain 1983; Side 1987). The State of Virginia enacted legislation that prohibits the use of tributyltin paints on nonaluminum vessels under 25 m (Anon. 1987). Similar legislation is pending in at least 12 coastal and Great Lakes States (Anon. 1988). In April 1987, England banned the retail sale of antifouling paints containing organotin compounds at concentrations greater than 4 grams of total tin per liter (Side 1987).

Because of their hazards, use of the more toxic triorganotin biocides should be curtailed to prevent their entry into the environment (Piver 1973). Continued monitoring of tributyltin levels is highly recommended at present, especially in areas of extensive boating activity (Simmonds 1986).

LITERATURE CITED

Aldridge, W. N., A. W. Brown, B. Brierly, R. D. Verschoyle, and B. W. Street. 1981. Brain damage due to trimethyltin compounds. Lancet, Sept. 26, 1981: 692-693.

Alzieu, C., J. Sanjuan, J. P. Deltreil, and M. Borel. 1986. Tin contamination in Arachon Bay: effects on oyster shell anomalies. Mar. Pollut. Bull. 17:494-498.

Anon. 1985. US Takes action on triorganotins. Mar. Pollut. Bull. 16:379.

Anon. 1987. Legislators consider plan to ban TBT paints on small craft only. Ecology USA, July 20, 1937: 124.

Anon. 1988. New York, Connecticut act to restrict TBT-based paints. Ecology USA, June 6, 1988: 107.

Arakawa, Y., and O. Wada, 1984. Inhibition of neutrophil chemotaxis by organotin compounds. Biochem. Biophys. Res. Comm. 123:543-548.

Arakawa, Y., O. Wada, and T. H. Yu. 1981. Dealkylation and distribution of tin compounds. Toxicol. Appl. Pharmacol. 60:1-7.

Barker, W. H., Jr., and V. Runte. 1972. Tomato juice-associated gastroenteritis, Washington and Oregon, 1969. Am. J. Epidemiol. 96:219-226.

Barnes, J. M., and H. B. Stoner. 1959. The toxicology of tin compounds. Pharmacol. Rev. 11:211-231.

Beaumont, A. R., and P. B. Newman. 1986. Low levels of tributyltin reduce growth of marine micro-algae. liar. Pollut. Bull. 17:457-461.

Blunden, S. J., and A. H. Chapman. 1982. The environmental degradation of organotin compounds - a review. Environ. Technol. Lett. 3:267-272.

Blunden, S. J., and A. Chapman. 1986. Organotin compounds in the environment. Pages 111-159 *in* P. J. Craig (ed.). Organometallic compounds in the environment. Longman Group Ltd., London.

Blunden, S. J., P. A. Cusack, and R. Hill. 1985. The industrial uses of tin chemicals. Royal Society of Chemistry, London. 337 pp.

Blunden, S. J., L. A. Hobbs, and P. J. Smith. 1984. The environmental chemistry of organotin compounds. Pages 49-77 *in* H. M. J. Bowen (ed.). Environmental chemistry, Vol. 3. Royal Society of Chemistry. London.

Brown, A. W., R. D. Verschoyle, B W. Street, and W. N. Aldridge. 1984. The neurotoxicity of trimethyltin chloride in hamsters, gerbils and marmosets. J. Appl. Toxicol. 4:12-21.

Brown, R. A., C. M. Nazario, R. S. de Tirado, J. Castrillon, and E. T. Agard. 1977. A comparison of the half-life of inorganic and organic tin in the mouse. Environ. Res. 13:56-61.

Bryan, G. W., P. E. Gibbs, G. R. Burt, and L. G. Hummerstone. 1987. The effects of tributyltin (TBT) accumulation on adult dog-whelks, *Nucella lapillus*: long-term field and laboratory experiments. J. Mar. Biol. Assoc. U.K. 67:525-544.

Bryan, G. W., P. E. Gibbs, L. Ii. Hummerstone, and G. R. Burt. 1986. The decline of the gastropod *Nucella lapillus* around south-west England: evidence for the effect of tributyltin from antifouling paints. J. Mar. Biol. Assoc. U.K. 66:611-640

Bushnell, P. J., and H. L. Evans. 1985. Effects of trimethyltin on homecage behavior of rats. Toxicol. Appl. Pharmacol. 79:134-142.

Byrd, J. T., and M. O. Andreae. 1986a. Concentrations and fluxes of tin in aerosols and rain. Atmos. Environ. 20:931-939.

Byrd, J. T., and M. O. Andreae. 1986b. Geochemistry of tin in rivers and estuaries. Geochim. Cosmochim. Acta 50:835-845.

Cardarelli, N. F., B. M. Cardarelli, E. P. Libby, and E. Dobbins. 1984a. Organotin implications in anticarcinogenesis. Effects of several organotins on tumor growth rite in mice. Aust. J. Exp. Biol. Med. Sci. 62:209-214.

Cardarelli, N. F., B. M. Quitter, A. Allen, E. Dobbins, E. P. Libby, P. Hager, and L. R. Sherman. 1984b. Organotin implications in anticarcinogenesis. Background and thymus involvement. Aust. J. Exp. Biol. Med. Sci. 62:199-208.

Cardwell, R. D., and A. W. Sheldon 1986. A risk assessment concerning the fate and effects of tributyltins in the aquatic environment. Pages 1117-1129 in G. L. Maton (ed.). Proceedings Oceans 86 Conference, September 23-25, 1986, Washington, D.C. Volume 4. Organotin symposium. Avail. from Marine Technology Society, 2000 Florida Ave. N.W., Washington, D.C.

CEC. 1978. Organotin compounds. Pages 1-18 *in* Noxious effects of dangerous substances in the aquatic environment. Comm. European Commun., Environ. Consumer Serv., Rustenborgvej 7, 2800 Copenhagen, Denmark.

Champ, M. A. 1986. Organotin symposium: introduction and review. Pages 1093-1100 *in* G. L. Maton (ed). Proceedings Oceans 86 Conference, September 23-25, 1986, Washington, D.C. Volume 4. Organotin symposium. Avail. from Marine Technology Society, 2000 Florida Ave N.W., Washington, D.C.

Chang, L. W. 1986. Neuropathology of trimethyltin: a proposed pathogenic mechanism. Fundam. Appl. Toxicol. 6:217-232.

Chau, Y. K., R. J. Maguire, P. T. S. Wong, B. A. Glen, G. A. Bengert, and R. J. Tkacz. 1984. Occurrence of methyltin and butyltin species in environmental samples in Ontario. Natl. Water Res. Inst. Rep. 8401. 25 pp. Avail. from Dep. Environment, Canada Centre for Inland Waters Burlington, Ontario, Canada L7R 4A6.

Chliamovitch, Y. P., and C. Kuhn. 1977. Behavioural, haematological and histological studies on acute toxicity of bis(tri-n-butyltin)oxide on *Salmo gairdneri* Richardson and *Tilapia rendalli* Boulenger. J. Fish Biol. 10:575-585.

Clark, J. R., J. M. Patrick, Jr., J. C. Moore, and E. M. Lores. 1987. Waterborne and sediment-source toxicities of six organic chemicals to grass shrimp (*Palaemonetes pugio* and amphioxus (*Branchiostoma caribaeum*). Arch. Environ. Contam. Toxicol. 16:401-407.

Cleary, J. J., and A. R. D. Stebbing. 1985. Organotin and total tin in coastal waters of southwest England. Mar. Pollut. Bull. 16:350-355.

Cleary, J. J., and A. R. D. Stebbing. 1987. Organotin in the surface microlayer and subsurface waters of southwest England. Mar. Pollut. Bull. 18:238-246.

Costa, L. G. 1985. Inhibition of ˜ . aminobutyric acid uptake by organotin compounds in vitro. Toxicol. Appl. Pharmacol. 79:471-479.

Costa, L. G., and R. Sulaiman. 1986. Inhibition of protein synthesis by trimethyltin. Toxicol. Appl. Pharmacol. 86:189-196.

Croft, B. A., S. C. Hoyt, and P. H. Westigard. 1987. Spider mite management on pome fruits revisited: organotin and acaricide resistance management. J. Econ. Entomol. 80:304-311.

Davies, A. G., and P. J. Smith. 1982. Tin. Pages 519-627 *in* G. Wilkinson (ed.). Comprehensive organometallic chemistry. Pergamon Press, New York.

Davies, I. M., S. K. Bailey, and D. C. Moore. 1987. Tributyltin in Scottish sea lochs, as indicated by degree of imposex in the dogwhelk, *Nucella lapillus* (L.). Mar. Pollut. Bull. 18:404-407.

Davies, I. M., and J. C. McKie. 1987. Accumulation of total tin and tributyltin in muscle tissue of farmed Atlantic salmon. Mar. Pollut. Bull. 18:405-407.

Davies, I. M., J. C. McKie, and J, D. Paul. 1986. Accumulation of tin and tributyltin from anti-fouling paint by cultivated scallops (*Pecten maximum*) and Pacific oysters (*Crassostrea gigas*). Aquaculture 55:103-114.

Dixon, D. R., and H. Prosser. 1986. An investigation of the genotoxic effects of an organotin antifouling compound (bis (tributyltin) oxide) on the chromosomes of the edible mussel, *Mytilus edulis*. Aquat. Toxicol. 8:185-195.

Donard, O. F. X., F. T. Short, and J. H. Weber. 1987. Regulation of tin and methyltin compounds by the green alga *Enteromorpha* under simulated estuarine conditions. Can. J. Fish. Aquat. Sci. 44-140-145.

Douglas, M. T., D. 0. Chanter, I. B. Pell, and G. M. Burney. 1986. A proposal for the reduction of minimal numbers required for the acute toxicity to fish test (LC50 determination). Aquat. Toxicol. 8:243-249.

Duncan, J. 1980. The toxicology of molluscicides. The organotins. Pharmacol. Ther. 10:407-429.

Dwivedi, R. S., G. Kaur, R. C. Srivastava, and C. R. K. Murti. 1985a. Metabolic activity of lysosomes in tin-intoxicated regenerating rat liver. Toxicol. Lett. 28:133-138.

Dwivedi, R. S., G. Kaur, R. C. Srivastava, and T. N. Srivastava. 1985b. Acute effects of organotins on brain, liver and kidney in rats. Ind. Health 23:9-15. on the chromosomes of the edible mussel, Toxicol. 8:185-195.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Elferink, J. G. R., M. Deierkauf, and J. V. Steveninck. 1986. Toxicity of organotin compounds for polymorphonuclear leukocytes. The effect on phagocytosis and exocytosis. Biochem. Pharmacol. 35:3727-3732.

EPA. 1986. Initiation of a special review of certain pesticide products containing tributyltins used as antifoulants; availability of support document. Federal Register 51(5):778-779.

EPA. 1987. Tributyltin. Technical support document. Position document 2/3. Mimeo. 152 pp. Avail. from U.S. Environ. Protection Agency, Office of Pesticides Programs, Registration Division, Special Review Branch, 401 M Street S.W., Washington, D.C. 20460.

Evans, D. W., and R. B. Laughlin, Jr. 1984. Accumulation of bis(tributyltin) oxide by the mud crab, *Rithropanopeus harrisii*. Chemosphere 13:213-219.

Floch, H., and R. Deschiens. 1962. Etude comparee de l'action molluscicide du 5,2'-dichloro-4'-nitro-salicylanilide (Bayer 73) et de sels (acetate et chlorine) de triphenyl-etain. Bull. Soc. Pathol. Exot. 55:816-825.

Floch, H., R. Deschiens, and T. Floch. 1964. Sur les proprietes molluscicides de l'oxyde et de l'acetate de tributyl-etain (prophylaxie des bilharzioses). Bull. Soc. Pathol. Exot. 57:454-465.

Gibbs, P. E., and G. W. Bryan. 1986. Reproductive failure in populations of the dog-whelk, *Nucella lapillus*, caused by imposex induced from tributyltin from antifouling paints. J. Mar. Biol. Assoc. U.K. 66:767-777.

Gibbs, P. E., G. W. Bryan, P. L. Pascoe, and G. R. Burt. 1987. The use of the dog-whelk, *Nucella lapillus*, as an indicator of tributyltin (TBT) contamination. J. Mar. Biol. Assoc. U.K. 67:507-523.

Gray, B. H., C. L. Gaworski, J. Horton, C. D. Flemming, and L. H. Lee. 1985. Comparative dermal irritation by tributyltin and organotin-containing antifouling paints. J. Toxicol. Cutaneous Ocul. Toxicol. 4:105-116.

Guard, H. E., A. B. Cobet, and W. M. Coleman III. 1981. Methylation of trimethyltin by estuarine sediments. Science 213:770-771.

Hall, L. W., Jr., S. J. Bushong, W. S. Hall, and W. E. Johnson. 1988. Acute and chronic effects of tributyltin on a Chesapeake Bay copepod. Environ. Toxicol. Chem. 7:'I-46.

Hall, L. W., Jr., M. J. Lenkevich, W. S. Hall, A. E. Pinkney, and S. J. Bushong. 1987. Evaluation of butyltin compounds in Maryland waters of Chesapeake Bay. Mar. Pollut. Bull. 18:78-83.

Hall, L. W., Jr., and A. E. Pinkney. 1985. Acute and sublethal effects of organotin compounds on aquatic biota: an interpretative literature evaluation. CRC Crit. Rev. Toxicol. 14:159-209.

Hall, R. A., E. G. Zook, and G. M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resource. U.S. Dep. Commerce NOAA Tech. Rep. NMFS SSRF-721. 313 pp.

Hassett, J. M., D. L. Johnson, J. A. Myers, A. Al-Mudamgha, M. E. Melcer, C. L. Kutscher, and M. M. Sembrat. 1984. The exposure of rats to inorganic tin: behavioral and systemic effects of different levels and modes of exposure. Pages 487-496 *in* D. D. Hemphill (ed.). Trace substances in environmental health-XVIII-. Univ. Missouri, Columbia.

Herwig, H. J., and D. A. Holwerda. 1986. Cytochemical localization of tin in freshwater mussels exposed to di-n-butyltin dichloride. Aquat. Toxicol. 9:117-128.

Hiles, R. A. 1974. Absorption, distribution, and excretion of inorganic tin in rats. Toxicol. Appl. Pharmacol. 27:366-379.

Holwerda, D. A., and H. J. Herwig. 1986. Accumulation and metabolic effects of di-n-butyltin dichloride in the freshwater clam, *Anodonta anatina*. Bull. Environ. Contam. Toxicol. 36:756-762.

Hunter, R. C. 1976. Organotin compounds and their use for insect and mite control. Environ. Health Perspect. 14:47-50.

Idemudia, S. O., and D. E. McMillan. 1986a. Effects of chemicals on delayed matching behavior in pigeons. III. Effects of triethyltin. Neurotoxicol. 7:109-118.

Idemudia, S. O., and D. E. McMillan. 1986b. Effects of chemicals on delayed matching in pigeons. IV: Effects of trimethyltin. Neurotoxicol. 7:75-88.

Jenkins, D. W. 1980. Biological monitoring of toxic trace metals. Volume 2. Toxic trace metals in plants and animals of the world. Part III. U.S. Environ. Protection Agency Rep. 600/3-80-092:1130-1148.

Karbe, L., C. Schier, and H. O Siewers. 1977. Trace elements in mussels (*Mytilus edulis*) from coastal areas of the North Sea and the Baltic. Multielement analyses using instrumental neutron activation analysis. J. Radioanal. Chem. 37:927-9411.

Kimbrough, R. D. 1976. Toxicity and health effects of selected organotin compounds: a review. Environ. Health Perspect. 14:51-56.

Krigman, M. R., and A. P. Silverman 1984. General toxicology of tin and its organic compounds. Neurotoxicol. 5:129-139.

Kumpulainen, J., and P. Koivistoinen. 1977. Advances in tin compound analysis with special reference to organotin pesticide residues. Residue Rev. 66:1-18.

Laughlin, R., and 0. Linden. 1982. Sublethal responses of the tadpoles of the European frog *Rana temporaria* to two tributyltin compounds. Bull. Environ. Contam. Toxicol. 28:494-499.

Laughlin, R., K. Nordlund, and O. Linden. 1984. Long-term effects of tributyltin compounds on the Baltic amphipod, *Gammarus oceanicus*. Mar. Environ. Res. 12:243-271.

Laughlin, R. B., Jr. 1987. Quantitative structure-activity studies of di- and triorganotin compounds. Pages 198-206 *in* K. L. E. Kaiser (ed.). QSAR in environmental toxicology - II. D. Reidel Publ., Dordrecht, The Netherlands.

Laughlin, R. B., Jr., W. French, and H. E. Guard. 1986a. Accumulation of bis(tributyltin) oxide by the marine mussel *Mytilus edulis*. Environ. Sci. Technol. 20:884-890.

Laughlin, R. B., Jr., H. E. Guard, and W. M. Coleman III. 1986b. Tributyltin in seawater: speciation and octanol-water partition coefficient. Environ. Sci. Technol. 20:201-204.

Laughlin, R. B., Jr., R. B. Johannesen, W. French, H. Guard, and F. E. Brinckman. 1985. structure-activity relationships for organotin compounds. Environ. Toxicol. Chem. 4:343-351.

Laughlin, R. B., Jr., and 0. Linden. 1985. Fate and effects of organotin compounds. Ambio 14:88-94.

Lawler, I. F., and J. C. Aldrich. 1987. Sublethal effects of bis(tri-n- butyltin)oxide on *Crassostrea gigas* spat. Mar. Pollut. Bull. 18:274-278.

Lee, R. F. 1985. Metabolism of tributyltin oxide by crabs, oysters and fish. Mar. Environ. Res. 17:145-148.

Lehotzky, K., M. J. Szeberenyi, F. Horkay, and A. Kiss. 1982. The neurotoxicity of organotin: behavioural changes in rats. Acta Biol. Acad. Sci. Hung. 33:15-22.

Linee, P., and M. C. Hennon. 1986. L'oedeme cerebral induit par le chlorure de triethyletain chez le rat, application a 1'etude de substances anti-oedemateuses cerebrales. J. Pharmacol. (Paris) 17:364-368.

Maguire, R. J., Y. K. Chau, G. A. Bengert, and E.J. Hale. 1982. Occurrence of organotin compounds in Ontario Lakes and rivers. Environ. Sci. Technol. 16:698-702.

Maguire, R. J., and R. J. Tkacz. 1985. Degradation of the tri-n-butyltin species in water and sediment from Toronto Harbor. J. Agric. Food Chem. 33:947-953.

Maguire, R. J., R. J. Tkacz, Y. K. Chau, G. A. Bengert, and P. T. S. Wong. 1986. Occurrence of organotin compounds in water and sediment in Canada. Chemosphere 15:253-274.

Maguire, R. J., P. T. S. Wong, and J. S. Rhamey. 1984. Accumulation and metabolism of tri-n-butyltin cation by a green alga, *Ankistrodesmus falcatus*. Can. J. Fish. Aquat. Sci. 41:537-540.

Maton, G. L. (ed.). 1986. Proceedings Oceans 86 conference, September 23-25, 1986, Washington, D.C. Volume 4. Organotin symposium: 1062-1330. Avail. from Marine Technology Society, 2000 Florida Ave. N.W., Washington, D.C.

McMillan, D. E., and G. R. Wenger. 1985. Neurobehavioral toxicology of trialkyltins. Pharmacol. Rev,. 37:365-380.

Messiha, N. N., and N. E. Ikladious. 1986. Antifouling performance of some new organotin polymers in the Mediterranean and Red Sea. J. Controlled Release 3:235-242.

Neumann, P. E., and F. Taketa. 1987. Effects of triethyltin bromide on protein phosphorylation in subcellular fractions from rat and rabbit brain. Mol. Brain Res. 2:83-87.

Noland, E. A., D. H. Taylor, and R. J. Bull. 1982. Monomethyl- and trimethyltin compounds induce learning deficiencies in young rats. Neurobeh. Toxicol. Teratol. 4:539-544.

Patel, B., and A. K. Ganguly. 1973. Occurrence of Se 75 and Sn 113 in oysters. Health Phys. 24:559-562.

Paul, J. D., and I. M. Davies. 1986. Effects of copper- and tin-based anti-fouling compounds on the growth of scallops (*Pecten maximus*) and oysters (*Crassostrea gigas*). Aquaculture 54:191-203.

Piver, W. T. 1973. Organotin compounds: industrial applications and biological investigation. Environ. Health Perspect. 4:61-79.

Randall, L., J. S. Han, and J. H. Weber. 1986. Determination of inorganic tin, methyltin, and butyltin compounds in sediments. Environ. Technol. Lett. 7:571-576.

Reiter, L. W., and P. H. Ruppert. 1984. Behavioral toxicity of trialkyltin compounds: a review. Neurotoxicol. 5:177-186.

Reuhl, K. R., and J. M. Cranmer. 1984. Developmental neuropathology of organotin compounds. Neurotoxicol. 5:187-204.

Reuhl, K. R., S. G. Gilbert, B. A. Mackenzie, J. E. Mallett, and D. C. Rice. 1985. Acute trimethyltin intoxication in the monkey (*Macaca fascicularis)*. Toxicol. Appl. Pharmacol. 79:436-452.

Rosenberg, D. W., M. K. Sardana, and A. Kappas. 1985. Altered induction response of hepatic cytochrome P-450 to phenobarbitol, 3-methylcholanthrene, and . napthoflavone in organotin-treated animals. Biochem. Pharmacol. 34:997-1005.

Saboski, E. M. 1977. Effects of mercury and tin on frustular ultrastructure of the marine diatom, *Nitzschia liebethrutti*. Water Air Soil Pollut. 8:461-466.

Salihoglu, I., C. Saydam, and S. Yemenicioglu. 1987. Two toxicants, mercury and tin in the Gulf of Iskenderun. Chemosphere 16:445-453.

Saxena, A., J. K. Koacher, and J. P. Tandon. 1985. Testicular changes in rats after administration of organotin complex. J. Toxicol. Environ. Health 15:503-507.

Seinen, W., T. Helder, H. Vernij, P. Penninks, and P. Leeuwangh. 1981. Short term toxicity of tri-n-butyltinchloride in rainbow trout (*Salmo gairdneri* Richardson) yolk sac fry. Sci. Total Environ. 19:155-166.

Seinen, W., J. G. Vos, R. Van Krieken, A. Penninks, R. Brands, and H. Hooykaas. 1977a. Toxicity of organotin compounds. III. Suppression of thymus-dependent immunity in rats by di-n-butyltindichloride and di-n-octyltindichloride. Toxicol. Appl. Pharmacol. 42:213-224.

Seinen, W., J. G. Vos, I. Van Spanje, M. Snoek, R. Brands, and H. Hooykaas. 1977b. Toxicity of organotin compounds II. Comparative *in vivo* and *in vitro* studies with various organotin and organolead compounds in different animal species with special emphasis on lymphocyte cytotoxicity. Toxicol. Appl. Pharmacol. 42:197-212.

Seligman, P. F., A. 0. Valkirs, and R. F. Lee. 1986. Degradation of tributyltin in San Diego Bay, California, waters. Environ. Sci. Technol. 20:1229-1235.

Short, J. W., and F. P. Thrower. 1986. Accumulation of butyltins in muscle tissue of chinook salmon reared in sea pens treated with tri-n-butyltin. Mar. Pollut. Bull. 17:542-545.

Side, J. 1987. Organotins--not so good relations. Mar. Pollut. Bull. 18:205-206.

Simmonds, M. 1986. The case against tributyltin. Oryx 20:217-220.

Smith, B. S. 1981a. Male characteristics on female mud snails caused by antifouling bottom paints. J. Appl. Toxicol. 1:22-25.

Smith, B. S. 1981b. Tributyltin compounds induce male characteristics on female mud snails *Nassarius obsoletus* = *Ilyanassa obsoleta*. J. Appl. Toxicol. 1:141-144.

Smith, P. J. 1978a- Toxicological data on organotin compounds, I.T.R.I. Publ. 538. 20 pp. Avail. from International Tin Research Institute, Greenford, Middlesex, U.K.

Smith, P. J. 1978b. Structure/activity relationships for di- and triorganotin compounds. I.T.R.I. Rep. 569. 16 pp. Avail. from International Tin Research Institute, Greenford, Middlesex, U.K.

Snoeij, N. J., A.H. Penninks, and W. Seinen. 1987. Biological activity of organotin compounds-an overview. Environ. Res. 44:335-353.

Snoeij, N. J., A. A. J. Van Iersel, A. H. Penninks, and W. Seinen. 1985. Toxicity of triorganotin compounds: comparative *in vivo* studies with a series of trialkyltin compounds and triphenyltin chloride in male rats. Toxicol. Appl. Pharmacol. 81:2;4-286.

Soderquist, C. J., and D. G. Crosby. 1980. Degradation of triphenyltin hydroxide in water. J. Agric. Food Chem. 28:111-117.

Stebbing, A. R. D. 1985. Organotins and water quality - some lessons to be learned. Mar. Pollut. Bull. 16:383-390.

Stoner, H. B., J. M. Barnes, and J. I. Duff. 1955. Studies on the toxicity of alkyl tin compounds. Br. J. Pharmacol. 10:16-25.

Stromgren, T., and T. Bongard. 1987. The effect of tributyltin oxide on growth of *Mytilus edulis.* Mar. Pollut. Bull. 18:30-31.

Subramanian, R. V. 1984. Biologically active organotin polymers. Ann. N.Y. Acad. Sci. 446:134-148.

Sylph, A. 1986a. Bibliography on the effects of organotin compounds on aquatic organisms. Libr. Biblio. No. 11. Mimeo. 76 pp. Avail. from International Tin Research Institute, Kingston Lane, Uxbridge, Middlesex UB8 3PJ, England.

Sylph, A. 1986b. Bibliography on the neurotoxicology of tin and organotin compounds. Libr. Biblio. No. 12. Mimeo. 72 pp. Avail. from International Tin Research Institute, Kingston Lane, Uxbridge, Middlesex UB8 3PJ, England.

Taylor, D., B. G. Maddock, and G. Mance. 1985. The acute toxicity of nine 'grey list' metals (arsenic, boron, chromium, copper, lead, nickel, tin, vanadium and zinc) to two marine fish species: dab (*Limanda limanda*) and grey mullet (*Chelon labrosus*). Aquat. Toxicol . 7:1 5-144.

Thain, J. E., and M. J. Waldock. 1986. The impact of tributyl tin (TBT) antifouling paints on molluscan fisheries. Water Sci. Technol. 18:193-202.

Thomas, T. E., and M. G. Robinson. 1986. The physiological effects of the leachates from a self-polishing organotin antifouling paint on marine diatoms. Mar. Environ. Res. 18:215-229.

Thomas, T. E., and M. G. Robinson. 1987. Initial characterization of the mechanisms responsible for the tolerance of *Amphora coffeaeformis* to copper and tributyltin. Bot. Mar. 30:47-53.

Thompson, J. A. J., M. G. Sheffer, R. C. Pierce, Y. K. Chau, J. J. Cooney, W. R. Cullen, and R. J. Maguire. 1985. Organotin compounds in the aquatic environment: scientific criteria for assessing their effects on environmental quality. Natl. Res. Coun. Canada, Publ. NRCC 22494. 284 pp. Avail. from Publications, NRCC/CNRC, Ottawa, Canada KIA OR6.

Tsuda, T., H. Nakanishi, Aoki, and J. Takebayashi. 1986. Bioconcentration of butyltin compounds by round Crucian carp. Toxicol. Environ. Chem. 12:137-143.

Tugrul, S., T. I. Balkas, aid E. D. Goldberg. 1983. Methyltins in the marine environment. Mar. Pollut. Bull. 14:297-303.

U'ren, S. C. 1983. Acute toxicity of bis(tributyltin)oxide to a marine copepod. Mar. Pollut. Bull. 14:303-306.

USN. 1984. Environmental assessment of fleetwide use of organotin antifouling paint. U.S. Naval Sea Systems Command, Washington, D.C. 184 pp.

Valkirs, A. O., B. M. Davidson, and P. F. Seligman. 1987. Sublethal growth effects and mortality to marine bivalves from long-term exposure to tributyltin. Chemosphere 16:201-220.

Valkirs, A. O., P. F. Seligman, P. M. Stang, V. Homer, S. H. Lieberman, G. Vata, and C. A. Dooley. 1986. Measurement of butyltin compounds in San Diego Bay. Mar. Pollut. Bull. 17:319-324.

Vighi, M., and D. Calamari. 1985. QSARs for organotin compounds on *Daphnia magna*. Chemosphere 14:1925-1932.

Vrijhof, H. 1985. Organotin compounds and international treaties on the pollution of water by dangerous substances: black or grey list substances. Sci. Total Environ. 43:221-231.

Waldock, M. J., and J. E. Thain. 1983. Shell thickening in *Crassostrea gigas*: organotin antifouling or sediment induced? Mar. Pollut. Bull. 14:411-415.

Walsh, G. E., L. L. McLaughlin, E. M. Lores, M. K. Louie, and C. H. Deans. 1985. Effects of organotins on growth and survival of two marine diatoms, *Skeletonema costatum* and *Thalassiosira pseudonana*. Chemosphere 14:383-392.

Walsh, G. E., M. K. Louie, L. McLaughlin, and E. M. Lores. 1986a. Lugworm (*Arenicola cristata*) larvae in toxicity tests: survival and development when exposed to organotins. Environ. Toxicol. Chem. 5:749-754.

Walsh, G. E., L. L. McLaughlin, M K. Louie, C. H. Deans, and E. M. Lores. 1986b. Inhibition of arm regeneration by *Ophioderma brevispina* (Echinodermata, Ophiuroidea) by tributyl tin oxide and triphenyltin oxide. Ecotoxicol. Environ. Safety 12:95-100.

Ward, G. S., G. C. Cramm, P. R. Parrish, H. Trachman, and A. Slesinger. 1981. Bioaccumulation and chronic toxicity of bis(tributyltin)oxide (TBTO): tests with a salt water fish. Pages 183-200 *in* D. R. Branson and K. L. Dickson (eds.). Aquatic toxicology and hazard assessment: fourth conference. ASTM Spec. Tech. Publ. 737, American Society for Testing and Materials, Philadelphia, Pennsylvania.

Watanabe, I. 1980. Organotins (triethyltin). Pages 545-557 *in* P. S. Spencer and H. C. Schaumburg (eds.). Experimental and clinical neurotoxicology. Williams and Wilkins, Baltimore, Maryland.

Weis, J. S., J. Gottlieb, and J. Kwiatkowski. 1987. Tributyltin retards regeneration and produces deformities of limbs in the fiddler crab, *Uca pugilator*. Arch. Environ. Contam. Toxicol. 16:321-326.

Weis, J. S., and K. Kim. 1988. Tributyltin is a teratogen in producing deformities in limbs of the fiddler crab, *Uca pugilator*. Arch. Environ. Contam. Toxicol. 17:583-587.

Weis, J. S., and J. Perlmutter. 1987. Effects of tributyltin on activity and burrowing behavior of the fiddler crab, *Uca pugilator*. Estuaries 10:342-346.

WHO. 1980. Tin and organotin compounds: a preliminary review. Environ. Health Crit. 15. World Health Organization, Geneva, Switzerland. 109 pp.

Wilkinson, R. R. 1984. Technoeconomic and environmental assessment of industrial organotin compounds. Neurotoxicol. 5:141-158.

Yemenicioglu, S., C. Saydam, and I. Salihoglu. 1987. Distribution of tin in the northeastern Mediterranean. Chemosphere 16:429-443.

Young, D. R., G. V. Alexander, and D. McDermott-Ehrlich. 1979. Vessel-related contamination of southern California harbours by copper and other metals. Mar. Pollut. Bull. 10:50-56.

Zuckerman, J. J., R. P. Reisdorf, H. V. Ellis III, and R. R. Wilkinson. 1978. Organotins in biology and the environment. Pages 388-424 *in* F. E. Brinckman and J. M. Bellama (eds.). Organometals and organometalloids, occurrence and fate in the environment. Am. Chem. Soc. Symp. Ser. 82, Washington, D.C.

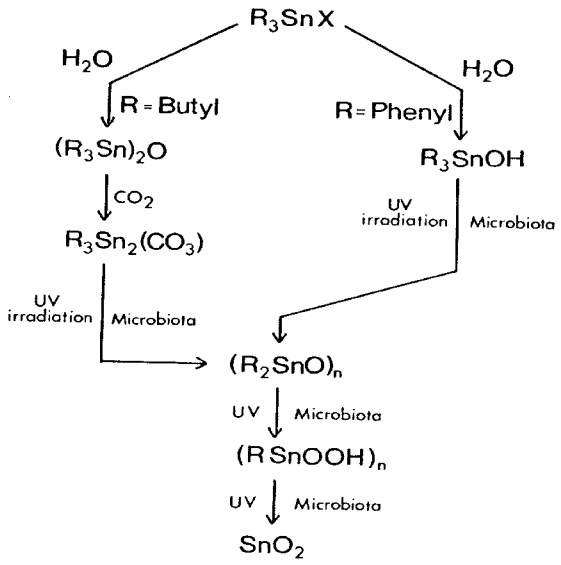


Figure 1. Environmental degradation scheme for tributyltin and triphenyltin compounds. Modified from Smith (1978b).

BIOLOGICAL REPORT 85(1.16)
FEBRUARY 1989

Contaminant Hazard Reviews
REPORT NO. 16

INDEX TO COMMON AND SCIENTIFIC NAMES OF SPECIES LISTED IN CONTAMINANT HAZARD REVIEWS 1 THROUGH 15

by
Ronald Eisler

and

Joyce Haber Corley

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

The Contaminant Hazard Review series emphasizes ecotoxicological aspects of selected chemical pollutants to fishery and wildlife resources, and includes reports on various agricultural pesticides (mirex, carbofuran, toxaphene, diazinon, chlorpyrifos), metals and metalloids (arsenic, cadmium, chromium, mercury, lead, selenium, tin), and organic industrial wastes (polycyclic aromatic hydrocarbons, dioxins, polychlorinated biphenyls). The present account is a cumulative index to the common and scientific names of all biological species listed in the first 15 reports in the Contaminant Hazard Review series, published as U.S. Fish and Wildlife Service Biological Reports 85(1.1) through 85(1.15), inclusive. Individual species were cross-referenced by contaminant and corresponding page numbers.

DISCLAIMER

Mention of trade names or commercial products does not constitute U.S. Government endorsement or recommendation for use.

Suggested citation for this report:

Eisler, R., and J. H. Corley. 1989. Index to common and scientific names of species listed in Contaminant Hazard Reviews 1 through 15. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.16).

ACKNOWLEDGMENTS

We thank Barbara A. Roberts and Julia L. Armstrong for secretarial assistance, Lynda J. Garrett for constructively reviewing the manuscript, and James R. Zuboy, Paul A. Opler, Paul H. Eschmeyer, and Nancy M. Wells for editorial services.

INTRODUCTION

A total of 15 Contaminant Hazard Reviews have been published since 1985 (Eisler 1985a,b,c,d; 1986a,b,c,d; 1987a,b; 1988a,b; 1989; Eisler and Jacknow 1985; Odenkirchen and Eisler 1988). These reviews briefly summarized ecological and toxicological aspects of various chemical pollutants, with particular emphasis on fishery and wildlife resources. Specifically, reviews were prepared on selected agricultural pesticides (mirex, carbofuran, diazinon, toxaphene, chlorpyrifos), metalloids (arsenic, selenium), metals (cadmium, lead, chromium, mercury, tin), and organic industrial wastes (polychlorinated biphenyls, dioxins, polycyclic aromatic hydrocarbons).

We present herein an index to the common and scientific names of all species listed in Contaminant Hazard Reviews 1 to 15. This report was prepared in response to a request from environmental specialists of the U.S. Fish and Wildlife Service. Taxonomic nomenclatures for plants, invertebrates, and vertebrates are under constant revision. Accordingly, we elected to conform as much as possible to the systems and spellings used by Swain and Swain (1948) for insects, Edwards (1974) for birds, American Fisheries Society (1980) for fishes, Johnson and Finley (1980) and Jenkins (1980) for invertebrates, Jenkins (1980) and Scott and Wasser (1980) for plants, and Nowak and Paradiso (1983) for mammals.

In this report, individual species are arranged alphabetically in the Index by scientific and common name. The scientific name is followed by an underlined number that refers to one of the Contaminant Hazard Reviews in the following list, and to the page numbers within the report.

1=Mirex (Eisler 1985a)
2=Cadmium (Eisler 1985b)
3=Carbofuran (Eisler 1985c)
4=Toxaphene (Eisler and Jacknow 1985)
5=Selenium (Eisler 1985d)
6=Chromium (Eisler 1986a)
7=Polychlorinated biphenyls (Eisler 1986b)
8=Dioxins (Eisler 1986c)
9=Diazinon (Eisler 1986d)
10=Mercury (Eisler 1987a)
11=Polycyclic aromatic hydrocarbons (Eisler 1987b)
12=Arsenic (Eisler 1988a)
13=Chlorpyrifos Odenkirchen and Eisler 1988)
14=Lead (Eisler 1988b)
15=Tin (Eisler 1989)

INDEX

NOTE: ISSUE AND PAGE NUMBERS HAVE BEEN DELIBERATELY OMITTED FROM THIS VERSION BECAUSE PAGE NUMBERS DO NOT CORRESPOND TO THOSE IN THE ORIGINAL ISSUES, AND BECAUSE INFORMATION ON INDIVIDUAL SPECIES CAN BE RETRIEVED BY ELECTRONIC SEARCH WITHIN EACH DOCUMENT.

Nitzschia, Nostoc, Oedogonium, Olisthodiscus, Platymonas, Scenedesmus, Scripsiella, Selenastrum, Skeletonema, Tetraedron, Tetraselmis, Thalassiosira, Ulva

Alligator, Alligator mississippiensis

Alligator mississipspiensis:

Allium porrum:

Allium sp.:

Allolobophophora caliginosa:

Alosa pseudoharengus:

Ambloplites rupestris:

Ambystoma opacum:

Ambystoma tigrinum:

Amnicola sp.:

Ampelisca abdita:

Amphioxus, Branchiostoma caribaeum

Amphipods, Ampelisca, Corophium, Elasmopus, Gammarus, Hyalella, Orchestia, Pontoporeia

Amphora coffeaeformis:

Anabaena variabilis:

Anabas testudineus:

Anacystis nidulans:

Anarhichas minor:

Anas acuta:

Anas americana:

Anas carolinensis:

Anas clypeata:

Anas discors:

Anas fulvigula:

Anas platyrhynchos:

Anas rubripes:

Anas spp.:

Anas strepera:

Anchovy, Engraulidae

Andropogon scoparius:

Anguilla anguilla:

Anguilla rostrata:

Anguilla sp.:

Anguilla vulgaris:

Anhinga, Anhinga anhinga

Anhinga anhinga:

Ankistrodesmus falcatus:

Ankistrodesmus sp.:

Annelids, Nereis, Tubifex

Anodonta anatina:

Anser anser:

Anser spp.:

Aster, Aster, Astragalus
Aster spp.:
Aster, tansy, Machaeranthera spp.
Asterias forbesi:
Asterionella formosa:
Asteroid, Echinus esculentus
Asteromonas gracilis:
Astragalus argillosus:
Astragalus beathii:
Astragalus bisculcatus:
Astragalus confertiflorus:
Astragalus crotulariae:
Astragalus racemosus:
Astragalus spp:
Astralium rogosum:
Atherinasoma microstoma:
Atherix sp.:
Atriplex spp.:
Auks, Alcidae
Australorbus glabratus:
Avena sativa:
Avocet, American, Recurvirostra americana
Aythya affinis:
Aythya americana:
Aythya ferina:
Aythya fuligula:
Aythya spp.:
Aythya valisineria:

Baboon, Papio anubis
Bacillus spp.:
Bacillus subtilis:
Bacteria, Aeromonas, Agrobacter, Arthrobacter, Bacillus, Escherichia, Flavobacterium, Klebsiella,
Pseudomonas, Salmonella
Balaenoptera physalis:
Balanus sp.:
Barley, Hordeum vulgare
Barnacle, Balanus sp.
Barn-owl, common, Tyto alba
Bass
Black sea, Centropristis striata
Largemouth, Micropterus salmoides
Rock, Ambloplites rupestris
Smallmouth, Micropterus dolomieui
Striped, Morone saxatilis

Bullfrog, Rana catesbeiana
Bullhead
    Black, Ictalurus melas
    Brown, Ictalurus nebulosus
Bunting, lark, Calamospiza melancorys
Bursaphelenchus xylophilus:
Buteo jamaicensis:
Buteo lineatus:
Buteo sp.:
Butorides striatus:
Butorides virescens:
Butterfly, large white, Pieris brassicae
Buzzard, honey, Pernis apivorus

Cabbage, Brassica oleracea capitata
Caddisfly, Triaenodus tardus
Calamospiza melanocorys:
Calcarius ornatus:
Calidris canutus:
Callinectes sapidus:
Callipepla californica:
Callithrix jacchus:
Callorhinus ursinus:
Calluna vulgaris:
Cambarus latimanus:
Cambarus sp.:
Campanularia flexuosa:
Cancer anthonyi:
Cancer irroratus:
Cancer magister:
Canis familiaris:
Canis latrans:
Canis sp.:
Canvasback, Aythya valisineria
Capitella capitata:
Capra hircus:
Capra sp.:
Capreolus capreolus:
Carassius auratus:
Carassius carassius grandoculis:
Carcharhinus longimanus:
Carcharhinus spp.:
Carcinus maenus:
Caretta caretta:
Caribou, Rangifer tarandus
Carnation, Dianthus sp.

Carp
    Common, Cyprinus carpio
    Indian, Saccobranchus fossilis
    Round Crucian, Carassius carassius grandoculis
Carpocapsa pomonella:
Carpodacus mexicanus:
Carrot, Daucus sp.
Cassia spp.:
Castilleja spp.:
Castor canadensis:
Cat, domestic, Felis domesticus
Caterpillar
    Eastern tent, Malacosoma americanum
    Gypsy, Porthetria dispar
    Saltmarsh, Estigmene acrea, Estigmene sp.
Catfish
    Air-breathing, Clarius batrachus
    African, Mystus vittatus
    Blue, Ictalurus furcatus
    Channel, Ictalurus punctatus
    Sea, Arius felis
    Various, Cnidoglanis, Ictalurus
Catharacta skua:
Catharacta spp.:
Catostomus commersoni:
Cattle, Bos sp.
Cauliflower, Brassica oleracea botrytis
Cavia cobaya:
Cavia porcellus:
Cavia sp.:
Celery, Apium graveolans
Centipede, Lithobius variegatus
Centropristis striata:
Ceratophyllum demersum:
Ceratophyllum sp.:
Ceratopogonidae:
Cervidae:
Cervus canadensis:
Cervus sp.:
Ceryle alcyon:
Champia parvula:
Channa punctatus:
Chaoborus punctipennis:
Chaoborus sp.:
Chard, Swiss, Beta vulgaris cicla
Chelon labrosus:

Chelonia mydas:
Chelydra serpentia:
Cherry
    Black, Prunus serotina
    Red, Prunus avium
Chicken
    Attwater's greater prairie, Tympanuchus cupido attwateri
    Domestic, Gallus gallus, Gallus sp.
    Prairie, Tympanuchus cupido
Chilomonas paramecium:
Chinocetes bairdii:
Chipmunk, Eutamias townsendii
Chironomid, Chironomus, Glyptotendipes
Chironomidae:
Chironomus plumosus:
Chironomus tentans:
Chlamydomonas reinhardi:
Chlamydomonas spp.:
Chlamys ferrei nipponensis:
Chlorella pyrenoidosa:
Chlorella vulgaris:
Chlorophyte, Hydrodictyon, Oedogonium
Choerodon azurio:
Chondrus crispus:
Choristoneura occidentalis:
Chroomonas sp.:
Chrysanthemum, Chrysanthemum
Chrysanthemum sp.:
Chrysemys scripta:
Chrysopa carnea:
Chukar, Alectoris chukar
Cichlasoma facetum:
Cichlid, Cichlasoma facetum
Cipangopaludina malleata:
Citharichthys stigmaeus:
Citrus tachibana:
Claassenia sp.:
Cladoceran, Bosmina, Daphnia, Simocephalus
Cladophora sp.:
Clam
    Asiatic, Corbicula fluminea
    Bentnose, Pitar morrhuana
    Giant, Tridacna maxima
    Hardshell or Quahaug, Mercenaria mercenaria
    Softshell, Mya arenaria
    Various, Donax, Glebula, Hormomya, Macoma, Rangia, Scrobicula, Tapes

Clams:
Clarias batrachus:
Clethrionomys glareolus:
Clinocardium nuttali:
Clover, Trifolium sp.
Clupea harengus pallasi:
Cnemidophorus sexlineatus:
Cnidoglanis macrocephalus:
Cockle, Clinocardium nuttali
Cockroach, German, Blattella germanica
Cod
    Atlantic, Gadus morhua
    Tom, Microgadus tomcod
Coleoptera:
Colinus virginianus:
Collembola:
Columba livia:
Columba sp.:
Colymbus (=Gavia) arcticus (= arctica):
Comandra spp.:
Condor
    Andean, Vultur gryphus
    California, Gymnogyps californianus
Coontail, Ceratophyllum demersum
Coot, American, Fulica americana
Copepod, Acartia, Eurytemora, Nitroca, Tisbe
Coral, Diploria, Montastrea
Corals:
Corbicula fluminea:
Corbicula manilensis:
Coregonus clupeaformis:
Coregonus spp.:
Cormorant
    Double-crested, Phalacrocorax auritus
    Various, Phalacrocorax spp.
Corn, Zea mays
Corophium volutator:
Cortinarius spp.:
Corvidae
Corvus brachyrhynchos:
Corvus monedula:
Cotton, Gossypium hirsutum
Cottontail, eastern, Sylvilagus floridanus
Coturnix coturnix:
Coturnix japonica:
Coturnix risoria:

Cow, Bos bovis
Cowbird, brown-headed, Molothrus ater
Cowpea, Vigna sp.
Coyote, Canis latrans
Crab
    Alaskan king, Paralithodes camtschatika
    Alaskan snow, Chionocetes bairdii
    Blue, Callinectes sapidus
    Drift-line, Sesarma cinereum
    Dungeness, Cancer magister
    Fiddler, Uca pugilator
    Hermit, Pagurus longicarpus
    Mud, Rithropanopeus harrisii
    Rock, Cancer irroratus
    Stone, Menippe mercenaria
    Various, Carcinus, Neptunus, Podophthalmus
Crabs:
Crane
    Lesser sandhill, Grus canadensis canadensis
    Sandhill, Grus canadensis
Crangon crangon:
Crappie, white, Pomoxis annularis
Crassostrea commercialis:
Crassostrea gigas:
Crassostrea spp.:
Crassostrea virginica:
Crataegus spp.:
Crawfish, Cambarus sp.
Crayfish, Astacus, Orconectes, Pacifastacus, Procambarus
Crayfishes
Crepidula fornicata:
Cricetus spp.:
Cricket, Gryllidae
Cristigera sp.:
Croaker, Atlantic, Micropogonias undulatus
Crocodile, American, Crocodylus acutus
Crocodylus acutus:
Crocothemis erythryaea:
Crow, American, Corvus brachyrhynchos
Ctenocephalides spp.
Culex pipiens quinquefasciatus:
Culex spp.:
Cunninghamella elegans:
Cutworm, Lepidoptera
Cygnus buccinator:
Cygnus columbianus:

Cygnus olor:
Cynodon dactylon:
Cynoscion nebulosus:
Cyprinodon variegatus:
Cyprinus carpio:

Dab, Limanda limanda
Damselflies, Odonata
Daphnia galeata mendotae:
Daphnia longispina:
Daphnia magna:
Daphnia pulex:
Daphnia sp.:
Daphnids
Daucus sp.:
Deer
    Mule, Odocoileus hemionus
    Roe, Capreolus capreolus
    Various, Cervidae
    White-tailed, Odocoileus virginianus
Dendrocygna bicolor:
Dianthus sp.:
Dicranum scoparium:
Digitaria sanguinalis:
Diomeda immutabilis:
Diplopoda, Millipedes
Diplodus sargus:
Diploria strigosa:.
Dog, Canis familiaris, Canis sp.
Dogfish
    Smooth, Mustelus canis
    Spiny, Squalus acanthias
Dolphin, striped, Stenella coeruleoalba
Donax venustus:
Dorosoma cepedianum:
Dorosoma petenense:
Dove
    Mourning, Zenaida macroura
    Ringed turtle, Streptopelia risoria
    Ring-necked, Streptopelia capicola
    Rock, Columba livia
Drosophila melanogaster:
Drum, freshwater, Aplodinotus grunniens
Duck
    American black, Anas rubripes
    American wood, Aix sponsa

Fulvous whistling, Dendrocygna bicolor
Tufted, Aythya fuligula
Mottled, Anas fulvigula
Various, Anas spp.
Duckweed, Lemna media, Lemna minor
Dugesia dorotocephala:
Dunaliella marina:
Dunaliella tertiolecta:

Eagle
Bald, Haliaeetus leucocephalus
White-tailed sea-, Haliaeetus albicilla
Earthworm
Australian, Lumbricus sp.
Various, Allolobophophora, Eisenia, Eisenoides, Lumbricus, Octochaetus
Earthworms:
Echinodermata:
Echinus esculentus:
Ecklonia radiata:
Eel, American, Anguilla rostrata
Eels, Anguilla
Egret, cattte, Bubulcus ibis
Eichhornia crassipes:
Eider, common, Somateria mollissima
Eisenia foetida:
Eisenia rosea:
Eisenoides carolinensis:
Egregia laevigata:
Elasmopus pectenicrus:
Elk, Cervus canadensis (=elaphus), Cervus sp.
Elm, Ulmus americana
Elodea canadensis:
Elodea sp.:
Engraulidae:
Enhydra lutris:
Enteromorpha linzi:
Enteromorpha sp.
Entosiphon sulcatum:
Eopsetta griporjewi:
Ephemerella sp.:
Eptesicus fuscus:
Equus caballus:
Eremophila alpestris:
Erethizon dorsatum:
Erithacus rubecula:
Erolia (= Calidris) spp.:

Escherichia coli:
Esox lucius:
Esox niger:
Estigmene acrea:
Eucyclops agilis:
Euphausid, Meganyctiphanes norvegica
Eurytemora affinis:
Eutamias townsendii:
Falco columbarius:
Falco mexicanus:
Falco peregrinus:
Falco rusticolus:
Falco sp:
Falco sparverius:
Falco tinnunculus:
Falcon
    Peregrine, Falco peregrinus
    Prairie, Falco mexicanus
    Swedish gyr, Falco rusticolus
Felis domesticus
Fern, ostrich, Matteuccia struthiopteris
Ferret, European, Mustela putorius furo
Fescue, Festuca arundinacea
Festuca arundinacea:
Festuca rubra:
Finch, house, Carpodacus mexicanus
Fish, harlequin, Rasbora heteromorpha
Flagfish, Jordanella floridae
Flatworm, see Dugesia dorotocephala
Flavobacterium:
Fleas, Ctenocephalides spp., Siphonaptera
Flounder
    Baltic or European, Platichthys flesus
    Roundnose, Eopsetta grigorjewi
    Summer, Paralichthys dentatus
    Windowpane, Scopthalmus aquosus
    Winter, Pseudopleuronectes americanus
    Witch, Glyptocephalus cynoglossus
    Yellowtail, Limanda limanda
Fly
    Crane, Tipula sp
    Damsel, Ischnura
    Dragon, Crocothemis, Macromia, Pseudagrion
    Fruit, Drosophila melanogaster
    Horn, Haematobia irritans, Muscidae
    House, Musca domestica, Musca sp.

May, Hexagenia, Siphlonurus
Snipe, Atherix sp.
Stone, Claassenia, Isoperla, Pteronarcella, Pteronarcys
Formicidae
Fox, red, Vulpes vulpes
Fragaria vesca:
Fratercula spp.
Frog
Bull, Rana catesbeiana
Cricket, Acris sp.
European, Rana temporaria
Green, Rana clamitans
Leopard, Rana sphenocephala
Tree, Hyla sp.
Various, Rana, Xenopus
Frogs:
Fruitworm, Lepidoptera
Fucus distichus:
Fucus spp.
Fucus vesiculosus
Fulica americana:
Fundulus heteroclitus:
Fundulus kansae:
Fundulus similis:
Fungi:
Fungus, Cortinarius spp., Cunninghamella elegans

Gadopsis marmoratus:
Gadus morhua:
Gadwall, Anas strepera
Galleria melonella:
Gallinule, purple, Porphyrula martinica
Gallus sp.:
Gambusia affinis:
Gammarus duebeni:
Gammarus fasciatus:
Gammarus lacustris:
Gammarus oceanicus:
Gammarus pseudolimnaeus:
Gammarus spp.:
Gar, spotted, Lepisosteus oculatus
Gasterosteus aculeatus:
Gastrophryne carolinensis:
Gastropods:
Gavia arctica:
Gavia immer:

Gazelle, Antilopinae
Gerbil, Gerbillus sp., Meriones unguiculatus
Gerbillus sp.:
Girella punctata:
Glebula rotundata:
Globicephala macrorhynchus:
Glycine max:
Glyptocephalus cynoglossus:
Glyptotendipes barbipes:
Goat, domestic, Capra hircus, Capra sp.
Goatfish, Mullus, Upeneus
Goby, edible, Boleophthalmus dussumieri
Goldenrod, Solidago graminifolia
Goldfish, Carassius auratus
Goose
    Canada, Branta canadensis
    Greylag, Anser anser
    Various, Anser spp.
Goosefish, Lophius piscatorius
Gopher, pocket, Thomomys sp.
Goshawk, Accipiter gentilis
Gossypium hirsutum:
Grackle
    Common, Quiscalus quiscala
    Great-tailed, Quiscalus mexicanus
Grape, Vitis sp.
Grass
    Bahia, Paspalum notatum
    Blue, Poa annua
    Brome, Bromus inermis, Bromus spp.
    Buffalo, Bouteloua dactyloides
    Colonial bent-, Agrostis tenuis
    Common Bermuda, Cynodon dactylon
    Crab, Digitaria sanguinalis
    Marsh, Spartina sp.
    Johnson, Sorghum halepense
    Red fescue, Festuca rubra
    Saltmarsh, Spartina alterniflora
    Western wheat, Agropyron smithii
Grasshopper, western, Melanoplus spp.
Grasshoppers:
Grebe
    Eared, Podiceps nigricollis
    Great crested, Podiceps cristata
    Pied-billed, Podilymbus podiceps
Grebes, Podicipediformes

Grindelia spp.:
Grindelia squarrossa:
Groundnut, Arachis hypogea
Grouse
    Ruffed, Bonasa umbellus
    Sharp-tailed, Tympanuchus phasianellus
Grunion, California, Leuresthes tenuis
Grus canadensis:
Grus canadensis canadensis:
Gryllidae:
Gudgeon, topmouth, Pseudorasbora parva
Gull
    California, Larus californicus
    Franklin's, Larus pipixcan
    Great black-backed, Larus marinus
    Herring, Larus argentatus
    Laughing, Larus atricilla
Lesser black-blacked, Larus fuscus
Ring-belled, Larus delawarensis
Gumweed, Grindelia spp., Grindelia squarrosa
Guppy, Poecilia reticulata
Gutierrezia spp.:
Gymnogyps californianus:
Haddock, Melanogrammus aeglifinus
Haematobia irritans:
Haematopus ostralegus:
Hagfish, Atlantic, Myxine glutinosa
Hake
    Blue, Antimora rostrata
    Red, Urophycus chuss
Haliaeetus albicilla:
Haliaeetus leucocephalus
Haliaeetus sp.:
Halibut, Atlantic, Hippoglossus hippoglossus
Halichoerus grypus hippoglossus
Halichoerus grypus:
Haliotis rufescens:
Hamster
    Chinese, Cricetus spp.
    Golden, Cricetus spp.
Haplopappus spp.:
Hardy head, small-mouthed, Atherinasoma microstoma
Hare, Lepus europaeus
Hawk
    Cooper's, Accipiter cooperii
    Pigeon (= Merlin), Falco columbarius

Red-shouldered, Buteo lineatus
Red-tailed, Buteo jamaicensis
Hawthorn, Crataegus spp.
Heather, Scotch, Calluna vulgaris
Helianthus spp.:
Helisoma campanulata:
Helisoma sp.:
Helisoma trivolvis:
Helix aspersa:
Helix spp.:
Hemicentrotus sp.:
Hemichromus bimaculatus:
Hemifusus spp.
Hen, guinea Gallus sp.
Hermione hystrix:
Heron
Black-crowned night-, Nycticorax nycticorax
Gray, Ardea cinerea
Great blue, Ardea herodias
Green-backer (=Green, Striated), Butorides striatus
Little green, Butorides virescens (=striatus)
Yellow-crowned night, Nycticorax violaceus
Herring, Pacific, Clupea harengus pallasi
Hexagenia bilineata:
Hexagenia sp.:
Himantopus mexicanus:
Hinnites multirugosus:
Hippoglossus hippoglossus:
Hirundo rustica:
Hog, Sus spp.
Hogchoker, Trinectes maculatus
Holothurian, sea cucumber, Stichopus
Homarus americanus:
Homo sapiens:
Honeybee, Apis mellifera, Apis spp.
Hordeum *vulgare*:
Hormomya mutabilis:
Hornworm, tobacco, Manduca sexta
Horse, Equus caballus
Hyacinth water, Eichhornia crassipes
Hyalella azteca:
Hydra, Hydra oligactis, Hydra sp.
Hydra oligactis:
Hydra sp.:
Hydrodictyon reticulatum
Hydroid, Campanularia

Hyla sp.:
Hymenomonas carterae:
Hypnum cupressiforme:
Hypogymnia physodes:

Ibis, white-faced, Plegadis chihi
Ictalurus furcatus:
Ictalurus melas:
Ictalurus nebulosus:
Ictalurus punctatus:
Ictalurus spp.:
Indoplanorbis exustus:
Ipomoea batatas:
Ischnura sp.:
Ischnura verticalis:
Isoperla sp.:
Isopod, Asellus sp.
Isurus oxyrinchus:

Jackdaw, Corvus monedula
Jewelfish, Hemichromus bimaculatus
Jordanella floridae:

Kale, Brassica oleracea acephala
Kelletia kelletia:
Kelp
    Brown, Ecklonia radiata
    Giant, Macrocystis pyrifera
Kestrel, Falco tinnunculus
Kestrel, American, Falco sparverius
Killifish
    Diamond, Adinia xenica
    Freshwater, Fundulus kansae
    Longnose, Fundulus similis
Kingfisher, belted, Ceryle alcyon
Kittiwake, black-legged, Rissa tridactyla
Klebsiella pneumoniae:
Knifejaw, striped Oplegnathus fasciatus
Knot, red, Calidris canutus
Knotted wrack, Ascophyllum nodosum

Lacewing, common green, Chrysopa carnea
Lactuca sativa:
Lactuca spp.:
Lagarosiphon major:
Lagodon rhomboides:

Lagopus lagopus:
Lagopus mutus:
Laminaria digitata:
Laminaria hyperborea:
Lamprey, Petromyzontidae
Lanistes carinatus:
Lanternfishes, Myctophidae
Laomedea loveni:
Lark
    Horned, Eremophila alpestris
    Southern meadow, Sturnella magna argutula
    Western meadow, Sturnella neglecta
Larus argentatus:
Larus atricilla:
Larus californicus:
Larus delawarensis:
Larus fuscus:
Larus marinus:
Larus pipixcan:
Lecanora conizaeoides:
Ledum sp.:
Leeches:
Leek, Allium porrum
Leiostomus xanthurus:
Lemna media:
Lemna minor:
Lepidoptera:
Lepisosteus oculatus:
Lepomis cyanellus:
Lepomis gibbosus:
Lepomis macrochirus:
Lepomis megalotis:
Lepomis microlophus:
Lepomis punctatus:
Leptinotarsa decemlineata:
Leptonychotes weddelli:
Lepus europaeus:
Lepus sp.:
Lettuce, Lactuca sativa, Lactuca spp.
Leuciscus idus melanotus:
Leucospius delineatus:
Leuresthes tenuis:
Lichen, Hypogymnia, Lecanora, Parmelia
Lily, water, Nuphar luteum
Limanda limanda:
Limanda sp.:

Limnodrilus hoffmeisteri:
Limnodrilus sp.:
Limpet,
    Slipper, Crepidula fornicata
    Various, Acmaea, Littorina, Patella
Limpkin, Aramus guarauna
Lithobius variegatus:
Littorina littorea:
Loach, Misgurnis fossilis
Lobster
    American, Homarus americanus
    Spiny, Nephrops, Panulirus
    Western rock, Panulirus cygnus
Lobsters:
Locoweed, Astragalus spp.
Loligo vulgaris:
Lolium perenne:
Longspur, chestnut-collared, Calcarius ornatus
Loon
    Arctic, Gavia arctica
    common, Gavia immer
Lophius piscatorius:
Lophodytes cucullatus:
Louse, wood, Oniscus, Porcellio
Lugworm, Arenicola cristata
Lumbricus herculeus:
Lumbricus rubellus:
Lumbricus sp.:
Lumbricus terrestris:
Lutjanus griseus:
Lutra canadensis:
Lycopersicon esculentum:
Lygaeidae:
Lymnaea palustris:
Lymnaea peregra:
Lymnaea stagnalis:
Lymnaea sp.:
Lynx rufus:
Lysmata caudata:
Lysmata seticaudata:

Macaca fascicularis:
Macaca iris:
Macaca mulatta:
Macaca sp.:
Machaeranthera spp.:

Mergus serrator:
Mergus spp.:
Meriones unguiculatus:
Merlin, Falco columbarius
Metamysidopsis elongate:
Mice
    Deer, Peromyscus maniculatus
    White-footed, Peromyscus leucopus
Microcystis aeruginosa:
Microgadus tomcod:
Micropogonias undulatus:
Micropterus dolomieui:
Micropterus ochrogaster, see Microtus ochrogaster
Micropterus salmoides:
Microtus agrestis:
Microtus arvalis:
Microtus ochrogaster:
Microtus pennsylvanicus:
Midge, Chaoborus, Chironomus, Tanytarsus
Midge, phantom, Chaoborus punctipennis
Milkvetch, Astragalus spp.
Millipedes:
Mimus polyglottos:
Mink, Mustela vison
Minnow,
    Cyprinid, Phoxinus, Puntius
    Eastern mud, Umbra pygmaea
    Fathead, Pimephales promelas
    Mud, Umbra limi
    Sheepshead, Cyprinodon variegatus
    Various, Poeciliopsis
Misgurnis fossilis:
Mite
    European red, Panonychus ulmi
    McDaniel spider, Tetranychus mcdanieli
    Two-spotted spider, Tetranychus urticae
    Various, Arachnids
Mockingbird, northern, Mimus polyglottos
Mole, Talpa europaea
Molothrus ater:
Monkey
    Cynomolgus, Macaca spp.
    Rhesus, Macaca mulatta
    Squirrel, Saimiri spp.
Monkeys:
Montastrea annularis:

Moose, Alces alces
Morone saxatilis:
Mosquito, Aedes, Culex,
Mosquitofish, Gambusia affinis
Moss
    Irish, Chondrus crispus
    Various, Brachythecium, Hylocomium, Hypnum, Sphagnum
Moth
    Codling, Carpocapsa pomonella
    Greater wax, Galleria melonella
    Pineapple gummosis, see Lepidoptera
Mouse
    Beach, or Old field, Peromyscus polionotus
    Field, Microtus arvalis
    Domestic, Mus spp.
    Western jumping, Zapus princeps
    Wood, Apodemus sylvaticus
Moxostoma duquesnei:
Mudalia potosensis:
Mugil cephalus:
Mullet
    Gray, Chelon labrosus
    Striped, Mugil cephalus
    Yellow-eye, Aldrichetta forsteri
Mullus barbatus:
Mummichog, Fundulus heteroclitus
Murre, common, Uria aagle
Murrel, Channa punctatus
Mus spp.:
Musca domestica:
Musca sp.:
Muscidae:
Muskrat, Ondatra zibethicus
Mussel
    Common, Mytilus edulis
    Duck, Anodonta anatina
    Various, M. californianus, M. edulis planulatus, M. galloprovincialis
Mussels:
Mustela putorius furo:
Mustela vison:
Mustelus antarcticus:
Mustelus canis:
Mya arenaria:
Myctophidae:
Myotis grisescens:
Myotis lucifugus:

Myotis spp.:
Myoxocephalus scorpius:
Myriophyllum spicatum:
Mysidopsis bahia:
Mysidopsis spp.:
Mysis relicta:
Mystus vittatus:
Mytilus californianus:
Mytilus edulis:
Mytilus edulis planulatus:
Mytilus galloprovincialis:
Myxine glutinosa:
Nais sp.:
Najus guadalupensis:
Nassarius obsoletus:
Natrix sp.:
Navicula sp.
Neanthes arenaceodentata:
Nematode, Brugia, Bursaphelenchus, Panagrellus, Parafilaria
Nematodes:
Nephrops norvegicus:
Nephtys hombergi:
Neptunus pelagicus:
Nereis diversicolor:
Nereis virens:
Neritina sp.:
Nerodia cyclopion:
Nerodia rhombifera:
Nerodia sipedon:
Nerodia spp.:
Nicotiana tabacum:
Nicrophorus tomentosus:
Nitroca spinipes:
Nitzschia liebethrutti:
Nostoc muscorum:
Notopterus notopterus:
Notropis hudsonius:
Notropis venustus:
Nucella lapillus:
Nucellus lapillus:
Nuphar luteum:
Nycticorax nycticorax:
Nycticorax violaceus:
Oak, Quercus spp.
Oat, Avena sativa
Oceanodroma furcata:

Octochaetus pattoni:
Octopus, Paroctopus sp.
Odobenus rosmarus:
Odocoileus hemionus:
Odocoileus virginianus:
Odonata:
Oedogonium cardiacum:
Oedogonium sp.:
Okra, Abelmoschus esculentus
Oligochaetes:
Olisthodiscus lutens:
Ommastrephes bartrami:
Oncorhynchus gorbuscha:
Oncorhynchus keta:
Oncorhynchus kisutch:
Oncorhynchus spp.:
Oncorhynchus tshawytscha:
Ondatra zibethicus:
Onion, Allium sp.
Oniscus asellus:
Oonopsis spp.:
Ophioderma brevispina:
Oplegnathus fasciatus:
Opsanus beta:
Orange, Mandarin, Citrus tachibana
Orchestia traskiana:
Orconectes immunes:
Orconectes limosus:
Orconectes nais:
Orconectes virilis:
Orfe, golden, Leuciscus idus melanotus
Oryctolagus cuniculus:
Oryza sativa:
Oryzaephilus surinamensis:
Oryzias latipes:
Osmerus mordax:
Osprey, Pandion haliaetus
Ostrea edulis:
Otter
    River, Lutra canadensis
    Sea, Enhydra lutris
Otus asio:
Ovis aries:
Ovis canadensis:
Owl
    Barn, Tyto alba

Eagle, Bubo bubo
Great horned, Bubo virginianus
Long-eared, Asio otus
Screech, Otus asio
Oyster
American, Crassostrea virginica
European flat, Ostrea edulis
Pacific, Crassostrea gigas
Sydney rock, Crassostrea commercialis
Oystercatcher, Eurasian, Haematopus ostralegus
Oysters:
Pachymetopan grande:
Pacifastacus sp.:
Pagophilus groenlandica:
Pagurus longicarpus:
Paintbrush, Indian, Castilleja spp.
Palaemon macrodactylus:
Palaemonetes kadiakensis:
Palaemonetes pugio:
Palaemonetes vulgaris:
Palm, Iraqi date, Phoenix sp.
Panagrellus redivivus:
Pandalus borealis:
Pandalus montagui:
Pandalus spp.:
Pandion haliaetus:
Panonychus ulmi:
Pantala hymenea:
Panthers:
Panulirus cygnus:
Panulirus interruptus:
Papio anubis:
Paracentrotus lividus:
Parafilaria bovicola:
Paralichthys dentatus:
Paralithodes camtschatika:
Paramecium caudatum:
Paranais sp.:
Parmelia baltimorensis:
Paroctopus sp.:
Parophrys vetulus:
Partridge, gray, Perdix perdix
Paspalum notatum:
Passer domesticus:
Patella caerulea:
Pea, Pisum sativum

Physa heterostropha:
Physeter macrocephalus:
Pica pica:
Picea abies:
Picea alba:
Pickerel, chain, Esox niger
Pieris brassicae:
Pig
    Guinea, Cavia spp.
    Domestic, Sus spp.
Pigeon, domestic, Columba livia
Pike, northern, Esox lucius
Pimephales promelas:
Pine
    Mugho, Pinus sp.
    Shortleaf, Pinus echinata
Pinfish, Lagodon rhomboides
Pinna nobilis:
Pinnipeds:
Pintail, northern, Anas acuta
Pinus echinata:
Pinus silvestris:
Pinus sp.:
Pisum sativum:
Pitar morrhuana:
Pitymys (= Microtus) pinetorium:
Placopecten magellanicus:
Plaice, Platichthys flesus, Pleuronectes platessa
Plant, marine flowering, Posidonia oceanica
Platichythys flesus:
Platymonas subcordiformis:
Plegadis chihi:
Pleuronectes flesus:
Pleuronectes platessa:
Plumaria elegans:
Poa annua:
Pochard, Aythya ferina
Podiceps cristata:
Podiceps nigricollis:
Podiceps spp.:
Podicipediformes:
Podilymbus podiceds:
Podoclavella moluccensis:
Podophthalmus vigil:
Poecilia reticulata:
Poeciliopsis spp.:

Polecat, Mustela putorius furo
Polychaetes, Capitella, Neanthes, Nereis
Pomatomus saltatrix:
Pomoxis annularis:
Pontoporeia affinis:
Pontoporeia hoyi:
Populus tremuloides:
Porcellio scaber:
Porcellio sp.:
Porcupine, Erethizon dorsatum
Porgy, Pachymetopan grande
Porgy, black, Sparus macrocephalus
Porphyrula martinica:
Porthetria dispar:
Porzana carolina:
Posidonia oceanica:
Potamogeton crispus:
Potamogeton foliosus;
Potamogeton richardsoni:
Potamogeton spp.:
Potato
    Common, Solanum tuberosum
    Sweet, Ipomoea batatas
Prawn
    Deep sea, Pandalus borealis
    Freshwater, Macrobrachium lamarrei, M. rosenbergii
    Various, Pandalus montagui, Pandalus spp., Penaeus indicus, Penaeus latisulcatus
Prionace glauca:
Pristina sp.:
Procambarus acutus acutus:
Procambarus blandingi:
Procambarus clarki:
Procambarus spp.:
Procyon lotor:
Pronghorn, Antilocapra americana
Prosopium cylindraceum:
Protozoan, Chilomonas, Cristigera, Entosiphon, Paramecium, Tetrahymena, Uronema
Prunus avium:
Prunus serotina:
Psettichthys melanostictus:
Pseudagrion spp.:
Pseudomonas sp.:
Pseudopleuronectes americanus:
Pseudorasbora parva:
Ptarmigan

Common, Lagopus mutus
Willow, Lagopus lagopus
Pteronarcella badia:
Pteronarcys californica:
Pteronarcys dorsata:
Pteronarcys sp.:
Ptychocheilus oregonensis:
Puffins, Fratercula spp.
Puffinus pacificus:
Pumpkinseed, Lepomis gibbosus
Puntius conchonius:
Pygoscelis adeliae:
Pyrus communis:
Pytiscidae:
Quail
California, Callipepla californica
Common, Coturnix coturnix
Coturnix, Coturnix risoria
Japanese, Coturnix japonica
Quelea, Quelea quelea
Quelea quelea:
Quercus spp.:
Quiscalus mexicanus:
Quiscalus quiscula:
Rabbit,
Various, Lepus, Oryctolagus, Sylvilagus
White, Oryctolagus cuniculus
Raccoon, Procyon lotor
Racerunner, six-lined, Cnemidophorus sexlineatus
Radish, Raphanus sativus
Rail
Clapper, Rallus longirostris
Sora, Porzana carolina
Raja erinacea:
Raja sp.:
Rallus longirostris:
Rana catesbeiana:
Rana clamitans:
Rana pipiens:
Rana sphenocephala:
Rana spp.:
Rana temporaria:
Rana temporia:
Rana utricularia:
Rangia cuneata:
Rangifer tarandus:

Raphanus sativus:
Rasbora heteromorpha:
Rat
    Cotton, Sigmodon hispidus
    Laboratory white, Rattus spp.
    Norway, Rattus norvegicus
Rattus norvegicus:
Rattus spp.:
Ray, Raja sp.
Recurvirostra americana:
Redhead Aythya americana
Redhorse, black, Moxostoma duquesnei
Redshank, Icelandic, Tringa totanus robusta
Rhizophora spp.:
Rice,
    Domestic, Oryza sativa
    Wild, Zizania aquatica
Rissa tridactyla:
Rithropanopeus harrisii:
Robin,
    American, Turdus migratorius
    European, Erithacus rubecula
Rotifer, Brachionus plicatilis
Rudd, Scardinus erythrophthalmus
Rye, Secale cereale
Rye, perennial, Lolium perenne
Rynchops niger:
Saccharum officinarum:
Saccobranchus fossilis:
Sagebrush, big, Artemisia tridentata
Saguinus fuscicollis:
Saimiri spp.:
Salamander
    Marbled, Ambystoma opacum
    Tiger, Ambystoma tigrinum
Salmo clarki:
Salmo gairdneri:
Salmo salar:
Salmo spp.:
Salmo trutta:
Salmon
    Atlantic, Salmo salar
    Chinook, Oncorhynchus tshawytscha
    Chum, Oncorhynchus keta
    Coho, Oncorhynchus kisutch
    Pink, Oncorhynchus gorbuscha

Seatrout, spotted, Cynoscion nebulosus
Secale cereale:
Selenastrum capricornutum:
Sepioteuthis australis:
Sergestes lucens:
Seriola quinqueradiata:
Sesarma cinereum:
Sesarma heamatocheir:
Shad
    Gizzard, Dorosoma cepedianum
    Threadfin, Dorosoma petenense
Shark
    Blue, Prionace glauca
    Shortfin mako, Isurus oxyrinchus
    Various, Carcharhinus, Mustelus, Sphyrna
    Whitetip, Carcharhinus longimanus
Sharks:
Shearwater, wedge-tailed, Puffinus pacificus
Sheep
    Bighorn, Ovis canadensis
    Domestic, Ovis aries, Ovis sp.
Shell
    Ivory, Buccinum striatissimum
    Spindle, Hemifusus
Shiner
    Blacktail, Notropis venustus
    Spottail, Notropis hudsonius
Shoveler, northern, Anas clypeata
Shrew
    Common, Sorex araneus
    Short-tailed, Blarina brevicauda
Shrimp
    Brine, Artemia salina
    Brown, Penaeus aztecus
    Glass, Palaemonetes kadiakensis
    Grass, Palaemonetes pugio, P. vulgaris
    Korean, Palaemon macrodactylus
    Mysid, Metamysidopsis, Mysidopsis, Mysis
    Pink, Penaeus duorarum
    Sand, Crangon crangon
    Various, Lysmata, Penaeopsis, Sergestes
    White, Penaeus setiferus
Shrimps:
Sicklepod, Cassia spp.
Sigmodon hispidus:
Silkworm, Bombyx mori

Sillago bassensis:
Silverside
    Atlantic, Menidia menidia
    Inland, Menidia beryllina
    Tidewater, Menidia peninsula
Simocephalus serrulatus:
Simocephalus sp.:
Simulium sp.:
Siphonsaptera:
Skate, little, Raja erinacea
Skeletonema costatum:
Skimmer, black, Rynchops niger
Skipper, mud, Boleophthalmus dussumieri
Skua, great, Catharacta skua
Slug, Agriolimax reticulatus
Smelt, rainbow, Osmerus mordax
Snail
    Land, Helix aspersa
    Mud, Nassarius obsoletus
    Pond, Cipangopaludina malleata
    Ram's horn, Helisoma trivolvis
    Red, Indoplanorbis exustus
    Various, Amnicola, Arcularia, Australorbus, Biomphalaria, Bulinus,
        Helisoma, Helix, Lanistes, Lymnaea, Mudalia, Neritina, Physa,
        Viviparus
Snake
    Garter, Thamnophis sp.
    Northern water, Nerodia sipedon
    Water, Natrix, Nerodia
Snapper, mangrove, Lutjanus griseus
Solanum tuberosum:
Sole
    English, Parophrys vetulus
    Sand, Psettichthys melanostictus
    Various, Limanda, Solea, Trinectes
Solea solea:
Solenopsis invicta:
Solidago graminifolia:
Somateria mollissima:
Sorex araneus:
Sorghum, Sorghum halopense
Sorghum halopense:
Soybean, Glycine max
Sparrow
    Chipping, Spizella passerina
    House, Passer domesticus

Sturnella neglecta:
Sturnus vulgaris:
Stylodrilus sp.:
Sucker, white, Catostomus commersoni
Sugar cane, Saccharum officinarum
Sula leucogaster:
Sula sula:
Sunfish
    Green, Lepomis cyanellus
    Longear, Lepomis megalotis
    Redear, Lepomis microlophus
    Spotted, Lepomis punctatus
Sunflower, Helianthus spp.
Sus spp.:
Swallow
    Barn, Hirundo rustica
    Northern rough-winged, Stelgidopteryx serripennis
Swan
    Mute, Cygnus olor
    Trumpeter, Cygnus buccinator
    Tundra, Cygnus columbianus
Swine, Sus spp.
Swordfish, Xiphias gladius
Sylvilagus floridanus:
Sylvilagus sp.:
Tadpoles:
Talpa europea:
Tamarin, Saguinus fuscicollis
Tanytarsus dissimilis:
Tapes decussatus:
Tapeworm:
Tea, Labrador, Ledum sp.
Teal
    Blue-winged, Anas discors
    Green-winged, Anas carolinensis
Termite
    Australian, Mastotermes darwiniensis
    Rhodesian, Trinervitersmes dispar
Tern
    Arctic, Sterna paradisaea
    Common, Sterna hirundo
    Forster's, Sterna forsteri
    Royal, Sterna maxima
    Sooty, Sterna fuscata
Terrapene carolina:
Tetraedron sp.:

Tetrahymena pyriformis:
Tetranychus mcdanieli:
Tetranychus urticae:
Tetraselmis chui:
Thais lapillus:
Thalassiosira aestivalis:
Thalassiosira pseudonana:
Thamnophis sp.:
Thomomys sp.:
Thynnus spp.:
Tilapia, Mozambique, Tilapia mossambica
Tilapia mossambica:
Timothy, Phleum pratense
Tipula sp.:
Tisbe holothuriae:
Toad
    European, Bufo bufo
    Narrow-mouthed, Gastrophryne carolinensis
    Various, Bufo sp., Bufo terrestris
Toadfish Gulf, Opsanus beta
Toadflax, bastard, Comandra
Tobacco, Nicotiana tabacum
Tomato, Lycopersicon esculentum
Tomcod, Microgadus tomcod
Triaenodus tardus:
Trichechus manatus:
Trichogaster pectoralis:
Tridacna maxima:
Trifolium sp.:
Trinectes maculatus:
Trinervitermes dispar:
Tringa solitaria:
Tringa totanus robusta:
Triticum aestivum:
Triticum vulgare:
Triturus cristatus:
Trout
    Brook, Salvelinus fontinalis
    Brown, Salmo trutta
    Cutthroat, Salmo clarki
    Lake, Salvelinus namaycush
    Rainbow, Salmo gairdneri
    Spotted sea, Cynoscion nebulosus
Tubifex costatus:
Tubifex sp.:
Tubifex tubifex:

Tuna
    Japanese, Scombridae
    Various, Thynnus spp.
Tunas:
Tunicate, Podoclavella moluccensis
Turdus merula:
Turdus migratorius:
Turkey, Meleagris gallopavo
Turnip, Brassica rapa
Turtle
    Atlantic green, Chelonia mydas
    Box, Terrapene carolina
    Slider, Chrysemys scripta
    Snapping, Chelydra serpentia
    Loggerhead, Caretta caretta
Turtle-dove, ringed, Streptopelia risoria
Tuskfish, scarbreast, Choerodon azurio
Tympanuchus cupido:
Tympanuchus cupido attwateri:
Tympanuchus phasianellus:
Tyto alba:
Uca minax:
Uca pugilator:
Uca sp.:
Ulmus americana:
Ulva sp.:
Umbra limi:
Umbra pygmaea:
Upeneus moluccensis:
Uria aalge:
Uronema marinum:
Uronema nigricans:
Uronema sp.:
Urophycus chuss:
Ursus maritimus:
Vaccinium angustifolium:
Vaccinium pallidum:
Vigna sp.:
Vitis sp.:
Vole
    Bank, Clethrionomys glareolus
    Field, Microtus agrestis
    Meadow, Microtus pennsylvanicus
    Pine, Pitymys (= Microtus) pinetorium
    Prairie, Micropterus ochrogaster, Microtus ochrogaster
Viviparus ater:

Xenopus laevis:
Xiphias gladius:
Yeasts:
Yellowtail, Seriola quinqueradiata (=lalandei)
Zalophus californianus:
Zapus princeps:
Zea mays:
Zebrafish, Brachydanio rerio
Zenaida (=Zenaidura) macroura:
Ziphius cavirostris:
Zizania aquatica:
Zylorhiza spp.:

LITERATURE CITED

American Fisheries Society. 1980. A list of common and scientific names of fishes from the United States and Canada. Am. Fish. Soc. Spec. Publ. 12. 174 pp.

Edwards, E. P. 1974. A coded list of birds of the world. Ernest P. Edwards, Sweet Briar, Virginia. 174 pp.

Eisler, R. 1985a. Mirex hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.1). 42 pp.

Eisler, R. 1985b. Cadmium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.2). 46 pp.

Eisler, R. 1985c. Carbofuran hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.3). 36 pp.

Eisler, R. 1985d. Selenium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.5). 57 pp.

Eisler, R. 1986a. Chromium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.6). 60 pp.

Eisler, R. 1986b. Polychlorinated biphenyl hazards to fish, wildlife, and invertebrates: a synoptic Review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.7). 72 pp.

Eisler, R. 1986c. Dioxin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.8). 37 pp.

Eisler, R. 1986d. Diazinon hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.9). 37 pp.

Eisler, R. 1987a. Mercury hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.10). 90 pp.

Eisler, R. 1987b. Polycyclic aromatic hydrocarbon hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.11). 81 pp.

Eisler, R. 1988a. Arsenic hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.12). 92 pp.

Eisler, R. 1988b. Lead hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.14). 134 pp.

Eisler, R. 1989. Tin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.15). 83 pp.

Eisler, R., and J. Jacknow. 1985. Toxaphene hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.4). 26 pp.

Jenkins, D. W. 1980. Biological monitoring of toxic trace metals. Vol. 1; Vol. 2, Parts I, II, and III. U. S. Environ. Protection Agency Rep. 600/3-80-092. 1274 pp.

Johnson, W. W., and M. T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U. S. Fish. Wildl. Serv. Resour. Publ. 137. 98 pp.

Nowak, R. M., and J. L. Paradiso. 1983. Walker's mammals of the world. Vol. I and II. Johns Hopkins Univ. Press, Baltimore, Maryland. 1362 pp. + LXXXI.

Odenkirchen, E. W., and R. Eisler. 1988. Chlorpyrifos hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.13). 34 pp.

Scott, T. G., and C. H. Wasser. 1980. Checklist of North American plants for wildlife biologists. The Wildlife Society, Suite 611, 7101 Wisconsin Ave. NW, Washington, DC 20014. 58 pp.

Swain, R. B., and S. N. Swain. 1948. The insect guide. Doubleday, New York. 261 pp.

Subject	Publication date	Publication number
Mirex	March 1985	85(1.1)
Cadmium	July 1985	85(1.2)
Carbofuran	August 1985	85(1.3)
Toxaphene	August 1985	85(1.4)
Selenium	October 1985	85(1.5)
Chromium	January 1986	85(1.6)
Polychlorinated Biphenyls	April 1986	85(1.7)
Dioxins	May 1986	85(1.8)
Diazinon	August 1986	85(1.9)
Mercury	April 1987	85(1.10)
Polycyclic Aromatic Hydrocarbons	May 1987	85(1.11)
Arsenic	January 1988	85(1.12)
Chlorpyrifos	March 1988	85(1.13)
Lead	April 1988	85(1.14)
Tin	January 1989	85(1.15)
Index to Species	February 1989	85(1.16)

Biological Report 85(1.17)
April 1989

Contaminant Hazard Reviews
Report No. 17

PENTACHLOROPHENOL HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

Pentachlorophenol (PCP) is a synthetic organochlorine compound that was first manufactured commercially in 1936 and is now used primarily as a wood preservative and secondarily as a herbicide, insecticide, fungicide, molluscicide, and bactericide. Current global production of PCP is estimated to be 50 million kg annually. Widespread use of PCP has resulted in the detection of residues in air, rain, snow, groundwater, surface water, drinking water, fish, and aquatic invertebrates, as well as in human urine, blood, and milk. Pentachlorophenol may be incorporated into animal tissues through inhalation, diet, or contact; its toxic action results from its ability to interfere with the production of high energy phosphate compounds essential for cell respiration. Pentachlorophenol has caused numerous occupational illnesses and deaths, and has had significant adverse effects on domestic animals. It is fetotoxic and teratogenic, but evidence for mutagenicity and carcinogenicity is incomplete or negative. Commercial PCP preparations often contain variable amounts of toxic impurities--including chlorophenols, hexachlorobenzene, phenoxyphenols, dioxins, and dibenzofurans--that contribute to its toxicity. Pentachlorophenol is rapidly accumulated and rapidly excreted, and has little tendency to persist in living organisms; it is readily degraded in the environment by chemical, microbiological, and photochemical processes.

In sensitive aquatic species, PCP adversely affected growth, survival, and reproduction at media concentrations of 8 to 80 ug PCP/1 in algae and higher plants, at 3 to 100 ug/l in invertebrates, and <1 to 68 ug/l in fish. In birds, PCP was fatal at 380 to 580 mg/kg body weight (BW) in oral doses, >3,580 mg/kg in the diet, and >285 mg/kg in contaminated nesting materials .(i.e., wood shavings). Residues >11 mg PCP/kg fresh weight in bird tissues were associated with acute toxicosis. Adverse sublethal effects in birds were noted at dietary levels as low as 1 mg/kg ration. In small laboratory mammals and domestic livestock, acute oral LD-50's ranged from 27 to 300 mg/kg BW. Tissue residues in mammals were elevated at PCP doses as low as 0.05 mg/kg BW, and at air levels >0.l mg/m^3. Histopathology, reproductive impairment, growth retardation, and other effects were evident in sensitive mammals at PCP concentrations of 0.2 to 1.25 mg/kg BW, and at dietary levels >30 mg/kg ration.

Pentachlorophenol is an undesirable pollutant whose use patterns should be carefully regulated to avoid contamination of soil, water, and food.

Recommendations for protection of sensitive fishery and wildlife resources follow; however, it is emphasized that some of these recommendations are markedly lower than those proposed by regulatory agencies. For protection of aquatic life, it is recommended that the PCP water concentration not exceed 3.2 ug/l; but even at this level certain species of fishes and oysters accumulate enough of the toxicant to retard their growth. In birds, dietary concentrations >1.0 mg/kg feed and tissue residues >2.0 mg/kg fresh weight should be viewed as presumptive evidence of significant environmental PCP contamination. Data are scarce for PCP and mammalian wildlife; until more data are collected, PCP levels recommended for human health protection (i.e., "no adverse effects" levels) are suggested as reasonable substitutes. In humans, no adverse effects were noted at daily PCP intakes equivalent to 39 ug/kg BW in food, or at concentrations of 21 ug/l in drinking water, 0.5 mg/m^3 in air, 0.5 mg/l in blood plasma, and 1.0 mg/l in blood.

DISCLAIMER

Mention of trade names or commercial products does not constitute endorsement or recommendation for use by the U.S. Government.

Suggested citation:

Eisler, R. 1989. Pentachlorophenol hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. Fish Wildl. Serv. Biol. Rep. 85 (1.17).

TABLES

ACKNOWLEDGMENTS

I thank Nancy A. Bushby, Lynda J. Garrett, and Joyce Haber Corley for literature search and retrieval; Barbara A. Roberts for secretarial help; Donald R. Clark, Laverne Cleveland, and Mark J. Melancon for technical and scientific review; and Paul H. Eschmeyer and James R. Zuboy for editorial services.

INTRODUCTION

Pentachlorophenol (PCP) and its water soluble salt, sodium pentachlorophenate, are commercially produced organochlorine compounds used primarily as preservatives of wood and wood products, and secondarily as herbicides, insecticides, fungicides, molluscicides, and bactericides (EPA 1980; Prescott et al. 1982). Both compounds have been sold for these purposes since 1936 under a variety of trade names (Knudson et al. 1974). Because of its widespread use, animals and humans are exposed to significant amounts of PCP; detectable PCP levels are found in most people living in industrialized societies, probably as a result of food chain exposure to PCP-treated wood products (Dougherty 1978; McConnell et al. 1980; Prescott et al. 1982). In Japan, PCP has been widely used as a herbicide in rice fields, but owing to its high toxicity to fishes, its use was limited (beginning in 1971) to upland fields (Nishimura 1984; Mikesell and Boyd 1986). The use of PCP in Japan has resulted in the contamination of all surface water in that country to concentrations of 0.01 to 0.1 ug/l (Lu et al. 1978). The chemical and its degradation products bioconcentrate in fish and are among the phenolic compounds known to taint fish flesh (Boyle et al. 1980). It has been detected in marine fishes and invertebrates, in drinking water, and in human blood and urine (Schimmel et al. 1978; Klemmer et al. 1980; (Trujillo et al. 1982). All samples of human milk from nursing mothers tested in Bavaria from 1979 to 1981 contained PCP (Gebefugi and Korte 1983).

In man, illnesses and deaths have been reported after exposure to PCP through diet or by direct contact with PCP-treated products (Prescott et al. 1982). For example, 20 of 80 infants who wore, for 8 days, diapers rinsed in an antimicrobial laundry neutralizer containing sodium pentachlorophenate developed enlarged livers and spleens, had high fevers, and sweated profusely; although most recovered spontaneously, 7 died (Knudsen et al. 1974; EPA 1980). At least 24 industrial PCP fatalities have been reported. The first deaths occurred at a wood preservative plant in France in 1952. Others were recorded at a chemical factory in Japan in 1953, during herbicide spraying in Australia in 1956, at a sawmill in Indonesia in 1958, in South Africa in 1961, and in Canada and the United States in 1965 (Wood et al. 1983). The acute toxic action of PCP in man and experimental animals is caused by the uncoupling of oxidative phosphorylation mechanisms, resulting in marked increases in metabolism (Murphy 1986).

Data are scarce on PCP effects on wildlife, although it is speculated that no wildlife losses should occur under normal PCP application conditions and that chronic toxicity would not be serious because PCP is rapidly excreted (Bevenue and Beckman 1967). However, mortality was heavy in two species of bats that came into contact with PCP-treated timbers up to 14 months after treatment (Racey and Swift 1986). Furthermore, evidence accumulating on the harmful effects of PCP to domestic animals suggests that the chemical may have considerable adverse effects on other species of wildlife. In the poultry industry, for example, PCP has been implicated in the cause of musty taint in chicken meat and eggs and in increased morbidity in chickens housed on PCP-contaminated wood shavings or given PCP-contaminated food (Prescott et al. 1982). Pentachlorophenol is repellent to animals; diets containing PCP have been rejected by rats, cats, and cattle (Bevenue and Beckman 1967). In farm animals, PCP intoxication has been increasing as a result of confinement in buildings recently treated with a PCP wood preservative, and through dermal contact with PCP-treated fences and feed bunks (Osweiler et al. 1984). Dairy cattle contaminated by PCP produced less milk, grew poorly, and developed skin lesions (Firestone et al. 1979; Greichus et al. 1979; Parker et al. 1980). The issue is confounded by the presence of various amounts of toxic impurities--primarily dioxins and dibenzofurans--in technical and commercial preparations of PCP; these contaminants are mainly responsible for its observed toxicity in rabbits, rats, pigs, cattle, and chickens (Dougherty 1978; McConnell et al. 1980; Prescott et al. 1982). In one example in 1957, millions of chickens died in the southeastern United States after eating poultry feeds containing fat from hides preserved with PCP. Nine dioxins were detected in the toxic animal fat, including the potent 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin isomer (Parker et al. 1980; Stedman et al. 1980; Prescott et al. 1982).

Useful reviews on the ecological and toxicological aspects of PCP have been published by Bevenue and Beckman (1967), Cote (1972), Rao (1978), EPA (1980), Williams (1982), and Choudhury et al. (1986). I here synthesize the available data on environmental aspects of PCP, with emphasis on fish and wildlife. It is part of a continuing series of reviews on chemical contaminants prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service.

ENVIRONMENTAL CHEMISTRY

GENERAL

Pentachlorophenol and its water soluble salt, sodium pentachlorophenate, are used extensively in agriculture and industry. Most--about 80%--of the 50 million kg of PCP manufactured each year is used in the protection and preservation of wood products. Commercial samples of technical grade PCP are heavily contaminated with many compounds, including chlorophenols, dioxins, dibenzofurans, hexachlorobenzene, and phenoxyphenols; the relative toxicities and accumulation potentials of some of these contaminants may exceed those of PCP by several orders of magnitude. Pentachlorophenol interferes with the production of high energy phosphate compounds essential for cell respiration. In general, it readily degrades in the environment by photochemical, chemical, and microbiological processes.

SOURCES AND USES

Although PCP was first synthesized in 1841, it was not produced commercially until 1936 (Wood et al. 1983; Menzer and Nelson 1986). It has since been registered for use as an insecticide, fungicide, herbicide, algicide, and disinfectant, and as an ingredient in antifouling paint; at least 578 products contain PCP (Cote 1972; Cirelli 1978; Choudhury et al. 1986;Murphy 1986). By 1967, PCP and its sodium salt, sodium pentachlorophenate (Na-PCP), were used extensively in industry and agriculture, due in large part to the solubility of PCP in organic solvents and of Na-PCP in water (Bevenue and Beckman 1967; Cirelli 1978). The major commercial application of technical grade preparations of PCP is in wood preservation formulations, where its fungicidal and bactericidal actions inhibit the growth of wood-destroying organisms (Kinzell et al. 1981).

In the United States, about 80% of the 23 million kg of technical PCP produced annually--or about 46% of worldwide production--is used for wood preservation (Pignatello et al. 1983; Kinzell et al. 1985; Zischke et al. 1985; Choudhury et al. 1986; Mikesell and Boyd 1986). It is the third most heavily used pesticide, preceded only by the herbicides atrazine and alachlor (Kinzell et al. 1981). There are about 470 wood preservative facilities in the United States, scattered among 45 states; they are concentrated in the south, southeast, and northwest--presumably due to the availability of preferred timber species in those regions (Cirelli 1978). Livestock facilities are often constructed of wood treated with technical PCP; about 50% of all dairy farms in Michigan used PCP-treated wood in the construction of various components of livestock facilities (Kinzell et al. 1985). The chemical is usually applied to wood products after dilution to 5% with solvents such as mineral spirits, No. 2 fuel oil, or kerosene. More than 98% of all wood processed is treated with preservative under pressure; about 0.23 kg of PCP is needed to preserve one cubic foot of wood (Cirelli 1978). Lumber treated with PCP retains its natural appearance, has little or no odor, and can be painted as readily as natural wood (Wood et al. 1983).

In addition to its extensive use by the construction and lumber industries to control damage by mold, termites, powder post beetles, and wood boring insects (Bevenue and Beckman 1967), PCP has been used as a bactericide and fungicide to protect many products, such as adhesives, paper and paperboard, cable coverings, leather, paints, textiles, rope, ink, rubber, and petroleum drilling muds (Bevenue and Beckman 1967; Firestone et al. 1979; Williams 1982). It has been used to control algae and fungi in cooling towers at electric plants (Williams 1982). It has also been added to fabrics for moth proofing, though derivatives such as pentachlorphenol laurate are more widely used for this purpose because their resistance to dry cleaning and washing exceeds that of PCP, and their toxicity to mammals is lower (Bevenue and Beckman 1967). It has been applied in agriculture and around industrial sites as an herbicide and preharvest desiccant, on pastureland, and in pineapple, rice, and sugarcane fields (Bevenue and Beckaman 1967). A Japanese manufacturer has added PCP to soy sauce--in violation of the law--as a preservative (Bevenue and Beckman 1967). It has also been used as a bird repellant: PCP discourages woodpeckers when it is mixed as a pellet and plugged into holes drilled by the bird (Cirelli 1978).

In Canada, the main use of PCP is in the protection and preservation of wood, and secondarily as an herbicide and insecticide for agricultural purposes. A total of 50 wood preserving plants--mostly in British Columbia, Alberta, and Ontario--used about 2.7 million kg of PCP in 1978 (Hoos 1978). Treatment with PCP significantly increased the life of timbers, construction lumber, telephone poles, and railway ties; for example, jackpine poles treated with PCP lasted at least 35 years, compared to 7 years for untreated poles (Hoos 1978).

Sodium pentachlorophenate has been used to control schistosomiasis by eliminating snails that are intermediate hosts of human schistosomes (Bevenue and Beckman 1967). It is also used as a fungicide, bactericide, and algicide in construction materials, emulsion polymers, paints, textiles, and finished paper products; as a preservative for ammonium alginate; and at concentrations of 15 to 40 mg/l, to control microbial growth in secondary oil recovery (Bevenue and Beckman 1967; Cirelli 1978).

PROPERTIES

Pentachlorophenol is readily soluble in most organic solvents, oils, and highly aromatic and olefinic petroleum hydrocarbons--a property that makes it compatible for inclusion in many pesticide formulations (Table 1; Bevenue and Beckman 1967). Purified PCP, however, is practically insoluble in water; therefore, the readily water-soluble sodium pentachlorophenate salt is substituted in many industrial applications (Table 1; Bevenue and Beckman 1967).

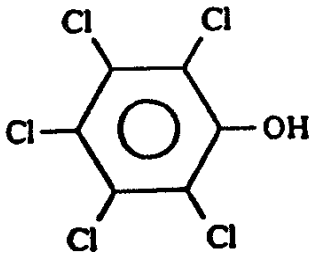
The solubility of sodium and potassium pentachlorophenate in water is pH-dependent; it increases from 79 mg/l at pH 5.0 to >4 g/l at pH 8.0 (Bevenue and Beckman 1967). But differential toxicity of PCP in solution is primarily attributable to variations in uptake as a function of pH (Jayaweera et al. 1982; Kaiser and Valdmanis 1982; Fisher and Wadleigh 1986; Smith et al. 1987), and not to water solubility. At pH 4.0, for example, PCP is fully protonated and therefore highly lipophilic, and has its greatest accumulation potential. Conversely, PCP is completely ionized at pH 9.0; lipophilicity is markedly reduced as is its toxicity to the alga *Selenastrum capricornutum* (Jayaweera et al. 1982; Smith et al. 1987) and the midge, *Chironomus riparius* (Fisher and Wadleigh 1986).

In recent years it has become clear that many commercial samples of technical grade PCP are heavily contaminated with a large number of potentially toxic compounds and materials (Fig. 1, Table 2). These contaminants include, in part, various isomers of chlorophenols, dibenzofurans, dioxins, hexachlorobenzene, and phenoxyphenols (Table 2), as well as various chlorinated diphenyl ethers, dihydroxybiphenyls, anisoles, catechols, guaiacols, and other chlorinated dibenzodioxin and dibenzofuran isomers (Kaufman 1978; Nilsson et al. 1978; Firestone et al. 1979; EPA 1980; Singh et al. 1985; Menzer and Nelson 1986; Mikesell and Boyd 1986; Murphy 1986; Holsapple et al. 1987). In relative toxicity and accumulation potential, some contaminants in technical grade PCP may exceed the parent compound by several orders of magnitude (Huckins and Petty 1981). For example, some isomers of hexachlorodibenzodioxin, which are present in technical grade PCP at concentrations of 1,000 to 17,300 ug/kg (Table 2), produce LD-50 values in guinea pigs of 60 to 100 ug/kg body weight--thus ranking them as extremely toxic chemicals (Eisler 1986; Murphy 1986).

FATE

Pentachlorophenol may be absorbed into the body through inhalation, diet, or skin contact (Bevenue and Beckman 1967; Williams 1982; Gray et al. 1985). Its acute toxicity results from its ability to interfere with the production of high energy phosphate compounds essential for cell respiration. This interference, or uncoupling, causes stimulation of the cell's metabolism to the toxic stage, which is accompanied by fever and other signs of stress (Bevenue and Beckman 1967; Hodson and Blunt 1981; Williams 1982). The metabolic consequences resemble those of vigorous exercise in some species (Hodson and Blunt 1981). In addition to the proven uncoupling effects on oxidative phosphorylation, the overall inhibitory effects on a variety of enzymes, metabolism of lipids and carbohydrates, ion transport, and protein synthesis may account for the broad spectrum biocidal effects of PCP and its salts (Rao et al. 1979; Gray et al., 1985; Smith et al. 1987). Pentachlorophenol is fetotoxic and teratogenic during early gestation; however, evidence of its mutagenic or carcinogenic properties is incomplete (Williams 1982).

Table 1. Chemical and other properties of pentachlorophenol (from Bevenue and Beckman 1967; Cote 1972; Cirelli 1978; EPA 1980; Williams 1982; Hudson et al. 1984; Choudhury et al. 1986; Hill and Camardese 1986; Mayer 1987).

Variable	Datum
Chemical name	Pentachlorophenol, CAS-87-86-5
Alternate names	Chem-Penta, Chemtrol, Chlorophen, Dow Pentachlorophenol, Dowicide 7, Dowicide EC-7, Dowicide G, DP-2, Durotox, Lauxtol A, Ontrack WE-1, PCP, Penchlorol, Penta, Penta General Weed Killer, Pentacon, Penta-kil, Pentanol, Pentasol, Penwar, Permacide, Permaguard, Permasem, Permatox, Priltox, Santobrite, Santophen, Sinituho, Term-l-trol, Weed-Beads, Weedone
Primary uses	Wood preservative, preharvest defoliant, herbicide, molluscicide, insecticide, fungicide
Producers:	Dow Chemical Company, Monsanto Company, Reichold Chemical Company, Vulcan Materials Company
Empirical formula	C_6Cl_5OH
Structural formula	
Physical state	White solid with needle-like crystals. Produced by chlorination of Molten phenol. Technical grade material is dark gray to brown
Molecular weight	266.35
Melting point	190 to 191 °C
Boiling point	309 to 310 °C (decomposes)
Specific gravity	1.978
Vapor pressure	
25 °C	0.0016 mm Hg
100 °C	0.02 mm Hg
211 °C	40.0 mm Hg
Solubility	
Water	
0 °C	5 mg/L

20 °C	14 mg/L
30 °C	20 mg/L
50 °C	35 mg/L
Carbon tetrachloride	20 to 30 g/L
Benzene	110 to 140 g/L
Ethanol	470 to 520 g/L
Methanol	570 to 650 g/L
Solubility of sodium salt (sodium pentachlorophenate, CAS 131-52-2) in water at 25 °C	330 g/L
Log octanol/water partition coefficient	5.01 to 5.12

Table 2. Partial list of contaminants detected in technical grade and purified pentachlorophenol. All values are in mg contaminant/kg product (ppm).

	Grade and concentration (% PCP)		
	Technical	Purified	
Contaminant	85% to 90%	>99%	Reference[a]
Chlorophenols			
Trichlorophenols[b]	1,000	--	1
Tetrachlorophenols			
2,3,4,6-tetrachlorophenol	49,000	0.25	2, 3
2,3,4,5-tetrachlorophenol	9,000	0.073	2, 3
Total	40,000 to 80,000	500	1, 4
Other chlorophenols[b]	20,000 to 60,000	--	1, 4
Dibenzofurans			
Pentachlorodibenzofurans[b]	40	--	5
Hexachlorodibenzofurans[b]	90	--	5
Heptachlorodibenzofurans[b]	400	--	5
Octachlorodibenzofurans[b]	29 to 260	--	5, 6
Dioxins			
Total	1,900 to 2,625	<7	7
Tetrachlorodioxins[b]	0.035 to 0.12	--	1, 5
Pentachlorodioxins[b]	0.03	--	5
Hexachlorodioxins[b]	1 to 173	0.00001	1, 2, 3, 4, 5, 8
Heptachlordioxins[b]	119 to 1,000	1.8	1, 5, 6, 8

Octachlorodioxins[b]	40 to 4,700	0.0002 to 3.0	1, 2, 3, 4, 5, 6, 8
Hexachlorobenzene	56 to 270	0.0014	2, 3, 6
Phenoxyphenols			
Heptachlorophenoxyphenols[b]	1,200	4.8	6
Octachlorophenoxyphenols[b]	28,000	300	6
Nonachlorophenoxyphenols[b]	15,000	500	6

[a]References: 1, Shull et al. 1986; 2, Zischke et al. 1985; 3, Pignatello et al. 1983; 4, Lamparski et al. 1980; 5, Williams 1982; 6, Cleveland et al. 1982; 7, Eisler 1986; 8, Singh et al. 1985.

[b]Total, when not indicated otherwise.

Pentachlorophenol readily degrades in the environment by chemical, microbiological, and photochemical processes (Kaufman 1978; Choudhury et al. 1986). Its suggested metabolic fates include oxidation and dechlorination to tri- and tetrachloro-p-hydroquinones, and glucuronide conjugation to PCP- and tetrachloro-p-hydroquinone conjugates (Williams 1982). In soils, reductive dehalogenation appears to be the most significant PCP degradation pathway, producing mono-, di-, tri-, and tetrachlorophenols, as well as various tetrachlorocatechols and tetrachlorohydroquinones. Further degradation results in ring cleavage, liberation of chloride, and carbon dioxide evolution; degradation is more rapid in flooded or anaerobic soils than in aerobic moist soils (Kaufman 1978). Irradiation of PCP solutions with sunlight or ultraviolet light produces photodegradation products that include chlorinated phenols, tetrachlorodihyroxyl benzenes, and nonaromatic fragments such as dichloromaleic acid (Wong and Crosby 1978; EPA 1980). Subsequent irradiation of the tetrachlorodiols produces hydroxylated trichlorobenzoquinones, trichlorodiols, dichloromaleic acid, and nonaromatic fragments (Wong and Crosby 1978; Boyle et al. 1980). Prolonged irradiation of PCP or its degradation products yielded colorless solutions containing no ether-extractable volatile materials; evaporation of the aqueous layer left no observable polymeric residue Wong and Crosby 1978). Photolytic condensation of PCP to form octachlorodioxins was observed on a wood substrate. Octachlorodioxin residues ranged from 4 mg/kg for purified PCP, to about 1,500 mg/kg for technical grade PCP (Lamparski et al. 1980).

Pentachlorophenol can be degraded by microbial flora both aerobically and anaerobically; degradation is more rapid under aerobic conditions but slows significantly at temperatures <19 C (Pignatello et al. 1985, 1986). Several strains of aerobic bacteria can metabolize and degrade PCP: *Flavobacterium* sp., a pseudomonad, a coryneform bacterium, and a strain of *Arthrobacter* (Pignatello et al. 1983; Mikesell and Boyd 1986; Steiert and Crawford 1986; Steiert et al. 1987). Microbial degradation under aerobic or anaerobic conditions was the major process by which PCP was degraded in estuarine sediments; tidal transport and photodegradation played minor roles (DeLaune et al. 1983). The biotic process requires a moderately long adaptive response by the aquatic microflora, but eventually becomes the predominant mechanism of PCP removal (Pignatello et al. 1983, 1985). Several significant observations were recorded when the degradation and transformation of PCP were documented in freshwater streams continuously dosed with PCP for 16 weeks (Pignatello et al. 1983): photolysis accounted for a 5% to 28% decline in initial PCP concentrations and was most rapid at the water surface under conditions of bright sunlight; adsorption to sediments and uptake by biota accounted for less than 5% loss in acclimated waters and probably less than 15% in unacclimatized waters; and microbial degradation of PCP became significant about 3 weeks after dosing and eventually became the primary mechanism of PCP removal, accounting for up to a 46% decline in initial PCP.

The half-life (Tb 1/2) of PCP in water ranged from 0.15 to 1.5 days; degradation was most rapid under conditions of high incident radiation, high dissolved oxygen, and elevated pH (Bevenue and Beckman 1967Wong and Crosby 1978; Boyle et al. 1980; Niimi and Cho 1983; Crossland and Wolff 1985; Smith et al. 1987). The Tb 1/2 in the water column controlled by microbial degradation alone is usually 5 to 12 hours (Pignatello et al. 1986). Technical grade PCP was initially degraded at the same rate as reagent grade PCP by anaerobic microorganisms in municipal sewage sludge, but was later degraded more slowly. Dechlorination and mineralization (to carbon dioxide and methane) of the reagent grade PCP was complete in 7 to 9 days, but only half the technical grade PCP had been transformed in 6 to 10 days (Mikesell and Boyd 1986).

In soils, PCP persisted for 15 to more than 60 days, depending on soil conditions and application rate. At initial concentrations of 100 mg PCP/kg soil, the Tb 1/2 was 10 to 40 days at 30°C under flooded conditions; however, in aerobic soils there was virtually no degradation after 2 months (Kaufman 1978). In rice paddy soils, initial concentrations of 4 mg PCP/kg fell to 2 mg/kg in 7 days (Bevenue and Beckman 1967). Pentachlorophenol was still measurable after 12 months in warm, moist soils (Cote 1972; EPA 1980). In estuarine sediments, degradation was most rapid under conditions of increased oxygen and a pH of 8.0 (DeLaune et al. 1983).

Pentachlorophenol solutions in water at the appropriate pH and dissolved oxygen content decompose in sunlight, and this makes a strong case for the likelihood of essentially total PCP destruction in aquatic environments (Wong .and Crosby 1978). The short residence time of PCP in an aquatic system before degradation further suggests that biological effects would be most pronounced in localized areas that receive PCP continuously from a point source (Niimi and Cho 1983).

BACKGROUND CONCENTRATIONS

GENERAL

Measurable PCP concentrations in field collections of living and nonliving materials over widespread geographic areas are almost certainly due to anthropogenic activities, especially to the use of the chemical as a wood preservative.

BIOLOGICAL AND NONBIOLOGICAL SAMPLES

Pentachlorophenol-contaminated air, rain, snow, surface waters, drinking waters, groundwaters, and aquatic biota are common in the United States (Table 3; Pignatello et al. 1983; Choudhury et al. 1986). Residues of PCP in food, water, and mammalian tissues may result from the direct use of PCP as a wood preservative and pesticide or as a result of use of other chemicals that form PCP as degradation products--i.e., hexachlorobenzene and lindane (EPA 1980; Choudhury et al. 1986). To confound matters, PCP was judged to be the source of dioxin and dibenzofuran contamination in chickens in Canada (Ryan et al. 1985). More than 50% of all chickens sampled contained hexachlorinated dibenzo-p-dioxins (hexs CDDS) at concentrations of 27 ng/kg fat and higher; 62% contained hepta CDDs at more than 52 ng/kg, and 46% contained octa CDDs at more than 90 ng/kg; concentrations of hexa-, and heptachlorinated dibenzofurans were similar.

Pentachlorophenol was found at high concentrations in all samples of sediments, waters, and biota collected near industrial facilities that used PCP as a wood preservative (Niimi and Cho 1983; Table 3). Fish can bioconcentrate PCP from water up to 10,000 times (Fox and Joshi 1984). However, similar concentrations were measured in blue mussel, *Mytilus edulis* (Folke and Birklund 1986), and softshell clam, *Mya arenaria* (Butte et al. 1985), from the vicinity of PCP-contaminated wastewater discharges as well as from more distant collection sites; thus PCP bioaccumulation in marine bivalve molluscs does not appear to be dose related.

Table 3. Pentachlorophenol concentrations in nonbiological and living materials.

Compartment and units	Concentration	Reference[a]
Nonbiological		
Aquatic (µg/L)		
Rivers, Southwest Japan	1 to 10	1
Willamette River, Oregon	0.1 to 0.7	1
Waters of British Columbia	up to 7.3	1
Drinking water	0.06	2, 3
Northern California		
Moss landing, seawater	<1	4

Sacramento, sewage discharge	<1	4
Oroville		
Drainage water	20	4
Drinking water	227 (1 to 800)	4
Surface water	0.7	3
Near wood preserving facility, Bay of Quinte, Lake Ontario, 1978		
Surface film	5.8	5
Water column	5.7	5
Air (ng/m^3)		
Uninhabited mountainous area	~0.25	6
Rooms containing PCP-treated wood or paint	up to 160	6
Near PCP wood preservative facility	Usually 263 to 1,188; Max. 297,000	2
PCP pressure treating room	Max. 15,000	2
PCP storage areas	9 to 9,000	2
Sediments (µg/kg dry weight)		
Bay of Quinte, Lake Ontario, 1978	60	5
Biological		
Freshwater organisms (µg/kg fresh weight)		
Lake Ontario, western basin		
Fish, whole less intestine		
Rainbow trout, *Salmo gairdneri*	24 (10 to 39)	7
Lake trout, *Salvelinus namaycush*	Max. 11	7
Coho salmon, *Oncorhynchus kisutch*	Max. 21	7
Brown trout, *Salmo trutta*	6, Max. 11	7
Rainbow smelt, *Osmerus mordax*	Max. 0.5	7
Alewife, *Alosa pseudoharengus*	Max. 0.3	7
Bay of Quinte, Lake Ontario, 1978		
Fish, whole		
Brown bullhead, *Ictalurus nebulosus*	260	5
Yellow perch,		

Perca flavescens	155	5
Invertebrates		
Annelids	Max. 85	5
Chironomids	Max. 1	5
Alga		
Cladophora sp.	7	5
Marine organisms (µg/kg)		
Blue mussel,		
Mytilus edulis		
Denmark, 1985, soft parts		
Fresh weight	5 to 33	8
Dry weight	32 to 244	8
Lipid weight	398 to 3473	8
Wildlife (mg/kg whole mummified body)		
Dutch pond bat,		
Myotis dasycneme		
Netherlands, found dead		
Berlikum roost (treated with PCP)		
1974	8 to 36	9
1977	410 to 795	9
1978	746 to 1,105	9
1979	10 to 283	9
Tjerkwerd roost (Control site)		
1978	<7	9
1979	<4	9
Livestock, Canada (µg/kg)		
Fat, chicken and pork		
Lipid weight	Usually (60% frequency) >10	10
Liver, pig		
Fresh weight	Always >50	10
Man (µg/kg fresh weight)		
Unexposed		
Urine	2 to 11	2, 11
Blood serum	4 to 10	2, 11
Adipose tissue	12 to 52	11
Milk, nursing mothers, Bavaria, 1979–81	0.67 (0.03 to 2.8)	10
Exposed		
Urine	80 to 300	2
Blood serum	1,000 to 2,000; Max. 3,900	2

Daily diet (mg)	1 to 6	12

[a]References: 1, Dominguez and Chapman 1984; 2, EPA 1980; 3, Menzer and Nelson 1986; 4, Wong and Crosby 1978; 5, Fox and Joshi 1984; 6, Pignatello et al. 1983; 7, Niimi and Cho 1983; 8, Folke and Birklund 1986; 9, Leeuwangh and Voute 1985; 10, Ryan et al. 1985; 11, Gebefugi and Korte 1983; 12, Choudhury et al. 1986.

LETHAL AND SUBLETHAL EFFECTS

GENERAL

The toxicity of commercial or technical grades of PCP significantly exceeds that of analytical or purified PCP. Some of this added toxicity is attributed to impurities such as dioxins, dibenzofurans, chlorophenols, and hexachlorobenzene. Pentachlorophenol is rapidly accumulated and rapidly excreted, and has little tendency to persist in living organisms. It acts by uncoupling oxidative phosphorylation.

Terrestrial plants and soil invertebrates were adversely affected at 0.3 mg PCP/l (root growth), and at 1 to 5 g PCP/m^2 soil (reduction in soil biota populations).

Pentachlorophenol was most toxic and most rapidly metabolized in aquatic environments at elevated temperatures and reduced pH. Adverse effects on growth, survival, and reproduction of representative sensitive species of aquatic organisms occurred at PCP concentrations of about 8 to 80 ug/l for algae and macrophytes, about 3 to 100 ug/l for invertebrates (especially molluscs), and <1 to 68 ug/l for fishes, especially salmonids.

Fatal PCP doses for birds were 380 to 504 mg/kg BW (acute oral), >3,850 mg/kg in diets, and >285 mg/kg in nesting materials. Adverse sublethal effects were noted at dietary levels as low as 1.0 mg/kg ration. Residues (mg/kg fresh weight) in birds found dead from PCP poisoning were >11 in brain, >20 in kidney, >46 in liver, and 50 to 100 in egg.

Data are scarce on the toxicity of PCP to mammalian wildlife, but studies with livestock and small laboratory animals show that the chemical is rapidly excreted. However, there is great variability between species in their ability to depurate PCP, as well as in their overall sensitivity. Acute oral LD-50's in laboratory animals were 27 to 300 mg/kg BW. Tissue residues were elevated at dietary levels as low as 0.05 mg/kg feed and at air levels >0.l mg/m^3. Histopathology, reproductive impairment, and retarded growth were evident at doses of 0.2 to 1.25 mg/kg BW, and when the diets fed contained >30 mg PCP/kg.

TERRESTRIAL PLANTS AND INVERTEBRATES

Pentachlorophenol is toxic to plant mitochondria; the mode of action is similar to that in other organisms--i.e., uncoupling of oxidative phosphorylation. At 267 ug PCP/L, 50% uncoupling was noted in isolated mitochondria of potato, *Solanum tuberosum*, and mung bean, *Phaseolus aureus* (Ravanel and Tissut 1986). Both PCP and its metabolite tetrachlorohydroquinone adversely affect cell growth and synthesis of RNA and ribosome in yeast, *Saccharomyces* sp., in a dose-related manner (Ehrlich et al. 1987).

Uptake of PCP by rice (*Oryza sativa*) grown over a 2-year period under flooded conditions was studied after a single application of radiolabeled PCP was applied to the soil at 23 kg/ha (Weiss et al. 1982). During the first year, PCP uptake was 12.9% of the application. Roots contained about 5 mg PCP/kg, distributed as follows (mg/kg): 3.95 as unextractable residues, 0.48 as polar nonhydrolyzable substances, 0.43 as free and conjugated lower chlorinated phenols, 0.14 as free PCP, 0.07 as anisoles, 0.06 as conjugated PCP, 0.03 as hydroxymonomethoxytetrachlorobenzenes, and 0.01 as dimethoxytetrachlorobenzenes. In the second year, PCP uptake was reduced to 2.5%, and soil residues corresponded to 8.4 kg/ha; the amounts of unextractable residues in plants increased, and lower chlorinated conjugated phenols were identified (Weiss et al. 1982). Root growth in rice seedlings was inhibited 50% at 0.3 mg PCP/1 (Nagasawa et al. 1981).

Pentachlorophenol applied to beech forest soils every 2 months for 2 years at the rate of 1.0 g/m^2 markedly reduced populations of soil organisms; at 5.0 g/m^2, it drastically reduced most of the soil animal species, and also the microflora (Zietz et al. 1987). Reduction of the soil metabolism by PCP retards decomposition and affects the overall nutrient balance of forest ecosystems (Zietz et al. 1987).

AQUATIC BIOTA

Pentachlorophenol affects energy metabolism by partly uncoupling oxidative phosphorylation and increasing oxygen consumption, by altering the activities of several glycolytic enzymes and the citric acid cycle enzymes, and by increasing the consumption rate of stored lipid (Johansen et al. 1985; Brown et al. 1987; McKim et al. 1987). Collectively, these events could reduce the availability of energy for maintenance and growth and thereby reduce the survival of larval fish and the ability of prey to escape from a predator (Brown et al. 1985, 1987).

The accumulation of PCP in fishes is rapid, and primarily by direct uptake from water rather than through the food chain or diet (Niimi and Cho 1983). Signs of PCP intoxication in fish include rapid swimming at the surface and increased opercular movements, followed by loss of balance, settling to the bottom, and death (Holmberg et al. 1972;Gupta 1983). The PCP is rapidly excreted by fishes after conjugates of PCP-glucuronide and PCP-sulfate are formed; half-lives in tissues are less than 24 hours (EPA 1980). Major roles were played by gall bladder and bile in PCP-glucuronide depuration kinetics, and by gill in PCP-sulfate depuration (Kobayashi 1978; Lech et al. 1978; McKim et al. 1986). It has been suggested that the efficient elimination of PCP should allow vertebrates to tolerate periodic low doses of PCP without toxic effects (McKim et al. 1986).

Many species of aquatic organisms were found dead in rice fields of Surinam, South America, after they were sprayed with PCP to control populations of snails (Vermeer et al. 1974). Residues of PCP in dead organisms (mg PCP/kg fresh body weight) were 8.1 in frogs (*Pseudis paradoxa*); 36.8 in snails (*Pomacea* spp.); and, in three species of fish, 31.2 in krobia (*Cichlasoma bimaculatum*), 41.6 in kwi kwi (*Hoplosternum littorale*), and 59.4 in srieba (*Astyanax bimaculatus*). Pentachlorophenol was also implicated in fish kills in Europe and North America, all of which were associated with the pulpwood industry (Schimmel et al. 1978). In December 1974, near Hattiesburg, Mississippi, water containing PCP in fuel oil that overflowed the banks of a holding pond of a wood-treatment waste water facility killed all fish in a 24 ha lake. Concentrations of PCP in water and fish returned to background concentrations 10 months after the spill; however, the chemical persisted in leaf litter and sediments for at least 17 months after the spill (Pierce and Victor 1978). In December 1976, another fish kill was observed near the same facility. Residues of PCP in surviving fish--including bluegills (*Lepomis macrochirus*), largemouth bass (*Micropterus salmoides*), and channel catfish (*Ictalurus punctatus*)--were greatly elevated one month later: 8 to 19 mg PCP/kg fresh weight in muscle, 42 to 48 mg/kg in gill, and 130 to 221 mg/kg in liver (Pierce and Victor 1978). Pentachlorophenol persisted in fish for 6 to 10 months before reaching background concentrations.

Studies with experimental ecosystems have indicated that the effects of PCP on community structure and activity are profound. These included a reduction in the number of individuals and species of estuarine macrobenthos after exposure to 55 to 76 ug PCP/l for 5 to 9 weeks (Tagatz et al. 1977, 1983) or 15.8 ug/l for 13 weeks (Tagatz et al. 1978); a decrease in periphyton biomass, fish growth, and larval drift, and a suppression of community metabolism at 48 ug PCP/l after 3 months exposure (Hedtke and Arthur 1985; Zischke et al. 1985; Yount and Richter 1986); elevated levels of PCP in postlarval shrimp, *Penaeus vannamei*, after chronic exposure to 10 ug PCP/1 (Seidler et al. 1986); and bioconcentration factors after exposure to radiolabeled PCP of 5X for an alga (*Oedogonium cardiacum*), 21X for a snail (*Physa* sp.), 26X for a mosquito larva (*Culex pipiens quinquefasciatus*), 132X for mosquitofish (*Gambusia affinis*), and 205X for *Daphnia magna* (^{14}C pentachlorophenol in laboratory model ecosystems. Pages 53-63 Lu et al. 1978)

In laboratory studies, increased accumulation and adverse effects on growth, survival, and reproduction were seen in sensitive species of aquatic organisms: in algae and macrophytes at water concentrations (ug PCP/1) of 7.5 to 80; in a wide variety of invertebrates, especially molluscs, at 2.5 to 100; and in fishes, especially salmonids, at <1.0 to 68 (Table 4).

Biocidal properties of PCP were significantly modified by water pH and temperature, and by the purity of PCP compounds tested. In general, PCP was most toxic and was metabolized most rapidly (Table 4) at elevated water temperatures (EPA 1980; Hodson and Blunt 1981; Niimi and Palazzo 1985; Fisher 1986) and at reduced pH (Bevenue and Beckman 1967; EPA 1980; Dave 1984; Choudhury et al. 1986; Fisher 1986; Seidler et al. 1986). Increasing pH of the water column decreases the hazard of PCP to aquatic biota: at pH above 4.8, for example, hydroxyl proton is dissociated and penetration in aquatic organisms is reduced (Fisher 1986). All authorities agree that commercial or technical grades of PCP are significantly more toxic to aquatic organisms

than is purified PCP (EPA 1980; Cleveland et al. 1982; Huckins and Petty 1983; Dominguez and Chapman 1984; Stuart and Robinson 1985; Hamilton et al. 1986; Nagler et al. 1986). The sublethal effects of low concentrations of commercial PCP to aquatic biota are due primarily to impurities composed mostly of octa- and nonachlorophenoxyphenols (Hamilton et al. 1986), and also to relatively large quantities of hexachlorobenzene, dioxins, and dibenzofurans (Cleveland et al. 1982).

BIRDS

Signs of PCP intoxication in birds include excessive drinking and regurgitation, rapid breathing, wing shivers or twitching, jerkiness, shakiness, ataxia, tremors, and spasms (Hudson et al. 1984). Signs sometimes appear within 10 minutes. Mallards usually die 2 to 24 hours posttreatment, and ring-necked pheasants 3 to 5 days posttreatment; remission in pheasants requires up to 2 weeks (Hudson et al. 1984).

Pentachlorophenol killed various species of birds at single oral doses of 380 to 504 mg/kg BW, at dietary concentrations of 3,850 mg/kg ration fed over a 5-day period, and when nesting materials contained >285 mg/kg. Residues (mg/kg fresh weight tissue) in birds found dead from PCP poisoning were 11 in brain, 20 in kidney, 46 in liver, and 50 to 100 in egg (Table 5). Sublethal effects, including liver histopathology and diarrhea, were reported in domestic chickens at dietary levels as low as 1 mg PCP/kg feed over an 8-week period; significant accumulations in tissues were measured after consumption for 14 days of diets containing 10 mg PCP/kg (Table 5). Residues in chickens fed PCP-containing diets for 8 weeks were dose-related and highest in kidney and liver and lower in other tissues; the high residues may reflect the principal routes of metabolism and excretion (Stedman et al. 1980). The loss of body fat in chickens, accomplished by feeding bile acid binding resins, hastens PCP excretion (Table 5; Polin et al. 1986).

Table 4. Lethal and sublethal effects of pentachlorphenol on selected species of aquatic organisms.

Species and other variables	Concentration, in µg PCP/L medium	Effect	Reference[a]
Algae and macrophytes			
Alga, *Chlorella pyrenoidosa*	7.5	Total chlorosis inhibition in 72 h	1
Alga, *Skeletonema costatum*	17 to 20	50% reduction in cell numbers at 96 h	1
Filamentous algae (*Chara* sp., *Enteromorpha* sp.)	50 to 100	Lethal in 30 days in outdoor ponds; Their decay was responsible for depression of dissolved oxygen and later fish deaths	2
Alga, *Scenedesmus costatum*	80	50% growth inhibition in 96 h	2
Alga, *Selenastrum capricornutum*	110 to 150	50% growth reduction in 96 h in soft water	3
S. capricornutum	290	50% growth inhibition in 96 h	2
S. capricornutum	760	50% growth reduction in 96 h in hard water	3
Alga, *Dunaliella tertiolecta*	170 to 206	50% reduction in cell numbers in 96 h	1
Alga, *Thalassiosira pseudonana*	179 to 189	50% reduction in cell numbers in 96 h	

Duckweed, *Lemna minor*	800	50% inhibition of chlorosis in 48 h	1
L. minor	1,000	Inhibition of photosynthetic oxygen production	5
L. minor	1,400	No measurable effect after exposure for 21 days	4
Invertebrates			
Eastern oyster, *Crassostrea virginica*	2.5	BCF of 78x in 28 days; 100% depuration within 4 days postexposure	6
C. virginica	25	BCF of 41x between days 4 and 28 of exposure; 100% depuration within 4 days postexposure	6
C. virginica	34	50% reduction in shell deposition in 8 days	1
C. virginica	40	50% abnormal development of larvae in 48 h	7
C. virginica	77	LC-50 (96 h)	1
Cladoceran, *Ceriodaphnia reticulata*	4.1	Reduction in number of young produced per female in lifetime exposure	4
C. reticulata	164	LC-50 (48 h)	8
Polychaete worm, *Ophryotrocha diadema*	10 to 13	No effect on reproduction in 41 days	8
O. diadema	23 to 75	50% inhibition in reproduction in 41 days	8
Clam, *Mulinia lateralis*	15.8	Populations reduced after 7 days	9
Razor clam, *Ensis minor*	15.8	Populations reduced after 7 days	9
Hydra, *Hydra littoralis*	19	Threshold for reproduction inhibition	8
Snail, *Physa gyrina*	26	Reproduction in number of egg masses produced and in egg survival during lifetime exposure	4, 10
P. gyrina	220	LC-50 (96 h) at 24 °C	4
P. gyrina	730	LC-50 (96 h) at 8.6 °C	11
P. gyrina	1,380	LC-50 (96 h) at 3.2 °C	4
Pacific oyster, *Crassostrea gigas*	55	62% of exposed embryos developed abnormally in 48 h	1
Midge, *Chironomus riparius*, 4th instar	84	LC-50 (24 h) at pH 4	12
C. riparius	465	LC-50 (24 h) at pH 6	12
C. riparius	631	50% locomotion inhibition at 35 °C	13
C. riparius	1,176	50% locomotion inhibition at 15 °C	13
C. riparius	1,948	LC-50 (24 h) at pH 9	12
Snail, *Lymnaea acuminata*	100	LC-16 (96 h)	14

L. acuminata	160	LC-50 (96 h)	14
L. acuminata	210	LC-84 (96 h)	14
Snail, *Australorbis glabratus*	100	Reduction in egg production and viability after exposure for 7 to 8 days	2
Sea urchin, *Paracentrotus lividus*, embryos	100	Reductions in various amino acid activity levels during exposure for 40 h	15
P. lividus	200	Number and size of swimming blastulae, gastrulae, and plutei reduced in 40-h exposure	15
Short-necked clam, *Tapes philippinarum*	100	Lethal in 120 h	16
Snail, *Lymnaea luteola*	112	LC-50 (96 h)	17
Flatworm, *Pugesia lugubris*	130	LC-50 (48 h)	8
Snail, *Lymnaea stagnalis*	180	LC-50 (16 days)	2
Cladoceran, *Daphnia magna*	180	No observable effect level in lifetime exposure	1
D. magna	320	Some adverse effects observed in lifetime exposure	1
D. magna	370 to 440	50% immobilization in 48 h	18
D. magna	475	LC-50 (96 h)	1
Cladoceran, *Simocephalus vetulus*	204	LC-50 (96 h) at 24 °C	4
S. vetulus	670	LC-50 (96 h) at 18 °C	11
Tubificid worm, *Tubifex tubifex*	286	LC-50 (24 h) at pH 7.5	1
T. tubifex	619	LC-50 (24 h) at pH 8.5	1
T. tubifex	1,294	LC-50 (24 h) at pH 9.5	1
Snail, *Gillia altilis*	300	LC-50 (96 h) in flow-through test	19
G. altilis	810	LC-50 (96 h) in static test	19
Mysid, *Mysidopsis bahia*	320	LC-50 (96 h)	20
Grass shrimp, *Palaemonetes pugio*	400 to 440	LC-50 (96 h) during molting	20, 21
P. pugio	473 to 637	Adversely affects initiation and progress of limb regeneration without altering duration of molt cycle	22
P. pugio	649 to 1,200	LC-50 (96 h)	1, 7
P. pugio	1,000	Histopathology of gill, hepatopancreas, and midgut epithelial cells after exposure for 12 days in shrimp that molted; normal tissues in shrimp that had not yet molted	21
P. pugio	2,500	LC-50 (96 h) during intermolt	20, 21

Polychaete worm, *Neanthes arenaceodentata*	435	LC-50 (96 h)	1
Amphipod, *Gammarus pseudolimnaeus*	770	Significant decreases in free amino acids after 5 days; in whole body glycogen, protein, and caloric content after 15 days; and in lipid content after 30 days	23
G. pseudolimnaeus	860	LC-50 (30 days)	23
G. pseudolimnaeus	1,150	LC-50 (96 h)	24
G. pseudolimnaeus	1,680	At 48 h, significant decrease in total free amino acid levels	24
Pond snail, *Vivparus bengalensis*	840	LC-50 (96 h)	25
Caddisfly, *Philarctus quaeris*	1,200	LC-50 (96 h)	11
Mayfly, *Callibaetis skokianus*	1,700	LC-50 (96 h)	11
Amphipod, *Crangonyx psedogracilis*	1,900	LC-50 (96 h)	11
Isopod, *Asellus racovitzai*	2,300	LC-50 (96 h) at 8.6 °C	11
A. racovitzai	4,320	LC-50 (96 h) at 4.2 °C	4
A. racovitzai	>7,770	LC-50 (96 h) at 3.2 °C	4
Crayfish, *Astacus fluviatilis*	9,000	LC-50 (8 days) at pH 6.5	26
A. fluviatilis	53,000	LC-50 (8 days) at pH 7.5	26
Vertebrates			
Rainbow trout, *Salmo gairdneri*	0.035	After 115 days, whole fish BCF 286x to 572x; half eliminated in 7 days	8, 57
S. gairdneri	0.7	After 115 days, BCF of 160x in whole fish; Tb1/2 elimination time of 7 days	8, 57
S. gairdneri	1.0	Whole body BCF of 221x in 18 h and 466x in 11.7 days; Tb1/2 of 65 h and 95% depuration in 12 days. Highest PCP tissue residues were bile >> liver >> blood > kidney > spleen > skin-bone-gill-gonad > muscle	27
S. gairdneri	7.4	27% inhibition of growth in 28 days	1
S. gairdneri	10 to 20	Some deaths during exposure from fertilization to yolk-sac absorption; 100% dead at 5 mg dissolved oxygen (DO)/L and 20 mg PCP/L; 100% dead at 3 mg DO/L and 10 mg PCP/L	28
S. gairdneri	11	No adverse effects observed during exposure from fertilization through day 72	29

S. gairdneri	19	Embryo mortality negligible during exposure from fertilization through day 72. Alevin mortality 3x greater than in controls. Growth in length and weight reduced. Fin erosion, mild cranial malformations, and lethargy reported	29
S. gairdneri	22	48% reduction in viable oocytes after exposure for 18 days	30
S. gairdneri	25	After 24 h, BCF of 40x in muscle, 240x in fat, 260x in blood, and 640x in liver. Tb1/2 values ranged from 7 h in muscle to 23 h in fat	31, 58
S. gairdneri	28	11% to 19% inhibition in growth in 20 to 38 days	1
S. gairdneri	34 to 121	LC-50 (96 h)	1, 29, 32, 33, 34
S. gairdneri	40	100% mortality during exposure from fertilization to yolk-sac absorption (72 days)	28
S. gairdneri	46	LC-100 (41 days)	1
S. gairdneri	49	81% reduction in oocytes available to complete oogenesis after exposure for 18 days	30
S. gairdneri	60	Eye abnormalities noted in developing embryos after exposure for 17 days; all dead at day 72 of exposure	29
S. gairdneri	10,000	LC-50 (3.5 h)	35
Sockeye salmon, *Oncorhynchus nerka*	3.2	10% growth inhibition in 6 weeks	1
O. nerka	63 to 68	LC-50 (96 h)	1, 56
Common carp, *Cyprinus carpio*	9.5	LC-50 (96 h), larvae	8
C. carpio	266	Reduction in liver glucose and glycogen release after 3 days; high accumulations in liver	36
C. carpio	1,500	LC-50 (3 h)	37
Largemouth bass, Micropterus salmoides	10	Food conversion efficiency significantly reduced in a concentration-dependent fashion at concentrations >10 µg/L	38
M. salmoides	25.2	Growth reduction after exposure for 52 days	38
M. salmoides	45	Decline in feeding activity after 8 weeks	38

M. salmoides	50	After 14 days, food conversion efficiency reduced 30%, reduction in ability to capture prey and in food consumed	39
M. salmoides	54	LC-50 (120 days)	38
M. salmoides	67	Exposure for 8 weeks produced hyperactivity and reductions in feeding rate and in prey capture	40
M. salmoides	136 to 287	LC-50 (96 h)	38, 39, 41
Rasbora, *Rasbora daniconius neilgeriensis*	10	LC-0 (96 h)	42
R.d. neilgeriensis	67	LC-16 (96 h)	42
R.d. neilgeriensis	148	LC-50 (96 h)	42
R.d. neilgeriensis	330	LC-84 (96 h)	42
Pinfish, *Lagodon rhomboides*	31 to 53	LC-50 (96 h)	1, 7, 20
Bluegill, *Lepomis macrochirus*	32 to 215	LC-50 (96 h)	1, 11, 32, 33
L. macrochirus	100	After exposure for 8 days, BCF 13x in muscle, 60x in gill, 210x in gastrointestinal tract, and 350x in liver. Rapid elimination, but some residues in muscle and liver were detectable 16 days postapplication	43
L. macrochirus	100	Liver histopathology after 32 days; degenerative changes detectable after 2 days	44
L. macrochirus	432	LC-100 (8 days)	10
Fathead minnow, *Pimephales promelas*	45	No observable effect level in lifetime exposure	1, 54
P. promelas	48	Growth and larval drift reduced after exposure for 12 weeks	10
P. promelas	50	Whole body BCF of 174x after 14 days; nondetectable residues after 14 days in clean water	45
P. promelas	73	Some adverse effects in lifetime exposure	1, 54
P. promelas	85	Growth reduction after 90 days exposure	46
P. promelas	120	LC-50 (96 h) at 16.6 °C	4
P. promelas	170	LC-50 (96 h) at 10.1 °C	4
P. promelas	200 to 350	LC-50 (96 h)	2, 11, 35
P. promelas	300	LC-50 (96 h) at 3.4 °C	4
Atlantic salmon, *Salmo salar*	46	Altered temperature preference in 24 h	1

S. salar	500	LC-50 (96 h)	35
S. salar	2,000	LC-50 (10.5 h)	35
S. salar	10,000	LC-50 (2.7 h)	35
Sheepshead minnow, *Cyprinodon variegatus*	47	No observable effect level in lifetime exposure	1
C. variegatus	88	12% mortality in lifetime exposure	47
C. variegatus	195	Life cycle exposure resulted in reduced hatch and survival of second generation fish	47
C. variegatus	223 to 392	LC-50 (96 h) for fry age 1 day to 6 weeks	7
C. variegatus	389	LC-100 (60 days)	47
C. variegatus	442	LC-50 (96 h)	1, 47
Flounder, *Pleuronectes platessa*	50	LC-50 (8 weeks), eggs	8
P. platessa	60 to 140	LC-50 (96 h), larvae	8
P. platessa	100 to 130	LC-50 (96 h), juveniles	8
Channel catfish *Ictalurus punctatus*	54 to 68	LC-50 (96 h)	8, 32, 33
Coho salmon, *Oncorhynchus kisutch*	55	LC-50 (96 h)	1
White crappie, *Pomoxis annularis*	56 to 75	LC-50 (96 h)	35
Longnose killifish, *Fundulus similis*	57 to 610	Whole body BCF of 53x after 168 h; Tb1/2 of 4. 7 days. Whole body residues up to 33 mg/kg fresh weight	48
Chinook salmon, *Oncorhynchus tshawytscha*	68 to 78	LC-50 (96 h)	1, 32, 55
White sucker, *Catostomus commersoni*	85	LC-50 (96 h)	4
Eel, *Anguilla anguilla*	100	Seawater-exposed eels, after exposure for 8 days, had 33 mg PCP/kg fresh weight in liver, 9 in muscle, and 4 in blood; after depuration for 8 days, values were 12 in liver, 4 in muscle, and 2 in blood. Eels exposed in freshwater for 4 days had 2 to 9 mg PCP/kg tissue, and <1.2 mg/kg 38 days postexposure	49
Goldfish, *Carassius auratus*	100	BCF of 1,000x after 12 h. Residues in dead fish were 82 to 116 mg PCP/kg	

		BW; no surviving fish contained more than 114 mg/kg	16, 48
C. auratus	200	Whole body residue of 116 mg/kg after exposure for 120 h	48
Tilapia, *Tilapia nilotica*	100	In 24-h tests, fish acclimatized to seawater were twice as resistant as freshwater-acclimatized fish to biocidal PCP properties, and contained lower residues	50
Mullet, *Rhinomugil corsula*	100	Metabolic rate elevated after 3 h	37
R. corsula	1,000	LC-50 (3 h)	37
Striped mullet, *Mugil cephalus*	112	LC-50 (96 h), whole body BCF of 38x	1, 6
Brook trout, *Salvelinus fontinalis*	128	LC-50 (96 h)	1
Salamander, *Ambystoma mexicanus*	130	LC-0 (48 h)	8
A. mexicanus	300	LC-50 (48 h)	8
Common shiner, *Notropis cornutus*	180	25% growth reduction after exposure for 7 days	51
N. cornutus	320	LC-100 (7 days)	51
Fish, 19 species	200 to 600	LC-50 (96 h)	35
Frog, *Xenopus laevis*	210	LC-0 (48 h)	8
X. laevis	260	LC-50 (48 h)	8
Guppy, *Poecilia reticulata*	500 to 700	Reduction in ability to escape from piscine predators	52
P. reticulata	700	LC-21 (30 days)	52
P. reticulata	1,000	LC-0 (12 days); possible acclimatization	53
P. reticulata	1,020	LC-50 (96 h)	52
Sea lamprey, *Petromyzon marinus*	924	LC-100 (4 h)	1

[a]References: 1, EPA 1980; 2, Crossland and Wolff 1985; 3, Smith et al. 1987; 4, Hedtke et al. 1986; 5, Huber et al. 1982; 6, Schimmel et al. 1978; 7, Borthwick and Schimmel 1978; 8, Choudhury et al. 1986; 9, Tagatz et al. 1981; 10, Zischke et al. 1985; 11, Hedtke and Arthur 1985; 12, Fisher and Wadleigh 1986; 13, Fisher 1986; 14, Gupta and Rao 1982; 15, Ozretic and Krajnovic-Ozretic 1985; 16, Kobayashi 1978; 17, Gupta et al. 1984; 18, Berglind and Dave 1984; 19, Stuart and Robinson 1985; 20, Mayer 1987; 21, Rao and Doughtie 1984; 22, Rao et al. 1978; 23, Graney and Giesy 1987; 24, Graney and Giesy 1987; 25, Gupta and Durve 1984; 26, Kaila and Saarikoski 1977; 27, McKim et al. 1986; 28, Chapman and Shumway 1978; 29, Dominguez and Chapman 1984; 30, Nagler et al. 1986; 31, Lech et al. 1978; 32, Johnson and Finley 1980; 33, Mayer and Ellersieck 1986; 34, McKim et al. 1987; 35, Cote 1972; 36, Yousri and Hanke 1985; 37, Peer et al. 1983; 38, Johansen et al. 1987; 39, Mathers et al. 1985; 40, Brown et al. 1987; 41, Johansen et al. 1985; 42, Gupta 1983; 43, Pruitt et al. 1977; 44, Owen and Rosso 1981; 45, Huckins and Petty 1983; 46, Cleveland et al. 1982; 47, Parrish et al. 1978; 48, Trujillo et al. 1982; 49, Holmberg et al. 1972; 50, Tachikawa et al. 1987; 51, Borgmann and Ralph 1986; 52, Brown et al. 1985; 53, Norup 1972; 54, Holcombe et al. 1982; 55, Iwama and Greer 1979; 56, Webb and Brett 1973; 57, Niimi and McFadden 1982; 58, Glickman et al. 1977.

Table 5. Effects of pentachlorophenol on selected species of birds.

Species and other variables	Effect and reference
Mallard, *Anas platyrhynchos*	Acute oral LD-50 of 380 mg/kg body weight (BW); 95% confidence interval 205 to 704 mg/kg BW (Hudson et al. 1984)
Japanese quail, *Coturnix japonica*. Birds age 14 days were fed treated diets for 5 days, then untreated feed for 3 days	No deaths at 3,100 mg/kg diet, 35% dead at 3,850, 50% at 5,139 (4,149 to 6,365), and 69% dead at 6,000 mg PCP/kg diet (Hill and Camardese 1986)
Domestic chicken, *Gallus gallus*. Fed diets containing 1, 10, 100, or 1,000 mg PCP/kg for 8 weeks	Liver histopathology and diarrhea recorded in all treated groups vs. non in controls. The 1,000 mg/kg diet was the only ration to adversely affect the weight of all organs analyzed. After 5 weeks on PCP-free diet, residues were still measurable in adipose tissues of all treated birds (Stedman et al. 1980)
Domestic chicken. Fed dietary levels of 600, 1,200, or 2,400 mg/kg for 8 weeks	No deaths in any group. Residues (mg/kg fresh weight) in 600 mg/kg group at 8 weeks were 2 in muscle, 10 in fat, 25 in liver and 80 in kidney vs. <0.02 in controls; no significant difference from controls in growth, blood chemistry, histopathology, or immune response. In the 1,200- and 2,400-mg/kg groups body weight decreased and liver weight increased; tissue residues were dose related (Prescott et al. 1982)
Domestic chicken. Raised over wood shavings containing 134 mg PCP/kg for 9 weeks	The PCP residues (mg/kg FW) were 3.7 in liver 0.4 in muscle, and 0.3 in fat, vs. <0.08 in controls (Newsome et al. 1984)

Domestic chicken. Fed diets containing 10 mg PCP/kg for 14 days, then 21 days on PCP-free diets containing either no additives, 5% mineral oil, or 5% colestipol hydrochloride	Body burden at 14 days was 362 µg/bird or 1.1 µg/kg BW. After 21 days, body burdens were 255 µg/bird in no-additive diet and nondetectable levels of <0.7 µg/bird in mineral oil and colestipol additive diets (Polin et al. 1986)
Domestic chicken. Eggs received single injected dose	Hatching reduced 50% at a dose of 50 mg PCP/kg egg and 100% at 100 mg/kg (none hatched) (Stedman et al. 1980)
Ring-necked pheasant, *Phasianus colchicus*	Acute oral LD-50 of 504 mg/kg BW; 95% confidence interval 343 to 743 mg/kg BW (Hudson et al. 1984)
Snail kite, *Rostrhamus sociabilis.* Found dead in rice fields after spraying to control populations of snails (*Pomacea glauca, P. lineata*)--the exclusive food of snail kites. Residues in soft parts of snails found dead after spraying were about 37 mg PCP/kg fresh weight	Residues in dead snail kites, in mg PCP/kg FW, were 46 in liver, 20 in kidney, and 11 in brain vs. <0.2 in controls, and 2 to 17 in birds surviving exposure (Vermeer et al. 1974)
Canary, *Serinus canarius*. Nesting on straw containing 285 mg PCP/kg	Reduced hatch, high mortality of young during the first week posthatch, and none surviving to age 3 months. Prior to death, young showed inhibited growth and feather development. Adult birds appeared normal (Dorrestein and Zelle 1979)

Spraying of PCP to control populations of water snails in rice fields of Surinam resulted in the death of fish and birds, including snail kites (*Rostrhamus sociabilis*), certain egrets and herons, and wattled jacanas (*Jacana jacana*). Levels of PCP in these birds and their food items suggested that PCP-contaminated food probably caused the deaths (Vermeer et al. 1974; Table 5).

Pentachlorophenol is widely used as a wood preservative, which often results in residues in wood shavings used as poultry litter. A moldy smell and taste in chicken tissue has been traced to the presence of chloroanisoles formed from PCP and tetrachlorophenol in the bedding. Several dioxins, diphenyl ethers,

dibenzofurans, and 2-phenoxyphenols have also been identified (Newsome et al. 1984). For example, PCP-contaminated (134 mg/kg) commercial wood shavings used as chicken litter contained detectable levels of heptachlorinated diphenyl ethers (18 ug/kg), octachlorinated diphenyl ethers (12 ug/kg) nonachlorinated diphenyl ethers (6 ug/kg), octachlorinated 2-phenoxyphenols (299 ug/kg), nonachlorinated 2-phenoxyphenols (50 ug/kg), heptachlorinated dibenzodioxins (19 ug/kg), and octachlorinated dibenzodioxins (143 ug/kg). After 9 weeks, PCP was detectable in liver, fat, and muscle; chlorinated diphenyl ethers were detectable in fat, but not in muscle or liver; octa- and nonachlorinated 2-phenoxyphenols were found in all three tissues; and dioxins only in liver and fat (Newsome et al. 1984). Exposure of domestic chickens to litter contaminated with PCP enhanced susceptibility to common poultry pathogens, perhaps due to immunosuppression by the chemical (Prescott et al. 1982).

MAMMALS

Data are scarce on the biological effects of PCP on mammalian wildlife, although evidence continues to accumulate on this subject for man, livestock, and small laboratory animals. Available data on PCP and mammals are briefly summarized, but it is not now clear if these findings are applicable to representative species of sensitive mammalian wildlife.

Pentachlorophenol tends to accumulate in mammalian tissues unless it is efficiently conjugated into a readily excretable form (Kinzell et al. 1985). The ability to conjugate PCP varies widely among species (Braun and Sauerhoff 1976; EPA 1980). For example, both laboratory rats (*Rattus* sp.) and humans eliminate about 75% of all PCP in the urine in an unconjugated form, but rhesus monkeys (*Macaca mulatta*) are unable to excrete PCP efficiently, whereas mice were the most efficient. As one result, Tb 1/2 values were low (about 24 hours) for mice, high (up to 360 hours) for rhesus monkey, and intermediate for rats and humans (EPA 1980). In man, however, the observed elimination half-life indicates that steady-state body burdens are 10 to 20 times higher than values extrapolated from animal pharmacokinetic data (Uhl et al. 1986).

Pentachlorophenol is not a carcinogen, and the evidence for mutagenicity is mixed. No carcinomas were produced in rodents, regardless of the composition of the PCP solution tested or route of exposure (EPA 1980; Choudhury et al. 1986). Some studies suggested that PCP may be mutagenic in the bacterium *Bacillus subtilis*, the yeast *Saccharomyces cerevisiae*, and in laboratory mice (*Mus* sp.), but not in two other species of bacteria tested--*Salmonella typhimurium* and *Escherichia coli* (Choudhury et al. 1986).

The primary sources of PCP in man include direct intake by way of diet, air, or water and through contact with PCP-contaminated materials (Uhl et al. 1986). The chief routes of exposure in an industrial setting are by way of inhalation and skin contact. Percutaneous absorption is significantly enhanced when PCP is dissolved in organic solvents, such as fuel oil, or when PCP comes in contact with open cuts and scratches (Wood et al. 1983). Pentachlorophenol has resulted in death in man through suicide and occupational and accidental exposures (EPA 1980; Rozman et al. 1982; Lambert et al. 1986).

Cases of PCP poisoning, including fatalities, were characterized by high fever, renal insufficiency, profuse perspiration, rapid heart beat and breathing, abdominal pain, dizziness, nausea, spasms, and death 3 to 25 hours after onset of symptoms (Knudsen et al. 1974; EPA 1980; Wood et al. 1983). Postmortem examination showed kidney degeneration, inflamed gastric mucosa, edematous lungs, and centrilobular degeneration of liver (EPA 1980; St. Omer and Gadusek 1987). Symptoms of nonfatal PCP intoxication in man include conjunctivitis, chronic sinusitus, nasal irritation, upper respiratory complaints, sneezing, coughing, recurring headache, neurological complaints, weakness, and several types of skin lesions (Knudsen et al. 1974; EPA 1980; Rozman et al. 1982). All symptoms were related to proximity to PCP-treated wood, and sometimes to elevated PCP residues in serum and urine (Lambert et al. 1986). At the cellular level, PCP--like other halogenated phenols--uncouples oxidative phosphorylation. A possible antidote to PCP poisoning is the administration of cholestyramine, a compound that interferes with the enterohepatic cycle of PCP, and also increases its elimination directly across the intestinal wall (Rozman et al. 1982).

The exposure of livestock to PCP can result from ingestion of feeds stored or fed in PCP-treated wooden structures, licking of treated wood, cutaneous absorption by direct contact with treated wood, and inhalation of air containing preservative chemicals--particularly volatile chlorophenols (Forsell et al. 1981). Acute signs of PCP intoxication in various domestic and laboratory animals include elevated blood sugar, vomiting, elevated blood pressure, increased respiration rate, tachycardia, motor weakness, weakened eye reflex, frequent

defecation, high fever, collapse, asphyxial convulsions, and death followed by rapid rigor mortis (Knudsen et al. 1974; Nishimura 1984; St. Omer and Gadusek 1987). In domestic cattle (*Bos* sp.) PCP has also been associated with decreased milk production, skin lesions, increased mastitis, persistent infections, and reduced survival (Forsell et al. 1981).

Among sensitive species of mammals tested against PCP (Table 6), acute oral LD-50 values ranged from 27 to 300 mg/kg BW, but most values were between 55 and 150 mg/kg BW. Sublethal effects were noted at much lower concentrations than those causing death. They included elevated tissue residues at dietary intake; equivalent to 0.05 mg/kg BW, or atmospheric concentrations >0.1. mg/m^3; organ damage at 0.2 to 2.0 mg/kg BW; reproductive impairment at >1.25 mg/kg BW; and retarded growth and reproduction in animals fed rations containing >30 mg/kg (Table 6).

Many commercial lots of technical PCP are known to contain small--but possibly biologically significant--amounts of highly toxic dioxins, dibenzofurans, and hexachlorobenzene. These contaminants may be responsible for most of the toxicity of technical PCP preparations (McConnell et al. 1980; Parker et al. 1980; Wollesen et al. 1986; Holsapple et al. 1987). However, both technical and analytical grade PCP can induce hepatic mixed function oxidases in intoxicated rats and cattle. In cattle, this effect was observed in both calves and adults, and in hepatic as well as pulmonary microsomes, and seemed to be dose related (Shull et al. 1986).

Table 6. Effects of pentachlorophenol on selected animals.

Organism, dose, and other variables	Effects and reference
Domestic cattle, *Bos taurus*	
Oral dose of 0.05 or 0.5 mg/kg BW	Maximal plasma values of 1.5 and 9.6 mg/L, respectively. Calves fed grain and hay from a PCP-treated feeder for 10 days contained plasma PCP levels of 1.1 mg/L, but levels returned to normal after access to feeder was denied (Osweiler et al. 1984)
Fed equivalent of 0.2 mg/kg BW daily for 75 to 84 days, then 2.0 mg/kg BW daily for 50 to 62 days	No effect on milk production, feed intake, body weight, lymphocyte function, or histopathology of spleen, thymus, or lymph nodes. Postmortem examination showed enlarged liver, lungs, kidneys, and adrenals; significant loss of renal function (Forsell et al. 1981; Kinzell et al 1981)
Fed 0.2 mg/kg BW daily for 95 days, then given single oral dose of uniformly ring-labeled C^{14}-PCP; analyzed 4 days postadministration	Highest residues were in liver, kidney, and lungs; in milk, the fat fraction contained the greatest amount. Tb1/2 for absorption was 4.3 h, and for elimination 43 h. Most excretion was by way of urine (76%), then milk, and feces (5% each). In urine, PCP was present in the conjugated form (Kinzell et al. 1985)
Fed 20 mg technical grade PCP/kg BW daily for 10 days, then 10 mg/kg BW for an additional 60 days	No clinical effects noted during the 70-day treatment or during a 165-day posttreatment period. Contaminants in PCP--including several dioxins and hexachlorobenzene--were found in milk, fat, and blood. PCP residues in whole milk rose to 4 mg/kg, but

	declined to <0.1 mg/kg within a few days after PCP cessation (Firestone et al. 1979)
Female yearling Holsteins were fed technical or analytical grade PCP in diets at 20 mg/kg BW daily for 42 days (647 mg/kg diet), then 15 mg/kg BW daily for 118 days (491 mg/kg diet)	Technical grade PCP was related to decreased body weight and feed conversion efficiency, anemia, enlarged liver and lungs, decreased thymus weight, and lesions in urinary bladder mucosa. Holsteins exposed to analytical grade PCP were comparable to controls. The toxicity of PCP in cattle seems to be due to its contamination with toxic impurities, especially dioxins (McConnell et al. 1980; Parker et al. 1980)
140 mg/kg BW	Acute oral LD-50 (Knudsen et al. 1974)
Domestic dog, *Canis familiaris*	
150 to 200 mg/kg BW	Acute oral LD-50 (Knudsen et al. 1974)
Guinea pig, *Cavia porcellus*	
100 mg/kg BW	Acute oral LD-50 (Choudhury et al. 1986)
Hamster, *Cricetus* spp.	
1.25 to 20 mg/kg BW	Fetal deaths and resorption (EPA 1980)
Man, *Homo sapiens*	
Average concentrations of 0.0012 to 0.18 mg/m^3 air for 3 to 34 years among occupationally exposed workers	Concentrations of PCP in blood of 20 workers ranged between 0.023 and 0.775 mg/L and were below the "biological tolerance value" of 1.0 mg/L; no effect on sister chromatid exchange or chromosomal aberrations (Ziemsen et al. 1987)
<0.02 to >0.1 mg/L urine in occupationally exposed woodworkers	During a 16-day vacation and plant shutdown, urinary excretion accounted for 90% elimination in those with high initial PCP levels (i.e., >0.1 mg/L) to 67% elimination in those with initial urinary levels of 0.02 to 0.1 mg PCP/L, and to 34% reduction in workers with <0.02 mg/L; Tb1/2 was estimated at 33 h in urine and 30 h in plasma (Kalman and Horstman 1983)
Single oral dose of 0.1 mg/kg BW	In urine of four subjects, 74% was eliminated unchanged and 12% as PCP-glucuronide; 4% was eliminated in feces as PCP and PCP-glucuronide. A peak blood level of 0.25 mg/L was reached 4 h after dosing (EPA 1980)
>1.0 mg/m^3 air	Painful irritation in upper respiratory tract, sneezing, and coughing in persons newly exposed to PCP; up to 2.4 mg/m^3 can be tolerated by conditioned individuals (EPA 1980)

Total dose of 3.9 to 18.0 mg	Steady state attained in about 3 months; Tb1/2 values of 20 days in whole body and about 17 days in urine and blood (Uhl et al. 1986)
8 to 1,130 mg/kg fresh weight tissue	Residues in tissues of 33-year-old male who died after working in chemical plant for 3 weeks; job involved breaking up large blocks of PCP with jackhammer. Before death, high body temperature and coma. After death, rigor mortis was profound and immediate. Postmortem examination showed cerebral edema, fatty degeneration of viscera, and PCP levels (mg/kg) of 8 in stomach contents, 29 in urine, 52 in liver, 116 in lung, 162 in blood, 639 in kidney, and 1,130 in bile (Wood et al. 1983; Gray et al. 1985)
28 to 225 mg/kg fresh weight tissue	Residues associated with acute toxicosis and death were 28 to 123 in kidney, 50 to 176 in blood, and 62 to 225 in liver (EPA 1980)
75 to 225 mg/kg fresh weight tissue	Residues in tissues of PCP suicide victim were 75 in urine, 116 in kidney, 173 in blood, and 225 in liver (EPA 1980)
4,000 mg/L solution	Immersion of hands for 10 min produced skin irritation (EPA 1980)
Domestic cat, *Felis domesticus*	
Pine wood shavings used as litter, containing 470 mg PCP/kg	Of 14 cats in contact with litter, 3 died and 8 became ill but recovered. Maximum PCP residues (mg/kg) in the dead cats were 20 in liver, 24 in kidney, and 10 in stomach contents (Peet et al. 1977)
Rhesus monkey, *Macaca mulatta*	
10 mg/kg BW, single oral dose	Residues highest in liver and GI tract; all other tissues contributed <4% of total body burden (EPA 1980)
10 mg/kg BW, single oral dose	Tb1/2 values in blood and urine were 41 to 72 h in males and 84 to 92 h in females (Braun and Sauerhoff 1976)
50 mg/kg BW, repeated 4 weeks later	During the first day after each dose, 20% was excreted into urine 0.5% into feces, and 20% into bile. The addition of 4% cholestyramine to diets for 6 days resulted in increased fecal excretion by a factor of 18x and increased total body burden excretion by 1.4x (Rozman et al. 1982)
Mouse, *Mus musculus*	
Fed diets equivalent to 3 mg/kg BW daily for 24 months	No measurable effect in females, based on clinical chemistry, hematology, routine histopathology, and organ weight changes (EPA 1980)

Fed diets equivalent to 10 mg/kg BW daily for 22 months	No measurable effect in males, based on clinical chemistry, hematology, routine histopathology, and organ weight changes (EPA 1980)
15 to 37 mg/kg BW through intraperitoneal or subcutaneous route	Tb1/2 of about 24 h through urinary excretion (EPA 1980)
Fed diets containing 50 mg pure (99%) PCP/kg or technical grade (86%) for 10 to 12 weeks	Mice exposed to technical grade PCP had enhanced tumor susceptibility (1.9x) from transplanted tumors; mortality increased 2.4x over controls after sarcoma virus inoculation. Mice exposed to pure PCP showed no enhanced growth of reduced tumors, but developed splenic tumors; 22% vs. none in controls (Kerkvliet et al. 1982)
65 to 252 mg/kg BW	Acute oral LD-50; females more sensitive than males (Knudsen et al. 1974; Borzelleca et al. 1985; Choudhury et al. 1986)
White rabbit, *Oryctolagus cuniculus*	
1 to 3 mg/kg BW daily for 90 days administered orally	No signs of intoxication (EPA 1980)
39 mg/kg BW	Lethal cutaneous dose administered in pine oil (Cote 1972)
60 to 200 mg/kg BW	Acute dermal lethal dose (EPA 1980)
100 to 130 mg/kg BW	Acute oral LD-50 (Knudsen et al. 1974; Choudhury et al. 1986)
350 mg/kg BW	Lethal cutaneous dose administered in olive oil (Cote 1972)
Domestic sheep, *Ovis aries*	
120 mg/kg BW	Acute oral LD-50 (Knudsen et al. 1974)
Pipistrelle bat, *Pipistrellus pipestrellus*	
Females roosting in contact with timbers treated with 5% PCP solutions	All bats introduced 6 weeks postapplication died in 3 to 7 days; those introduced 8 weeks postapplication died in 1 to 2 days; bats in contact with timbers 14 months postapplication died in 5 to 23 days
Laboratory rat, *Rattus norvegicus*	
Dietary levels of 20, 100, and 500 mg/kg feed equivalent to 1.2, 6, and 30 mg/kg BW daily, respectively	No effect after exposure for 8 months to pure grade PCP at doses of 20 and 100 mg/kg. Technical grade PCP produced disruptions in liver enzyme activity in females at 20 and 100 mg/kg. At 500 mg/kg body weight gain was reduced in both sexes and by both grades of PCP (EPA 1980)

Diets containing 25, 50, or 200 mg PCP/kg, equivalent to 1.5, 3, and 12 mg/kg BW daily, respectively	After 12 weeks, no observable effect at 25 mg/kg diet; dose-related adverse effects on liver, kidney calcium deposits, and blood chemistry at higher dietary levels (Knudsen et al. 1974)
Dietary level of 50 mg/kg, equivalent to about 3 mg/kg BW daily	After 62 days, no observable effect on reproduction, neonatal growth, survival, or development. After 12 weeks, males had decreased hemoglobin and erythrocytes. After 2 years, no significant adverse effects on growth, survival, reproduction, or development (Schwetz et al. 1978; EPA 1980; McConnell et al. 1980)
5.0 to 5.8 mg/kg BW on days 6 to 15 of gestation	Delayed ossification of skull (EPA 1980)
10 mg/kg BW	After a single oral dose, 0.44% remained after 9 days; 82% of total residue was in kidney and liver, and lowest residues were in brain, spleen, and fat. A maximum residue of 45 mg/L was attained in blood plasma; the Tb1/2 in plasma was 13 to 121 h (EPA 1980)
10 or 100 mg/kg BW	After a single dose, elimination occurred by way of several routes: catabolism to tetrachlorohydroquinone; excretion of unchanged PCP and its glucuronide conjugate in urine; excretion of PCP or its metabolites into bile. More than 90% was eliminated during the rapid phase, the Tb1/2 being 13 to 17 h (Braun et al. 1977)
Dietary levels of 200 mg/kg, equivalent to about 13 mg/kg BW daily	After 181 days, reduction in crown-rump length and increase in fetal skeletal variations (Welsh et al. 1987)
15 mg/kg daily of purified PCP on days 6 to 15 of gestation	No measurable effect on development (EPA 1980)
27 to 300 mg/kg BW	Acute oral LD-50 range. Lower values in tests when PCP dissolved in fuel oil, in weanling rats, and in adult rats; higher values in tests with juveniles and when immersion vehicle is peanut oil (Knudsen et al. 1974; McConnell et al. 1980; Borzelleca et al. 1985; Choudhury et la. 1986; St. Omer and Gadusek 1987)
Dietary levels equivalent to 30 mg/kg BW daily	Decrease in neonatal survival and growth after 62 days. After 2 years, no evidence of carcinogenicity but adverse effects on adult growth and serum enzyme activity levels (Schwetz et al. 1978)

50 mg/kg BW on days 6 to 15 of gestation	100% fetal resorption (EPA 1980)
60 mg/kg BW	Single dose on day 9 or 10 of gestation produced reduction in fetal weight; no effect when given on days 11, 12, or 13 (EPA 1980)
120 mg/kg BW	Single dose results in early hepatic glycogen depletion and elevation in blood glucose (Nishimura 1984)
Domestic pig, *Sus* spp.	
5, 10, or 15 mg purified PCP/kg BW daily for 30 days	No effect on weight gain, food consumption, or kidney weight. Significanlty enlarged liver in 10 and 15 mg/kg groups. Elevated PCP residues in all groups. Residues in 5 mg/kg group vs. controls, in mg/kg fresh weight, were: 78.1 vs. 0.7 for blood, 6.7 vs. 0.2 for muscle, 22.0 vs. 0.2 for kidney, and 28.9 vs. 0.5 for liver (Greichus et al. 1979)
27 to 55 mg/kg BW	Fatal chronic dose (Schipper 1961)
30 mg/kg BW daily for 7 days	Acute toxicosis (Greichus et al. 1979)
Pregnant swine in direct contact with lumber freshly treated with PCP	Extensive mortality in newborn swine (Schipper 1961)
Eastern chipmunk, *Tamias striatus*	
138 mg/kg BW	Acute oral LD-50 (Ege 1985)
200 mg/kg BW	Acute oral LD-100 (Ege 1985)
Fed diets containing 250 or 500 mg PCP/kg for 2 weeks	No increase in metabolic activity. Some weight loss due to food avoidance; enlarged livers (Ege 1985)

CURRENT RECOMMENDATIONS

Commercial PCP preparations often contain variable amounts of chlorophenols, hexachlorobenzene, phenoxyphenols, dioxins, dibenzofurans, chlorinated diphenyl ethers, dihydroxybiphenyls, anisoles, catechols, and other chlorinated dibenzodioxin and dibenzofuran isomers. These contaminants contribute to the toxicity of PCP, sometimes significantly, although the full extent of their interactions with PCP and with each other in PCP formulations are unknown. Unless these contaminants are removed or sharply reduced in existing technical and commercial grade PCP formulations, efforts to establish sound PCP criteria for protection of natural resources may be hindered.

Proposed PCP ambient water quality criteria to protect freshwater and marine life now range from 48 to 55 ug/l for acute effects, 3.2 to 34 ug/l for chronic effects, and daily mean concentrations of 6.2 ug/l, not to exceed 140 ug/l (Table 7). Available data, however, suggest that significant adverse effects occur at much lower PCP concentrations--i.e., between 0.035 and 19 ug/l. In rainbow trout (*Salmo gairdneri*), for example, concentrations of 0.035 to 1.0 ug/l produced elevated issue residues (Choudhury et al. 1986; McKim et al. 1986), 7.4 ug/l caused growth inhibition in 28 days (EPA 1980), and 10 to 19 ug/l produced adverse effects and some deaths

(Chapman and Shumway 1978; Dominguez and Chapman 1984). Other sensitive fish species include sockeye salmon (*Oncorhynchus nerka*), showing growth inhibition after prolonged exposure to 1.8 or ug PCP/1 (EPA 1980; Choudhury et al. 1986); larvae of common carp (*Cyprinus carpio*), having an 96-hour LC-50 of 9.5 ug/l (Choudhury et al. 1986); and largemouth bass (*Micropterus salmoides*), exhibiting reduced food conversion efficiency at 10 ug/l (Johansen et al. 1987). Among sensitive species of plants and invertebrates, American oysters (*Crassostrea virginica*) have elevated tissue residues after exposure for 28 days to 2.5 ug/l (Schimmel et al. 1978); cladocerans have impaired reproduction at 4.1 ug/l (Hedtke et al. 1986); alga show chlorosis inhibition in 72 hours at 7.5 ug/l (EPA 1980); and estuarine macrobenthos populations decreased in abundance and species after exposure for 13 weeks to 15.8 ug/l (Tagatz et al. 1981). Also, an air concentration of 0.2 mg/m^3--a tolerable level to humans (Table 7)--interfered with photosynthesis in duckweed, *Lemna minor* (Huber et al. 1982).

As judged by these studies, it seems appropriate to suggest modification of certain aquatic PCP criteria. A maximum PCP concentration of 3.2 ug/l is indicated, and this level would probably protect most aquatic species, although it would not prevent accumulations and growth inhibition in salmonids or accumulations in oysters. Additional research is needed to establish sound water quality criteria for PCP, and also to interpret the significance of its residues and their metabolites in tissues of representative species.

Table 7. Proposed pentachlorophenol criteria for protection of fish, wildlife, and humans.

Resource and criterion	Concentration or dose	Reference[a]
Aquatic biota		
Freshwater life		
Acute	48 to <55 µg/L	1,2,3
Chronic	<3.2 µg/L	1
24-h mean	<6.2 µg/L	2
Maximum concentration	<140 µg/L	2
Fish		
Warmwater species	10 to <15 µg/L	4
Coldwater species	20 to <40 µg/L	4
Saltwater life		
Acute	<53 µg/L	1
Chronic	<34 µg/L	1, 5
Birds		
Tissue residues		
Contaminated	>2 mg/kg fresh weight	6
Life-threatening	>11 mg/kg fresh weight	6
Diets		
Adverse effects	>1.0 mg/kg diet	7
Fatal	>3,850 mg/kg diet	8
Wood shavings		
Litter	<134 mg/kg	9
Nesting materials	<285 mg/kg	10
Livestock and laboratory mammals		
No measurable adverse		

effects		
Rat		
Females	3 mg/kg BW daily for 24 months	1, 11
Males	10 mg/kg BW daily for 22 months	1, 11
Rabbit	3 mg/kg BW daily for 90 days	1
Adverse effects		
Elevated tissue residues, cattle		
Blood plasma	0.05 mg/kg BW, single dose	12
Internal organs	0.2 mg/kg BW for 95 days	13
Histopathology, cattle		
Internal organs	0.2 mg/kg BW daily for about 80 days, then 2.0 mg/kg BW daily for about 59 days	14, 15
Internal organs	50 mg/kg diet for 12 weeks, equivalent to 3 mg/kg BW daily	16
Reproductive impairment		
Hamster	1.25 to 20 mg/kg BW, single dose	1
Rat	5 mg/kg BW daily or 50 mg/kg diet daily, chronic	5
Rat	5 to 5.8 mg/kg BW daily	1, 17
Increased tumor frequency		
Mice	50 mg/kg diet, chronic	18
Death, various species		
Acute oral LD-50	55 to 200 mg/kg BW	5, 16, 19, 20
Acute dermal LD-50	60 to 200 mg/kg BW	1
Contaminated wood shavings, dermal contact	470 mg/kg	21
Human health		
Current exposure levels, 70 kg adult		
Food	15 µg daily, or 0.21 µg/kg BW daily	1
Water	0.12 µg daily, or 1.7 µg/kg BW daily	1
No adverse effect levels		
Food, upper safe limit, 70 kg adult	30 µg/kg BW, or 2.1 mg per person	1
Wood, in contact with food	Up to 50 mg/kg	1
Drinking water	21 µg/L[b]	1, 5, 22
Upper safe limit	1.01 mg/L	1
Air, 8 h exposure		

daily, 5 days weekly	<0.5 mg/m^3	1, 5, 23, 24
Blood	<1.0 mg/L	25
Blood plasma	<0.5 mg/L	24
Total intake	<3 µg/kg BW daily[c]	
Total intake, 70 kg adult	<30 µg/kg BW daily or	
	2.1 mg daily[d]	5
Expectant mothers	No safe level established to	
	guard against fetal toxicity	17
Adverse effect levels		
Air	>1.0 mg/m^3	1
Dermal solutions	4,000 mg/L	1
Tissue residues associated		
with acute toxicosis		
Kidney	>28 mg/kg fresh weight	1
Blood	>40 to 80 mg/L	1, 23
Liver	>62 mg/kg fresh weight	1
Tissue residues associated		
with death		
Stomach contents	8 mg/kg fresh weight	24, 26
Urine	29 to 75 mg/L	1, 24, 26
Liver	52 to 225 mg/kg fresh	
	weight	1, 24, 26
Lung	116 mg/kg fresh weight	24, 26
Blood	162 to 176 mg/L	1, 24, 26
Kidney	116 to 639 mg/kg fresh	1, 24, 26
	weight	
Bile	1,130 mg/kg fresh weight	24, 26

[a]References: 1, EPA 1980; 2, Zischke et al. 1985; 3, Johansen et al. 1987; 4, Hodson and Blunt 1981; 5, Choudhury et al. 1986; 6, Vermeer et al. 1974; 7, Stedman et al. 1980; 8, Hill and Camardese 1986; 9, Newsome et al. 1974; 10, Dorrestein and Zelle 1979; 11, Schwetz et al. 1978; 12, Osweiler et al. 1984; 13, Kinzell et al. 1985; 14, Forsell et al. 1981; 15, Kinzell et al. 1981; 16, Knudsen et al. 1974; 17, Williams 1982; 18, Kerkvliet et al. 1982; 19, Schlipper 1961; 20, Ege 1985; 21, Peet et al. 1977; 22, Lu et al. 1978; 23, Cote 1972; 24, Wood et al. 1983; 25, Ziemsen et al. 1987; 26, Gray et al. 1985.

[b]Based on no observable adverse effect level of 3 mg/kg BW daily in rat study, uncertainty factor of 1,000x and water consumption of 2 liters daily.

[c]Based on animal data and uncertainty factor of 1,000x.

[d]Based on rat chronic oral no observable effect level of 3 mg/kg BW daily and uncertainty factor of 100.

Dietary concentrations of 1.0 mg/kg and higher produced diarrhea and liver histopathology in chickens (*Gallus* spp.) after 8 weeks (Stedman et al. 1980), and deaths occurred at relatively high dietary concentrations, i.e., 3,850 mg/kg, in Japanese quail (*Coturnix japonica*) after 5 days (Hill and Camardese 1986). Wood shavings contaminated with PCP produced elevated residues when used as litter for domestic chickens (Newsome et al. 1984), and death in canaries (*Serinus canarius*), when used as nesting materials (Dorrestein and Zelle 1979). Tissue residues >2 mg/kg fresh weight are considered to be indicative of significant

environmental PCP contamination, and those >11 mg/kg fresh weight were associated with birds that died or were recovering from PCP exposure (Table 7; Vermeer et al. 1974). No data are now available on avian wildlife and PCP contamination in their diets, residues in their tissues, or frequency of use of PCP-contaminated wood shavings for nesting materials and other purposes.

As judged by studies with domestic and small laboratory mammals, no observable adverse effects have been noted at dietary levels equivalent to 3 to 10 mg PCP/kg BW (Table 7). Variability is great among species, however, and adverse effects have been documented in some species (Table 7) at doses as low as 0.05 to 0.2 mg/kg BW (elevated tissue residues), 0.2 to 2.0 mg/kg BW or 50 mg/kg diet (histopathology, reproductive impairment, increased tumor frequency), and 55 to 60 mg/kg BW (death). Based on guidelines for carcinogen risk assessment and inadequate evidence for animal carcinogenicity or absence of human cancer data, PCP is classified as group D, meaning that it is not classified as a human carcinogen (Choudhury et al. 1986).

Data for man indicate that adverse effects occur at concentrations in air >1.0 mg PCP/m^3 and in tissues >8 mg/kg fresh weight (Table 7). No adverse effects were noted at daily intakes of 2.1 mg per 70-kg adult or 30 ug/kg BW, up to 1.01 mg/l in drinking water, <0.5 mg/m^3 in air, <0.5 mg/l in blood plasma, and <1.0 mg/l in blood (Table 7). It is noteworthy that the currently recommended PCP air concentration of 0.5 mg/m^3 results in a daily intake of 2.5 to 3.8 mg (based on 15 to 23 m^3 of air inhaled daily, 8 hour exposure), equivalent to 42 to 63 ug/kg BW for a 60 kg female. These levels are higher than the currently recommended no adverse effect level of 30 ug/kg BW daily (Table 7), and overlap or exceed the 58 to 74 ug/kg BW daily range--a level recommended by Williams (1982). Air concentrations >1.0 mg PCP/m^3 can produce respiratory irritation in unacclimatized individuals, but concentrations as high as 2.4 mg/m^3 can be tolerated by conditioned individuals (EPA 1980). The biological tolerance value of <1,000 ug PCP/1 in blood, recommended by Ziemsen et al. (1987), is based on occupational air exposure studies: exposure to maximum average air concentrations of 0.18 mg PCP/m^3 for up to 34 years produced blood PCP residues of 23 to 775 ug/l, with no measurable adverse effects. The authors concluded that PCP and its impurities in occupationally relevant concentrations below the maximum concentration in the workplace and below the biological tolerance value do not produce genotoxic damage that can be detected on the chromosomal level, either in vivo or in vitro.

The human taste threshold for PCP in drinking water is about 30 ug/l (EPA 1980), a level far below the upper safe limit of 1.01 mg/l and near the no observable effect level of 21 ug/l (Table 7). Odor detection is not as sensitive as taste: the odor threshold for PCP ranges from about 857 ug/l at 30 C, to 1,600 ug/l at 20 to 22 C, to 12,000 ug/l at 60 C (EPA 1980). It is not clear whether the determined organoleptic threshold values made the water undesirable or unfit for consumption (EPA 1980). If fish and wildlife species of concern have PCP organoleptic thresholds that are similar to those of humans, or lower, will they too avoid contaminated habitats or diets?

Data for PCP and terrestrial wildlife are incomplete and--in view of the large interspecies variations in sensitivity--need to be collected. Until they are, it seems reasonable to apply to wildlife the same levels recommended for human health protection.

LITERATURE CITED

Berglind, R., and G. Dave. 1984. Acute toxicity of chromate, DDT, PCP, TPBS, and zinc to *Daphnia magna* cultured in hard and soft water. Bull. Environ. Contam. Toxicol. 33:63-68.

Bevenue, A., and H. Beckman. 1967. Pentachlorophenol: a discussion of its properties and its occurrence as a residue in human and animal tissues. Residue Rev. 19:83-134.

Borgmann, U., and K. M. Ralph. 1986. Effects of cadmium, 2,4-dichlorophenol, and pentathlorophenol on feeding, growth, and particle-size-conversion efficiency of white sucker larvae and young common shiners. Arch. Environ. Contam. Toxicol. 15:473-480.

Bothwick, P. W., and S. C. Schimmel. 1978. Toxicity of pentachlorophenol and related compounds to early life stages of selected estuarine animals. Pages 141-146

Borzelleca, J. F., J. R. Hayes, L. W. Condie, and J. L. Egle, Jr. 1985. Acute toxicity of monochlorophenols, dichlorophenols and pentachlorophenol in the mouse. Toxicol. Lett. 29:39-42.

Boyle, T. P., E. F. Robinson-Wilson, J. D. Petty, and W. Weber. 1980. Degradation of pentachlorophenol in simulated lentic environment. Bull. Environ. Contam. Toxicol. 24:177-184.

Braun, W. H., and M. W. Sauerhoff. 1976. The pharmacokinetic profile of pentachlorophenol in monkeys. Toxicol. Appl. Pharmacol. 38:525-533.

Braun, W. H., J. D. Young, G. E. Blau, and P. J. Gehring. 1977. The pharmacokinetic and metabolism of pentachlorophenol in rats. Toxicol. Appl. Pharmacol. 41:395-406.

Brown, J. A., P. H. Johansen, P. W. Colgan, and R. A. Mathers. 1985. Changes in the predator-avoidance behaviour of juvenile guppies (*Poecilia reticulata*) exposed to pentachlorophenol. Can. J. Zool. 63:2001-2005.

Brown, J. A., P. H. Johansen, P. W. Colgan, and R. A. Mathers. 1987. 59 Impairment of early feeding behavior of largemouth bass by pentachlorophenol exposure: a preliminary assessment. Trans. Am. Fish. Soc. 116:71-78.

Butte, W., J. Denker, M. Kirsch, and T. Hopner. 1985. Pentachlorophenol and tetrachlorophenols in Wadden sediment and clams *Mya arenaria* of the Jadebusen after a 14-year period of wastewater discharge containing pentachlorophenol. Environ. Pollut. 9B:29-39.

Chapman, G. A., and D. L. Shumway. 1978. Effects of sodium pentachlorophenate on survival and energy metabolism of embryonic and larval steelhead trout. Pages 285-299

Choudhury, H., J. Coleman, C. T. De Rosa, and J. F. Stara. 1986. Pentachlorophenol: health and environmental effects profile. Toxicol. Ind. Health 2:483-571.

Cirelli, D. P. 1978. Patterns of pentachlorophenol usage in the United States of America--an overview. Pages 13-18

Cleveland, L., D. R. Buckler, F. L. Mayer, and D. R. Branson. 1982. Toxicity of three preparations of pentachlorophenol to fathead minnows--a comparative study. Environ. Toxicol. Chem. 1:205-212.

Cote, R. P. 1972. A literature review of the toxicity of pentachlorophenol and pentachlorophenates. Environ. Can. EPS Manus. Rep. 72-4. 14 pp.

Crossland, N. O., and C. J. M. Wolff. 1985. Fate and biological effects of pentachlorophenol in outdoor ponds. Environ. Toxicol. Chem. 4:73-86.

Dave, G. 1984. Effect of pH on pentachlorophenol toxicity to embryos and larvae of zebrafish (*Brachydanio rerio*). Bull. Environ. Contam. Toxicol. 33:621-630.

DeLaune, R. D., R. P. Gambrell, and K. S. Reddy. 1983. Fate of pentachlorophenol in estuarine sediment. Environ. Pollut. 6B:297-308.

Dominguez, S. E., and G. A. Chapman. 1984. Effect of pentachlorophenol on the growth and mortality of embryonic and juvenile steelhead trout. Arch. Environ. Contam. Toxicol. 13:739-743.

Dorrestein, G. M., and R. Zelle. 1979. Pentachlorophenol poisoning in nestlings of canaries (*Serinus canarius*). Tijdschr. Diergeneesk. 104:268-273.

Dougherty, R. C. 1978. Human exposure to pentachlorophenol. Pages 351-361

Ege, M. K. 1985. The effect of pentachlorophenol on the metabolic activity of the eastern chipmunk (*Tamias striatus*) during social interaction. M.S. Thesis. Ohio State University, Columbus, Ohio. 70 pp.

Ehrlich, W., M Mangir, and E. R. Lochmann. 1987. The effect of pentachlorophenol and its metabolite tetrachlorohydroquinone on RNA, protein, and ribosome synthesis in *Saccharomyces* cells. Ecotoxicol. Environ. Safety 13:7-12.

Eisler, R. 1986. Dioxin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85(1.8). 37 pp.

EPA. 1980. Ambient water quality criteria for pentachlorophenol. U.S. Environ. Protection Agency Rep. 440/5-80-065. 89 pp.

Firestone, D., M. Clower, Jr., A. P. Borsetti, R. H. Teske, and P. E. Long. 1979. Polychlorodibenzo-p-dioxin and pentachlorophenol residues in milk and blood of cows fed technical pentachlorophenol. J. Agric. Food Chem. 27:1171-1177.

Fisher, S. W. 1986. Effects of temperature on the acute toxicity of PCP in the midge *Chironomus riparius* Meigen. Bull. Environ. Contam. Toxicol. 36:744-748.

Fisher, S. W., and R. W. Wadleigh. 1986. Effects of pH on the acute toxicity and uptake of (^{14}C) pentachlorophenol in the midge, *Chironomus riparius*. Ecotoxicol. Environ. Safety 11:1-8.

Folke, J., and J. Birklund. 1986. Danish coastal water levels of 2,3,4,6-tetrachlorophenol, pentachlorophenol, and total organohalogens in blue mussels (*Mytilus edulis*). Chemosphere 15:895-900.

Forsell, J. H., L. R. Shull, and J. R. Kateley. 1981. Subchronic administration of technical pentachlorophenol to lactating dairy cattle: immunotoxicologic evaluation. J. Toxicol. Environ. Health 8:543-558.

Fox, M. E., and S. R. Joshi. 1984. The fate of pentachlorophenol in the Bay of Quinte, Lake Ontario. J. Great Lakes Res. 10:190-196.

Gebefugi, I., and F. Korte. 1983. Pentachlorophenol contamination of human milk samples. Chemosphere 12:1055-1060.

Glickman, A. H., C. N. Statham, A. Wu, and J. J. Lech. 1977. Studies on the uptake, metabolism, and disposition of pentachlorophenol and pentachloroanisole in rainbow trout. Toxicol. Appl. Pharmacol. 41:649-658.

Graney, R. L., and J. P. Giesy, Jr. 1986. Effects of long-term exposure to pentachlorophenol on the free amino acid pool and energy reserves of the freshwater amphipod *Gammarus pseudolimnaeus* Bousfield (Crustacea, Amphipoda). Ecotoxicol. Environ. Safety 12:233-251.

Graney, R. L., and J. P. Giesy, Jr. 1987. The effect of short-term exposure to pentachlorophenol and osmotic stress on the free amino acid pool of the freshwater amphipod *Gammarus pseudolimnaeus* Bousfield. Arch. Environ. Contam. Toxicol. 16:167-176.

Gray, R. E., R. D. Gilliland, E. E. Smith, V. G. Lockard, and A. S. Hume. 1985. Pentachlorophenol intoxication: report of a fatal case, with comments on the clinical course and pathologic anatomy. Arch. Environ. Health 40:161-164.

Greichus, Y. A., G. W. Libal, and D. D. Johnson. 1979. Diagnosis and physiologic effects of pentachlorophenols on young pigs. Part I. Effects of purified pentachlorophenol. Bull Environ. Contam. Toxicol. 23:418-422.

Gupta, P. K. 1983. Acute toxicity of pentachlorophenol to a freshwater teleost, *Rasbora daniconius neilgeriensis* (Hamilton). Arch. Hydrobiol. 98:127-132.

Gupta, P. K., and V. S. Durve. 1984. Evaluation of the toxicity of sodium pentachlorophenate, pentachlorophenol and phenol to the snail *Viviparus bengalensis* (L.). Arch. Hydrobiol. 101:469-475.

Gupta, P. K., and P. S. Rao. 1982. Toxicity of phenol, pentachlorophenol and sodium pentachlorophenate to a freshwater pulmonate snail *Lymnaea acuminata* (Lamarck). Arch. Hydrobiol. 94:210-217.

Gupta, P. K., P. S. Rao, and V. S. Mujumdar. 1984. Studies on the toxicity of pentachlorophenol, sodium-pentachlorophenate and phenol to a pulmonate snail *Lymnaea luteola* (Lamarck). Arch. Hydrobiol. 102:123-130.

Hamilton, S. J., L. Cleveland, L. M. Smith, J. A. Lebo, and F. L. Mayer. 1985. Toxicity of pure pentachlorophenol and chlorinated phenoxyphenol impurities to fathead minnows. Environ. Toxicol. Chem. 5:543-552.

Hedtke, S. F., and J. W. Arthur. 1985. Evaluation of a site-specific water quality criterion for pentachlorophenol using outdoor experimental streams. Pages 551-564 *in* R. D. Cardwell, R. Purdy, and R. C. Bahner (eds.). Aquatic toxicology and hazard assessment: seventh symposium. ASTM STP 854. American Society for Testing and Materials, Philadelphia, Pennsylvania.

Hedtke, S. F., C. W. West, K. N. Allen, T. J. Norkerg-King, and D. I. Mount. 1986. Toxicity of pentachlorophenol to aquatic organisms under naturally varying and controlled environmental conditions. Environ. Toxicol. Chem. 5:531-542.

Hill, E. F., and M. B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to Coturnix. U.S. Fish Wildl. Serv. Fish Wildl. Tech. Rep. 2. 147 pp.

Hodson, P. V., and B. R. Blunt. 1981. Temperature-induced changes in pentachlorophenol chronic toxicity to early life stages of rainbow trout. Aquat. Toxicol. 1:113-127.

Holcombe, G. W., G. L. Phipps, and J. T. Fiandt. 1982. Effects of phenol, 2,-4 dimethylphenol, 2,4-dichlorophenol, and pentachlorophenol on embryo, larval, and early-juvenile fathead minnows (*Pimephales promelas*). Arch. Environ. Contam. Toxicol. 11:73-78.

Holmberg, B., S. Jensen, A. Larsson, K. Lewander, and M. Olsson. 1972. Metabolic effects of technical pentachlorophenol (PCP) on the eel *Anguilla anguilla* L. Comp. Biochem. Physiol. 43B:171-183.

Holsapple, M. P., P. J. McNerney, and J. A. McCay. 1987. Effects of pentachlorophenol on the in vitro and in vivo antibody response. J. Toxicol. Environ. Health 20:229-239.

Hoos, R. A. W. 1978. Patterns of pentachlorophenol usage in Canada--an overview. Pages 3-11 *in* K. R. Rao (ed.). Pentachlorophenol chemistry, pharmacology, and environmental toxicology. Plenum Press, New York.

Huber, W., V. Schubert, and C. Sautter. 1982. Effects of pentachlorophenol on the metabolism of the aquatic macrophyte *Lemna minor* L. Environ. Pollut. 29A:215-223.

Huckins, J. N., and J. D. Petty. 1981. Problems associated with the purification of pentachlorophenol for biological studies. Bull. Environ. Contam. Toxicol. 27:836-841.

Huckins, J. N., and J. D. Petty. 1983. Dynamics of purified and industrial pentachlorophenol in fathead minnows. Arch. Environ. Contam. Toxicol. 12:667-672.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U. S. Fish Wildl. Serv. Resour. Publ. 153. 90 pp-

Iwama, G. K., and G. L. Greer. 1979. Toxicity of sodium pentachlorphenate to juvenile chinook salmon under conditions of high loading density and continuous-flow exposure. Bull. Environ. Contam. Toxicol. 23:711-716.

Jayaweera, R., R. Petersen, and P. Smejtek. 1982. Induced hydrogen ion transport in lipid membranes as origin of toxic effect of pentachlorophenol in an alga. Pestic. Biochem. Physiol. 18:197-204.

Johansen, P. H., R. A. Mathers, and J. A. Brown. 1987. Effect of exposure to several pentachlorophenol concentrations on growth of young-of-year largemouth bass, *Micropterus salmoides*, with comparisons to other indicators of toxicity. Bull. Environ. Contam. Toxicol. 39:379-384.

Johansen, P. H., R. A. S. Mathers, J. A. Brown, and P. W. Colgan. 1985. Mortality of early life stages of largemouth bass, *Micropterus salmoides* due to pentachlorophenol exposure. Bull. Environ. Contam. Toxicol. 34:377-384.

Johnson, W. W., and M. T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U. S. Fish Wildl. Serv. Resour. Publ. 137. 98 pp.

Kaila, K., and J. Saarikoski. 1977. Toxicity of pentachlorophenol and 2,3,6-trichlorophenol to the crayfish (*Astacus fluviatilis* L.). Environ. Pollut. 12:119-123.

Kaiser, K. L. E., and 1. Valdmanis. 1982. Apparent octanol/water partition coefficients of pentachlorophenol as a function of pH. Can. J. Chem. 60:2104-2106.

Kalman, D. A., and S. W. Horstman. 1983. Persistence of tetrachlorophenol and pentachlorophenol in exposed woodworkers. J. Toxicol.-Clin. Toxicol. 20:343-352.

Kaufman, D. D. 1978. Degradation of pentachlorophenol in soil, and by soil microorganisms. Pages 27-39

Kerkvliet, N. I., L. Baecher-Steppan, and J. A. Schmitz. 1982. Immunotoxicity of pentachlorophenol (PCP): increased susceptibility to tumor growth in adult mice fed technical PCP-contaminated diets. Toxicol. Appl. Pharmacol. 62:55-64.

Kinzell, J. H., N. K. Ames, S. D. Sleight, J. D. Krehbiel, C. Kuo, M. J. Zabik, and L. R. Shull. 1981. Subchronic administration of technical pentachlorophenol to lactating dairy cattle: performance, general health, and pathologic changes. J. Dairy Sci. 64:42-51.

Kinzell, J. H., R. M. McKenzie, B A. Olson, D. K. Kirsch, and L. R. Shull. 1985. Metabolic fate of (U- ^{14}C) pentachlorophenol in a lactating dairy cow. J. Agric. Food Chem. 33:827-833.

Klemmer, H. W., L. Wong, M. M. Sato, E. L. Reichert, R. J. Korsak, and M. N. Rashid. 1980. Clinical findings in workers exposed to pentachlorophenol. Arch. Environ. Contam. Toxicol. 9:715-725.

Knudsen, I., H. G. Verschuuren, E. M. D. Tonkelaar, R. Kroes, and P. F. W. Helleman. 1974. Short-term toxicity of pentachlorophenol in rats. Toxicology 2:141-152.

Kobayashi, K. 1978. Metabolism of pentachlorophenol in fishes. Pages 89-105 *in* K. R. Rao (ed.). Pentachlorophenol: chemistry, pharmocology, and environmental toxicology. Plenum Press, New York.

Lambert, J., P. Schepens, J. Janssens, and P. Dockx. 1986. Skin lesions as a sign of subacute pentachlorophenol intoxication. Acta Derm. Venereol. 66:170-172.

Lamparski, L. L., R. H. Stehl, and R. L. Johnson. 1980. Photolysis of pentachlorophenol-treated wood. Chlorinated dibenzo-p-dioxin formation. Environ. Sci. Technol. 14:196-200.

Lech, J. J., A. H. Glickman, and C. N. Statham. 1978. Studies on the uptake, disposition and metabolism of pentachlorophenol and pentachloroanisole in rainbow trout (*Salmo gairdneri*). Pages 107-113

Leeuwangh, P., and A. M. Voute. 1985. Bats and woodpreservatives. Pesticide residues in the Dutch Pond bat (*Myotis dasycneme*) and its implications. Mammalia 49:517-524.

Lu, P Y., R. L. Metcalf, and L. K. Cole. 1978. The environmental fate of ^{14}C pentachlorophenol in laboratory model ecosystems. Pages 53-63

Mathers, R. A., J. A. Brown, and P. H. Johansen. 1985. The growth and feeding behaviour responses of largemouth bass (*Micropterus salmoides*) exposed to PCP. Aquat. Toxicol. 6:157-164.

Mayer, F. L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U. S. Environ. Protection Agency Rep. 600/8-87/017. 274 pp.

Mayer, F. L., Jr., and M. R. Ellersieck. 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals. U. S. Fish Wildl. Serv. Resour. Publ. 160. 579 pp.

McConnell, E. E., J. A. Moore, B. N. Gupta, A. H. Rakes, M. 1. Luster, J. A. Goldstein, J. K. Haseman, and C. E. Parker. 1980. The chronic toxicity of technical and analytical pentachlorophenol in cattle. 1. Clinicopathology. Toxicol. Appl. Pharmacol. 52:468-490.

McKim, J. M., P. K. Schmieder, R. W. Carlson, and E. P. Hunt. 1987. Use of respiratory-cardiovascular responses of rainbow trout (*Salmo gairdneri*) in identifying acute toxicity syndromes in fish: part 1. Pentachlorophenol, 2,4-dinitrophenol, tricaine methanesulfonate and 1-octanol. Environ. Toxicol. Chem. 6:295-312.

McKim, J. M., P. 14 K. Schmieder, and R. J. Erickson. 1986. Toxicokinetic modeling of (^{14}C) pentachlorophenol in the rainbow trout (*Salmo gairdneri)*. Aquat. Toxicol. 9:59-80.

Menzer, R. E., and J. 0. Nelson. 1986. Water and soil pollutants. Pages 825-853 *in* C. D. Klaassen, M. 0. Amdur, and J. Doull (eds.). Casarett and Doull's Toxicology. Third edition. Macmillan Publ. Co., New York.

Mikesell, M. D., and S. A. Boyd. 1986. Complete reductive dechlorination and mineralization of pentachlorophenol by anaerobic microorganisms. Appl. Environ. Microbiol. 52:861-865.

Murphy, S. D. 1986. Toxic effects of pesticides. Pages 519-581 *in* C. 0. Klaassen, M. 0. Amdur, and J. Doull (eds.). Casarett and Doull's Toxicology. Third edition. Macmillan Publ. Co., New York.

Nagasawa, S., M. Kondo, and M. Kasuya. 1981. Concentration of PCP inhibiting the development of roots at the early growth stage of rice and the difference of susceptibilities in varieties. Bull. Fac. Agric. Shimane Univ. 15:101-108 (in Japanese, English summary).

Nagler, J. J., P. Aysola, and S. M. Ruby. 1986. Effect of sublethal pentachlorophenol on early oogenesis in maturing female rainbow trout (*Salmo gairdneri*). Arch. Environ. Contam. Toxicol. 15:549-555.

Newsome, W. H., F. Iverson, J. J. Ryan, P. Y. Lau, and H. A. McLeod. 1984. Chlorinated compounds in tissues of chickens raised on pentachlorophenol-contaminated litter. Food Addit. Contam. 1:3-9.

Niimi, A. J., and C. Y. Cho. 1983. Laboratory and field analysis of pentachlorophenol (PCP) accumulation by salmonids. Water Res. 17:1791-1795.

Niimi, A. J., and C. A. McFadden. 1982. Uptake of sodium pentachlorophenate (NaPCP) from water by rainbow trout (*Salmo gairdneri*) exposed to concentrations in the ng/l range. Bull. Environ. Contam. Toxicol. 28:11-19.

Niimi, A. J., and V. Palazzo. 1985. Temperature effect on the elimination of pentachlorophenol, hexachlorobenzene and mirex by rainbow trout (*Salmo gairdneri*). Water Res. 19:205-207.

Nilsson, C. A., A. Norstrum, K. Andersson, and C. Rappe. 1978. Impurities in commercial products related to pentachlorophenol. Pages 313-324

Nishimura, H. 1984. Effect of pentachlorophenol on hepatic glycogen metabolism in rats. Jpn. J. Hyg. 39:662-669.

Norup, B. 1972. Toxicity of chemicals in paper factory effluents. Water Res. 6:1585-1588.

Osweiler, G. D., B. Olesen, and G. E. Rottinghaus. 1984. Plasma pentachlorophenol concentrations in calves exposed to treated wood in the environment. Am. J. Vet. Res. 45:244-246.

Owen, J. W., and S. W. Rosso. 1981. Effects of sublethal concentrations of pentachlorophenol on the liver of bluegill sunfish, *Lepomis macrochirus*. Bull. Environ. Contam. Toxicol. 26:594-600.

Ozretic, B., and M. Krajnovic-Ozretic. 1985. Morphological and biochemical evidence of the toxic effect of pentachlorophenol on the developing embryos of the sea urchin. Aquat. Toxicol. 7:255-263.

Parker, C. E., W. A. Jones, H. B. Matthews, E. E. McConnell, and J. R. Hass. 1980. The chronic toxicity of technical and analytical pentachlorophenol in cattle. II. Chemical analyses of tissues. Toxicol. Appl. Pharmacol. 55:359-369.

Parrish, P. R., E. E. Dyar, J. M. Enos, and W. G. Wilson. 1978. Chronic toxicity of chlordane, trifluralin, and pentachlorophenol to sheepshead minnows (*Cyprinodon variegatus*). U. S. Environ. Protection Agency Rep. 600/3-78-010. 53 pp.

Peer, M. M., J. Nirmala, and M. N. Kutty. 1983. Effects of pentachlorophenol (Na PCP) on survival, activity and metabolism in *Rhinomugil corsula* (Hamilton), *Cyprinus carpio* (Linnaeus) and *Tilapia mossambica* (Peters). Hydrobiologia 107:19-24.

Peet, R. L., G. MacDonald, and A. Keefe. 1977. Possible pentachlorophenol poisoning in cats. Aust. Vet. J. 53:602.

Pierce, R. H., Jr., and D. M. Victor. 1978. The fate of pentachlorophenol in an aquatic ecosystem. Pages 41-52

Pignatello, J. J., L. K. Johnson, M. M. Martinson, R. E. Carlson, and R. L. Crawford. 1985. Response of the microflora in outdoor experimental streams to pentachlorophenol: compartmental contributions. Appl. Environ. Microbiol. 50:127-132.

Pignatello, J. J., L. K. Johnson, M. M. Martinson, R. E. Carlson, and R. L. Crawford. 1986. Response of the microflora in outdoor experimental streams to pentachlorophenol: environmental factors. Can. J. Microbiol. 32:38-46.

Pignatello, J. J., M. M. Martinson, J. G. Steiert, R. E. Carlson, and R. L. Crawford. 1983. Biodegradation and photolysis of pentachlorophenol in artificial freshwater streams. Appl. Environ. Microbiol. 46:1024-1031.

Polin, D., B. Olson, S. Bursian, and E. Lehning. 1986. Enhanced withdrawal from chickens of hexachlorobenzene (HCB) and pentachlorophenol (PCP) by colestipol, mineral oil, and/or restricted feeding. J. Toxicol. Environ. Health 19:359-368.

Prescott, C. A., B. N. Wilke, B. Hunter, and R. J. Julian. 1982. Influence of a purified grade of pentachlorophenol on the immune response of chickens. Am. J. Vet. Res. 43:481-487.

Pruitt, G. W., B. J. Grantham, and R. H. Pierce, Jr. 1977. Accumulation and elimination of pentachlorophenol by the bluegill, *Lepomis macrochirus*. Trans. Am. Fish. Soc. 106:462-465.

Racey, P. A., and S. M. Swift. 1986. The residual effects of remedial timber treatments on bats. Biol. Conserv. 35:205-214.

Rao, K. R. (ed.). 1978. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology. Plenum Press, New York. 402 pp.

Rao, K. R., P. J. Conklin, and A. C. Brannon. 1978. Inhibition of limb regeneration in the grass shrimp, *Palaemonetes pugio* by sodium pentachlorophenate. sPages 193-203 *in* K. R. Rao (ed.). Pentachlorophenol: chemistry, pharmacology, and environmental toxicolgy. Plenum Press, New York.

Rao, K. R., and D. G. Doughtie. 1984. Histopathological changes in grass shrimp exposed to chromium, pentachlorophenol and dithiocarbamates. Mar. Environ. Res. 14:371-395.

Rao, K. R., F. R. Fox, P. J. Conklin, A. C. Cantelmo, and A. C. Brannon. 1979. Physiological and biochemical investigations of the toxicity of pentachlorophenol to crustaceans. Pages 307-339 *in* W. B. Vernberg, A. Calabrese, F. P. Thurberg, and F. J. Vernberg (eds.). Marine pollution: functional responses. Academic Press, New York.

Ravanel, P., and M. Tissut. 1986. Toxicity of pentachlorophenol on isolated plant mitochondria. Phytochemistry. 25:577-583.

Rozman, T., L. Ballhorn, K. Rozman, C. Klaassen, and H. Greim. 1982. Effect of cholestyramine on the disposition of pentachlorophenol in rhesus monkeys. J. Toxicol. Environ. Health 10:277-283.

Ryan, J. J., R. Lizotte, T. Sakuma, and B. Mori. 1985. Chlorinated dibenzo-p-dioxins, chlorinated dibenzofurans, and pentachlorophenol in Canadian chicken and pork samples. J. Agric. Food Chem. 33:1021-1026.

Schimmel, S. C., J. M. Patrick, Jr., and L. F. Fass. 1978. Effects of sodium pentachlorophenate on several estuarine animals: toxicity, uptake, and depuration. Pages 147-155

Schipper, I. A. 1961. Toxicity of wood preservatives for swine. Am. J. Vet. Res. 22:401-405.

Schwetz, B.. A., J. F. Quast, P. A. Keeler, C. G. Humiston, and R. J. Kociba. 1978. Results of two-year toxicity and reproduction studies on pentachlorophenol in rats. Pages 301-309 in K. R. Rao (ed.). Pentachlorophenol: chemistry, pharmacology, and environmental toxicology. Plenum Press, New York.

Seidler, J. J., M. Landau, F. E. Dierberg, and R. H. Pierce. 1986. Persistence of pentachlorophenol in a wastewater-estuarine agriculture system. Bull. Environ. Contam. Toxicol. 36:101-108.

Shull, L. R., B. A. Olson, B. J. Hughes, R. M. McKenzie, and J. H. Kinzell. 1986. Effect of pentachlorophenol on microsomal mixed-function oxidases in cattle. Pest. Biochem. Physiol. 25:31-39.

Singh, J., W. Miles, and J. P. Barrette. 1985. Determination of polychlorinated dibenzo-p-dioxins in technical pentachlorophenol. J. Assoc. Off. Anal- Chem. 68:583-586.

Smith, P. D., D. L. Brockway, and F. E. Stancil, Jr. 1987. Effects of hardness, alkalinity and pH on the toxicity of pentachlorophenol to *Selenastrum capricornutum* (Printz). Environ. Toxicol. Chem. 6:891-900.

St. Omer, V. E. V., and F. Gadusek. 1987. The acute oral LD-50 of technical pentachlorophenol in developing rats. Environ. Toxicol. Chem. 6:147-149.

Stedman, T. M., Jr., N. H. Booth, P. B. Bush, R. K. Page, and D. D. Goetsch. 1980. Toxicity and bioaccumulation of pentachlorophenol in broiler chickens. Poult. Sci. 59:1018-1026.

Steiert, J. G., and R. L. Crawford. 1986. Catabolism of pentachlorophenol by a *Flavobacterium* sp. Biochem. Biophys. Res. Commun. 141:825-830.

Steiert, J. G., J. J. Pignatello, and R. L. Crawford. 1987. Degradation of chlorinated phenols by a pentachlorophenol-degrading bacterium. Appl. Environ. Microbiol. 53:907-910.

Stuart, R. J., and J. B. Robertson. 1985. Acute toxicity of pentachlorophenol in the freshwater snail, *Gillia altilis*. Bull. Environ. Contam. Toxicol. 35:633-640.

Tachikawa, M., A. Hasegawa, R. Sawamura, A. Takeda, S. Okada, and M. Nara. 1987. Difference between fresh- and seawater fishes in the accumulation and effect of environmental chemical pollutants. I. Intakes of chlordane and pentachlorophenol by seawater-acclimated tilapia (nilotica). Eisei Kagaku 33:98-105 (in Japanese, English summary).

Tagatz, M. E., C. H. Deans, G. R. Plaia, and J. D. Pool. 1983. Impact on and recovery of experimental macrobenthic communities exposed to pentachlorophenol. Northeast Gulf Sci. 6:131-136.

Tagatz, M. E., J. M. Ivey, N. R. Gregory, and J. L. Oglesky. 1981. Effects of pentachlorophenol on field-and laboratory-developed estuarine benthic communities. Bull. Environ. Contam. Toxicol. 26:137-143.

Tagatz, M. E., J. M. Ivey, J. C. Moore, and M. Tobia. 1977. Effects of pentachlorophenol on the development of estuarine communities. J. Toxicol. Environ. Health 3:501-506.

Tagatz, M. E., J. M. Ivey, and M. Tobia. 1978. Effects of Dowicide® G-ST on development of experimental estuarine macrobenthic communities. Pages 157-163

Trujillo, D. A., L. E. Murray, and C. S. Giam. 1982. Bioaccumulation of pentachlorophenol by killifish (*Fundulus similis*). Chemosphere 11:25-31.

Uhl, S., P. Schmid, and C. Schlatter. 1986. Pharmacokinetics of pentachlorophenol in man. Arch. Toxicol. 58:182-186.

Vermeer, K., R. W. Risebrough, A. L. Spaans, and L. M. Reynolds. 1974. Pesticide effects on fishes and birds in rice fields of Surinam, South America. Environ. Pollut. 7:217-236.

Webb, P. W., and J. R. Brett. 1973. Effects of sublethal concentrations of sodium pentachlorophenate on growth rate, food conversion efficiency,, and swimming performance in underyearling sockeye salmon (*Oncorhynchus nerka*). J. Fish. Res. Board Can. 30:499-507.

Weiss, V. M., P. Moza, I. Scheunert, A. Haque, and F. Korte. 1982. Fate of pentachlorophenol- ^{14}C in rice plants under controlled conditions. J. Agric. Food Chem. 30:1186-1190.

Welsh, J. J., T. F. X. Collins, T. N. Black, S. L. Graham, and M. W. O'Donnell, Jr. 1987. Teratogenic potential of purified pentachlorophenol and pentachloroanisole in subchronically exposed Sprague-Dawley rats. Food Chem. Toxicol. 25:163-172.

Williams, P. L. 1982. Pentachlorophenol, an assessment of the occupational hazard. Am. Ind.. Hyg. Assoc. J. 43:799-810.

Wollesen, C., S. Schulzeck, T. Stork, U. Betz, and 0. Wassermann. 1986. Effects of pure and technical grade pentachlorophenol on cultured rat hepatocytes. Chemosphere 15:9-12.

Wong, A. S., and D. G. Crosby. 1978. Photolysis of pentachlorophenol in water. Pages 119-25

Wood, S., W. N. Rom, G. L. White, and D. C. Logan. 1983. Pentachlorophenol poisoning. J. Occupat. Med. 25:527-530.

Yount, J. D., and J. E. Richter. 1986. Effects of pentachlorophenol on periphyton communities in outdoor experimental streams. Arch. Environ. Contam. Toxicol 15:51-60.

Yousri, R., and W. Hanke. 1985. The effects of pentachlorophenol, phenol and other pollutants on the liver of carp (*Cyprinus carpio* L.). Comp. Biochem. Physiol. 82C:283-290.

Ziemsen, B., J. Angerer, and G. Lehnert. 1987. Sister chromatid exchange and chromosomal breakage in pentachlorophenol (PCP) exposed workers. Int. Arch. Occup. Environ. Health 59:413-417.

Zietz, E., K. Dumpert, and J. Rombke. 1987. Effects of pentachlorophenol and 2,4,5-trichlorophenol on a soil ecosystem. I. Application and residue analysis. Sci. Total Environ. 61:153-165.

Zischke, J. A., J. W. Arthur, R. 0. Hermanutz, S. F. Hedtke, and J. C. Helgen. 1985. Effects of pentachlorophenol on invertebrates and fish in outdoor experimental channels. Aquat. Toxicol. 7:37-58.

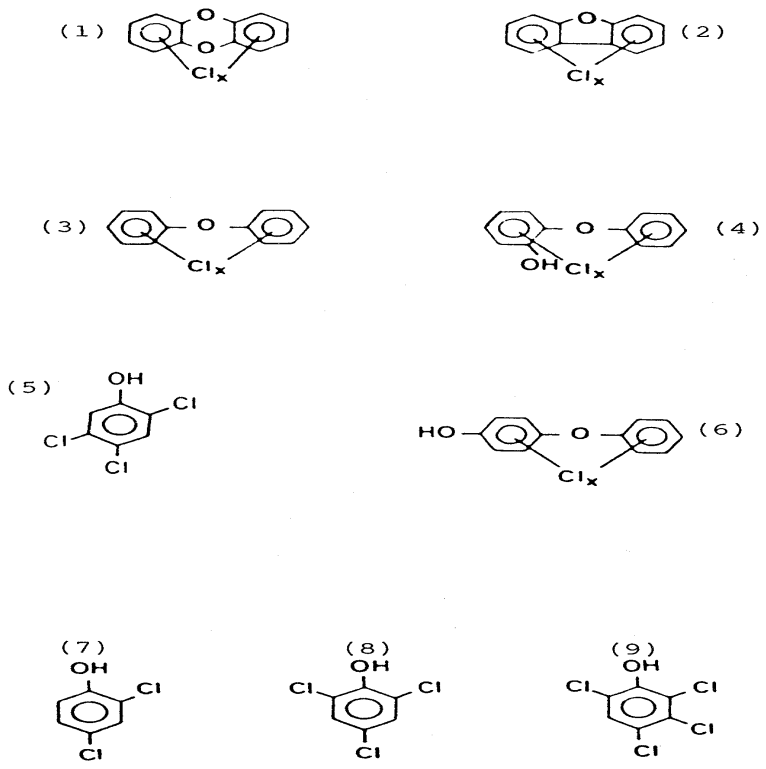


Figure 1. Some impurities found in technical grade pentachlorophenol (from Nilsson et al. 1978). Compounds are: (1) dibenzo-p-dioxins, (2) dibenzofurans, (3) diphenyl ethers, (4) 2- phenoxyphenols, (5) 2,4,5- trichlorophenol, (6) 4- phenoxyphenols, (7) 2,4- dichlorophenol, (8) 2,4,6- trichlorophenol, (9) 2,3,4,6- tetrachlorophenol.

Biological Report 85(1.8)
May 1989

Contaminant Hazard Reviews
Report No. 18

ATRAZINE HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

The herbicide atrazine (2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine) is the most heavily used agricultural pesticide in North America. In the United States alone, more than 50 million kg (110 million pounds) are applied annually to more than 25 million ha (62 million acres), primarily to control weeds in corn and sorghum. Residues have been detected at phytotoxic concentrations in groundwater, lakes, and streams as a result of runoff from treated fields. Atrazine degrades rapidly, usually by way of hydrolysis, nitrogen dealkylation, and splitting of the triazine ring to less toxic compounds not normally inhibitory to plants and animals. The half-time persistence of atrazine in soils is usually about 4 days, but may range up to 385 days in dry, sandy, alkaline soils, under conditions of low temperature and low microbial densities. Half-time persistence is about 3 days in freshwater, 30 days in marine waters, 35 days in marine sediments, and less than 72 hours in vertebrate animals.

Sensitive species of aquatic plants experience temporary, but reversible, adverse effects at concentrations in the range of 1 to 5 ug atrazine/l. However, potentially harmful phytotoxic concentrations of atrazine, i.e., >10 ug/l for extended periods, have not been documented in the environment, and are probably unrealistic under current application and degradation rates. Aquatic fauna are indirectly affected at atrazine concentrations of 20 ug/l and higher, partly through reduction of the food supply of herbivores, and partly through loss of macrophyte habitat. Direct adverse effects to aquatic invertebrates and fishes were measured at 94 ug/l and higher. Bioaccumulation of atrazine is limited, and food chain biomagnification is negligible in aquatic ecosystems. Birds are comparatively resistant to atrazine, having a low probability for uptake and retention. Known acute oral LD-50 values for birds are >2,000 mg/kg body weight, and dietary LD-50s are >5,000 mg/kg ration. However, indirect ecosystem effects of atrazine on seed- and insect-eating birds are unknown, and should be investigated. Data are lacking for atrazine toxicity to mammalian wildlife, but tests with domestic livestock and small laboratory animals indicate that this group is also comparatively resistant. Acute oral LD-50s for mammals are >1,750 mg/kg body weight; no adverse effects were measured at chronic dietary levels of 25 mg/kg (about 1.25 mg/kg body weight) and, for some species, 100 mg/kg diet.

Proposed criteria for aquatic life protection include <5 ug atrazine/1 for sensitive species of aquatic flora, and <11 ug/l for most species of aquatic plants and animals. No criteria have been promulgated for human or animal health protection, although it has been suggested that <7.5 ug/l in drinking water, and <0.0375 mg atrazine/kg body weight (<2.25 mg daily for a 60 kg adult, <1.5 mg/kg diet based on consumption of 1.5 kg food daily) would pose a negligible risk to human health. Additional data are needed on toxicity, environmental fate, and chemistry of atrazine and its metabolites in order to maintain existing registrations or to permit new registrations. In particular, more research is needed on possible synergistic or additive effects of atrazine with other agricultural chemicals in aquatic environments.

DISCLAIMER

Suggested citation:

Eisler, R. 1989. Atrazine hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. Fish Wildl. Serv. Biol. Rep. 85(1.18).

TABLES

ACKNOWLEDGMENTS

I thank Nancy A. Bushby, Lynda J. Garrett, and Joyce Haber Corley for literature search and retrieval; Barbara A. Roberts for secretarial help; W. James Fleming, Gary H. Heinz, A. Dennis Lemly, Harry M. Ohlendorf, and David L. Trauger for technical and scientific review; and Paul H. Eschmeyer and James R. Zuboy for editorial services.

INTRODUCTION

Atrazine (2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine) is the most heavily used agricultural pesticide in North America (DeNoyelles et al. 1982; Stratton 1984; Hamilton et al. 1987), and is currently registered for use in controlling weeds in numerous crops, including corn (*Zea mays*), sorghum (*Sorghum vulgare*), sugarcane (*Saccharum officinarum*), soybeans (*Glycine max*), wheat (*Triticum aestivum*), pineapple (*Ananas comusus*). and various range grasses (Reed 1982). Atrazine was first released for experiment station evaluations in 1957 and became commercially available in 1958 (Hull 1967; Jones et al. 1982). In 1976, 41 million kg (90 million pounds) were applied to 25 million ha (62 million acres) on farms in the United States, principally for weed control in corn, wheat, and sorghum crops; this volume represented 16% of all herbicides and 9% of all pesticides applied in the United States during that year (DeNoyelles et al. 1982; Hamala and Kollig 1985). By 1980, domestic usage had increased to 50 million kg (Reed 1982). In Canada, atrazine was the most widely used of 77 pesticides surveyed (Frank and Sirons 1979). Agricultural use of atrazine has also been reported in South Africa, Australia, New Zealand, Venezuela, and in most European countries (Reed 1982). Resistance to atrazine has developed in various strains of weeds typically present in crop fields--sometimes in less than two generations (Bettini et al. 1987; McNally et al. 1987)--suggesting that future agricultural use of atrazine may be limited.

Atrazine has been detected in lakes and streams at levels ranging from 0.1 to 30.3 ug/l; concentrations peak during spring, which coincides with the recommended time for agricultural application (Hamilton et al. 1987). In runoff waters directly adjacent to treated fields, atrazine concentrations of 27 to 69 ug/l have been reported, and may reach 1,000 ug/l (DeNoyelles et al. 1982). Some of these concentrations are demonstrably phytotoxic to sensitive species of aquatic flora (DeNoyelles et al. 1982; Herman et al. 1986; Hamilton et al. 1987). Although atrazine runoff from Maryland corn fields was suggested as a possible factor in the decline of submerged aquatic vegetation in Chesapeake Bay, which provides food and habitat for large populations of waterfowl, striped bass (*Morone saxatilis*), American oysters (*Crassostrea virginica*), and blue crabs (*Callinectes sapidus*), it was probably not a major contributor to this decline (Forney 1980; Menzer and Nelson 1986).

This report was prepared in response to requests for information from environmental specialists of the U. S. Fish and Wildlife Service. It is part of a continuing series of brief reviews on hazards of selected chemicals to natural resources.

ENVIRONMENTAL CHEMISTRY

Atrazine is a white crystalline substance that is sold under a variety of trade names for use primarily as a selective herbicide to control broadleaf and grassy weeds in corn and sorghum (Table 1). It is only slightly soluble in water (33 mg/l at 27 °C), but soluble (360 to 183,000 mg/1) in many organic solvents. Atrazine is usually applied in a water spray at concentrations of 2.2 to 4.5 kg/ha before weeds emerge. Stored atrazine is stable for several years, but degradation begins immediately after application (Table 1). The chemical is available as a technical material at 99.9% active ingredient and as a manufacturing-use product containing 80% atrazine for formulation of wettable powders, pellets, granules, flowable concentrates, emulsifiable concentrates, or tablets (EPA 1983).

There are three major atrazine degradation pathways: hydrolysis at carbon atom 2, in which the chlorine is replaced with a hydroxy group; N-dealkylation at carbon atom 4 (loss of the ethylpropyl group) or 6 (loss of the isopropyl group); and splitting of the triazine ring (Knuesli et al. 1969; Reed 1982). The major atrazine metabolite in both soil and aquatic systems is hydroxyatrazine. In soils, it accounts for 5% to 25% of the atrazine originally applied after several months compared to 2% to 10% for all dealkylated products combined, including deethylated atrazine and deisopropylated atrazine (Stratton 1984; Schiavon 1988a,b). Atrazine may be converted to nonphytotoxic hydroxyatrazine by chemical hydrolysis, which does not require a biological system (Dao 1977; Wolf and Jackson 1982). Bacterial degradation, however, proceeds primarily by N-dealkylation (Giardi et al. 1985). In animals, N-dealkylation is a generally valid biochemical degradation mechanism (Knuesli et al. 1969). In rats, rabbits, and chickens, most atrazine is excreted within 72 hours; 19 urinary metabolites--including hydroxylated, N-dealkylated, oxidized, and conjugated metabolites--were found (Reed 1982). There is general agreement that atrazine degradation products are substantially less toxic than the parent compound and not normally present in the environment at levels inhibitory to algae, bacteria, plants, or animals (DeNoyelles et al. 1982; Reed 1982; Stratton 1984).

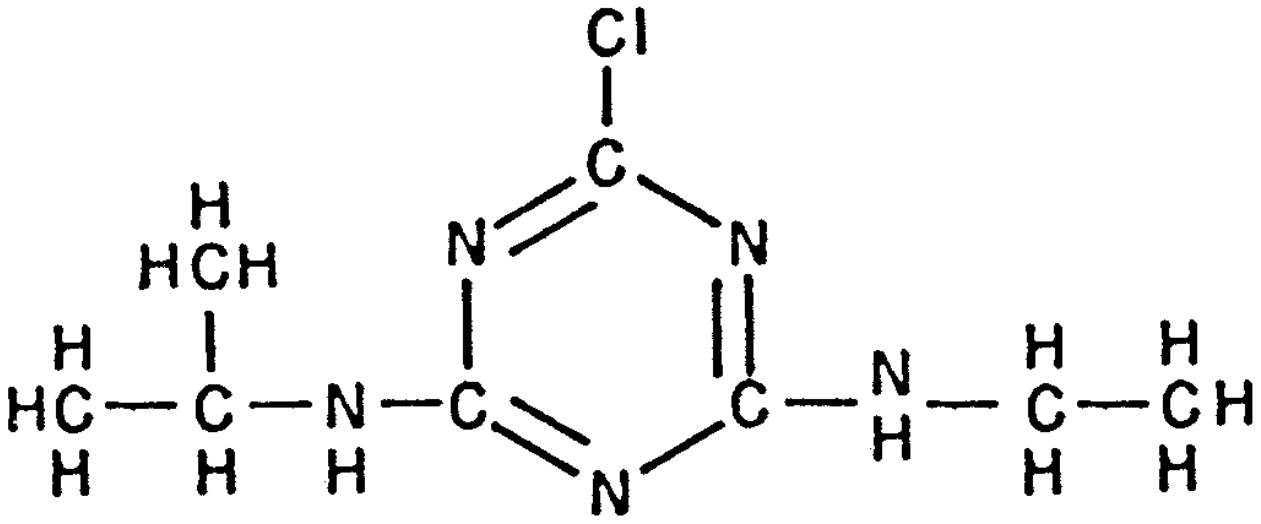
Residues of atrazine rapidly disappeared from a simulated Northern Prairie freshwater wetland microcosm during the first 4 days, primarily by way of adsorption onto organic sediments (Huckins et al. 1986). This is consistent with the findings of others who report 50% loss (Tb 1/2) from freshwater in 3.2 days (Moorhead and Kosinski 1986), 82% loss in 5 days, and 95% loss in 55 days (Lay et al. 1984), although one report presents evidence of a 300-day half-life for atrazine (Yoo and Solomon 1981). In estuarine waters and sediments, atrazine is inactivated by adsorption and metabolism: half-time persistence in waters has been estimated to range between 3 and 30 days, being shorter at elevated salinities; for sediments this range was 15 to 35 days (Stevensen et al. 1982; Glotfelty et al. 1984; Isensee 1987). The comparatively rapid degradation of atrazine to hydroxyatrazine in estuarine sediments and water column indicates a low probability for atrazine accumulation in the estuary, and a relatively reduced rate of residual phytotoxicity in the estuary for the parent compound (Jones et al. 1982).

Table 1. Chemical and other properties of atrazine

(Anon. 1963; Hull 1967; Knuesli et al. 1969; Gunther and Gunther 1970; Reed 1982; Beste 1983; Hudson et al. 1984; Huber and Hock 1986; Huckins et al. 1986; EPA 1987).

Variable	Datum
Chemical name	2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine
Alternate names	CAS 1912-24-9, ENT 28244, G-30027, Aatrex, Aatrex 4L, Aatrex 4LC, Aatrex Nine-0, Aatrex 80W, Atranex, ATratol, Atratol 8P, Atratol 80W, Atrazine 4L, Atrazine 80W, Atred, Bicep 4.5L, Co-Op, Co-Op Atra-pril, Cristatrina, Crisazine, Farmco atrazine, Gesaprim, Griffex, Primatol A, Shell atrazine herbicide, Vectal, Vectal SC
Primary uses	Selective herbicide for control of most annual broadleaf and grassy weeds in corn, sugar cane, sorghum, macadamia orchards, rangeland, pineapple, and turf grass sod. Nonselective herbicide for weed control on railroads, storage yards, along highways, and industrial sites. Sometimes used as selective weedicide in conifer reforestation, Christmas tree plantations, and grass seed fields
Major producer	Ciba-Geigy Corporation
Application methods	Usually as water spray or in liquid fertilizers applied preemergence, but also may be applied preplant or postemergence. Rates of 2 to 4 pounds/acre (2.24 to 4.48 kg/ha) are effective for most situations; higher rates are used for nonselective weed control, and on high organic soils
Compatibility with other pesticides	Compatible with most other pesticides and fertilizers when used at recommended rates. Sold in formulation with Lasso®, Ramrod®, and Bicep®
Stability	Very stable over several years of shelf life, under normal illumination and extreme temperatures. Stable in neutral, slightly acid or basic media. Sublimes at high temperatures and when heated, especially at high temperatures in acid or basic media, hydrolyzes to hydroxyatrazine (2-hydroxy-4-ethylamino-6-isopropylamino-*s*-triazine), which

	has no herbicidal activity
Empirical formula	$C_8H_{14}ClN_5$
Structural formula	



Molecular weight	215.7
Melting point	173 ºC to 175 ºC
Vapor pressure	5.7×10^{-8} mm mercury at 10 ºC, 3.0×10^{-7} at 20 ºC, 1.4×10^{-6} at 30 ºC, and 2.3×10^{-5} at 50 ºC
Henry's Law constant	6.13×10^{-8} to 2.45×10^{-7} atm-m^3/mole
Physical state	The technical material is a white, crystalline, noncombustible, noncorrosive substance
Purity	No impurities or contaminants that resulted from the manufacturing process were detected
Solubility	
Water	22 mg/L at 0 ºC, 32 mg/L at 25 ºC, 320 mg/L at 85 ºC
N-pentane	360 mg/L at 27 ºC
Petroluem ether	12,000 mg/L at 27 ºC
Methanol	18,000 mg/L at 27 ºC
Ethyl acetate	28,000 mg/L at 27 ºC
Chloroform	52,000 mg/L at 27 ºC
Dimethyl sulfoxide	183,000 mg/L at 27 ºC
Log Kow	2.71

Atrazine is leached into the soil by rain or irrigation water. The extent of leaching is limited by the low water solubility of atrazine and by its adsorption onto certain soil constituents (Anon. 1963). Runoff loss in soils ranges from 1.2% to 18% of the total quantity of atrazine applied, but usually is less than 3% (Wolf and Jackson

1982). Surface runoff of atrazine from adjacent conventional tillage and no-tillage corn watersheds in Maryland was measured after single annual applications of 2.2 kg/ha for 4 years (Glenn and Angle 1987). Most of the atrazine in surface runoff was lost during the first rain after application. In 1979, the year of greatest precipitation, 1.6% of the atrazine applied moved from the conventional tillage compared to 1.1% from the no-tillage watershed, suggesting that no-tillage should be encouraged as an environmentally sound practice (Glenn and Angle 1987). Lateral and downward movement of atrazine was measured in cornfield soils to a depth of 30 cm when applied at 1.7 kg/ha to relatively moist soils; in lower elevation soils, atrazine accumulated by way of runoff and infiltration (Wu 1980). Downward movement of atrazine through the top 30 cm of cornfield soils indicates that carryover of atrazine to the next growing season is possible: between 5% and 13% of atrazine was available one year after application (Wu 1980; Wu and Fox 1980). Atrazine is not usually found below the upper 30 cm of soil in detectable quantities, even after years of continuous use; accordingly, groundwater contamination by atrazine is not expected at recommended application rates (Anon. 1963; Hammons 1977; Wolf and Jackson 1982; Beste 1983).

Atrazine persistence in soils is extremely variable: reported Tb 1/2 values ranged from 20 to 100 days in some soils to 330 to 385 days in others (Jones et al. 1982); intermediate values were reported by Forney (1980), Stevenson et al. (1982), and Stratton (1984). Atrazine activity and persistence in soils is governed by many physical, chemical, and biological factors. In general, atrazine loss was more rapid under some conditions than others: it was more rapid from moist soils than from dry soils, during periods of high temperatures than during periods of low temperatures, from high organic and high clay content soils than from sandy mineral soils, during summer than in winter, from soils with high microbial densities than from those with low densities, from soils of acidic pH than from those of neutral or alkaline pH, during storm runoff events than during normal flows, at shallow soil depths than at deeper depths, and under conditions of increased ultraviolet irradiation (Anon. 1963; McCormick and Hiltbold 1966; Hull 1967; Gunther and Gunther 1970; Dao 1977; Hammons 1977; Frank and Sirons 1979; Forney 1980; Stevenson et al. 1982; Wolf and Jackson 1982; Beste 1983; EPA 1987). Microbial action, usually by way of N-dealkylation and hydrolysis to hydroxyatrazine, probably accounts for the major breakdown of atrazine in the soil, although nonbiological degradation pathways of volatilization, hydroxylation, dealkylation, and photodecomposition are also important (Hull 1967; Gunther and Gunther 1970; Reed 1982; Menzer and Nelson 1986).

BACKGROUND CONCENTRATIONS

Atrazine concentrations in human foods are negligible. Monitoring of domestic and imported foods in the human diet by the U.S. Food and Drug Administration between 1978 and 1982 showed that only 3 of 4,500 samples analyzed had detectable atrazine residues. Two samples in 1980 contained 0.01 and 0.08 mg atrazine/kg and one in 1978, following a known contamination incident, contained 47 mg/kg (Reed 1982).

Atrazine and its metabolites have been observed in freshwater streams contiguous to agricultural lands; 0.1% to 3% of the atrazine applied to the fields was lost to the aquatic environment (Jones et al. 1982). Atrazine concentrations in runoff waters from treated cornfields may exceed 740 ug/l (Table 2). Elevated levels were associated with high initial treatment rates, major storms shortly after application, conventional tillage practices (vs. no tillage), and increased flow rates, increased suspended solids, and increased dissolved nitrates and nitrites. Concentrations in runoff water usually declined rapidly within a few days (Forney 1980; Setzler 1980; Stevenson et al. 1982). Groundwater contamination by way of atrazine treatment of cornfields has been unexpectedly reported in parts of Colorado, Iowa, and Nebraska. Contamination was most pronounced in areas of highly permeable soils that overlie groundwater at shallow depths (Wilson et al. 1987).

The total amount of atrazine reaching the Wye River, Maryland, estuary depended on the quantity applied in the watershed and the timing of runoff. In years of significant runoff, 2% to 3% of the atrazine moved to the estuary within 2 weeks after application and effectively ceased after 6 weeks (Glotfelty et al. 1984). In Chesapeake Bay waters, a leakage rate of 1% of atrazine from agricultural soils resulted in aqueous concentrations averaging 17 ug/1--concentrations potentially harmful to a variety of estuarine plants (Jones et al. 1982). The maximum recorded atrazine concentration in runoff water entering Chesapeake Bay was 480 ug/l (Forney 1980). However, these concentrations seldom persisted for significant intervals, and only rarely approached those producing long-term effects on submerged aquatic vegetation (Glotfelty et al. 1984).

Atmospheric transport of atrazine-contaminated aerosol particulates, dusts, and soils may contribute significantly to atrazine burdens of terrestrial and aquatic ecosystems. The annual atmospheric input of atrazine

in rainfall to the Rhode River, Maryland, as one example, was estimated at 1,016 mg/surface ha in 1977, and 97 mg/ha in 1978 (Wu 1981). A similar situation exists with fog water. When fog forms, exposed plant surfaces become saturated with liquid for the duration of the fog (Glotfelty et al. 1987).

Table 2. Atrazine concentrations in selected watersheds.

Locale and other variables	Concentration[a] In ug/1 or up/kg	Reference[b]
Atrazine-treated cornfields		
Iowa, shortly after application		
Runoff water	4,900	1
Sediments	7,350	1
Kansas, 1974		
Runoff water		
May	1,074	1
June	739	1
Soil from drainage canal	50	1
Water from drainage canal		
Summer	100	1
Winter	10	1
Ontario, Canada (1.7 kg/ha)		
Clay-dominated soils	Max. 25	2
Loam-dominated soils	Max. 14	2
Sand-dominated soils	Max. 4	2
Streamwater, Quebec		
Atrazine	(0.01 to 26.9)	3
Metabolites	(<0.01 to 1.3)	3
Northern Ohio streams, 1980		
Sandusky River Basin	(1.0 to 45.7)	4
Others	(0.1 to 23.2)	4
Streams entering Great Lakes from Canada		
To Lake Erie	4.0	2
To Lake Huron	1.4	2
To Lake Ontario	1.1	2
Susquehanna Drainage Basin, Pennsylvania, 1980		
May	Max. 67.8	2
Other months	(1.1 to 2.5)	2
Drinking water		

Colorado	Usually <1.8, Max. 2.3	5
Tiffin, Ohio, 1980		
May 30	16.4	4
June 16	7.2	4
June 26	5.3	4
July 1	3.3	4
Fog water, Beltsville, Maryland	(0.27 to 0.82)	6
Chesapeake Bay watershed		
Runoff water	Max. 480.0	1
Chesapeake Bay, 1980		
April	Max. 0.3	2
June	Max. 1.1	2
July	Max. 0.4	2
Chesapeake Bay tributaries		
Horn Point		
May–July, 1980	(0.1 to 18.3)	7
May, 1981	(0.7 to 46.0)	7
Choptank, estuary		
May–July, 1980	(0.0 to 0.8)	7
May, 1981 (runoff event)	(0.2 to 9.3)	7
Wye River, Maryland	Usually <3.0 at peak loadings; Max. ~15.0	8
Rhode River, Maryland		
1977–78		
Water column, depth -0.3 m	0.04 (0.003 to 0.19)	9
Microsurface layer	0.13 (0.01 to 3.3)	9
Rainwater, May	Max. 2.2	10

[a]Concentrations are shown as mean, range (in parenthesis), and maximum (Max.).

[b]References: 1, Forney 1980; 2, Stevenson et al. 1982; 3, Frank and Sirons 1979; 4, Setzler 1980; 5, Wilson et al. 1987; 6, Glotfelty et al. 1987; 7, Kemp et al. 1985; 8, Glotfelty et al. 1984; 9, Lu et al. 1980; 10, Wu 1981.

LETHAL AND SUBLETHAL EFFECTS

GENERAL

In terrestrial ecosystems, atrazine effectively inhibits photosynthesis in target weeds, and may also affect certain sensitive crop plants. Atrazine metabolites are not as phytotoxic as the parent compound. Degradation is usually rapid, although atrazine may persist in soils for more than one growing season. Soil fauna may be adversely affected shortly after initial atrazine application at recommended levels, but long-term population effects on this group are considered negligible.

As discussed later, sensitive species of aquatic flora experience temporary adverse effects at concentrations as low as 1.0 to 5.0 ug/l; however, most authorities agree that potentially harmful levels, i.e., >10 ug/l for long periods, have not been documented and are probably unrealistic under current application protocols

and degradation rates. The observed declines in submerged aquatic vegetation in the Chesapeake Bay are not now directly attributable to atrazine use. Atrazine indirectly affects aquatic fauna at concentrations of 20 ug/l and higher by reducing the food supply of herbivores and, to some extent, their macrophyte habitat. Direct adverse effects on growth and survival of aquatic fauna were evident in the range of 94 to 500 ug/l. Bioaccumulation of atrazine is limited and food chain biomagnification is negligible in aquatic ecosystems.

Birds show a low probability for atrazine uptake and accumulation. Known acute oral LD-50s and dietary LD-50s are high: >2,000 mg/kg body weight, and 5,000 mg/kg diet. Indirect ecosystem effects of atrazine on insect- and seed-eating birds are not known, and seem to merit study.

Data are lacking for mammalian wildlife, but tests with domestic livestock and small laboratory animals strongly indicate that this group is comparatively resistant to atrazine. Acute oral LD-50s are >1,750 mg/kg body weight, and no adverse effects are evident at dietary levels of 25 mg/kg food (about 1.25 mg/kg body weight) and sometimes 100 mg/kg food over extended periods.

TERRESTRIAL PLANTS AND INVERTEBRATES

Atrazine enters plants primarily by way of the roots and secondarily by way of the foliage, passively translocated in the xylem with the transpiration stream, and accumulates in the apical meristems and leaves (Hull 1967; Forney 1980; Reed 1982; Wolf and Jackson 1982). The main phytotoxic effect is the inhibition of photosynthesis by blocking the electron transport during Hill reaction of photosystem II. This blockage leads to inhibitory effects on the synthesis of carbohydrate, a reduction in the carbon pool, and a buildup of carbon dioxide within the leaf, which subsequently causes closure of the stomates, thus inhibiting transpiration (Stevenson et al. 1982; Jachetta et al. 1986; Shabana 1987).

Atrazine is readily metabolized by tolerant plants to hydroxyatrazine and amino acid conjugates. The hydroxyatrazine can be further degraded by dealkylation of the side chains and by hydrolysis of resulting amino groups on the ring and some carbon dioxide production (Hull 1967; Reed 1982; Beste 1983). Resistant plant species degrade atrazine before it interferes with photosynthesis. Corn, for example, has an enzyme (2,4-dihydroxy-7-methoxy-1, 4 [2H]-berzoxazin-3 [4H]-one) that degrades atrazine to nonphytotoxic hydroxyatrazine (Wu 1980; Stevenson et al. 1982). In sensitive plants, such as oats, cucumber, and alfalfa, which are unable to detoxify atrazine, the compound accumulates, causing chlorosis and death (Anon. 1963; Hull 1967). Corn and sorghum excrete about 50% of accumulated atrazine and metabolize the rest to insoluble residues that are indigestible to sheep (*Ovis aries*) and rats (*Rattus* sp.). These results strongly suggest that the final disposition of atrazine metabolites does not occur in either plants or animals, but ultimately through microbial breakdown (Bakke et al. 1972b).

Long-term applications of atrazine for weed control in corn result in degradation products, mainly hydroxylated analogues, that may persist in soil for at least 12 months after the final herbicide application, and may enter food crops planted in atrazine-treated soil in the years after cessation of long-term treatment (Frank and Sirons 1979; Kulshrestha et al. 1982). In one example, atrazine was applied to a corn field for 20 consecutive years at rates of 1.4 to 2.2 kg/ha (Khan and Saidak 1981). Soils collected 12 months after the last application contained atrazine (55 ug/kg dry weight), hydroxyatrazine (296 ug/kg), and various mono dealkylated hydroxy analogues (deethylatrazine at 14 ug/kg, deethylhydroxyatrazine, at 17 ug/kg, and deisopropylhydroxyatrazine at 23 ug/kg). Oat (*Avena sativa*) seedlings grown in this field contained hydroxyatrazine (64 to 73 ug/kg fresh weight) and deisopropylhydroxyatrazine (84 to 116 ug/kg); similar results were obtained with timothy, *Phleum pratense* (Khan and Saidak 1981). In areas with a relatively long growing season, a double cropping of soybeans (*Glycine max*)--planted after corn is harvested for silage or grain--is gaining acceptance. Under conditions of warm weather, relatively high rainfall, and sandy soils, soybeans can be safely planted after corn (14 to 20 weeks after atrazine application) when rates of atrazine normally recommended for annual weed control (1.12 to 4.48 kg/ha) are used (Brecke et al. 1981).

Seed germination of sensitive species of plants was reduced by 50% at soil atrazine concentrations between 0.02 and 0.11 mg/kg (Table 3). Mustard (*Brassica juncea*) was especially sensitive, and died shortly after germination. Soil atrazine residues of this magnitude were typical of those remaining at the beginning of a new growing season following corn in sandy loam under tropical conditions (Kulshrestha et al. 1982). Reduction in seed germination was also noted at soil atrazine concentrations of 0.25 to 0.46 mg/kg for the lentil *Lens esculenta*, the pea *Pisum sativum*, and the gram *Cicer arietinum* (Kulshrestha el al. 1982). Many species of

mature range grasses are tolerant of atrazine but are susceptible as seedlings; seedlings of the most sensitive three species of eight tested were adversely affected in soils containing 1.1 mg atrazine/kg (Bahler et al. 1984; Table 3).

Soil fungi and bacteria accumulated atrazine from their physicochemical environment by factors between 87X and 132X (Wolf and Jackson 1982), probably through passive adsorption mechanisms. Atrazine stimulated the growth of at least two common species of fungal saprophytes known to produce antibiotics: *Epicoccum nigrum* and *Trichoderma viride* (Richardson 1970). *Trichoderma*, for example, grew rapidly at all treatments tested (up to 80 mg/kg soil) and showed optimal growth 3 to 10 days postinoculation (Rodriguez-Kabana et al. 1968). Atrazine suppressed the growth of various species of soil fungi, including *Rhizoctonia solani*, *Sclerotium rolfsii*, and *Fusarium* spp., and stimulated the growth of other species known to be antagonistic to *Fusarium*. This selectivity is likely to induce a shift in the fungal population of atrazine-treated soil that would be either harmful or beneficial to subsequent crops, depending on whether saprophytic or pathogenic fungi attained dominance (Richardson 1970).

At 2.5 mg atrazine/kg soil, equivalent to 2 kg/ha in the top 10 cm, field and laboratory studies demonstrated that mortality in arthropod collembolids (*Onchiurus apuanicus*) was 47% in 60 days; however, fecundity was not affected at dose levels up to 5.0 mg/kg soil. It was concluded that atrazine applications at recommended treatment levels had negligible long-term population effects on sensitive species of soil fauna (Mola et al. 1987). At 5 or 8 kg atrazine/ha, all species of soil fauna tested, except some species of nematodes, were adversely affected (Popovici et al. 1977). One month postapplication, population reductions of 65% to 91% were recorded in protozoa, mites, various insect groups, and collembolids at 5 kg/ha; after 4 months, populations were still depressed by 55% to 78% (Popovici et al. 1977). At 9 kg atrazine/ha, soil faunal populations of beetles, collembolids, and earthworms remained depressed for at least 14 months after initial treatment (Mola et al. 1987).

Table 3. Atrazine effects on selected species of terrestrial plants.

Species, dose, and other variables	Effect and reference
Soil alga, *Chlorella vulgaris*	
0.1 and 0.5 ug/L soil water	Chlorophyll production stimulated (Torres and O'Flaherty 1976)
1.0 ug/L and higher	Chlorophyll production inhibited; more-than-additive toxicity observed in combination with simazine and malathion (Torres and O'Flaherty 1976)
Mustard, *Brassic juncea*	
20 ug/kg dry weight soil	Seed germination reduced 50%; death shortly thereafter (Kulshrestha et al. 1982)
Cyanobacteria, 4 species, isolated from rice-cultivated soils in Egypt	
50 ug/L soil water for 7 days	Suppressed pigment biosynthesis in *Aulosira fertilissima* and *Tolypothrix tenuis*, reduced growth in *Anabaena oryzae* and *Nostoc muscorum*, and reduced carbohydrate content in *Nostoc* and

	Tolypothrix (Shabana 1987)
100 to 500 ug/L soil water for 7 days	All variables affected in all species (Shabana 1987)
Barley, *Hordeum vulgare*	
50 ug/kg dry weight soil	Seed germination reduced 50% (Kulshrestha et al. 1982)
Oat, *Avena sativa*	
70 ug/kg dry weight soil	Seed germination reduced 50% (Kulshrestha et al. 1982)
Wheat, *Triticum aestivum*	
110 ug/kg dry weight soil	Seed germination reduced 50% (Kulshrestha et al. 1982)
0.6 kg/ha	Effectively controls weeds in wet sandy soils; some damage to crop possible in dry clay soils (Amor et al. 1987)
Range grasses, four species, seedlings	
1.1 mg/kg soil	Survival reduced, and growth reduced in surviving seedlings (Bahler et al. 1984)
Weed, *Chenopodium album*, seedlings from French garden never treated with chemicals	
0.5 kg/ha	Survival 12%; progeny of these survivors were resistant to 1 kg/ha treatment (Bettini et al. 1987)
1.0 kg/ha	Fatal to 100% (Bettini et al. 1987)
Corn, *Zea mays*	
1.25 kg/ha	No effect on growth or yield (Malan et al. 1987)
5.0 kg/ha	Severe phytotoxicity 25 to 30 days after planting; growth inhibition during early development. Recovery, with no negative effect on final yield (Malan et al. 1987)
Soybean, *Glycine max*, planted after corn, *Zea mays*	
2.24 kg/ha	No effect on yield when planted at least 8 weeks after atrazine application (Brecke et al. 1981)
4.48 kg/ha	At least 10-week interval required after atrazine application for successful germination (Brecke et al. 1981)

AQUATIC PLANTS

Since the mid-1960's, seagrasses and freshwater submersed vascular plants have declined in many aquatic systems, especially Chesapeake Bay (Forney and Davis 1981; Stevenson et al. 1982; Kemp et al. 1983; Cunningham et al. 1984). These plants provide food and habitat to diverse and abundant animal populations. In Chesapeake Bay, this decline has been associated with an overall decline in the abundance of fish and

wildlife, and has been interpreted as an indication of serious disturbance in the ecological balance of the estuary. More than 10 native species of submerged aquatic plants in Chesapeake Bay have decreased in abundance. In the upper estuary, this decline was preceded by an invasion of Eurasian watermilfoil (*Myriophyllum spicatum*), which eventually also died back (Kemp et al. 1983). Runoff of herbicides, including atrazine, from treated agricultural lands has been suggested as a possible factor involved in the disappearance of Chesapeake Bay submerged vegetation. During the past 20 years, the most widely used herbicide in the Chesapeake Bay watershed--and in the surrounding coastal plain--has been atrazine. Since its introduction into the region in the early 1960's, atrazine use has grown to about 200,000 kg annually in Maryland coastal communities alone (Kemp et al. 1983). Potentially phytotoxic concentrations of atrazine would be expected in estuaries with the following characteristics (which seem to apply in most of upper Chesapeake Bay): immediately adjacent to cornfields in the watershed; rains occur shortly after atrazine application; clay soils in fields producing more rapid runoff; soils with circumneutral pH and relatively low organic content; and large estuarine areas of low salinity and poor mixing (Stevenson et al. 1982).

At this time, most authorities agree that atrazine could induce some loss in aquatic vegetation but was not likely to have been involved in the overall decline of submerged plants in Chesapeake Bay (Forney 1980; Plumley and Davis 1980; Forney and Davis 1981; Kemp et al. 1983, 1985; Jones et al. 1986), and that nutrient enrichment and increased turbidity probably played major roles (Kemp et al. 1983, 1985). In the open waters of Chesapeake Bay, atrazine concentrations have rarely exceeded 1 ug/l; in major tributaries, such as the Choptank and Rappahanock Rivers, concentrations of 5 ug/l may occur after a major spring runoff. These runoffs sometimes generate transient, 2- to 6-hour concentrations up to about 40 ug/l in secondary tributaries (Kemp et al. 1983). In some small coves on the Chesapeake Bay, submerged plants may be exposed periodically to atrazine concentrations of 5 to 50 ug/l for brief periods during runoffs; however, dilution, adsorption, and degradation tend to reduce concentrations in the water phase to <5 ug/l within 6 to 24 hours (Jones et al. 1986). Since atrazine degrades rapidly in estuarine conditions Tb 1/2 1 to 6 weeks), concentrations of atrazine on suspended and deposited estuarine sediments were seldom >5 ug/kg, suggesting little potential for accumulation (Kemp et al. 1983). The photosynthesis of redheadgrass (*Potamogeton perfoliatus*) was significantly inhibited by atrazine concentrations of 10 to 50 ug/l; however, it returned to normal levels within 1 hour after atrazine was removed (Jones et al. 1986). Recovery of redheadgrass within several weeks has also been documented after exposure to 130 ug/l for 4 weeks (Cunningham et al. 1984). In Chesapeake Bay, potential long-term exposure of submersed aquatic plants to concentrations of atrazine in excess of 10 ug/l is doubtful; therefore, any observed reductions in photosynthesis by these plants under such conditions would be minor and reversible (Jones et al. 1986).

Some authorities, however, suggest that the effects of atrazine on aquatic plants may be substantial. For example, atrazine concentrations between 1 and 5 ug/l adversely affect phytoplankton growth and succession; this, in turn, can adversely affect higher levels of the food chain, beginning with the zooplankton (DeNoyelles et al. 1982). Also, exposure to environmentally realistic concentrations of 3.2 to 12 ug atrazine/l for about 7 weeks was demonstrably harmful to wildcelery (*Vallisneria americana*), a submersed vascular plant in Chesapeake Bay (Correll and Wu 1982 . At highest concentrations of 13 to 1,104 ug/l for 3 to 6 weeks, growth of representative submerged macrophytes in Chesapeake Bay was significantly depressed, and longer exposures were fatal to most species (Forney 1980). Atrazine concentrations of 100 ug/l reportedly cause permanent changes in algal community structure after exposure for 14 days, including decreased density and diversity, altered species composition, and reduced growth (Hamala and Kollig 1985). It seems that additional research is needed on the role of atrazine and on its interactions with other agricultural chemicals in regard to observed declines in submerged plants. It is emphasized that degradation products of atrazine did not play a role in the disappearance of the submerged vascular plants from the Chesapeake Bay. For example, 500 ug/l of deethylated atrazine was needed to produce 20% to 40% photosynthetic inhibition in four major species of submerged macrophytes in 2 hours, but only 95 ug/l of the parent atrazine caused 50% inhibition in a similar period (Jones and Winchell 1984).

Many studies have been conducted on the effects of atrazine on various species of aquatic flora under controlled conditions (Table 4). At concentrations of 1 to 5 ug/l, and exposure periods of 5 minutes to 7 weeks, documented adverse effects in sensitive species included inhibition in photosynthesis, growth, and oxygen evolution (Table 4). Higher concentrations were associated with altered species composition, reduced carbon uptake, reduced reproduction, high accumulations of atrazine, decreased chlorophyll *a* production, ultrastructural changes on chloroplasts, and death (Table 4). Phytotoxic effects were significantly increased at

elevated levels of incident illumination, elevated water temperatures, decreased water pH, decreased dissolved oxygen concentrations, decreased nutrient content, and at increasing atrazine concentrations in the water column (Forney and Davis 1981; Karlander et al. 1983; Jones and Estes 1984; Malanchuk and Kollig 1985; Mayasich et al. 1986). Phytotoxicity was not significantly influenced by atrazine concentrations in the sediments or hydrosoils, or by the salinity of the medium (Forney 1980; Forney and Davis 1981; Jones and Estes 1984; Huckins et al . 1986).

Atrazine was 4 to 10 times more effective than its degradation products in producing growth reduction, photosynthesis inhibition, and acetylene-reducing ability in two species of green algae, *Chlorella pyrenoidosa*, *Scenedesmus quadricauda*, and three species of cyanobacteria, *Anabaena* spp. (Stratton 1984). Atrazine reduced growth 50% at 0.03 to 5.0 mg/l and inhibited photosynthesis 50% at 0.1 to 0.5 mg/l. Comparable values for deethylated atrazine were 1.0 to 8.5 mg/l for growth reduction, and 0.7 to 4.8 mg/l for photosynthesis inhibition; for deisopropylated atrazine, these values were 2.5 to >10 mg/l for growth reduction and 3.6 to 9.3 mg/l for photosynthesis inhibition; hydroxyatrazine and diaminoatrazine were nontoxic to most cultures tested (Stratton 1984). Smooth cordgrass (*Spartina alterniflora*), the major emergent species in North American salt marshes, is only slightly affected by relatively high levels of atrazine, due possibly to its ability to metabolize this compound (Davis et al. 1979; Forney and Davis 1981; Stevenson et al. 1982). Studies with radiolabeled atrazine and *Spartina* roots were conducted during 2-day exposures, followed by 28 days in atrazine-free solution (Pillai et al. 1977; Weete et al. 1980). After 2 days, 90% of the atrazine had translocated to the shoots. Atrazine was readily metabolized to chloroform-soluble substances, then to water-soluble substances, and finally to insoluble substances. Atrazine in the chloroform-soluble fraction decreased from 85% to 24% by day 28; the aqueous fraction contained 15% at the start and 60% at day 28. The basis of *Spartina* resistance is due primarily to its ability to convert atrazine to N-dealkylation products, such as 2-chloro-4-amino-6-isopropylamino-s-triazine. However, at least 14 water-soluble metabolites were isolated; about half contained the fully alkylated triazine rings, and most of the others had the 4-amino-6-isopropylamino derivative. Acid hydrolysates of the metabolites contained small amounts of amino acids, suggesting that a conjugation pathway, in addition to N-deakylation, may be operative in *Spartina*.

Table 4. Atrazine effects on selected species of aquatic plants.

Species, dose, and other variables	Effect and reference
Phytoplankton communities in experimental microcosms	
0.5 to 5.0 ug/L, 39 weeks	No measurable adverse effects (Brockway et al. 1984)
1.0 to 5.0 ug/L, several days	Reduced photosynthesis in sensitive species (DeNoyelles et al. 1982)
>17.9 ug/L, 21 days	Decreased oxygen production, decreased content of calcium and magnesium (Pratt et al. 1988)
20 ug/L, 20 days	Altered species composition (DeNoyelles and Kettle 1985)
20 ug/L, 136 days	Reduced growth, altered succession; atrazine resistant species now dominant (DeNoyelles et al. 1982)
50 ug/L, 12 days	Oxygen production decreased 20% to 30% (Brockway et al. 1984)
100 ug/L, 14 days	Algal densities and biomass reduced, diversity decreased, and species composition altered. Within 16 days after removal of atrazine stress, net productivity was indistinguishable from controls, but

	community structure remained altered at day 21 (Hamala and Kollig 1985)
100 ug/L, 20 days	Carbon uptake reduced >40% (DeNoyelles and Kettle 1985)
500 ug/L, 53 days	Immediate decline in primary productivity and community metabolism; no recovery (Stay et al. 1985)
5,000 ug/L, 12 days	Death (Brockway et al. 1984)
Alga, *Cyclotella meneghiniana*	
1.0 ug/L, 5 min	Some inhibition in oxygen evolution (Millie and Hersh 1987)
99 to 243 ug/L, 5 min	Oxygen evolution reduced 50% (Millie and Hersh 1987)
500 ug/L, 5 min	Oxygen evolution 100% inhibited (Millie and Hersh 1987)
Wildcelery, *Vallisneria americana*	
1.3 ug/L, 47 days	No measurable effect (Correll and Wu 1982)
3.2 ug/L, 49 days	Some reduction in leaf area (Correll and Wu 1982)
12 ug/L, 47 days	LC-50; reduced reproduction and leaf area in survivors (Correll and Wu 1982)
75 ug/L, 12 to 28 days	Inhibited photosynthesis (Correll and Wu 1982)
100 ug/L, 6 weeks	Growth inhibited 29% (Forney and Davis 1981)
120 ug/L, 30 days	LC-100 (Correll and Wu 1982)
163 ug/L, 21 to 42 days	Growth inhibition of 50% (Forney 1980)
320 ug/L, 6 weeks	Growth inhibited 36% (Forney and Davis 1981)
Elodea, *Elodea canadensis*	
3.2 ug/L, 3 to 4 weeks	Growth inhibited 1% (Stevenson et al. 1982)
13 ug/L, 21 to 42 days	Growth inhibited 50% (Forney 1980)
32 ug/L, 3 to 4 weeks	Growth inhibited 15% to 39% (Forney and Davis 1981)
100 ug/L, 3 to 4 weeks	Growth inhibited 53% (Forney and Davis 1981)
Redheadgrass, *Potamogeton perfoliatus*	
4 ug/L, 4 weeks	Photosynthesis reduced 10% (Kemp et al. 1985)
10 ug/L, 3 weeks	Growth inhibited 15% (Forney and Davis 1981)
50 ug/L, 2 h	Equilibrium reached within 15 min, maximum residues of 3.5 mg/kg dry weight (Jones et al. 1986)
55 ug/L, 4 weeks	Photosynthesis reduced 50% (Kemp et al. 1985; Larsen et al. 1986)
80 ug/L, 2 h	Photosynthesis inhibited 50% (Jones et al. 1986)
100 ug/L, 2 h	Photosynthesis inhibition and residues of about 9.0 mg/kg dry weight; recovery rapid in atrazine-free medium but some photo-synthetic depression for up to 77 h (Jones et al. 1986)
100 ug/L, 4 weeks	Photosynthesis inhibition; water levels of 87 ug atrazine/L at 4 weeks; recovery in 2 to 3 weeks in atrazine-free medium (Kemp et al. 1985)
130 ug/L, 4 weeks	Decreased oxygen production immediately on exposure; significant recovery within 2

	weeks despite constant atrazine concentrations (Cunningham et al. 1984)
320 ug/L, 3 weeks	Growth inhibited 45% to 54% (Forney and Davis 1981)
450 to 650 ug/L, 2 h	Photosynthesis inhibited 87%; residues of about 5 mg/kg dry weight (Jones et al. 1986)
474 ug/L, 21 to 42 days	Growth reduced 50% (Forney 1980)
1,200 ug/L, 4 weeks	Pronounced phytotoxic effects; no recovery (Cunningham et al. 1984)
Eurasian watermilfoil, *Myriophyllum spicatum*	
5 ug/L, 4 weeks	Enhanced oxygen production (Kemp et al. 1985)
11 ug/L, 4 weeks	Photosynthesis reduced 1% (Kemp et al. 1985)
50 ug/L, 4 weeks	Oxygen production depressed (Kemp et al. 1985)
117 ug/L, 4 weeks	Photosynthesis reduced 50% (Kemp et al. 1985; Larsen et al. 1986)
320 ug/L, 4 weeks	Growth inhibited 22% (Forney and Davis 1981)
1,000 ug/L, 4 weeks	Growth inhibited 62% (Forney and Davis 1981)
1,000 ug/L, 4 weeks	Residues <1 ug/kg (Kemp et al. 1985)
1,104 ug/L, 21 to 42 days	Growth inhibited 50% (Forney 1980)
Common cordgrass, *Spartina alterniflora*	
10 ug/L, 3 to 4 weeks	Biomass reduction of 6% (Stevenson et al. 1982)
100 ug/L, 3 to 4 weeks	Biomass reduction of 34% (Stevenson et al.1982)
1,000 ug/L, 3 to 4 weeks	Biomass reduction of 46% (Steveneson et al. 1982)
Shoal grass, *Halodule wrightii*	
10, 40, or 120 ug/L, 22 days	Enhanced growth when compared to controls (Mitchell 1985)
420 ug/L, 22 days	Above ground biomass reduced 26% (Mitchell 1985)
1,490 ug/L, 22 days	Above ground biomass reduced 45% compared to controls (Mitchell 1985)
Marine alga, *Nannochlsoris oculata*	
15 ug/L, 7 days	Growth reduction (Mayasich et al. 1987)
50 ug/L, 72 h	Some growth inhibition; inhibition greatest under conditions of elevated temperature and illumination (Karlander et al. 1983)
Alga and macrophytes, various species	
20 ug/L, 6 weeks	Bioconcentration factors up to 32x Huckins et al. 1986)
Submerged aquatic macrophytes, 4 species: *Potamogeton* sp., *Ruppia* sp., *Myriophyllum* sp., *Zannichellia* sp.	
20 ug/L, 2 h	Photosynthesis inhibition of about 1% (Jones and Winchell 1984)
95 ug/L, 2 h	Photosynthesis inhibition 50%; atrazine significantly more effective than deethylated atrazine, seisopropylated atrazine, and hydroxyatrazine, in that order, in effecting

	inhibition (Jones and Winchell 1984)
Algae, various species	
22 ug/L, 7 days	No effect on photosynthesis rate, chlorophyll content, or cell numbers (Plumley and Davis 1980)
37 to 308 ug/L, 24 h	Carbon uptake reduced 50% (Larsen et al. 1986)
60 to 100 ug/L, 72 h	Growth inhibited 50% in seven species (Mayer 1987)
60 to 460 ug/L, 1 h	Oxygen evolution inhibited 50% in 18 species (Hollister and Walsh 1973)
77 to 102 ug/L, 24 h	Photosynthesis reduction of 50% (Larsen et al. 1986)
80 to 907 ug/L, 3 weeks	Growth inhibited 50% (Larsen et al. 1986)
100 ug/L, 2 h	Growth inhibited 50% in three species (Mayer 1987)
100 ug/L, 3 days	Reduced productivity; complete recovery by day 7 (Moorhead and Kosinski 1986)
100 to 300 ug/L, 10 days	Growth inhibited 50% in four species (Mayer 1987)
100 to 460 ug/L, 72 h	Growth inhibited 50% in eight species (Mayer 1987)
220 ug/L, 7 days	Reduced photosynthesis; no effect on chlorophyll production and cell division rate in three estuarine species (Plumley and Davis 1980)
Algae, *Chlorella* spp.	
54 ug/L, 10 days	Growth reduction of 30% (Gonzalez-Murua et al. 1985)
200 ug/L, 48 h	Photosynthesis reduced 30%, but no effect on growth (Lay et al. 1984)
250 ug/L, 7 days	Growth reduction; 90% of atrazine passively accumulated within 1 h (Veber et al. 1981)
Submersed vascular plant, *Zannichellia palustris*	
75 ug/L, 21 to 42 days	Photosynthesis inhibition (Correll and Wu 1982)
Submersed vascular plant, *Potamogeton pectinatus*	
75 ug/L, 21 to 42 days	Photosynthesis stimulation (Correll and Wu 1982)
650 ug/L, 21 to 42 days	Photosynthesis inhibition (Correll and Wu 1982)
Submersed vascular plant, *Zostera marina*	
75 ug/L, 21 to 42 days	Photosynthesis stimulation (Correll and Wu 1982)
650 ug/L, 21 to 42 days	Photosynthesis inhibition (Correll and Wu 1982)
Periphyton communities in freshwater enclosures	
80 to 1,560 ug/L, 10 months	Declines in net production, cell numbers, biomass, number of taxa, and chlorophyll activity; larger algal species (*Mougeotia, Oedogonium*, *Tolypothrix*, *Epithemia*) were the most sensitive. At higher concentrations, population shifted from a chlorophyte-dominated to a diatom-dominated community

	(Hamilton et al. 1987)
100 ug/L, 2 treatments, 6 weeks apart	After initial application, all blue green algae disappeared and organic matter significantly decreased. Within 3 weeks of second treatment, a 36% to 67% reduction in organic matter, chlorophyll, algal biomass, and rate of carbon assimilation was measured. Some species of green algae decreased in abundance, but others increased (Herman et al. 1986)
Duckweed, *Lemna minor*	
250 ug/L, 15 days	Ultrastructural changes on chloroplasts of mesophyll cells; no effect on chlorophyll and lipid distribution (Beaumont et al. 1980; Grenier et al. 1987)

Estuarine fungi contribute substantially to plant detritus due to their abundance and degradative potential. Fungi are known to accumulate soluble atrazine from seawater through sorption, and release up to *2.2%* as hydroxyatrazine and other atrazine metabolites; another 4.6% is more tightly associated and less available to the external environment. The combined processes result in atrazine accumulation, and may contribute to its transport and redistribution through the estuary (Schocken and Speedie 1982, 1984).

AQUATIC FAUNA

A marine copepod (*Acartia tonsa*) was the most sensitive aquatic animal tested against direct effects of atrazine, having a 96-hour LC-50 of 94 ug/l (Table 5). Adverse effect levels to selected species of aquatic invertebrates and fishes ranged from 120 ug/l to 500 ug/l, based on lifetime exposure studies (Table 5). The most sensitive criterion measured during long-term chronic exposure varied among species. Among freshwater invertebrates, for example, the most useful criterion was survival for *Gammarus*, the number of young produced for *Daphnia*, and developmental retardation for *Chironomus* (Macek et al. 1976).

Table 5. Lethal and sublethal effects of atrazine on selected species of aquatic fauna. Concentrations listed are in micrograms of atrazine per liter of medium.

Ecosystem, organism, and other variables	Concentration (ug/L)	Effect	Reference [a]
Freshwater Invertebrates			
Midge, *Chironomus riparius*			
Adults	20	Whole body residue of 160 ug/kg in 6 weeks	1
Larvae	20	Whole body residue of 569 ug/kg in 6 weeks	1
Cladoceran, *Daphnia magna*	20	After 6 weeks, whole body residue of 300 ug/kg	1
D. magna	200	Exposure for six generations. Number of	

		young per female in 21 days did not differ from controls in generations 1, 2, and 3, but significant reduction measured in generations 4, 5, and 6	2
D. magna	6,900 (5,200 to 8,100)	LC-50 (48 h)	3
Scud, *Gammarus fasciatus*	60 to 140	MATC[b]	3
G. fasciatus	>2,400	Some deaths in 48 h	3
G. fasciatus	5,700 (3,600 to 8,000)	LC-50 (48 h)	3
Midge, *Chironomus tentans*	110 to 230	MATC[b]	3
C. tentans	500	Some deaths in 48 h	3
C. tentans	720 (360 to 1,440)	LC-50 (48 h)	3
Leeches, two species (*Glossiphonia complanata, Helobdella stagnalis*)	<1,000	Adverse effects on growth, food intake, and egg production	11
Leeches, two species	6,300 to 9,900	LC-50 (28 days)	11
Leeches, two species	16,000	No deaths in 96 h	11
Freshwater fishes			
Brook trout, *Salvelinus fontinalis*	60 to 120	MATC[b]	3
S. fontinalis	450	Reduced incubation time of developing embryos	3
S. fontinalis	740	After 44 weeks, concentration in muscle <0.2 mg/kg fresh weight	3
S. fontinalis	6,300 (4,100 to 9,700)	LC-50 (8 days)	3
Bluegill, *Lepomis macrochirus*	90 to 500	MATC[b]	3
L. macrochirus	94	After 78 weeks, concentration in muscle <0.2 mg/kg fresh weight	3
L. macrochirus	500	At 28 days, fish were lethargic and ate poorly, and swam erratically	3
L. macrochirus	6,700 (5,400 to 8,400)	LC-50 (7 days)	3
L. macrochirus	8,000 to 42,000	LC-50 (96 h)	3, 4, 5, 6
L. macrochirus	46,000	LC-50 (24 h)	6
Fathead minnow, *Pimephales promelas*	210	After 43 weeks, concentration in	

		eviscerated carcass was <1.7 mg/kg fresh weight	3
P. promelas,	210 to 520	MATC[b]	3
P. promelas fry	520	LC-25 (96 hours)	3
P. promelas	15,000 (11,000 to 20,000)	LC-50 (8 days)	3
Rainbow trout, *Salmo gairdneri*	4,500 to 24,000	LC-50 (96 h)	4, 6
Marine invertebrates			
Mysid shrimp, *Mysidopsis bahia*	80 to 190	MATC[b]	7
M. bahia	1,000 (650 to 3,100)	LC-50 (96 h)	7
Copepod, *Acartia tonsa*	94 (52 to 167)	LC-50 (96 h)	7
Brown shrimp, *Penaeus aztecus*	1,000	50% immobilized in 48 h	8
American oyster, *Crassostrea virginica,*	1,000	No effect on survival or growth	9
C. virginica	>1,000	Growth reduced 50% in 96 h	8
C. virginica	>30,000	No effect on development in 48 h	7
"Shrimp"	1,000	LC-30 (96 h)	9
Pink shrimp, *Penaeus duorarum*	6,900	LC-50 (96 h)	7
Grass shrimp, *Palaemonetes pugio*	9,000	LC-50 (96 h)	7
Fiddler crab, *Uca pugilator*	>29,000	LC-50 (96 h)	7
Fiddler crab, *Uca pugnax*	100,000	Interfered with escape response when exposed in August; negligible effects in November; young males most sensitive	10
U. pugnax	1,000,000 to 10,000,000	Reduced survival after 10 weeks	10
Mud crab, *Neopanope texana*	750,000	No deaths in 96 h	9
N. texana	1,000,000	LC-50 (96 h)	9
Marine fishes			
Sheepshead minnow, *Cyprinodon variegatus*	1,900 to 3,400	MATC[b]	7
C. variegatus	>16,000	LC-50 (96 h)	7
Spot, *Leiostomus xanthurus*	8,500	LC-50 (96 h)	7

[a]References: 1, Huckins et al. 1986; 2, Kaushik et al. 1985; 3, Macek et al. 1976; 4, Beste 1983; 5, Klaassen and Kadoum 1979; 6, Mayer and Ellersieck 1986; 7, Ward and Ballantine 1985; 8, Mayer 1987; 9, Stevenson et al. 1982; 10, Plumley et al. 1980; 11, Streit and Peter 1978.

[b]Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing measurable effect.

Ambient concentrations as low as 20 ug atrazine/l have been associated with adverse effects on freshwater aquatic fauna, including benthic insects (Dewey 1986) and teleosts (Kettle et al. 1987), although effects were considered indirect. For example, the abundance of emerging chironomids (*Labrundinia pilosella*), and other aquatic insects declined at 20 ug atrazine/l (Dewey 1986). Richness of benthic insect species and total emergence declined significantly with atrazine addition. The effects were primarily indirect, presumably by way of reduction in food supply of nonpredatory insects, and to some extent their macrophyte habitat. Dietary habits and reproductive success were negatively affected in three species of fish after exposure for 136 days in ponds containing 20 ug atrazine/l (Kettle et al. 1987). About 70% of the original concentration applied was present in water at the end of the study. The reproduction of channel catfish (*Ictalurus punctatus*) and gizzard shad (*Dorosoma cepedianum*) failed, and that of bluegills, as measured by number of young per pond, was reduced more than 95%. Also, the number of prey items in the stomachs of bluegills were significantly higher in control ponds (25.6) than in a treated pond (3.8), and number of taxa represented were significantly greater. Macrophyte communities in treated ponds were reduced more than 60% in 2 months. The authors concluded that the effects of atrazine on bluegills were probably indirect, and that the reduction of macrophytes that had provided habitat for food items led to impoverished diets and more cannibalism by adult bluegills (Kettle et al. 1987).

Bioaccumulation of atrazine from freshwater is limited, and food chain biomagnification is negligible. In a farm pond treated once with 300 ug atrazine/l, residues at 120 days posttreatment ranged between 204 and 286 ug/kg in mud and water, and from not detectable in bullfrog (*Rana catesbeiana*) tadpoles to 290 ug/kg (all fresh weights) in whole bluegills; values were intermediate in zooplankton and clams. No residues were detectable in biological components one year posttreatment, when residues were <21 ug/kg in water and mud (Klaassen and Kadoum 1979). In a laboratory stream treated four times with 25 ug atrazine/l for 30 days, followed by depuration for 60 days, maximum accumulation factors ranged from about 4X in annelids to 480X in mayfly nymphs; however, residue concentrations declined to posttreatment levels within a few days after depuration began. Maximum atrazine concentrations recorded, in mg/kg whole organism fresh weight, were 0.2 in the clam *Strophitis rugosus*, 0.4 in the snail *Physa* sp., 0.9 in crayfish, *Orconectes* sp., 2.4 in the mottled sculpin *Cottus bairdi*, 3.0 in the amphipod *Gammarus pseudolimnaeus*, and 3.4 in mayflies, *Baetis* sp. (Lynch et al. 1982). In studies with the freshwater snail *Ancylus fluviatilis* and fry of the whitefish *Coregonus fera*, atrazine was rapidly accumulated from the medium by both species and saturation was reached within 12 to 24 hours; bioconcentration factors were 4X to 5X at ambient water concentrations of 50 to 250 ug atrazine/l (Gunkel and Streit 1980; Gunkel 1981). Elimination of atrazine was rapid: 8 to 62 minutes for *Coregonus*, and 18 minutes for *Ancylus*. No accumulation of atrazine was recorded in molluscs, leeches, cladocerans, or fish when contamination was by way of the diet (Gunkel and Streit 1980; Gunkel 1981). Atrazine accumulations in *Daphnia pulicaria* were significantly correlated with whole body protein content at low (8 °) water temperatures, and with fat content at elevated (20°C) water temperatures (Heisig-Gunkel and Gunkel 1982).

Atrazine is rapidly degraded in boxcrabs (*Sesarma cinereum*) feeding on smooth cordgrass (*Spartina alterniflora*) grown in radiolabeled atrazine solution. After 10 days, only 1.2% of the total radioactivity in the crab was unchanged atrazine, compared to 24% in the food source. The accumulation of water-soluble atrazine metabolites (86% of total radioactivity) in *Sesarma* suggested that glutathione conjugation, or a comparable pathway, was responsible for the almost complete degradation and detoxification of atrazine in crabs (Davis et al. 1979; Pillai et al. 1979). Atrazine does not appear to be a serious threat to crabs in Chesapeake Bay, where water concentrations of 2.5 ug/l have been recorded, although it could have an indirect effect on crabs by decreasing the algal population, which composes a portion of their diet (Plumley et al. 1980).

BIRDS

Atrazine is not acutely lethal to birds at realistic environmental levels, i.e., oral LD-50 values were >2,000 mg/kg BW and dietary LC-50s were >5,000 mg/kg (Table 6). Also, the probability is low for chronic effects of atrazine on wetland aquatic organisms and for biomagnification of toxic residues through waterfowl food chains (Huckins et al. 1986). However, indirect effects of atrazine on insect- and seed-eating birds have not been investigated, and this may be critical to the survival of certain species during nesting and brood-rearing. Studies are needed on the potential indirect ecosystem effects of atrazine, with special reference to seed-eating birds.

Domestic chickens (*Gallus* sp.) rapidly metabolized atrazine by way of partial N-dealkylation accompanied by hydrolysis; dealkylation occurred mainly at the ethylamino group, resulting in intermediate degradation products (Foster and Khan 1976; Khan and Foster 1976). In vitro studies with bird liver homogenates also demonstrated active transformation of atrazine and its metabolites. Chicken liver homogenates released nonextractable atrazine residues that had accumulated in corn plants, present mainly as 2-chloro mono N-dealkylated compounds, and subsequently metabolized them to 2-hydroxy analogues (Khan and Akhtar 1983). Liver homogenates in the goose (*Anser* sp.) contained enzyme systems that metabolized atrazine by partial N-dealkylation and hydrolysis; hydrolysis predominated and resulted in the formation of hydroxyatrazine, which does not undergo further degradation by dealkylation. But partly N-dealkylated metabolites, such as deethylatrazine and deisopropylatrazine, were further hydrolyzed to the corresponding hydroxy analogues (Foster et al. 1980).

MAMMALS

Data are lacking for atrazine's effects on mammalian wildlife, although there is a growing body of evidence on domestic and small laboratory mammals. Available data demonstrate that mammals are comparatively resistant to atrazine, and that the compound is not carcinogenic, mutagenic, or teratogenic (Reed 1982; Table 7). There have been no established cases of skin irritation resulting from experimental or commercial applications of atrazine, and no documented cases of poisoning in man (Anon. 1963; Hull 1967). No observable ill effects were detected in cattle, dogs, horses, or rats fed diets that included 25 mg atrazine/kg food over extended periods (Beste 1983). Most members of the triazine class of herbicides, including atrazine, have low acute oral toxicities--usually >1,000 mg/kg body weight (Murphy 1986; Table 7). But at dosages bordering on lethality, rats showed muscular weakness, hypoactivity, drooped eyelids, labored breathing, prostration (Beste 1983), altered liver morphology and renal function (Santa Maria et al. 1986, 1987), and embryotoxicity (Peters and Cook 1973).

Animals feeding-on atrazine-treated crops are at limited toxicological risk. Crop plants metabolize atrazine to hydroxyatrazine, dealkylated analogues, and cysteine-and glutathione-conjugates of atrazine; mature plants contain little unchanged atrazine. Bound atrazine residues in plants are of limited bioavailability to animals (Bakke et al. 1972a; Khan and Akhtar 1983; Khan et al. 1985). Metabolic degradation of atrazine in mammals is usually rapid and extensive; unchanged atrazine was recovered only from the feces (Anon. 1963). Liver enzyme systems in pigs, rats, and sheep metabolize atrazine by partial N-dealkylation and hydrolysis (Bakke et al. 1972a; Dauterman and Muecke 1974; Foster et al. 1980). However, atrazine is reportedly converted in vivo to N-nitrosoatrazine in mice, *Mus* sp. (Krull et al. 1980). Since N-nitrosoatrazine is carcinogenic and mutagenic to laboratory animals (Krull et al. 1980), more research is recommended on the extent of nitrosation of atrazine in the environment.

Table 6. Atrazine effects on selected species of birds.

Species, dose, and other variables	Effect and reference
Chicken, *Gallus* sp.	
Laying hens were fed diets containing 100 mg/kg for 7 days	No visible adverse physiological effects or signs of toxicity. No effect on egg production or growth. No residues of atrazine or its metabolites detected in eggs. In excreta, however, atrazine and atrazine metabolites were detected after 24 h on treated diet and remained measurable until day 11, or after 4 days on an untreated diet (Foster and Khan 1976; Reed 1982)
Adults fed diets containing 100 mg/kg for 7 days, followed by uncontaminated diet for 7 days. Residues of atrazine and its metabolites were determined in selected tissues	Residues, in mg/kg FW, were as follows: atrazine, 38.8 in abdominal fat and 0.04 in muscle; hydroxyatrazine, 16.2 in liver, 4.3 in kidney 2.5 in oviduct, 0.7 in abdominal fat, and 0.5 in gizzard; and deethylhydroxyatrazine in liver, 2.3 in kidney, 0.8 to 1.8 in muscle, and 0.3 in gizzard (Khan and Foster 1976)
Ring-necked pheasant, *Phasianus colchicus*	
Males, age 3 months, given 2,000 mg/kg body weight (BW), administered orally	Survivors showed weakness, hyperexcitability, ataxia, and tremors; remission by day 5 posttreatment (Hudson et al. 1984)
Mallard, *Anas platyrhynchos*	
Females, age 6 months, given 2,000 mg/kg BW, administered orally	Survivors showed weakness, tremors, ataxia, and weight loss. Signs of poisoning appeared within one hour posttreatment and persisted up to 11 days (Tucker and Crabtree 1970; Hudson et al. 1984)
19,650 mg/kg diet for 8 days	LD-50 (Beste 1983)
Coturnix, *Coturnix japonica*	
Chicks, age 7 days, given diets containing 5,000 mg/kg for 5 days plus 3	One of 14 birds tested died on day 3 of feeding; no other adverse effects reported (Hill and Camardese 1986)

days on untreated feed	
Northern bobwhite, *Colinus virginianus*	
5,760 mg/kg diet for 8 days.	LD-50 (Beste 1983)

Table 7. Lethal and sublethal effects of atrazine on selected species of mammals.

Species, dose, and other variables	Effect and reference
Cattle, Cow, *Bos* spp.	
30 mg atrazine/kg diet for 21 days	Tissue residues <0.1 mg/kg fresh weight (Reed 1982)
100 mg atrazine/kg diet for 21 days	No detectable atrazine (<0.04 mg/kg) or hydroxyatrazine (<0.05 mg/kg) found in milk (Reed 1982)
Domestic sheep, *Ovis aries*	
30 mg atrazine/kg diet for 28 days	Tissue residues <0.1 mg/kg fresh weight (Reed 1982)
100 mg atrazine/kg diet for 28 days	No adverse effects (Reed 1982)
Mice, *Mus* spp.	
46.4 mg/kg body weight (BW) given daily on days 6 through 14 of pregnancy	No effect on reproduction (Peters and Cook 1973)
82 mg/kg diet for 18 months	Negative oncogenicity results (Reed 1982)
1,750 to 3,900 mg/kg BW	Acute oral LD-50 value (Anon. 1963; Hull 1967; Reed 1982)
Dog, *Canis familiaris*	
150 mg/kg diet for two years, equivalent to 3.75 mg/kg BW daily	No observable effect level (Reed 1982)
1,500 mg/kg diet for two years	No oncogenic effects; decreased body weight, reduced hemoglobin and hematocrit (Reed 1982)
Rat, *Rattus* spp.	
Inhalation exposure to a dust aerosol of Atrazine 80W (80% wettable powder) for one hour to concentrations between 1.8 and 4.9 mg/L atmosphere	No deaths, or signs of toxicological or pharmacological effects (Hull 1967)

100 mg/kg diet for 2 years, equivalent to 5 mg/kg BW daily	No gross microscopic signs of toxicity (Anon. 1963; Reed 1982; Beste 1983)
100 mg/kg diet for three generations, equivalent to 5 mg/kg BW daily	No teratogenic or reproductive effects (Reed 1982)
Daily oral administration on days 6 to 15 of gestation, in mg/kg BW	
10	No adverse maternal or fetal effects (Infurna et al. 1988)
70	Increased salivation; initial reduction in feed consumption (Infurna et al. 1988)
700	Mortality 78% before necropsy; increased incidences of salivation, ptosis, bloody ulva, swollen abdomen, and fetal skeletal malformations (Infurna et al. 1988)
100, 200, 400, or 600 mg/kg BW daily, given orally for 14 days	All dose levels increased elimination of sodium, potassium, chloride, and urine protein; interference with creatinine clearance at 200 mg/kg BW and higher (Santa Maria et al. 1986)
100, 200, 400 or 600 mg/kg BW daily for 14 days	At 100 mg/kg, significant increases in serum lipids, serum alkaline phosphatase, and serum alanine aminotransferase; no liver histopathology At 200 mg/kg, a significant reduction in body weight. At 400 mg/kg, liver enlargement and loss in body weight. A dose-dependent decrease in growth and in serum glucose and a dose-related increase in total serum lipids were recorded. At 600 mg/kg, liver histopathology (Santa Maria et al. 1987)
100, 300, or 900 mg/kg diet for 3 weeks	Except for lymphoenia, which was observed at all dose levels, no other effects were measured in the 100 and 300 mg/kg groups. At 900 mg/kg, significant decreases occurred in body weight, food intake, blood lymphocytes and thymus weight, and significant increases occurred in thyroid weight, mesenteric lymph nodes, and histopathology (Vos et al. 1983)
200 mg/kg BW injected subcutaneously on days 3, 6, and 9 of gestation	No effect on number of pups per litter or on weight at weaning (Peters and Cook 1973)
800, 1,000, or 2,000 mg/kg BW injected	At 2,000 mg/kg BW, most pups born dead; at 800 and 1,000 mg/kg BW, litter size

subcutaneously on days 3, 6, and 9 of gestation	reduced 50% to 100% (Peters and Cook 1973)
1,000 mg atrazine/kg diet from first day of pregnancy throughout gestation	No effect on number of pups per litter or on weight on weaning (Peters and Cook 1973)
1,000 mg/kg diet for two years, equivalent to 50 mg/kg BW daily	No signs of oncogenicity, but reduced food intake and lower body weight (Reed 1982)
1,800 to 5,100 mg/kg BW	Acute oral LD-50 (Anon. 1963; Hull 1967; Reed 1982; Beste 1983)
White rabbit, *Oryctolagus cuniculus*	
Daily oral administration on gestational days 7 through 19, in mg/kg BW	
1	No adverse maternal or fetal affects (Infurna et al. 1988)
5	Moderate reductions in food consumption and body weight gain (Infurna et al. 1988)
75	Increased abortion rate; no death of does. Weight loss, reductions in feed consumption and fetal and embryotoxic effects, including reduced fetal weight and increased incidence in skeletal variations (Infurna et al. 1988)
9,300 mg/kg BW	Acute dermal LD-50 (Beste 1983)

CURRENT RECOMMENDATIONS

Labels on products containing atrazine are required to contain information on acceptable uses and potential hazards to groundwater and to fish and wildlife (EPA 1983). At present, atrazine is approved for use as an herbicide to control broadleaf and grassy weeds on corn, sorghum, sugarcane, pineapple, macadamia nuts, rangeland, turf grass sod, conifer reforestation areas, Christmas tree plantations, grass seed fields, noncrop land, guava, grass in orchards, millet, perennial ryegrass, and wheat. Because atrazine is expected to leach into groundwater, it was recommended (EPA 1983) that labels of atrazine products bear the following statement: "Atrazine leaches readily and accepted label rates have been found to result in contamination of water supplies by way of groundwater. Therefore users are advised to avoid use of atrazine in well drained soils, particularly in areas having high groundwater tables." Cautionary statements on potential hazards to living resources is another labeling requirement: "This pesticide is toxic to aquatic invertebrates. Do not apply to water or wetlands. Runoff and drift from treated areas may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning of equipment or disposal of wastes. Do not discharge into lakes, streams, ponds, or public water supplies unless in accordance with an [approved EPA] permit" (EPA 1983).

Current permissible tolerances for atrazine range from 0.02 mg/kg (the limit of detection of the analytical method) in meat, milk, and eggs, to 15 mg/kg in orchard grass forage, fodder, and hay (Reed 1982; EPA 1983). However, the current 15 mg/kg tolerance in forage is considered high, and a new upper limit of 4 mg/kg is proposed. This limit would be expressed in terms of atrazine and three major metabolites: 2-amino-4-chloro-6-isopropylamino-1, 3, 5-triazine; 2-amino-4-chloro-6-ethylamino-1, 3, 5-triazine; and 2-chloro-4, 6-diamino-1, 3, 5-triazine (Reed 1982; EPA 1983).

The maximum recommended safe level of atrazine to algal diatoms is 10 ug/l (Karlander et al. 1983), although temporary inhibition of chlorophyll production in sensitive algal species has been reported in the range of 1 to 5 ug/l (Torres and O'Flaherty 1976). Proposed atrazine concentrations for aquatic life protection range from about 1 to 11 ug/l: 1 to 2 ug/l for protection of estuarine productivity (Stevenson et al. 1982; Ward and Ballantine 1985); 1 to 7 ug/l for no adverse effect levels to most species of submerged aquatic vegetation (Glotfelty et al. 1984); 5 to 10 ug/l for minor reductions in photosynthesis in sensitive species of aquatic macrophytes (Glotfelty et al. 1984); 9 ug/l for sensitive aquatic invertebrates, as judged by an uncertainty factor of 10 applied to a 96-hour LC-50 (Ward and Ballantine 1985); and 11 ug/l for salt marsh algae, based on the least effect level of 110 ug/l, and an uncertainty factor of 10 (Plumley and Davis 1980). Atrazine concentrations >11 ug/l sometimes occur during periods of runoff and non-flushing (Stevenson et al. 1982), but rarely persist at levels necessary to markedly inhibit photosynthesis in aquatic plants, i.e., 60, to 70 ug/l (Glotfelty et al. 1984).

In laboratory animals, atrazine is only slightly toxic on an acute basis; no carcinogenic, mutagenic, or reproductive effects have been seen at low doses, and reduced food intake and body weight were the primary adverse effects seen at high doses in chronic studies with rats and dogs (Reed 1982). However, data are lacking on indirect ecosystem effects of atrazine application on terrestrial wildlife--especially on insectivores and granivores; studies should be initiated in this subject area.

No allowable daily intake of atrazine in the human diet has been established, although 0.0375 mg/kg body weight daily has been proposed --equivalent to 2.25 mg daily for a 60-kg adult, or 1.5 mg/kg diet based on 1.5 kg food daily (Reed 1982). In man, the theoretical maximum residue contribution (TRMC)--a worst case estimate of dietary exposure--is 0.77 mg daily, assuming 1.5 kg of food eaten daily; this is equivalent to 0.51 mg/kg diet, or 0.013 mg/kg body weight daily for a 60-kg person (EPA 1983). Another TRMC calculation is based on 0.233 mg daily per 1.5 kg diet, equivalent to 0.156 mg/kg diet, or 0.0039 mg/kg body weight daily for a 60-kg person (Reed 1982). Both TRMC estimates are substantially below the proposed limit of 0.0375 mg/kg body weight daily. Lifetime exposure to drinking water concentrations of 2.3 ug atrazine/l poses negligible risk to human health, as judged by the no adverse effect level of 7.5 ug/l when 1% of the allowable daily intake is obtained from this source (EPA 1987; Wilson et al. 1987). Higher allowable concentrations are proposed over short periods: 123 ug/l for adults and 35 ug/l for children over a 10-day period (EPA 1987).

Additional data are needed on toxicity, environmental fate, and chemistry of atrazine in order to maintain existing registrations or to permit new registrations (EPA 1983). Specifically, data are needed on mobility and degradation rates of atrazine and its metabolites in soils; accumulation studies in rotational crops, fish, and aquatic invertebrates; and chronic testing with representative flora and fauna on survival, reproduction, carcinogenesis, teratogenesis, and mutagenesis (EPA 1983). Animal metabolism studies are required if tolerances for residues in animal products are expressed in terms of atrazine and its metabolites (EPA 1983). Finally, more research on aquatic species is merited on synergistic and additive effects of atrazine in combination with other agricultural chemicals at realistic environmental levels of 1 to 50 ug/l, and on the toxic effects of dealkylated atrazine metabolites (Stevenson et al. 1982).

LITERATURE CITED

Amor, R. L., A. Kent, P. E. Ridge, and R. M. Binns. 1987. Persistence of atrazine in chemical fallows in the Victorian Wimmera and Mallee. Plant Protection Q. 21:38-40.

Anon. 1963. Atrazine- Geigy Agric. Chem. Tech. Bull. 63-1. 14 pp. Avail. from Geigy Chem. Corp., P.O. Box 430, Yonkers, New York.

Bahler, C. C., K. P. Vogel, and L. E. Moser. 1984. Atrazine tolerance in warm-season grass seedlings. Agron. J. 76:891-895.

Bakke, J. E., J. D. Larson, and C. E. Price. 1972a. Metabolism of atrazine and 2-hydroxyatrazine by the rat. J. Agric. Food Chem. 20:602-607.

Bakke, J. E., R. H. Shimabukuro, K. L. Davison, and G. L. Lamoureux. 1972b. Sheep and rat metabolism of the insoluble ^{14}C-residues present in ^{14}C-atrazine-treated sorghum. Chemosphere 1:21-24.

Beaumont, G., A. Lord, and G. Grenier. 1980. Effets physiologiques de l'atrazine a doses subletales sur *Lemna minor*. V. Influence sur l'ultrastructure des chloroplastes. Can. J. Bot. 58:1571-1577.

Beste, C. E. (ed.). 1983. Herbicide handbook of the Weed Science Society of America. Weed Science Society of America, 309 West Clark Street, Champaign, Illinois. 515 pp.

Bettini, P., S. McNally, M. Sevignac, H. Darmency, J. Gasquez, and M. Dron. 1987. Atrazine resistance in *Chenopodium album*. Plant Physiol. 84:1442-1446.

Brecke, B. J., W. L. Cuney, and D. H. Teem. 1981. Atrazine persistence in a corn-soy bean doublecropping system. Agron. J. 73:534-537.

Brockway, D. L., P. D. Smith, and F. E. Stancil. 1984. Fate and effects of atrazine in small aquatic microcosms. Bull. Environ. Contam. Toxicol. 32:345-353.

Correll, D. L., and T. L. Wu. 1982. Atrazine toxicity to submersed vascular plants in simulated estuarine microcosms. Aquat. Bot. 14:151-158.

Cunningham, J. J., W. M. Kemp, M. R. Lewis, and J. C. Stevenson. 1984. Temporal responses of the macrophyte *Potamogeton perfoliatus* L., and its associated autotrophic community to atrazine exposure in estuarine microcosms. Estuaries 7(4B):519-530.

Dao, T. H. 1977. Factors affecting atrazine adsorption, degradation, and mobility in soil. Ph. D. Thesis. University of Nebraska, Lincoln. 68 pp

Dauterman, W. C., and W. Muecke. 1974. *In vitro* metabolism of atrazine by rat liver. Pestic. Biochem. Physiol. 4:212-219.

Davis, D. E., J. D. Weete, C. G. P. Pillai, F. G. Plumley, J. T. McEnerney, J. W. Everest, B. Truelove, and A. M. Diner. 1979. Atrazine fate and effects in a salt marsh. U. S. Environ. Protection Agency Rep. 600/3-79-111. 84 pp.

DeNoyelles, F., Jr., and W. D. Kettle. 1985. Experimental ponds for evaluating bioassay predictions. Pages 91-103 *in* T. P. Boyle (ed.). Validation and predictability of laboratory methods for assessing the fate and effects of contaminants in aquatic ecosystems. ASTM Spec. Tech. Publ. 865. American Society for Testing and Materials, 1916 Race Street, Philadelphia, Pennsylvania 19103.

DeNoyelles, F., W. D. Kettle, and D. E. Sinn. 1982. The responses of plankton communities in experimental ponds to atrazine, the most heavily used pesticide in the United States. Ecology 63:1285-1293.

Dewey, S. L. 1986. Effects of the herbicide atrazine on aquatic insect community structure and emergence. Ecology 67:148-162.

EPA. 1983. Guidance for the reregistration of pesticide products containing atrazine as the active ingredient. U. S. Environ. Protection Agency Rep. 540-RS-83-002. 90 pp.

EPA. 1987. Atrazine. Health advisories for 50 pesticides. Draft report. Office of Drinking Water, U. S. Environ. Protection Agency, 401 M Street SW, Washington, DC 20460. 21 pp.

Forney, D. R. 1980. Effects of atrazine on Chesapeake Bay aquatic plants. M. S. Thesis. Auburn University, Auburn, Alabama. 76 pp.

Forney, D. R., and D. E. Davis. 1981. effects of low concentrations of herbicides on submersed aquatic plants. Weed Sci. 29:677-685.

Foster, T. S., and S. U. Khan. 1976. Metabolism of atrazine by the chicken. J. Agric. Food Chem. 24:566-570.

Foster, T. S., S. U. Khan, and M. H. Akhtar. 1980. Metabolism of deethylatrazine, deisopropylatrazine, and hydroxyatrazine by the soluble fraction (105000 g) from goose liver homogenates. J. Agric. Food Chem. 28:1083-1085.

Frank, R., and G. J. Sirons. 1979. Atrazine: its use in corn production and its loss to stream waters in southern Ontario, 1975-1977. Sci. Total Environ. 12:223-239.

Giardi, M. T., M. C. Giardina, and G. Filacchioni. 1985. Chemical and biological degradation of primary metabolites of atrazine by a *Nocardia* strain. Agric. Biol. Chem. 49:1551-1558.

Glenn, S., and J. S. Angle. 1987. Atrazine and simazine in runoff from conventional and no-till corn watersheds. Agric. Ecosys. Environ. 18:273-280.

Glotfelty, D. E., J. N. Seiber, and L. A. Liljedahl. 1987. Pesticides in fog. Nature (Lond.) 325:602-605.

Glotfelty, D. E., A. W. Taylor, A. R. Isensee, J. Jersey, and S. Glenn. 1984. Atrazine and simazine movement to Wye River estuary. J. Environ. Qual. 13:115-121.

Gonzalez-Murua, C., A. Munoz-Rueda, F. Hernando, and M. Sanchez-Diaz. 1985. Effect of atrazine and methabenzthiazuron on oxygen evolution and cell growth of *Chlorella pyrenoidosa*. Weed Res. 25:61-66.

Grenier, G., L. Protean, J. P. Marier, and G. Beaumont. 1987. Effects of a sublethal concentration of atrazine on the chlorophyll and lipid composition of chlorophyll-protein complexes of *Lemna minor*. Plant Physiol. Biochem. 25:409-413.

Gunkel, G. 1981. Bioaccumulation of a herbicide (atrazine, s-triazine) in the whitefish (*Coregonus fera* J.): uptake and distribution of the residue in fish. Arch. Hydrobiol. Suppl. 59(2/3):252-287.

Gunkel, G., and B. Streit. 1980. Mechanisms of a herbicide (atrazine, s-triazine) in a freshwater mollusc (*Ancylus fluviatilis* Mull.) and a fish (*Coregonus fera* Jurine). Water Res. 14:1573-1584.

Gunther, F. A., and J. D. Gunther (eds.). 1970. The triazine herbicides. Residue Rev. 32:1-413.

Hamala, J. A., and H. P. Kollig. 1985. The effects of atrazine on periphyton communities in controlled laboratory ecosystems. Chemosphere 14:1391-1408.

Hamilton, P. B., G. S. Jackson, N. K. Kaushik, and K. R. Solomon. 1987. The impact of atrazine on lake periphyton communities, including carbon uptake dynamics using track autoradiography. Environ. Pollut. 46:83-103.

Hammons, R. H. 1977. Atrazine persistence in a Valentine loamy fine sand profile. M. S. Thesis. Univ. Nebraska, Lincoln. 48 pp.

Heisig-Gunkel, G., and G. Gunkel. 1982. Distribution of a herbicide (atrazine, s-triazine) in *Daphnia pulicaria*: a new approach to determination. Arch. Hydrobiol. Suppl. 59(4):359-376.

Herman, D., N. K. Kaushik, and K. R. Solomon. 1986. Impact of atrazine on periphyton in freshwater enclosures and some ecological consequences. Can. J. Fish. Aquat. Sci. 43:1917-1925.

Hill, E. F., and M. B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to coturnix. U. S. Fish Wildl. Serv. Tech. Rep. 2. 147 pp.

Hollister, T. A., and G. E. Walsh. 1973. Differential responses of marine phytoplankton to herbicides: oxygen evolution. Bull. Environ. Contam. Toxicol. 9:291-295.

Huber, S. J., and B. Hock. 1986. Atrazine in water. Pages 438-451 *in* H. U. Bergmeyer, J. Bergmeyer, and M. Grassl (eds.). Methods of enzymatic analysis. Vol. XII. Drugs and pesticides, third edition. VCH Publishers, Deerfield Beach, Florida.

Huckins, J. N., J. D. Petty, and D. C. England. 1986. Distribution and impact of trifluralin, atrazine, and fonofos residues in microcosms simulating a northern prairie wetland. Chemosphere 15:563-588.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U. S. Fish Wildl. Serv. Resour. Publ. 53. 90 pp.

Hull, H. M. 1967. Herbicide handbook of the Weed Society of America. W. F. Humphery Press, Geneva, New York. 293 pp.

Infurna, R., B. Levy, C. Meng, E. Yau, and V. Traina. 1988. Teratological evaluations of atrazine technical, a triazine herbicide, in rats and rabbits. J. Toxicol. Environ. Health 24:307-319.

Isensee, A. R. 1987. Persistence and movement of atrazine in a salt marsh sediment microecosystem. Bull. Environ. Contam. Toxicol. 39:516-523.

Jachetta, J., A. P. Appleby, and L. Boersma. 1986. Apoplastic and symplastic pathways of atrazine and glyphosate transport in shoots of seedling sunflower. Plant Physiol. 82:1000-1007.

Jones, T. W., and P. S. Estes. 1984. Uptake and phytotoxicity of soil-sorbed atrazine for the submerged aquatic plant, *Potamogeton perfoliatus* L. Arch. Environ. Contam. Toxicol. 13:237-241.

Jones, T. W., W. M. Kemp, P. S. Estes, and J. C. Stevenson. 1986. Atrazine uptake, photosynthetic inhibition, and short-term recovery for the submersed vascular plant, *Potamogeton perfoliatus* L. Arch. Environ. Contam. Toxicol. 15:277-283.

Jones, T. W., W. M. Kemp, J. C. Stevenson, and J. C. Means. 1982. Degradation of atrazine in estuarine water/sediment systems and soils. J. Environ. Qual. 11:632-638.

Jones, T. W., and L. Winchell. 1984. Uptake and photosynthetic inhibition by atrazine and its degradation products on four species of submerged vascular plants. J. Environ. Qual. 13:243-247.

Karlander, E. P., J. M. Mayasich, and D. E. Terlizzi. 1983. Effects of the herbicide atrazine on an oyster-food organism. Univ. Maryland Water Resour. Res. Cen., Tech. Rep. 73. 20 pp. Univ. Maryland, College Park.

Kaushik, N. K., K. R. Solomon, G. Stephenson, and K. Day. 1985. Assessment of sublethal effects of atrazine on zooplankton. Can. Tech. Rep. Fish. Aquat. Sci. 1368:377-379.

Kemp, W. M., W. R. Boynton, J. J. Cunningham, J. C. Stevenson, T. W. Jones, and J. C. Means. 1985. Effects of atrazine and linuron on photosynthesis and growth of the macrophytes, *Potamogeton perfoliatus* L. and *Myriophyllum spicatum* L. in an estuarine environment. Mar. Environ. Res. 16:255-280.

Kemp, W. M., W. R. Boynton, J. C. Stevenson, J. C. Means, R. R. Twilley, and T. W. Jones (eds.). 1983. Submerged aquatic vegetation in upper Chesapeake Bay: studies related to possible causes of the recent decline in abundance. Final report submitted to U. S. Environ. Protection Agency, 2083 West Street, Annapolis, Maryland 21401. 331 pp

Kettle, W. D., F. DeNoyelles, Jr., B. D. Heacock, and A. M. Kadoum. 1987. Diet and reproductive success of bluegill recovered from experimental ponds treated with atrazine. Bull. Environ. Contam. Toxicol. 38:47-52.

Khan, S. U., and M. H. Akhtar. 1983. In vitro release of bound (nonextractable) atrazine residues from corn plants by chicken liver homogenate and bovine rumen liquor. J. Agric. Food Chem. 31:641-644.

Khan, S. U., and T. S. Foster. 1976. Residues of atrazine (2-chloro-4-ethylamino-6-isopropylamino-s -triazine) and its metabolites in chicken tissues. J. Agric. Food Chem. 24:768-771.

Khan, S. U., S. Kacew, and S. J. Molnar. 1985. Bioavailability in rats of bound ^{14}C residues from corn plants treated with [^{14}C] atrazine. J. Agric. Food Chem. 33:712-717.

Khan, S. U., and W. J. Saidak. 1981. Residues of atrazine and its metabolites after prolonged usage. Weed Res. 21:9-12.

Klaassen, H. E., and A. M. Kadoum. 1979. Distribution and retention of atrazine and carbofuran in farm pond ecosystems. Arch. Environ. Contam. Toxicol. 8:345-353.

Knuesli, E., D. Berrer, G. Depuis, and H. Esser. 1969. s-Triazines. Pages 51-78 *in* P. C. Kearney and D. D. Kaufman (eds.). Degradation of herbicides. Marcel Dekker, New York.

Krull, I. S., K. Mills, G. Hoffman, and D. H. Fine. 1980. The analysis of N-nitrosoatrazine and N-nitrosocarbaryl in whole mice. J. Anal. Toxicol. 4:260-262.

Kulshrestha, G., N. T. Yaduraju, and V. S. Mani. 1982. The relative toxicity of the s -triazine herbicides atrazine and simazine to crops. J. Environ. Sci. Health B17:341-354.

Larsen, D. P., F. DeNoyelles, Jr., F. Stay, and T. Shiroyama. 1986. Comparisons of single-species, microcosm and experimental pond responses to atrazine exposure. Environ. Toxicol. Chem. 5:179-190.

Lay, J. P., A. Muller, L. Peichl, W. Klein, and F. Korte. 1984. Longterm effects of the herbicides atrazine and dichlobenil upon the phytoplankton density and physico-chemical conditions in compartments of a freshwater pond. Chemosphere 13:821-832.

Lu, T. W., L. Lambert, D. Hastings, and D. Banning. 1980. Enrichment of the agricultural herbicide atrazine in the microsurface water of an estuary. Bull. Environ. Contam. Toxicol. 24:411-414.

Lynch, T. R., H. E. Johnson, and W. J. Adams. 1982. The fate of atrazine and a hexachlorobiphenyl isomer in naturally-derived model stream ecosystems. Environ. Toxicol. Chem. 1:179-192.

Macek, K. J., K. S. Buxton, S. Sauter, S. Gnilka, and J. W. Dean. 1976. Chronic toxicity of atrazine to selected aquatic invertebrates and fishes. U. S. Environ. Protection Agency Rep. 600/3-76-047. 58 pp.

Malan, C., J. H. Visser, and H. A. van de Venter. 1987. Atrazine metabolism in field-grown maize and the effect of atrazine phytotoxicity on yield. S. Afr. J. Plant Soil 4:7-11.

Malanchuk, J. L., and H. P. Kollig. 1985. Effects of atrazine on aquatic ecosystems: a physical and mathematical modeling assessment. Pages 212-224 *in* T. P. Boyle (ed.). Validation and predictability of laboratory methods for assessing the fate and effects of contaminants in aquatic ecosystems. ASTM Spec. Tech. Publ. 865. American Society for Testing and Materials, 1916 Race Street, Philadelphia, Pennsylvania 19103.

Mayasich, J. M., E. P. Karlander, and D. E. Terlizzi, Jr. 1986. Growth responses of *Nannochloris oculata* Droop and *Phaeodactylum tricornutum* Bohlin to the herbicide atrazine as influenced by light intensity and temperature. Aquat. Toxicol. 8:175-184.

Mayasich, J. M., E. P. Karlander, and D. E. Terlizzi, Jr. 1987. Growth responses of *Nannochloris oculata* Droop and *Phaeodactylum tricornutum* Bohlin to the herbicide atrazine as influenced by light intensify and temperature in unialgal and bialgal assemblage. Aquat. Toxicol. 10:187-197.

Mayer, F. L. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U. S. Environ. Protection Agency Rep. 600/8-87/017. 274 PP-

Mayer, F. L., Jr., and M. R. Ellersieck. 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals. U. S. Fish Wildl. Serv. Resour. Publ. 160. 579 PP-

McCormick,. L. L., and A. E. Hiltbold. 1966. Microbiological decomposition of atrazine and diuron in soil. Weeds 14:77-82.

McNally, S., P. Bettini, M. Sevignac, H. Darmency, J. Gasquez, and M. Dron. 1987. A rapid method to test for chloroplast DNA involvement in atrazine resistance. Plant Physiol. 83:248-250.

Menzer, R. E., and J. 0. Nelson. 1986. Water and soil pollutants. Pages 825-853 *in* C. D. Klaassen, M. 0. Amdur, and J. Doull (eds.). Casarett and Doull's toxicology, third edition. Macmillan Publ. Co., New York.

Millie, D. F., and C. M. Hersh. 1987. Statistical characterizations of the atrazine-induced photosynthetic inhibition of *Cyclotella meneghiniana* (Bacillariophyta). Aquat. Toxicol. 10:239-249.

Mitchell, C. A. 1985. Effects of atrazine on *Halodule wrightii* Ascherson in the laboratory. M. S. Thesis. Corpus Christi State Univ., Corpus Christi, Texas. 82 pp.

Mola, I., M. A. Sabatini, B. Fratello, and R. Bertolani. 1987. Effects of atrazine on two species of Collembola (Onychiuridae) in laboratory tests. Pedobiologia 30:145-149.

Moorhead, D. L., and R. J. Kosinski. 1986. Effect of atrazine on the productivity of artificial stream algal communities. Bull. Environ. Contam. Toxicol. 37:330-336.

Murphy, S. D. 1986. Toxic effects of pesticides. Pages 519-581 *in* C. D. Klaassen, M. 0. Amdur, and J. Doull (eds.). Casarett and Doull's toxicology, third edition. Macmillan Publ. Co., New York.

Peters, J. W., and R. M. Cook . 1973. Effects of atrazine on reproduction in rats. Bull. Environ. Contam. Toxicol. 9:301-304.

Pillai, C. G. P., J. D. Weete, and D. E. Davis. 1977. Metabolism of atrazine by *Spartina alterniflora*. I. Chloroform-soluble metabolites. J. Agric. Food Chem. 25:852-855.

Pillai, P., J. D. Weete, A. M. Diner, and D. E. Davis. 1979. Atrazine metabolism in box crabs. J. Environ. Qual. 8:277-280.

Plumley, F. G., and D. E. Davis. 1980. The effect of a photosynthesis inhibitor atrazine, on salt marsh edaphic algae, in culture, microecosystems, and in the field. Estuaries 3:271-277.

Plumley, F. G., D. E. Davis, J. T. McEnerney, and J. W. Everest. 1980. Effects of a photosynthesis inhibitor, atrazine, on the salt-marsh fiddler crab, *Uca pugnax* (Smith). Estuaries 3:217-223.

Popovici, I., G. Stan, V. Stefan, R. Tomescu, A. Dumea, A. Tarta, and F. Dan. 1977. The influence of atrazine on soil fauna. Pedobiologia 17:209-215.

Pratt, J. R., N. J. Bowers, B. R. Niederlehner, and J. Cairns, Jr. 1988. Effects of atrazine on freshwater microbial communities. Arch. Environ. Contam. Toxicol. 17:449-457.

Reed, D. 1982. Atrazine. (Unpubl. mimeo.) Available from U. S. Food and Drug Administration, Bureau of Foods, Washington, DC. 6 pp.

Richardson, L. T. 1970. Effects of atrazine on growth response of soil fungi. Can. J. Plant Sci. 50:594-596.

Rodriguez-Kabana, R., E. A. Curl, and H. H. Funderburk, Jr. 1968. Effect of atrazine on growth activity of *Sclerotium rolfsii* and *Trichoderma viride* in soil. Can. J. Microbiol. 14:1283-1288.

Santa Maria, C., J. Moreno, and J. L. Lopez-Campos. 1987. Hepatotoxicity induced by the herbicide atrazine in the rat. J. Appl. Toxicol. 7:373-378.

Santa Maria, C., M. G. Vilas, F. G. Muriana, and A. Relimpio. 1986. Subacute atrazine treatment effects on rat renal functions. Bull. Environ. Contam. Toxicol. 36:325-331.

Schiavon, M. 1988a. Studies of the leaching of atrazine, of its chlorinated derivatives, and of hydroxyatrazine from soil using ^{14}C ring-labeled compounds under outdoor conditions. Ecotoxicol. Environ. Safety 15:46-54.

Schiavon, M. 1988b. Studies of the movement and the formation of bound residues of atrazine, of 14 its chlorinated derivatives, and of hydroxyatrazine in soil using ^{14}C ring-labeled compounds under outdoor conditions. Ecotoxicol. Environ. Safety 15:55-61.

Schocken, M. J., and M. K. Speedie. 1982. Interaction of higher marine fungi with the herbicide atrazine. II. Sorption of atrazine to four species of marine fungi. Bull. Environ. Contam. Toxicol. 29:101-106.

Schocken, M. J., and M. K. Speedie. 1984. Physiological aspects of atrazine degradation by higher marine fungi. Arch. Environ. Contam. Toxicol. 13:707-714.

Setzler, J. V. 1980. Atrazine residues in northern Ohio streams--1980. U. S. Army Corps Engineers, Tech. Rep., Lake Erie Wastewater Manage. Study, 1776 Niagara St., Buffalo, New York. 29 pp.

Shabana, E. F. 1987. Use of batch assays to assess the toxicity of atrazine to some selected cyanobacteria. 1. Influence of atrazine on the growth, pigmentation and carbohydrate contents of *Aulosira fertilissima*, *Anabaena oryzae*, *Nostoc muscorum* and *Tolypothrix tenuis*. J. Basic Microbiol. 2:113-119.

Stay, F. S., D. P. Larsen, A. Katko, and C. M. Rohm. 1985. Effects of atrazine on community level responses in Taub microcosms. Pages 75-90 *in* T. P. Boyle (ed.). Validation and predictability of laboratory methods for assessing the fate and effects of contaminants in aquatic ecosystems. ASTM Spec. Tech. Publ. 865. American Society for Testing and Materials, 1916 Race Street, Philadelphia, Pennsylvania 19103.

Stevenson, J. C., T. W. Jones, W. M. Kemp, W. R. Boynton, and J. C. Means. 1982. An overview of atrazine dynamics in estuarine ecosystems. Pages 71-94 *in* Proceedings of the workshop on agrichemicals and estuarine productivity, Beaufort, North Carolina, September 18-19, 1980. Avail. from Natl. Ocean. Atmos. Admin., Off. Mar. Pollut. Assess., Boulder Colorado.

Stratton, G. W. 1984. Effects of the herbicide atrazine and its degradation products, alone and in combination, on phototrophic microorganisms. Arch. Environ. Contam. Toxicol. 13:35-42.

Streit, B., and H. M. Peter. 1978. Long-term effects of atrazine to selected freshwater invertebrates. Arch. Hydrobiol. Suppl. 55:62-77.

Torres, A. M. R., and L. M. O'Flaherty. 1976. Influence of pesticides on *Chlorella*, *Chlorococcum*, *Stigeoclonium* (Chlorophyceae), *Tribonema*, *Vaucheria* (Xanthophyceae) and *Oscillatoria* (Cyanophyceae). Phycologia 15:25-36.

Tucker, R. K., and D. G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. U. S. Fish Wildl. Serv. Resour. Publ. 84. 131 PP-

Veber, K., J. Zahradnik, I. Breyl, and F. Kredi. 1981. Toxic effect and accumulation of atrazine in algae. Bull. Environ. Contam. Toxicol. 27:872-876.

Vos, J. G., E. I. Krajnc, P. K. Beekhof, and M. J. van Logten. 1983. Methods for testing immune effects of toxic chemicals: evaluation of the immunotoxicity of various pesticides in the rat. Pages 497-504 *in* J. Miyamoto and P. C. Kearney (eds.). Pesticide chemistry, human welfare and the environment. Vol. 3. Mode of action metabolisms and toxicology. Pergamon Press, Oxford, England.

Ward, G. S., and L. Ballantine. 1985. Acute and chronic toxicity of atrazine to estuarine fauna. Estuaries 8:22-27.

Weete, J. D., P. Pillai, and D. D. Davis. 1980. Metabolism of atrazine by *Spartina alterniflora*. 2. Water-soluble metabolites. J. Agric. Food Chem. 28:636-640.

Wilson, M. P., E. P. Savage, D. D. Adrian, M. J. Aaronson, T. J. Keefe, D. H. Hamar, and J. T. Tessari. 1987. Groundwater transport of the herbicide, atrazine, Weld County, Colorado. Bull. Environ. Contam. Toxicol. 39:807-814.

Wolf, D. C., and R. L. Jackson. 1982. Atrazine degradation, sorption and bioconcentration in water systems. Arkansas Water Resour. Res. Cen. Publ. 87. 40 pp.

Wu, T. L. 1980. Dissipation of the herbicides atrazine and alachlor in a Maryland cornfield. J. Environ. Qual. 9:459-465.

Wu, T. L. 1981. Atrazine in estuarine water and the aerial deposition of atrazine into Rhode River, Maryland. Water Air Soil Pollut. 15:173-184.

Wu, T. L., and B. M. Fox. 1980. Rate of disappearance of atrazine and alachlor in cornfield soils. Proc. Northeast Weed Sci. Soc. 34:147-154.

Yoo, J. Y., and K. R. Solomon. 1981. Persistence of permethrin, atrazine and methoxychlor in a natural lake system. Can. Tech. Rep. Fish. Aquat. Sci. 1151:164-167.

Biological Report 85(1.19)
August 1989

Contaminant Hazard Reviews
Report No. 19

MOLYBDENUM HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, MD 20708

SUMMARY

The element molybdenum (Mo) is found in all living organisms and is considered to be an essential or beneficial micronutrient. However, the molybdenum poisoning of ruminants has been reported in at least 15 States and 8 foreign countries.

Molybdenum is used primarily in the manufacture of steel alloys. Its residues tend to be elevated in plants and soils near Mo mining and reclamation sites, fossil-fuel power plants, and Mo disposal areas. Concentrations of Mo are usually lower in fish and wildlife than in terrestrial macrophytes.

Aquatic organisms are comparatively resistant to Mo salts: adverse effects on growth and survival usually appeared only at water concentrations >50 mg Mo/l. But in one study, 50% of newly fertilized eggs of rainbow trout (*Oncorhynchus mykiss*) died in 28 days at only 0.79 mg Mo/l. High bioconcentration of Mo by certain species of aquatic algae and invertebrates--up to 20 grams of Mo/kg dry weight--has been recorded without apparent harm to the accumulator; however, hazard potential to upper trophic organisms (such as waterfowl) that may feed on bioconcentrators is not clear. Data on Mo effects are missing for avian wildlife and are inadequate for mammalian wildlife. In domestic birds, adverse effects on growth have been reported at dietary Mo concentrations of 200 mg Mo/kg, on reproduction at 500 mg/kg, and on survival at 6,000 mg/kg.

Molybdenum chemistry is complex and inadequately known. Its toxicological properties in mammals are governed to a remarkable extent through interaction with copper and sulfur; residues of Mo alone are not sufficient to diagnose Mo poisoning. Domestic ruminants, especially cattle, are especially sensitive to Mo poisoning when copper and inorganic sulfate are deficient. Cattle are adversely affected--and die if not removed--when grazing on pastures where the ratio of copper to Mo is <3, or if they are fed low copper diets containing Mo at 2 to 20 mg/kg diet; death usually occurs when tissue residues exceed 10 mg/kg body weight. The resistance of other species of mammals tested, including domestic livestock, small laboratory animals, and wildlife, was at least 10X that of cattle. Mule deer (*Odocoileus hemionus*), for example, showed no adverse effects at dietary levels of 1,000 mg/kg.

Additional research is needed in several fields: the role of Mo on inhibition of carcinomas and dental caries; the establishment of minimum, optimal, and upper daily requirements of Mo in aquatic and wildlife species of concern; the improvement in diagnostic abilities to distinguish molybdenum poisoning from copper deficiency; and the determination of sensitivity of early developmental stages of fishes to Mo insult.

Suggested citation:

Eisler, R. 1989. Molybdenum hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish Wildl. Serv. Biol. Rep. 85 (1.19).

TABLES

ACKNOWLEDGMENTS

I thank Nancy A. Bushy, Joyce Haber Corley, and Lynda J. Garrett for literature search and retrieval services; Barbara A. Roberts for secretarial assistance; Kirk A. King and B. Thomas Johnson for technical review of the manuscript; and Paul H. Eschmeyer and James R. Zuboy for editorial services.

INTRODUCTION

Molybdenum (Mo) is present in all plant, human, and animal tissues, and is considered an essential micronutrient for most life forms (Schroeder et al. 1970; Underwood 1971; Goyer 1986). The first indication of an essential role for Mo in animal nutrition came in 1953 when it was discovered that a flavoprotein enzyme, xanthine oxidase, was dependent on Mo for its activity (Underwood 1971). It was later determined that Mo is essential in the diet of lambs, chicks, and turkey poults (Underwood 1971). Molybdenum compounds are now routinely added to soils, plants, and waters to achieve various enrichment or balance effects (Friberg et al. 1975; Friberg and Lener 1986).

There are certain locations where plants will not grow optimally because of a deficiency in Mo, and other places where the levels of Mo in plants are toxic to livestock grazing on the plants (Chappell and Peterson 1976). Molybdenum poisoning in cattle was first diagnosed in England in 1938; molybdenosis was shown to be associated with consumption of herbage containing large amounts of this element, and to be controllable by treatment with copper sulfate (Underwood 1971). Molybdenum poisoning of ruminants, especially cattle, has been reported in at least 15 States, and in Canada, England, Australia, New Zealand, Ireland, the Netherlands, Japan, and Hungary. Molybdenosis was most pronounced in areas where soils were alkaline, high in Mo and low in copper, or near industrial point sources such as coal, aluminum, uranium, or molybdenum mines; steel alloy mills; or oil refineries (Dollahite et al. 1972; Alloway 1973; Kubota 1975; Buck 1978; Ward 1978; Chappell et al. 1979; Kincaid 1980; King et al. 1984; Kume et al. 1984; Sas 1987). All cattle are susceptible to molybdenosis, milking cows and young stock being the most sensitive (Underwood 1971). Industrial molybdenosis in domestic cattle and sheep, which usually involved a single farm or pasture, has been widely documented: in Colorado in 1958 from contaminated river waters used in irrigation, in Alabama in 1960 from mine spoil erosion, in North Dakota in 1968 from fly ash from a lignite burning plant, in Missouri in 1970-1972 from clay pit erosion, in Pennsylvania in 1971 from aerial contamination by a molybdenum smelter, in South Dakota in 1975 from Mo-contaminated magnesium oxide, and in Texas in 1965-1972 from uranium mine waste leachate (Ward 1978). In humans, a gout-like disease in two villages in Armenia was attributed to the ingestion of local foods high in Mo and grown in high Mo soils (Friberg and Lener 1986). Esophageal cancer was prevalent in various parts of southern Africa where food was grown in low Mo soils; it was reported in China in a low frequency rate that was significantly correlated with increasing Mo concentrations in cereals and drinking water (Luo et al. 1983). Additional and more extensive data on ecological and toxicological aspects of Mo in the environment were reviewed by Schroeder et al. (1970), Underwood (1971), Friberg et al. (1975), Chappell and Peterson (1976, 1977), Ward (1978), Chappell et al. (1979), Gupta and Lipsett (1981), and Friberg and Lener (1986).

This report was prepared in response to an informational request from environmental specialists of the U. S. Fish and Wildlife Service. It is part of a continuing series of brief reviews on chemical contaminants and natural resources.

ENVIRONMENTAL CHEMISTRY

GENERAL

Molybdenum is a comparatively rare element that is used primarily in the manufacture of steel alloys for the aircraft and weapons industries. Most of the recent global production of about 100,000 tons annually comes from the United States--primarily Colorado. Anthropogenic activities that have contributed to environmental Mo contamination include combustion of fossil fuels, and smelting, mining, and milling operations for steel, copper, and uranium, as well as for molybdenum. In general, the chemistry of Mo is complex and inadequately known. Its toxicological properties are governed to a remarkable extent by interactions with copper and sulfur, although other metals and compounds may confound this interrelation.

SOURCES AND USES

Molybdenum, discovered about 200 years ago, entered the commercial market in the 1920's as a result of extensive metallurgical research into its alloying properties and to the finding at Climax, Colorado, of the largest proven reserves of Mo worldwide (King et al. 1973). Molybdenum does not occur free in nature and is found only in combination with sulfur, oxygen, tungsten, lead, uranium, iron, magnesium, cobalt, vanadium, bismuth, or calcium. The most economically important ores are molybdenite (MoS_2), jordisite (amorphous MoS_2), and

ferrimolybdate ($FeMoO_3$ - H_20); less important are wulfenite ($PbMoO_4$) powellite ($CaMoO_4$), and ilsemannite (Mo_3O_8) (Friberg et al. 1975; Chappell et al. 1979; Friberg and Lener 1986; Goyer 1986).

World Mo production has increased from about 90 metric tons in 1900--half from Australia and Norway, half from the United States--to 136 tons in 1906, 1,364 in 1932 (an order of magnitude increase in 26 years), 10,909 in 1946, and 91,000 tons in 1973. Through the years, Mo has been produced in about 30 countries; in 1973, about 60% of the worldwide production was from the United States, 15% from Canada, 15% from the USSR and China combined, and 10% from other nations--Chile, Japan, Korea, Norway, and Mexico (King et al. 1973). By 1979, the United States produced about 62% of the world production of 103,000 metric tons, and exported about half, chiefly to western Europe and Japan; other major producers in 1979 were Canada, Chile, and the USSR (Kummer 1980). In the United States, only three mines in Colorado account for almost 70% of domestic production. Other active Mo mining sites in North America are in Arizona, Nevada, New Mexico, Utah, and California; Mo reserves have also been proven in Idaho, Alaska, Pennsylvania, and British Columbia (Kummer 1980). About 65% of domestic Mo is recovered from ores rich in Mo; the rest is a by-product from ores of copper, tungsten, and uranium (Chappell et al. 1979).

As a result of various human activities, Mo enters the environment from many sources (King et al. 1973; Friberg et al. 1975; Chappell et al. 1979). Coal combustion is the largest atmospheric source of Mo, contributing about 550 metric tons annually, or 61% of all atmospheric Mo worldwide that comes from anthropogenic sources. In Sweden alone, about 2.5 tons of Mo are emitted into the atmosphere yearly from oil combustion (Friberg et al. 1975). Molybdenum mining and milling are the source of about 100 metric tons annually to aquatic systems. At the world's largest Mo mine in Climax, Colorado, where about 36,000 tons of tailings are generated daily, the operation releases up to 100 tons of Mo annually as aqueous effluent. Other sources are Mo smelting, uranium mining and milling, steel and copper milling, oil refining, shale oil production, and claypit mining.

Molybdenum is used in the manufacture of high-strength low-alloy steels and other steel alloys in the aircraft and weapons industries, and in the production of spark plugs, X-ray tubes and electrodes, catalysts, pigments, and chemical reagents (Friberg et al. 1975; Kummer 1980; Goyer 1986). The most important industrial compound is the trioxide, MoO_3, which is resistant to most acids, and is oxidized in air at >500 °C (Shamberger 1979).

CHEMICAL PROPERTIES

Molybdenum, which can function both as a metal and metalloid, is an essential component in a large number of biochemical systems--including xanthine oxidase. At least four metalloenzymes are known that are Mo-dependent, and all are molybdoflavoproteins (Schroeder et al. 1970). Molybdenum is characterized by the following physical and chemical properties: atomic number 42; atomic weight 95.94; density 10.2; melting point 2,617 C; boiling point 4,612 °C; oxidation states 0, +2, +3, +4, +5, and +6; crystalline forms as gray-black powder, or silver-white metal; mass numbers (percent contribution of naturally occurring Mo) of 92 (15.86%), 94 (9.12%), 95 (15.7%), 96 (16.5%), 97 (9.45%), 98 (23.75%), and 100 (9.62%.); and radioactive isotopes of mass number 90, 91, 93, 99 (Tb 1/2 of 67 hours, frequently used as a tracer), 101, 102, and 105 (Busev 1969; Schroeder et al. 1970; Shamberger 1979; Friberg and Lener 1986). In water at pH >7, Mo exists primarily as the molybdate ion, MoO_4^{2-};at pH <7, various polymeric compounds are formed, including the paramolybdate ion, $Mo_7O_{24}^{6-}$ (Busev 1969). In soils, molybdate was sorbed most readily to alkaline, high calcium, high chloride soils; retention was least in low pH, low sulfate soils (Smith et al. 1987). There is general agreement that molybdenum chemistry is complex and inadequately known. Additional and more extensive information on its properties were summarized in major reviews by Busev (1969), Boschke (1978), Brewer (1980), Coughlan (1980), Newton and Otsuka (1980), Parker (1983), and Mitchell and Sykes (1986).

MODE OF ACTION

Interactions among some trace metals are so pervading and so biologically influential that the results of nutritional and toxicological studies conducted with a single element can be misleading unless the dietary and body tissue levels of interacting elements are clearly defined (Underwood 1979). For molybdenum, interactions are so dominant--especially in ruminant species--that a particular level of intake in the diet can lead to Mo

deficiency or to Mo toxicity in the animal, depending on the relative intakes of copper and inorganic sulfate (Schroeder et al. 1970; Underwood 1971, 1979; Clawson et al. 1972; Suttle 1973, 1983a; Friberg et al. 1975; Buck 1978; Ward 1978; Chappell et al. 1979; Shamberger 1979; Van Ryssen and Stielau 1980; Gupta and Lipsett 1981; Ivan and Veira 1985; Friberg and Lener 1986; Goyer 1986; Kincaid et al. 1986).

The first indications of interaction between copper and Mo came more than 40 years ago from studies of grazing cattle in certain areas of England. Afflicted animals lost weight, developed severe diarrhea, and (in extreme cases) died. The disease is sometimes called teart (rhymes with heart) or molybdenosis, and is caused by eating herbage rich in Mo--i.e., 20 to 100 mg/kg dry weight diet compared to <5 mg/kg in nearby healthy pastures--and low or deficient in copper and inorganic sulfate (Underwood 1979). Molybdenosis is a copper-deficiency disease that occurs particularly in cattle and sheep and is usually caused by the depressing effect of Mo on the physiological availability of copper (Clawson et al. 1972; Dollahite et al. 1972; Alloway 1973; Erdman et al. 1978; Mills and Breamer 1980; Van Ryssen and Stielau 1980; Nederbragt 1982; Suttle 1983a; Goyer 1986). The disease was treated successfully with copper sulfate at 1 to 2 grams daily in the diet, or 200 to 300 mg daily by intravenous injection (Buck 1978; Underwood 1979; Ivan and Veira 1985). When ruminant diets contained copper at 8 to 11 mg/kg weight--a normal range--cattle were poisoned at Mo levels of 5 to 6 mg/kg and sheep at 10 to 12 mg/kg. When dietary copper was low (i.e., <8 mg/kg) or sulfate ion level was high, Mo at 1 to 2 mg/kg ration was sometimes toxic to cattle. Increasing the copper in diets to 13 to 16 mg/kg protected cattle against concentrations up to 150 mg/kg of dietary Mo (Buck 1978). Studies of Mo metabolism are of limited value unless one knows the status in the diet of inorganic sulfate, which alleviates Mo toxicity in all known species by increasing urinary Mo excretion (Underwood 1971, 1979).

Copper prevents the accumulation of Mo in the liver and may antagonize the absorption of Mo from food. The antagonism of copper to Mo depends on sulfate, which may displace molybdate (Goyer 1986). In certain sheep pastures, for example, the herbage may contain up to 15 mg copper/kg dry weight and <0.2 mg Mo/kg dry weight--conditions favoring the development of a high copper status that may lead to copper poisoning. Treatment consists of providing molybdate salt licks, which are highly effective in reducing copper levels in grazing sheep (Buck 1978; Underwood 1979).

A low copper:molybdenum ratio (i.e., <2), rather than the absolute dietary concentration of Mo, is the primary determinant of susceptibility to molybdenum poisoning; molybdenosis is not expected when this ratio is near 5 (Buck 1978; Ward 1978; Mills and Breamer 1980). Ratios of copper to molybdenum in sweet clover (*Melilotus* spp., a known Mo accumulator plant) growing in coal mine spoils in the Dakotas, Montana, and Wyoming ranged from 0.4 to 5, suggesting that molybdenosis can be expected to occur in cattle and sheep grazing in low Cu:Mo areas (Erdman et al. 1978). A similar situation existed in British Columbia, where 19% of all fodders and grains had a Cu:Mo ratio <2 (Underwood 1979).

There are several explanations for the high sensitivity of ruminants to increased dietary Mo and sulfur, the most plausible being the role of thiomolybdates (Penumarthy and Oehme 1978; Lamand et al. 1980; Nederbragt 1980, 1982; Suttle 1980, 1983b; Mills et al. 1981; Suttle and Field 1983; Weber et al. 1983; Hynes et al. 1985; Friberg and Lener 1986; Allen and Gawthorne 1987; Sas 1987; Strickland et al. 1987). Thiomolybdates are compounds formed by the progressive substitution for sulfur and oxygen in the molybdate (MoO_4^{2-}) anion when hydrogen sulfide and MoO_4^{2-} interact in vitro at neutral pH. Di-, tri-, and tetra-thiomolybdates are formed, but only the last of these effectively impairs copper absorption. When sufficient tetrathiomolybdate (MoS_4) is formed in the rumen, it and copper in the gut combine and the resultant complex is bound strongly to proteins of high molecular weight. The molybdoproteins so formed are strong chelators of copper, and may be the agents responsible for copper deficiency through formation of biologically unavailable copper complexes in gut, blood, and tissues of animals that consume diets containing high concentrations of Mo. To confound matters, the complex molybdenum-copper-sulfur interrelation can be modified, or disrupted entirely, by many compounds or mixtures. These include the salts of tungsten (Schroeder et al. 1970; Underwood 1971; Mills and Breamer 1980; Luo et al. 1983; Goyer 1986), zinc (Penumarthy and Oehme 1978; Parada 1981; Alary et al. 1983), lead and manganese (Underwood 1971), iron (Phillippo et al. 1987b), vanadium (Vaishampayan 1983), chromium (Vaishampayan 1983; Chung et al. 1985), phosphorus (Underwood 1971; Baldwin et al. 1981), cystine and methionine (Underwood 1971, 1979), fluoride (Goyer 1986), and proteins (Underwood 1971, 1979; Friberg and Lener 1986; Kincaid et al. 1986).

BACKGROUND CONCENTRATIONS

GENERAL

Molybdenum levels tend to be elevated in nonbiological materials and in terrestrial flora in the vicinity of Mo mining and reclamation activities, fossil-fuel power plants, and disposal areas for Mo-contaminated sewage sludge, fly ash, and irrigation waters. Concentrations of Mo in fish, wildlife, and invertebrates were low when compared to those in terrestrial plants, although certain aquatic invertebrates were capable of high bioconcentration. Concentrations of Mo alone, however, were not sufficient to diagnose Mo deficiency or toxicosis.

NONBIOLOGICAL SAMPLES

Elevated levels of Mo in nonbiological materials have been reported near certain mines, power plants, and oil shale deposits, as well as in various sewage sludges, fertilizers, and agricultural drainwaters (Table 1).

Molybdenum is concentrated in coal and petroleum, and the burning of these fuels contributes heavily to atmospheric Mo (King et al. 1973). Combustion of fossil fuels contributes about 5,000 metric tons of Mo annually to the atmosphere; atmospheric particulates contain about 0.001 ug Mo/m^3 air (Goyer 1986).

Natural Mo concentrations in ground and surface waters rarely exceed 20 ug/l; significantly higher concentrations are probably due to industrial contamination. Existing wastewater and water treatment facilities remove less than 20% of the Mo; accordingly, drinking water concentrations are near those of the untreated source (Chappell et al. 1979). Molybdenum concentrations in saline waters appear to be directly related to salinity (Prange and Kremling 1985; Sloot et al. 1985). In the Wadden Sea, for example, Mo concentrations were 0.08, 0.4, and 1.0 ug/l at salinities of 0.07, 1.2, and 3.3%, respectively (Sloot et al. 1985).

Table 1. Molybdenum concentrations in selected nonbiological materials.

Material, unit and location	Concentration [a]	Reference [b]
Seawater (ug/L)		
Worldwide	<1 to 10	1, 2, 3
Worldwide	4 to 12	4
Pacific Ocean, all depths	10.3 + 0.2	5
Drinking water (ug/L)		
USSR		
Winter	0.03 to 0.06	1
Summer	0.11 to 0.15	1
USA	0.1 to 6.2	2
USA	Usually <5, sometimes	
up to 500	1, 4	
Switzerland	Usually <1, Max. 29	1
Surface water (ug/L)		
North American rivers	0.4	4
California lakes	0.4 (<3 to 100)	1
USA rivers	1.2 to 4.1	1
Mineral waters	2 to 3	2
Near Mo mine and mill, Colorado	100 to 10,000	4

Ash pond effluent from coal fired power plant, New Mexico	170	4
Power station effluent, Vicotria Australia	330	6
Near Mo tailings pile, New Mexico	600	4
Evaporation ponds, California, 1985–86	1,100 (630 to 2,600)	7
Leachate from oil shale retort, Colorado	4,100 (2,500 to 8,300)	4
Irrigation water from Mo mining and reclamation	5,000 to 100,000	8
Groundwater (ug/L)		
USA	Usually <1	4
USSR	3	4
California, agricultural drain-water, 1985–86	1,200 to 5,500	7
Colorado		
Mining areas	Max. 25,000	1
Near urnaium mill	50,000	4
Sediments (mg/kg, dry weight)		
USA rivers	5 to 57	1
Evaporation ponds, California	18 (<2 to 22)	7
Near Mo tailings pile, Colorado	21	4
Baltic Sea	80	3
Near Mo mine and mill, Colorado	530, Max. 1,800	1, 4
Soils (mg/kg, dry weight)		
Natural soils		
Worldwide	0.1 to 10, usually 0.2 to 0.7	1, 2
Worldwide	1 to 2 (0.6 to 3.5)	4
USA	1.2 (0.1 to 40)	4
Molybdenosis areas	2 to >6	9
Elevated Mo	12 to 76 (2 to 190)	4
Economic Mo deposits	>200	4
Impacted soils		
In upper 5 cm at 0.3 or 3 km from Mo ore processing plant in 1982 and 1983		
0.3 km		
1982, Total	28	10
1982, Extractable	5	10
1983, Total	73	10
1983, Extractable	3	10

3 km		
1982, Total	3	10
1982, Extractable	0.4	10
1983, Total	8	10
1983, Extractable	0.8	10
Near Mo mine and mill, Colorado		
Irrigated with Mo-contaminated		
effluent from uranium mill	61 (49 to 72)	4
Ireland, highly mineralized	170 (11 to 4,000)	17
Sewage sludge (mg/kg, dry weight)		
Iowa	<1 to 75	11
USA	2 to 30	2
Most states, USA	5 to 39	11
North America	<10 (2 to 100)	1, 12
Michigan	32 (6 to 3,700)	11
Air (ugm^3)		
Rural, USA	0.0001 to 0.003	1, 2
Urban, USA	0.01 to 0.03	1, 2
Worldwide	<0.0005	13
Fertilizers (mg/kg, dry weight)		
Domestic	3 to 6	1, 14
Oil, oil shale, coal, and waste products		
(liquids, mg/L; solids, mg/kg dry weight)		
Coal conversion process waters	0.001 to 0.5	15
Oil shale retort water	0.06 to 0.3	15
Light oil	<0.1	1
Heavy oil	Max. 0.5	1
Spent oil shale	0.6	15
Coal	1 to 73	15
Coal	3 (0.3 to 15)	1, 16
Oil shale	5 to 87	15
Coal ash	7 to 160	16
Fly ash from power stations	Usually 10 to 40, Max 180	1

[b]References: 1, Friberg et al. 1975; 2, Friberg and Lener 1986; 3, Prange and Kremling 1985; 4, Chappell et al. 1979; 5, Collier 1985; 6, Ahsanullah 1982; 7, Fujii 1988; 8, Smith et al. 1987; 9, Kubota et al. 1967; 10, Schalscha et al. 1987; 11, Pierzynski and Jacobs 1986; 12, Lahann 1976; 13, Schroeder et al. 1970; 14, Goyer 1986; 15, Birge et al. 1980; 16, Elseewi and Page 1984; 17, Talbot and Ryan 1988.

The Mo content of soil may vary by more than an order of magnitude, causing both deficient and excessive concentrations for plants and ruminants in some parts of the world (Friberg et al. 1975). Native soils may contain enough Mo to cause molybdenosis in range livestock in some areas of the United States, particularly in Oregon, Nevada, and California (Kubota et al. 1967; Erdman et al. 1978). Elevated soil Mo levels can result from both natural and industrial sources. Usually when soil Mo levels exceed 5 mg/kg dry weight, a geological anomaly or industrial contamination is the likely explanation (Chappell et al. 1979). Molybdenum is more

available biologically to herbage plants in alkaline soils than in neutral or acidic soils (Underwood 1971; Friberg et al. 1975; Shacklette et al. 1978; Wright and Hossner 1984). Liming of acidic soils or treatment with Mo-containing fertilizers can effectively raise the Mo content of herbage (Underwood 1971; Pierzynski and Jacobs 1986).

The disposal of sewage sludge, fly ash from coal combustion, and Mo-contaminated irrigation waters to agricultural fields may result in the production of Mo-rich herbage. Sewage sludges rich in Mo and applied to agricultural soils resulted in elevated Mo content in corn and soybeans in a dose-dependent pattern (Pierzynski and Jacobs 1986). Similarly, fly ash from coal combustion applied to pasture and croplands at rates sufficient to provide Mo at concentrations of 40 g/kg and higher resulted in potentially hazardous levels in vegetation to ruminant grazers. Molybdenum in fly ash applied to soils remained biologically available for extended periods, especially in calcareous soils (Elseewi and Page 1984). Irrigation has also been proposed as a possible disposal method for large quantities of water having Mo concentrations of 5 to 100 mg/l that result from mining and reclamation activities. This method of disposal is not recommended unless all animals are kept off irrigated sites and the vegetation can be harvested and destroyed until Mo levels in the plants remain below 10 mg/kg dry weight (Smith et al. 1987).

BIOLOGICAL SAMPLES

All plants contain Mo and it is essential for the growth of all terrestrial flora (Schroeder et al. 1970). Molybdenum concentrations were elevated in terrestrial plants, especially in those collected from soils amended with fly ash, liquid sludge, or Mo-contaminated irrigation waters, in naturally occurring teart pastures, and in the vicinity of Mo mining and ore processing activities, steelworks, and other metal processors; Mo concentrations greater than 20 mg/kg dry weight were frequently documented in plants from contaminated areas (Table 2). Legumes, especially trefoil clovers (*Lotus* sp.) selectively accumulated Mo; concentrations of 5 to 30 mg/kg dry weight were common in Mo-contaminated areas (Friberg et al. 1975; Shacklette et al. 1978). The Mo levels were sometimes high and potentially toxic in legumes from poorly drained acidic soils (Kubota et al. 1967; Underwood 1971). Some terrestrial grasses displayed copper:Mo ratios between 0.5 and 3.7. Since ratios greater than 2 were within the range where molybdenosis is likely, and since most of the Mo concentrations were greater than the maximum tolerable level of 6 mg/kg dry weight, hypocuprosis (molybdenosis) in cattle was expected (Schalscha et al. 1987). Major sources of Mo overload in fodder were in plants grown on high-Mo alkaline soils and from industrial contamination by coal and uranium mines and alloy mills (Sas 1987). Variations in Mo content of pasture species ranged from 0.1 to 200 mg/kg dry weight, and most variations were due to soil and species differences (Underwood 1971). Pasture plants collected from mountainous areas of southern Norway were usually deficient in copper, and low to partly deficient in Mo. As a result, the copper:Mo ratios were generally high and may explain the occurrence of chronic copper poisoning in grazing sheep in that region (Garmo et al. 1986).

Except in terrestrial plants, Mo concentrations were low in all groups examined; maximum concentrations reported from all sampling locales were about 6 mg/kg dry weight in aquatic plants, about 4 mg/kg fresh weight in aquatic invertebrates, 2 mg/kg fresh weight in fishes (except for rainbow trout liver and kidney--26 to 43 mg/kg fresh weight--from fish collected near a Mo tailings outfall), 4 mg/kg dry weight in birds, 30 mg/kg dry weight in domestic ruminant liver, 85 mg/kg dry weight in the horse, and <4 mg/kg dry weight in mammalian wildlife and man (Table 2).

There are large interspecies differences among aquatic organisms in their ability to accumulate Mo from the medium. Marine bivalve molluscs usually contained 30X to 90X more Mo than the ambient seawater; however, some species from Greek waters had bioconcentration factors up to 1,300X (Eisler 1981). Marine plankton accumulated Mo from seawater by factors up to 25X (Goyer 1986). But growth in aquatic phytoplankton populations was inhibited under conditions of low or missing Mo, nitrogen, and organic matter concentrations; the role of Mo in this process requires clarification (Paerl et al. 1987). In rainbow trout (*Oncorhynchus mykiss*), residues of Mo in tissues were affected only slightly by the concentrations in water; tissue residues ranged from 5 to 118 ug/kg fresh weight in water containing trace (<6 ug/1) concentrations, 10, to 146 ug/kg in water containing low (6 ug/1) concentrations, and from 13 to 322 ug/kg in water containing high (300 ug/1) concentrations (Ward 1973). A similar pattern was reported for kokanee salmon, *Oncorhynchus nerka* (Ward 1973). Rainbow trout held for 2 weeks in live traps 1.6 km downstream from a Mo mine tailings outfall survived, but liver and kidney had significantly elevated levels of Mo, calcium, manganese, iron, zinc, strontium, and

zirconium, and 10% less potassium; the observed mineral changes may have been due to outfalls from nonmolybdenum mines discharged into the river system (Kienholz 1977).

Molybdenum mining operations are not detrimental to mammalian wildlife, as judged by normal appearance and low Mo levels in liver and kidney of nine species--including deer, squirrel, chipmunk, badger, beaver, marmot, and pika--collected from areas of high environmental Mo levels (Kienholz 1977). I must emphasize, however, that Mo levels in animal tissues give little indication of the dietary Mo status, and are of little diagnostic value for this purpose unless the sulfate, protein, and copper status of the diet are also known. This point is discussed in greater detail later.

Table 2. Molybdenum concentration in field collections of selected species of animals and plants. Values shown are Mo in mg/kg (ppm Mo) fresh weight (FW), dry weight (DW), or ash weight (AW).

Taxonomic group, organism tissue, and other variables	Concentration, [a] in mg/kg	Reference [b]
Terrestrial plants		
Bermuda grass, *Cynodon dactylon*		
Soil amended with Mo-contaminated irrigation water		
Control	5 DW	1
6 mg Mo/kg soil	225 DW	1
13 mg Mo/kg soil	309 DW	1
26 mg Mo/kg soil	447 DW	1
Herbage (forage)		
Normal	1 to 3 DW	2
Teart pastures	20 to 100 DW	2
Barley, *Hordeum vulgare*		
Soil amended with fly ash		
40 g/kg soil	6 DW	3
80 g/kg soil	11 DW	3
Moss, *Hypnum cupressiforme*,		
Sweden		
Normal	1 DW	4
Near waste disposal plant	8 DW	4
Near metal processor	400 DW	4
Near steelworks	560 DW	4
Legumes		
From molybdenosis areas	17 to 125 DW	5
From nonmolybdenosis areas	6 to 28 DW	5
Black medic, *Medicago lupulina*		
Carson Valley, Nevada	Max. 372 DW	6
Alfalfa, *Medicago sativa*		
Soil amended with fly ash		
40 g/kg soil	10 DW	3
80 g/kg soil	12 DW	3
Pasture plants, southern Norway	0.3 (0.01 to 4) DW	7

Peas, *Pisum sativum*		
Canada	0.2 FW	4
USA	0.3 to 5 FW	4
India	0.7 to 2 FW	4
Romania, Germany	1 FW	4
USSR	6 FW	4
Ballica grass, *Lolium perenne*		
Distance from Mo ore processing plant		
1982		
0.3 km	29 to 40 DW	8
1.0 km	8 to 10 DW	8
1983		
0.3 km	6 to 10 DW	8
1.0 km	7 to 10 DW	8
9.0 km	4 to 5 DW	8
In soil amended with liquid sludge to contain 410 mg Mo/ha	20 DW	9
White clover, *Trifolium repens*		
Soil amended with fly ash		
40 g/kg soil	27 DW	3
80 g/kg soil	36 DW	3
Soil amended with liquid sludge		
17 mg Mo/ha	31 DW	9
410 mg Mo/ha	90 DW	9
Wheat, *Triticum aestivum*		
Germany, Romania, USSR	0.2 to 0.8 FW	4
India	0.5 FW	4
USA	0.6 to 6 FW	4
Vegetables		
Mo symptoms in man	11 to 82 DW	4
Control site	3 to 5 DW	4
Vegetation		
Near Mo mine	Max. 5,400 AW	6
Normal	<2 to 500 AW	6
Aquatic plants		
Algae, whole		
Marine	0.03 to 0.2 FW; 0.1 to 1.3 DW	4
Canada, 11 species	0.2 to 1.4 DW	10
Marine plants	0.5 FW	11
Marsh plants, whole		
Texas, 14 species	0.4 to 2.5 DW	10
Seaweeds, whole		
UK, 5 species	0.2 to 1.3 DW; 0.04 to 0.2 FW	10

Norway, 11 species	0.3 to 6 DW	4
Aquatic invertebrates		
Aquatic insects, 4 species		
Near low Mo waters (<1.0 ug Mo/L)	0.3 to 1.4 DW	12
Upstream	Max. 0.2 DW	12
Downstream	Max. 0.3 DW	12
Corals, marine,		
34 species	<2 DW	13
Crustaceans, marine		
Tissues sold for human consumption,		
16 species	0.1 to 0.4 FW	14
Molluscs, marine		
Soft parts		
15 species	<0.1 to 0.6 FW	14
3 species	0.7 to 4 FW	14
Mussel, *Mytilus edulis aoteanus*		
Soft parts	0.6 DW	15
Gill	0.6 DW	15
Visceral mass	2 DW	15
Shell	11 DW	15
Other tissues	<0.1 DW	15
Scallop, *Pecten novae-zelandiae*		
Soft parts	0.9 DW	15
Mantle	2 DW	15
Gill	3 DW	15
Intestine	4 DW	15
Kidney	3 DW	15
Foot	0.4 DW	15
Plankton, Baltic Sea	2 DW	16
Fish		
Fishes, marine		
Liver		
43 species	0.1 to 0.3 FW	14
29 species	0.4 to 2.0 FW	14
2 species	0.4 to 1.0 DW	17
Muscle		
130 species	0.1 to 0.3 FW	14
29 species	0.4 to 0.6 FW	14
2 species	0.3 to 0.12 DW	17
Various	Max. 0.04 FW	11
Whole		
17 species	0.1 to 0.6 FW	14
8 species	0.012 to 0.15 FW	18

Rainbow trout, *Oncorhynchus mykiss*		
From low Mo waters (<6 ug/L)		
Liver	0.04 to 0.1 FW	19
Spleen	0.05 to 0.9 FW	19
Kidney	0.1 FW	19
Skin	0.07 FW	19
Bone	0.1 to 0.15 FW	19
Muscle	0.01 FW	19
Intestine	0.01 to 0.07 FW	19
Stomach	0.04 FW	19
Brain	0.02 FW	19
From high Mo waters (300 ug/L)		
Liver	0.2 FW	19
Spleen	0.2 FW	19
Kidney	0.15 FW	19
Skin	0.1 FW	19
Bone	0.2 FW	19
Muscle	0.01 FW	19
Intestine	0.1 FW	19
Stomach	0.3 FW	19
Brain	0.09 FW	19
Held 2 weeks in live traps 1.6 km downstream from Mo tailings outfall		
Liver	43 DW	20
Kidney	26 DW	20
Control location		
Liver	1 DW	20
Kidney	<2 DW	20
Birds		
Chicken, *Gallus* sp.		
Liver	3.6 DW	21
Kidney	4.4 DW	21
Muscle	0.1 DW	21
Robin, *Turdus migratorius*		
From Mo mine site		
Liver	1.6 DW	20
Kidney	1.9 DW	20
Mammals		
Alaskan moose, *Alces alces gigas*		
Hair	0.1 to 0.6 DW	22
Cattle, cows, *Bos* spp.		
Normal		
Blood	0.06 FW	2

Milk	0.07 (0.02 to 0.2) FW	2, 4
Liver	0.7 to 2 FW; 2.9 to 5.4 DW	2, 11, 23
Kidney	0.3 FW; 1.3 to 2.7 DW	2, 23
Muscle	0.1 FW; 0.5 DW	2, 23
Feces	1.1 to 2.1 DW	23
Elevated or poisoned		
Blood	0.6 to 0.8 FW	2
Kidney	21 FW	11
Rumen contents	21 to 28 DW	24
Horse, *Equus caballus*		
Liver	3 to 85 DW	21
Man, *Homo sapiens*		
Liver	0.5 to 1.0 FW; 3.2 DW	21, 25
Liver cortex	0.9 FW	21, 25
Kidney	0.2 to 0.3 FW; 1.6 DW	21, 25
Kidney cortex	0.2 FW	21, 25
Adrenal	0.7 FW	21, 25
Amnion	3.5 FW	21, 25
Chorion	0.6 FW	21, 25
Spleen	0.2 DW	21, 25
Lung	0.15 DW	21, 25
Brain	0.14 DW	21, 25
Muscle	0.14 DW	21, 25
Hair	0.06 (0.02 to 0.13) DW	21, 25
Blood	<0.005 to 0.1 FW	21, 25
Mule deer, *Odocoileus hemionus*		
Liver		
Mo mining area	1.0 FW	26
Control site	0.6 FW	26
Healthy	1.3 FW	26
Sheep, *Ovis aries*		
Wool	0.2 (0.03 to 0.6) DW	21
Liver		
Normal diet		
Adults	2 to 4 DW	21
Newborn lambs	2 to 4 DW	21
High Mo diet		
Adults	25 to 30 DW	21
Newborns	12 to 20 DW	21
Milk		
Grazing on low Mo		
(<1 mg/kg) pasture	<0.01 FW	21
Grazing on high Mo (13 mg/kg) pasture	>1 FW	21

Grazing on high Mo (25 mg/kg) pasture, and given high sulfate (23 g/daily) for 3 days	0.1 FW	21
As above, without sulfate administration	1 FW	21
Rat, *Rattus* sp.		
Liver	2 DW	21
Kidney	1 DW	21
Spleen	0.5 DW	21
Lung	0.4 DW	21
Brain	0.2 DW	21
Muscle	0.06 DW	21
Wildlife, 9 species		
From areas of high environmental Mo levels		
Liver	0.1 to 4 DW	20
Kidney	0.3 to 3 DW	20

[a]Concentrations are listed as means, minimum-maximum (in parentheses), and maximum (Max.).

[b]References: 1, Smith et al. 1987; 2, Penumarthy and Oehme 1978; 3, Elseewi and Page 1984; 4, Friberg et al. 1975; 5, Kubota et al. 1967; 6, Shacklette et al. 1978; 7, Garmo et al. 1986; 8, Schalscha et al. 1987; 9, Pierzynski and Jacobs 1986; 10, Eisler 1981; 11, Schroeder et al. 1970; 12, Colborn 1982; 13, Livingston and Thompson 1971; 14, Hall et al. 1978; 15, Brooks and Rumsby 1965; 16, Prange and Kremling 1985; 17, Papadopoulu et al. 1981; 18, Rao 1984; 19, Ward 1973; 20, Kienholz 1977; 21, Underwood 1971; 22, Flynn et al. 1976; 23, Kume et al. 1984; 24, Sas 1987; 25, Friberg and Lener 1986; 26, King et al. 1984.

EFFECTS

GENERAL

Trace quantities of Mo are beneficial and perhaps essential for normal growth and development of plants and animals. In mammals, Mo can protect against poisoning by copper, mercury, and probably other metals, and may have anticarcinogenic properties. For all organisms, the interpretation of Mo residues depends on knowledge of Mo, copper, and inorganic sulfate concentrations in diet and in tissues.

Some Mo compounds have insecticidal properties at low concentrations and have been proposed as selective termite control agents.

Aquatic flora and fauna seem to be comparatively resistant to Mo salts; adverse effects on growth and survival were usually noted only at water concentrations of 50 mg Mo/l, and higher. However, one study with newly fertilized eggs of rainbow trout produced an LC-50 (28 day) value of 0.79 mg Mo/l compared to an LC-50 (96 hour) value of 500 mg/l for adults. Also, bioconcentration of Mo by selected species of algae and invertebrates (up to 20 g/kg dry weight) poses questions on risk to higher trophic level organisms.

In birds, adverse effects of Mo have been reported on growth at dietary concentrations of 200 to 300 mg/kg, on reproduction at 500 mg/kg, and on survival at 6,000 mg/kg.

In mammals, cattle are especially sensitive to Mo poisoning, followed by sheep, under conditions of copper and inorganic sulfate deficiency. Cattle were adversely affected when grazing pastures with a copper:Mo ratio <3, or when fed low copper diets containing 2 to 20 mg Mo/kg diet, or when total daily intake approaches 141 mg Mo; cattle usually die at doses of 10 mg Mo/kg body weight. Other mammals, including horses, pigs,

rodents, and ruminant and nonruminant wildlife are comparatively tolerant to Mo. Deer, for example, are at least 10 times more resistant than domestic ruminants to Mo; no adverse effects in deer were noted at dietary levels of 1,000 mg/kg after 8 days, slight effects at 2,500 mg/kg after 25 days, and reduction in food intake and diarrhea at 5,000 mg/kg diet after 15 days.

TERRESTRIAL PLANTS

In a major literature review, Gupta and Lipsett (1981) concluded that Mo was essential for plant growth due to its role in the fixation of nitrogen by bacteria using the enzymes nitrogenase and nitrate reductase, and that plants readily accumulated MoO_4^{2-} except under conditions of low pH, high sulfate, and low phosphate, and in some highly organic soils. Molybdenum deficiency has been recorded in a variety of crops worldwide, but there is an extremely narrow range between adequacy and deficiency. In lettuce (*Lactuca sativa*), for example, adverse effects were noted at 0.06 mg/kg (dry weight) in plants, but sufficiency was attained at 0.08 to 0.14 mg/kg; a similar case is made for *Brassica* spp., i.e., Brussels sprouts, cabbage, and cauliflower (Gupta and Lipsett 1981). In certain species, such as beets (*Beta vulgaris*) and corn (*Zea mays*), the ratio between deficiency and sufficiency may differ by more than 10X (Gupta and Lipsett 1981).

Okra (*Abelmoschus esculentus*), grown in soils supplemented with Mo at 1, 2, or 3 mg/kg, as sodium molybdate, showed increasing growth and yields when compared to nonsupplemented soils; fruiting occurred earlier and persisted longer with increasing Mo concentration (Singh and Mourya 1983). The cashew (*Anacardium occidentale*)--one of the most valuable plantation crops in India--developed yellow- leaf spots accompanied by low Mo levels and excess manganese in low pH soils; in extreme cases the tree was defoliated (Subbaiah et al. 1986). The disorder was corrected by foliar spraying of Mo salts or by liming the soil. A similar case was reported for Florida citrus in the 1950's, which was shown to be due to Mo deficiency (Subbaiah et al. 1986).

Soils amended with sewage sludge containing 12 to 39 mg Mo/kg dry weight (soil contained 2 mg Mo/kg dry weight at start and 4.8 to 6 mg/kg after treatment) were planted with corn and bromegrass (*Bromus inermis*). A lime-treated sludge increased Mo concentrations in plant tissues after several years of sludge application; maximum values recorded were 1.9 mg Mo/kg dry weight in bromegrass and 3.7 in corn (Soon and Bates 1985). No toxicity of Mo has yet been observed in field-grown crops, although forages containing 10 to 20 mg/kg dry weight are considered toxic to cattle and sheep (Soon and Bates 1985).

TERRESTRIAL INVERTEBRATES

Sodium molybdate and other molybdenum compounds in toxic baits have potential for termite control (Brill et al. 1987). Baits containing 1,000 mg Mo/kg were fatal to 99% of the termite *Reticulitermes flavipes* in 48 days. After 8 to 10 days, termites became steel-gray in color, but appeared otherwise normal; mortality began only after day 16. Termites did not avoid the poisoned bait, even at concentrations of 5,000 mg Mo/kg. Yoshimura et al. (1987) reported similar results with another species of termite; sodium molybdate killed 100% of the workers in a colony of *Coptotermes formosanus* within 24 hours after they ate filter paper treated with a 5% solution. Some other species of insects--including fire ants (*Solenopsis* sp.) and various species of beetles and cockroaches--were not -affected when exposed to baits containing 5,000 mg Mo/ kg for 48 days (Brill et al. 1987).

AQUATIC ORGANISMS

Aquatic plants are comparatively resistant to Mo; in sensitive species adverse effects were evident on growth at 50 mg/l, and on development at 108 mg/l (Table 3). Bioconcentration of Mo from the medium by certain freshwater algae can result in residues up to 20 grams/kg dry weight without apparent damage (Table 3); the implications of this phenomenon to waterfowl and to other species that consume Mo-laden algae need to be explored.

Molybdenum is considered essential for aquatic plant growth, but the concentrations required are not known with certainty and are considered lower than those for any other essential element (Schroeder et al. 1970; Henry and Tundusi 1982). Molybdenum starvation restricts nitrogen fixation in algae, thereby limiting photosynthetic production during depleted conditions. Blue-green alga (*Anabaena oscillaroides*) cultured in Mo-deficient media containing 0.004 to 0.005 ug Mo/l rapidly depleted Mo in the medium; this ability was lost at higher

concentrations of added Mo, when *Anabaena* began to accumulate the element (Steeg et al. 1986). The addition of tungstate to Mo-deficient media enhances dinitrogenase inactivation, resulting in inhibited algal growth; this process is reversed at Mo levels of 0.005 to 0.04 ug/l (Steeg et al. 1986). On the other hand, algal growth was significantly enhanced when vanadium (V) was present at 12.5 ug/l, although higher concentrations of V were growth inhibitory in 7 days (Vaishampayan 1983).

Algal uptake of Mo is rapid during the first 2 hours, and slower thereafter; the sequential biological reduction of hexavalent to pentavalent to trivalent Mo occurs intracellularly in green algae (Sakaguchi et al. 1981). Uptake is greater in freshwater than in seawater, greater at increased doses, and greater at reduced algal densities (Sakaguchi et al. 1981); it is also greater at elevated temperatures (Penot and Videau 1975).

Molybdenum occurs naturally in seawater as molybdate ion, MoO_4^{2-}, at about 10 ug/l (Abbott 1977). Despite the high concentrations of dissolved Mo in offshore seawater, phytoplankton from offshore locales contain extremely low Mo residues, almost typical of Mo-deficient terrestrial plants (Howarth and Cole 1985). This phenomenon is attributed to the high concentrations of sulfate in seawater; sulfate inhibits molybdate assimilation by phytoplankton, making it less available in seawater than in freshwater. As one result, nitrogen fixation and nitrate assimilation--processes that require Mo--may require greater energy expenditure in marine than in fresh waters and may explain, in part, why marine ecosystems are usually nitrogen-limited and lakes are not (Howarth and Cole 1985). Experimentally increasing the ratio of sulfate to molybdate inhibits molybdate uptake by marine algae, slows nitrogen fixation rates, and slows the growth of organisms that use nitrate as a nitrogen source (Howarth and Cole 1985).

Table 3. Molybdenum effects on selected species of aquatic organisms.

Organism, Mo concentration, and other variables	Effect	Reference [a]
Aquatic plants		
Blue-green alga, *Anabaena oscillaroides*		
0.005 ug/L	Bioconcentration factor (BCF) of 3,300 in 60 min	1
0.073 ug/L	BCF of 550 in 60 min	1
25 ug/L	BCF of 7 to 24 in 60 min	1
Green alga, *Chlorella vulgaris*		
10 mg/L	Residues of about 20,000 mg/kg dry weight in 20 h. Dead (heat-killed) *Chlorella* contained 4,902 mg/kg dry weight in 1 h versus 3,264 mg/kg in live cells	2
20 mg/L	Normal growth in 96 h	2
50 mg/L	Reduced growth in 96 h	2
Euglena, *Euglena gracilis*		
5.4 mg/L	Normal growth and reproduction	3
96 mg/L	No abnormal cells in 48 h	3
108 mg/L	Abnormal development, cells forming clusters. Culture is photosensitive with blue color	3
>960 mg/L	No growth	3
Freshwater alga, *Nitella flexilis*		
0.014 ug/L	BCF of 628 in 25 days	4
3.3 mg/L	BCF of 39 in 24 days; elevated	

	residues of 130 mg/kg fresh weight	4
Blue-green alga, *Nostoc muscorum*		
17.7 ug/L	Required for growth	5
Invertebrates		
Amphipod, *Allorchestes compressa*		
60 mg/L	No deaths (=LC-0) in 96 h	6
247 mg/L	50% dead (=LC-50) in 96 h	6
450 mg/L	97% dead (=LC-97) in 96 h	6
Starfish, *Asterias rubens*		
127 mg/L	LC-50 (24 h) at pH 5.8	7
254 mg/L	LC-50 (24 h) at pH 8.2	7
Copepod, *Calanus marshallae*		
20 mg/L	Minor increase in oxygen consumption in 24 h	8
100 mg/L	Decreased oxygen consumption in 24 h	8
560 mg/L	LC-50 (19 days)	8
Green crab, *Carcinus maenus*		
1,018 mg/L	LC-50 (48 h)	7
American oyster, *Crassostrea virginica*		
1,375 mg/L	Reduction of 50% in shell growth in 96 h	9
Hermit crab, *Eupagurus bernhardus*		
100 mg/L	LC-0 (50 days)	7
222 mg/L	LC-50 (48 h)	7
Euphausiid, *Euphausia pacifica*		
560 mg/L	LC-50 (112 h)	8
Amphipod, *Gammarus* sp.		
3.3 mg/L	BCF of 4.8 in whole animal in 24 days	4
Lake periphyton		
0.014 ug/L	BCF of 3,570 in 24 days	4
Clam, *Margaretifera margaretifera*		
3.3 mg/L	Maximum BCF values in 15 to 24 days were 1.8 in shell, 0.9 in soft parts, and 0.3 in muscle	4
Mysid shrimp, *Mysidopsis bahia*		
1,205 mg/L	LC-50 (96 h)	9
Mussel, *Mytilus edulis*, larvae		
147 mg/L	Development reduced 50% in 48 h, based on survival and abnormalities	10
Crayfish, *Pacifiastacus leniusculus*		
3.3 mg/L	BCF in 24 days of 5.7 for muscle and 9.8 for carapace	4
Pink shrimp, *Penaeus duorarum*		
1,909 mg/L	LC-50 (96 h)	9
Pullet-shell (clam), *Venerupis pallustra*		
381 mg/L	LC-50 (24 h)	7

Fish		
Sheepshead minnow, *Cyprinodon variegatus*		
3,057 mg/L	LC-50 (96 h)	9
Bluegill, *Lepomis macrochirus*		
1,320 mg/L	LC-50 (96 h)	11
Fathead minnow, *Pimephales promelas*		
70 mg/L	LC-50 (96 h), soft water	11
360 mg/L	LC-50 (96 h), hard water	11
Steelhead trout, *Oncorhynchus mykiss*		
0.014 ug/L	Max. BCF of 1,143 in liver and gastrointestinal tract after chronic exposure	4
3.3 mg/L	Max. BCF in 24 days of 5.4 in spleen 4.5 in liver, 2.3 in muscle, 1.8 in gill, and 0.6 in gastrointestinal tract	4
Rainbow trout, *O. mykiss*		
Embryo and larval stages exposed for a total of 28 days starting at fertilization through 4 days posthatch		
28 ug/L	LC-1 (28 days)	12
125 ug/L	LC-10 (28 days)	12
790 (610 to 990) ug/L	LC-50 (28 days)	12
17.0 to 18.5 mg/L, exposed continuously for one year from eyed eggs to juvenile stage	No significant effect on survival, growth, or blood hematocrit	10, 11
500 mg/L	LC-25 (96 h), mean length 20 mm	11
800 mg/L	LC-50 (96 h), mean length 20 mm	11
1,320 mg/L	LC-50 (96 h), mean length 55 mm	11

[a]References: 1, Steeg et al. 1986; 2, Sakaguchi et al. 1981; 3, Colmano 1973; 4, Short et al. 1971; 5, Vaishampayan 1983; 6, Ahsanullah 1982; 7, Abbott 1977; 8, Anderson and Mackas 1986; 9, Knothe and Van Riper 1988; 10, Morgan et al. 1986; 11, McConnell 1977; 12, Birge et al. 1980.

Limited data suggested that aquatic invertebrates were very resistant to Mo; adverse effects were observed on survival at >60 mg Mo/l and on growth at >1,000 mg Mo/l (Table 3). Bioconcentration factors were low, but depending on initial dose, measured residues (mg/kg fresh weight) were as high as 16 in amphipods, and were 3 in clams, 18 in crayfish muscle, and 32 in crayfish carapace (Short et al. 1971). The host organisms seemed unaffected under these Mo burdens, but effects on upper trophic level consumers were not clear. Tailings from a pilot molybdenum mine on the North American Pacific coast were acutely lethal at concentrations of >61,000 mg tailings solids/1 seawater to larvae of the mussel *Mytilus edulis*, and to adults of the amphipod *Rhepoxynius abronius* and the euphausiid *Euphausia pacifica*; acute sublethal effects were observed at >277,000 mg/l (Mitchell et al. 1986). All species of invertebrates tested in this preliminary study were more sensitive than juvenile coho salmon, *Oncorhynchus kisutch* (Mitchell et al. 1986). In another study, zooplankton exposed to Mo mine tailings <8 um in diameter at high sublethal concentrations ingested and excreted these particles (-

Anderson and Mackas 1986). The lowest tailing concentration tested at which a deleterious effect was observed was 100 mg/l for depression of respiration in the copepod *Calanus marshallae*, and 560 mg/l for increased mortality in copepods and the euphausiid *Euphausia pacifica*; concentrations of Mo mine tailings were always <15 mg/l at 0.5 km downstream from a Mo tailings outfall (Anderson and Mackas 1986).

Freshwater and marine fishes were--with one exception--extremely resistant to Mo; LC-50 (96 hour) values ranged between 70 mg/l and <3,000 mg/l (Table 3). The exception was newly fertilized eggs of rainbow trout exposed for 28 days through day 4 posthatch; the LC-50 (28 day) value was only 0.79 mg/l (Birge et al. 1980), and suggested that additional research is needed on the sensitivity of early life stages to Mo. In general, Mo was more toxic to teleosts in fresh water than in seawater and more toxic to younger fish than to older fish; in rainbow trout it bioconcentrated up to 16 mg/kg fresh weight in liver, 18 in spleen, 7 in muscle, 6 in gill, and 2 in gastrointestinal tract (Table 3; Short et al. 1971). Environmental levels of molybdenum as molybdate measured in the Mo mining areas of Colorado were not considered harmful to rainbow trout (McConnell 1977). Molybdenum enrichment of Castle Lake, California (a high mountain lake in which Mo was determined to be the limiting micronutrient), coupled with favorable environmental conditions, led to record high yields of trout. The addition of 16 kg of sodium molybdate, or 6.4 kg Mo, to Castle Lake in July 1963 was followed by larger standing crops of zooplankton and bottom fauna, which probably promoted survival of the 1965 year class and resulted in record yields to the angler of rainbow trout and brook trout (*Salvelinus fontinalis*) in 1967 (Cordone and Nicola 1970). Enrichment of Mo-deficient waters to improve angler success merits additional research.

BIRDS

Data are missing on the effects of Mo on avian wildlife under controlled conditions. All studies conducted with birds have been restricted to domestic poultry.

Signs of Mo deficiency in domestic chickens included loss of feathers, lowered tissue Mo concentrations, reduced xanthine dehydrogenase activity in various organs, decreased uric acid excretion, disorders in ossification of long bones, and changes in joint cartilage that led to complete immobility; signs were eliminated when diets were supplemented with Mo at concentrations of 0.2 to 2.5 mg/kg (Reid et al. 1956; Friberg and Lener 1986). Efforts to produce a Mo deficiency syndrome in birds and mammals by feeding diets low in Mo have been unsuccessful (Friberg et al. 1975). Thus, it has been necessary to introduce a compound with a known property of inhibiting Mo, namely wolframate (Na_2WO_4), a tungsten compound. Wolframate increases Mo excretion, leading to Mo deficiency in rats and chickens. With this technique it has been possible to produce an assumed Mo deficiency in chicks consisting of reduced weight gain and sometimes death (Friberg et al. 1975). Dietary requirements to maintain normal growth in rats and chicks were probably less than 1 mg Mo/kg food, and thus substantially less than that of any other trace element recognized as essential (Mills and Breamer 1980). In fact, birds may require Mo at concentrations up to 6 mg/kg in their diets for optimal growth (Kienholz 1977). Dietary Mo counteracts adverse effects in chicks on growth and survival induced by hexavalent chromium. Chicks fed 900 mg chromium/kg ration for 4 weeks showed significantly depressed growth, 25% mortality, and elevated liver chromium; however, diet supplementation to 150 mg Mo/kg resulted in normal growth and liver chromium values, and no deaths (Chung et al. 1985).

Early studies with chicks and turkey poults showed that the addition of only 13 to 25 ug Mo per kg--as molybdate or molybdic acid--to basal diets containing 1.0 to 1.5 mg Mo/kg resulted in a growth advantage of 14% to 19% in 4 weeks over that in unsupplemented groups (Reid et al. 1956, 1957). Roosters given dietary supplements of 100 or 400 ug Mo per bird daily for 4 weeks to basal diets containing 0.51 mg Mo/kg had reduced serum uric acid values when compared to those of controls; the significance of this finding is not clear (Karring et al. 1981). Birds are relatively resistant to Mo. For example, day-old chicks fed diets containing 20% Mo mine tailings for 23 days were unaffected, and those fed diets containing 40% Mo mine tailings showed only a slight reduction in body weight during the same period (Kienholz 1977). Dietary levels of 200 mg Mo/kg ration results in minor growth inhibition of chicks; and at 300 mg/kg feed, the growth of turkey poults was reduced (Underwood 1971). Dietary supplements of 500 mg Mo/kg ration produced a slight decrease in growth rate of chicks after 4 weeks; hens, however, laid 15% fewer eggs than controls, and all eggs contained embryolethal concentrations of 16 to 20 mg Mo/kg (Friberg et al. 1975). At dietary supplements of 1,000 mg Mo/kg, egg production was reduced 50% in domestic chickens (Friberg et al. 1975). Dietary loadings of 2,000 mg/kg induced severe growth depression and a 100X increase in Mo content in tibia (Underwood 1971), and an 80% reduction in egg production (Friberg et al. 1975). At 4,000 mg/kg diet, severe anemia was reported in chickens

(Underwood 1971). Mortality of chicks fed 6,000 mg Mo/kg diet for 4 weeks was 33%; at 8,000 mg Mo/kg diet for 4 weeks, 61% of the chicks died and survivors weighed only 16% as much as the controls (Friberg et al. 1975). Chicks, unlike mammals, did not experience Mo reduction in tissues after sulfate administration--although sulfate markedly reduced the signs of No toxicity (Underwood 1971).

MAMMALS

Data on the effects of Mo on mammalian wildlife are scarce. Almost all studies conducted to date on Mo effects under controlled conditions have been on livestock, especially cattle and sheep.

Molybdenum is beneficial and perhaps essential to adequate mammalian nutrition; moreover, it can protect against poisoning by copper or mercury, and may be useful in controlling cancer. Evidence of functional roles for Mo in the enzymes xanthine oxidase, aldehyde oxidase, and sulphite oxidase suggests that Mo is an essential trace nutrient for animals (Underwood 1971; Earl and Vish 1979; Mills and Breamer 1980). Signs of Mo deficiency include decreased intestinal and liver xanthine oxidase activity (Mills and Breamer 1980). Molybdenum prevents damage to the liver in sheep recieving excess copper; accumulations of copper and Mo in kidney were present in a biologically unavailable form and of negligible physiological significance (Van Ryssen et al. 1982). Dietary supplements of 70 mg Mo per day for a restricted period is recommended for reduction of liver Cu in sheep, provided dietary Cu levels are simultaneously reduced (Van Ryssen et al. 1986). Molybdenum, as sodium molybdate, protects against acute inorganic mercury toxicity in rats by altering the metabolism of cysteine-containing proteins in the cytoplasm of liver and kidney, resulting in lowered mercury content in these organs (Yamane and Koizumi 1982; Koizumi and Yamane 1984). Anticarcinogenic properties of Mo in rats have been reported, although the mechanisms of action are unknown. In one study, 2 or 20 mg Mo/1 in drinking water significantly inhibited cancer of the esophagus and forestomach experimentally induced by N-nitrososarcosine ethyl ester (Luo et al. 1983). In another study with virgin female rats, 10 mg Mo/l in drinking water reduced by half the number of mammary carcinomas experimentally induced by N-nitroso-N-methylurea (Wei et al. 1985). Additional research seems warranted on the role of Mo in cancer inhibition.

Molybdenosis has been produced experimentally in many species of mammals, including cattle, sheep, rabbits, and guinea pigs (Friberg et al. 1975). Signs of Mo poisoning vary greatly among species, but generally include the following: copper deficiency, especially in serum; reduced food intake and growth rate; liver and kidney pathology; diarrhea and dark-colored feces; anemia; dull, wiry, and depigmented hair; reproductive impairment, including delayed puberty, female infertility, testicular degeneration, and abnormal or delayed oestrus cycle; decreased milk production; joint and connective tissue lesions; bone abnormalities; and loosening and loss of teeth (Underwood 1971; Dollahite et al. 1972; Friberg et al. 1975; Erdman et al. 1978; Penumarthy and Oehme 1978; Ward 1978; Chappell et al. 1979; Mills and Breamer 1980; Alary et al. 1981; Baldwin et al. 1981; Friberg and Lener 1986; Van Ryssen et al. 1986; Phillippo et al. 1987a). These authorities also agree on three additional points: first, early signs of molybdenosis are often irreversible, especially in young animals; second, the severity of the signs depends on the level of Mo intake relative to that of copper and inorganic sulfate; and third, if afflicted animals are not removed promptly from Mo-contaminated diets and given copper sulfate therapy, death may result.

Molybdenum poisoning in ruminants, or teart disease, has been known since the mid 1800's and affects only ruminants of special pastures. Degree of teartness varies from field to field and season to season, and is usually proportional to the Mo content in herbage. Molybdenum levels in typical teart pastures range from 10 to 100 mg/kg dry weight compared to normal levels of 3 to 5 mg/kg (Friberg and Lener 1986). If herbage contains more than 12 mg Mo/kg dry weight, problems should be expected in cattle, and to a lesser extent in sheep (Friberg et al. 1975). In situations where cattle are accidentally exposed to high Mo levels, the administration of copper sulphate should result in Mo excretion, up to 50% in 10 days (Penumarthy and Oehme 1978). Aside from cattle and sheep, all evidence indicates that other mammals are comparatively tolerant of high dietary intakes of Mo, including horses, pigs, small laboratory animals, and mammalian wildlife (Underwood 1971; Buck 1978; Chappell et al. 1979; Friberg and Lener 1986; Table 4). Cattle excrete Mo primarily through feces, but other (more tolerant) species such as pigs, rats, and man, rapidly excrete Mo through urine and this may account, in part, for the comparative sensitivity of cattle to Mo (Underwood 1971). Cattle normally excrete about 67% of all administered MoO_3 in feces and urine in 7 days; guinea pigs excreted 100% in urine in 8 days; and swine excreted 75% in urine in 5 days (Penumarthy and Oehme 1978). Cattle are adversely affected when they graze copper-deficient pastures containing 2 to 20 mg/kg Mo, and the copper to Mo ratio is less than 3; or when

they are fed low copper diets containing 5 mg (or more) Mo/kg dry weight; or when total daily intake approaches 141 mg Mo; or when body weight residues exceed (a fatal) 10 mg Mo/kg (Table 4). It is clear that both the form of Mo administered and the route of exposure affect Mo metabolism and survival (Table 4). By comparison, adverse effects (some deaths) were noted at 250 mg Mo/kg body weight (BW) (in guinea pigs), at 50 mg/kg BW in domestic cats (central nervous system impairment), at 10 mg/l drinking water in mice (survival), at 10 to 15 mg total daily intake in man (high incidence of gout-like disease), and at to 3 mg/m^3 air in man for 5 years (respiratory difficulties), or 6 to 19 mg/m^3 in man for 4 years (Table 4).

Table 4. Molybdenum effects on selected species of mammals.

Species, dose, and other variables	Effects (reference) [a]
Cattle, cows, *Bos* spp.	
Near steelworks, 20 kg Mo as MoO_3 emitted daily in gaseous form; fallout deposits ~2 mg/m^2 monthly, corresponding to a pasture Mo content from 2 to 20 mg Mo/kg dry weight. Pasture had slight copper deficiency of natural origin, with copper:Mo ratio in pastures <3	About 40% of 5,000 grazing cows with signs of molybdenosis. No signs of poisoning before steelworks began operations. Signs evident almost immediately in first grazing season; most pronounced in younger animals closest to source. Remedial actions included copper glycine administration to cattle, and installation of additional emission filters at the steelworks (1)
Low dietary Mo (<5 mg Mo/kg), adequate copper	Growth normal; fertilization rate 100% liver copper >70 mg/kg dry weight; 63% of embryos developed normally (2)
Fed diets containing 5 mg Mo/kg dry weight and 4 mg copper/kg dry weight for 84 weeks	Decreased food intake, reduced efficiency of food use, altered iron metabolism, clinical signs of copper deficiency. Onset of puberty delayed 10 weeks, decreased conception rate (fertility 12% to 33% vs. 57% to 80% in controls), disrupted oestrus cycle (67% were anoestrus vs. 7% in controls), and other signs consistent with decreased releases of luteinizing hormones associated with altered ovarian secretion (3, 4)
High dietary Mo (15 to 20 mg Mo/kg), copper-deficient	Growth and fertilization normal; liver copper 10 mg/kg dry weight; only 16% of embryos developed normally (2)

Fed diets of normal copper, and high Mo (30 mg/kg feed)	Blood Mo level of 0.6 to 0.8 mg/L (5)
Diets containing 40 mg Mo/kg and 6 mg copper/kg fed to lactating cows for 9 weeks	Reduction of 30% in milk yield; rapid decline in plasma copper; milk Mo levels of 1.6 mg/L; growth reduction in nursing calves (6)
Fed diets of 60 mg Mo/kg dry weight	Low liver copper, intestinal disturbances, brittle bones prone to fracture (7)
Dairy herd fed pelleted feed containing 140 mg Mo/kg fresh weight and up to 10 mg copper/kg fresh weight	Molybdenosis. Contaminated magnesium oxide (12,200 mg Mo/kg) added to ration at 1% was the source of the excess Mo (8)
Drinking water with Mo as ammonium molybdate. Basal diet with 13 mg copper/kg and 2,900 mg sulfur/kg	
1 or 10 mg Mo/L in drinking water for 21 days	In 5-week-old calves, there was no effect on liver or plasma copper levels (9)
50 mg Mo/L in drinking water for 21 days	Copper liver concentration reduced to 201 mg/kg dry weight vs. 346 in controls; copper in plasma elevated to 1,100 ug/L vs. 690 in controls. No effect on growth, or food and water consumption (9)
Total daily intake of 100 mg Mo	Normal milk Mo level of 0.06 mg/L (5)
Total daily intake of 141 mg Mo	Anorexia, darrhea, and weight loss in Swiss beef cattle (10)
Total daily intake of 500 mg Mo	Milk Mo level of 0.37 mg/L (5)
Total daily intake of 1,360 mg Mo daily as soluble molybdate	Signs of molybdenum poisoning (7)
10 mg Mo/kg body weight	Lethal dose (11)
Guinea pig, *Cavia* sp.	
Chronic exposure, daily dose in mg Mo/animal	

25, as MoO_3	75% mortality (12)
200, as calcium molybdate	25% mortality (12)
Air concentrations of 28 to 285 mg Mo/m^3	Hexavalent Mo compounds absorbed appreciably, but not disulfide compounds (10, 13)
Dose, in mg Mo/kg body weight, various administration routes	
80	LD-0 (12)
250	Some deaths (11)
400	LD-75 (4 days) (12)
800	LD-100 (4 months) (12)
Domestic ruminants	
Pastures containing 10 to 20 mg Mo/kg dry weight	"Risk" zone for molybdenosis (12)
Pastures containing 20 to 100 mg Mo/kg dry weight	"Teart" disease characterized by anemia, poor growth, diarrhea; prolonged exposure resulted in joint deformities, and death (13)
Horses, ponies, *Equus* sp.	
Feeding on teart pastures with elevated Mo content	No effect (5)
Given single oral dose of radio Mo-99, as molybdate, or about 20 to 28 mg	Mo appeared rapidly in plasma as Mo-99 molybdate, but quickly cleared with Tb 1/2 of 7 to 10 h (14)
Fed diets containing 20 mg Mo/kg dry weight for 4.5 months; diet supplemented with sulfur for one month at 1.2 g/kg feed	Animals remained healthy. No decline in total plasma copper or increase in plasma insoluble copper (14)
Fed diets containing up to 107 mg Mo/kg for 14 days	Increasing dietary Mo resulted in decreasing copper retention due to increasing excretion of copper in feces; up to 1.45 g Mo/kg body weight absorbed and retained with no obvious adverse effects (15)
Cat, *Felis domesticus*	
Intravenous injection, in mg Mo/kg body weight	
25	Increased arterial blood pressure (12)
50	Central nervous system impairment (12)

Man, *Homo sapiens*	
Drinking water, in ug/L	
50	No effect (11)
200	Increased urinary excretion, normal serum Mo levels, no change in copper metabolism (11)
Total intake, in mg Mo daily	
0.18	Average intake in United States (11)
0.5 to 1	Increased urinary copper excretion (11)
10	Increase in blood and urine Mo levels, increases in serum ceruloplasmin, increased xanthine oxidase activity (11)
10 to 15	Increased uric acid, decreased copper excretion, high incidence of gout-like disease (11)
Atmospheric concentrations, in mg Mo/m^3 air	
1 to 3; 5-year exposure	Respiratory difficulties (12)
6 to 19; 4-year exposure	Respiratory difficulties (12)
Mouse, *Mus* spp.	
10 mg Mo/L in drinking water of breeding mice	Decrease in survival of F_2 and F_3 generations (16)
Sheep, *Ovis* spp.	
Mo deficient diets of 0.03 mg/kg	High incidence of renal xanthine calculi (5)
Mo adequate diet of 0.4 mg/kg, due to resowing of pasture and lime treatment	Zero incidence of renal calculi (5)
Mo content of pasture 0.4 to 1.5 mg/kg dry weight	Mo concentrations, in mg/kg fresh weight, were 0.0 to 0.03 in plasma, 2.0 to 2.4 in liver, and 0.4 to 0.5 in kidney. No lameness or connective tissue lesions (17)

2.4 mg Mo/kg diet in lambs	Significantly enhanced growth when compared to sheep fed 0.36 mg Mo/kg diet; growth associated with increased cellulose digestibility by rumen biota (5)
Grazing pastures treated 3x with 420 g Mo/ha: at start, week 45 and week 72. Mo content of pasture usually 5.5 to 12.5 mg/kg dry weight	Mo concentrations, in mg/kg fresh weight, were 1.7 to 2.4 in plasma, 6.0 to 6.4 in liver, and 6.9 to 8.1 in kidney. Lameness and connective tissue lesions in most sheep (17)
Given diets of high copper (82 mg/kg) and sulfur (3.8 g/kg), and Mo at 20, 40, or 60 mg/kg for 193 days	Liver damage due to copper at low Mo (20 mg/kg) diets; at 40 and 60 mg Mo/kg, both metals accumulated in kidney cortex but no evidence of liver histopathology or kidney damage (18)
Breeding ewes fed diets of normal copper, high Mo (30 mg/kg feed)	Blood Mo level of 2.4 to 3.4 mg/L (5)
Diets of 50 mg Mo/kg	Avoidance by lambs; may be learned olfactory recognition (19)
Lambs grazing on soils where copper:Mo ratio is <0.4	Swayback observed in 15% to 39% (10)
Ram lambs fed diets of adequate sulfate and copper (7.7 mg/kg dry weight). Copper to Mo ratios of 5.5, 5.3, 1.1, or 0.7 for 105 days	No significant measurable effects at ratios of 5.5 and 5.3. Secondary copper deficiency (molybdenosis) at 1.1 ratio evident in blood and plasma, and in liver at 0.7 (20)
Lambs fed daily intake of 8 mg Mo, 36.3 mg copper, and 3.7 g sulfur for 125 days	No effect on growth of food intake; significant increases in levels of kidney cortex copper, liver Mo, and plasma copper; major differences in responses among breeds tested (21)
Total intake raised from 0.4 daily mg daily to 96 mg daily	Blood Mo level of 4.95 mg/L (5)
Fed 75 mg copper daily for 50 days,	Molybdenosis within 8 days (22)

followed by 140 mg Mo and 4 g sulfur daily for 13 days with no added copper	
As above, but 70 mg Mo daily at day 13 for 34 days	40% reduction in liver copper (22)
White rabbit, *Oryctolagus* sp.	
Dietary Mo concentrations, in mg Mo/kg ration	
100; lifetime exposure	Reduced growth, hair loss, dermatosis, anemia, skeletal and joint deformities, decreased thyroxin (11)
500; 12 weeks	No obvious effects (12)
1,000; 12 weeks	Some growth retardation (12)
2,000 to 4,000	Many deaths of weanlings in about 37 days, and of adults in 53 days. Survivors were anorexic, diarrhetic, anemic, and had front-leg abnormalities; successful recovery after copper therapy (12)
5,000	Thyroid dysfunction (11)
Rat, *Rattus* spp.	
Drinking water, in mg Mo/L	
10; chronic exposure of 3 years	Disrupted calcium metabolism (29). Increased sensitivity to cold stress, elevated tissue residues of 50 to 60 mg Mo/kg dry weight (23, 24)
20; 30 weeks exposure	No effect on growth or organ histology (25)
50; lifetime exposure	Some growth retardation (11)
1,000; lifetime exposure	No severe signs observed in breeding adults. Resultant pups, however, maintained on this regimen were stunted, rough haired, sterile (males), and hyperactive (11)
Dose, in mg Mo per animal daily for up to 232 days	
10	LD-25 to LD-50 for hexavalent Mo compounds (12)

100	LD-50 for calcium molybdate (12)
125	LD-50 for MoO_3 (12)
333	LD-50 for ammonium molybdate (12)
Atmospheric concentrations, in mg Mo/m^3	
64; 2 h	Outwardly normal, some microscopic damage due to MoO_3 exposure (12)
Up to 5,000 ammonium paramolybdate, 12,000 molybdenum dioxide, 15,000 molybdenum trioxide, or 30,000 metallic Mo; one-hour exposure	Four weeks postexposure, there were no adverse effects except for some irritation of upper respiratory passage (12)
Feeding levels, in mg Mo/kg diet	
50	Diet avoidance (19). In low sulfate diets and 5 weeks exposure, rats had reduced growth and mandibular exostoses (10)
80; copper-deficient	Inhibited growth and reduced survival (5, 26)
80; 35 mg $CuSO_4$/kg	No measurable effects (5, 26)
100; lifetime exposure	Appetite loss, weight loss, reduced growth, anemia, mandibular exostoses, bone deformities, liver and kidney histopathology, increased liver copper residues, male sterility (11)
400	After 5 weeks, growth depression, anemia, mandibular exostoses; some deaths at lifetime exposures (12)
500 or 800	No deaths in 6 weeks; growth retardation and anemia (12)
500 or 1,000; 77 mg copper/kg	Poor growth (5, 26)
500 or 1,000;	Normal growth (5, 26)
5,000	Lethal in 2 weeks (11, 12)
Dose, in mg Mo/kg body weight	

0.00002 to 0.001	50% excretion (Tb 1/2) in 60 h to 113 h for kidney, liver, spleen, small intestine, and skin (10)
0.003	Tb 1/2 in 47 h (10)
>0.003	Tb 1/2 in 3 h when administered subcutaneously, 6 h for intragastric application (10)
4.5, intravenous injection	Biliary excretion of Mo^{+6} compounds was more rapid than Mo^{+5} compounds (27)
100	When inhaled as MoO_3, irritating to eyes and mucous membranes and eventually lethal. Repeated oral administration leads to histopathology of liver and kidney (13)
100 to 150	Lethal (11)
114	All recovered after intraperitoneal injection of sodium molybdate (12)
117	All dead within a few hours after intraperitoneal injection of sodium molybdate (12)
500; daily	Tolerated when given as disulfide (13)
500; 28 days	Reduced growth, disrupted blood and enzyme chemistry, histopathology of liver and kidney; partly reversed by 20% protein diet (28)
Domestic pig, *Sus* sp.	
Fed diets containing 1,000 mg Mo/kg for 3 months	No effect (5)

[a]References: 1, Alary et al. 1981; 2, O'Gorman et al. 1987; 3, Phillippo et al. 1987a; 4, Phillippo et al. 1987b; 5, Underwood 1971; 6, Wittenberg and Devlin 1987; 7, Penumarthy and Oehme 1978; 8, Lloyd et al. 1976; 9, Kincaid 1980; 10, Friberg and Lener 1986; 11, Chappell et al. 1979; 12, Friberg et al. 1975; 13, Goyer 1986; 14, Strickland et al. 1987; 15, Cymbaluk et al. 1981; 16, Earl and Vish 1979; 17, Pitt et al. 1980; 18, Van Ryssen et al. 1982; 19, White et al. 1984; 20, Robinson et al. 1987; 21, Harrison et al. 1987; 22, Van Ryssen et al. 1986; 23, Winston et al. 1973; 24, Winston et al. 1976; 25, Luo et al. 1983; 26, Underwood 1979; 27, Lener and Bibr 1979; 28, Bandyopadhyay et al. 1981; 29, Solomons et al. 1973.

In newborn lambs from ewes that consumed high-Mo diets during pregnancy, demyelinization of the central nervous system was severe, accompanied by low copper contents in the liver (Earl and Vish 1979). Sheep are

more tolerant than cattle to Mo poisoning due, in part, to a lower turnover of ceruloplasmin, a copper-transporting enzyme that is inhibited by Mo; however, this characteristic makes sheep more sensitive than cattle to copper poisoning (Ward 1978). For example, chronic copper poisoning in sheep in several districts in Norway is probably due to Mo-deficient forages rather than to excess copper intake (Froslie et al. 1983). Swayback is a spastic paralysis in lambs born of ewes that were copper deficient during pregnancy Todd 1976). In northern Ireland, where cases have been reported, pastures were not copper deficient and swayback was due to an imbalance of copper, Mo, and sulfur. Very severely affected lambs were paralyzed in all limbs and died shortly after birth because they were unable to stand and suckle. Lambs less severely affected developed signs in about 2 weeks, but usually only the hind limbs were affected. Brain and spinal cord lesions were present, resulting in demyelination of spinal cord and cavitation of brain tissues; lesions were irreversible, but death might have been avoided with adequate copper therapy (Todd 1976).

Horses are generally considered to be tolerant of dietary copper deficiencies and of copper and Mo excesses that affected ruminants. Yet Mo accumulated in equine liver and has been implicated as a possible contributory factor in bone disorders in foals and yearlings grazing pastures containing 5 to 25 mg Mo/kg (Cymbaluk et al. 1981; Strickland et al. 1987). Cattle and horses are highly susceptible to pyrrolizidine alkaloids, an ingredient in certain poisonous plants such as tansy ragwort (*Senecio jacobaea*). Signs of poisoning included elevated copper levels in liver followed by fatal hemolytic crisis. Sheep are more resistant to alkaloids than equines or bovines, and sheep grazing has been recommended as a means of controlling tansy ragwort. However, dietary supplements of 10 mg Mo/kg increased the susceptibility of sheep to tansy ragwort intoxication, despite the observed increase in copper excretion (White et al. 1984).

In rodents, Mo is neither teratogenic nor embryocidal to golden hamsters at doses up to 100 mg/kg body weight, and has no measurable effect on fertility or gestation of female rats given similar high doses (Earl and Vish 1979). Voluntary rejection of high-Mo diets by rats results in anorexia. This phenomenon implies sensory, probably olfactory, recognition of molybdate in combination with other dietary constituents to form compounds with a characteristic odor detectable by rats (Underwood 1971). The ability to reject high-Mo diets requires a learning or conditioning period because it is lacking or weak with freshly prepared diets and extends to a discrimination between a toxic (high Mo) and nontoxic (high Mo plus sulfate) diet. Rats may associate a gastrointestinal disturbance with a sensory attribute of diets containing toxic levels of Mo (Underwood 1971).

Data on Mo effects to mammalian wildlife are scarce, although those available strongly suggest that domestic livestock are at far greater risk (Table 4). Studies with mule deer (*Odocoileus hemionus*) showed that this species was at least an order of magnitude more tolerant to high levels of dietary Mo than were domestic ruminants, and at least as resistant as swine, horses, and rabbits (Ward and Nagy 1976; Ward 1978; Chappell et al. 1979). Female mule deer showed no visible effects after 33 days on diets containing up to 200 mg Mo/kg feed, or after 8 days at 1,000 mg/kg. Only slight effects--some reduction in food intake and some animals with diarrhea--were observed at diets of 2,500 mg/kg for 25 days. At feeding levels of 5,000 and 7,000 mg/kg for periods of 3 to 15 days, signs were more pronounced; however, recovery began almost immediately after transfer to uncontaminated feed. Signs of copper deficiency and of molybdenosis are very similar, and careful diagnosis is necessary to ensure use of the correct remedial action. For example, some populations of Alaskan moose (*Alces alces gigas*) showed faulty hoof keratinization and decreased reproductive rates, but this was attributed to copper-deficient browse growing on low copper soils, and not to increased Mo levels in herbage (Flynn et al. 1977). In another case, a high proportion of white-tailed deer (*Odocoileus virginianus*) feeding near uranium-mine spoil deposits in several Texas counties--areas in which extreme molybdenosis has been documented in grazing cattle--had antlers that were stunted, twisted, and broadened or knobby at the tips (King et al. 1984). However, the copper levels in liver of these deer were similar to those of deer in a control area--16.7 mg/kg fresh weight vs. 18.0--and only 1 of 19 deer examined from the mining district had a detectable Mo concentration in liver (0.7 mg/kg fresh weight) vs. none in any control sample. On the basis of low contents of copper in soils and vegetation, it was concluded that white-tailed deer examined were experiencing copper deficiency (hypocuprosis), with signs similar to molybdenosis (King et al. 1984).

In humans, Mo is low at birth, increases until age 20 years, and declines thereafter (Goyer 1986). Although conclusive evidence that Mo is required by humans is lacking, there is general agreement that it should be considered as one of the essential trace elements. The absence of any documented deficiencies in man indicates that the required level is much less than the average daily intake of 180 ug Mo in the United States (Chappell et al. 1979). Human discomfort has been reported in workers from copper-Mo mines, and in those

eating food products containing 10 to 15 mg Mo/kg and <10 mg copper/kg and grown on soils containing elevated Mo of 77 mg/kg and 39 mg copper/kg. Symptoms included general weakness, fatigue, headache, irritability, lack of appetite, epigastric pain, pain in joints and muscles, weight loss, red and moist skin, tremors of the hands, sweating, dizziness (Friberg et al. 1975), renal xanthine calculi, uric acid disturbances (Schroeder et al. 1970), and increased serum ceruloplasmin (Friberg and Lener 1986). The typical human adult contains only 9 mg of Mo, primarily in liver, kidney, adrenal, and omentum (Goyer 1986). Most of the ingested Mo is easily absorbed from the GI tract and excreted within hours or days in urine, mostly as molybdate; excesses may be excreted also by the bile, particularly as hexavalent Mo (Friberg et al. 1975; Goyer 1986; Friberg and Lener 1986). At high dietary levels Mo reportedly prevents dental caries (Schroeder et al. 1970), but this requires verification.

RECOMMENDATIONS

Although Mo is generally recognized as an essential trace metal for plants and animals, and may reduce the incidence and severity of carcinomas in rats (Luo et al. 1983; Wei et al. 1985) and dental caries in humans (Shamberger 1979), there is no direct evidence of Mo deficiency being detrimental to animal health. The minimum daily Mo requirements in diets are not yet established due to problems in preparing Mo-free rations (Chappell et al. 1979). As a consequence, no regulatory agency recognizes Mo as safe and necessary, and Mo can not be legally incorporated into animal feeds (Penumarthy and Oehme 1978).

The richest natural sources of Mo (i.e., 1.1 to 4.7 mg Mo/kg fresh weight) are plants unusually high in purines such as legumes and whole grains (Schroeder et al. 1970), followed by leafy vegetables, liver, and kidney (Shamberger 1979); the poorest sources are fruits, sugars, oils, and fat (Schroeder et al. 1970).

The greatest economic importance of molybdenosis is associated with subclinical manifestations of copper deficiency resulting from forages containing a low copper:Mo ratio. Unfortunately, these conditions are often difficult to diagnose accurately, and animal response to copper may be difficult to demonstrate (Ward 1978). One recommended treatment for afflicted cattle is 2 grams daily of copper sulfate to cows and 1 gram daily to young stock, or intravenous injection of 200 to 300 mg of copper sulfate daily for several days (Underwood 1971).

The animals most sensitive to Mo insult are domestic ruminants, especially cattle. Diets containing >15 mg Mo/kg dry weight and with a low copper to Mo ratio, or drinking water levels >10 mg Mo/l were frequently associated with molybdenosis in cattle (Table 5). By contrast, adverse effects were documented in birds at dietary levels >200 mg Mo/kg ration, in ruminant wildlife at dietary levels >2,500 mg Mo/kg, and in aquatic organisms--with one exception--at >50 mg Mo/l (Table 5). The exception was newly fertilized eggs of rainbow trout, which were about 21X more sensitive to Mo than were zygotes about 1/3 through embryonic development, and about 90X more sensitive than adult fish (Table 5).

Table 5. Proposed Mo criteria for the protection of living resources and human health.

Resource, criterion, and other variables	Concentration	Reference [a]
Terrestrial plants		
Okra, *Abelmoschus esculentus*		
Increased growth	3 mg/kg soil	1
Lettuce, *Lactuca sativa*		
Mo deficiency	~0.06 mg/kg dry weight (DW) plant	2
Mo sufficiency	>0.08 mg/kg DW	2
Corn, *Zea mays*		

No adverse effect	3.7 mg/kg DW plant	3
Terrestrial invertebrates		
Toxic baits		
Termites	~1,000 mg/kg	4
Other insect species	>5,000 mg/kg	4
Aquatic life		
Algae		
Deficiency levels	<0.005 to 17.7 ug/L	5, 6
High bioconcentration	>0.014 ug/L	7
Growth reduction	>50 mg/L	8
Invertebrates		
Reduced survival	>60 mg/L	9
Fish		
Adults		
High bioconcentration	>0.014 ug/L	7
Reduced survival	>70 mg/L	10
Eggs		
Newly fertilized		
Reduced survival	>0.79 mg/L	11
No adverse effects	<28 ug/L	11
Eyed		
Adverse effects	>17.0 mg/L	10, 12
Birds		
Mo deficiency	13 to 200 ug/kg diet	13, 14, 15
Normal growth	~1.0 mg/kg diet	16
Optimal growth	6.0 mg/kg diet	17
Growth reduction	200 to 300 mg/kg diet	18
Reproductive impairment	500 mg/kg diet	19
Reduced survival	6,000 mg/kg diet	19
Mammals		
Cattle, Cows (*Bos* spp.)		
Forage		
Healthy pasture	3 to 5 mg/kg DW	18
Possibility of molybdenosis	10 to 20 mg/kg DW	19
Probability of molybdenosis	20 to 100 mg/kg DW	18, 19
Toxic	15 to 30 mg/kg DW	20
Maximum tolerable level	6 mg/kg DW	20, 21
Recommended	0.1 to 0.5 mg/kg DW	22
Ratio of Copper to Mo in diet		
Mo in diet		
Molybdenosis probable	<0.4	23

Critical	<2.0	20
Critical	>20.0	22
Optimal for growth and reproduction	6.1 to 10.1	22, 23
Drinking Water		
Safe level	<10 mg/L	24
Minimum toxic concentration for calves	10 to 50 mg/L	24
Guinea pig, *Cavia* sp.		
No effect on survival	80 mg/kg body weight	19
Cat, *Felis domesticus*		
Adverse nonlethal effects	25 to 50 mg/kg body weight	19
Mule deer, *Odocoileus hemionus*		
No effect	200 to 1,000 mg/kg diet	25, 26, 27, 28
Reduction in food intake	2,500 mg/kg diet	25, 26, 27, 28
Nonlethal adverse effects	5,000 to 7,000 mg/kg diet	25, 26, 27, 28
Sheep, *Ovis* sp.		
Forage, recommended	<0.5 mg/kg dry weight	22
Rat, *Rattus* sp.		
Minimum daily need	0.5 ug	29
Disrupted calcium metabolism, elevated tissue residues	10 mg/L drinking water	30, 31, 32
Cancer inhibition	2 to 20 mg/L drinking water	33, 34
Food avoidance	50 mg/kg diet	35
Human health		
Total daily intake, 70 kg adult		
Minimal need	120 ug	29
Average range	100 to 500 ug	18, 19, 28, 29, 36, 37
Maximum	10 to 15 mg	28
In Mo mining areas	>1 mg	19
From food		
USA	170 ug	28
USA	335 (210 to 460) ug	19
USSR		
Children	159 ug	19
Adults	353 ug	19
UK	128 (110 to 1,000) ug	19
From drinking water	<5 ug	28
No effect level	<500 ug	28
Adverse effects		
Biochemical	0.5 to 10 mg	28
Clinical	10 to 15 mg	28

Drinking water		
Safe level	<50 ug/L	28
Irrigation water		
Safe level	<10 ug/L	28
Air		
Maximum permissible concentration		
USSR	6 mg/m^3	3
USA, 8 h daily, 5 days weekly	9.5 to 10 mg/m^3	15, 36
Blood		
"Normal"	14.7 ug/L	

[a]References: 1, Singh and Mourya 1983; 2, Gupta and Lipsett 1981; 3, Soon and Bates 1985; 4, Brill et al. 1987; 5, Vaishampayan 1983; 6, Steeg et al. 1986; 7, Short et al. 1971; 8, Sakaguchi et al. 1981; 9, Ahsanullah 1982; 10, McConnell 1977; 11, Birge et al. 1980; 12, Morgan et al. 1986; 13, Reid et al. 1956; 14, Reid et al. 1957; 15, Friberg and Lener 1986; 16, Mills and Bremner 1980; 17, Kienholz 1977; 18, Underwood 1971; 19, Friberg et al. 1975; 20, Schalscha et al. 1987; 21, Kume et al. 1984; 22, Garmo et al. 1986; 23, Baldwin et al. 1981; 24, Kincaid 1980; 25, Nagy et al. 1975; 26, Ward and Nagy 1976; 27, Ward 1978; 28, chappell et al. 1979; 29, Schroeder et al. 1970; 30, Solomons et al. 1973; 31, Winston et al. 1973; 32, Winston et al. 1976; 33, Luo et al. 1983; 34, Wei et al. 1985; 35, White et al. 1984; 36, Goyer 1986; 37, Shamberger 1979.

Proposed criteria for human health protection include drinking water concentrations <50 ug Mo/l, and daily dietary intakes <7 ug Mo/kg food--based on a 70 kg adult (Table 5). Molybdenum concentrations in blood of "healthy" people averaged 14.7 ug Mo/l, distributed between the plasma and erythrocytes. Anemic people had significantly lower blood Mo levels; in leukemia patients Mo levels increased significantly in whole blood and erythrocytes but not in plasma (Shamberger 1979). Additional work is recommended on the use of blood in fish and wildlife as an indicator of Mo stress and metabolism.

Increasing problems associated with marginal mineral deficiencies and unfavorable mineral interaction--as has been the case in the older agricultural areas of northern Europe--can be anticipated as pasture and forage production becomes more intensive (Ward 1978). Research has been recommended in areas having a high Mo content in soils and vegetation, and also in non-contaminated areas where consumption habits favor a high Mo intake and an imbalance in relation to other dietary constituents of importance, such as copper (Friberg et al. 1975). In some parts of the world where Mo has been substituted for lime, the soils have become more acidic, thus making them difficult to farm. Liming under these conditions may elevate soil Mo from levels, previously considered safe to levels potentially hazardous to grazing animals through high Mo herbage (Gupta and Lipsett 1981). The addition of Mo fertilizers to sheep pastures resulted in small increments in Mo content with negligible risk of induced copper deficiency. But it would be unwise to apply Mo fertilizers to temperate grasslands grazed by animals of low initial copper status, as judged by growth retardation of lambs from pastures supplemented with Mo (Suttle 1983a).

LITERATURE CITED

Abbott, 0. J. 1977. The toxicity of ammonium molybdate to marine invertebrates. Mar. Pollut. Bull. 8:204-205.

Ahsanullah, M. 1982. Acute toxicity of chromium, mercury, molybdenum and nickel to the amphipod *Allorchestes compressa*. Aust. J. Mar. Freshwater Res. 33:465-474.

Alary, J., P. Bourbon, J. Esclassan, J. C. Lepert, J. Vandaele, and F. Klein. 1983. Zinc, lead, molybdenum contamination in the vicinity of an electric steelworks and environmental response to pollution abatement by bag filter. Water Air Soil Pollut- 20:137-145.

Alary, J., P. Bourbon, J. Esclassan, J. C. Lepert, J. Vandaele, J. M. Lecuire, and F. Klein. 1981. Environmental molybdenum levels in industrial molybdenosis of grazing cattle. Sci. Total Environ. 19:111-119.

Allen, J. D., and J. M. Gawthorne. 1987. Involvement of the solid phase of rumen digesta in the interaction between copper, molybdenum and sulphur in sheep. Brit. J. Nutr. 58:265-276.

Alloway, B.J. 1973. Copper and molybdenum in swayback pastures. J. Agric. Sci. (Cambridge) 80:521-524.

Anderson, E. P., and D. L. Mackas. 1986. Lethal and sublethal effects of a molybdenum mine tailing on marine zooplankton: mortality, respiration, feeding and swimming behavior in *Calanus marshallae*, *Metridia pacifica* and *Euphausia pacifica*. Mar. Environ. Res. 19:131-155.

Baldwin, W. K., D. W. Hamar, M. L. Gerlach, and L. D. Lewis. 1981. Copper-molybdenum imbalance in range cattle. Bovine Practice 2:9-16.

Bandyopadhyay, S. K., K. Chatterjee, R. K. Tiwari, A. Mitra, A. Banerjee, K. K. Ghosh, and G. C. Chatterjee. 1981. Biochemical studies on molybdenum toxicity in rats: effects of high protein feeding. Int. J. Vit. Nutr. Res. 51:401-409.

Birge, W. J., J. A. Black, A. G. Westerman, and J. E. Hudson. 1980. Aquatic toxicity tests on inorganic elements occurring in oil shale. Pages 519-534 *in* C. Gale (ed.). Oil shale symposium: sampling, analysis and quality assurance. U. S. Environ. Protection Agency Rep. 600/9-80-022.

Boschke, F. L. (ed.). 1978. Aspects of molybdenum and related chemistry. Topics in current chemistry 76. Springer-Verlag, New York. 159 pp.

Brewer, L. (ed.). 1980. Molybdenum: physico-chemical properties of its compounds and alloys. Atom. Ener. Rev. Spec. issue No. 7. 714 pp. Avail. from UNIPUB, 345 Park Ave. S., New York, 10010.

Brill, W. J., S. W. Ela, and J. A. Breznak. 1987. Termite killing by molybdenum and tungsten compounds. Naturwissenschaften 74:494-495.

Brooks, R. R., and M. G. Rumsby. 1965. The biogeochemistry of trace element uptake by some New Zealand bivalves. Limnol. Oceanogr. 10:521-527.

Buck, W. B. 1978. Copper/molybdenum toxicity in animals. Pages 491-515 *in* F. W. Oehme (ed.). Toxicity of heavy metals in the environment. Part I. Marcel Dekker, New York.

Busev, A. I. 1969. Analytical chemistry of molybdenum. Ann Arbor-Humphey Sci. Publ., Ann Arbor, Michigan. 283 pp.

Chappell, W. R., R. R. Meglen, R. Moure-Eraso, C. C. Solomons, T. A. Tsongas, P. A. Walravens, and P. W. Winston. 1979. Human health effects of molybdenum in drinking water. U. S. Environ. Protection Agency Rep. 600/1-79-006. 101 pp.

Chappell, W. R., and K. K. Petersen (eds.). 1976. Molybdenum in the environment. Vol. 1. The biology of molybdenum. Marcel Dekker, New York: 1-315.

Chappell, W. R., and K. K. Peterson (eds.). 1977. Molybdenum in the environment. Vol. 2. The geochemistry, cycling, and industrial uses of molybdenum. Marcel Dekker, New York: 316-812.

Chung, K. H., Y. O. Suk, and M. H. Kang. 1985. The toxicity of chromium and its interaction with manganese and molybdenum in the chicks. Korean J. Anim. Sci. 27:391-395.

Clawson, W. J., A. L. Lesperance, V. R. Bohman, and D. C. Layhee. 1972. Interrelationship of dietary molybdenum and copper on growth and tissue composition of cattle. J. Anim. Sci. 34:516-520.

Colborn, T. 1982. Measurement of low levels of molybdenum in the environment by using aquatic insects. Bull. Environ. Contam. Toxicol. 29:422-428.

Collier, R. L. 1985. Molybdenum in the northeast Pacific Ocean. Limnol. Oceanogr. 30:1351-1354.

Colmano, G. 1973. Molybdenum toxicity: abnormal cellular division of teratogenic appearance in *Euglena gracilis*. Bull. Environ. Contam. Toxicol. 9:361-364.

Cordone, A. J., and S. J. Nicola. 1970. Influence of molybdenum on the trout and trout fishing of Castle Lake. Calif. Fish Game 56:96-108.

Coughlan, M. P. (ed.). 1980. Molybdenum and molybdenum-containing enzymes. Pergamon Press, Elmsford, New York. 577 pp.

Cymbaluk, N. F., H. F. Schryver, H. F. Hintz, D. F. Smith, and J. E. Lowe. 1981. Influence of dietary molybdenum on copper metabolism in ponies. J. Nutr. 111:96-106.

Dollahite, J. W., L. D. Rowe, L. M. Cook, D. Hightower, E. M. Bailey, and J. R. Kyzar. 1972. Copper deficiency and molybdenosis intoxication associated with grazing near a uranium mine. Southwest. Vet. 26:47-50.

Earl, F. L., and T. J. Vish. 1979. Teratogenicity of heavy metals. Pages 617-639 *in* F. W. Oehme (ed.). Toxicity of heavy metals in the environment. Part 2. Marcel Dekker, New York.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Elseewi, A. A., and A. L. Page. 1984. Molybdenum enrichment of plants grown on fly ash-treated soils. J. Environ. Qual. 13:394-398.

Erdman, J. A., R. J. Ebens, and A. A. Case. 1978. Molybdenosis: a potential problem in ruminants grazing on coal mine spoils. J. Range Manage. 31:34-36.

Flynn, A., A. W. Franzmann, and P. D. Arneson. 1976. Molybdenum-sulfur interactions in the utilization of marginal dietary copper in Alaskan moose (*Alces alces gigas*). Pages 115-124 *in* W. R. Chappell and K. K. Peterson (eds.). Molybdenum in the environment. Vol. 1. The biology of molybdenum. Marcel Dekker, New York.

Flynn, A., A. W. Franzmann, P. 0. Arneson, and J. L. Oldemeyer. 1977. Indications of copper deficiency in a subpopulation of Alaskan moose. J. Nutr. 107:1182-1189.

Friberg, L., P. Boston, G. Nordberg, M. Piscator, and K. H. Robert. 1975. Molybdenum--a toxicological appraisal. U. S. Environ. Protection Agency Rep. 600/1-75-004. 142 pp.

Friberg, L., and J. Lener. 1986. Molybdenum. Pages 446-461 *in* L. Friberg, G. F. Nordberg, and V. B. Vouk (eds.). Handbook of the toxicology of metals. Vol. II: specific metals. Elsevier Science Publ., New York.

Froslie, A., G. Norheim, and N. E. Soli. 1983. Levels of copper, molybdenum, zinc, and sulphur in concentrates and mineral feeding stuffs in relation to chronic copper poisoning in sheep in Norway. Acta Agric. Scand. 33:261-267.

Fujii, R. 1988. Water-quality and sediment-chemistry data of drain water and evaporation ponds from Tulare Lake drainage district, Kings County, California, March 1985 to March 1986. U. S. Geol. Surv. Open-File Rep. 87-700. 19 pp. Avail. from U. S. Geological Survey, Federal Center, Building 810, Box 25425, Denver, Colorado 80225.

Garmo, T. H., A. Froslie, and R. Hole. 1986. Levels of copper, molybdenum, sulphur, zinc, selenium, iron and manganese in native pasture plants from a mountain area in southern Norway. Acta Agric. Scand. 36:147-161.

Goyer, R. A. 1986. Toxic effects of metals. Pages 582-635 *in* C. D. Klaassen, M. O. Amdur, and J. Doull (eds.). Casarett and Doull's toxicology. Third edition. Macmillan Publ., New York.

Gupta, U. C., and J. Lipsett. 1981. Molybdenum in soils, plants, and animals. Adv. Agron. 34:73-115.

Hall, R. A., E. G. Zook, and G. M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resources. U. S. Dep. Commerce NOAA Tech. Rep. NMFS SSRF-721. 313 pp.

Harrison, T. J., J. B. J. van Ryssen, and P. R. Barrowman. 1987. The influence of breed and dietary molybdenum on the concentration of copper in tissues of sheep. S. Afr. J. Anim. Sci. 17:104-110.

Henry, R., and J. G. Tundisi. 1982. Evidence of limitation by molybdenum and nitrogen on the growth of the phytoplankton community of the Lobo Reservoir (Sao Paulo, Brazil). Rev. Hydrobiol. Trop. 15:201-208.

Howarth, R. W., and J. J. Cole. 1985. Molybdenum availability, nitrogen limitation, and phytoplankton growth in natural waters. Science 229:653-655.

Hynes, M., M. Woods, D. Poole, P. Rogers, and J. Mason. 1985. Some studies on the metabolism of labelled molybdenum compounds in cattle. J. Inorg. Biochem. 24:279-288.

Ivan, M., and D. M. Veira. 1985. Effects of copper sulfate supplement on growth, tissue concentration, and ruminal solubilities of molybdenum and copper in sheep fed low and high molybdenum diets. J. Dairy Sci. 68:891-896.

Karring, M., R. Pohjanvirta, T. Rahko, and H. Korpela. 1981. The influence of dietary molybdenum and copper supplementation on the contents of serum uric acid and some trace elements in cocks. Acta Vet. Scand. 22:289-295.

Kienholz, E. W. 1977. Effects of environmental molybdenum levels upon wildlife. Pages 731-737 *in* W. R. Chappell and K. K. Peterson (eds.). Molybdenum in the environment. Vol. 2. The geochemistry, cycling, and industrial uses of molybdenum. Marcel Dekker, New York.

Kincaid, R. L. 1980. Toxicity of ammonium molybdate added to drinking water of calves. J. Dairy Sci. 63:608-610.

Kincaid, R. L., R. M. Blauwiekel, and J. D. Cronrath. 1986. Supplementation of copper as copper sulfate or copper proteinate for growing calves fed forages containing molybdenum. J. Dairy Sci. 69:160-163.

King, K. A., J. Leleux, and B. M. Mulhern. 1984. Molybdenum and copper levels in white-tailed deer near uranium mines in Texas. J. Wildl. Manage. 48:267-270.

King, R. U., D. R. Shawe, and E. M. MacKevett, Jr. 1973. Molybdenum. Pages 425-435 *in* D. A. Brobst and W. P. Pratt (eds.). United States mineral resources. U. S. Geol. Surv. Prof. Paper 820. Avail. from U. S. Govt. Printing Office, Washington, D. C. 20402.

Knothe, D. W., and G. G. Van Riper. 1988. Acute toxicity of sodium molybdate dehydrate (Molhibit 100) to selected saltwater organisms. Bull. Environ. Contam. Toxicol. 40:785-790.

Koizumi, T., and Y. Yamane. 1984. Protective effect of molybdenum on the acute toxicity of mercuric chloride. III. Chem. Pharm. Bull. 32:2316-2324.

Kubota, J. 1975. Areas of molybdenum toxicity to grazing animals in the western United States. J. Range Manage. 28:252-256.

Kubota, J., V. A. Lazar, G. H. Simonson, and W. W. Hill. 1967. The relationship of soils to molybdenum toxicity in grazing animals in Oregon. Soil Sci. Soc. Am. Proc. 31:667-671.

Kume, S., A. Mukai, and M. Shibata. 1984. Effects of dietary copper and molybdenum levels on liver and kidney minerals in Holstein cattle. Jpn. J. Zootech. Sci. 55:670-676.

Kummer, J. T. 1980. Molybdenum. Pages 615-628 *in* U. S. Bur. Mines. Minerals yearbook 1978-79. Vol. I. Metals and minerals. Avail. from Sup. Doc., U. S. Govt. Printing Office, Washington, D. C. 20402.

Lahann, R. W. 1976. Molybdenum hazard in land disposal of sewage sludge. Water Air Soil Pollut. 6:3-8.

Lamand, M., C. Lab, J. C. Tressal, and J. Mason. 1980. Biochemical parameters useful for the diagnosis of mild molybdenosis in sheep. Ann. Rech. Vet. 11:141-145.

Lener, J., and B. Bibr. 1979. Biliary excretion and tissue distribution of penta- and hexavalent molybdenum in rats. Toxicol. Appl. Pharmacol. 51:259-263.

Livingston, H. D., and G. H. Thompson. 1971. Trace element concentrations in some modern corals. Limnol. Oceanogr. 16:786-795.

Lloyd, W. E., H. T. Hill, and G. L. Meerdink. 1976. Observations of a case of molybdenosis-copper deficiency in a South Dakota dairy herd. Pages 85-95 *in* W. R. Chappell and K. K. Peterson (eds.). Molybdenum in the environment. Vol. 1. The biology of molybdenum. Marcel Dekker, New York.

Luo, X. M., H. J. Wei, and S. P. Yang. 1983. Inhibitory effects of molybdenum on esophageal and forestomach carcinogensis in rats. J. Natl. Cancer Inst. 71:75-80.

McConnell, R. P. 1977. Toxicity of molybdenum to rainbow trout under laboratory conditions. Pages 725-730 *in* W. R. Chappell and K. K. Peterson (eds.). Molybdenum in the environment. Vol. 2. The geochemistry, cycling, and industrial uses of molybdenum. Marcel Dekker, New York.

Mills, C. F., and I. Breamer. 1980. Nutritional aspects of molybdenum in animals. Pages 517-542 *in* M. P. Coughlan (ed.). Molybdenum and molybdenum-containing enzymes. Pergamon Press, Elmsford, New York.

Mills, C. F., T. T. El-Gallad, I. Breamer, and G. Wenham. 1981. Copper and molybdenum absorption by rats given ammonium tetrathiomolybdate. J. Inorg. Biochem. 14:163-175.

Mitchell, D. G., J. D. Morgan, J. C. Cronin, D. A. Cobb, G. A. Vigers, and P. M. Chapman. 1986. Acute lethal marine bioassay studies for the U. S. Borax Quartz Hill project. Can. Tech. Rep. Fish. Aquat. Sci. No. 1480:48-49.

Mitchell, P. C. H., and A. G. Sykes (eds.). 1986. The chemistry and uses of molybdenum. Proceedings of the Climax Fifth International Conference. Polyhedron. 5(1/2):1-606.

Morgan, J. D., D. G. Mitchell, and P. M. Chapman. 1986. Individual and combined toxicity of manganese and molybdenum to mussel, *Mytilus edulis*, larvae. Bull. Environ. Contam. Toxicol. 37:303-307.

Nagy, J. G., W. Chappell, and G. M. Ward. 1975. Effects of high molybdenum intake in mule deer. J. Anim. Sci. 41:412.

Nederbragt, H. 1980. The influence of molybdenum on the copper metabolism of the rat at different Cu levels of the diet. Brit. J. Nutr. 43:329-338.

Neberbragt, H. 1982. Changes in the distribution of copper and molybdenum after Mo administration and subsequent additional oral or intraperitoneal Cu administration to rats. Brit. J. Nutr. 48:353-364.

Newton, W. E., and S. Otsuka (eds.). 1980. Molybdenum chemistry of biological significance. Plenum Press, New York. 425 pp.

O'Gorman, J., F. H. Smith, D. B. R. Poole, M. P. Boland, and J. F. Roche. 1987. The effect of molybdenum-induced copper deficiency on reproduction in beef heifers. Theriogenology 27:265.

Paerl, H. W., K. M. Crocker, and L. E. Prufert. 1987. Limitation of N fixation in coastal marine waters: relative importance of molybdenum, iron, phosphorus, and organic matter availability. Limnol. Oceanogr. 32:525-536.

Papadopoulu, C., I. Hadjistelios, M. Ziaka, and D. Zafiropoulos. 1981. Stable molybdenum in plankton and pelagic fish from the Aegean Sea. Rapp. P.-V. Reun. Comm. Int. Explor. Sci. Mer Mediterr. 27:135-138.

Parada, R. 1981. Zinc deficiency in molybdenum poisoned cattle. Vet. Human Toxicol. 23:16-21.

Parker, G. A. 1983. Analytical chemistry of molybdenum. Springer-Verlag, New York. 175 pp.

Penot, M., and C. Videau. 1975. Absorption du ^{86}Rb et du ^{99}Mo par deux algues marines: le *Laminaria digitata* et le *Fucus serratus*. Z. Pflanzenphysiol. Bd. 76 (Suppl.):285-293.

Penumarthy, L., and F. W. Oehme. 1978. Molybdenum toxicosis in cattle. Vet. Human Toxicol. 20:11-12.

Phillippo, M., W. R. Humpheries, T. Atkinson, G. D. Henderson, and P. H. Garthwaite. 1987a. The effect of dietary molybdenum and iron on copper status, puberty, fertility and oestrus cycles in cattle. J. Agric. Sci. (Cambridge) 109:321-326.

Phillippo, M., W. R. Humphries, and P. H. Garthwaite. 1987b. The effect of dietary molybdenum and iron on copper status and growth in cattle. J. Agric. Sci. (Cambridge) 109:315-320.

Pierzynski, G. M., and L. W. Jacobs. 1986. Molybdenum accumulation by corn and soybeans from a molybdenum-rich sewage sludge. J. Environ. Qual. 15:394-398.

Pitt, M., J. Fraser, and D. C. Thurley. 1980. Molybdenum toxicity in sheep: epiphysiolysis, exostoses and biochemical changes. J. Compar. Pathol. 90:567-576.

Prange, A., and K. Kremling. 1985. Distribution of dissolved molybdenum, uranium and vanadium in Baltic Sea waters. Mar. Chem. 16:259-274.

Rao, T. A. 1984. Iron, copper and molybdenum in the different body parts of some clupeoids. Indian J. Fish. 31:357-360.

Reid, B. L., A. A. Kurnick, R. N. Burroughs, R. L. Svacha, and J. R. Couch. 1957. Molybdenum in poult nutrition. Proc. Soc. Exp. Biol. Med. 94:737-740.

Reid, B. L., A. A. Kurnick, R. L. Svacha, and J. R. Couch. 1956. The effect of molybdenum on chick and poult growth. Proc. Soc. Exp. Biol. Med. 93:245-248.

Robinson, J. A., T. J. Devlin, K. M. Wittenberg, and N. E. Stanger. 1987. The influence of molybdenum and sulfur on various copper parameters of afaunated ram lambs of different sire breeds. Can. J. Anim. Sci. 67:65-74.

Sakaguchi, T., A. Nakajima, and T. Horikoshi. 1981. Studies on the accumulation of heavy metal elements in biological systems. Accumulation of molybdenum by green microalgae. European J. Appl. Microbiol. Biotechnol. 12:84-89.

Sas, B. 1987. Accidental molybdenum contamination induced fatal secondary copper deficiency in cattle. Acta Vet. Hung. 35:281-289.

Schalscha, E. B., M. Morales, and P. F. Pratt. 1987. Lead and molybdenum in soils and forage near an atmospheric source. J. Environ. Qual. 16:313-315.

Schroeder, H. A., J. J. Balassa, and I. H. Tipton. 1970. Essential trace metals in man: molybdenum. J. Chron. Dis. 23:481-499.

Shacklette, H. T., J. A. Erdman, T. F. Harms, and C. S. E. Papp. 1978. Trace elements in plant food stuffs. Pages 25-68 *in* F. W. Oehme (ed.) Toxicity of heavy metals in the environment. Part 1. Marcel Dekker, New York.

Shamberger, R. J. 1979. Beneficial effects of trace elements. Pages 689-796 *in* F. W. Oehme (ed.). Toxicity of heavy metals in the environment. Part 2. Marcel Dekker, New York.

Short, Z. F., P. R. Olson, R. F. Palumbo, J. R: Donaldson, and F. G. Lowman. 1971. Uptake of molybdenum, marked with ^{99}Mo, by the biota of Fern Lake, Washington, in a laboratory and a field experiment. Pages 474-485 *in* D. J. Nelson (ed.). Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology. Vol. 1. May 10-12, 1971, Oak Ridge, Tennessee.

Singh, S. S., and A. N. Mourya. 1983. Effect of molybdenum on growth, yield, and quality of okra (*Abelmoschus esculentus* (L.) Moench). Agric. Sci. Dig. 3:105-107.

Sloot, H. A. van der, D. Hoede, J. Wijkstra, J. C. Duinker, and R. F. Nolting. 1985. Anionic species of V, As, Se, Mo, Sb, Te, and W in the Scheldt and Rhine estuaries and the Southern Bight (North Sea). Estuar. Coastal Shelf Sci. 21:633-651.

Smith, C., K. W. Brown, and L. E. Deuel, Jr. 1987. Plant availability and uptake of molybdenum as influenced by soil type and competing ions. J. Environ. Qual. 16:377-382.

Solomons, C. C., D. J. Ernisse, and E. M. Handrich. 1973. Skeletal biology of molybdenum. Pages 233-239 *in* D. D. Hemphill (ed.). Trace substances in environmental health-VII. Univ. Missouri, Columbia, Missouri.

Soon, Y. K., and T. E. Bates. 1985. Molybdenum, cobalt and boron uptake from sewage-sludge-amended soils. Can. J. Soil Sci. 65:507-517.

Steeg, P. F. ter, P. J. Hanson, and H. W. Paerl. 1986. Growth-limiting quantities and accumulation of molybdenum in *Anabaena oscillaroides* (Cyanobacteria). Hydrobiologia 140:143-147.

Strickland, K., F. Smith, M. Woods, and J. Mason. 1987. Dietary molybdenum as a putative copper antagonist in the horse. Equine Vet. J. 19:50-54

Subbaiah, C. C., P. Manikandan, and Y. Joshi. 1986. Yellow leaf spot of cashew: a case of molybdenum deficiency. Plant Soil 94:35-42.

Suttle, N. F. 1973. The nutritional significance of the Cu:Mo interrelationship to ruminants and non-ruminants. Pages. 245-249 *in* D. D. Hemphill (ed.). Trace substances in environmental health-VII. Univ. Missouri, Columbia, Missouri.

Suttle, N. F. 1980. The role of thiomolybdates in the nutritional interactions of copper, molybdenum, and sulfur: fact or fantasy? Ann. N.Y. Acad. Sci. 355:195-207.

Suttle, N. F. 1983a. Effects of molybdenum concentration in fresh herbage, hay and semi-purified diets on the copper metabolism of sheep. J. Agric. Sci. (Cambridge) 100:651-656.

Suttle, N. F. 1983b. A role for thiomolybdates in the Cu x Mo x S interaction in ruminant nutrition. Pages 599-610 *in* P. Bratter and P. Schramel (eds.). Trace element-analytical chemistry in medicine and biology, Vol. 2. Walter de Gruyter, New York.

Suttle, N. F., and A. C. Field. 1983. Effects of dietary supplements of thiomolybdates on copper and molybdenum metabolism in sheep. J. Comp. Pathol. 93:379-389.

Talbot, V., and P. Ryan. 1988. High molybdenum land values in Ireland: possible implications. Sci. Total Environ. 76:217-228.

Todd, J. R. 1976. Problems of copper-molybdenum imbalance in the nutrition of ruminants in northern Ireland. Pages 33-49 *in* W. R. Chappell and K. K. Peterson (eds.). Molybdenum in the environment. Vol. 1. The biology of molybdenum. Marcel Dekker, New York.

Underwood, E. J. 1971. Trace elements in human and animal nutrition. Chapter 4. Molybdenum. Academic Press, New York: 116-140.

Underwood, E. J. 1979. Interactions of trace elements. Pages 641-668 *in* F. W. Oehme (ed.). Toxicity of heavy metals in the environment. Part 2. Marcel Dekker, New York.

Vaishampayan, A. 1983. Mo-V interactions during N_2- and NO_3 - metabolism in a N_2- fixing blue-green alga *Nostoc muscorum*. Experientia 39:358-360.

Van Ryssen, J. B. J., W. S. Botha, and W. J. Stielau. 1982. Effect of a high copper intake and different levels of molybdenum on the health of sheep. J. S. Afr. Vet. Assoc. 53:167-170.

Van Ryssen, J. B. J., S. van Malsen, and P. R. Barrowman. 1986. Effect of dietary molybdenum and sulphur on the copper status of hypercuprotic sheep after withdrawal of dietary copper. S. Afr. J. Anim. Sci. 16:77-82.

Van Ryssen, J. B. J., and W. J. Stielau. 1980. The effect of various levels of dietary copper and molybdenum on copper and molybdenum metabolism in sheep. S. Afr. J. Anim. Sci. 10:37-47.

Ward, G. M. 1978. Molybdenum toxicity and hypocuprosis in ruminants: a review. J. Anim. Sci. 46:1078-1085.

Ward, G. M., and J. G. Nagy. 1976. Molybdenum and copper in Colorado forages, molybdenum toxicity in deer, and copper supplementation in cattle. Pages 97-113 *in* W. R. Chappell and K. K. Peterson (eds.). Molybdenum in the environment. Vol. 1. The biology of molybdenum. Marcel Dekker, New York.

Ward, J. V. 1973. Molybdenum concentrations in tissues of rainbow trout (*Salmo gairdneri*) and kokanee salmon (*Oncorhynchus nerka*) from waters differing widely in molybdenum content. J. Fish Res. Board Can. 30:841-842.

Weber, K. M., R. C. Boston, and D. D. Leaver. 1983. The effect of molybdenum and sulfur on the kinetics of copper metabolism in sheep. Aust. J. Agric. Res. 34:295-306.

Wei, H-J., X-M. Luo, and S. P. Yang. 1985. Effects of molybdenum and tungsten on mammary carcinogensis in SD rats. J. Natl. Cancer Inst. 74:469-473.

White, R. D., R. A. Swick, and P. R. Cheeke. 1984. Effects of dietary copper and molybdenum on tansy ragwort (*Senecio jacobaea*) toxicity in sheep. Am. J. Vet. Res. 45:159-161.

Winston, P.W., M. S. Heppe, L. Hoffman, L. J. Kosarek, and R. S. Spangler. 1976. Physiological adaptations to excess molybdenum ingested over several generations. Pages 185-200 *in* W. R. Chappell and K. K. Peterson eds). Molybdenum in the environment. Vol. 1. The biology of molybdenum. Marcel Dekker, New York.

Winston, P. W., L. Hoffman, and W. Smith. 1973. Increased weight loss in molybdenum-treated rats in the cold. Pages 241-244 *in* D. D. Hemphill (ed.). Trace substances in environmental health-VII. Univ. Missouri, Columbia, Missouri.

Wittenberg, K. M., and T. J. Devlin. 1987. Effects of dietary molybdenum on productivity and metabolic parameters of lactating beef cows and their offspring. Can. J. Anim. Sci. 67:1055-1066.

Wright, R. J., and L. R. Hossner. 1984. Molybdenum release from three Texas soils. Soil Sci. 138:374-377.

Yamane, Y., and T. Koizumi. 1982. Protective effect of molybdenum on the acute toxicity of mercuric chloride. Toxicol. Appl. Pharmacol. 65:214-221.

Yoshimura, T., K. Tsunoda, and K. Nishimoto. 1987. Effect of molybdenum and tungsten compounds on the survival of *Coptotermes formosanus* Shiraki (Isoptera: Rhinotermitidae) in laboratory experiments. Mater. Org. (Berl.) 22:47-56.

Biological Report 85(1.20)
April 1990

Contaminant Hazard Reviews
Report 20

Boron Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20709

ABSTRACT. Ecological and toxicological aspects of boron (B) in the environment are reviewed, with emphasis on natural resources. Subtopics covered include environmental chemistry, background concentrations, effects, and current recommendations for the protection of living resources.

The United States is the major producer of boron compounds and supplies about 70% of the annual global demand. Although boron is ubiquitous in the environment, human activities such as mining, coal burning, drainwater disposal, and use of borax laundry detergents have resulted in elevated boron loadings in the atmosphere and in irrigation waters. The chemistry of boron is complex and rivals that of carbon in its diversity. However, most boron compounds enter or degrade in the environment to B-0 compounds (borates)such as borax and boric acid--and these are considered to be the most significant ecologically.

Boron is an essential trace element for the growth of terrestrial crop plants and for some species of fungi, bacteria, and algae, but excess boron is phytotoxic. Representative species of aquatic organisms, including plants, invertebrates, fishes, and amphibians, usually tolerated up to 10 mg B/L of medium for extended periods without harm. In waterfowl, growth was adversely affected at dietary levels of 30 to 100 mg B/kg fresh weight, tissue boron concentrations were elevated at 100 to 300 mg B/kg diet, and survival was reduced at dietary levels of 1,000 mg B/kg; all of these dietary levels currently exist near agricultural drainwater disposal sites in the western United States. Boron is not now considered essential in mammalian nutrition, although low dietary levels protect against fluorosis and bone demineralization. Excessive consumption (i.e., > 1,000 mg B/kg diet, > 15 mg B/kg body weight daily, > 1.0 mg B/L drinking water, or > 210 mg B/kg body weight in a single dose) adversely affects growth, survival, or reproduction in sensitive mammals. Boron and its compounds are potent teratogens when applied directly to the mammalian embryo, but there is no evidence of mutagenicity or carcinogenicity. Boron's unique affinity for cancerous tissues has been exploited in neutron capture radiation therapy of malignant human brain tumors.

Current boron criteria recommended for the protection of sensitive species include < 0.3 mg B/L in crop irrigation waters, < 1.0 mg B/L for aquatic life, < 5.0 mg B/L in livestock drinking waters, < 30 mg B/kg in waterfowl diets, and < 100 mg B/kg in livestock diets.

This publication may be cited as follows:

Eisler, R. 1990. Boron hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. Fish Wildl. Serv., *Biol*. *Rep*. 85(1.20).

TABLES

Introduction

Borax ($Na_2B_40_7$ .10 H_20) was the first of the boron (B) minerals to be traded by the Babylonians more than 4,000 years ago for use in the working and welding of gold (Greenwood and Thomas 1973). Borax has been known as a cleaning agent since the days of the ancient Greek and Roman empires and was used as a food preservative in Europe and America, although its use for the latter purpose has been discontinued (Weir and Fisher 1972). Boron and its compounds were used in Egyptian and Roman eras to prepare borosilicate glass. Borax glazes were known from about the year 200; by 1556, borax was widely used throughout Europe as a flux (Greenwood and Thomas 1973). Boric acid (H_3BO_3) was first synthesized in 1707 (Greenwood and Thomas 1973). Boric acid and borates are the main boron compounds of ecological significance; other boron compounds usually degrade or are transformed to borates or boric acid (Sprague 1972).

Boron is an essential trace element for the growth and development of higher plants, although the range between insufficiency and excess is generally narrow, varying with the plant; boron is not required in fungi and animals (Sprague 1972; Weir and Fisher 1972; Birge and Black 1977; Goldbach and Amberger 1986). In the southwestern United States, naturally elevated boron concentrations in surface waters used for irrigation may be sufficiently high to cause toxicity to plants of commercial importance (Benson et al. 1984). Another major source of boron entering ground and surface waters results from the use of borax-containing laundry products coupled with ineffective removal of boron by conventional sewage processes (Benson et al. 1984). Agricultural drainwaters contaminated with boron are considered potentially hazardous to waterfowl and other wildlife populations throughout areas of the western United States (Smith and Anders 1989).

Medical and household uses of boric acid solutions as antiseptics have led to numerous accidental poisonings by ingestion or absorption through abraded skin, particularly in infants (Environmental Protection Agency 1975; Dixon et al. 1976; Landolph 1985; Siegel and Wason 1986). Poisonings have been reported in English children consuming milk containing 0.7 g boric acid/L, and in burn patients treated topically with saturated boric acid solutions (National Academy of Sciences 1980). In the 1940's, topical preparations of boric acid became a popular remedy for diaper rash in England. By 1953, at least 60 fatal cases of boric acid poisoning had been reported in English infants (O'Sullivan and Taylor 1983). Inhalation of boranes, especially diborane (B_2H_6), pentaborane (B_5H_9), and decaborane ($B_{IO}H_{14}$)--which is used as a rocket propellant--is toxic to exposed workers (Dixon et al. 1976; NAS 1980). Boron compounds, especially boric acid, can also accumulate in animal tissues and produce a reduction in fertility, an increase in developmental abnormalities--especially those involving the skeletal system--stillbirth, and death (Weir and Fisher 1972; Lee et al. 1978; Landolph 1985). At present, there seems to be a reasonable margin between a toxic dose in humans and other vertebrates and in boron levels that may occur as incidental residues from the use of borax and boric acid in agriculture and industry (Weir and Fisher 1972). Additional information on ecological and toxicological aspects of boron in the environment is presented in reviews by Sprague (1972), Environmental Protection Agency (EPA; 1975), National Academy of Sciences (NAS; 1980), Anonymous (1983), Klasing and Pilch (1988), and Butterwick et al. (1989).

In this report, I summarize available data on boron in the environment, with emphasis on fishery and wildlife resources. It is part of a continuing series of brief reviews on chemical contaminants and natural resources that are prepared in response to informational requests from environmental specialists of the U.S. Fish and Wildlife Service.

Environmental Chemistry

General

The United States supplies about 70% of the global boron demand, and Turkey supplies 18%. Of the total annual United States production of about 500,000 tons, 45% is used in the manufacture of glass and glassware, 15% in laundry products, 10% in enamels and glazes, and 8% in agricultural chemicals. It is estimated that boron compounds enter the North American environment at a rate of 32,000 tons annually as a result of human activities, primarily from laundry products, irrigation drainwater, agricultural chemicals, coal combustion, and mining and processing (Table 1). Boron compounds tend to accumulate in aquatic ecosystems because of the relatively high water solubility of these compounds (EPA 1975).

The chemistry of boron is exceedingly complex and rivals that of carbon in its diversity. Most boron compounds, however, enter or degrade in the environment to borates (B-0 compounds), such as borax and boric acid, and these are considered to be the most significant ecologically.

Toxicosis in animals has resulted from ingestion of boric acid or borax solutions, from topical applications of boric acid solutions to damaged skin, and from inhalation of boranes; the exact mechanisms of action are not understood. Boron and its compounds are potent teratogens when applied directly to the embryo, but there is no evidence of mutagenicity or carcinogenicity. Boron's unique affinity for cancerous tissues has been exploited in neutron capture radiation therapy of malignant human brain tumors.

Sources and Uses

Boron is a dark brown element that is widespread in the environment but occurs naturally only in combined form, usually as borax, colemanite ($Ca_2B_60_{11} \cdot 5H_20$), boronatrocalcite ($CaB_40_7NaBO_2 \cdot 8H_20$), and boracite ($Mg_7Cl_2B_{16}O_{30}$; EPA 1975; NAS 1980). In the United States, boron deposits in the form of borax are concentrated in the desert areas of southern California, especially near Boron, California (EPA 1975). Proven deposits of sodium tetraborates--from which borax is prepared and from which boron can be isolated--also exist in Nevada, Oregon, Turkey, Russia, and China (Sprague 1972; NAS 1980). The United States supplies about 70% of the world boron demand, and Turkey supplies 18%; the most common commercial compounds are boric acid and borax (Sprague 1972; Butterwick et al. 1989).

The majority of the 555,000 tons of boron produced annually in the United States--of which half is usually exported--is in the form of sodium tetraborate compounds. Of the total production, about 42% occurs as anhydrous borax ($Na_2B_40_7$), 29% as borax pentahydrate ($Na_2B_40_7 \cdot 5H_20$), 10% as borax decahydrate or borax, and 16% as boric acid or boric oxide (B_20_3; Sprague 1972; EPA 1975). Boron and its compounds are used in the manufacture of glassware (40 to 45%); soaps and cleansers (15%); enamels, frits, and glazes (10%); fertilizers (5%); and herbicides (2 to 3%); 22 to 28% goes for other uses (Sprague 1972; EPA 1975; NAS 1980). Borates have some toxicity to insects and, in relatively high concentrations, can control cockroaches, woodboring insects, gypsy moths, and larvae of flies in manure piles and in dog runs (Sprague 1972; EPA 1975). Some organoboron compounds are used to sterilize fuel distribution and storage systems against fungi and bacteria (Sprague 1972). Radioboron-10 is widely used in radiation therapy against brain tumors, especially in Japan (Hatanaka 1986). Various boron compounds are also used widely as thermal protection materials in space probes, in fireproofing of fabrics and wood, in leather manufacture, in numerous pharmaceuticals and hygienic products, in steel hardening, in deoxidation of bronze, as a high-energy fuel, as neutron-absorbing shielding near atomic reactors, and as water softeners, pH adjusters, emulsifiers, neutralizers, stabilizers, buffers, and viscosifiers (NAS 1980; Parry and Kodama 1980; Schillinger et al. 1982; Siegel and Wason 1986).

Most boron ends up in the aquatic environment because of the relatively high water solubility of all boron compounds, especially B-containing laundry products and sewage (EPA 1975). Conventional sewage treatment removes little or no boron (EPA 1975). Of the total boron in coal, as much as 71% may be lost to the atmosphere upon combustion; more than 50% of the boron found in coal ash is readily water soluble (Pagenkopf and Connolly 1982). The release of boron from coal fly ash to leachate water is dependent on the ash to water ratio: at 1 g ash/L up to 90% of the boron is soluble; at 50 g/L only 40% is released; at 100 g/L less than 30% is released. Coating of coal ash with aluminum solution reduces boron solubility by about 90% because of the formation of an insoluble aluminum-borate complex (Pagenkopf and Connolly 1982).

Table 1. Environmental sources of domestic boron (EPA 1975).

Source	Metric tons, annually
Laundry products	14,000
Agricultural chemicals and fertilizers	7,000
Coal combustion	4,000
Mining and processing	3,000
Glass and ceramics	1,500
Miscellaneous	2,500
Total	32,000

Boron compounds listed in the "Commodity List of Explosives and Other Dangerous Articles" are boron trichloride ($BC1_3$), boron trifluoride (BF_3), decaborane ($B_{10}H_{14}$), and pentaborane (B_5H_9; EPA 1975). Boron trichloride is a corrosive liquid; the maximum quantity allowed in containers by rail is 1 L, and by air only one container is permitted per aircraft. Boron trifluoride is a nonflammable gas restricted to 140 kg in one outside container by rail, and to 140 kg in cargo planes only. Decaborane is a flammable solid, and transport by rail or air is limited to 12 kg. Pentaborane is a flammable liquid and is prohibited for transport by air or rail. Diborane (B_2H_6) and higher boranes are unstable and are classified as dangerous articles in transport; no more than 0.1 kg can be shipped in a cylinder (EPA 1975). Organic boron-oxygen compounds readily hydrolyze and should be stored and transferred in an inert atmosphere; usually, glass containers are used for shipping small quantities, and steel containers or tank cars are used for bulk items. Hazardous atmospheric conditions resulting from high concentrations of boron compounds are localized and are not considered a serious environmental problem (EPA 1975).

Chemical Properties

The element boron has an atomic number of 5, a molecular weight of 10.811, an oxidation state of 3 for simple compounds (but other oxidation states for carboranes and other polyhedral cage boron compounds), a specific gravity of 2.34, a melting point of 2,300 °C, sublimation at 2,550 °C, and is almost insoluble in water. Boron exists as B-10 (19.78%) and B-11 (80.22%) isotopes, and it contributes about 0.001% to the Earth's crust, although it does not occur free in nature (EPA 1975; Smith 1985). The chemistry of boron is exceedingly complex and rivals that of carbon in diversity. Reviews on boron's chemistry are especially abundant and include those by Steinberg and McCloskey (1964), Brotherton and Steinberg (1970a, b), Greenwood and Thomas (1973), Grimes (1982), Evans and Sparks (1983), Smith (1985), Emin et al. (1986), Heller (1986), Niedenzu and Trofimenko (1986), and Hermanek (1987).

Most boron compounds degrade in the environment to B-0 (borate) compounds, and these are the boron compounds of ecological significance-especially borax and boric acid (Sprague 1972; Antia and Cheng 1975; Thompson et al. 1976). Sodium tetraborate decahydrate (borax) has a melting point of 75°C, a boiling point of 320°C, and is soluble in water to 20 g/L at O°C and to 1,700 g/L at 100°C (EPA 1975). Boric acid has a melting point of 169°C, a boiling point of 300°C and, like borax, is exceedingly soluble in water: 63.5 g/L at 30°C and 276 g/L at 100°C (EPA 1975).

Boron exists in several forms in the soil (EPA 1975), and in soil solution it exists largely as the undissociated weak monobasic acid that accepts hydroxyl groups (Gupta and Macleod 1982). Most plant-available boron in soils is associated with soil organic matter (Gupta and Macleod 1982), with the hot-water soluble boron fraction (Hingston 1986), and with soil solution pH ranges of 5.5 to 8.5 and 10 to 11.5 (Goldberg and Glaubig 1986). It is assumed that boron adsorbs to soil particles and aluminum and iron oxide minerals (Goldberg and Glaubig 1986).

The predominant boron species in seawater is boric acid (Thompson et al. 1976); concentrations are higher at higher salinities and in proximity to industrial waste discharges (Liddicoat et al. 1983; Narvekar et al. 1983). In seawater, borate or boric acid occurs naturally at 4.5 to 5.5 mg/L. About 76% of the total inorganic boron in seawater occurs as undissociated boric acid [$B(OH)_3$], and the remainder is identified as the borate ion

$[B(OH)_4^-]$. Of the total borate ion, 44% seems to be complexed with sodium, magnesium, and calcium (Antia and Cheng 1975). Other evidence suggests additional complexation of borate with ferric ions and polyhydroxylated organic compounds (Antia and Cheng 1975).

Mode of Action

The complexing ability of the boron atom is considered to be the key explanation of why it is essential to higher plants (EPA 1975), although the exact mechanism of action is still unknown. Boron's complexing ability is thought to beneficially influence transport of sugars and other organic compounds, production of plant growth regulators, biosynthesis of nucleic acids and phenolic acid, carbohydrate metabolism, respiration, and pollen germination (EPA 1975; Nielson 1986).

Boron poisoning in animals is primarily an experimental phenomenon, although livestock in certain regions may be exposed to high concentrations in drinking water--up to 80 mg B/L--that have not been shown to be toxic (NAS 1980). Toxicosis in humans has resulted from ingestion of boric acid or borax solutions, topical applications of boric acid solutions to burn-damaged skin, and inhalation of boranes (NAS 1980). In mammals, boron is thought to regulate parathyroid function through metabolism of phosphorus, magnesium, and especially calcium. Boron has a close relation with calcium metabolism, most likely at the cell membrane level (Nielsen 1986).

Dietary boron at nontoxic concentrations, as sodium borate or boric acid, is rapidly and almost completely absorbed from the gastrointestinal tract, doesn't seem to accumulate in healthy tissues, and is excreted largely in urine, usually within hours; similar patterns are evident for humans, dogs, cows, rabbits, and guinea pigs (NAS 1980; Benson et al. 1984; Nielsen 1986; Siegel and Wason 1986). Boric acid poisoning in animals, regardless of route of administration, is characterized by the following signs: generalized erythema (boiled lobster appearance) starting in the axillary, inguinal, and facial regions, eventually covering the entire body with conjunctival redness, followed by massive desquamation 2 to 3 days later; acute gastroenteritis, including nausea and vomiting; diarrhea; anorexia; cardiac weakness; excessive urinary excretion of riboflavin; decreased oxygen uptake by the brain; hypoacidity; altered enzyme activity levels; impaired growth and reproduction; and death from circulatory collapse and shock, usually within 5 days (Dani et al. 1971; Sprague 1972; EPA 1975; NAS 1980; Schillinger et al. 1982; Settimi et al. 1982; Siegel and Wason 1986).

Boron hydrides or boranes, such as B_2H_6, B_4H_{10}, and B_5H_9, from chemical processes produce acute central nervous system pulmonary damage and lung disease through inhalation (NAS 1980; Klaassen et al. 1986). Boranes produce toxic effects by creating embolisms of hydrogen gas as they react with tissue, and by depleting biogenic amines of the central nervous system and inhibiting aminotransferases and other pyridoxol-dependent enzymes (Korty and Scott 1970; EPA 1975). Boranes produce similar effects in humans and animals, and these are generally ascribable to central nervous system depression and excitation (Naeger and Leibman 1972; Smith 1985). Symptoms of borane intoxication include pulmonary irritation, headache, chills, fatigue, muscular weakness and pain, cramps, dizziness, chest tightness, and pneumonia (NAS 1980). Boranes may adversely affect male reproductive capacity (Klaassen et al. 1986), but this requires verification. Decaborane ($B_{l0}H_{14}$), as one example, is a highly lipid-soluble compound that can enter the body through inhalation, ingestion, or the skin. In water, decaborane is rapidly transformed into intermediate products that are eventually degraded to boric acid. The intermediate products, but not decaborane or boric acid, reduce phosphomolybdic acid and inhibit glutamic-oxaloacetic transaminase; treatment of intermediates with pyridoxol phosphase tends to reverse the inhibitory activity (Naeger and Leibman 1972). Low decaborane doses cause behavioral effects such as depression, catatonia, and convulsions (EPA 1975).

Inorganic borates are quite toxic, seemingly complexing hydroxy compounds and interfering with protein synthesis (EPA 1975). Organoborate compounds exert physiological effects on the central nervous system and peripheral nervous system, acting as spasmolytics, sedatives, and convulsants, depending on their structure (EPA 1975). Boron trihalides, such as BBr_3, $BC1_3$, and BF_3, are corrosive to the eyes, skin, and mucous membranes, and will cause burns on the skin seemingly because of the hydrolysis of the trihalides to their halogen acids, and not to boron (EPA 1975; Smith 1985).

Boron is a potent teratogen when applied directly to the embryo. Boric acid injected into chicken and amphibian embryos produced abnormal development of the neural tube, notochord, tail, and limbs, perhaps through complexing polyhydroxy compounds and interfering with riboflavin metabolism (Landauer 1952, 1953a, 1953b, 1953c; Landauer and Clark 1964; EPA 1975; Settimi et al. 1982). Boron and its compounds, however, are neither mutagenic nor carcinogenic (Landolph 1985). Nonmutagenicity is based on results of the *Salmonella typhimurium*-mammalian microsome mutagenicity assay; boron neither enhances nor inhibits the activity of benzo(a)pyrene, a known mutagen (Anonymous 1983; Benson et al. 1984). There is no evidence that boron is a possible carcinogen, although long-term, selective uptake of boron by tumors has been reported (EPA 1975).

Boron seems to have an affinity for cancerous tumors, and this property has been exploited in radiation therapy (Hamada et al. 1983; Hatanaka 1986). Boron-10 has been used in neutron capture therapy to cure malignant sarcomas implanted in the hind legs of mice, as well as spontaneous malignant melanomas in pigs (Slatkin et al. 1986). The sulfhydral borane monomer $(B_{12}H_{11}SH)^{2-}$ is used as a B-10 carrier in neutron therapy of malignant human brain tumors and seems to be most effective at 30 µ*g* B-10/kg tissue (Hatanaka 1986). Polyhedral boranes attached to monoclonal antibodies that are tumor-specific may become useful in tumor therapy by neutron irradiation (Parry and Kodama 1980). It is possible, however, that uptake of boron may be a nonspecific attribute of tumors and of a variety of normal tissues that lack a blood-brain barrier. Thus, the potential usefulness of selected B-10 carriers for treating extracranial neoplasms seems questionable (Slatkin et al. 1986).

Background Concentrations

General

Terrestrial plants are normally rich sources of boron. Levels in meat and fish are usually low. These generalizations, however, are based on extremely limited data. Boron is ubiquitous in the environment, although human activities such as mining, coal burning, and use of borax laundry detergents have resulted in elevated boron loadings in the atmosphere and in irrigation waters. Comparatively high levels of boron were recorded in fish, insects, and aquatic plants at Kesterson National Wildlife Refuge, which was contaminated by agricultural drainwater; the significance of the contamination is under investigation.

Nonbiological

Boron is distributed widely in the environment (Ahl and Jonsson 1972; EPA 1975). Naturally elevated boron levels are usually associated with marine sediments, thermal springs, large deposits of boron minerals, seawater, and certain groundwaters (Table 2). Human activities, however, have resulted in elevated boron concentrations near coal-fired plants, in mine drainage waters, in municipal wastes, and in agricultural drainage waters. In one instance, agricultural drainwater practices in western California produced boron concentrations in local rivers, groundwaters, and surface waters that exceeded the established limits for the protection of crops and aquatic life (Table 2; Schuler 1987; Klasing and Pilch 1988).

Coal-fired power plants are major sources of atmospheric boron contamination; at least 30% of boron in coal is lost in this manner (Cox et al. 1978; Gladney et al. 1978). The seemingly large amounts of boron lost to the environment through stack emissions may be directly related to the organic content of coal (Table 2; Gladney et al. 1978). Also, disposal of B-laden drainage waters from boron mines is a major problem in certain geographic areas. In Turkey, for example, which possesses about 60% of the world's boron reserves--localized in a rectangular area about 100 x 200 km near the Simav River--drainage waters discharged from the mines as a result of borate production have elevated boron concentrations in the Simav River to levels unsuitable for crop irrigation. About 68,000 ha of agricultural land irrigated by the Simav River are now threatened by boron pollution (Okay et al. 1985). In the United States, laundry detergents originating from household use may contribute as much as 50% of the boron loadings in effluents discharged into aquatic environments; lesser amounts are contributed by soil minerals, rainfall, and industry and sewage effluents (EPA 1975).

Table 2. Boron concentrations in selected nonbiological materials. Concentrations are in mg B/kg fresh weight (FW), dry weight (DW), or ash weight (AW).

Material	Concentration (mg/kg or mg/L)	Reference[a]
Coal-fired power plants		
Chalk Point Power Plant, New Mexico		
Coal	13 AW	1
Bottom slag	19 AW	1
Fly ash	33 AW	1
Four Corners Power Plant, New Mexico		
Coal	92 AW	1
Bottom slag	120 AW	1
Fly ash	240 AW	1
Coal ash		
Anthracite	90 AW	1
Volatile bituminous		
Low	123 AW	1
Medium	218 AW	1
High	770 AW	1
Lignite	1,020 AW	1
Coal ash	5–200 DW	2, 15
Sediments		
Nonmarine clays	<10 DW	3
Postglacial marine	Max. 500 DW	3
Mine drainage waters		
Turkish boron mines		
Avsar mine	16 FW	4
Simav mine	260 FW	4
Yenikoy mine	390 FW	4
Soil		
Worldwide	Usually 45–124 DW, range 4–200, mostly as biologically unavailable tourmaline	5, 6
United States	30 (10–300) DW	7
Thermal springs, Greece	43 FW	4
Surface fresh waters		
Worldwide	0.0001–<0.5 FW	8, 9, 10, 16
Norway, 1970	Usually <0.004 FW, median 0.013, range 0.001–1.05 FW	3
Sweden, 1970	0.12 (0.001–1.0) FW	3, 7
Southeastern United States 1969–70		
Streams, swamps, ponds	Usually <0.1 FW	11
Reservoirs	0.007 (<0.001–0.09) FW	11
In regions where marine deposits are common	>0.006 FW	3
United States	Generally <0.1 FW	12
United States	0.1–0.3 FW	8
Nevada		
Humboldt River	0.2 FW	6
Borax Flat	Up to 80 FW	6
Turkey		
Uncontaminated	<0.5 FW	4
Contaminated with boron mine wastes	4 (Max. 7) FW	4
Western United States	Sometimes 5–15 FW	10, 12

Japan	1–15 FW	7
Seawater		
British Columbia		
Surface	3.5 (0.2–4.7) FW	13
Depth 5 m	3.9 FW	13
Open ocean	4.5 FW	8
Coastal	4.6 FW	8
Total inorganic	4.5–5.5 FW	14
As undissociated boric acid	3.4–4.2 FW	14
As borate ion, $B(OH)_4^-$	1.1–1.3 FW	14
As complex with sodium, magnesium, and calcium	0.5–0.6 FW	14
Groundwaters		
Worldwide	Usually <0.5 FW	9
Greece	2.3–5.4 FW	4
United States	Max. 5.0 FW	12
Sewage waters, Scandinavia	0.4 (Max. 0.7) FW	3
Well water, India	0.08–0.5 FW	7
Rain		
Sweden	0.002 FW	7
France	0.002–0.004 FW	7
United States		
Mississippi	Usually <0.01 FW	11
Florida	~0.01 FW	7, 8
India	0.03 (0.002–0.007) FW	11
England	0.08 FW	7
Japan	0.1 FW	7
Affected by agricultural drainage waters		
Western San Joaquin Valley, California		
River waters	Median 1.1 FW	16
Surface waters	Median 3.1 (Max. 83.0) FW	16
Groundwaters	Median 7.4 (Max. 70.0) FW	16
Kesterson National Wildlife Refuge, 1984		
Subsurface waters	20 (12–41) FW	17
Sediments	20 (10–71) DW	17

[a]1, Gladney et al. 1978; 2, Pagenkopf and Connolly 1982; 3, Ahl and Jonsson 1972; 4, Okay et al. 1985; 5, Gupta and Macleod 1982; 6, NAS 1980; 7, Sprague 1972; 8, EPA 1975; 9, Benson et al. 1984; 10, Lewis and Valentine 1981; 11, Boyd and Walley 1972; 12, Birge and Black 1977; 13, Thompson et al. 1976; 14, Antia and Cheng 1975; 15, Cox et al. 1978; 16, Klasing and Pilch 1988; 17, Schuler 1987.

Biological

Boron occurred at high concentrations in plants, insects, and fish at Kesterson National Wildlife Refuge in California--the recipient of contaminated agricultural drainwater--when compared to a nearby control area (Table 3; Ohlendorf et al. 1986; Schuler 1987). These authors indicated that little is known about the effect of boron ingestion on bird reproduction, although both boric acid and borax produced mortality and teratogenic development when injected into eggs. Recent studies on effects of boron on waterfowl growth, physiology (Hoffman et al. 1990), and reproduction (Smith and Anders 1989) are discussed later.

Table 3. Boron concentrations in field collections of selected species of plants and animals. Concentrations are in mgB/kg fresh weight (FW), dry weight (DW), or ash weight (AW).

Ecosystem, organism, and other variables	Concentration (mg/kg)	Reference[a]
Terrestrial plants		
Cereal grains	1–5 DW	1, 2
Box thorn, *Lycium andersonii*		
Stem 7–26 DW	8	
Leaf 26–163 DW	8	
Root 25–74 DW	8	
Prunes, raisins, dates	9–27 DW	2
Tropical fruits	Usually <10 FW	1
Nuts 16–23 DW	2	
Vegetables	Usually <13 DW	2
Angiosperms	Mean 50 DW	8
Gymnosperms	Mean 63 DW	8
Pteridophytes	Mean 77 DW	8
Big sagebrush, *Artemisia tridentata*		
On high B soil		
Whole	Max. 250 DW	8
Leaf Max. 156 DW	8	
Stem Max. 54 DW	8	
Apple, pear, tomato, red pepper	440–1,250 DW	2
Freshwater organisms		
Lake trout, *Salvelinus namaycush*, muscle	0.2–0.6 FW	8
Cattail, *Typha latifolia*, whole	15–30 DW	8
Aquatic macrophytes		
22 species	Usually <20 DW; mean 11.3 (1.2–100) DW	4
Macrophytes, various	2–19 DW	5
Waterweed, *Elodea* sp., whole	18–44 DW	8
Pondweed, *Potamogeton* sp., whole	18–170 DW	8
Yellow pond lily, *Nuphar* sp., whole	23–31 DW	8
Watermilfoil, *Myriophyllum* sp., whole	25–54 DW	8
Kesterson National Wildlife Refuge, California, contaminated with irrigation drainwater		
1983		
Aquatic plants	382 (270–510) DW	3
Aquatic insects	45 (36–54) DW	3
Mosquitofish, *Gambusia affinis*, whole	11 (8–20) DW	3
1984		
Widgeongrass, *Ruppia maritima*		
Whole	371 (120–780) DW	9
Seeds	1,860 (450–3,500) DW	9
Filamentous algae	501 (390–787) DW	9
Aquatic insects	43 to 186 (22–340) DW	9
Volta Wildlife area, California, control area		
1983		
Aquatic plants	34 DW	3
Aquatic insects	13 (6–35) DW	3
Mosquitofish, whole	2.8 (Max. 3.6) DW	3
1984		
Widgeongrass		

Whole	100 (37–540) DW	9
Seeds	36 (32–43) DW	9
Filamentous algae	85 (64–140) DW	9
Aquatic insects	12 to 32 (7–47) DW	9
Western San Joaquin Valley, California, contaminated with irrigation drainwater		
Vegetation and seeds	Max. 3,390 DW	10
Clams, 2 species, muscle	Max. 9.3 FW	10
Bluegill, *Lepomis macrochirus*, whole	<0.8–1.9 FW, Max. 3.9 FW	10
Common carp, *Cyprinus carpio*, whole	0.5–5.7 FW, Max. 6.2 FW	10
Marine organisms		
Seaweeds, whole, Japan, 41 species	106 (16–319) DW 762 (231–3,308) AW	6
Marine algae	4–120 DW	8
Zooplankton	18–216 DW	7
Ctenophore, *Beroe cucumis*	115 AW	6
Corals, 34 species		
Deep open ocean	50–85 DW	6
Shallow open ocean	65–100 DW	6
Shallow coastal zone	40–110 DW	6
Tunicate, *Salpa fusiformis*, whole	50 AW	6
Chaetognath, *Sagitta elegans*	130 AW	6
Dungeness crab, *Cancer magister*, whole	1.8 (0.9–3.3) FW	6, 7
Molluscs, bivalves		
Soft parts, 11 species	1.6–4.5 FW	6
Soft parts, British Columbia		
Clams, 8 species	0.9–5.3 FW	7
Oysters, 2 species	3.1–4.0 FW	7
Mussels, 2 species	2.0–5.5 FW	7
Octopus, *Polypus bimaculatus*, whole	1.3 FW	7
Sockeye salmon, *Oncorhynchus nerka*		
Soft tissues	0.5–0.7 FW	6, 7
Bone	1.5 (1.1–4.4) FW	6, 7
Anchovetta, *Cetengraulis mysticetus*, whole	3.3–3.8 AW	8
Yellowfin tuna, *Thunnus albacares*		
Muscle	39.0 AW	8
Whole	9.0 AW	8
Eyeball	5.6 AW	8
Spleen	3.3 AW	8
Gill	1.8 AW	8
Heart	1.5 AW	8
Harbor seal, *Phoca vitulina*		
Blood	2.0 FW	8
Spleen	0.5 FW	8
Muscle	0.3 FW	8
Liver	0.2 FW	8
Heart	0.1 FW	8
Kidney	0.01 FW	8
Mammals, terrestrial		
Humans		
Teeth	18.2 (0.5–69) DW	1
Rib	6.2–10.2 AW	1
Kidney, lung, lymph nodes	0.6 FW	1, 2
Blood	0.1–0.4 FW	1, 2

Serum	0.2 FW	2
Muscle	0.1 FW	1, 2
Testes	0.09 FW	2
Milk	0.06–0.08 FW	2
Brain	0.06 FW	1, 2
Animal meat for human consumption	0.2 DW	2
Animal muscle and organs	0.5–1.5 DW	1
Milk, cow	0.5–1.0 FW	1
Dairy products	1.1 DW	2

[a]1, NAS 1980; 2, Nielsen 1986; 3, Ohlendorf et al. 1986; 4, Boyd and Walley 1972; 5, Ahl and Jonsson 1972; 6, Eisler 1981; 7, Thompson et al. 1976; 8, Jenkins 1980; 9, Schuler 1987; 10, Klasing and Pilch 1988.

Terrestrial plants, especially nuts, some fruits, and vegetables, are rich sources of boron (Table 3). Honey is another good source of boron, and concentrations up to 7.2 mg/kg dry weight (DW) have been reported (Nielsen 1986). Boron concentrations are also elevated in marine plants, zooplankton, and corals, but are low in fish and certain marine invertebrates (Table 3). No data are available on boron levels in terrestrial mammalian wildlife. Data for humans and domestic animals indicate that boron levels are elevated in bony tissues, but are always less than 0.6 mg B/kg fresh weight (FW) or 1.5 mg/ kg DW in other tissues examined (Table 3).

Effects

General

Boron is essential for the growth of higher plants and has been applied to B-deficient soils for at least 50 years to improve yields of many crops. Phytotoxic levels of B occur usually as a result of human activities, such as B-contaminated irrigation waters and excess applications of B-rich fertilizers, sewage sludges, and fly ashes. Boron compounds at comparatively high concentrations are used to control pestiferous insects through direct biocidal action, through enhancement of disease sensitivity, or through use as a chemosterilant.

Representative species of aquatic plants, invertebrates, fishes, and amphibians can usually tolerate up to 10 mg B/L medium for extended periods without adverse effects, although it has been suggested that concentrations >0.l mg B/L may ultimately affect reproduction in rainbow trout (*Oncorhynchus mykiss*), and >0.2 mg/L may impair survival of other fish species.

In waterfowl, diets that contain 30 or 100 mg B/kg FW adversely affect growth rate. Elevated tissue residues were recorded in ducks fed diets containing between 100 and 300 mg B/kg, and reduced survival occurred at dietary levels of 1,000 mg B/kg. Boron is a potent avian teratogen when injected directly into embryos during the first 96 h of development.

In mammals, the lethal dose of boron, as boric acid, varies according to species, and usually ranges between 210 and 603 mg B/kg body weight (BW); early developmental stages are especially sensitive. Excessive boron consumption adversely affects growth and reproduction in sensitive species of mammals (i.e., > 1,000 mg B/kg diet, > 15 mg B/kg BW daily, >1.0 mg B/L drinking water, or >3 g B/kg BW single dose on the first day of pregnancy). Boron is not considered essential for mammalian growth, but does protect against fluorosis and bone demineralization.

Terrestrial Plants

The role of boron in nutrition and toxicity of terrestrial crops has been reviewed extensively by Eaton (1944), EPA (1975), Gupta (1979, 1983), Gupta and Macleod (1982), Pilbeam and Kirkby (1983), and Gupta et al. (1985). It is generally agreed that boron is essential for the growth of higher plants and some species of fungi, bacteria, and algae, and that excess B is phytotoxic. It is also agreed that plants vary greatly in their sensitivity to B toxicity (Boyd and Walley 1972; EPA 1975; Birge and Black 1977; Goldberg and Glaubig 1986; Dear and Lipsett 1987). The exact mode of action of boron is unknown; however, its complexing ability facilitates the movement of sugars and other materials, and it is involved in cell wall bonding, conversion of glucose-l-phosphate to starch, and metabolism of nucleic acids (Sprague 1972; Gupta et al. 1985; Goldbach and Amberger 1986). Boron level in plants depends on the content and availability of soil boron, season, disease

state, inherent species or variety differences, and interactions with other substances (EPA 1975; Gestring and Soltanpour 1987). Most of the plant-available boron comes from the decomposition of soil organic matter and from boron adsorbed and precipitated onto soil surface particles; however, soil solution boron is the most important form, and plants take it up directly from this source (Gupta et al. 1985). Boron availability to plants is strongly associated with the hot-water-soluble fraction. This usually ranges from 0.4 to 4.7% of the total boron; the highest percentage occurs in fine-textured soils, and the lowest occurs in coarse-textured soils (Gupta and Macleod 1982). Uptake of boron by plants is about x 4 higher at pH 4 than at pH 9, highest in the temperature range 10 to 30°C, and higher with increased light intensity (Sprague 1972).

For the past 50 years, boron has been applied to B-deficient soils to improve crop yields of grains, fruits, vegetables, legumes, pine trees, tobacco, cotton, sunflowers, and peanuts (EPA 1975; Gupta 1979; Lipsett et al. 1979; Shorrocks and Nicholson 1980; Hopmans and Flinn 1984; Gupta and Cutcliffe 1985; Willett et al. 1985; Combrink and Davies 1987; Dear and Lipsett 1987; Mozafar 1987; Nuttall et al. 1987; Rerkasem et al. 1988). Boron is unique among the essential micronutrients because it is the only element normally present in soil solution as a nonionized molecule over the pH range suitable for plant growth (Gupta 1979). Boron deficiency in plants is widespread and has been reported in one or more crops in at least 43 States, almost all Canadian Provinces, and many countries (Gupta 1979). Boron deficiency in crops is more widespread than that of any other micronutrient (Gupta et al. 1985). It is more likely to occur in light-textured acid soils in humid regions because of boron's tendency to leach; however, deficiency may also occur in heavy-textured soils with high pH because boron is readily adsorbed under these conditions (Gupta et al. 1985). Deficiency signs include browning and spotting of leaves, chlorosis, abnormal thickening of cell walls, increased production of indoleacetic acid, accumulation of polyphenolic compounds, changes in membrane permeability, necrosis, and finally death (EPA 1975; Gupta 1979). Visible signs of deficiency in corn are accentuated by calcium deficiency, and are least evident when calcium is added to excess. Under conditions of boron and calcium deficiency combined, yields are low, and starch phosphorylase activity in corn leaves increases markedly, as does that of ribonuclease and polyphenol oxidase (Chatterjee et al. 1987). Interaction effects were also measured between B and potassium in alfalfa (Walker et al. 1987). Boron deficiency is usually corrected by application of 0.5 to 3 kg B/ha, depending on crop and formulation (Gupta 1979). Adding boron promotes the translocation rate of photosynthetic products and increases $C0_2$ incorporation into free amino acids (Gupta 1979).

Boron toxicity has been reported in many species of grasses, fruits, vegetables, grains, trees, and other terrestrial plants (Table 4; Gupta and Macleod 1982; Dye et al. 1983; Glaubig and Bingham 1985; Francois 1986; Nicholaichuk et al. 1988). Toxic levels generally do not occur on agricultural lands unless boron compounds have been added in excessive quantities, such as with fertilizer materials, irrigation water sewage sludge, or coal ash (Gupta and Macleod 1982; Gestring and Soltanpour 1987). Boron-contaminated irrigation water is one of the main causes of boron toxicity to plants. The continued use and concentration of boron in the soil due to evapotranspiration is the reason for eventual toxicity problems (Gupta et al. 1985). Borates have also been used as herbicides for complete kill of vegetation at application rates of 2,244 kg/ha (equivalent to 2,000 pounds/acre; Sprague 1972). Borates are frequently applied at elevated concentrations (i.e., >2 g/kg soil) in combination with organic pesticides to produce bacteriostatic effects; the resultant B-produced reduction in microbial degradation of the pesticide effectively extends the pesticide's biocidal properties (Sprague 1972). In some instances, cooling tower drift from geothermal steam containing boron may cause foliar boron toxicity near generating units (Glaubig and Bingham 1985; Sage et al. 1989).

Boron poisoning in plants is characterized by stunted growth, leaf malformation, browning and yellowing, chlorosis, necrosis, increased sensitivity to mildew, wilting, and inhibition of pollen germination and pollen tube growth (EPA 1975; Glaubig and Bingham 1985; Mitchell et al. 1987). In barley (*Hordeum vulgare*), for example, excess boron caused decreased growth and grain yield, elevated residues in leaves, and increased rate of leaf senescence (Table 4; Riley 1987). Barley grown on zinc-deficient soils tended to accumulate boron up to x 2.5 within 7 days; a similar pattern was evident for excess phosphorus (Graham et al. 1987). Thus, under conditions of marginally high boron in the rooting zone, low zinc, and high phosphorus, boron may accumulate to toxic levels in plants (Graham et al. 1987). Toxic effects in plants—including leaf injury—were observed in 26% of plants at or below substrate concentrations that resulted in greatest growth, indicating considerable overlap between injurious and beneficial effects of boron in plants (Eaton 1944). In general, deficiency effects in plants were evident when boron concentrations in soil solution were <2 mg/L; optimal growth occurred at 2 to 5 mg/L; and toxic effects were evident at 5 to 12 mg B/L (Gupta et al. 1985). However, considerable variation

exists in resistance to boron between species (Table 5). Sensitive species are known to include citrus, stone fruits, and nut trees; semitolerant species include cotton, tubers, cereals, grains, and olives; tolerant species usually include most vegetables (Gupta et al. 1985).

Table 4. Boron toxicity to some terrestrial plants.

Species, dose, and other variables	Effect	Reference[a]
Bigleaf maple, *Acer macrophyllum*		
0.9–5.4 mg B/L in saturated soil extracts	Reduced growth; >25% foliar damage; leaf residues of 76–324 mg B/kg ash weight (AW)	1
Madrone, *Arbutus menziesii*		
2.2–5.4 mg B/L in saturated soil extracts	Growth inhibition; >25% foliar damage; leaf residues of 216–540 mg B/kg AW	1
Beet, *Beta vulgaris*		
Soil B solutions		
5 mg/L	Optimal growth	2
15 mg/L	Injury evident	2
Broccoli, *Brassica oleracea italica*		
Grown in nutrient solutions containing		
0.08 mg B/L	Chlorophyll levels and net photosynthetic rates were significantly lower than those for plants grown in 0.41–0.81 mg B/L solutions	3
4.1 and 8.1 mg B/L	Leaf damage evident; lower chlorophyll levels and lower net photosynthetic rate than 0.4 and 0.8 mg B/L groups	3
Rhodes grass, *Chloris gayana*		
Grown in fly ash containing 3 mg hot-water-soluble B/L	Toxic. Residues >149 mg/kg dry weight (DW)	4
Lemon, *Citrus limonia osbeck*		
Soil B concentrations		
0.03–0.04 mg/L	Optimal growth	2
1 mg/L	Injury evident	2
Soybean, *Glycine max*		
Grown in soils amended with scrubber sludge residues (4.1 g B/kg) from coal-fired power plant for 2–3 years	Higher sludge B levels of 2 mg B/kg soil surface at year 1, and 1.2 mg B/kg at year 2 produced signs of B toxicity, including decreased growth and elevated residues in leaf (>83 mg/kg DW) and in seeds (>47 mg/kg DW)	5
Sunflower, *Helianthus annuus*		
50 mg B/L growth medium	Adversely affects phospholipid composition and synthesis in roots and microsomes from seedlings by inhibition of choline phosphotransferasse	6
10 mg B/L growth medium	Tolerated level	6

Barley, *Hordeum vulgare*		
Residues, in mg B/kg DW		
0.5–1.0 in soil	Residues of 46–100 mg/kg DW in leaves	7
30 in shoots	Damage to older leaves	8
50–70 in shoots	Reduction of 10% in DW of shoots	7
60–80 in leaf	Toxicity evident	8
80–120 in shoots	Toxic signs, but no yield reductions	8
120–130 in shoots	Grain yield reduced 10%	8
Alfalfa, *Madicago sativa*		
850–975 mg B/kg DW plant	Reduced yield	9
Rice, *Oryza sativa*		
Whole plant B residues		
38 mg/kg DW	No signs of toxicity	10
43–55 mg/kg DW	Signs of toxicity evident	10
Soil waters		
2.5–5 mg B/L	Toxic	10
French bean, *Phaseolus vulgaris*		
Grown in fly ash containing 3 mg hot-water-soluble B/L	Toxic. Residues >209 mg/kg DW	4
Residues in whole plant, in mg B/kg DW		
9–12	Slow flowering and pod formation; general yellowing of tips	11
>125	Reduced growth; burned older leaves dark brown	11
Digger pine, *Pinus sabiniana*, seedlings	Growth reduction; foliar damage >25%; needle	
13–17 mg B/L in saturated soil extracts	residues 1,242–1,512 mg B/kg AW	1
Pear, *Pyrus communis*		
82–164 kg B/ha applied to soil around pear trees in a nonirrigated orchard over a 6-year period	Toxicity observed during application and during 4 years postapplication. Toxicity was associated with residues, in mg B/kg DW, of 90–115 in blossom clusters and 45–55 in fruit. Within 5 years postapplication, soil B levels were <2 mg/kg, and all visible signs of toxicity had disappeared	12
Vegetation, various species		
2,244 kg borates/ha (2,000 lbs/acre)	Total kill of most species	2
Soil B concentrations		
1 mg/L	Optimal growth	2
5 mg/L	Injury evident	2
Plant residues		
>98 mg B/kg DW	Marginal burning and dark brown tips of older leaves	11

[a]1, Glaubig and Bingham 1985; 2, Sprague 1972, 3, Petracek and Sams 1987; 4, Aitken and Bell 1985; 5, Ransome and Dowdy 1987; 6, Belver and Donaire 1987; 7, Riley 1987; 8, Kluge and Podlesak 1985; 9, Gestring and Soltanpour 198; 10, Cayton 1985; 11, Gupta 1983; 12, Crandall et al. 1981.

Table 5. Boron concentrations in soil water associated with optimal growth and plant injury (from Sprague 1972).

Plant category	Boron concentration in soil water (mg/L) — Optimal growth	Boron concentration in soil water (mg/L) — Plant injury (usually)
Sensitive species	Trace to 1	1–5
Semitolerant species	Usually 1–5	5–15
Tolerant species	Usually 5–10	5–25

Table 6. Lethal and sublethal effects of boron on terrestrial invertebrates.

Organism, dose, and other variables	Effect	Reference[a]
Fruit fly, *Anastrepha ludens*		
Baits containing cottonseed hydrolysate and borax	Reduced infestation in oranges by 68%, and in mangoes by 98%	1
Honey bee, *Apis mellifera*		
8.7 mg B/L syrup (50 mg boric acid/L)	No effect on survival	2
17.5 mg B/L syrup (100 mg boric acid/L)	Fatal to about 50%	2
German cockroach, *Blattella germanica*		
Baits containing 25% boric acid plus honey	Population reduction of 50% in about 5 days, 80% in 4 weeks, and 98% in 6 to 9 months	3
Sugar diet containing		
11% boric acid	44% dead in 72 h	1
25% boric acid	79% dead in 72 h	1
50% boric acid	80% dead in 72 h	1
100% boric acid	91% dead in 72 h	1
Baits containing 20% boric acid	88% population reduction in 2 weeks; 92 to 95% reduction in 4 to 12 weeks	4
Gypsy moth, *Lymantria dispar*, larvae		
0.25% boric acid solution (436 mg B/L)	No effect on gypsy moth nucleopolyhedrosis virus (NPV)	5
0.5% boric acid	Enhanced NPV activity by x2	5
1% boric acid	Enhanced NPV activity by x11	5
Houseflies, *Musca domestica*		
250–5,000 mg B/kg diet, as boric acid	Inhibits reproduction	2
Isobornyl thiocyanoacetate		
27.3 µg/fly	LD50	1
Aerosols, >2%	50% knockdown in 6 min	1
American cockroach, *Periplaneta americana*		
Baits containing 1.5% boric acid	All dead in 6 days	6

Woodboring insects		
Common houseborer		
430 mg boric acid/m^3 wood	Adequate wood protection	2
Termites, 3 species		
>10,000 mg boric acid/m^3 wood	Required for wood protection	2

[a]1, EPA 1975; 2, Sprague 1972; 3, Gupta and Parrish 1984; 4, Wright and Dupree 1982; 5, Shapiro and Bell 1982; 6, Lizzio 1986.

Terrestrial Invertebrates

Relatively high concentrations of boron compounds are used to control fruit flies, cockroaches, gypsy moth larvae, houseflies, and woodboring insects (Table 6; Sprague 1972; EPA 1975). Boric acid is an effective stomach poison for several insect species (including German cockroaches [*Blattella germanica*], which are unable to detect the presence of boric acid (EPA 1975). Insect infestation of wood and other substrates can be prevented by pretreatment with boric acid or borax at doses of 0.25 to 0.55 kg/m^3 of wood (EPA 1975). Boric acid and other boron compounds are effective chemosterilants of the cotton boll weevil (*Anthonomus grandis*) and houseflies (EPA 1975).

Aquatic Organisms

Boron effects on aquatic plants are highly species-specific (Rao 1981; Table 7). Borate, like silicate, is an essential micronutrient for the growth of aquatic plants, such as diatoms, and it seems that a chemical combination of both nutrients in the form of silicoborate may be required by certain diatoms (Antia and Cheng 1975). In aquatic plants, boron affects nucleic acid metabolism, carbohydrate biosynthesis and transport, membrane integrity, and it interacts with growth substances (Frick 1985). Diatoms (*Cylindrotheca fusiformis*) cultured under B-deficient conditions stop dividing and swell in size despite increased photosynthetic rates. Boron-deficient diatoms accumulate rubidium, phenolic compounds, nitrates, and phosphates, and they show increased activity of various enzymes, especially glucose-6-phosphate dehydrogenase; however, respiratory adjustment is negligible until nutrient stress becomes irreversible in about 48 h (Smyth and Dugger 1980, 1981). Boron, under conditions of excess, alleviates nutrient deficiency in some phytoplankters and may cause temporal variations of phytoplankton composition in coastal waters (Rao 1981). Phytoplankton can tolerate up to 10 mg inorganic B/L in the absence of stress from pH adversity and nutrient deficiency, although higher borate concentrations up to 100 mg/L are expected to cause species redistribution by favoring the growth of some species and suppressing that of others (Table 7; Antia and Cheng 1975).

Data are limited for aquatic invertebrates and boron, although those data available suggest that the no-observable-effect levels were 13.6 mg B/L for freshwater organisms and 37 mg B/L for marine biota (Table 7). Juvenile Pacific oysters (*Crassostrea gigas*) accumulated boron in relation to availability, but showed no prolonged retention following cessation of exposure (Thompson et al. 1976). At current industrial discharge levels of about 1.0 mg B/L, no hazard is clear to oysters and aquatic vertebrates (Thompson et al. 1976).

The most sensitive aquatic vertebrates tested for which data are available were coho salmon (*Oncorhynchus kisutch*), with an LC50 (16-day) value of 12 mg B/L in seawater, and sockeye salmon (*O. nerka*), showing elevated tissue residues after exposure for 3 weeks in seawater containing 10 mg B/L (Table 7). Boron concentrations between 0.001 and 0.1 mg/L had little effect on survival of rainbow trout embryos after exposure for 28 days (Table 7). These low levels may represent a reduction in reproductive potential of rainbow trout, and >0.2 mg B/L may impair survival of other fish species, according to Birge and Black (1977); however, additional data are needed to verify these speculations. Birge and Black (1977) reported that concentrations of 100 to 300 mg B/L killed all species of aquatic vertebrates tested, that embryonic mortality and teratogenesis were greater in hard water than in soft water, but that larval mortality of fish and amphibians was higher in soft water than in hard water, and that boron compounds were more toxic to embryos and larvae than to adults. Moreover, they found no measurable effect of boron toxicity to aquatic vertebrates in water temperature in the range of 13 to 29°C, dissolved oxygen between 6.4 and 10.3 mg/L, and pH between 7.5 and 8.5.

Table 7. Lethal and sublethal effects of boron on aquatic organisms.

Taxonomic group, organism, compound, dose, and other variables	Effect	Reference[a]
Aquatic plants		
Blue green alga, *Anacystis nidulans*, boric acid, H_3BO_3		
0.01–4.0 mg B/L	Grows well in B-deficient media; growth neither stimulated nor inhibited at higher levels	1, 15
50 mg B/L	No effect on growth or organic constituents	2
75–100 mg B/L	Growth and chlorophyll content reduced; at 72 h, photosynthetic pigments depleted	2
100 mg B/L	Decrease in protein content causing inhibition in nitrate uptake and nitrate reductase activity. Decreased chlorophyll content and photosynthesis inhibition within 72 h	2, 15
Green alga, *Chlorella pyrenoidosa*, boric acid		
10 mg B/L	No effect on growth or cell composition. Bioconcentration factor (BCF) of x4 after 7 days	3
50 mg B/L	BCF of x5 after 7 days	3
50–100 mg B/L	Altered cell division and amino acid activity after 72 h; reversible photosynthesis inhibition. Giant cells formed with increased nitrate and protein	4
100 mg B/L	BCF of x4.8 after 7 days	3
>100 mg B/L	Totally inhibitory for cell division and biomass synthesis in 72 h	4
Duckweed, *Lemna minor*, boric acid		
Control media, 10–20 mg B/L, pH 5.0	Normal growth	5
100 mg B/L, pH 5.0	Growth inhibited; recovery on transfer to control media	5
20 mg B/L, pH 4.0	Residues of 93 mg B/kg fresh weight (FW) v. 63 in controls	5
20 mg B/L, pH 7.0	Growth inhibited. Residues of 257 mg/kg FW v. 49 in controls	5
Marine algae, 19 species, boric acid		
5–10 mg B/L	No inhibitory effect on growth rate in 60 days; stimulatory to some species	6
10–50 mg B/L	Prolonged survival of peak populations of certain diatoms after growth cessation: *Bellerochea polymorpha* at 10 mg B/L, *Skeletonema costatum* at 50 mg B/L	6
50 mg B/L	Growth inhibition in 26% of species tested; adaptation and recovery by most species	6
100 mg B/L	Growth inhibition in 12 of 19 species tested; 8 species did not recover and died	6
Marine phytoplankton		
30 mg B/L, high nitrates, phosphates, silicates, and low temperatures	Increased primary production and carbon assimilation	7
30 mg B/L, low nutrients, high temperatures	Photosynthesis inhibited up to 62%	7

30 mg B/L, unialgal cultures, 5-days-old	Photosynthesis inhibition	7
As above, 14-days-old	Enhanced photosynthesis in certain species	7
Invertebrates		
Sea urchin, *Anthocidaris crassispina*, embryos, boric acid		
37 mg B/L	Normal development	8
75 mg B/L	Fatal	8
Cladoceran, *Daphnia magna*, boric acid		
6.4 mg B/L	Highest concentration tested in 21-day exposure producing no measurable effect	9, 10
13.6 mg B/L	Lowest concentration tested in 21-day exposure causing reduction in number of broods, total young produced, mean brood size, and mean size	9, 10
27 mg B/L	LC14 (21 days)	10
53 mg B/L	LC50 (21 days)	10
54–200 mg B/L	No deaths (48 h)	9, 10
106 mg B/L	LC100 (21 days)	10
115–246 mg B/L	LC50 (48 h)	9, 10
420 mg B/L	LC100 (48 h)	9
Mosquito larvae, 3 species, boric acid, mg/L		
250 (43.7 mg B/L)	LC97-LC99 through hatching	11
4,000 (700 mg B/L)	LC100 (48 h), freshly hatched	11
3,000 (524 mg B/L)	LC100 (48 h), second instar	11
10,000 (1,748 mg B/L)	LC100 (48 h), third instar	11
16,000 (2,797 mg B/L)	LC100 (48 h), pupae	11
Vertebrates		
Fowler's toad, *Bufo fowleri*, embryos, through day 4 posthatch		
Boric acid		
Soft water, 50 mg $CaCO_3$/L		
25 mg B/L	LC1 (7.5 days)	12
145 mg B/L	LC50 (7.5 days)	12
Hard water, 200 mg $CaCO_3$/L		
5 mg B/L	LC1 (7.5 days)	12
123 mg B/L	LC50 (7.5 days)	12
Toad, *Bufo vulgaris*, embryos		
874 mg B/L, as boric acid. Exposure for 24 h from 2-cell stage to tailbud stage	Malformations included edema, microcephalia, short tail, and suppressed forebrain development	11
Goldfish, *Carassius auratus*, embryos, through day 4 posthatch		
Boric acid		
Soft water		
0.6 mg B/L	LC1 (7 days)	12
46 mg B/L	LC50 (7 days)	12
Hard water		
0.2 mg B/L	LC1 (7 days)	12
75 mg B/L	LC50 (7 days)	12
Borax, $Na_2B_4O_7 \cdot 10H_2O$		
Soft water		
0.5 mg B/L	LC1 (7 days)	12

65 mg B/L	LC50 (7 days)	12
Hard water		
0.9 mg B/L	LC1 (7 days)	12
59 mg B/L	LC50 (7 days)	12
Mosquitofish, *Gambusia affinis*, adults		
Boric acid		
5,600 mg/L (979 mg B/L)	LC50 (96 h)	12
Sodium borate		
3,600 mg/L	LC50 (96 h)	12
Channel catfish, *Ictalurus punctatus*, embryos, through day 4 posthatch		
Boric acid		
Soft water		
0.5 mg B/L	LC1 (9 days)	12
155 mg B/L	LC50 (9 days)	12
Hard water		
0.2 mg B/L	LC1 (9 days)	12
22 mg B/L	LC50 (9 days)	12
Borax		
Soft water		
5.5 mg B/L	LC1 (9 days)	12
155 mg B/L	LC50 (9 days)	12
Hard water		
1.7 mg B/L	LC1 (9 days)	12
71 mg B/L	LC50 (9 days)	12
Bluegill, *Lepomis macrochirus*		
Boron trifluoride, BF_3		
15,000 mg B/L	LC50 (24 h)	12
Dab, *Limnada limnada*		
74.0 mg B/L	LC50 (96 h)	13
88.3 mg B/L	LC50 (24 h)	13
Coho salmon, *Oncorhynchus kisutch*, underyearlings		
12 mg B/L	LC50 (283–384 h), seawater	14
113 mg B/L	LC50 (283–552 h), fresh water	14
Rainbow trout, *Oncorhynchus mykiss*, embryos, through day 4 posthatch		
Boric acid		
Soft water		
0.1 mg B/L	LC1 (28 days)	12
100 mg B/L	LC50 (28 days)	12
Hard water		
0.001 mg B/L	LC1 (28 days)	12
79 mg B/L	LC50 (28 days)	12
Borax		
Soft water		
0.07 mg B/L	LC1 (28 days)	12
27 mg B/L	LC50 (28 days)	12
Hard water		
0.07 mg B/L	LC1 (28 days)	12
54 mg B/L	LC50 (28 days)	12
Adults		
339 mg B/L	LC50 (48 h)	10, 12, 16
350 mg B/L	No effect in 30 min	16
3,500 mg B/L	All alive after 30 min, but in obvious distress	16
14,000 mg B/L	After exposure for 30 min, all recovered if	16

	placed in flowing B-free water	
Sockeye salmon, *Oncorhynchus nerka*		
10 mg B/L, exposure in seawater for 3 weeks	Maximum residues, in mg/kg FW, were 17 in bone, 12 in kidney, 10 in gill, 9 in liver, and 8 in muscle. Maximum control values were always <1.0, except bone, which was 4.4 mg/kg FW	14
Leopard frog, *Rana pipiens*, embryos, through day 4 posthatch		
Boric acid		
Soft water		
13 mg B/L	LC1 (7.5 days)	12
130 mg B/L	LC50 (7.5 days)	12
Hard water		
22 mg B/L	LC1 (7.5 days)	12
135 mg B/L	LC50 (7.5 days)	12
Borax		
Soft water		
5 mg B/L	LC1 (7.5 days)	12
47 mg B/L	LC50 (7.5 days)	12
Hard water		
3 mg B/L	LC1 (7.5 days)	12
54 mg B/L	LC50 (7.5 days)	12

[a]1, Martinez et al. 1986b; 2, Martinez et al. 1986a; 3, Fernandez et al. 1984; 4, Maeso et al. 1985; 5, Frick 1985; 6, Antia and Cheng 1975; 7, Rao 1981; 8, Kobayashi 1971; 9, Gerisch 1984; 10, Lewis and Valentine 1981; 11, EPA 1974; 12, Birge and Black 1977; 13, Taylor et al. 1985; 14, Thompson et al. 1976; 15, Mateo et al 1987; 16, Sprague 1972.

Birds

Boron is a potent teratogen to domestic chicken embryos when injected into eggs. Injection of boron into the yolk sac of chicken embryos during the first 96 h of development with 1.0 to 2.5 mg of boric acid--equivalent to 3.2 to 8.0 mg B/kg FW egg (55 g egg)--produced a wide range of developmental abnormalities (Table 8). Several compounds are known to counteract B-induced avian developmental abnormalities, or to reduce the frequency of malformations, although the mode of action is unclear. These compounds include sodium pyruvate, to counteract rumplessness (Landauer 1952); nicotinamide, to decrease frequency of facial defects (Landauer 1952) and melanin formation (Landauer 1953c); and riboflavin, which greatly reduced the teratogenic effects of boric acid (Landauer 1952, 1953a, 1953b; Landauer and Clark 1964). Other polyhydroxy compounds, such as D-ribose, pyridoxine hydrochloride, and D-sorbitol hydrate, also reduced or abolished boric acid-induced teratogencity in chick embryos (Landauer 1953b).

High concentrations of boron have been found in the San Joaquin Valley of California in irrigation drainwater and in aquatic plants consumed by waterfowl. Measured boron concentrations in that locale exceeded 20 mg/L in subsurface agricultural drainage waters, 400 mg/kg DW in widgeongrass (*Ruppia maritime*) and algae, 150 mg/kg DW in aquatic insects, 1,860 mg/kg DW in some aquatic plants, and up to 3,390 mg/kg DW in seeds consumed by waterfowl (Schuler 1987; Klasing and Pilch 1988; Smith and Anders 1989; Hoffman et al. 1990). At present, only selenium has been implicated as the cause of abnormal development among waterfowl in western areas affected by irrigation drainwaters (Ohlendorf et al. 1986; Hoffman et al. 1988, 1990). However, recent studies by Smith and Anders (1989) and Hoffman et al. (1990) with mallards demonstrate that dietary boron concentrations well below levels that can occur in the environment represent a toxicological hazard that has not been considered in the management of agricultural drainwater. For example, dietary concentrations of 300 to 400 mg B/kg of feed FW--substantially lower than boron levels reported near some western wildlife refuges contaminated by agricultural drainwater--adversely affect mallard growth, behavior, and brain biochemistry and are often associated with elevated tissue boron levels (Table 8). Dietary levels of 100 mg B/kg FW resulted in reduced growth of female mallard ducklings (Hoffman et al. 1990), and diets containing as little

as 30 mg B/kg FW fed to mallard adults adversely affected growth rate of their ducklings (Smith and Anders 1989). Resource managers must now consider boron, as well as selenium, and their possible interactions, as a toxic hazard to wildlife populations throughout areas of the western United States (Smith and Anders 1989).

Table 8. Lethal and sublethal effects of boron on birds.

Species, dose, and other variables	Effect	Reference[a]
Domestic chicken, *Gallus domesticus*		
Embryo, yolk injection		
Boric acid		
0.01 mg B/kg body weight (BW)	LD1	1
1.0 mg B/kg BW	LD50	1
1.0 mg at 28 h of development	Developmental abnormalities	2
2.0 mg at 28 h of development	Malformations of nervous system, eyes, and spinal cord	3
2.5 mg at 24 h of development	Rumplessness	7
2.5 mg at 84 h of development	Skeletal deformities, cleft palate, missing toes, eye deformities	4, 5, 6
15.8 mg B/kg egg at 96 h of development	LD50 (96 h). Most (70 to 85%) of the survivors at age 18 days had edema, inhibited feather growth, pale body coloration, and reduced BW	10
Borax		
0.01 mg B/kg BW	LD1	1
0.5 mg B/kg BW	LD50	1
Adult		
875 mg B/kg diet, as boric acid, for 6 days	Egg production ceased; production normal 14 days after B withdrawn	1
Mallard, *Anas platyrhynchos*		
Adults fed diets containing various concentrations of B, as boric acid, for 3 weeks, then mated. Resultant ducklings continued on same diets for 21 days. Data collected on reproduction, survival, residues, and histopathology when ducklings were age 21 days		
8 mg B/kg diet fresh weight (FW) (controls). Diets contained about 10% moisture	Boron residues in egg, liver, and brain of adults and ducklings were always <3 mg B/kg dry weight (DW)	8
30 mg B/kg diet FW	Duckling weight gain reduced compared to controls. Residues in egg and duckling liver and brain about 3–4 mg B/kg DW; residues <3 in adult liver and brain	8
300 mg B/kg FW	Duckling BW at hatch significantly lower than controls; duckling weight gain reduced. Mean residues, in mg B/kg DW, were 13 in egg, 15 in adult liver (Max. 24), 17 in duckling liver (Max. 36), 14 in adult brain (Max. 24), and 19 in duckling brain (Max. 44)	8
1,000 mg B/kg diet FW	No observable effect on adults. No effect on egg fertility or shell thickness. Significantly reduced hatching success; duckling mortality through age 7 days significantly greater than controls; body weight lower. Total number of 21-day-old	8

	ducklings produced per female, and brain to BW ratios were significantly higher than controls. Mean B residues, in mg/kg DW, were 49 in egg, 33 in adult liver (Max. 74), 51 in duckling liver (Max. 89), 41 in adult brain (Max. 89), and 66 in duckling brain (Max. 110). No histopathology evident in liver, brain, kidney, or heart	
Ducklings, age 1 day, 2-week dietary exposure		
1,000 mg B/kg FW diet, as boric acid	Adverse effects on growth	9
5,000 mg B/kg diet, as boric acid	Some deaths	9
Ducklings, age 1 day, 10-week dietary exposure to boric acid		
Controls, 13 mg B/kg FW diet. Diets contained 12–14% moisture	Brain B concentration of 2 mg/kg DW	9
100 mg B/kg FW diet	Delayed growth of females, plasma triglyceride levels evaluated, abnormal liver metabolism, brain residue of 4 mg/kg DW	
400 mg B/kg FW diet	Delayed growth of females, plasma triglyceride elevated, brain B residue of 5 mg/kg DW, decrease in brain ATP, altered duckling behavior in bathing and resting	9
1,600 mg B/kg FW diet	Some deaths (10%), delayed growth, decreased food consumption, plasma triglyceride elevated, brain B residue of 51 mg/kg DW (Max. 99), decrease in brain calcium and ATP, reduction in time spent bathing and standing, increase in time spent resting, increased serum calcium, lower hematocrit and hemoglobin; no histopathology of brain, liver, or kidney	9

[a]1, Birge and Black 1977; 2, Schowing and Cuevas 1975; 3, Schowing et al. 1976; 4, Landauer 1953a; 5, Landauer 1953b; 6, Landauer 1953c; 7, Landauer 1952; 8, Smith and Anders 1989; 9, Hoffman et al. 1990; 10, Ridgeway and Karnofsky 1952.

Mammals

Epidemics and sporadic cases of oral intoxication in humans are often due to inadvertent addition of boric acid to infant formulas (Siegel and Wason 1986). Pacifiers and some other products containing boron compounds have been sold in Ireland despite a recommendation from the Pharmaceutical Society of Great Britain that these products should not be sold because of hazards to infants (O'Sullivan and Taylor 1983). Fatal cases of boron poisoning have involved misuse of boron compounds in hospitals, either from accidental substitution of boric acid solution for water in infant formula or from accidental use of boric acid as a diapering powder (EPA 1975). In an adult fatality, the victim died after inundation by borax solution (EPA 1975). In one case, a 12-month-old girl developed violent vomiting, coughing, irritability, tremors, seizures, and a delirious reaction after accidentally swallowing a mixture containing 3 g of boric acid and 300 mg of cinchocaine chloride prescribed for a painful dental protrusion (Egfjord et al. 1988). Her plasma boric acid level 6 h later was 26 mg/L; the half-time persistence (Tb l/2) for boric acid in plasma is about 7 h (Egfjord et al. 1988). The lethal dose of boric acid varies according to the species. In mammals it ranges from 210 to 603 mg B/kg BW, and death is due to central nervous system paralysis and gastrointestinal irritation (Table 9; NAS 1980). Human newborns are especially sensitive, and accidental deaths have been recorded at doses between 50 and 140 mg B/kg BW (Table 9).

Table 9. Lethal and sublethal effects of boron on mammals.

Organism, route of administration, dose, and other variables	Effect	Reference[a]
Cattle, *Bos* spp.		
Drinking water		
Supplemented with 15, 30, 60, or 120 mg B/L for 10 days	Boron levels in plasma rose from 2.7 mg/L in controls to 4.4 (15 mg/L group), 5.3 (30 mg/L group), 8.3 (60 mg/L group), and 13.4 mg/L in the 120 mg B/L drinking water supplement	5
29 mg B/L, and higher	When given a choice, cattle preferred tap water to drinking water supplemented with B compounds	1
120 mg B/L, as borax, for 10 days	No effect on feed or water consumption; no overt signs of toxicosis	2
150 mg B/L, as borax, for 30 days equivalent to 15.3 mg B/kg body weight (BW) daily	Decreased feed consumption, weight loss, edema, inflammation of legs, daily elevated plasma B levels of 1.2 mg/L v. 0.5 in controls, abnormal blood chemistry	1, 2, 3, 4, 5
Diet		
Consumed feed containing 157 mg B/kg, as borax, for 42 days	No adverse effects	3
Fed 2 to 2.5 g of boron daily as borax, for 40 days	No observable adverse effects; all B excreted, mostly in urine	6
Fed 20 g of borax daily	Milk B residues increased from <1.0 mg/L to >3 mg/L	5
Ingested total dose of 100–300 g of boron equivalent to 200–600 mg B/kg BW	Toxic dose	7
Found dead after consuming 1 kg of borax, or about 250 g of B	Residues in mg B/kg fresh weight (FW) were 1,300 in ruminal fluids, 1,900 in abomasal fluids, 24 in liver, 19 in rumen, and 21 in abomasums	7
Dog, *Canis familiaris*		
Diet		
350 mg B/kg feed, 2 years	Tolerated	8
1,540 mg borax/kg or 3,000 mg boric acid/kg, chronic study (174–524 mg B/kg diet)	No adverse effects	6, 9
1,170 mg B/kg, 38 weeks	Testicular degeneration, spermatogenesis cessation	5, 8
Inhalation		
92 mg pentaborane/m^3 for 15 min	LC50	9
Guinea pig, *Cavia* sp.		
Inhalation		
0.018 mg decaborane/m^3, 6 h daily, 5–6 exposures	Eye inflammation, listlessness, emaciation, convulsions	3
Human, *Homo sapiens*		
Dermal		
7-month-old infant treated for dermatitis with 3% boric acid powder	Fatal. Boron concentrations elevated in bile, intestinal contents, and spleen	9

Adult administered about 645 g of boric acid dermally	Toxicosis observed	
Inhalation		
Borax dust, 1.1–14.4 mg/m^3, occupational exposure for at least 5 years	At 14.4 mg/m^3, 33% of workers noted dryness of mouth, nose, or throat; 28% had eye irritation problems; 15% had nosebleeds and cough; 13% had sore throat or shortness of breath and ches tightness. At 4.0 and 1.1 mg/m^3, no symptoms except eye irritation were noted by more than 5 and 3% of exposed participants	11
Boranes, various	Pulmonary irritation, headache, nausea, fatigue, muscular weakness, liver and kidney pathology	3
Oral		
3 mg B daily for 119 days in diet containing 0.25 mg B	Reduction in urinary excretion of calcium and magnesium by postmenopausal women	12
20 mg B daily	Normal adult intake	6
Solutions >88 mg B/L or >500 mg boric acid/L	Fatal to infants	13
1–3 g boric acid, or 0.3–0.8 g/kg BW	Lethal to newborns	14
2–4.5 g boric acid or 0.5–1.2 g/kg BW	Nonfatal to infants, but serum levels elevated from 20–150 mg borate/L	14
>3.5 g boric acid daily	Probably harmful or lethal to infants and newborns	10
4 g boric acid or borates daily	No toxicosis in adults	6, 9
4.5–15 g of boric acid, equivalent to 1.25–4.2 g/kg BW, in accidentally contaminated formula in newborn nursery	Death preceded by severe symptomology; serum levels of 400–1,000 mg borate/L	13, 14
5–6 of borates, or 0.7 g/kg BW	Fatal to infants	14, 15
15–20 g of boric acid, equivalent to 0.25–0.3 g/kg BW	Fatal to adults	9, 14, 15
Infants, age 6–16 weeks		
Given pacifiers dipped in a proprietary borax (107 g/L) and honey compound. Dose during 1-month-exposure period estimated at 3–9 g borax	Some developed seizure disorders characterized by vomiting, loose stools, irritability, diarrhea; elevated blood B values of 2.6–8.5 mg B/L v. <0.6 in controls. When preparation witheld, seizures stopped and children remained well for at least 5 years	13
Injections, intravenous		
Adult males, age 22–28 years, given single infusion of 562–611 mg boric acid equivalent to 8.0–8.7 mg B/kg BW	Boric acid half-time persistence was 21 h. Most was excreted in urine 24 h, 94% in 96 h, and ~99% in 120 h; plasma boric acid concentration after infusion was about 16 mg/L v. 0.5 at start; no discomfort during or after infusion	16
Adults given dose of 20 g boric acid	No permanent adverse effects	9
Monkey, *Macaca* sp.		
Inhalation		
Pentaborane, 640 mg/m^3, 2 min	LC50	9
Intraperitoneal injection		
Decaborane, 1 mg/kg BW daily, multiple	Altered brain wave activity	9

injections		
Decaborane, 6 mg/kg BW, single injection	LC50	9
Mice, *Mus* sp.		
Drinking water		
5 mg B/L, lifetime exposure	No effect on growth, longevity, or tumor incidence	2, 5
Ingestion		
3 g B/kg BW, first day of pregnancy	94% of embryos failed to develop past blastocyst stage v. 9% in controls	9
Diet		
1,500 mg boric acid/kg (262 mg B/kg)	All dead within 10 days	17
Injection, intravenous		
1.32 g sodium borate/kg BW, single dose	LD50	18
Injection, intraperitoneal		
25.2 mg decaborane/kg BW, single dose	LD50	9
44.7 mg decaborane/kg BW, single dose, prior treatment for 8 days at 250 mg/kg BW with pyridoxine hydrochloride	LD50	9
2,817 mg sodium borate/kg BW, single dose	LD50	18
Inhalation		
Pentaborane		
0.011 mg/m^3 for 4 h	LC50	3
50 mg/m^3, 15 min	LC50	9
342 mg/m^3, 2 min	LC50	9
1,034 mg/m^3, 30 s	LC50	9
Rabbit, *Oryctolagus* sp.		
Diet		
Equivalent to 800–1,000 mg borates/kg BW daily for 4 days	Growth retardation	18
Intragastric route		
Daily dose of 100 mg calcium borate 4 months	Altered serum chemistry	9
Intravenous injection		
Single dose of 800–900 mg boric acid/kg BW	LD50	18
Intraperitoneal injection		
30 mg decaborane/kg BW	Death within 24 h	3
Dermal		
25–200 mg boric acid/kg BW daily	Nonirritative and nontoxic when applied to intact skin	18
Sodium borate solutions of 50,000 or 100,000 mg borates/L applied to skin	Mildly or moderately irritating	18
Boron oxide dust	Application to skin produced erythema that lasted 2–3 days; instillation in eyes produced immediate conjunctivitis as a result of exothermic hydration of boron oxide to boric acid	19
Inhalation		
120–150 mg calcium borate/m^3, 2 h daily, 10-week exposure	Respiratory tract pathology, growth inhibition, enlarged liver	9
Rat, *Rattus* sp.		

Drinking water		
Free access for 90 days to drinking water containing 0.3, 1.0, or 6.0 mg B/L	Rats refused to drink water at 1.0 or 6.0 mg/L	15
0.3 mg boric acid/L for 6 months	No effect on gonadotoxicity	20
1.0 mg boric acid/L for 6 months, equivalent to 0.05 mg B/kg BW daily	Decreased spermatozoid count, reduction in spermatozoid activity	20
6 mg B/L, 90 days	No toxic effect on male reproductive system, blood chemistry, or growth	5, 15
6 mg B/L for 6 months, equivalent to 0.3 mg B/kg BW daily	Gonadotoxicity in male rats; altered enzyme activity levels in blood and liver	20, 21
75 mg B/L, as borax, for 45 days	No effect on growth or reproduction	3
100 mg B/L for 21 days	Tissue B levels in kidney, liver, brain, and blood increased for first 9 days but returned to normal by day 21 except for blood, which continued to rise	
150 mg/L for 70 days, or 170 mg B/L for 25 days	Slight reduction in growth rate	
>150 mg B/L for extended periods	Adverse effects probable	5
300 mg B/L for 49–70 days	Growth rate reduced 21% but no change in food consumption; coarse coat; atrophied scrotal sacs	4
440 mg B/L for 25 days	Growth inhibition	4
3 g sodium tetraborate/L for 10–14 weeks	Increase in activity of cerebral succinic dehydrogenase, brain acid proteinase, and in brain RNA concentration; decrease in liver cytochrome P-450 activity	22
Diet		
0.09–1.71 mg boric acid/kg BW daily for 6 months (0.015–0.3 mg B/kg BW daily)	Adverse changes in testes	18
350 or 525 mg B/kg diet, as borax or boric acid, for 2 years	No observable adverse effects on fertility, lactation, litter size, weight, or appearance	6
500, 1,000, or 2,000 mg B/kg diet, as borax, for 30–60 days, equivalent to 12, 25, or 50 mg B ingested daily	No adverse effects at 500 mg B/kg diet for 60 days. At 1,000 and 2,000 mg B/kg, adverse effects measured on male reproductive capacity, including germinal aplasia and infertility; effects persisted for at least 8 months following B exposure at highest dose	23
525 mg B/kg diet for 90 days	Tolerated	8
1,000 mg boric acid or borax/kg BW daily	Weight loss after 1 week on borax diet or 2 weeks on boric acid diet; toxic signs after 3 weeks on both diets	24
1,050 mg B/kg diet, as borax or boric acid, for 2 years	Testicular degeneration	6
1,060 mg B/kg diet, as sodium borate, chronic exposure	Growth retardation and testicular atrophy	18
1,170 mg B/kg diet, 2 months	Coarse coat, scaly tails, hunched position, bloody discharge from eyes, depressed hemoglobin and hematocrit	5
1,170 mg B/kg diet, as borax or boric acid 2 years	Sterility in males and females	6, 8
1,750 mg B/kg diet, 25 days	Reduction of 50% in growth rate	4
1,750 mg B/kg diet, as sodium borate, chronic	Severe testicular atrophy	18

Oral, single dose		
450 mg B/kg BW	No effect on male fertility	15
510–690 mg B/kg BW, as borax	LD50	8, 9, 24
550–710 mg B/kg BW, as boric acid	LD50	8, 9, 24
600 mg B/kg BW	LD50	2
3.45–5.14 g sodium borate/kg BW	LD50	18
5.1 g boric acid/kg BW	LD50	6
6.1 g borax/kg BW	LD50	6
Injection subcutaneous		
1.4 g boric acid/kg BW	LD50	18
Injection, intravenous		
5–75 mg boric acid/kg BW	Slight reduction in arterial blood pressure	21
Injection, intraperitoneal		
42 mg sodium borate/kg BW, single injection	Tissue residues after 30 min, in mg B/kg FW, were 25 in blood, 30 in liver, and 50 in kidney v. <5 in all control tissues. After 3 months, residues were 20 mg B/kg FW in brain, 45 in heart, 60 in liver, and 75 in kidney	21
Inhalation, boron trifluoride		
2, 6, or 17 mg BF_3/m^3, 6 h daily, 5 days weekly, 13 weeks	At 17 mg/m^3, altered proximal tubluar epithelium of kidney and abnormal serum chemistry. At 6 mg/m^3, elevated fluoride levels in urine, serum, and bone, but no toxic response. No difference from controls at 2 mg/m^3	26
24 or 66 mg/m^3, 6 h daily, 9 days	Clinical signs of respiratory irritation, nasal discharge, weight loss, increased lung weight, depressed liver weight, kidney pathology at 66 but not 24 mg/m^3	26
55 mg/m^3, 4–7 h daily, 5 days weekly, 6 weeks	Some deaths in rats and other rodent species tested, but no deaths in nonrodent species	26
180 mg/m^3, 6 h daily, consecutive days	All dead prior to sixth exposure	26
259 mg/m^3, 4–7 h daily, 2 days	All dead. Mortality was lower for guinea pigs, dogs, rabbits, mice, and cats. Lung and kidney damage in all species	26
1,210 mg/m^3, 4 h	50% dead	26
Inhalation, boron oxide		
470 mg/m^3, 10 weeks	Reddish exudates from nose, but no deaths or signs of lung damage	19
470 mg/m^3, 24 weeks	No signs of toxicosis	9
Inhalation, decaborane		
20 mg/m^3, 6 h daily, 5 days weekly	Tremors, convulsions, nervousness, restlessness, weight loss, belligerency	3
36 mg/m^3, 4 h	LC50	3
Inhalation, pentaborane		
3 mg/m^3, 6 h daily, 5 days weekly	Extreme belligerency, tremors, weight loss	3
18 mg/m^3, 4 h	LC50	3

[a]1, Green and Weeth 1977; 2, Weeth et al. 1981; 3, NAS 1980; 4, Seal and Weeth 1980; 5, Nielsen 1986; 6, Sprague 1972; 7, Brockman et al. 1985; 8, Weir and Fisher 1972; 9, EPA 1975; 10, Gupta and Parrish 1984; 11, Garabrant et al. 1985; 12, Nielsen et al. 1987; 13, O'Sullivan and Taylor 1983; 14, Siegel and Wasson 1986; 15,

Dixon et al. 1976; 16, Jansen et al. 1984; 17, Lizzio 1986; 18, Anonymous 1983; 19, Garabrant et al. 1984; 20, Krasovskii et al. 1976; 21, Magour et al. 1982; 22, Settimi et al. 1982; 23, Lee et al. 1978; 24, Dani et al. 1971; 25, Benson et al. 1984; 26; Rusch et al. 1986.

Table 10. Proposed boron criteria for the protection of natural resources and human health.

Resource and other variables	Criterion	Reference[a]
Crops		
Irrigation waters		
Sensitive crops	0.3–1.25 mg B/L	1, 2, 3
Semitolerant crops	0.67–2.5 mg B/L	1, 2, 3
Tolerant crops	1–4 mg B/L	1, 2, 3
Maximum safe concentration	4 mg B/L	2
Residues in crops		
Boron deficiency	<15 mg B/kg dry weight (DW) plant	4, 5
Toxicosis	>200 mg B/kg DW plant	4, 5
Aquatic organisms		
Nonhazardous levels in water		
Fish, oysters	1 mg B/L	6
Aquatic plants	4 mg B/L	2
Fish	5 mg B/L	2
"Safe" levels in water		
Largemouth bass, *Micropterus salmoides*	<30 mg B/L	1
Bluegill, *Lepomis macrochirus*	<33 mg B/L	1, 7
Adverse effects, sensitive species	10–12 mg/L	6
Waterfowl		
Diet		
No observed adverse effect	<13 mg/kg fresh weight (FW)	17
Adverse effects	30–100 mg/kg FW	17, 18
Fatal	1,000 mg/kg FW	18
Livestock		
Diet		
Boron deficiency	<0.4 mg B/kg DW	5
Toxic signs probable	>100 mg B/kg DW	5
Maximum tolerable level, as borax	150 mg B/kg DW	4, 5
Total dose, toxic	100–300 g of B (equivalent to 200–600 mg B/kg body weight)	9
Drinking water		
Maximum allowable	5 mg B/L	4, 8, 10, 11
Maximum tolerated	40 mg B/L	10
"Safe"	40–150 mg B/L	11
Adverse effects	>150 mg B/L	5
Pesticide applications		
Boric acid, 99% powder	Effective for control of household cockroaches, ants, and fleas	2
Boric acid, 8% solution	Fungicide for vegetables, fruits, and trees	12
Human health		
Daily intake		
Worldwide	Range 0.3–41 mg B, means usually 10–20 mg B	4, 5, 13
Finland	1.7 mg B	5
England	2.8 mg B	5
United States	3 mg B	4

No effect level	4 g boric acid	14
Adverse effect level		
Chronic intoxication	4–5 g boric acid	14
Lethal to infants and small children	5–6 g boric acid	14
Lethal to adults	18–20 g boric acid, single dose	14
Drinking water		
Recommended	<0.3 mg B/L	15
USSR	<0.5 mg B/L	10
United States	<1.0 mg B/L	4, 11
"Safe"	<20 mg B/L	2, 10
No toxic effects	20–30 mg B/L	2
Dermal, ocular		
Sodium borate and boric acid	Safe as cosmetic ingredients at <5% concentrations; not recommended on infant skin or injured skin	12, 16
Air, Threshold Limit Value (8 h daily, 5 days weekly)		
Pentaborane	0.01 mg/L	4
Dioborane	0.1 mg/L	4
Decaborane	0.5 mg/L	4
Sodium borate	1–5 mg/m^3	16, 17
Boron trifluoride	3 mg/m^3	3
Calcium borate	4–6 mg/m^3	3
Boron tribromide	10 mg/m^3	3
Boron oxide	10 mg/m^3	3

[a]1, Sprague 1972; 2, Papchristou et al. 1987; 3, EPA 1975; 4, NAS 1980; 5, Nielsen 1986; 6, Thompson et al. 1976; 7, Birge and Black 1977; 8, Weeth et al. 1981; 9, Brockman et al. 1985; 10, Seal and Weeth 1980; 11, Green and Weeth 1977; 12, Siegel and Wason 1986; 13, Benson et al. 1984; 14, Schillinger et al. 1982; 15, Krasovskii et al. 1976; 16, Anonymous 1983; 17, Hoffman et al. 1989; 18, Smith and Anders 1989.

In mammals, excessive boron consumption results in a reduced growth rate and sometimes loss in body weight; these may not be entirely due to reduced feed and water consumption (Table 9; Seal and Weeth 1980). Growth retardation has been reported in cattle Even 150 mg B/L drinking water (about 15 mg B/kg BW daily), in dogs consuming diets containing 1,760 mg B/kg, in rabbits eating rations equivalent to > 140 mg B/kg BW daily, and in rats given 150 mg B/L drinking water or 1,060 mg B/kg diet (Table 9). In some instances, animals will avoid B-contaminated drinking water if given a choice. Rats, for example, will reject drinking water containing as little as 1.0 mg B/L (Dixon et al. 1976), and cattle will avoid water containing > 29 mg B/L (Green and Weeth 1977).

Male workers engaged in boric acid production showed weakened sexual activity, decreased seminal volume, low sperm count and motility, and increased seminal fructose (EPA 1975). Adverse effects on reproduction of laboratory animals have been reported in sensitive species fed diets containing more than 1,000 mg B/kg, given drinking water containing 1.0 mg B/L (equivalent to about 0.3 mg B/kg BW daily), or given a single oral dose of 3,000 mg B/kg BW on the first day of pregnancy (Table 9).

Volatile boron compounds, especially boranes, are usually more toxic than boric acid or soluble borates (Table 9; NAS 1980). However, there is little commercial production of synthetic boranes, except for sodium borohydride—one of the least toxic boranes (Sprague 1972). Boron trifluoride is a gas used as a catalyst in several industrial systems, but on exposure to moisture in air it reacts to form a stable dihydride (Busch et al. 1086). For boric oxide dusts, occupational exposures to 4.1 mg/m^3 (range 1.2 to 8.5), are associated with eye irritation; dryness of mouth, nose and throat; sore throat; and cough (Garabrant et al. 1984).

No requirement for boron in mammals is known. Boron may accumulate in tissues because of slow excretion rates, although the significance of elevated residues is largely unknown (EPA 1975). Boron dietary

supplements to postmenopausal women age 48 to 82 years induced changes consistent with the prevention of calcium loss and bone demineralization (Nielson et al. 1987). In cattle, increases in boron ingestion were associated with elevated boron levels in plasma and urine, increased boron excretion, decreased plasma phosphate concentrations, and increased renal and urinary clearance of phosphates (Weeth et al. 1981). Boron accumulations in rat testes were associated with progressive germ cell depletion that persisted long after toxic exposure to boron had occurred (Lee et al. 1978).

Boron effectively counteracts symptoms of fluoride intoxication in humans (Zhou et al. 1987) and in experimentally poisoned rabbits (Elsair et al. 1980a, 1980b, 1981). Men suffering from skeletal fluorosis experienced 50 to 80% improvement after drinking solutions containing 300 to 1,100 mg of borax/L daily, 3 weeks a month for 3 months (Zhou et al. 1987). Boron enhances sequestration of fluoride from bone and excretion through kidneys and possibly the intestinal tract (Elair et al. 1980a, 1981).

Recommendations

Many boron criteria have been proposed for the protection of crops, aquatic life, waterfowl, livestock, and human health (Table 10).

Boron concentrations in contaminated industrial effluents seldom exceed 1.0 mg B/L, a level considered nonhazardous to aquatic life (Table 10; Thompson et al. 1976). However, future accumulations of boron in groundwaters through wider uses of B-containing cleansing agents may adversely affect aquatic organisms and other species of plants and animals, as now occurs in areas where natural boron deposits exist (EPA 1975). Long-term monitoring of groundwaters and surface waters for boron levels seems warranted.

Results of chronic feeding studies using mallards demonstrate that diets containing 13 mg B/kg FW produce no adverse effects, but those containing 30 or 100 mg B/kg FW are associated with elevated tissue boron residues and growth reduction, and diets containing 1,000 mg B/kg are fatal (Table 10). More research is needed on the fate and effects of boron on waterfowl and raptors, especially in those areas where high dietary boron loadings are encountered as a result of agricultural drainwater disposal practices.

Minimum concentrations of dietary boron needed to maintain animal health are not known with certainty. However, diets containing < 0.4 mg B/kg FW may adversely affect metabolism of rats and chicks; accordingly, animal diets should contain >0.3 mg B/kg FW until necessary feeding data become available (Nielsen 1986). Also, the defensible boron maximum for livestock drinking water may be considerably higher than 5 mg/L (Table 10) because several “safe” water sources in Nevada exceeded this upper maximum and approached 80 mg B/L (Green and Weeth 1977). Data are unavailable on boron effects on terrestrial wildlife. Until these data become available, it seems reasonable to apply the same criteria proposed for livestock protection (Table 10) to mammalian wildlife; that is, diets should contain more than 0.4 mg B/kg DW but less than 100 mg/kg, and drinking water < 5 mg/L.

Medicinal use of boric acid and borax for babies has resulted in anorexia, nausea, vomiting, diarrhea, marked cardiac weakness, a red eruption over the entire body, and (rarely) death (NAS 1980). The medical community has abandoned the use of boric acid solutions as irritants and antiseptics (Siegel and Wason 1486), abandoned all medical uses in Denmark (Egfjord et al. 1988), and severely limited availability (prescription only) in Ireland (O'Sullivan and Taylor 1983). Increased use of boric acid as a household pesticide should be viewed with concern, especially in households where children have access to nonsafety-capped boric acid containers (Siegel and Wason 1986).

The fact that boron is essential to plants is firmly established (NAS 1980). However, when boron concentrations in irrigation waters exceed 2 mg/L, extensive plant toxicity should be expected (Pagenkopf and Connolly 1982). High boron concentrations in some potential irrigation waters in the western United States (at levels capable of causing crop damage) have prompted implementation of boron criteria for irrigation waters (Table 10), although no legally enforceable boron standards have been promulgated (EPA 1975). Information is needed on crop plants in the following subjects: interaction of boron with other elements in the soil and its effects on boron availability to plants, the role of boron on pollination as it affects seed yield and sugar content of crops, and distinguishing signs of boron deficiency in plants from similar signs of molybdenum deficiency (Gupta and Macleod 1982).

Acknowledgments

I thank N. A. Bushby, L. J. Garrett, and J. Haber Corley for technical services; B. A. Roberts for secretarial help; N. C. Coon, D. J. Hoffman, A. D. Lemly, and G. J. Smith for technical review of the manuscript; and J. R. Zuboy for editorial services.

References

Ahl, T., and E. Jonsson. 1972. Boron in Swedish and Norwegian fresh waters. Ambio 1:66-70.

Aitken, R. L., and L. C. Bell. 1985. Plant uptake and phytotoxicity of boron in Australian fly ashes. Plant Soil 84:245-257.

Anonymous. 1983. Final report on the safety assessment of sodium borate and boric acid. J. Am. Coll. Toxicol. 2:87-125.

Antia, N. J., and J. Y. Cheng. 1975. Culture studies on the effects from borate pollution on the growth of marine phytoplankters. J. Fish. Res. Board Can. 32:2487-2494.

Belver, A., and J. P. Donaire. 1987. Phospholipid metabolism in roots and microsomes of sunflower seedlings: inhibition of choline phosphotransferase activity by boron. Phytochemistry (Oxf.) 26:2923-2927.

Benson, W. H., W. J. Birge, and H. W. Dorough. 1984. Absence of mutagenic activity of sodium borate (borax) and boric acid in the *Salmonella* preincubation test. Environ. Toxicol. Chem. 3:209-214.

Birge, W. J., and J. A. Black. 1977. Sensitivity of vertebrate embryos to boron compounds. U.S. Environ. Prot. Agency Rep. 560/1-76-008. 66 pp.

Boyd, C. E., and W. W. Walley. 1972. Studies of the biogeochemistry of boron. I. Concentrations in surface waters, rainfall and aquatic plants. Am. Midl. Nat. 88:1-14.

Brockman, R. P., R. J. Audette, and M. Gray. 1985. Borax toxicity. Can. Vet. J. 26:147.

Brotherton, R. J., and H. Steinberg, editors. 1970a. Progress in boron chemistry. Vol. 2. Pergamon Press, New York. 299 pp.

Brotherton, R. J., and H. Steinberg, editors. 1970b. Progress in boron chemisty. Vol. 3. Pergamon Press, New York. 392 pp.

Butterwick, L., N. De Oude, and K. Raymond. 1989. Safety assessment of boron in aquatic and terrestrial environments. Ecotoxicol. Environ. Safety 17:339-371.

Cayton, M. T. C. 1985. Boron toxicity in rice. Int. Rice Res. Inst., Res. Pap. Ser. 113:3-10.

Chatterjee, C., P. Sinha, N. Nautiyal, S. C. Agarwala, and C. P. Sharma. 1987. Metabolic changes associated with boron-calcium interactions in maize. Soil Sci. Plant Nutr. 33:607-617.

Combrink, N. J. J., and E. A. Davies. 1987. Effect of Ca, K and B supply on growth of cotton (*Gossypium hirsutum* L.) and tobacco (*Nicotiana tabacum* L.). S. Afr. J. Plant Soil 4:143-144.

Cox, J. A., G. C. Lundquist, A. Przyjazmy, and C. D. Schmulback. 1978. Leaching of boron from coal ash. Environ. Sci. & Technol. 12:722-723.

Crandall, P. C., J. D. Chamberlain, and J. K. L. Garth. 1981. Toxicity symptoms and tissue levels associated with excess boron in trees. Comm. Soil Sci. Plant. Anal. 12:1047-1057.

Dani, H. M., H. S. Saini, 1. S. Allag, B. Singh, and K. Sareen. 1971. Effect of boron toxicity on protein and nucleic acid contents of rat tissues. Res. Bull. (N.S.) Panjab Univ. 22:229-235.

Dear, B. S., and J. Lipsett. 1987. The effect of boron supply on the growth and seed production of subterranean clover (*Trifolium subterraneum* L.). Aust. J. Agric. Res. 38:537-546.

Dixon, R. L., I. P. Lee, and R. J. Sherins. 1976. Methods to assess reproductive effects of environmental chemicals: studies of cadmium and boron administered orally. Environ. Health Perspect. 13:59-67.

Dye, M. H., L. Buchanan, F. D. Dorofaeff, and F. G. Beecroft. 1983. Die-back of apricot trees following soil application of boron. N.Z. J. Exp. Agric. 11:331-342.

Eaton, F. M. 1944. Deficiency, toxicity, and accumulation of boron in plants. J. Agric. Res. 69:237-277.

Egfjord, M., J. A. Jansen, H. Flachs, and J. S. Schou. 1988. Combined boric acid and cinchocaine chloride poisoning in a 12-month-old infant: evaluation of haemodialysis. Hum. Toxicol. 7:175-178.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Elsair, J., R. Merad, R. Denine, M. Azzouz, K. Khelfat, M. Hamrour, B. Alamir, S. Benali, and M. Reggabi. 1981. Boron as antidote to fluoride: effect on bones and claws in subacute intoxication of rabbits. Fluoride 14:21-29.

Elsair, J., R. Merad, R. Denine, M. Reggabi, S. Benali, M. Azzouz, K. Khelfat, and M. T. Aoul. 1980a. Boron as an antidote in acute fluoride intoxication in rabbits: its action on the fluoride and calcium-phosphorus metabolism. Fluoride 13:30-38.

Elsair, J., R. Merad, R. Denine, M. Reggabi, B. Alamir, S. Benali, M. Azzouz, and K. Khelfat. 1980b. Boron as a preventive antidote in acute and subacute fluoride intoxication in rabbits: its action on fluoride and calcium-phosphorus metabolism. Fluoride 13:129-138.

Emin, D., T. Aselage, C. L. Beckel, I. A. Howard, and C. Wood, editors. 1986. Boron-rich solids. American Inst. Physics, 21 Congress St., Salem, Mass. 389 pp.

Environmental Protection Agency (EPA). 1975. Preliminary investigation of effects on the environment of boron, indium, nickel, selenium, tin, vanadium and their compounds. Vol. 1. Boron. U.S. Environ. Prot. Agency Rep. 56/2-75-005A. 111 pp.

Evans, C. M., and D. L. Sparks. 1983. On the chemistry and mineralogy of boron in pure and in mixed systems: a review. Comm. Soil Sci. Plant Anal. 14:827-846.

Fernandez, E., E. Sanchez, 1. Bonilla, P. Mateo, and P. Ortega. 1984. Effect of boron on the growth and cell composition of *Chorella pyrenoidosa*. Phyton 44:125-131.

Francois, L. E. 1986. Effect of excess boron on broccoli, cauliflower, and radish. J. Am. Hort. Soc. 111:494-498.

Frick, H. 1985. Boron tolerance and accumulation in the duckweed, *Lemna* minor. J. Plant Nutr. 8:1123-1129.

Garabrant, D. H., L. Bernstein, J. M. Peters, and T. J. Smith. 1984. Respiratory and eye irritation from boron oxide and boric acid dusts. J. Occup. Med. 26:584-586.

Garabrant, D. H., L. Bernstein, J. M. Peters, T. J. Smith, and W E. Wright. 1985. Respiratory effects of borax dust. Br. J. Ind. Med. 42:831-837.

Gersich, F. M. 1984. Evaluation of a static renewal chronic toxicity test method for *Daphnia magna* Straus using boric acid. Environ. Toxicol. Chem. 3:89-94.

Gestring, W D., and R N. Soltanpour. 1987. Comparison of soil tests for assessing boron toxicity to alfalfa. Soil Sci. Soc. Am. J. 51:1214-1219.

Gladney, E. S., L. E. Wangen, D. R Curtis, and E. T Jurney. 1978. Observations on boron release from coal-fired power plants. Environ. Sci. & Technol. 12:1084-1085.

Glaubig, B. A., and F. T. Bingham. 1985. Boron toxicity characteristics of four northern California endemic tree species. J. Environ. Qual. 14:72-77.

Goldbach, H., and A. Amberger. 1986. Influence of boron nutrition on cell wall polysaccharides in cell cultures of *Daucus carota* L. J. Plant Physiol. 123:263-269.

Goldberg, S., and R. A. Glaubig. 1986. Boron adsorption on California soils. Soil Sci. Soc. Am. J. 50:1173-1176.

Graham, R. D., R. M. Welch, D. L. Grunes, E. E. Cary, and W A. Norvell. 1987. Effect of zinc deficiency on the accumulation of boron and other mineral nutrients in barley. Soil Sci. Soc. Am. J. 51:652-657.

Green, G. H., and H. J. Weeth. 1977. Responses of heifers ingesting boron in water. J. Anim. Sci. 46:812-818.

Greenwood, N. N., and B. S. Thomas. 1973. The chemistry of boron. Pergamon Press, Elmsford, New York. 326 pp.

Grimes, R. N., editor. 1982. Metal interactions with boron clusters. Plenum Press, New York. 327 pp.

Gupta, A. P., and M. D. Parrish. 1984. Effectiveness of a new boric acid bait (roach killer cream) on German cockroach (*Blattella germanica*) populations in urban dwellings. Uttar Pradesh J. Zool. 4:51-56.

Gupta, U. C. 1979. Boron nutrition of crops. Adv. Agron. 31:273-307.

Gupta, U. C. 1983. Boron deficiency and toxicity symptoms for several crops as related to tissue boron levels. J. Plant Nutr. 6:387-395.

Gupta, U. C., and J. A. Cutcliffe. 1985. Boron nutrition of carrots and table beets grown in a boron deficient soil. Comm. Soil Sci. Plant Anal. 16:509-516.

Gupta, U. C., Y W Jame, C. A. Campbell, A. J. Leyshon, and W. Nicholaichuk. 1985. Boron toxicity and deficiency: a review. Can. J. Soil Sci. 65:381-409.

Gupta, U C., and J. A. Macleod. 1982. Role of boron in crop production. Ind. J. Agric. Chem. 15:117-132.

Hamada, T., K. Aoki, T. Kobayashi, and K. Kanda. 1983. The in vivo measurement of the time-dependent 10B movement in tumor of hamsters. Annu. Rep. Res. Reactor Inst. Kyoto Univ. 16:112-116.

Hatanaka, H., editor. 1986. Boron-neutron capture therapy for tumors. MTP Press, 101 Philip Dr., Norwell, Mass. 463 pp.

Heller, G. 1986. A survey of structural types of borates and polyborates. Pages 39-100 *in* F. L. Boschke, ed. Structural chemistry of boron and silicon. Springer-Verlag, Berlin.

Hermanek, S., editor. 1987. Sixth international meeting on boron chemistry. World Scientific Publ. Co., Teaneek, New Jersey. 509 pp.

Hingston, F. J. 1986. Biogeochemical cycling of boron in native eucalypt forests of south-western Australia. Aust. For. Res. 16:73-83.

Hoffman, D. J., M. B. Camardese L. J. LeCaptain, and G. W Pendleton. 1990. Effects of boron on growth and physiology in mallard ducklings. Environ. Toxicol. Chem. 9:335-346.

Hoffman, D. J., H. M. Ohlendorf, and T. W. Aldrich. 1988. Selenium teratogenesis in natural populations of aquatic birds in central California. Arch. Environ. Contam. Toxicol. 17:519-525.

Hopmans, P., and D. W. Flinn. 1984. Boron deficiency in *Pinus radiata* D. Don and the effect of applied boron on height growth and nutrient uptake. Plant Soil 79:295-298.

Jansen, J. A., J. Andersen, and J. S. Schou. 1984. Boric acid single dose pharmacokinetics after intravenous administration to man. Arch. Toxicol. 55:64-67.

Jenkins, D. W 1980. Biological monitoring of toxic trace metals. Vol. 2. Toxic trace metals in plants and animals of the world. Part 1. U.S. Environ. Prot. Agency Rep. 600/3-80-090:150-171.

Klaassen, C. D., M. 0. Amdur, and J. Doull, editors. 1986. Casarett and Doull's toxicology. Third edition. Macmillan Publ., New York. 974 pp.

Klasing, S. A., and S. M. Pilch. 1988. Agricultural drainage water contamination in the San Joaquin Valley: a public health perspective for selenium, boron, and molybdenum. Available from San Joaquin Valley Drainage Program, 2800 Cottage Way, Sacramento, Calif. 135 pp.

Kluge, R., and W Podlesak. 1985. Plant critical levels for the evaluation of boron toxicity in spring barley (*Hordeum vulgare* L.). Plant Soil 83:381-388.

Kobayashi, N. 1971. Fertilized sea urchin eggs as an indicatory material for marine pollution bioassay, preliminary experiments. Publ. Seto Mar. Biol. Lab. 18:379-406.

Korty, P., and W. N. Scott. 1970. Effects of boranes upon tissues of the rat. II. Tissue amino acid content in rats on a normal diet. Proc. Soc. Exp. Biol. Med. 135:629-632.

Krasovskii, G. N., S. P. Varshavskaya, and A. I. Borisov. 1976. Toxic and gonadotropic effects of cadmium and boron relative to standards for these substances in drinking water. Environ. Health Perspect. 13:69-75.

Landauer, W. 1952. Malformations of chicken embryos produced by boric acid and the probable role of riboflavin in their origin. J. Exp. Zool. 120:469-508.

Landauer, W 1953a. Genetic and environmental factors in the teratogenic effects of boric acid on chicken embryos. Genetics 38:216-228.

Landauer, W. 1953b. Complex formation and chemical specificity of boric acid in production of chicken embryo malformations. Proc. Soc. Exp. Bio. Med. 82:633-636.

Landauer, W. 1953c. Abnormality of down pigmentation associated with skeletal defects of chicks. Proc. Nat. Acad. Sci. USA 39:54-58.

Landauer, W, and E. M. Clark. 1964. On the role of riboflavin in the teratogenic activity of boric acid. J. Exp. Zool. 156:307-312.

Landolph, J. R. 1985. Cytotoxicity and negligible genotoxicity of borax ores to cultured mammalian cells. Am. J. Ind. Med. 7:31-43.

Lee, 1. P., R. J. Sherins, and R. L. Dixon. 1978. Evidence for induction of germinal aplasia in male rats by environmental exposure to boron. Toxicol. Appl. Pharmacol. 45:577-590.

Lewis, M. A., and L. C. Valentine. 1981. Acute and chronic toxicities of boric acid to *Daphnia magna* Straus. Bull. Environ. Contam. Toxicol. 27:309-315.

Liddicoat, M. I., D. R. Turner, and M. Whitfield. 1983. Conservative behaviour of boron in the Tamar estuary. Estuarine Coastal Shelf Sci. 17:467-472.

Lipsett, J., A. Pinkerton, and D. J. David. 1979. Boron deficiency as a factor in the reclamation by liming of a soil contaminated by mine waste. Environ. Pollut. 20:231-240.

Lizzio, E. F. 1986. A boric acid-rodenticide mixture used in the control of coexisting rodent-cockroach infestations. Lab. Anim. Sci. 36:74-76.

Maeso, E. S., E. F. Valiente, 1. Bonilla, and P. Mateo. 1985. Accumulation of proteins in giant cells, induced by high boron concentrations in *Chlorella pyrenoidosa*. J. Plant Physiol. 121:301-311.

Magour, S., P. Schramel, J. Ovcar, and H. Maser. 1982. Uptake and distribution of boron in rats: interaction with ethanol and hexobarbital in the brain. Arch. Environ. Contam. Toxicol. 11:521-525.

Martinez, F., P. Matio, 1. Bonilla, and E. Fernandez-Valiente. 1986a. Cellular changes due to boron toxicity in the blue-green alga *Anacystis nidulans*. Phyton 46:145-152.

Martinez, F., P. Mateo, I. Bonilla, E. Fernandez-Valiente, and A. Garate. 1986b. Growth of *Anacystis nidulans* in relation to boron supply. Isr. J. Bot. 35:17-21.

Mateo, P., F. Martinez, 1. Bonilla, E. F. Valiente, and E. S. Maeso. 1987. Effects of high boron concentrations on nitrate utilization and photosynthesis in blue-green algae *Anabaena* PCC 7119 and *Anacystis nidulans*. J. Plant Physiol. 128:161-168.

Mitchell, R. J., H. E. Garrett, G. S. Cox, A. Atalay, and R. K. Dixon. 1987. Boron fertilization, ecotomycorrhizal colonization, and growth of *Pinus echinata* seedlings. Can. J. For. Res. 17:1153-1156.

Mozafar, A. 1987. Effect of boron on ear formation and yield components of two maize (*Zea mays* L.) hybrids. J. Plant Nutr. 10:319-332.

Naeger, L. L., and K. C. Leibman. 1972. Mechanisms of decaborane toxicity. Toxicol. Appl. Pharmacol. 22:517-527.

Narvekar, P. V., M. D. Zingde, and V. N. K. Dalal. 1983. Behaviour of boron, calcium and magnesium in a polluted estuary. Estuarine Coastal Shelf Sci. 16:9-16.

National Academy of Sciences (NAS). 1980. Boron. Pages 71-83 *in* Mineral tolerance of domestic animals. Natl. Acad. Sci., Natl. Res. Coun., Comm. Anim. Nutr. Washington, D.C.

Nicholaichuk, W., A. J. Leyshon, Y. W. Jame, and C. A. Campbell. 1988. Boron and salinity survey of irrigated projects and the boron adsorption characteristics of some Saskatchewan soils. Can. J. Soil Sci. 68:77-90.

Niedenzu, K., and S. Trofimenko. 1986. Pyrazole derivatives of boron. Pages 1-37 *in* F. L. Boschke, ed. Structural chemistry of boron and silicon. Springer-Verlag, Berlin.

Nielsen, F. H. 1986. Other elements: Sb, Ba, B, Br, Cs, Ge, Rb, Ag, Sr, Sn, Ti, Zr, Be, Bi, Ga, Au, In, Nb, Sc, Te, Tl, W. Pages 415-463 *in* W. Mertz, ed. Trace elements in human and animal nutrition. Vol. 2. Academic Press, New York.

Nielsen, F. H., C. D. Hunt, L. M. Mullen, and J. R. Hunt. 1987. Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. FASEB J. 1:394-397.

Nuttall, W. F., H. Ukrainetz, J. W. B. Stewart, and D. T. Spurr. 1987. The effect of nitrogen, sulphur and boron on yield and quality of rapeseed (*Brassica napus* L. and *B. campestris* L.). Can. J. Soil Sci. 67:545-559.

Ohlendorf, H. M., D. J. Hoffman, M. K. Saiki, and T. W. Aldrich. 1986. Embryonic mortality and abnormalities of aquatic birds: apparent impacts of selenium from irrigation drainwater. Sci. Total Environ. 52:49-63.

Okay, O., H. Guclu, E. Soner, and T. Balkas. 1985. Boron pollution in the Simav River, Turkey and various methods of boron removal. Water Res. 19:857-862.

O'Sullivan, K., and M. Taylor. 1983. Chronic boric acid poisoning in infants. Arch. Dis. Child. 58:737-739.

Pagenkopf, G. K., and J. M. Connolly. 1982. Retention of boron by coal ash. Environ. Sci. & Technol. 16:609-613.

Papachristou, E., R. Tsitouridou, and B. Kabasakalis. 1987. Boron levels in some groundwaters of Halkidiki (a land at northern Aegean Sea). Chemosphere 16:419-427.

Parry, R. W., and G. Kodama, editors. 1980. Boron chemistry-4. Pergamon Press, New York. 161 pp.

Petracek, P. D., and C. E. Sams. 1987. The influence of boron on the development of broccoli plants. J. Plant Nutr. 10:2095-2107.

Pilbeam, D. J., and E. A. Kirkby. 1983. The physiological role of boron in plants. J. Plant Nutr. 6:563-582.

Ransome, C. S., and R. H. Dowdy. 1987. Soybean growth and boron distribution in a sandy soil amended with scrubber sludge. J. Environ. Qual. 16:171-175.

Rao, D. V. S. 1981. Effect of boron on primary production of nanoplankton. Can. J. Fish. Aquat. Sci. 38:52-58.

Rerkasem, B. I R. Netsangtip, R. W. Bell, J. F. Loneragen, and N. Hiranburana. 1988. Comparative species responses to boron on a typic tropaqualf in northern Thailand. Plant Soil 106:15-21.

Ridgeway, L. P., and D. A. Karnofsky. 1952. The effects of metals on the chick embryo: toxicity and production of abnormalities in development. Ann. N.Y. Acad. Sci. 55:203-215.

Riley, M. M. 1987. Boron toxicity in barley. J. Plant Nutr. 10:2109-2115.

Rusch, G. M., G. M. Hoffman, R. F. McConnell, and W. E. Rinehart. 1986. Inhalation toxicity studies with boron trifluoride. Toxicol. Appl. Pharmacol. 83:69-78.

Sage, R. F., S. L. Ustin, and S. J. Manning. 1989. Boron toxicity in the rare serpentine plant, *Streptanthus morrisonii*. Environ. Pollut. 61:77-93.

Schillinger, B. M., M. Berstein, L. A. Goldberg, and A. R. Shalita. 1982. Boric acid poisoning. J. Am. Acad. Dermatol. 7:667-673.

Schowing, J., and P. Cuevas. 1975. Teratogenic effects of boric acid upon the chick. Macroscopic results. Teratology 12:334.

Schowing, J., P. Cuevas, and J. Ventosa. 1976. Influence de l'acide borique sur]e developpment de 1'embryon de poulet traite a un stade precoce resultats preliminaires. Arch. Biol. (Brussels) 87:385-392.

Schuler, C. A. 1987. Impacts of agricultural drainwater and contaminants on wetlands at Kesterson Reservoir, California. M.S. thesis, Oregon State University, Corvallis. 136 pp.

Seal, B. S., and H. J. Weeth. 1980. Effect of boron in drinking water on the male laboratory rat. Bull. Environ. Contam. Toxicol. 25:782-789.

Settimi, L., E. Elovaara, and H. Savolaninen. 1982. Effects of extended peroral borate ingestion on rat liver and brain. Toxicol. Lett. 10:219-223.

Shapiro, M., and R. A. Bell. 1982. Enhanced effectiveness of *Lymantria dispar* (Lepidoptera: Lymantriidae) nucleopolyhedrosis virus formulated with boric acid. Ann. Entomol. Soc. Am. 75:346-349.

Shorrocks, V. M., and D. D. Nicholson. 1980. The influence of boron deficiency on fruit quality. Acta Hortic. 92:103-108.

Siegel, E., and S. Wason. 1986. Boric acid toxicity. Pediatr. Clin. North Am. 33:363-367.

Slatkin, D., P. Micca, A. Forman, D. Gabel, L. Wielopolski, and R. Fairchild. 1986. Boron uptake in melanoma, cerebrum and blood from $Na_2B_{I2}H_{11}SH$ and $Na_4B_{24}H_{22}S_2$ administered to mice. Biochem. Pharmacol. 35:1771-1776.

Smith, G. J., and V. P. Anders. 1989. Toxic effects of boron on mallard reproduction. Environ. Toxicol. Chem. 8:943-950.

Smith, K., editor. 1985. Organometallic compounds of boron. Chapman and Hall, New York. 304 pp.

Smyth, D. A., and W. M. Dugger. 1980. Effects of boron deficiency on ^{86} rubidium uptake and photosynthesis in the diatom *Cylindrotheca fusiformis* . Plant Physiol 66:692-695.

Smyth, D. A., and W. M. Dugger. 1981. Cellular changes during boron-deficient culture of the diatom *Cylindrotheca fusiformis*. Physiol. Plant. 51:111-117.

Sprague, R. W. 1972. The ecological significance of boron. United States Borax and Chemical Corp., Los Angeles. 58 pp.

Steinberg, H., and A. L. McCloskey, editors. 1964. Progress in boron chemistry. Vol. 1. Pergamon Press, New York. 487 pp.

Taylor, D., B. G. Maddock, and G. Mance. 1985. The acute toxicity of nine grey list metals (arsenic, boron, chromium, copper, lead, nickel, tin, vanadium and zinc) to two marine fish species: dab (*Limanda limanda*) and grey mullet (*Chelon labrosus*). Aquat. Toxicol. 7:135-144.

Thompson, J. A. J., J. C. Davis, and R. E. Drew. 1976. Toxicity, uptake and survey studies of boron in the marine environment. Water Res. 10:869-875.

Walker, W. M., D. W. Grains, and C. D. Faulkner. 1987. Effect of potassium and boron upon yield and nutrient concentration of alfalfa. J. Plant Nutr. 10:2169-2180.

Weeth, H. J., C. F. Speth, and D. R. Hanks. 1981. Boron content of plasma and urine as indicators of boron intake in cattle. Am. J. Vet. Res. 42:474-477.

Weir, R. J., Jr., and R. S. Fisher. 1972. Toxicologic studies on borax and boric acid. Toxicol. Appl. Pharmocol. 23:351-364.

Willett, I. R., P. Jakobsen, and B. A. Zarcinas. 1985. Nitrogen-induced boron deficiency in lucerne. Plant Soil 86:443-446.

Wright, C. G., and H. E. Dupree, Jr. 1982. Efficacy of experimental formulations of acephate, boric acid, encapsulated diazinon, permethrin, pirimphos-methyl, and propetamphos in control of German cockroaches. J. Ga. Entomol. Soc. 17:26-32

Zhou, L. Y., Z. D. Wei, and S. Z. Ldu. 1987. Effect of borax in treatment of skeletal fluorosis. Fluoride 20:24-27

Biological Report 85(1.21)
July 1990

Contaminant Hazard Reviews
Report 21

Chlordane Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

By
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

Tables

Suggested citation for this report:

Eisler, R. 1990. Chlordane hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. Fish Wildl. Serv., Biol. Rep 85 (1.21).

Abstract

ABSTRACT.-Technical chlordane is an organochlorine compound first introduced into the United States in 1947 in a variety of formulations for use as a broad-spectrum pesticide. By 1974, about 9.5 million kilograms of chlordane were produced annually. Concern over the potential carcinogenicity of chlordane has led to sharply curtailed production. Since 1983, chlordane use in the United States has been prohibited, except for control of underground termites.

Technical chlordane consists of about 45 components, primarily *cis*-chlordane (19%), *trans*-chlordane (24%), heptachlor (10%), *cis*- and *trans*-nonachlor (7%), and various chlordane isomers (22%). Chemical analysis of technical chlordane is difficult because of analytical interferences from other organochlorine compounds, nonstandardization of analytical techniques, variations in the number and relative composition of components in weathered chlordane, and, uncertainty of structural formulas and other properties of several compounds present.

Past chlordane use, coupled with atmospheric transport as the major route of dissemination, produced global contamination of fish and wildlife resources and human populations. The chemical and its metabolites were frequently detected in all species examined, but usually at low concentrations. Residues in fish muscle sometimes exceeded the U.S. Food and Drug Administration action level of 0.3 mg/kg fresh weight recommended for human health protection. In general, chlordane in animals is highest near areas where the chemical has been applied to control termites; concentrations are highest in fat and liver, especially in predatory species.

The half-life of chlordane in water is comparatively short; *cis*-chlordane, for example, usually persists less than 18 h in solution. In soils, however, some chlordane isomers persist for 3 to 14 years because of low solubility in water, high solubility in lipids, and relatively low vapor pressure. There seems to be little accumulation of chlordane in crops grown in contaminated soils.

Chlordane is readily absorbed by warm-blooded animals through skin, diet, and inhalation, and distributed throughout the body. In general, residues of chlordane and its metabolites are not measurable in tissues 4 to 8 weeks after exposure, although metabolism rates varied significantly between species. Food chain biomagnification is usually low, except in some marine mammals. In most mammals, the metabolite oxychlordane has proven much more toxic and persistent than the parent chemical.

Many species of aquatic organisms are adversely affected at concentrations in water between 0.2 and 3.0 µg/L technical chlordane. Sensitive bird species had reduced survival on diets containing 1.5 mg chlordane per kilogram in their diet, or after a single oral dose as low as 14.1 mg chlordane per kilogram body weight. Chlordane has produced liver cancer in laboratory strains of domestic mice, but carcinogenicity has not been established in other mammals.

Chlordane criteria for protection of marine life (0.004 µg/L, 24-h mean; not to exceed 0.09 µg/L) seem satisfactory. Proposed criteria for freshwater life protection (0.0043 µg/L, 24-h mean; not to exceed 2.4 µg/L) however, overlap the range of 0.2 to 3.0 µg/L shown to adversely affect certain fish and aquatic invertebrates, suggesting that some downward modification in the maximum permissible level is needed. Chlordane criteria for protection of birds and mammals are inadequate because the data base is incomplete. Until these data become available, a reasonable substitute is the criteria proposed for human health protection, namely, daily intake not to exceed 0.001 mg chlordane per kilogram body weight, and diet not to exceed 0.3 mg chlordane per kilogram fresh weight.

Most authorities agree that more studies are needed in several areas: monitoring of oxychlordane concentrations in wildlife; interpretation of the biological significance of residue levels found in wildlife; standardization of analytical extraction and other techniques for quantitation of chlordane and its metabolites; reexamination of aquatic toxicity data where test concentrations exceeded the solubility of chlordane in water (6 to 9 µg/L); interaction effects with other agricultural chemicals; reevaluation of the cancer risk of chlordane on representative organisms at realistic environmental levels; effects of depleted soil fertility from chlordane-induced earthworm suppression; and continuance of epidemiological studies on exposed workers.

Technical chlordane is a mixture of chlorinated hydrocarbons that has been used as an insecticide since its introduction in 1947. Chlordane was the first cyclodiene insecticide to be used in agriculture and was the second most important organochlorine insecticide in the United States in 1976-77, behind toxaphene, with an estimated annual production of 9 million kilograms (Nomeir and Hajjar 1987). Chlordane is now the leading insecticide in controlling termites, with about 1.2 million homes in the United States alone treated annually for this purpose (Nomeir and Hajjar 1987).

Chlordane has been detected in human milk in Canada, Hawaii, Japan, Mexico, Mississippi, and Spain (World Health Organization [WHO] 1984; Ohno et al. 1986). Chlordane compounds have been detected in oysters from the South Atlantic Ocean and Gulf of Mexico, in fish from the Great Lakes and major river basins of the United States, in the blubber of cetaceans from the coastal waters of North America, and the Antarctic atmosphere (Kawano et al. 1988). In fact, all available evidence suggests that chlordane is ubiquitous in the environment. Air and water transport of technical chlordane has resulted in the detection of chlordane and its metabolites in rainwater, drinking water, air, surface waters, soils, sediments, plankton, earthworms, fish, shellfish, birds and their eggs, aquatic invertebrates, cats, dogs, livestock, and humans (Zitko 1978; Environmental Protection Agency 1980; Sudershan and Khan 1980; Kerkhoff and Boer 1982; Wickstrom et al. 1983; Johnson et al. 1986; Nomeir and Hajjar 1987; Suzaki et al. 1988). Despite its widespread use, persistence, and tendency to accumulate in fat, there was no firm evidence of direct lethal or sublethal effects on terrestrial vertebrate wildlife until Blus et al. (1983) recorded several chlordane-related mortalities. A North Dakota marsh treated with chlordane had decreased reproductive success and some deaths of young of several bird species but this was attributed to depletion of invertebrate prey and not to acute poisoning (Hanson 1952). More recently, chlordane was implicated as the principal toxicant in 30 pesticide poisoning cases of hawks, owls, herons, and other birds in New York between 1982 and 1986 (Stone and Okoniewski 1988).

The U.S. Environmental Protection Agency (EPA) considers chlordane as a probable human carcinogen (defined as inadequate evidence from human studies and sufficient evidence from animal studies), as judged by chlordane-induced cancer of the liver in domestic mice (Arruda et al. 1987). In 1978, EPA restricted chlordane use to subterranean termite control, nonfood plants, and root dip. Limited agricultural use was permitted until 1980. In 1987, EPA registered chlordane again, limiting its sale and use to licensed applicators for subterranean termite control (Arruda et al. 1987). However, it seems that significant home and garden use exists, especially for control of termites and undesirable lawn insects (Wood et al. 1986). Reviews on ecological and toxicological aspects of chlordane in the environment are available; particularly useful are those by Ingle (1965), Menzie (1974), National Research Council of Canada [NRCC] (1975), International Agency for Research on Cancer [IARC] (1979), EPA (1980, 1988), WHO (1984), Klaassen et al. (1986), and Nomeir and Hajjar (1987).

This report was prepared in response to requests for information on chlordane from regional environmental contaminant specialists of the U.S. Fish and Wildlife Service. It is part of a continuing series of brief reviews on chemicals in the environment, with emphasis on fishery and wildlife resources.

Chemical and Biochemical Properties

Technical chlordane (64 to 67 % chlorine) is produced by the condensation of cyclopentadiene and hexachlorocyclopentadiene to yield chlordene (Figure). Addition of chlorine across the 2-3 olefinic bond of chlordene forms *cis*-chlordane and *trans*-chlordane; substitution of chlorine into position 1 of chlordene forms heptachlor, and further addition of chlorine across the 2-3 olefinic bond forms *cis*-nonachlor and *trans*-nonachlor (Ribick and Zajicek 1983). Technical chlordane includes about 45 components. Its approximate composition is 19% *cis*-chlordane ($C_{10}H_6Cl_8$), 24% *trans*-chlordane ($C_{10}H_6Cl_8$), 21.5% chlordene isomers ($C_{10}H_6Cl_6$), 10% heptachlor ($C_{10}H_5Cl_7$), *7% cis*- and *trans*-nonachlor ($C_{10}H_5Cl_9$), 2% Diels-Alder adduct of cyclopentadiene and pentachlorocyclopentadiene, 1 % hexachlocycloropentadiene, 1 % octachlorocyclopentene, and 15.5% miscellaneous constituents (NRCC 1975; IARC 1979; EPA 1980; WHO 1984). Oxychlordane and heptachlor epoxide are toxicologically significant degradation products (Figure; Perttila et al. 1986).

Chlordane produced before 1951 contained a significant quantity of hexachlorocyclopentadiene--a toxic irritant to warm-blooded animals; chlordane produced after 1951 contains little or none of this compound (Ingle 1965). A high-purity chlordane formulation containing about 74% *cis*-chlordane and 24% *trans*-chlordane is also available (Nomeir and Hajjar 1987).

Chemical analysis of technical chlordane is difficult because of frequent variations in both the number and relative composition of components in weathered chlordane (Ribick and Zajicek 1983). Other difficulties are encountered from analytical interferences from various organochlorine compounds; furthermore, the exact structure has not been determined for a number of compounds in technical chlordane, and the majority of compounds have not been isolated or synthesized for use as comparative standards (Ribick and Zajicek 1983).

Cis-chlordane (CAS number 5103-71-9) and *trans*-chlordane (CAS number 5103-74-2) are characterized by the following properties: molecular weight of 409.76; chemical formula of ($C_{10}H_6Cl_8$); viscous, amber-colored liquid; boiling point between 104 and 105° C for *trans*-chlordane, and between 106 and 107° C for *cis*-chlordane; density of 1.59 to 1.63 at 25° C; soluble in most organic solvents, but only sparingly soluble in water, that is, 9µg/L at 25° C; vapor pressure of 0.00001 mm mercury at 25° C; and a log Kow (octanol/water partition coefficient) of 5.16 (Ingle 1965; NRCC 1975; IARC 1979; EPA 1980, 1988; WHO 1984). Pesticides containing chlordane or technical chlordane have been sold under a variety of names including 1068, Aspon, Belt, CD-68, Chlor-dan, Chlordan, Chlorindan, Chlor-kil, Chlorodane, Chlortox, Cortilanneu, Corodane, Dichlorochlordene, Dichlorodene, Dowchlor, ENT 9932, HCS 3260, Kypclor, M 140, M 410, Niran, Niran 5% granular bait, Octachlor, Octa-klor, Octaterr, Ortho-klor, Synklor, Tat Chlor 4, Topiclor 20, Toxichlor, and Velsicol 1068 (IARC 1979; Johnson and Finley 1980; Hudson et al. 1984; WHO 1984; Hill and Camardese 1986; Mayer 1987; EPA 1988).

Technical chlordane is stable under ultraviolet (UV) light, although some components, such as chlordane, heptachlor, *cis*-chlordane, and *trans*-chlordane, will form photoisomers under high intensity UV in the presence of sensitizers, such as ketones (NRCC 1975; Menzie 1978). Several compounds were measured in alfalfa grown on soils treated with chlordane, including 1,2-dichlorochlordene, oxychlordane, and photo-*cis*-chlordane, as well as the parent chlordane compounds (WHO 1984). The half-life (Tb 1/2) of *cis*-chlordane in water is comparatively short, between 1.1 and 17.5 h (Feroz and Khan 1979a). In soils, technical chlordane has a half-life ranging from 0.5 to 1.0 years for some samples, and 4 to 10 years for other samples. The lower Tb 1/2 values refer to the initial rapid disappearance of chlordane from the soil; if studies continue over several years, the remaining chlordane is relatively persistent, with a Tb 1/2 of 5 to 7 years (NRCC 1975). Measurable residues of chlordanes in soil were present more than 14 years after application (EPA 1988). Chlordane persists in soils because of its low solubility in water, relatively low vapor pressure, and high tendency to adsorb to soil particles; accordingly, soil-bound chlordanes are not likely to become serious contaminants of the lower soil strata or deep water sources (WHO 1984). Transport into the hydrosphere from contaminated soils will occur through erosion of soil particles or sediments, not by desorption and dissolution (Klaassen et al. 1986).

Chlordane is a nerve stimulant; at low chronic doses it produces hyperexcitability and lack of coordination in animals, and at high acute doses causes tremors and convulsions (Ingle 1965; Klaassen et al. 1986). Chlordane induces hepatic microsomal drug-metabolizing enzymes, resulting in enhanced biotransformation at low doses, although high doses may result in liver hypertrophy (Klaassen et al. 1986). The physiological target sites are in nerve and muscle membranes, presumably on proteins and phospholipids; the ultimate effect is axonic with membrane disruption, resulting in spasmic muscle twitching and death (Greenhalgh 1986).

Chlordane is readily absorbed by warm-blooded animals through skin, diet, and inhalation. It is quickly distributed in the body and tends to concentrate in liver and fat (WHO 1984). Up to 75% of a single oral dose of chlordane administered to rats and mice was absorbed in the gut, and up to 76% of an aerosol dose was absorbed in the respiratory tract (Nomeir and Hajjar 1987); rabbits absorbed 33% in the gut following oral administration (EPA 1988). Chlordane residues in mammals were usually not measurable 4 to 8 weeks after cessation of exposure (Ingle 1965). Chlordane persistence in human serum and whole body was estimated at 88 days and 21 days, respectively; this compares to a Tb 1/2 of about 23 days in rats fed chlordane for 56 days (EPA 1980).

Excretion kinetics of chlordane are complex, and different isomers exit through different pathways (EPA 1980, 1988). In rats, chlordane elimination was almost complete 7 days after receiving single oral doses up to 1 mg/kg body weight (BW); 24 h after treatment, 70% of the *cis*-chlordane and 60% of the *trans*-chlordane had been excreted (WHO 1984). In rodents, chlordane and its metabolites were usually excreted in feces, regardless of the administration route; the *cis*-isomer was excreted slightly faster than the *trans*-isomer, although identical metabolites seemed to be formed (EPA 1980; Menzie 1969, 1980; WHO 1984; Nomeir and

Hajjar 1987). In rabbits, however, up to 47 % of the administered dose was voided in the urine, and *cis*- and *trans*-chlordane were excreted at the same rate (Nomeir and Hajjar 1987).

Microorganisms such as *Nocardiopsis* sp., an actinomycete, can metabolize *cis*- and *trans*-chlordane to at least eight solvent-soluble substances, including dichlorochlordene, oxychlordane, heptachlor, heptachlor *endo*-epoxide, chlordene chlorohydrin, and 3-hydroxy-*trans*-chlordane (Beeman and Matsumura 1981). Based on studies of chlordane metabolism in animals, four metabolic pathways arc proposed: (1) hydroxylation to form 3-hydroxychlordane, which on dehydration forms 1,2-dichlorochlordene, with subsequent epoxidation to oxychlordane (*trans*-chlordane is converted to oxychlordane 7 times faster than is *cis*-chlordane); (2) dehydrochlorination to form heptachlor, from which heptachlor epoxide and other hydroxylation products may be formed; (3) dechlorination to monochlorodihydrochlordene; and (4) the replacement of chlorine by hydroxyl groups resulting in the formation of hydroxy metabolites, which are excreted or further transformed by conjugation with glucuronic acid (Feroz and Khan 1979a; WHO 1984; Nomeir and Hajjar 1987; EPA 1988). Metabolism of chlordanes and nonachlors to oxychlordane is orders of magnitude greater in fish-eating and carnivorous birds than in marine mammals (Kawano et al. 1988). The reasons for this are unclear and merit further research.

Trans-nonachlor, a major component of technical chlordane, was frequently found as the major chlordane residue in humans, whereas oxychlordane was the major component in rats fed technical chlordane (Nomeir and Hajjar 1987). *Trans*-nonachlor is converted efficiently by rat liver microsomes to *trans*-chlordane, but this ability is lacking in humans, resulting in the accumulation of *trans*-nonachlor in humans (Nomeir and Hajjar 1987).

Although technical chlordane is a mixture of compounds, two metabolites--heptachlor epoxide and oxychlordane--can kill birds when administered through the diet (Blus et al. 1983). These two metabolites originate from biological and physical breakdown of chlordanes in the environment, or from metabolism after ingestion. Heptachlor can result from breakdown of *cis*- and *trans*-chlordane, eventually oxidizing to heptachlor epoxide; oxychlordane can result from the breakdown of heptachlor, *cis*-chlordane, *trans*-chlordane, or *trans*-nonachlor (Blus et al. 1983). Heptachlor epoxide has been identified in soil, crops, and aquatic biota, but its presence is usually associated with the use of heptachlor, not technical chlordane--which also contains some heptachlor (NRCC 1975). Various components in technical chlordane may inhibit the formation of heptachlor epoxide or accelerate the decomposition of the epoxide, but the actual mechanisms are unclear (NRCC 1975).

In mammals, oxychlordane ($C_{10}H_4Cl_8O$) is a metabolite *of cis*- and *trans*-chlordanes and *trans*-nonachlor (Miyazaki et al. 1980), and has proven much more toxic and persistent than the parent chemicals (WHO 1984; Kawano et al. 1988). Oxychlordane has been measured in the fat of rats, dogs, and pigs fed either isomer, and in milk and cheese from cows fed alfalfa treated with technical chlordane (WHO 1984; Nomeir and Hajjar 1987; EPA 1988). Oxychlordane was isolated and identified from adipose tissues of pigs fed diets (for 90 days) containing 300 mg/kg of *cis*-chlordane or *trans*-chlordane (Schwemmer et al. 1970). Sharply elevated oxychlordane levels were detected in milk from cows fed chlordane for 60 days; when chlordane was removed from their diet, oxychlordane residues in milk dropped rapidly during the week following termination, and stabilized after 2 weeks (EPA 1980). The Tb 1/2 for oxychlordane in beef cattle grazing in heptachlor-contaminated pastures for 4 weeks was about 92 days (Petterson et al. 1988). Rats and rabbits given chlordane orally or through the diet retained the highest levels in adipose tissue, followed by liver, kidney, brain, and muscle; oxychlordane was the most persistent residue after chlordane was removed from the diet (WHO 1984; EPA 1988).

Uses

Chlordane was first produced commercially in the United States in 1947 and became available in five basic formulations, including 5% granules, oil solutions containing 2 to 200 g/L, and emulsifiable concentrates containing chlordane at 400 to 800 g/L (WHO 1984). Production of chlordane in the United States in 1971 was estimated at 11.3 million kg (Glooschenko and Lott 1977). By 1974, about 9.5 million kilograms of chlordane were used domestically to control commercial pests (35%); in homes, lawns, and gardens (30%); on corn (20%); turf (6%); potatoes (5%); tomatoes (2%); and other uses (IARC 1979). On 6 March 1978, the EPA issued a cancellation proceeding on chlordane, allowing limited use on certain crops and pests until 1 July 1983, but no use thereafter except for underground termite control (IARC 1979; EPA 1988). A similar situation exists

in Japan, where the only permitted use of chlordane is for control of termites and powder post beetles (Miyazaki et al. 1980). Use in Japan is estimated at 500,000 kg a year (Yamagishi et al. 1981 b).

In Canada, chlordane had been used in soils (usually at 0.45 to 4.5 kg/ha) against corn rootworms, strawberry root weevils, wireworms, white grubs, and subterranean cutworms infesting a wide range of crops (Glooschenko and Lott 1977). In the past, at least 75 different formulations containing chlordane as the active insecticidal ingredient had been registered for sale in Canada; the most widely sold formulation, accounting for about 60% of chlordane in soils, was the 25% granular type that was used extensively for corn rootworm control (NRCC 1975). Sales of chlordane in Canada increased about tenfold between 1969 and 1971 because of restrictions on DDT and other organochlorines; however, chlordane use was restricted in Canada in 1978 (Elliott et al. 1988).

Background Concentrations

General

Chlordanes and their metabolites are ubiquitous in the environment at low concentrations, but at a high occurrence in samples analyzed. Atmospheric transport is considered to be the major route of global dissemination. Some chlordane isomers persist in soils for 3 to 15 years, although there seems to be little accumulation of chlordanes by crop plants grown in these soils. Lengthy persistence of various chlordane isomers, especially *cis*-chlordane and *trans*-nonachlor, has been reported in certain organisms, but this has varied greatly between species and tissues.

In living organisms, chlordane concentrations are usually highest in samples collected near areas where chlordane was applied to control termites or other pests, in predatory species, and in tissues with high lipid content. Food chain biomagnification is usually low except in certain marine mammals. In some fishes, chlordane levels in muscle have been sufficient to endanger fish health (100 µg/kg fresh weight) or human consumers of fish (300 µg/kg fresh weight).

Nonbiological Samples

Air and water transport of technical chlordane has resulted in the detection of chlordane and its metabolites in nonbiological samples worldwide (Table 1). Chlordane enters the atmosphere mainly through aerial applications of dust and spray formulations, soil erosion by wind, and volatilization from soil and water (WHO 1984). In aquatic systems, chlordane enters by way of surface runoff and rainfall; chlordane is rapidly adsorbed onto bottom sediments, where it persists (WHO 1984). Atmospheric transport of chlordanes is considered the major route of global dissemination (Pyysalo et al. 1981; Wickstrom et al. 1981). Levels of chlordane compounds in the marine atmosphere of the Southern Hemisphere are nearly the same as those of DDT and its metabolites; this strongly suggests that chlordane compounds are globally distributed and dispersed (Kawano et al. 1985). The yearly input of *cis*-chlordane to the Arctic Ocean from atmospheric sources is estimated at 3,000 kg; if *cis*-chlordane constitutes 19% of technical chlordane, then more than 600,000 kg of technical chlordane has entered the Arctic Ocean since 1948 (Hoff and Chan 1986). Chlordane is frequently measured in the air of buildings where the compound has been used for insect control (WHO 1984). Chlordane has been found in household dust in the homes of farmers and pesticide formulators at exceedingly high mean levels: 5.8 to 23.1 mg/kg air-dried dust (WHO 1984).

Chlordane has been detected in both groundwater and surface water at low levels of 0.001 to 0.01 µg/L (EPA 1988). A high frequency of chlordane was detected in seawater samples collected from a Hawaiian marina: up to 90% of all samples contained *cis*-chlordane, and 68 % contained *trans*-chlordane (IARC 1979). Because of chlordane's use as a soil-injected insecticide, and its persistence, it has the potential to contaminate groundwater, particularly when it is applied near existing wells (EPA 1988).

In soils, chlordane is comparatively immobile and persistent and has only a limited capacity for translocation into edible portions of food crops (NRCC 1975). Total chlordane content in cropland soils nationwide in 1971-72 averaged 0.05 to 0.06 mg/kg dry weight, and ranged between 0.01 and 7.9 mg/kg dry weight (Table 1); maximum values, in excess of 3.0 mg/kg, were recorded in soils from Illinois (7.0), Ohio (5.0), Indiana (4.1), and Iowa (Carey et al. 1978, 1979). The half-life of chlordane in soil when used at agricultural rates is about 1 year (IARC 1979), but residues may be measurable much longer, depending on soil type (NRCC 1975). For example, 10 years after application of 8.5 kg technical chlordane per hectare, up to 20% of the active

ingredients were still measurable; in another study, 15 % of the active ingredients remained in turf soils after 15 years (WHO 1984). *Cis*- and *trans*-chlordanes were less persistent in mineral soils than in organic mucky soils (WHO 1984). Chlordanes were usually detected in surface soils of basins receiving urban runoff water at a maximum concentration of 2.7 mg/kg; this decreased with soil depth to <0.03 mg/kg at depths below 24 cm (Nightingale 1987). Chlordane levels in soils near Air Force bases in the United States in 1975-76 were similar to those found in nonmilitary urban environments (Lang et al. 1979).

Chlordanes in sediments usually were highest in those sediments with the highest organic content, especially downstream from the center of anthropogenic activities (Smith et al. 1987). Sediments from a lake in which the overlying water column initially was treated to contain 10 µg technical chlordane per liter contained measurable residues 2.8 years after application: total chlordanes--consisting of *cis*-chlordane, *trans*-chlordane, and *trans*-nonachlor--averaged 20 µg/kg and ranged up to 46 µg/kg (Albright et al. 1980). The yearly flux of chlordanes from sediments to the overlying water column has been estimated at 0.02 $\mu g/m^2$, based on measurements made in the Sargasso Sea and deep North Atlantic Ocean between 1978 and 1980 (Knap et al. 1986).

Terrestrial Crops

Maximum total chlordane concentrations in corn (*Zea mays*) and sorghum (*Sorghum halepense*) samples collected nationwide in 1971, in µ/kg dry weight, were 480 in corn kernel, 1,260 in cornstalk, and 420 in sorghum (Carey et al. 1978); these values were somewhat lower in 1972: 150 in kernels, 410 in stalks, and 150 in sorghum (Carey et al. 1979). Concentrations in various crops grown in soils treated with 15 kg technical chlordane per hectare were always <260 µg/kg dry weight when clay content was 12 %, and < 150 µg/kg when clay content was 28% (WHO 1984).

Table 1. Chlordane concentration in selected nonbiological samples.

Sample, units of measurement, chlordane Isomer, and other variables	Concentration[a]	Reference[b]
Air, in ng/m^3		
Between Bermuda and Rhode Island, February–		
June 1973, total chlordanes	(<0.005–0.9)	1
United States, 16 States		
2,477 of 2,479 samples	ND	2
2 samples	84,204	2
Southern Hemisphere, 1980–84, various locations,		
total chlordanes	(0.005–0.19)	3
Northern Hemisphere, 1973–78, Atlantic Ocean,		
total chlordanes	(0.009–0.084)	3
Pacific Ocean, 1979–81, total chlordanes	0.013	3
Canadian Arctic, summer 1984		
cis-chlordane	~0.0015	4
trans-chlordane	(0.0005–0.002)	4
cis-nonachlor	(ND to 0.0004)	4
trans-nonachlor	~0.0012	4
Fresh water, in ug/L		
Nova Scotia		
cis-chlordane	(ND to 31.3)	1

trans-chlordane	(ND to 17.9)	1
Ontario, Canada		
trans-chlordane	(<0.001–0.021)	1
Lower Mississippi River		
trans-chlordane	(0.0004–0.0012)	1
Iraq, Tigris-Euphrates Delta, 1986		
cis-chlordane	0.057, Max. 0.067	5
trans-chlordane	0.015, Max. 0.021	5
Urban runoff	0.1, Max. 0.3	6
Lake water, total chlordanes		
Start (treated)	10.0	7
Day 421 after treatment	(0.008–0.011)	7
Seawater, in ug/L		
Northern Pacific Ocean and Bering Sea, 1980–82		
cis-chlordane	(0.004–0.005)	8
trans-chlordane	(0.004–0.005)	8
cis-nonachlor	<0.0002	8
trans-nonachlor	(0.0013–0.0015)	8
oxychlordane	<0.0002	8
Sargasso Sea		
cis-chlordane	<0.001	8
trans-chlordane	<0.001	8
Tokyo Bay, Japan, total chlordanes	~0.002	8
Soils, in mg/kg dry weight		
Everglades National Park, Florida, 1976, total chlordanes		
In National Park	Max. 0.005	9
Adjacent agricultural area	Max. 0.195	9
United States, total chlordanes		
Croplands		
1970	0.08 (0.01–13.3)	10
1971	0.06 (0.01–7.0)	11
1972	0.05 (0.01–7.9)	12
35 States	(0.01–13.3)	1
Urban areas		
8 cities	(0.02–20.5)	1
14 cities	(0.04–13.9)	1
Near U.S. military bases, 1975–76, upper 7.6 cm		
Residential areas		
1975	5.4 (ND to 52.1)	13
1976	0.2 (ND to 1.2)	13

Nonuse areas		
1975	0.09 (ND to 1.8)	13
1976	0.2 (ND to 3.4)	13
Golf course		
1975	0.7 (ND to 4.6)	13
1976	0.6 (ND to 3.1)	13
Sediments, in ug/kg		
Total chlordanes		
Lake Superior, 1973	ND	14
Long Island, New York	Usually 20–200, Max. 580	15
Streams tributary to San Francisco Bay	(4–8)	1
Upper Rockaway River, New Jersey	(<1–510)	16
Hawaiian marina		
cis-chlordane	3.0 (0.4–5.3)	1
trans-chlordane	2.3 (1.3–5.1)	1
Bottom muds, Ontario, Canada		
trans-chlordane	<0.1–3.1	1
Stream beds, drainage ditches, Nova Scotia		
cis-chlordane	(0–664)	1
trans-chlordane	(0-51)	1

[a]Concentrations are shown as mean, extremes in parentheses, maximum (Max.), and nondetectable (ND).
[b]1, IARC 1979; 2, EPA 1980; 3, Kawano et al. 1985; 4, Hoff and Chan 1986; 5, DouAbul et al. 1988; 6, Nightingale 1987; 7, Albright et al. 1980; 8, Kawano et al. 1988; 9, Requejo et al. 1979; 10, WHO 1984; 11, Carey et al. 1978; 12, Carey et al. 1979; 13, Lang et al. 1979; 14, Frank et al. 1980; 15, Wood et al. 1986; 16, Smith et al. 1987.

Aquatic Invertebrates

Extremely high levels of chlordanes (e.g., 1,746 to 7,643 µg/kg FW) were measured in several species of south Florida corals collected in 1985 (Table 2). Researchers speculate that the elevated levels were because of the illegal disposal of chlordanes off Key Largo, Florida, in 1982 (Glynn et al. 1989).

Maximum concentrations of chlordanes in American oysters (*Crassostrea virginica*) taken in the Gulf of Mexico in 1976 were near 0.1 µg/kg dry weight (Table 2). Chlordane concentrations were substantially lower than concentrations of other organochlorines measured in oysters, such as DDT (28 µ/kg) and polychlorinated biphenyls (90 µg/kg), suggesting a need for additional studies on interaction effects of chlordane residues with those of other environmental chemicals (Rosales et al. 1979).

Marine clams and worms tended to underrepresent chlordane concentrations in the ambient sediments; concentration factors were less than 0.2 for clams and 0.6 for worms (Ray et al. 1983). Similarly, chlordane concentrations in clams from the Shatt al-Arab River in Iraq closely reflected chlordane concentrations in water particulates when compared to levels in water columns or in sediments (DouAbul et al. 1988).

Table 2. Chlordane concentrations in field collections of selected animals. Values shown are in micrograms per kg (parts per billion) fresh weight (FW), dry weight (DW), or lipid weight (LW).

Taxonomic group, organism, chlordane isomer, and other variables	Concentrationa (ug/kg)	Reference[b]
Aquatic invertebrates		
Bivalve mollusks, 3 species, Ebro River, Spain, 1980, soft parts		
Total chlordanes	(<1–21) DW	1
Corals, 10 species, Biscayne National Park, near Miami, Florida, July–September 1985, *cis*-chlordane and *trans*-chlordane		
Scleractinian corals		
Colpophyllia amaranthus	Max. 6 FW	84
Colpophyllia natans	Max. 62 FW	84
Diploria clivosa	Max. 32 FW	84
Diploria strigosa	Max. 6 FW	84
Montastrea annularis	Max. 1,746 FW	84
Porites asteroides	Max. 2,256 FW	84
Siderastrea sierea	Max. 145 FW	84
Octacorals		
Briareum abestinum	Max. 1,180 FW	84
Gorgonia flabellum	Max. 6,626 FW	84
Pseudopterogorgia acerosa	Max. 7,643 FW	84
Asiatic clam, *Corbicula fluminea*, Iraq, 1986, soft parts		
cis-chlordane	6 FW; Max. 10 FW	2
trans-chlordane	5 FW; Max. 9 FW	2
American oyster, *Crassostrea virginica*, Gulf of Mexico, Mexico, summer, 1976, soft parts		
cis-chlordane	Max. 0.1 DW	3
Krill, *Euphausia superba*, Antarctic Ocean, 1980–82, whole		
cis-chlordane	0.58 LW	4
trans-chlordane	0.51 LW	4
cis-nonachlor	0.22 LW	4
trans-nonachlor	0.8 LW	4
oxychlordane	0.1 LW	4
Eight-armed squid, *Gonatopsis borealis*, North Pacific Ocean, 1980–82 whole		
cis-chlordane	15 (11–18) LW	4
trans-chlordane	8.1 (6.3–9.9) LW	4
cis-nonachlor	2.4 (2.2–2.8) LW	4
trans-nonachlor	18 (14–20) LW	4

oxychlordane	1.2 (0.8–1.6) LW	4
total chlordanes	44 (35–52) LW	5
American lobster, *Homarus americanus*, east coast of Canada, 1971–77, hepatopancreas		
cis- and *trans*-chlordane	80–100 LW	6
cis-nonachlor	30 LW	6
trans-nonachlor	(380–440) LW	6
Mysid shrimp, *Mysis relicta*, Lake Michigan, 1980–81, whole		
July		
cis-chlordane	Max. 35 DW	7
trans-chlordane	Max. 44 DW	7
October		
cis-chlordane	ND	7
trans-chlordane	(72–151) DW	7
Sandworm, *Neanthes* sp., Portland, Maine, 1980, whole		
Total chlordanes	Max. 5.4 FW	8
Oysters, Hawaii, soft parts		
cis-chlordane	13 (1.6–58) FW	9
trans-chlordane	8 (1.4–23) FW	9
Amphipod, *Pontoporeia hoyi*, Lake Michigan, 1980–81, whole		
cis-chlordane	Max. 68 DW	7
trans-chlordane	Max. 184 DW	7
Crawfish, *Procambarus clarkii*, Louisiana, 1978–79, whole		
cis-chlordane	Max. 20 FW	10
trans-chlordane	Max. 26 FW	10
Short-necked clam, *Tapes philippinarum*, Tokyo Bay, Japan, 1978		
Muscle		
cis-chlordane	5.1 FW	11
trans-chlordane	2.3 FW	11
cis-nonachlor	0.7 FW	11
trans-nonachlor	1.3 FW	11
oxychlordane	0.2 FW	11
total chlordanes	40.6 FW	11
Viscera		
cis-chlordane	19.0 FW	11
trans-chlordane	11.0 FW	11
cis-nonachlor	3.1 FW	11
trans-nonachlor	7.9 FW	11
oxychlordane	0.2 FW	11
total chlordanes	40.6 FW	
Soft parts		
cis-chlordane	10.0 FW	11

trans-chlordane	5.7 FW	11
cis-nonachlor	3.7 FW	11
trans-nonachor	4.4 FW	11
oxychlordane	0.3 FW	11
total chlordanes	21.0 FW	11
Zooplankton, North Pacific Ocean, 1980–82, whole		
cis-chlordane	19 (13–27) LW	4
trans-chlordane	13 (7–20) LW	4
cis-nonachlor	5 (3.2–8.7) LW	4
trans-nonachlor	14 (12–15) LW	4
oxychlordane	3 (2.3–3.8) LW	4
total chlordanes	54 (40–72) LW	5
Fish		
Goby, *Acanthogobius flavimanus*, Tokyo Bay, Japan, 1978 whole		
cis-chlordane	6 FW; Max. 62 FW	11, 12
trans-chlordane	9 FW; Max. 15 FW	11, 12
cis-nonachlor	8 FW; Max. 21 FW	11, 12
trans-nonachlor	18 FW; Max. 120 FW	11, 12
oxychlordane	3 FW; Max. 25 FW	11, 12
White shark, *Carcharodon carcharius*, liver, east coast of Canada, 1971		
cis- and *trans*-chlordanes	2,600 LW	6
cis-nonachlor	1,700 LW	6
trans-nonachlor	8,500 LW	6
Baltic herring, *Clupea harengus*, Baltic Sea, 1978–82, whole		
Total chlordanes		
1978	(200–600) LW	13
1982	(400–800) LW	13
Atlantic herring, *Clupea harengus harengus*, oil, east coast of Canada, 1977		
cis- and *trans*-chlordanes	(40–110) LW	6
cis-nonachlor	Max. 30 LW	6
trans-nonachlor	Max. 170 LW	6
Lake whitefish, *Coregonus clupeaformis*		
Great Lakes, 1978, whole		
cis-chlordane	(16–94) FW	14
trans-chlordane	(21–87) FW	14
total chlordanes	111 FW	14
Lake Superior, Siskiwit Lake, Isle Royale, 1983, whole		
chlordanes	260 LW; Max. 330 LW	15
nonachlors	450 LW; Max. 500 LW	15
oxychlordane	16 LW; Max. 200 LW	15

Common carp, *Cyprinus carpio*		
Great Lakes, 1979, whole		
cis-chlordane	Max. 390 FW	16
trans-chlordane	Max. 360 FW	16
cis-nonachlor	Max. 390 FW	16
trans-nonachlor	Max. 300 FW	16
San Joaquin River, California, 1981, whole		
Total chlordanes	Max. 273 FW; Max. 3,578 LW	17
Shad, *Dorosoma* spp., Louisiana, 1978–79, whole body		
cis-chlordane	Max. 76 FW	10
trans-chlordane	Max. 82 FW	10
cis-nonachlor	Max. 26 FW	10
trans-nonachlor	Max. 12 FW	10
Northern pike, *Esox lucius*, Baltic Sea, 1971–82		
Total chlordanes		
Muscle		
1971	(100–1,000) LW	13
1972	(100–1,300) LW	13
1973	100 LW	13
1974	800 LW	13
1975	1,900 LW	13
1978	(2,600–3,100) LW	13
1982	(2,300–6,300) LW	13
Liver		
1971	(100–400) LW	13
1972	(100–300) LW	13
1973	500 LW	13
1974	600 LW	13
1975	700 LW	13
1978	700 LW	13
1982	(1,100–2,100) LW	13
Fish, 2 species, muscle, Belmont Lake, Long Island, New York		
Total chlordanes	380–5,200 FW	18
Fish, 4 species, Chesapeake Bay, Maryland, 1976–80		
Total chlordanes		
Muscle	70–120 FW; Max. 310–700 FW	19
Gonad	(10–1,900) FW	19
Fish, 4 species, eastern Finland, 1979–82		
Liver		
cis-chlordane	(ND to 76) FW	20
trans-chlordane	(ND to 277) FW	20

trans-nonachlor	(ND to 20) FW	20
total chlordanes	Max. 320 FW; Max. 410 LW	21
Muscle		
cis-chlordane	(ND to 53) FW	20
trans-chlordane	(ND to 232) FW	20
trans-nonachlor	(ND to 20) FW	20
total chlordanes	Max. 1,770 LW	21
Fish, 11 species, Lake Texoma, Texas and Oklahoma, 1979		
Total chlordanes		
Whole fish	(ND to 24) FW	22
Fish, Mississippi River, 1984–86		
Total chlordanes		
Shovelnose sturgeon, *Scaphirhynchus platyrynchus*		
Muscle	325–2,285 FW	75
Eggs	163–1,926 FW	75
Common carp, muscle	55–556 FW	75
Channel catfish, *Ictalurus punctatus*, muscle	322 to 1,389 FW	75
Fish, Mississippi River, 1988, muscle		
Total chlordanes		
Channel catfish	Max. 853 FW	75
Common carp	Max. 614 FW	75
Freshwater drum, *Aplodinotus grunniens*	Max. 19 FW	75
Flathead catfish, *Pylodictis olivaris*	Max. 272 FW	75
River carpsucker, *Carpiodes carpio*	Max. 160 FW	75
Smallmouth buffalo, *Ictiobus bubalus*	Max. 200 FW	75
Sauger, *Stizosteiden canadense*	Max. 19 FW	75
Paddlefish, *Polyodon spathula*	Max. 93 FW	75
Blue catfish, *Ictalurus furcatus*	Max. 895 FW	75
Bigmouth buffalo, *Ictiobus cyprinellus*	Max. 360 FW	75
White bass, *Morone chrysops*	Max. 436 FW	75
Fish, Missouri River, 1984–86		
Total chlordanes, 3 locations		
Shovelnose sturgeon		
Muscle	146–860 FW	75
Eggs	921–6,735 FW	75
Channel catfish, muscle	205–777 FW	75
Common carp, muscle	118–548 FW	75
Fish, Missouri River, 1988, muscle		
Near Rockport, 6 species		
total chlordanes	Max. 438 FW	75
heptachlor epoxide	Max. 15 FW	75
heptachlor	ND	75

oxychlordane	Max. 11 FW	75
trans-chlordane	Max. 25 FW	75
cis-chlordane	Max. 24 FW	75
trans-nonachlor	Max. 51 FW	75
cis-nonachlor	Max. 25 FW	75
total chlordenes	Max. 4 FW	75
Above, Kansas City, 2 species		
total chlordanes	Max. 290 FW	75
heptachlor epoxide	Max. 39 FW	75
heptachlor	ND	75
oxychlordane	Max. 48 FW	75
trans-chlordane	Max. 20 FW	75
cis-chlordane	Max. 25 FW	75
trans-nonachlor	Max. 55 FW	75
cis-nonachlor	Max. 14 FW	75
total chlordenes	Max. 35 FW	75
Below Kansas City, 6 species		
total chlordanes	95–2,450 FW	75
heptachlor epoxide	3–24 FW	75
heptachlor	ND	75
trans-chlordane	4–266 FW	75
cis-chlordane	7–260 FW	75
trans-nonachlor	9–167 FW	75
cis-nonachlor	5–66 FW	75
total chlordenes	4–144 FW	75
Fish, various species, whole		
Wabash River, Indiana		
cis-chlordane	13 FW	16
trans-chlordane	9 FW	16
cis-nonachlor	5 FW	16
trans-nonachlor	20 FW	16
oxychlordane	<0.5 FW	16
Ashtabula River, Ohio, total chlordanes	<0.5 FW	16
Great Lakes area, 1978		
cis- and *trans*-chlordanes	Max. 2,680 FW	23
cis- and *trans*-nonachlors	Max. 3,070 FW	23
oxychlordane	Max. 167 FW	23
Fish, United States, nationwide, 1976–84, whole		
cis-chlordane		
1976–77	60 FW; Max. 930 FW; 600 LW	24, 76
1978–79	70 FW; Max. 2,530 FW; 700 LW	24, 76

1980–81	30 FW; Max. 360 FW; 300 LW	24, 76
1984	30 FW; Max. 660 FW	76
trans-chlordane		
1976–77	20 FW; Max. 320 FW; 300 LW	24, 76
1978–79	20 FW; Max. Max. 540 FW; 300 LW	24, 76
1980–81	20 FW; Max. 220 FW; 200 LW	24, 76
1984	20 FW; Max. 350 FW	76
cis-nonachlor		
1976–77	10 FW; Max. 490 FW; 100 LW	24, 76
1978–79	30 FW; Max. 710 FW; 300 LW	24, 76
1980–81	20 FW; Max. 270 FW; 300 LW	24, 76
1984	20 FW; Max. 450 FW	76
trans-nonachlor		
1976–77	30 FW; Max. 950 FW; 300 LW	24, 76
1978–79	50 FW; Max. 2,710 FW; 600 LW	24, 76
1980–81	40 FW; Max. 770 FW; 100 LW	24, 76
1984	30 FW; Max. 1,000 FW	76
oxychlordane		
1978–79	10 FW; Max. 740 FW; 100 LW	24, 76
1980–81	10 FW; Max. 330 FW; 100 LW	24, 76
1984	10 FW; Max. 290 FW	76
heptachlor epoxide		
1976–77	10 FW; Max. 780 FW	76
1978–79	20 FW; Max. 1,170 FW	76
1980–81	10 FW; Max. 270 FW	76
1984	10 FW; Max. 290 FW	76
Atlantic cod, *Gadus morhua*		
East coast Canada, 1977, liver		
cis- and *trans*-chlordanes	ND	6
cis-nonachlor	70 LW	6
trans-nonachlor	(60–1,900) LW	6

Northern Baltic Sea, liver		
cis- and *trans*-chlordanes	Max. 50 LW	25
Shad, *Konosirus punctatus*, Tokyo Bay, Japan, 1979		
Total chlordanes		
Muscle	Max. 41 FW	11
Viscera	Max. 95 FW	11
Sea bass, *Lateolabrax japonicus*, Tokyo Bay, Japan, 1979		
Total chlordanes		
Gill	11 FW	11
Muscle	5 FW	11
Brain	41 FW	11
Kidney	37 FW	11
Liver	81 FW	11
Abdominal fat	279 FW	11
Bluegill, *Lepomis macrochirus*, San Joaquin River, California, whole fish, 1981		
Total chlordanes	Max. 14 FW; Max. 759 LW	17
Fourhorn sculpin, *Myoxocephalus quadricornis*, Lake Michigan, 1980–81, whole		
cis-chlordane	Max. 15 DW	7
trans-chlordane	Max. 70 DW	7
Cutthroat trout, *Oncorhynchus clarki*, liver, from lake sprayed with 10 µg technical chlordane per liter		
Total chlordanes		
Time, after application		
13.3 weeks	Max. 46,449 LW	26
39.8 weeks	Max. 3,940 LW	26
1.15 years	Max. 870 LW	26
2.78 years	ND	26
Chum salmon, *Oncorhynchus keta*, North Pacific Ocean, 1980–81, whole		
cis-chlordane	9 (8–11) LW	4
trans-chlordane	5.2 (5.1–5.9) LW	4
cis-nonachlor	2 (1.6–2.7) LW	4
trans-nonachlor	17 (13–21) LW	4
oxychlordane	2.5 (2.4–2.6) LW	4
total chlordanes	36 LW	5
Sea lamprey, *Petrolmyzon marinus*, Great Lakes, 1978, whole		
cis-chlordane	(9–202) FW	14
trans-chlordane	(3–243) FW	14
total chlordanes	88 FW	14
Lizard goby, *Rhinogobius flumineus*, Nagaragawa River, Japan, whole fish		

Total chlordanes		
1968–74	(ND to 7.6) FW	85
1977–86	(13–40) FW	85
Atlantic salmon, *Salmo salar*, east coast of Canada, 1976		
Egg		
cis- and *trans*-chlordanes	150 LW	6
cis-nonachlor	60 LW	6
trans-nonachlor	(130–210) LW	27
Lake trout, *Salvelinus namaycush*, Great Lakes, 1977–82, whole fish, oxychlordane		
Lake Michigan		
1977	250 FW	28
1978	180 FW	28
1979	240 FW	28
1980	160 FW	28
1981	60 FW	28
1982	70 FW	28
Lake Huron		
1978	40 FW	28
1979	60 FW	28
1980	60 FW	28
1981	60 FW	28
1982	60 FW	28
Lake Superior		
1977	120 FW	28
1978	40 FW	28
1979	140 FW	28
1980	30 FW	28
1981	60 FW	28
1982	40 FW	28
Great Lakes, 1979, whole		
cis-chlordane	Max. 25 FW	18
trans-chlordane	Max. 75 FW	18
cis-nonachlor	Max. 160 FW	18
trans-nonachlor	Max. 42 FW	18
Great Lakes, Lake Superior, Siskiwit Lake, Isle Royale, 1983, whole		
chlordanes	420 LW; Max. 770 LW	15
nonachlors	570 LW; Max. 1,100 LW	15
oxychlordane	73 LW; Max. 170 LW	15
Shovelnose sturgeon		
Muscle, Mississippi River, 1988		
total chlordanes	Max. 1,025 FW	75

heptachlor epoxide	Max. 31 FW	75
heptachlor	Max. 3 FW	75
oxychlordane	Max. 42 FW	75
trans-chlordane	Max. 75 FW	75
cis-chordane	Max. 90 FW	75
trans-nonachlor	Max. 95 FW	75
cis-nonachlor	Max. 65 FW	75
Eggs		
total chlordanes	Max. 1,484 FW	75
heptachlor epoxide	Max. 51 FW	75
heptachlor	Max. 5 FW	75
oxychlordane	Max. 56 FW	75
trans-chlordane	Max. 123 FW	75
cis-chlordane	Max. 148 FW	75
trans-nonachlor	Max. 146 FW	75
cis-nonachlor	Max. 90 FW	75
Walleye pollock, *Terhagra chalcogramma*, North Pacific Ocean, 1980–82, whole		
cis-chlordane	44 (34–54) LW	4
trans-chlordane	17 (16–20) LW	4
cis-nonachlor	10 (6–12) LW	4
trans-nonachlor	62 (47–92) LW	4
oxychlordane	8 (5–11) LW	4
total chlordanes	140 (110–190) LW	5
Benthic fish, *Trematomus bernacchii*, Antarctic Ocean, 1980–82, whole		
cis-chlordane	4 (2–8) LW	4
trans-chlordane	1.7 (0.8–3.4) LW	4
cis-nonachlor	3 (0.8–7) LW	4
trans-nonachlor	11 (2–29) LW	4
oxychlordane	1 (0.2–1.8) LW	4
Amphibians		
Frogs, *Rana* spp., Louisiana, 1978–79, chlordanes, muscle, whole body	ND	10
California newt, *Taricha torosa*, liver, from lake sprayed with 10 µg technical chlordane per liter		
Total chlordanes		
Time, after application		
14 days	Max. 34, 094 LW	26
9.3 months	Max. 10,094 LW	26
1.24 years	Max. 4,882 LW	26
2.84 years	Max. 601 LW	26
Reptiles		

American crocodile, *Crocodylus acutus*, infertile eggs		
cis-chlordane	Max. 10 FW	29
cis-nonachlor	Max. 30 FW	29
trans-nonachlor	Max. 40 FW	29
oxychlordane	Max. 70 FW	29
Northern water snake, *Nerodia sipedon*, Lake Michigan, 1978, chlordanes		
All tissues, stomach contents	ND	30
Common garter snake, *Thamnophis sirtalis*, Lake Michigan, 1978, *trans*-nonachlor		
Carcass	(100–250) FW	30
Stomach contents	ND	30
Other chlordane isomers	ND	30
Birds		
Mallard, *Anas platyrhynchos*, wing, nationwide		
1976–77		
Chlordane isomers		
Atlantic Flyway	(10–60) FW	31
Mississippi Flyway	(10–20) FW	31
Central Flyway	(10–20) FW	31
Pacific Flyway	(10–20) FW	31
1981–82		
cis-chlordane	Max. 20 FW	32
trans-nonachlor	Max. 50 FW	32
American black duck, *Anas rubripes*, chlordane isomers		
Atlantic Flyway, 1978, egg		
Maryland	50 FW	33
Massachusetts	80 FW	33
Maine	120 FW	33
New Hampshire	(130–160) FW	33
Atlantic Flyway, 1976–77, wing	10–50 FW	31
Great blue heron, *Ardea herodias*, northwestern United States, 1977–82		
Egg		
oxychlordane	Max. 570 FW	78
heptachlor epoxide	Max. 460 FW	78
cis-chlordane	Max. 1,360 FW	78
cis-nonachlor	Max. 690 FW	78
trans-nonachlor	Max. 2,250 FW	78
Whole body, oxychlordane	Max. 470 FW	78
Brain, oxychlordane	Max. 230 FW	78
Canvasback, *Aythya valisineria*		
Egg, breeding areas, 1972–73		

cis-chlordane	<1,000 FW	34
cis-nonachlor	ND	34
oxychlordane	<1,000 FW	34
Carcass (less GI tract, skin, feet, beak) Chesapeake Bay, Maryland, winter		
cis-chlordane		
1973	ND	35
1975	9,000 FW	35
trans-nonachlor		
1973	ND	35
1975	11,000 FW	35
oxychlordane		
1973	ND	35
1975	5,000 FW	35
Birds, 4 species, eastern and southern United States, 1972–74, egg, total chlordanes	<100 FW	36
Birds, New York State, 1982–86, found dead or debilitated, brain tissue, chlordane implicated as primary cause of distress		
Cooper's hawk, *Accipiter cooperii*		
oxychlordane	Max. 5,800 FW	79
heptachlor epoxide	Max. 4,300 FW	79
trans-nonachlor	Max. 1,300 FW	79
Sharp-shinned hawk, *Accipiter striatus*		
oxychlordane	Max. 4,300 FW	79
heptachlor epoxide	Max. 3,500 FW	79
trans-nonachlor	Max. 1,000 FW	79
Great blue heron		
oxychlordane	Max. 2,400 FW	79
heptachlor epoxide	Max. 600 FW	79
Great horned owl, *Bubo virginianus*		
oxychlordane	Max. 8,700 FW	79
heptachlor epoxide	Max. 7,700 FW	79
trans-nonachlor	Max. 2,300 FW	79
Blue jay, *Cyanocitta cristata*		
oxychlordane	Max. 5,000 FW	79
heptachlor epoxide	Max. 3,700 FW	79
trans-nonachlor	Max. 2,000 FW	79
Eastern screech owl, *Otus asio*		
oxychlordane	Max. 2,600 FW	79
heptachlor epoxide	Max. 1,800 FW	79
trans-nonachlor	Max. 1,800 FW	79
Common grackle, *Quiscalus quiscula*		

oxychlordane	Max. 10,800 FW	79
heptachlor epoxide	Max. 9,100 FW	79
Eastern bluebird, *Sialia sialis*		
oxychlordane	Max. 3,000 FW	79
heptachlor epoxide	Max. 2,200 FW	79
European starling, *Sturnus vulgaris*		
oxychlordane	Max. 7,700 FW	79
heptachlor epoxide	Max. 5,000 FW	79
trans-nonachlor	Max. 500 FW	79
American robin, *Turdus migratorius*		
oxychlordane	Max. 1,300 FW	79
heptachlor epoxide	Max. 2,700 FW	79
trans-nonachlor	Max. 1,900 FW	79
Cackling Canada goose, *Branta canadensis minima*, 1973–74, carcass, breeding areas, total chlordanes		
Uncontaminated	<1 FW	37
Contaminated (Oregon, California)		
Immature male	<0.2 FW	37
Adult male	1.7 FW	37
Adult female	2.0 FW	37
Common goldeneye, *Bucephala clangula*, fat, oxychlordane		
On arrival at wintering grounds, New York		
Juveniles	40 (10–300) LW	38
Adults	220 (120–370) LW	38
Just before to spring migration		
Adults	250 (190–320) LW	38
Dunlin, *Calidris alpina*, Washington State, 1980, whole		
Total chlordanes	Max. 60 FW	39
Peregrine, *Falco peregrinus*, Alaska, 1979–84, egg		
trans-nonachlor	Max. 290 FW	40
oxychlordane	130 FW; Max. 960 FW	40
Atlantic puffin, *Fratercula arctica*, Hornoy, Norway, 1982–83, oxychlordane plus *trans*-nonachlor		
Adults		
Uropygial gland	1,429 (48–2,815) LW	41
Liver	93 (262–1,531) LW	41
Chicks		
Brain	833 (445–1,289) LW	41
Chicken, *Gallus* sp., contaminated through use of former chlordane container to hold cage disinfectants, Australia		
Egg	300 DW	42
Pullets, fat		
30 weeks old	920 DW	42

80 weeks old	670 DW	42
Nationwide, egg		
cis-chlordane	1 FW	9
trans-chlordane	2 FW	9
Gull-billed tern, *Sterna nilotica*, South Carolina, 1972–75		
Egg		
Oxychlordane	Max. 290 FW	80
trans-nonachlor	ND	80
Bald eagle, *Haliaeetus leucocephalus*		
Egg, total chlordanes		
Maryland, Virginia, 1980–84	1,100 FW	82
Maine, 1980–84	500 FW	82
Ohio, 1981–84	840 FW	82
Oregon, 1980–83	220 FW	82
Arizona, 1982–84	160 FW	82
Wisconsin, 1980–83	330 FW	82
Nationwide, found dead or moribund		
1971–74		
Brain		
cis-chlordane plus *trans*-chlordane	270 FW	43
cis-nonachlor	290 FW	43
oxychlordane	150 FW	43
Carcass (less skin, beak, feet, GI tract, liver)		
cis-chlordane plus *trans*-chlordane	27,000 LW	43
cis-nonachlor	30,000 LW	43
oxychlordane	15,000 LW	43
1975–77		
Brain		
cis-chlordane	90–190 FW; Max. 6,400 FW	44
cis-nonachlor	130–170 FW; Max. 750 FW	44
trans-nonachlor	200–330 FW; Max. 7,400 FW	44
oxychlordane	180–290 FW; Max. 2,600 FW	44
Carcass (less skin, viscera)		
cis-chlordane	220–320 FW; Max. 4,500 FW	44
cis-nonachlor	100–150 FW; Max. 1,700 FW	44
trans-nonachlor	280–380 FW; Max. 6,000 FW	44
oxychlordane	130–180 FW; Max. 2,300 FW	44
1978–81		
Brain		
cis-chlordane	90–190 FW; Max. 2,300 FW	45
cis-nonachlor	100–230 FW; Max. 1,600 FW	45
trans-nonachlor	180–410 FW; Max. 4,100 FW	45
oxychlordane	120–260 FW; Max. 2,700 FW	45

Carcass (less skin, viscera)		
cis-chlordane	120–290 FW; Max. 2,200 FW	45
cis-nonachlor	120–190 FW; Max. 1,200 FW	45
trans-nonachlor	230–370 FW; Max. 4,100 FW	45
oxychlordane	90–130 FW; Max. 1,450 FW	45
Herring gull, *Larus argentatus*		
Egg, Canada, 1973		
cis- and *trans*-chlordanes	220 LW	6
cis-nonachlor	20 LW	6
trans-nonachlor	520 LW	6
Egg, Maine, 1977		
trans-nonachlor	50 (ND to 500) FW	46
Egg, Virginia, 1977		
trans-nonachlor	40 (ND to 440) FW	46
oxychlordane	20 (ND to 180) FW	46
Chicks, age 21 days		
Liver, oxychlordane	6 (2–13) FW	47
Muscle, oxychlordane	4–140 FW	47
Glaucous-winged gull, *Larus glaucescens*, Alaska, 1973–76		
Egg		
cis-chlordane	Max. 75 FW	48
cis-nonachlor	Max. 26 FW	48
oxychlordane	Max. 250 FW	48
Great black-backed bull, *Larus marinus,* Maine, 1977		
Egg		
cis-chlordane	40 (ND to 500) FW	46
oxychlordane	220 (ND to 430) FW	46
Red breasted merganser, *Mergus serrator*, Lake Michigan, United States, 1978, carcass		
trans-nonachlor	Max. 480 FW	30
Long-billed curlew, *Numenius americanus*, Oregon, 1981–83, convulsions noted, brain		
cis-chlordane	(110–300) FW	49
trans-chlordane	(ND to 50) FW	49
cis-nonachlor	(ND to 470) FW	49
trans-nonachlor	(140 –4,100) FW	49
oxychlordane	(2,500–4,400) FW	49
heptachlor epoxide	(1,000–4,800) FW	49
Yellow-crowned night-heron, *Nycticorax violaceus*, Louisiana, 1978–79, whole body		
Total chlordanes	ND	10
Osprey, *Pandion haliaetus*		
Eastern United States, 1975–82, dead or moribund, carcass		

(less skin, feet, and back)		
cis-chlordane	Max. 680 FW	50
cis-nonachlor	Max. 480 FW	50
trans-nonachlor	Max. 280 FW	50
oxychlordane	Max. 350 FW	50
Eagle Lake, California, 1973–84, egg		
cis-chlordane	Max. 10 FW	51
trans-nonachlor	Max. 6 FW	51
oxychlordane	Max. 6 FW	51
Fourteen states, United States, 1970–79, egg		
cis-chlordane	Usually <100; Max. 1,100	52
cis-nonachlor	Usually <100; Max. 400	52
trans-nonachlor	Usually <100; Max. 500	52
oxychlordane	Usually <100; Max. 400	52
Passeriformes, 38 species, western United States, 1980, carcass (less beak, feet, GI tract, feathers)		
oxychlordane	Usually <50 FW; Max. 290 FW	53
Brown pelican, *Pelecanus occidentalis*, South Carolina, 1974–75, egg		
oxychlordane	Max. 530 FW	81
heptachlor epoxide	Max. 500 FW	81
cis-chlordane	Max. 960 FW	81
trans-nonachlor	Max. 980 FW	81
cis-nonachlor	Max. 630 FW	81
Adelie penguin, *Pygoscelis adeliae*, Antarctic Ocean, 1980–82, subcutaneous fat		
cis-chlordane	0.9 LW	4
trans-chlordane	<0.05 LW	4
cis-nonachlor	1.7 LW	4
trans-nonachlor	15 LW	4
oxychlordane	16 LW	4
Black skimmer, *Rynchops niger*, South Carolina, 1972–75		
Egg		
oxychlordane	Max. 520 FW	80
trans-nonachlor	Max. 520 FW	80
Adults, found dead		
oxychlordane		
Brain	Max. 880 FW	80
Carcass	Max. 560 FW	80
cis-chlordane		
Brain	Max. 540 FW	80
Carcass	Max. 150 FW	80

Shorebirds, 7 species, Corpus Christi, Texas, winter 1976–77, skinned carcasses		
Total chlordanes	Usually <1,000 FW; Max. 1,700 FW	54
Forster's tern, *Sterna forsteri*, egg, Lake Michigan, 1983		
cis-chlordane	(<10–60) FW	77
trans-chlordane	(<10–20) FW	77
trans-nonachlor	(<10–170) FW	77
oxychlordane plus heptachlor epoxide	(10–230) FW	77
heptachlor	(10–300) FW	77
European starling, *Sturnus vulgaris*, whole (less beak, wing tip, feet, skin), nationwide		
1972		
oxychlordane	Max. 100 FW	55
1979		
total chlordanes	Max. 290 FW	56
1982		
cis-chlordane	Max. 30 FW	57
cis-noncachlor	Max. 70 FW	57
trans-nonachlor	Max. 40 FW	57
oxychlordane	Max. 140 FW	57
Northern gannet, *Sula bassanus*, eastern Canada, 1969–84		
Egg		
cis-chlordane		
1969	Max. 550 FW	58
1970	Max. 520 FW	58
1984	Max. 150 FW	58
cis-nonachlor		
1969	Max. 380 FW	58
1970	Max. 370 FW	58
1984	Max. 150 FW	58
oxychlordane		
1969	Max. 208 FW	58
1970	Max. 202 FW	58
1984	Max. <100 FW	58
Tree swallow, *Tachycineta bicolor*, Alberta, Canada, 1978–79		
Eggs and nestlings		
cis-chlordane	<30 FW	59
oxychlordane	<30 FW	59
Thick-billed murre, *Uria lomvia*, northern Pacific Ocean, 1980–82, subcutaneous fat		
cis-chlordane	3 (1.4–3.9) LW	4
trans-chlordane	<0.05 LW	4

cis-nonachlor	10 (3–15) LW	4
trans-nonachlor	3 (1.7–4.5) LW	4
oxychlordane	82 (63–130) LW	4
total chlordanes	98 (63–150) LW	4
Waterbirds, 3 species, Galveston Bay, Texas, 1980–82, total chlordanes		
Carcass (less skin, feet, bill, GI tract)	Max. 1,200 FW	60
Egg	Max. 900 FW	60
Mammals		
Bats, 3 species, Maryland and West Virginia, 1973, near high chlordane use area, oxychlordane		
Carcass	Max. 3,000 FW	61
Guano	Max. 100 FW	61
Cow, *Bos bovis*, milk, total chlordanes		
Nationwide	20–60 FW	9
Illinois, 1971–73	50 FW	62
Cattle, *Bos* sp., grazing heptachlor-contaminated pastures for 4 weeks (some deaths), oxychlordane, subcutaneous fat		
End of grazing	5,700 FW	63
48 days later	180 FW	63
Dog, *Canis familiaris*, Tokyo, 1979, adipose tissue		
trans-nonachlor	17 FW	11
oxychlordane	71 FW	11
total chlordanes	88 FW	11
Cat, *Felis domesticus*, Tokyo, 1979, adipose tissue		
cis-nonachlor	60 FW	11
trans-nonachlor	51 FW	11
oxychlordane	50 FW	11
total chlordanes	160 FW	11
Long-finned pilot whale, *Globicephala melaena*, Newfoundland, 1980, blubber		
Total chlordanes		
Males	1,600 (1,000–3,200) FW	64
Females	700 (200–1,900) FW	64
Grey seal, *Halichoerus grypus*, Gulf of Finland, 1976–82		
Blubber		
cis-chlordane	50 FW	65
trans-chlordane	130 FW	65
trans-nonachlor	700 FW	65
oxychlordane	210 FW	65
total chlordanes	970 FW	65
Human, *Homo sapiens*		
Mother's milk		

Hawaii, 1979		
trans-nonachlor	2.5 FW	66
oxychlordane	1.9 FW	66
Arkansas and Mississippi, 1973–74		
Total chlordanes	5 FW; Max. 20 FW	62
Japan, 1979		
cis-chlordane	0.1 FW	66
trans-chlordane	0.2 FW	66
cis-nonachlor	0.2 FW	66
trans-nonachlor	0.8 FW	66
oxychlordane	0.5 FW	66
Japan, 1983		
cis-chlordane	0.1 FW; 3.1 LW	67
trans-chlordane	0.04 FW; 1.2 LW	67
cis-nonachlor	0.1 FW; 4.0 LW	67
trans-nonachlor	0.5 FW; 15.7 LW	67
oxychlordane	0.4 FW; 11.5 LW	67
Finland, 1982		
cis-chlordane	<0.05 FW; <1.0 LW	66
trans-chlordane	<0.05 FW; <1.0 LW	66
cis-nonachlor	0.08 FW; 2.0 LW	66
trans-nonachlor	0.4 FW; 10.0 LW	66
oxychlordane	0.2 FW; 5.0 LW	66
Blood, Tokushima City, Japan		
cis-chlordane	0.05 FW; Max. 0.14 FW	68
trans-chlordane	0.1 FW; Max. 0.22 FW	68
cis-nonachlor	0.03 FW: Max. 0.08 FW	68
trans-nonachlor	0.08 FW; Max. 0.29 FW	68
oxychlordane	0.2 FW; Max. 0.75 FW	68
total chlordanes	0.51 FW; Max. 1.1 FW	68
Fat, worldwide, oxychlordane	140 (30–400) FW	69
White-beaked dolphin, *Lagenorhynchus albirostris*, Newfoundland, 1982, blubber		
Total chlordanes		
Males	12,700 (6,300–25,000) FW	64
Females	8,300 (3,700–15,000) FW	64
Weddell seal, *Leptonychotes weddelli*, Antarctic Ocean, 1980–82, blubber		
cis-chlordane	7 LW	4
trans-chlordane	<0.05 LW	4
cis-nonachlor	8 LW	4
trans-nonachlor	41 LW	4
oxychlordane	13 LW	4

River otter, *Lutra canadensis,* liver, Alberta, Canada, 1980–83		
cis-chlordane	Max. 6 FW	70
oxychlordane	Max. 13 FW	70
Gray bat, *Myotis grisescens*, Missouri, 1976–77, found dead		
Brain		
cis-chlordane	Max. 1,000 FW	71
trans-nonachlor	Max. 2,100 FW	71
oxychlordane	Max. 2,300 FW	71
Carcass		
cis-chlordane	6,300 (15,000–108,000) LW	71
trans-nonachlor	159,000 (91,000–252,000) LW	71
oxychlordane	68,000 (16,000–167,000) LW	71
Pacific walrus, *Odobenus rosmarus divergens*, oxychlordane, blubber		
Alaska, 1981–84	20–60 FW	83
Soviet Union, 1984	100 FW	83
Saimaa ringed seal, *Phoca hispida saimensis*, Finland, 1977–81		
Total chlordanes		
Blubber	590 (110–1,700) LW	72
Liver	200 (10–400) FW	72
Muscle	20 (10–30) FW	72
Harbor seal, *Phoca vitulina*, Netherlands, blubber		
trans-nonachlor	2,700 LW	73
oxychlordane	3,000 LW	73
Dall's porpoise, *Phocoenoides dalli*, North Pacific Ocean, 1980–82, blubber		
cis-chlordane	440 (360–550) LW	4
trans-chlordane	63 (53–73) LW	4
cis-nonachlor	270 (240–310) LW	4
trans-nonachlor	1,800 (1,600–2,000) LW	4
oxychlordane	250 (160–340) LW	4
total chlordanes	2,800 (2,700–3,000) LW	5
Raccoon, *Procyon lotor*, Louisiana, 1978–79, muscle		
cis-chlordane	17 FW	10
trans-chlordane	17 FW	10
Gray squirrel, *Sciurus carolinensis*, Jacksonville, Florida, 1974, fat		
nonachlors	Max. 110 LW	74
oxychlordane	Max. 62 LW	74

[a]Concentrations are shown as mean, extremes in parentheses, maximum (Max.), and nondetectable (ND).

[b]Risebrough et al. 1983; 2, DouAbul et al. 1988; 3, Rosales et al. 1979; 4, Kawano et al. 1988; 5, Kawano et al. 1986; 6, Zitko 1978; 7, Evans et al. 1982; 8, Ray et al. 1983; 9, IARC 1979; 10, Dowd et al. 1985; 11, Yamagishi et al. 1981; 12, Miyazaki et al. 1980; 13, Moilanen et al. 1982; 14, Kaiser 1982; 15, Swackhamer and Hites 1988; 16, Kuehl et al. 1980; 17, Saiki and Schmitt 1986; 18, Kuehl et al. 1983; 19, Eisenberg and Topping 1985; 20, Pyysalo et al. 1981; 21, Pyysalo et al. 1983; 22, Hunter et al. 1980; 23, veith et al. 1981; 24, Schmitt et al. 1985; 25, Wickstrom et al. 1981; 26, Albright et al. 1980; 27, Zitko and Saunders 1979; 28, DeVault et al. 1986; 29, Hall et al. 1979; 30, Heinz et al. 1980; 31, White 1979; 32, Prouty and Bunck 1986; 33, Haseltine et al. 1980; 34, Stendell et al. 1977; 35, White et al. 1979; 36, Klaas et al. 1980; 37, Anderson et al. 1984; 38, Foley and Batcheller 1988; 39, Schick et al. 1987; 40, Ambrose et al. 1988; 41, Ingebrigtsen et al. 1984; 42, Reece et al. 1985; 43, Barbehenn and Reichel 1981; 44, Kaiser et al. 1980; 45, Reichel et al. 1984; 46, Szaro et al. 1979; 47, Peakall et al. 1986; 48, Ohlendorf et al. 1982; 49, Blus et al. 1985; 50, Wiemeyer et al. 1987; 51, Littrell 1986; 52, Wiemeyer et al. 1988; 53, De Weese et al. 1986; 54, White et al. 1980; 55, Nickerson and Barbehenn 1975; 56, Cain and Bunck 1983; 57, Bunck et al. 1987; 58, Elliott et al. 1988; 59, Shaw 1984; 60, King and Krynitsky 1986; 61, Clark and Prouty 1976; 62, EPA 1980; 63, Petterson et al. 1988; 64, Muir et al. 1988; 65, Perttila et al. 1986; 66, Wickstrom et al. 1983; 67, Tojo et al. 1986; 68, Wariishi et al. 1986; 69, WHO 1984; 70, Somers et al. 1987; 71, Clark et al. 1980; 72, Helle et al. 1983; 73, Kerkhoff and Boer 1982; 74, Nalley et al. 1978; 75, Bush and Grace 1989; 76, Schmitt et al. 1990; 77, Kubiak et al. 1989; 78, Fitzner et al. 1988; 79, Stone and Okoniewski 1988; 80, Blus and Stafford 1980; 81, Blus et al. 1979; 82, S. Wiemeyer, Patuxent Wildlife Research Center, personal communication; 83, Taylor et al. 1989; 84, Glynn et al. 1989; 85, Loganathan et al. 1989.

Fishes

Health advisories have been issued near Lawrence Kansas, based on chlordane levels in edible fish tissues. In fish from the Kansas River, Kansas, in 1986, chlordanes were detected more frequently and at higher levels than other contaminants measured (Arruda et al. 1987). More than 80% of the sites sampled in Kansas had detectable chlordanes in fish; at more than 50% of these sites, levels exceeded 0.1 mg/kg fresh weight--a guideline for the protection of predatory fish. At three urban sites in Kansas, concentrations of chlordanes in fish have approached or exceeded the Food and Drug Administration action level of 0.3 mg chlordane per kilogram of fresh weight for protection of human health. The most likely source of chlordane in fish from the Kansas River is urban and suburban use of chlordane as a termite control agent (Arruda et al. 1987). Other health advisories based on chlordane contamination have been issued. In 1985, people were warned not to eat shovelnose sturgeon (*Scaphirhynchus platyrynchus*) from the Missouri and Mississippi rivers. In 1987, advisories warned against the consumption of sturgeon from the Missouri River between Kansas City and St. Louis, and against bullhead catfishes, suckers, carps, sturgeons, and sturgeon eggs from the Mississippi River near St. Louis (Bush and Grace 1989).

Chlordane residues were detected in 36% of all fish samples collected in major domestic watersheds in 1976 (Veith et al. 1979). In the Great Lakes region in 1979, chlordane residues in fish tissues exceeded 100 µ/kg on a fresh weight basis in about 40% of the samples measured; residues were highest in samples collected near Alton, Illinois, and Fairborn, Ohio (Kuehl et al. 1983).

The two most abundant components of technical chlordane found in fish tissues from Tokyo Bay, Japan, were *trans*-nonachlor and *cis*-chlordane (Yamagishi et al. 1981 b; Table 2). However, this may vary between locales. For example, *cis*-chlordane and *trans*-chlordane were the most abundant components in fish samples collected throughout Japan during the past 20 years, followed, in order, by *cis*-nonachlor, *trans*-nonachlor, and oxychlordane (Loganathan et al. 1989). Of the total chlordanes measured in muscle of northern pike *(Esox lucius)* from the Baltic Sea, 37% was *cis*-chlordane, 34% *trans*-chlordane, and 15% each *trans*-nonachlor and oxychlordane (*(Esox lucius)* and Baltic herring (Moilanen et al. 1982). For liver tissue of northern pike, 35 % was oxychlordane, 28% *trans*-chlordane, 22% *cis*-chlordane, and 14% *trans-non*achlor (*(Esox lucius)* and Baltic herring *(*Moilanen et al. 1982). In the United States, only chlordanes and nonachlors have been detected as significant residues in fish collected nationwide. The most abundant component was *cis*-chlordane, followed by *trans*-nonachlor, *trans*-chlordane, and *cis*-nonachlor (Ribick and Zajicek 1983). The two most abundant components were detected in about 93 % of all fish samples collected in 1978 and 1979; residues were usually highest in Hawaii, the Great Lakes, and the Corn Belt (Ribick and Zajicek 1983). Fish from Manoa Stream in Hawaii had high residues because of heavy use of technical chlordane in pineapple culture and termite control (Ribick and Zajicek 1983). Nationwide monitoring of freshwater fishes showed that chlordane concentrations in

whole fish did not change from 1980 to 1994, following a period of decline; however, *trans*-nonachlor replaced *cis*-chlordane as the most abundant component, suggesting a lower influx of chlordane to the aquatic environment from terminated use of chlordane in agriculture in the mid- 1970's (Schmitt et al. 1990; Table 2). Residues of *cis*-chlordane and *trans*-nonachlor--the most abundant and persistent of the chlordane components measured --were present at 85 and 89% of the stations sampled in 1984 (Schmitt et al. 1990). Maximum chlordane levels in fish in 1984 occurred in the Great Lakes, Hawaii, watersheds of the Ohio, Missouri, and Mississippi rivers, and in the Delaware and Raritan rivers in the Northeast (Schmitt et al. 1990).

Atmospheric transport may be the main source of chlordane in Finland --a country that prohibits chlordane use— because chlordanes are distributed evenly in the Finnish environment (Pyysalo et al. 1983). No chlordane compounds were detected in rainbow trout (*Oncorhynchus mykiss*) taken from lakes in eastern Finland, although measurable residues were detected in other fish species. This phenomenon is attributed to the superior ability of rainbow trout to metabolize chlordanes to oxychlordane (Pyysalo et al. 1981).

Amphibians and Reptiles

Chlordane residue data for amphibians and reptiles are extremely limited. Maximum concentrations of chlordane isomers did not exceed 70 µg/kg FW of oxychlordane in eggs of the American crocodile, *Crocodylus acutus,* or 250 µg/kg FW in carcass of the common garter snake, *Thamnophis sirtalis* (Table 2). However, California newts, *Taricha torosa*, taken near a lake treated with 10 µg/L technical chlordane had greatly elevated chlordane residues in liver and comparatively low concentrations in carcass, stomach, and stomach contents. After 14 days, livers contained about 34 mg/kg total chlordanes lipid weight--about 19% chlordanes, 9% nonachlors, and 6% chlordanes (Albright et al. 1980). After 2.8 years, 98% of the total chlordanes was lost. *Trans*-nonachlor was the most persistent component in newt liver, accounting for up to 55% of the total chlordanes in specimens collected 2.8 years after application (Albright et al. 1980; Table 2).

Birds

Technical chlordane components and their metabolites--especially oxychlordane--are comparatively elevated in tissues with high lipid content, in older birds, and in raptors (Table 2).

Chlordane isomers occur frequently in birds collected nationwide. In 1976, for example, 41 % of European starlings (Cain and Bunck 1983). In 1982, oxychlordane was detected in 45 % of all starlings analyzed, *trans*-nonachlor in 40%, *cis*-nonachlor in 9%, and *cis*- and *trans*-chlordanes in fewer than 2% (Bunck et al. 1987). Chlordane isomers were detected at frequencies exceeding 50% in wings of American black ducks *(Anas rubripes)* and mallards *(Anas platyrhynchos)* from the Atlantic Flyway in 1976-77 (White 1979), in eggs of 19 species of Alaskan seabirds in 1973-76 (Ohlendorf et al. 1982), and in carcasses of ospreys (Pand*ion haliaetus)* found dead in the eastern United States between 1975 and 1982 (Wiemeyer et al. 1987). Frequency of detection for chlordane isomers ranging between 14 and 40% has been reported in wings of American black ducks and mallards from flyways other than the Atlantic Flyway (White 1979), in 19 species of passeriformes from the western United States in 1980 (DeWeese et al. 1976), and in 7 species of Texas shorebirds in 1976-77--although residues in shorebirds were below levels known to adversely affect reproduction or survival (White et al. 1980).

Carcasses of bald eagles (*Haliaeetus leucocephalus*) collected between 1978 and 1981 usually contained oxychlordane at 45 to 56% frequency, *trans*-nonachlor at 62 to 74%, *cis*-chlordane at 38 to 45%, and *cis*-nonachlor at 38 to 47%. Frequency of occurrence in the brain was lower, ranging between 19 and 55% for individual isomers (Reichel et al. 1984). However, a positive correlation was established in bald eagles between concentration of chlordanes in brain on a fresh weight basis and in carcass on a lipid weight basis; this relation seems to extend to other birds as well (Barbehenn and Reichel 1981). Bald eagles also contained appreciable quantities of other organochlorine compounds, and a few--for example, dieldrin--were sometimes present at concentrations considered life-threatening (Reichel et al. 1984). A similar situation exists in other species of raptors (Ambrose et al. 1988).

Some chlordane isomers tend to persist in avian tissues for lengthy periods. In northern gannets (*Sula bassanus*), the half-time persistence of *cis*-chlordane, *cis*-nonachlor, and oxychlordane was estimated at 11.2, 19.4, and 35.4 years (Elliott et al. 1988). Oxychlordane residues in the thick-billed murre *(Uria lomvia)* tend to be high because of rapid excretion through uropygial gland secretions of *cis*- and *trans*-chlordanes and

nonachlors, and to biotransformation of these and other chlordane components to oxychlordane (Kawano et al. 1988). This observation is alarming because the metabolite oxychlordane has proven much more toxic and persistent than the parent chemicals (Kawano et al. 1988). Secondary poisonings of raptors after consumption of poisoned bait or prey that had accumulated a large quantity of chlordane were documented for the red-shouldered hawk *(Buteo lineatus)* and the great horned owl (*Bubo virginianus*); concentrations of oxychlordane and heptachlor epoxide found in brain and carcass of both species (Blus et al. 1983) were within the lethal range reported in experimental studies (Stickel et al. 1979).

Chlordane-induced mortality of the long-billed curlew *(Numenius americanus)* has been documented at least four times since 1978, despite restriction of technical chlordane use since 1980 to subterranean applications for termite control (Blus et al. 1985). Death of these curlews was probably due to over-winter accumulations of oxychlordane of 1.5 to 5.0 mg/kg brain FW and of heptachlor epoxide at 3.4 to 8.3 mg/kg--joint lethal ranges for oxychlordane and heptachlor epoxide in experimental birds— compared with 6 mg/kg brain for oxychlordane alone, and 9 mg/kg for heptachlor epoxide alone (Blus et al. 1985). Additional research is needed on toxic interactions of chlordane components with each other and with other chemicals in the same environment.

Mammals

Chlordane levels in mammals were usually highest in lipids, in animals collected near areas of high chlordane use, and in aquatic mammals, especially marine species (Table 2). Biomagnification of total chlordane through the food chain was strongly evident in marine mammals; chlordanes were concentrated gradually from zooplankton, through squid and fish, to porpoises and dolphins (Kawano et al. 1986; Muir et al. 1988; Table 2). Chlordane residues in marine mammals were positively related to lipid content and not to the age of the animal (Perttila et al. 1986).

A high death rate over a 2-year period was evident in the little brown bat (*Myotis lucifugus*) following application of chlordane; young bats were most affected in the first year after application and adults in the second year (Kunz et al. 1977). Residues were greatly elevated in the brain and carcass of another bat, the gray bat (*Myotis grisescens*)-an endangered species--found dead near areas of high chlordane use (Table 2).

Chlordane levels in human blood were comparatively elevated among individuals living in residences treated with chlordane during the past 5 years, and in termite control operators; oxychlordane levels were usually significantly higher than *trans*-nonachlor except among those who consumed large quantities of fish (Wariishi et al. 1986; Wariishi and Nishiyama 1989).

Lethal and Sublethal Effects

General

Chlordane has been applied extensively to control pestiferous soil invertebrates, usually at rates between 0.6 and 2.24 kg/ha; within this range sensitive nontarget species, especially earthworms, were adversely affected.

Nominal water concentrations between 0.2 and 3.0 µg/L were harmful to various species of fish and aquatic invertebrates. Effects included a reduction in survival, immobilization, impaired reproduction, histopathology, and elevated chlordane accumulations. *Cis*-chlordane, when compared with *trans*-chlordane, was more toxic, preferentially stored, and concentrated to a greater degree. In aquatic organisms, *cis*-chlordane photoisomers were frequently more toxic than the parent form. Oxychlordane was not a major metabolite in aquatic fauna.

Sensitive bird species had reduced survival after consumption of diets as low as 1.5 mg chlordane per kilogram of ration, or after a single oral dose as low as 14.1 mg/kg BW; accumulations were documented in tissues following consumption of diets containing 0. 1 to 0.3 mg chlordane per kilogram of feed. Oxychlordane was the most persistent metabolite in avian brain tissue.

Concern for the continued widespread use of chlordane centers on its ability to cause liver cancer in domestic mice. Other adverse effects in mammals, such as elevated tissue residues and growth inhibition, were frequently associated with diets containing between 0.76 and 5.0 mg chlordane per kilogram of feed. Metabolism of technical chlordane by mammals results primarily in oxychlordane, a metabolite that is about 20 times more toxic than the parent compound and the most persistent metabolite stored in adipose tissues.

Chlordane interactions with other agricultural chemicals produced significant biological effects in warm-blooded organisms, indicating a need for additional research on this subject.

Terrestrial Invertebrates

Chlordane has been used extensively to control grubs, ants, snails, and terrestrial invertebrates. Chlordane applied to wheat crops in India at 0.6 kg/ha and higher controlled infestation by two species of termites *(Odontotermes obesus, Microtermes obesi)* and increased grain yield; chlordane applications of 0.4 kg/ha and lower were ineffective (Khan and Singh 1985). Chlordane has been used to control the imported fire ant *(Solenopsis invicta),* although registration for this purpose by EPA has now been withdrawn (Williams and Lofgren 1983). Application of 4.5 g of chlordane per ant mound, applied as an emulsifiable concentrate, resulted in 83 to 94% control 4 to 5 weeks after treatment (Williams and Lofgren 1983). Cricket (*Acheta pennsylvanicus*) nymphs died within one minute of contact with technical chlordane; dead crickets showed cellular disruption of the caecal lining, the malpighian tubules, and the digestive tract (Greenhalgh 1986).

Chlordane, at 1. 12 to 2.24 kg/ha, was lethal to fly and beetle larvae and also caused reductions in populations of various species of soil invertebrates (WHO 1984). Among nontarget soil species, earthworms were especially sensitive. Significant reductions in earthworm populations were recorded following application of 2.2 kg/ha; metabolism was adversely affected in 2 weeks at 13 kg/ha and remained depressed for at least 5 years; at 80 kg/ha, 46% died in 4 days (NRCC 1975). In soil, chlordane effects decreased with increasing soil temperature and organic content; the heptachlor component in technical chlordane had the greatest biological activity to soil fauna (NRCC 1975).

Aquatic Organisms

Signs of chlordane poisoning in fish included hyperexcitability, increased respiration rate, erratic swimming, loss of equilibrium and convulsions; death frequently occurred within 12 h of exposure (NRCC 1975). Chlordane adversely affected sensitive species of fish and aquatic invertebrates at nominal water concentrations between 0.2 and 3.0 µg/L (Table 3). Specifically, reduced survival was measured in shrimp and crabs at water concentrations of 0.2 to 2.0 µg/L, and in freshwater and marine fishes between 1.7 and 3.0 µg/L; immobilization, impaired reproduction, and histopathology were recorded in shrimp, fish, and planarians between 0.8 and 3.0 µg/L; and high accumulations were evident in fish, shrimp, and oysters between 0.2 and 4.2 µg/L. Growth stimulation and high residues were measured in resistant species of algae, such as *Scenedesmus quadricauda,* at media concentrations up to 100 µg chlordane per liter; in sensitive algal species, however, growth was inhibited at water concentrations as low as 10 µg/L (Table 3).

Large intraspecfic and interspecific differences in sensitivity to chlordane were evident (Table 3). Some of this variability was attributed to variations in water temperature, salinity, and sediment loadings; some to the age, condition, and nutritional history of the test organism; and some to the chlordane formulation and isomer tested (NRCC 1975; EPA 1980; and Finley 1980; McLeese and Metcalf 1980; Mayer and Ellersieck 1986). In general, granular chlordane formulations were most toxic, organisms at a young developmental stage and organisms with reduced lipid content were most sensitive, and adverse effects were most pronounced under conditions of elevated water temperatures, reduced salinities, decreased sediment loadings, and increased duration of exposure. Reduced bioavailability and lessened toxicity of chlordane to daphnids was associated with increasing concentrations (up to 200 mg/L) of suspended solids and their associated carbon content (Hall et al. 1986). Sediment loadings of 5.8 mg chlordane per kilogram were fatal to 50% of sandworms *(*McLeese et al. 1982). Resistance or adaptation to chlordane has been reported in mosquitofish *(Gambusia affinis)* collected from ditches near treated cotton fields; these fish were up to 20 times more resistant than newly exposed fish (NRCC 1975).

Residues of *cis*-chlordane were preferentially stored and magnified over *trans*-chlordane by freshwater fish and invertebrates in ponds treated with technical chlordane at concentrations up to 1.14 µg/L; the *cis* isomer, with an estimated Tb 1/2 of 46 days, persisted longer than did the *trans*- isomer (Johnson and Finley 1980). Tissue concentrations of 106,000 µg total chlordenes per kilogram, on a lipid weight basis, were associated with reduced survival of estuarine invertebrates (Zitko 1978). Moribund amphipods *(Hyallela azteca),* for example, contained 137,000 to 2,180,000 µg/kg lipid of various chlordanes, heptachlors, and chlordenes (Zitko 1978). In fish, chlordane concentrations of 300,000 to 4,000,000 µg/kg lipid weight in tissues were lethal (Zitko 1978).

Cis-chlordane was 8 times more toxic to bluegill *(Lepomis macrochirus)* than was *trans*-chlordane (Johnson and Finley 1980). *Cis*-chlordane was also more toxic to goldfish *(Carassius auratus)* than was *trans*-chlordane because of its comparatively rapid uptake from the medium and lengthy storage in body tissues, estimated at 99 % after 25 days (Feroz and Khan 1979b). The elimination rate of *cis*-chlordane from a cichlid (*Cichlasoma* sp.) was estimated at 2.9% weekly over a 20-week period, with a Tb 1/2 of about 17 weeks; metabolites accounted for 12.5% (dichlorochlordene, oxychlordane, chlordene chlorohydrin, dihydroxyheptachlor, dihydroxydihydrochlordene, plus four unidentified compounds) and unchanged *cis*-chlordane for 87.5 % (Feroz and Khan 1979a).

Table 3. Chlordane effects on selected aquatic organisms. Compound tested was technical chlordane, unless indicated otherwise.

Organism and concentration in medium in ug/L	Effect	Reference[b]
Algae		
Blue-green alga, *Chlamydomonas* sp.		
0.1–50	Stimulatory to growth	1
>100	Inhibitory to growth	1
Estuarine phytoplankton, mixed species		
5	No effect on growth in 5 days	2
10	Daily additions of 10 µg/L for 8 days reduced algal growth rate and carbon uptake. Inhibition persisted for 2–48 h and did not affect community composition	2
Marine dinoflagellate, *Exuviella baltica*		
50	Exposure for 7 days resulted in disintegration of many cells, reduced cell density and reduced carbon fixation. Particle size distribution altered, and this could affect availability of food for particle feeding herbivores	3
Green alga, *Scenedesmus quadricauda*		
0.1–100	Stimulatory to respiration and growth; bioconcentration factor (BCF) ranged from x6,000 to x15,000 in 24 h for all doses, and from x6,700 to x103,000 in 5 days	1, 4
>1,000	Growth inhibition	4
Invertebrates		
Blue crab, *Callinectes sapidus*		
260	50% immobilization in 48 h	5
Dungeness crab, *Cancer magister*		
0.015	No effect on survival or molting	6
0.15	LC50 (37 days), molting inhibited	6
1.3	LC50 (96 h), zoeae	6
220	LC50 (96 h), adults	6
Sand shrimp, *Crangon septemspinosa*		

2	LC50 (96 h)	7
American oyster, *Crassostrea virginica*		
4.2	8% reduction in shell growth in 96 h, BCF of x2,619 in soft parts	8
6.2–10	50% reduction in shell growth in 96 h, BCFof x3,200–x8,300	5, 6, 8
100	BCF of x7,300 after exposure for 10 days	9
Daphnid, *Daphnia magna*		
12.1 and 21.6	Maximum acceptable toxicant concentration (MATC)[a]	6
28	50% immobilization in 96 h	10
97	LC50 (48 h) for chlorinated chlordane	11
152	LC50 (48 h) for chlorinated emulsifiable concentrate	11
270	LC50 (48 h)	12
813	LC50 (48 h) for dechlorinated chlordane	11
1,174	LC50 (48 h) for dechlorinated emulsifiable concentrate	11
Daphnid, *Daphnia pulex*		
2.3	50% immobilization in 48 h for *trans*-nonachlor	13
24	LC50 (48 h)	14, 15
57	LC50 (96 h) for *cis*-chlordane	16
269	LC50 (96 h) for *trans*-chlordane	16
550	LC50 (96 h) for *cis*-photochlordane	16
930	LC50 (96 h) for oxychlordane	16
Planarian, *Dugesia dorotocephala*		
0.2	No deaths in 5 days	17
>1.0	Impaired reproduction after 10-day exposure	17
~3.0	LC50 (5 days)	17
10.0	LC100 (10 days)	17
Amphipod, *Gammarus fasciatus*		
40	LC50 (96 h), 95% confidence interval of 21–60 µg/L	14, 15
Amphipod, *Hyallela azteca*		
97	50% immobilization in 168 h	10
Freshwater bivalve mollusk, *Lamellidens marginalis*, exposed to 0.12 mg technical chlordane/L for up to 30 days		
2 days	Residues, in mg/kg FW, were 5.0 in gill, 3.6 in foot, 3.1 in muscle, and 2.2 in intestine	26
8 days	Residues, in mg/kg FW, ranged between 2.4 in gill and 1.1 in muscle	26

30 days	Residues, in mg/kg FW, were 1.0 in gill, 1.0 in foot, 0.4 in intestine, and 0.1 in muscle	26
Sandworm, *Nereis virens*		
220	LC50 (12 days), but no deaths in 96 h. At 96 h, signs of stress included everted proboscis, loss of equilibrium, emergence from sediments, and failure to burrow	18
Crayfish, *Orconectes nais*		
31.6	LC50 (35 days)	14
50	LC50 (96 h)	14
Korean shrimp, *Palaemon macrodactylus*		
11	LC50 (96 h)	15
Grass shrimp, *Palaemonetes pugio*		
4.2	LC15 (19 h), BCF about x1,070	8
4.8	LC50 (96 h), BCF of x1,900–x2,300	8
Brown shrimp, *Penaeus aztecus*		
2.4	50% immobilization in 48 h	5
Pink shrimp, *Penaeus duorarum*		
0.24	LC10 (96 h), whole body BCF of x2,960 in survivors	8
0.4	BCF of x4,000–x6,000 in 96 h	8
4.4	LC50 (48 h)	8
Stonefly, *Pteronarcy californica*		
15	LC50 (96 h), 95% confidence interval of 9–24 µg/L	14, 15
Daphnid, *Simocephalus serrulatus*		
20	LC50 (48 h)	14, 15
Fish		
Goldfish, *Carassius auratus*		
13	LC50 (96 h) for *cis*-photochlordane	16
15	LC50 (96 h) for oxychlordane	16
26	Exposed for 24 h to *cis*-chlordane. Whole body BCF at 10 and 25 days after exposure were x2,280 and x1,820, respectively	19
27	LC50 (96 h) for *cis*-chlordane	16
82	LC50 (96 h)	6
440	LC50 (96 h) for *trans*-chlordane	16
Sheepshead minnow, *Cyprinodon variegatus*		
0.5 and 0.8	MATC[a]	20
0.8	Reduced hatch during continuous exposure	20
1.7	Some deaths in second-generation fish during	20

	continuous exposure	
2.8	Some deaths in adult fish during exposure for 189 days	20
3.3	No deaths in 28 days, whole body BCF of x3,333	8
7.1	Equilibrium loss in fry after exposure for 10 days	8
12.5–24.5	LC50 (96 h)	8, 20
15	LC25 (96 h), BCF up to x18,700 in survivors	8
36	No effect on fertilization success or embryo survival after adults exposed for 28 days	8
Common carp, *Cyprinus carpio*		
3.0	LC50 (96 h)	6
Threespine stickleback, *Gasterosteus aculeatus*		
90–160	LC50 (96 h)	6, 15
Freshwater catfish, *Heteropneustes fossilis*		
150	No deaths in 96 h	21
247	Muscle glycogenolysis and hyperglycemia in 2–12 h	21
275	LC50 (96 h)	21
3,500	LC100 (96 h)	21
Channel catfish, *Ictalurus punctatus*		
7–46	LC50 (96 h)	14
Pinfish, *Lagodon rhomboides*		
5.4	LC30 (94 h), whole body BCF of x3,070	8
6.4	LC50 (96 h), BCF up to x7,500	8
Bluegill, *Lepomis macrochirus*		
1.2 and 2.2	MATC[a]	10
7.1–17	LC50 (96 h) for *cis*-chlordane	14, 16
9.2	LC50 (96 h) for oxychlordane	16
12	LC50 (48 and 96 h) for *cis*-photochlordane	16, 22
19–85	LC50 (96 h)	6, 10, 14, 15
41	LC50 (96 h) for chlorinated technical chlordane	11
50.5–140	LC50 (96 h) for *trans*-chlordane	14, 16
62	LC50 (96 h) for chlorinated emulsifiable concentrate	11
582	LC50 (96 h) for dechlorinated technical chlordane	11
800	LC50 (96 h) for dechlorinated emulsifiable concentrate	11

Largemouth bass, *Micropterus salmoides*		
3.0	LC50 (96 h)	14
Striped bass, *Morone saxatilis*		
11.8	LC50 (96 h)	6
Striped mullet, *Mugil cephalus*		
3.2	LC50 (48 h)	5
Cutthroat trout, *Oncorhynchus clarki*		
27	LC50 (96 h)	14
Coho salmon, *Oncorhynchus kisutch*		
14–56	LC50 (96 h)	6, 14, 15
Rainbow trout, *Oncorhynchus mykiss*		
8–47	LC50 (96 h)	6, 14, 15, 24
Chinook salmon, *Oncorhynchus tshawytscha*		
57	LC50 (96 h)	15
Sea lamprey, *Petromyzon marinus*		
1,000	LC100 (14 h)	9
Fathead minnow, *Pimephales promelas*		
25–115	LC50 (96 h)	10, 14, 15
Indian carp, *Saccobranchus fossilis*		
420	LC50 (96 h)	23
Brown trout, *Salmo trutta*		
11	LC50 (96 h)	14
Brook trout, *Salvelinus fontinalis*		
0.32	Adverse effects during chronic exposure	10
22	No deaths in 96 h	25
30-47	LC50 (96 h)	6, 10, 25

[a] MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

[b] 1. Glooschenko et al. 1979; 2. Biggs et al. 1978; 3. Magnani et al. 1978; 4. Glooschenko and Lott 1977; 5. Mayer 1987; 6. EPA 1980; 7. McLeese and Metcalfe 1980; 8. Parrish et al. 1976; 9. NRCC 1975; 10. Cardwell et al. 1977; 11. Randall et al. 1979; 12. Hall et al. 1986; 13. Passino and Smith 1987; 14. Johnson and Finley 1980; 15. EPA 1973; 16. Podowski et al. 1979; 17. Best et al.; 1981; 18. McLeese et al. 1982; 19. Feroz and Khan 1979b; 20. Parrish et al. 1978; 21. Mirsha and Srivastava 1984; 22. Sudershan and Khan 1980; 23. Verma et al. 1982; 24. Mayer and Ellersieck 1986; 25. Zitko 1979; 26. Agrawal 1986.

Photoisomers seem to be more toxic than the parent form. For example, *cis*-photochlordane was about twice as lethal to bluegills and goldfish than was *cis*-chlordane (Sudershan and Khan 1980). Bluegills exposed to 5 µg/L of radiolabeled *cis*-photochlordane or *cis*-chlordane for 48 h accumulated *cis*-chlordane from the medium by a factor of x78, and *cis*-photochlordane by a factor of x 140 (Sudershan and Khan 1980). During the next 6 weeks, 20% of the cis-chlordane was eliminated in a linear pattern, and about 50% was eliminated in 46 days. Elimination of *cis*-photochlordane followed a biphasic pattern and was most rapid during the first 3 weeks; 40% was eliminated in the fast 6 weeks, and 50% was eliminated in 15 weeks. Less than 7% of the radioactivity retained in *cis*-chlordane-treated bluegills was in the form of two conjugates, compared with 16% in the form of 14 metabolites for *cis*-photochlordane. No oxychlordane was found in bluegill tissues after treatment; this

compound is one of the predominant metabolites found in chlordane-treated rodents and cockroaches. Thus, absence of epoxidation and presence of a mechanism of hydroxylation followed by conjugation seems to be the most active mode of chlordane metabolism in bluegill (Sudershan and Khan 1980).

Cis-photochlordane was about one-tenth as toxic to *Daphnia pulex* than was *cis*-chlordane (Podowski et al. 1979). This is in sharp contrast to the pattern shown in bluegill and goldfish (Sudershan and Khan 1980); further, *cis*-photochlordane and *cis*-chlordane toxicity to mice and houseflies was about the same (Podowski et al. 1979), which demonstrates the difficulty in generalizing about the comparative toxicity of chlordane isomers.

Amphibians and Reptiles

Shortly after chlordane was applied to wooden huts in Australia for termite control, large numbers of dead skinks *(Morethia boulengeri, Lerista puctorittata)* and frogs *(Litoria caerulea, L. peronii)* were discovered, presumably killed by the chlordane (Henle 1988). Toad *(Bufo arenarum)* embryos survived 0.5 mg technical chlordane per liter for 8 days but died by day 20; all embryos held in 15 mg/L were dead by day 15 (Juarez and Guzman 1984). For tadpoles of the common toad *(Bufo bufo)* a 48-h LC50 of 2 mg/L was reported (WHO 1984).

Birds

Signs of chlordane intoxication in birds include sluggishness, drooped eyelids, fluffed feathers, low crouching on perch, reduced food intake, and weight loss. Later, afflicted animals rested on their breasts, wings spread, quivering and panting rapidly, back arched, neck arched over the back, and convulsing (Stickel et al. 1983). Signs of intoxication appeared within 5 min, and death usually occurred in the first 8 days of exposure; remission took up to 4 weeks in some birds (Hudson et al. 1984).

The most sensitive birds tested against technical chlordane were California quail *(Callipepla californica),* with an acute oral LD50 of 14.1 mg/kg BW; ring-necked pheasant (*Phasianus colchicus*), with an acute oral LD50 of 24 to 72 mg/kg BW; and European starlings (*Sturnus vulgaris*) fed diets containing 1.5 mg/kg ration for 57 days or 6.25 mg/kg for 24 days (Table 4). Accumulations of various chlordane isomers and metabolites were evident in chickens (*Gallus* sp.) fed diets containing as little as 0.1 mg technical chlordane per kilogram of feed for 6 weeks or 0.3 mg/kg for 4 weeks (NRCC 1975). Vapor toxicity of chlordane is persistant. In one instance, a room used for housing rock doves was sprayed with a chlordane solution; walls and floors were then scrubbed and the room left unoccupied for 2 months. When rock doves were returned to the room, enough chlordane remained to be lethal to all birds (Ingle 1965). Similar cases are reported for mice, presumably after use of very concentrated chlordane solutions (Ingle 1965).

Table 4. Chlordane effects on selected birds.

Organism and other variables	Effect	Reference
Red-winged blackbird, *Agelaius phoeniceus*, fed diets containing		
10 mg/kg for 84 days	Residue of 1.8 mg *cis*-chlordane per kilogram body weight (BW), fresh weight (FW)	Stickel et al. 1983
50 mg/kg for 42 days	Whole body *cis*-chlordane content of 9.2 mg/kg FW	Stickel et al. 1983
100 mg/kg for 21 days	Whole body *cis*-chlordane content of 14.8 mg/kg FW	Stickel et al. 1983
Plus 3 or 7 days off dosage	Whole body *cis*-chlordane content of 5.4 and 2.6 mg/kg FW, respectively	Stickel et al. 1983
200 mg/kg diet	LD50 within 9 days	Stickel et al. 1983
Mallard, *Anas platyrhynchos*		
Single oral dose, age 4–5 months, 1,200 mg/kg BW	LD50	Hudson et al. 1984

858 mg/kg diet for 5 days followed by 3 days of clean diet, ducklings age 10 days	LD50	Hill et al. 1975
709 mg/kg diet	LD50	NRCC 1975
Birds, 4 species, from marsh treated with 1.12 kg chlordane per hectare	No reproduction in blue-winged teal (*Anas discors*) and northern shovelers (*Anas clypeata*); reproduction inhibited by 60% in coots (*Fulica americana*) and red-winged blackbirds (*Agelaius phoeniceus*); disruption of food cycles in marsh was probable cause	NRCC 1975
Birds, 4 species, fed diets containing 71% cis-chlordane and 23% *trans*-chlordane at 50–500 mg/kg diet	Oxychlordane concentrations in brain of dead birds ranged from 9.4–22.1 mg/kg FW in brown-headed cowbirds (*Molothrus ater*), common grackles (*Quiscalus quiscula*), and red-winged blackbirds. In European starlings (*Sturnus vulgaris*), oxychlordane ranged from 5.0 to 19.1 mg/kg FW in birds that died, and from 1.4 to 10.5 mg/kg FW in sacrificed birds	Stickel et al. 1983
Birds, 3 species, fed diets containing 150 mg technical chlordane per kilogram	LD50 reached in 6–7 days for starlings, cowbirds, and red-winged blackbirds	Stickel et al. 1979
California quail, *Callipepla californica*		
Single oral dose of 14.1 mg/kg BW	LD50	Hudson et al. 1984
Northern bobwhite, *Colinus virginianus*		
10–120 mg/kg diet for 14 weeks	LD50	NRCC 1975; WHO 1984
250 mg/kg diet for 10 days, juveniles	LD50	WHO 1984
250 mg/kg diet for 100 days, adults	LD50	WHO 1984
Japanese quail, *Coturnix japonica*		
25 mg/kg diet, 4 weeks	No effect on survival, weight gain, or activity	NRCC 1975
200 mg/kg diet, 7 days	LD100	NRCC 1975
14-day-old chicks fed treated diets for 5 days, then untreated diets for 3 days		
203 mg/kg diet	No effect on survival or food consumption	Hill and Camardese 1986
308 mg/kg diet	LD50	Hill and Camardese 1986
370 mg/kg diet	LD73, reduced food consumption	Hill and Camardese 1986
500 mg/kg diet	LD93, reduced food consumption	Hill and Camardese 1986
Chicken, *Gallus* sp.		
Fed diet containing 0.1 mg/kg for 6 weeks	Egg chlordane residue about 0.2 mg/kg FW, and fat residue about 0.33 mg/kg FW	NRCC 1975
Adults fed diet containing 0.3 mg/kg for 4 weeks	No adverse effects on growth, egg hatchability, or chick growth	NRCC 1975
Fed diet containing 10 mg/kg for 5 days	Egg chlordane residue about 4 mg/kg FW	NRCC 1975
220–230 mg/kg BW	Acute oral LD50	NRCC 1975
Ring-necked pheasant, *Phasianus colchicus*		
Single oral dose of 24–72 mg/kg BW	LD50	Hudson et al. 1984
50 mg/kg diet for 100 days, juveniles	LD50	WHO 1984
318 mg/kg diet	LD50	NRCC 1975
430 mg/kg diet for 5 days, then clean diet	LD50	Hill et al. 1975

for 3 days, juveniles		
European starling, *Sturnus vulgaris*		
Fed diet containing 1.5, 6.25, 25 or 100 mg chlordane per kilogram	Time for 50% mortality was 57 days for 1.5 mg/kg diet, 24 days for 6.25 mg/kg diet, 6.5 days for the 25 mg/kg diet, and 3.25 days for the 100 mg/kg diet	Stickel et al. 1979
Fed diet containing 100 mg nonachlor per kilogram for 35 days	8% dead	Stickel et al. 1983
200 mg chlordane per kilogram diet	LD50 usually within 14 days	Stickel et al. 1983
500 mg chlordane per kilogram diet	LD50 in 5 days	Stickel et al. 1983
Common barn owl, *Tyto alba*, adults		
Fed diets containing 75 mg/kg until 50% died; survivors sacrificed and residues measured	Mortality reached 50% on day 40. Maximum residues in brains of birds dying during exposure (or sacrificed), in mg/kg FW, were 6.5 (9.0) for *cis*-chlordane, 4.5 (9.0) for trans-nonachlor, 3.2 (9.0) for trans-chlordane, and 1.0 (2.0) for cis-nonachlor	O. H. Pattee, Patuxent Wildlife Research Center, personal communication
Fed diets containing 150 mg/kg until 50% died; survivors sacrificed and residues measured	Mortality reached 50% on day 17. Maximum residues in brains of owls dying during exposure (or sacrificed), in mg/kg FW, were 5.1 (1.8) for *cis*-chlordane, 3.6 (1.8) for *trans*-chlordane, 3.2 (2.1) for *trans*-nonachlor, and 0.9 (0.4) for *cis*-nonachlor	O. H. Pattee, Patuxent Wildlife Research Center, personal communication

Reproductive impairment was reported in several species of waterfowl from a marsh treated with 1.12 kg technical chlordane per hectare (Table 4). Recent studies by Lundholm (1988) with two species of ducks *(Anas* spp.) and the domestic chicken (*Gallus* sp.) demonstrated that various organochlorine compounds, including chlordane, interfered (in a dose-dependent manner) with reproduction by reducing the binding of progesterone to its cytoplasmic receptor in the shell gland mucosa of birds, especially ducks.

The lethal effect of technical chlordane in birds is attributed primarily to chlordane metabolites, especially oxychlordane, and to a lesser extent heptachlor epoxide (Stickel et al. 1983). Oxychlordane was the most persistent chlordane component in avian brain tissues. The half-time persistence of oxychlordane in brain was 63 days, and 95% loss was estimated in 280 days; the Tb 1/2 for heptachlor epoxide was 29 days, and for *trans*-nonachlor it was 19 days (Stickel et al. 1979). Oxychlordane residues in brain tissue approaching 5 mg/kg FW were considered within the lethal hazard zone to birds (Stickel et al. 1979).

Technical heptachlor contains about 15 % *cis*-chlordane and 2.5% *trans*-chlordane. Diets containing 50 mg technical heptachlor per kilogram fed to brown-headed cowbirds *(Molothrus ater),* red-winged blackbirds *(Agelaius phoeniceus),* common grackles *(Quiscalus quiscula),* and European starlings produced 50% mortality in 9 to 24 days; birds that died contained 9.2 to 27 mg oxychlordane per kilogram of FW brain and survivors contained 2.7 to 7.8 mg/kg (Stickel et al. 1979). Red-winged blackbirds were fed diets containing 10 mg technical chlordane per kilogram for 84 days, 50 mg/kg for 42 days, or 100 mg/kg for 21 days; all contained about 17% of the total diet fed as *cis*-chlordane, with whole body residues in mg/kg FW of 1.8, 9.2, and 14.8; accumulations of *trans*-chlordane were negligible (Sticker et al. 1983).

Chlordane interactions with other agricultural chemicals are significant and merit additional research. In one study, male Japanese quail *(Coturnix japonica)* pretreated for 8 weeks with 10 mg chlordane per kilogram of diet had increased resistance to parathion, but not to paraoxon, as judged by cholinesterase activity (Ludke 1977). In another study, northern bobwhites *(Colinus virginianus)* treated with 10 mg chlordane per kilogram of diet for 10 weeks, followed by endrin stress, had greater accumulations of chlordane in the brain than did birds treated only with chlordane (Ludke 1976).

Mammals

Concern for the continued widespread use of chlordane is centered around its carcinogenicity in mice, *Mus* sp. (Ewing et al. 1985). Chlordane produced liver cancer in both sexes of two different strains of domestic mice (EPA 1980; WHO 1984; Tojo et al. 1986; Table 5). A dose-dependent incidence of hepatocellular carcinoma was evident in mice fed chlordane in their diets; frequency of liver carcinomas was not significantly different from controls at dietary levels of 5 mg/kg and lower but were greatly elevated (i.e., 70% frequency) at dietary levels of 50 mg/kg and higher (EPA 1980). In contrast to mice, chlordane was not a hepatic carcinogen in rats at dietary levels up to 64 mg/kg ration (WHO 1984; EPA 1988); however, a dose-related increase in follicular cell thyroid neoplasms and malignant fibrous histocytomas was recorded in chlordane-exposed rats Ohno et al. 1986). In humans, no increased evidence of cancer was proven among employees in chlordane manufacturing facilities, although there was a statistically significant increase in death rate from cerebrovascular disease in that group (Klaassen et al. 1986).

Human toxicity data for chlordane usually are obtained after accidental exposure through spillage onto clothing or ingestion (Ingle 1965; NRCC 1975; EPA 1980). In one case, a 15-month-old girl accidentally swallowed a mouthful of chlordane suspension and within 3 h displayed tremors and incoordination. Repeated seizures developed and she was treated with ethyl chloride, amobarbitol, and gastric lavage with magnesium sulfate; ataxia and excitability disappeared in about 3 weeks. At age 26, she was in excellent health and seemed not to have experienced latent effects from the childhood incident (WHO 1984). Other cases of accidental chlordane poisoning in children are documented, and all seem to have recovered completely after treatment (WHO 1984).

Symptoms of acute chlordane poisoning in humans include irritability, salivation, labored respiration, muscle tremors, brain wave abnormalities, incoordination, convulsions, deep depression, and sometimes death (IARC 1979; EPA 1980, 1988). Signs of acute chlordane intoxication in other mammal species are similar to those in humans and may also include aplastic anemia and acute leukemia; cyanosis; pathology of gastrointestinal tract, liver, kidney, lung, and heart; pulmonary congestion; degenerative changes in the central nervous system; impaired uptake and utilization of glucose; interference with immunocompetence response; diarrhea; avoidance of food and water; enhanced estrone metabolism; increased production of hepatic mixed function oxidase enzymes; altered enzyme activity in brain and in kidney cortex; enlarged liver; hair loss; abdominal distention; hunched appearance; inhibited oxidative phosphorylation in liver mitochondria; and thyroid carcinoma (Saxena and Karel 1976; IARC 1979; Reuber and Ward 1979; WHO 1984; Barnett et al. 1985; Johnson et al. 1986, 1987; Klaassen et al. 1986; EPA 1988; Suzaki et al. 1988). Acute oral LD50 values for technical chlordane and sensitive mammals usually ranged between 25 and 50 mg/kg BW (Table 5). Chlordane-related compounds (i.e., *cis*-chlordane, *trans*-chlordane, heptachlor, heptachlor epoxide) stimulate superoxide (O_2^-) generation in guinea pig leucocytes, alter membrane potential, and increase intracellular calcium concentration; toxicity of individual compounds seems to be related to superoxide generation (Suzaki et al. 1988). Metabolism of chlordane isomers results in oxychlordane, a metabolite that is about 20 times more toxic to rats than is the parent compound and is the most persistent metabolite stored in rat adipose tissue (Menzie 1978; EPA 1980). Oxychlordane accounted for 53% in females and 63% in males of all chlordane isomers in fat of rats killed 24 h after a single oral dose of 1.0 mg/kg BW technical chlordane (Nomeir and Hajjar 1987). Acute oral LD50 values in the rat, in mg/kg BW, were 19.1 for oxychlordane; 89 to 392 for *cis*-chlordane; 200 to 590 for technical chlordane; 327 for *trans*-chlordane; >4,600 for chlordane, 3-chlordene, 1-hydroxychlordene, chlordene epoxide, 1-hydroxy, and 2,3-epoxy chlordane; and >10,000 for 2-chlorochlordene (Table 5).

Chlordane adversely affects growth and fertility of laboratory animals (Talamantes and Jang 1977; IARC 1979; Klaassen et al. 1986; EPA 1988; Table 5). Neonatal exposure of mice to chlordane retards growth, as judged by lowered body weights during the first 12 weeks (Talamantes and Jang 1977). No fetotoxic or teratogenic effects were observed in rats born to dams fed chlordane in their diets for 2 years at levels up to 300

mg/kg diet; however, pups nursed by dams consuming chlordane at 150 or 300 mg/kg diet developed signs of toxicity (EPA 1988). In uterine mucosa of the rabbit, chlordane isomers (as well as isomers of DDE and polychlorinated biphenyls) reduced the binding of progesterone to its cytoplasmic receptor in a dose-dependent manner, which suggests a pathway to account for chlordane-induced reproductive impairment (Lundholm 1988).

Table 5. Chlordane effects on selected mammals.

Organism, dose, and other variables	Effects	Reference
Cow, *Bos bovis*		
Oral doses equivalent to 1, 10, or 100 mg/kg diet for 60 days, then no dose for 30 days	At 1 mg/kg diet equivalent, total chlordane in fat increased from 0.24 mg/kg at day 30 to 0.47 at day 60; 30 days later, residues remained elevated at 0.45 mg/kg. The same pattern was seen at higher dose levels but residues were higher at 1.2–1.5 mg/kg in the 10 mg/kg diet group, and 2.6–4.0 in the 100 mg/kg group	Nomeir and Hajjar 1987
Fed diets containing 10 mg/kg for 10 days	Milk contained less than 50 µg/L	NRCC 1975
Fed diets containing 20 mg/kg for 150 days	Milk contained less than 200 µg/L	NRCC 1975
25–90 mg/kg body weight (BW)	Acute oral LD50	WHO 1984
Dog, *Canis familiaris*		
Fed diets containing 0.3, 3, 15, or 30 mg chlordane per kilogram of food for 2 years	Liver abnormalities in 15 and 30 mg/kg groups; no adverse effects at lower doses on behavior, appearance, survival, weight gain, or blood chemistry. In the 3 mg/kg group, equivalent to 0.075 mg/kg BW daily, maximum residue in fat was 3.6 mg/kg	NRCC 1975; WHO 1984; EPA 1988
Daily oral dose ranging between 5 and 200 mg/kg BW	Dose-dependent mortality. All died between 25 days and 93 weeks	WHO 1984
Single oral dose of 200–700 mg/kg BW	No deaths	WHO 1984
Goat, *Capra* sp.		
180 mg/kg BW	Acute oral LD50	WHO 1984
Guinea pig, *Cavia* spp.		
Males exposed daily for 90 days to 67 mg/kg BW through dermal painting	Mild degenerative changes in skin and testes	WHO 1984
Hamster, *Cricetus* spp.		
1,720 mg/kg BW	Acute oral LD50	EPA 1980; WHO 1984
Human, *Homo sapiens*		
100 µg/L	Reduced growth and altered cell morphology in human cell cultures	EPA 1980
25–50 mg/kg BW	Acute lethal oral dose	WHO 1984
100 mg/kg BW	Fatal	IARC 1979
Female swallowed 6g of chlordane, equivalent to 104 mg/kg BW	Death in 9 days	WHO 1984
Contamination of water supply in Chattanooga, Tennessee, by up to 1.2 g	Gastrointestinal and neurological symptoms in 13 reported cases	WHO 1984

chlordane per liter		
Cynomolgus monkey, *Macaca* spp.		
Inhalation for 90 days of air containing 10 µg technical chlordane per liter	No measurable effect	Khasawinah et al. 1989
Indian desert gerbil, *Meriones hurrianae*		
Males dosed intramuscularly at 2.5 mg/kg BW every 3 days for 45 days	Hyperproteinemia, hyperglycemia, and enhanced serum alkaline and acid phosphatase activities	WHO 1984
Single intramuscular injection of 25, 50, or 75 mg/kg BW	Dose-dependent hyperglycemia, due to increased production of liver glucose in blood of treated animals, reaching a maximum glucose level about 1 h after injection, persisting for up to 3 days, and approaching control levels within 1 week	Saxena and Karel 1976
Mouse, *Mus* spp.		
On days 2, 3, and 4 of life, each received 0.075 or 0.15 mg of either *cis*-chlordane or *trans*-chlordane	Depressed growth and delayed development in eye and vaginal opening during first 12 weeks; all normal at necropsy after 15 weeks	Talamantes and Jang 1977
Oral doses of 0.08 or 0.25 mg daily for 30 days, equivalent to 100 and 300 mg/kg BW	Significant dose-related reduction in size of seminiferous tubules and in percentage of damaged tubules. High dose group experienced 24–58% reduction in spermatogenesis (and high death rate), low dose group 11–21% reduction, and controls 0.5–6.1% reduction	Balash et al. 1987
0.09 mg/kg BW daily for 2 years, equivalent to 0.76 mg/kg diet	Increased liver to BW ratios in both sexes. At higher dietary concentrations equivalent to 0.43 and 1.1 mg/kg BW daily, liver necrosis was observed in males	EPA 1988
Daily oral doses for 14 days of 0.1, 4, or 8 mg *trans*-chlordane per kilogram BW	Significant dose-related increase in liver weight and leukocytes; no effect on immunocompetence	Johnson et al. 1986
Pregnant females treated with 0.16 or 8 mg/kg BW throughout gestation	Decreased immune competence in offspring of high-dose group challenged with oxazolone at age 101 days	WHO 1984
Single oral dose of *cis*-chlordane of 1.0 mg/kg BW	Peak tissue concentrations reached, in µg/kg FW, were 1,180 in liver, 880 in fat, 349 in kidney, 248 in lungs, 164 in muscle, 92 in testes, and 68 in brain. Peak concentration in blood of 113 µg/L reached in 8 h; 34% of total dose excreted in feces by 12 h after treatment. After 14 days, measurable residues detected in gonad, muscle, fat, and kidney	Ewing et al. 1985
Offspring from parents given 1.0 or 2.5 mg/kg BW for 7 consecutive days	Impaired conditioned avoidance response behavior, and hyperactivity	WHO 1984

Fed diets containing 5, 25, or 50 mg technical chlordane per kilogram ration for 18 months	Dose-related incidence of hepatic nodular hyperplasias in the 25 and 50 mg/kg diets and an increased incidence of hepatomas in the male 5 and 25 mg/kg groups. Controls experienced a high incidence of premature deaths	Epstein 1976
Females injected intraperitoneally with 25 mg/kg BW once weekly for 3 weeks	Fertility reduced by about 50%	EPA 1988
Fed diets containing 25 to 100 mg chlordane per kilogram food for six generations	At 100 mg/kg, decreased viability in first and second generations and no offspring in third generation. At 50 mg/kg, viability was reduced in fourth and fifth generations. No significant effects in the 25 mg/kg group, even after six generations	WHO 1984
Males fed diets containing 29.9 or 56.2 mg technical chlordane per kilogram for 80 weeks	Frequency of liver tumors was 88% in high-dose group, 33% in low-dose group, and 19% in controls	EPA 1980
Females fed diets containing 30 or 64 mg technical chlordane per kilogram for 80 weeks	Frequency of liver tumors was 70% in high-dose group, 6% in low-dose group, and 4% in controls	EPA 1980
Males given single dose of 50 or 100 mg/kg BW, then mated with untreated females	No dominant lethal changes produced	EPA 1980
390–430 mg/kg BW	Acute oral LD50	IARC 1979; EPA 1980
Rabbit, *Oryctolagus* sp.		
Oral doses of 1, 5, or 15 mg/kg BW daily on days 6–18 of gestation	Some miscarriages in 1 and 15 mg/kg groups; no changes in behavior, appearance, or body weight; no teratogenic effects observed	WHO 1984
Dosed orally with 14.3 mg of radiolabeled *trans*-chlordane daily for 10 weeks and killed 2 weeks after the last dose	Residues were highest in abdominal and subcutaneous fat (235 mg/kg FW), followed by heart and spleen (75–91 mg/kg), then liver, brain, and blood (25–44 mg/kg)	Nomeir and Hajjar 1987
20 mg/kg BW, single intravenous injection	LD74	Ingle 1965
Dermal exposure for 90 days, equivalent to 20–40 mg/kg BW	LD50	WHO 1984
Dosed orally with *cis*-chlordane at 67 mg/kg BW, or *trans*-chlordane at 30 mg/kg BW every 4 days for a total of 4 doses, then killed 5 days after the last dose	Residues in the *trans*-chlordane group were higher (17–77 mg/kg) than in the *cis*-chlordane group (8–67 mg/kg) although *trans*-chlordane was administered at a much lower dose. Fat and kidney usually contained the highest concentrations, and brain the lowest. Oxychlordane was measured in all tissues at 0.1 mg/kg in brains, 11 mg/kg in fat, and 0.5 to 2 mg/kg in liver, muscle, and kidney	Nomeir and Hajjar 1987
100–500 mg/kg BW	Acute oral LD50	Ingle 1965; EPA 1980
780–1,200 mg/kg BW	Acute dermal LD50; death preceded by skin	WHO 1984

	irritation, tremors, and convulsions	
Sheep, *Ovis aries*		
Single oral dose of 500 mg/kg BW	Incoordination and partial blindness; full recovery in 5–6 days	WHO 1984
Single oral dose of 1,000 mg/kg BW	Severe respiratory and nervous signs in 16 h, and death in 48 h	WHO 1984
Baboon, *Papio anubis*		
Fed diets containing chlordane, equivalent to 0.1–1.0 mg/kg BW daily, for 2 years	At 1.0 mg/kg BW, cytochrome P-450 activity was significantly increased, but no other significant effects were recorded on general health or on any major organ system	WHO 1984
Rat, *Rattus* spp.		
Inhalation of air for various intervals containing technical chlordane		
0.1 µg/L, 90 days	Adverse biological response	Khasawinah et al. 1989
5.8 or 28.2 µg/L, 28 days	No measurable difference from controls at low dose; impaired liver function at high dose	Khasawinah et al. 1989
154 µg/L, 5 days	Death	Khasawinah et al. 1989
413 µg/L, 2 days	Death	Khasawinah et al. 1989
Fed technical chlordane at dietary levels of 1, 5, or 25 mg/kg, equivalent to daily doses of 0.045, 0.229, and 1.175 mg/kg BW respectively, for 130 weeks (2.5 years)	No significant effects on hematology, clinical chemistry, body weight, or survival rate. Dose-dependent hepatocellular necrosis (34% in high-dose group); liver adenomas in males and hepatocellular swelling in females from the high-dose group	EPA 1988
0.05 mg radiolabeled *trans*-chlordane per kilogram BW, single oral dose, residues measured over 96 h after exposure	Maximum resides, in mg/kg FW, and time after administration were: liver, 0.1, 2 h; adipose tissue, 0.09, 96 h; kidney, 0.07, 4 h; skin, 0.03, 8 h; brain, 0.01, 4 h; muscle, 0.008 4 h; and blood 0.003, 4 h. Half-time persistence was 6.5–13 h for the rapidly decreasing phase and 4.8–8.9 days for the slowly decreasing phase	Ohno et al. 1986
Daily intraperitoneal injections of technical chlordane at 0.15, 1.75, or 25 mg/kg daily for 42 days	Dose-dependent alterations of brain potentials without behavioral signs of chronic toxicity	EPA 1980
Single oral dose of 0.2 mg/kg BW of *cis*-chlordane, *trans*-chlordane, or oxychlordane	Maximum residues in fat after 24 h, in mg/kg FW, were 0.3 for *cis*-chlordane, 0.7 for *trans*-chlordane, and 0.5 for oxychlordane	Nomeir and Hajjar 1987
Single oral dose of 0.2 or 1.0 mg/kg BW technical chlordane	Maximum residues in fat at 24 h, in mg/kg FW, were 0.5 for the low-dose group, and 3.7 for the high-dose group	Nomeir and Hajjar 1987
Fed diets containing 0.3, 3, 15, 30, or 60 mg technical chlordane per kilogram diet for 3 generations	Levels up to and including 30 mg/kg diet had no measurable effect on fertility, number of young produced, growth, or mortality rate; no gross or microscopic differences between the	NRCC 1975; WHO 1984

	groups. At 60 mg/kg, the second F_3 generation litters had elevated mortality (11%) during the latter part of the nursing period; these animals also showed gross and microscopic pathology	
Single oral dose of 1.0 mg *cis*-chlordane per kilogram BW	Peak tissue concentration, in mg/kg FW, were noted within 4 h after treatment: liver, 1.9; fat, 1.2; kidney, 0.7; lung, 0.3; brain 0.2; testes, 0.1; muscle, 0.1; and blood, 0.08. After 12 h, 7% was excreted, and after 3 days, 83% was voided	Ewing et al. 1985
Single oral dose of 1.0 mg/kg BW	About 50% excreted in feces after 1 day and 90% in 7 days; only 2–3% of the dose was detected in the urine	Nomeir and Hajjar 1987
Fed oxychlordane in diets for 90 days at rate equivalent to 2.0 mg/kg BW daily	No gross pathology or histological lesions	NRCC 1975; WHO 1984
Fed 2.5, 25, or 75 mg technical chlordane per kilogram of diet for 2 years	Severe toxic signs at 25 and 75 mg/kg; liver damage at 2.5 mg/kg diet	WHO 1984
Long-term feeding studies at dietary concentrations between 5 and 320 mg technical chlordane per kilogram	Reduced survival and growth at dietary levels >150 mg/kg; liver enlargement and micropathology at >20 mg/kg; no effect on reproduction at 150 mg/kg diet; no adverse effects at 5 mg/kg diet	Ingle 1965
Fed *cis*-chlordane at dietary levels of 0.5, 15, 25, or 35 mg/kg	Increased mortality and growth retardation in 4–5 months at 35 mg/kg diet; growth normal in other groups; some liver damage in 25 and 35 mg/kg groups	WHO 1984
Daily oral dose of 6.5–25 mg technical chlordane per kilogram BW, for 15 days	No tremors or convulsions; however, dose-related liver pathology was noted	WHO 1984
Single oral dose of 10 mg radiolabeled *trans*-chlordane per kilogram BW	Maximum residues, in mg/kg FW and time after administration were: liver, 21, 4 h; kidney, 18, 4h; adipose tissue, 11, 16 h; skin, 5, 8 h; brain, 3.4, 4 h; muscle 1.4, 4 h; and blood, 0.6, 4 h; half-life of 5–12 h for the fast component, and 4.3–7.3 days for the slow component	Ohno et al. 1986
Fed diets containing 15 or 25 mg/kg of *cis*-chlordane for 78 weeks	No adverse effects on liver at 15 mg/kg diet; some effects at 25 mg/kg	NRCC 1975
Fed *trans*-chlordane at dietary levels of 15, 25, 35, or 75 mg/kg diet	Decreased survival, liver damage, and growth retardation of males in 8 months at 75 mg/kg diet; growth normal at other doses	WHO 1984
19.1 mg oxychlordane per kilogram BW	Acute oral LD50	WHO 1984
20 mg technical chlordane per kilogram diet for 350 days	Residues in mg/kg FW, were about 20 for adipose tissue, 0.8 for liver, and 0.2 for heart	NRCC 1975
Daily oral doses of 25 mg/kg BW for 15 days	No toxic signs	EPA 1980

Fed diets containing 35 mg/kg *trans*-chlordane for 78 weeks	No adverse effects on liver	NRCC 1974
Daily oral dose of 50 mg technical chlordane per kilogram BW for 15 days	2 of 5 rats died; toxic signs in survivors	WHO 1984
83–392 mg/kg BW	Acute oral LD50 for *cis*-chlordane	EPA 1980, 1988
Fed diets containing 100 or 200 mg/kg ration of *cis*-chlordane or *trans*-chlordane for 11–15 days	Maximum residues, in mg/kg lipid, in females fed 100 mg/kg *cis*-chlordane were 23 for *cis*-chlordane and 100 for oxychlordane; for the 200 *cis*-chlordane group, levels were 48 for *cis*-chlordane and 182 for oxychlordane. Females fed 100 mg/kg *trans*-chlordane had 10 mg/kg lipid of *trans*-chlordane and 201 of oxychlordane; for the 200 mg/kg group, residues were 23 mg/kg lipid of *trans* chlordane and 470 of oxychlordane; for all groups, residues in males were x6–21 lower than in females	Nomeir and Hajjar 1987
Fed diets averaging 121 and 241 mg/kg feed (females) and 203 and 407 mg technical chlordane per kilogram diet (males) for 80 weeks	Increased mortality, tremors, growth reduction; elevated incidence of thyroid neoplasms and malignancies in all treated animals, but no hepatocellular carcinomas	IARC 1979; EPA 1988
137 mg/kg BW	Acute oral LD50 for rats fed a low protein diet	EPA 1980
200–590 mg technical chlordane per kilogram BW	Acute oral LD50	NRCC 1975; EPA 1980; WHO 1984
205 mg technical chlordane per kilogram BW	Acute dermal LD50 for females	WHO 1984
Fed diets containing 300, 500, or 1,000 mg technical chlordane per kilogram	75% dead at 300 mg/kg diet after 100 days; all dead in 70 days at 500 mg/kg, or in 10 days at 1,000 mg/kg	WHO 1984
311 mg/kg BW	Acute oral LD50 for rats fed a normal protein diet	EPA 1980
Fed diets containing 320 mg technical chlordane per kilogram from weaning	Reduced sexual activity, reduction in number of viable litters, increase rate of death of progeny before weaning	WHO 1984
327 mg *trans*-chlordane per kilogram BW	Acute oral LD50	EPA 1980; WHO 1984
335 mg/kg BW	Acute oral LD50 for males	IARC 1979
343 mg/kg BW	Acute intraperitoneal (IP) LD50 for adults	EPA 1980
350 mg/kg BW	IP injection produced mild tremors and disorientation within a few minutes, and death within 60 min	EPA 1980
530–690 mg/kg BW	Acute dermal LD50 for females	EPA 1980; WHO 1984
539 mg/kg BW	Acute IP LD50 for newborns pretreated with 40 mg/kg BW phenobarbitol	EPA 1980
840 mg/kg BW	Acute dermal LD50 for males	EPA 1980
1,121 mg/kg BW	Acute IP LD50 for newborns	EPA 1980
Oral administration, in mg/kg BW, of 4,600	Less than 50% dead	WHO 1984

chlordene, 4,600 3-chlorochlordene, 4,600 1-hydroxychlordene, 4,600 chlordene epoxide, 4,600 1-hydroxy, 2, 3-epoxy chlordene, or 10,200 2-chlorochlordene		
Pig, *Sus* spp.		
Fed diet containing 300 mg/kg of *cis*-chlordane or *trans*-chlordane for 60–90 days	Residues of total chlordanes in fat ranged from 9 mg/kg to 72 mg/kg; values were highest for *trans*-chlordane and lowest for *cis*-chlordane	NRCC 1975

Chlordane tends to accumulate in adipose tissues and, to a lesser extent, in liver (Table 5). In general, animals given a single oral dose of chlordane eliminated 80 to 90% of the dose within 7 days, usually by way of the feces; the *cis* isomer is eliminated more rapidly than the *trans* isomer and results in preferential accumulations of *trans*-chlordane (Nomeir and Hajjar 1987). In rats, *trans*-chlordane is rapidly absorbed and distributed to liver and kidney at single oral dosages as low as 0.05 mg/kg BW Ohno et al. 1986). Rabbits fed *trans*-chlordane for 10 weeks excreted 70% of accumulated chlordane during the following 2 weeks on a chlordane-free diet (Menzie 1974). Treatment with *trans*-chlordane resulted in a greater percentage of oxychlordane in fat than did treatment with *cis*-chlordane. When chlordane was removed from the diet of treated animals, levels in fat declined 60% at a relatively steady rate over 4 weeks, but then only slightly thereafter; accumulations in liver, kidney, brain, and muscle were much lower than in fat, but excretion kinetics were similar (Nomeir and Hajjar 1987).

Results of chronic feeding studies show that dietary concentrations of chlordane between 0.76 and 5 mg/kg ration did not affect survival but did produce adverse effects on various species of laboratory animals and livestock (Table 5). Dietary concentrations of 0.76 mg/kg (equivalent to 0.09 mg/kg BW daily) were associated with enlarged livers in mice, 1.0 mg/kg produced elevated residues in cow's milk, 2.5 mg/kg resulted in liver pathology in rats, 3 mg/kg (equivalent to 0.075 mg/kg BW daily) produced high residues in fat of dogs, and 5 mg/kg caused liver pathology in mice (Table 5).

Negative results for mutagenicity of *cis*-chlordane and *trans*-chlordane were reported in various strains of bacteria and in hepatocyte cultures of small mammals. But technical chlordane proved mutagenic to selected strains *of Salmonella typhimurium* and induced gene conversions in certain strains of the yeast *Saccharomyces cervisiae* (IARC 1979; EPA 1980, 1988; WHO 1984).

Chlordane interacts with other chemicals to produce additive or more than additive toxicity. For example, chlordane increased hepatotoxic effects of carbon tetrachloride in the rat (EPA 1980; WHO 1984), and in combination with dimethylnitrosamine acts more than additively in producing liver neoplasms in mice (Williams and Numoto 1984). Chlordane in combination with endrin, methoxychlor, or aldrin is additive or more-than-additive in toxicity to mice (Klaassen et al. 1986). Protein deficiency doubles the acute toxicity of chlordane to rats (WHO 1984). In contrast, chlordane exerts a protective effect against several organophosphorus and carbamate insecticides (WHO 1984) protects mouse embryos against influenza virus infection and mouse newborns against oxazolone delayed hypersensitivity response (Barnett et al. 1985). More research seems warranted on interactions of chlordane with other agricultural chemicals.

Recommendations

All use of chlordane was banned in Norway in 1967 (Ingebrigtsen et al. 1984). In August 1975, EPA issued its intent to suspend registrations and prohibit production of all pesticides containing heptachlor or chlordane, based on evidence of carcinogenicity (Glooschenko and Lott 1977). On 1 July 1983, chlordane use was prohibited in the United States for any purpose except to control underground termites; a similar situation exists in Japan (Ohno et al. 1986; Tojo et al. 1986).

The continued use of chlordane, coupled with its general persistence in the environment, suggests that extreme caution be taken in all stages of its manufacture, transport, storage, and application (Greenhalgh 1986).

In particular, chlordane use near marine environments is not recommended because of chlordane's high toxicity to marine life (EPA 1988). At elevated risk of chlordane toxicity in the human population are children, as a result of the milk they consume; fisherman and their families, because of high consumption of fish and shellfish; people living downwind from fields treated with chlordane; and individuals residing in houses treated with chlordane-containing pesticides (EPA 1980).

The proposed criterion for marine life protection of 0.004 µg/L as a 24-hour mean, not to exceed 0.09 µg/L at any time (Table 6), seems to offer a reasonable degree of protection. But the proposed freshwater criterion of 0.0043 µg/L 24-hour average, not to exceed 2.4 µg/L at any time (Table 6), overlaps the range of 0.2 to 3.0 µg/L, shown earlier to be harmful to sensitive species of fish and aquatic invertebrates; accordingly, the maximum permissible freshwater value should be adjusted downward. "Safe" residues in tissues of aquatic biota require clarification, and probably additional research effort. Criteria on chlordane for protection of mammalian wildlife are missing, and those formulated for birds are incomplete and require data on no-observable-effect levels from lifetime exposures (Table 6). Until this information becomes available, it seems prudent to use criteria developed for human health protection as temporary guidelines for the protection of vertebrate wildlife. Specifically, daily intake should not exceed 0.001 mg total chlordane, including chlordane, *trans*-chlordane, and oxychlordane per kilogram BW; and food items should not exceed 0.3 mg/kg FW (Table 6).

Table 6. Proposed chlordane criteria for protection of natural resources of human health.

Resource	Criterion or effective chlordane concentration	Reference[a]
Aquatic life		
Water concentration, safe level		
Fresh water	<0.0043 ug/L, 24-h average; not to exceed 2.4 ug/L at any time	1
Salt water	<0.004 µg/L, 24-h average; not to exceed 0.09 ug/L at any time	1
Tissue concentrations		
Fish		
Reduced survival	>300 mg/kg tissue, lipid weight (LW) basis	2
No observed adverse effect level (NOEL)	<0.1 mg/kg fresh weight (FW) tissue	3
Estuarine invertebrates, lethal	>106 mg/kg tissue LW	2
Birds		
Concentration in brain		
Joint lethal range	1.1–5.5 mg/kg FW for oxychlordane and 3.4–8.3 mg/kg FW for heptachlor epoxide	4, 12
Single lethal range	6 mg/kg FW for oxychlordane or 9 mg/kg FW for heptachlor epoxide	4, 12
Diet, acceptable range, but producing slight elevation in tissue concentrations	0.1–0.3 mg/kg diet	6
Mammals		
Dog, *Canis familiaris*, NOEL	<3 mg/kg diet, equivalent to <0.075 mg/kg body weight (BW) daily	5, 6
Rat, *Rattus* sp., NOEL	<5 mg/kg diet, equivalent to 0.25 mg/kg BW daily	5
Livestock water use, United States	<3 ug/L	

Human health		
Drinking water		
Worldwide	<0.3 ug/L	5
Canada, United States	<3.0 ug/L	1, 7
Chronic, child, United States	<0.5 ug/L	7
Maximum 1-day exposure, adult, USA	63.0 ug/L	7
Increased lifetime risk of cancer, 70-kg adult, 2 L daily[b]		
10^{-4}	2.7 ug/L	7
10^{-5}	0.27 ug/L	7
10^{-6}	0.027 ug/L	7
Acceptable daily intake[e] 70-g adult	<70 ug, equivalent to <0.001 mg/kg BW	1, 3, 5, 6, 8
Diet		
U.S. Food and Drug Administration "action level"	0.3 mg/kg FW	3, 8, 9, 10
Australia	<0.05 mg/kg FW in meats, including oxychlordane	11
Worldwide	Usually <0.3 mg/kg FW, but residue tolerances vary between 0.02 and 0.5 mg/kg FW, based on the sum of *cis*-chlordane, *trans*-chlordane, and oxychlordane	5, 8
Air		
USSR	Maximum allowable concentration of 0.01 mg/m^3	5
Romania	<0.3 mg/m^3, maximum allowed is 0.6 mg/m^3	5
Belgium, Finland, United States, Japan, the Netherlands	<0.5 mg/m^3	1, 5, 7, 8
15-min exposure limit, United States	<2 mg/ m^3	1

[a] 1. EPA 1980; 2. Zitko 1978; 4. Blus et al. 1983; 5. WHO 1984; 6. NRCC 1975; 7. EPA 1988; 8. IARC 1979; 9. 1965; 10. Wood et al. 1986; 11. Petterson et al. 1988; 12. Stickel et al. 1979.

[b] One excess cancer per million (10^{-6}) is associated with lifetime exposure to chlordane in drinking water at concentrations as low as 0.027 µg/L, the most conservative estimate. A lifetime health advisory computation was not possible because chlordane is a probable human carcinogen (EPA 1988).

[c] Consumed fish are considered to be the only source of chlordane; up to 98% of chlordane exposure results from aquatic organisms with high top (up to 14,100 times) bioconcentration potential (EPA 1980). Urban residents should not consume more than 8 ounces (227 g) of dish daily containing 0.03 mg total chordanes per kilogram FW, and nonurban residents up to 1, 135 mg of fish daily containing 0.03 mg/kg FW (Arruda et al. 1987). The value of 0.001 mg/kg BW is based on the no-observed-effect level of 5 mg/kg in the diet of the rat, equivalent to 0.25 mg/kg BW, and 3 mg/kg in the diet of the dog, equivalent to 0.075 mg/kg BW (WHO 1984).

Additional research on chlordane is recommended in nine general areas: (1) monitoring of background concentrations of oxychlordane in wildlife, since this metabolite is more toxic and persistent than the parent chemical (Kawano et al. 1988); (2) interpretation of the biological significance of residue levels found in wildlife; (3) adoption of improved uniform methods of quantitation so that residue levels can be compared, and so that a time estimate of their environmental significance can be made (NRCC 1975; EPA 1988); (4) reexamination of aquatic toxicity data where concentrations tested exceeded the solubility of chlordane in water of 6 to 9 µg/L (WHO 1984); (5) evaluation of interaction of chlordane with other agricultural chemicals, including heptachlor, to clearly delineate any additive, synergistic, or antagonistic effects (WHO 1984); (6) reevaluation of the cancer risk of chlordane to experimental animals (WHO 1984); (7) measurement of chronic exposures of fish and wildlife to realistic environmental levels (WHO 1984); (8) measurement of effects of depleted soil fertility from chlordane-induced earthworm suppression on migratory birds and other wildlife (NRCC 1975; WHO 1984); and (9) continuance of epidemiological studies on workers who have been exposed to chlordane (WHO 1984).

Acknowledgments

I thank N. Bushby, J. Corley, and L. Garrett for literature search and retrieval; B. A. Roberts for secretarial assistance; L. J. Blus, R. Crunkilton, N. C. Coon, J. B. Hunn A. J. Krynitsky, D. H. White, and J. L. Zajicek for technical and scientific review; and C. M. Lemos, C. E. Puckett, and J. R. Zuboy for editorial services.

References

Agrawal, H. P 1986. The accumulation of biocide residues in a few tissues of *Lamellidens marginalis.* J. Anim. Morphol. Physiol. 33:45-50.

Albright L J., R C. Oloffs, and S. Y. Szeto. 1980. Residues in cutthroat trout *(Salmo clarki)* and California newts *(Tarichiatorosa)* from a lake treated with technical chlordane. J. Environ. Sci. Health M B. Pestic. Food Contam. Agric. Wastes 15:313-349.

Ambrose, R. E., C. J. Henny, R. E. Hunter, and J. A. Crawford. 1988. Organochlorines in Alaskan peregrine eggs and their current impact on productivity. Pages 385-393 *in* T J. Cade, J. H. Enderson C. G. Thelander, and C. M. White, eds. Peregrine falcon populations: their management and recovery. The Peregrine Fund, Inc., Boise, Idaho.

Anderson, D. W, D. G. Raveling, R. W. Risebrough, and A. M. Springer. 1984. Dynamics of low-level organochlorines in adult cackling geese over the annual cycle. J. Wildl. Manage. 48:1112-1127.

Arruda, J. A., M. S. Cringan, D. G. Gilliand S. G. Haslouer, J. E. Fry, R. Broxterman, and K. L Brunson. 1987. Correspondence between urban areas and the concentrations of chlordane in fish from the Kansas River. Bull. Environ. Contam. Toxicol. 39:563-570.

Balash, K. J., M. A. Al-Omer, and B. M. A. Latif. 1987. Effect of chlordane on testicular tissues of Swiss mice. Bull. Environ. Contam. Toxicol. 39:434-442.

Barbehenn, K. R., and W. L. Richel. 1981. Organochlorine concentrations in bald eagles: brain/body lipid relations and hazard evaluation. J. Toxicol. Environ. Health 8:325-330.

Barnett, J. B., L S. F Soderberg, and J. H. Menna. 1985. The effect of prenatal chlordane exposure on the delayed hypersensitivity response of BALB/c mice. Toxicol. Lett. Amst. 25:173-183.

Beeman, R. W, and R. Matsumura. 1981. Metabolism of *cis*- and *trans*-chlordane by a soil microorganism. J. Agric. Chem. 29:94- 99.

Best, J.B., M. Morita, and B. Abbotts. 1981. Acute toxic responses of the freshwater planarian, *Dugesia dorotocephala, to*chlordane. Bull. Environ. Contam. Toxicol. 26:502- 507.

Biggs, D. C., R. G. Rowland H. B. O'Connors, Jr., C. D. Powers, and C. F. 1978. A comparison of the effects of chlordane and PCB on the growth, photosynthesis and cell size of phytoplankton. Environ. Pollut. 15:253-263.

Blus, L. .J., C. J. Henny, and A. J. Krynitsky. 1985. Organochlorine-induced mortality and residues in long-billed curlews from Oregon. Condor 87:563-565.

Blus, L. J., C. J. Lamont, and B. S. Neely, Jr. 1979. Effects of organochlorine residues on eggshell thickness, reproduction, and population status of brown pelicans (*Pelecanus occidentalis*) in South Carolina and Florida, 1969 - 76. Pestic. Monit. J. 12:172- 184.

Blus, L. J., 0. H. Pattee, C. J. Henny, and R. M. Prouty. 1983. First records of chlordane-related mortality in wild birds. J. Wildl. Manage. 47:196- 198.

Blus, L. J., and C. 1. Stafford. 1980. Breeding biology and relation of pollutants to black skimmers and gull-billed terns in South Carolina. U.S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 230. 18 pp.

Bunck, C. M., R. M. Prouty, and A. J. Krynitsky. 1987. Residues of organochlorine pesticides and polychlorobiphenyls in starlings *(Sturnus vulgaris),* from the continental United States, 1982. Environ. Monit. Assess. 8:59-75.

Bush, J., and T B. Grace. 1989. Fish contaminant study of the Missouri and Mississippi rivers. Final report, National Marine Fisheries Service, Program 2-416-R-3, Project II. 102 pp.

Cain, B. W., and C. M. Bunck. 1983. Residues of organochlorine compounds in starlings *(Sturnus vulgaris),* 1979. Environ. Monit. Assess. 3:161- 172.

Cardwell, R. D., D. G. Foreman, T R. Payne, and D. J. Wilbur. 1977. Acute and chronic toxicity of chlordane to fish and invertebrates. U.S. Environ. Prot. Agency Rep. 600/3-77-019. 125 pp.

Carey, A. E., J. A. Gowen, H. Tai, W. G. Mitchell, and G. B. Wiersma. 1978. Pesticide residue levels in soils and crops, 1971--National Soils Monitoring Program (III). Pestic. Monit. J. 12:117-136.

Carey, A. E., J. A. Gowen, H. Tai, W. G. Mitchell, and G. B. Wiersma. 1979. Pesticide residue levels in soils and crops from 37 States, 1972--National Soils Monitoring Program (IV). Pestic. Monit. J. 12:209 - 229.

Clark, D. R., Jr., R. K. LaVal, and A. J. Krynitsky. 1980. Dieldrin and heptachlor residues in dead gray bats, Franklin County, Missouri- 1976 versus 1977. Pestic. Monit. J. 13:137- 140.

Clark, D. R., Jr., and R. M. Prouty. 1976. Organochlorine residues in three bat species from four localities in Maryland and West Virginia, 1973. Pestic. Monit. J. 10:44- 53.

DeVault D. S., W. A. Willford, R. J. Hesseberg, D. A. Nortrupt E. G. S. Rundberg, A. K. Alwan, and C. Bautista. 1986. Contaminant trends in lake trout *(Salvelinus namaycush)* from the upper Great Lakes. Arch. Environ. Contam. Toxicol. 15:349-356.

DeWeese, L. R., L. C. McEwen, G. L Hensler, and B. E. Petersen. 1986. Organochlorine contaminants in passeriformes and other avian prey of the peregrine falcon in the western United States. Environ. Toxicol. Chem. 5:675- 693.

DouAbul, A. A., H. T Al-Saad, A. A. Al-Timari, and H. N. Al-Rekabi. 1988. Tigris-Euphrates Delta: a major source of pesticides to the Shatt al-Arab River (Iraq). Arch. Environ. Contam. Toxicol. 17:405- 418.

Dowd, P E, G. U. Hayfield, D. R Coulon, J. B. Graves, and J. D. Newsom. 1985. Organochlorine residues in animals from three Louisiana watersheds in 1978 and 1979. Bull. Environ. Contam. Toxicol. 3:832- 84 1.

Eisenberg, M., and J. J. Topping. 1985. Organochlorine residues in finfish from Maryland waters 1976-1980. J. Environ. Sci. Health Part B. Pestic. Food Contam. Agric. Wastes 20:729-742.

Elliott, J. E., R. J. Norstrom, and J. A. Keith. 1988. Organochlorines and eggshell thinning in northern gannets *(Sula bassanus)* from eastern Canada, 1968-1984. Environ. Pollut. 52:81-102.

Environmental Protection Agency (EPA). 1973. Water quality criteria 1972. U.S. Environ. Prot. Agency Rep. R3-73-033. 594 pp.

Environmental Protection Agency (EPA). 1980. Ambient water quality criteria for chlordane. U.S. Environ. Prot. Agency Rep. 440/5- 80- 027. 60 pp.

Environmental Protection Agency (EPA). 1988. United, States Environmental Protection Agency Office of Drinking Water Health Advisories. Chlordane. Rev. Environ. Contam. Toxicol. 104:47-62.

Epstein, S. S. 1976. Carcinogenicity of heptachlor and chlordane. Sci. Total Environ. 6:103- 154.

Evans, M. S., R. W. Bathelt, and C. P Rice. 1982. PCB's and other toxicants in *Mysis relicta*. Hydrobiologia 93:205- 2151.

Ewing, A. D., A. M. Kadry, and H. W. Dorough. 1985. Comparative disposition and elimination of chlordane in rats and mice. Toxicol. Lett. Amst. 26:233- 239.

Feroz, M., and M. A. Q. Khan. 1979a. Metabolism tissue distribution, and elimination of *cis*-[^{14}C] chlordane in the tropical freshwater fish *Cichlasoma* sp. J. Agric. Food Chem. 27:1190-1197.

Feroz, M., and M. A. Q. Khan. 1979b. Fate of ^{14}C-*cis*-chlordane goldfish *Carassius auratus* (L.). Bull. Environ. Contam. Toxicol. 23:64- 69.

Fitzner, R. E., L. J. Blus, C. J. Henny, and D. W. Carlile. 1988. Organochlorine residues in great blue herons from the northwestern United States. Colon. Waterbirds 11:293- 300.

Foley, R. E., and G. R. Batcheller. 1988. Organochlorine contaminants in common goldeneye wintering on the Niagara River. J. Wildl. Manage. 52:441- 445.

Frank, R., R. L. Thomas, H. E. Braun, J. Rasper, and R. Dawson. 1980. Organochlorine insecticides and PCB in the surficial sediments of Lake Superior (1973). J. Gt. Lakes Res. 6:113-120.

Glooschenko, V., M. Holdrinet J. N. A. Lott, and R. Frank. 1979. Bioconcentration of chlordane by the green alga *Scenedesmus quadricauda*. Bull. Environ. Contam. Toxicol. 21:515- 520.

Glooschenko, V., and J. N. A. Lott. 1977. The effects of chlordane on the green alga *Scenedesmus quadricauda* and *Chlamydomonas* sp. Can. J. Bot. 55:2866-2872.

Glynn, P. W., A. M. Szmant, E. F. Corcoran, and S. V. Cofer-Shabica. 1989. Condition of coral reef cnidarians from the northern Florida reef tract: pesticides, heavy metals, and histopatholgical examination. Mar. Pollut. Bull. 20:568-576.

Greenhalgh, E. A. 1986. The effects of chlordane and rotenone on the alimentary tract of the field cricket. Toxicology 42:317-330.

Hall, R. J., T E. Kaiser, W. B. Robertson, Jr., and R C. Patty. 1979. Organochlorine residues in eggs of the endangered American crocodile *(Crocodylus acutus).* Bull. Environ. Contam. Toxicol. 23:87-90.

Hall, W. S., K. L. Dickson, F. Y. Saleh, and J. H. Rodgers, Jr. 1986. Effects of suspended solids on the bioavailability of chlordane to *Daphnia magna.* Arch. Environ. Contam. Toxicol. 15:529-534.

Hanson, W. R. 1952. Effects of some herbicides and insecticides on biota of North Dakota marshes. J. Wildl. Manage. 16:299-308.

Haseltine, S. D., B. M. Muthern, and C . Stafford. 1980. Organochlorine and heavy metal residues in black duck eggs from the Atlantic Flyway, 1978. Pestic. Monit. J. 14:53- 57.

Heinz, G. H., S. D. Haseltine, R. J. Hall, and A. J. Krynitsky. 1980. Organochlorine and mercury residues in snakes from Pilot and Spider islands, Lake Michigan- 1978. Bull. Environ. Contam. Toxicol. 25:738-743.

Helle, E., H. Hyvarinen, H. Pyysalo, and K. Wickstrom. 1983. Levels of organochlorine compounds in an inland seal population in eastern Finland. Mar. Pollut. Bull. 14:256-260.

Henle, K. 1988. Amphibian and reptile fatalities caused by chlordane spraying? Victorian Nat. 105:216-217.

Hill, E. E, R. G. Heath, J. W Spann, and J. S. Williams. 1975. Lethal dietary toxicities of environmental pollutants to birds. U.S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 191. 61 pp.

Hill, E. F., and M. B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to coturnix. U.S. Fish Wildl. Serv., Tech. Rep. 2. 147 pp.

Hoff, R. M., and K. W. Chan, 1986. Atmospheric concentrations of chlordane at Mould Bay, N.W.T, Canada. Chemosphere 15:449-452.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish Wildl. Serv., Resour. Publ. 153. 90 pp.

Hunter, R. G., J. H. Carroll, and J. C. Randolph. 1980. Organochlorine residues in fish of Lake Texoma, October 1979. Pestic. Monit. J. 14:102- 107.

Ingebrigtsen K., J. U. Skaare, and S. W. Teigen. 1984. Organochlorine residues in two Norwegian puffin *(Fratercula arctica)* colonies. J. Toxicol. Environ. Health 14:813- 828.

Ingle, L. 1965. A monograph on chlordane. Toxicological and pharmacological properties. Library of Congress Number 65- 28686. 88 pp.

International Agency for Research on Cancer (IARC). 1979. Chlordane. Int. Agen. Res. Cancer, Monographs. Eval. Carcinogen. Risk Chem. Hum. 20:45- 65.

Johnson, K. W., M. P. Holsapple, and A. E. Munson. 1986. An immunotoxicological evaluation of -chlordane. Fund. Appl. Toxicol. 6:317- 326.

Johnson, K. W., N. E. Kaminski, and A. E. Munson. 1987. Direct suppression of cultured spleen cell responses by chlordane and the basis for differential effects on in vivo and in vitro immunocompetence. J. Toxicol. Environ. Health 22:497-515.

Johnson, W. W., and M. T Finley. 1980. Handbook of acute toxicity of chemicals to fish and invertebrates. U.S. Fish Wildl. Serv., Resour. Publ. 137. 98 pp.

Juarez, A., and J. A. Guzman. 1984. Chronic effect of five organochlorine insecticides on larvae of *Bufo arenarum.* Commun. Biologicas 2:411- 415.

Kaiser, K. L. E. 1982. Early trend determination of organochlorine contamination from residue ratios in the sea lamprey *(Petromyzon marinus)* and its lake whitefish *(Coregonus clupeaformis)* host. Can. J. Fish. Aquat. Sci. 39:571-579.

Kaiser, T E., W. L. Reichel, L. N. Locke, E. Chromartie, A. J. Krynitsky, T. G. Lamont B. M. Mulhern, R. M. Prouty, C. J. Stafford, and D. M. Swineford. 1980. Organochlorine pesticide, PCB, and PBB residues and necropsy data for bald eagles from 29 States--1975-77. Pestic. Monit. J. 13:145-149.

Kawano, M., T. Inoue, T. Wada, H. Hidaka, and R. Tatsukawa. 1988. Bioconcentration and residue patterns of chlordane compounds in invertebrates, fish, mammals, and seabirds. Environ. Sci. Technol. 22:792- 797.

Kawano, M., S. Matsushita, T. Inoue, H. Tanaka, and R. Tatsukawa. 1986. Biological accumulation of chlordane compounds in marine organisms from the northern North Pacific and Bering Sea. Mar. Pollut. Bull. 17:512- 516.

Kawano, M., S. Tanabe, T. Inoue, and R. Tatsukawa. 1985. Chlordane compounds found in the atmosphere from the Southern Hemisphere. Trans. Tokyo Univ. Fish. 6:59- 66.

Kerkhoff, M., and J. D. Boer. 1982. Identification of chlordane compounds in harbour seals from the coastal waters of the Netherlands. Chemosphere 11:841- 845.

Khan, R. M., and A. P Singh. 1985. Control of termites in wheat crop with insecticides applied through irrigation. Entomon 10:197-201.

Khasawinah, A. M., C. J. Hardy, and G. C. Clark. 1989. Comparative inhalation toxicity of technical chlordane in rats and monkeys. J. Toxicol. Environ. Health 28:327- 347.

King, K. A., and A. J. Krynitsky. 1986. Population trends, reproductive success, and organochlorine chemical contaminants in waterbirds nesting in Galveston Bay, Texas. Arch. Environ. Contam. Toxicol. 15:367-376.

Klaas, E. E., H. M. Ohlendorf, and E. Cromartie. 1980. Organochlorine residues and shell thicknesses in eggs of the clapper rail, common gallinule, purple gallinule, and limpkin (Class Aves), eastern and southern United States, 1972-74. Pestic Monit. J. 14:90-94.

Klaassen C. D., M. 0. Amdur, and J. Doull. 1986. Casarett and Doull's toxicology. 3rd ed. Macmillan Publishing Company, New York. 974 pp.

Knap, A. H., K. S. Binkley, and W G. Deuser. 1986. Synthetic organic chemicals in the deep Sargasso Sea. Nature 319:572-574.

Kubiak, T J., H. J. Harris, L M. Smith, T R. Schwartz, D. L Stalling, J. A. Trick, L Sileo, D. E. Docherty, and T. C. Erdman 1989. Microcontaminants and reproductive impairment of the Forster's tern on Green Bay, Lake Michigan-1983. Arch. Environ. Contam. Toxicol. 18:706- 727.

Kuehl, D. W, E. N. Leonard, B. C. Butterworth, and K. L. Johnson. 1983. Polychlorinated chemical residues in fish from major watersheds near the Great Lakes, 1979. Environ. Int. 9:293- 299.

Kuehl, D. W, E. N. Leonard, K. J. Welch, and G. D. Vieth. 1980. Identification of hazardous organic chemicals in fish from the Ashtabula River, Ohio, and Wabash River, J. Assoc. Off. Anal. Chem. 63:1238-1244.

Kunz, T. H., E. L. P. Anthony, and W. T. Rumage, III. 1977. Mortality of little brown bats following multiple pesticide applications. J. Wildl. Manage. 41:476-483.

Lang, J. T., L. L. Rodriguez, and J. M. Livingston. 1979. Organochlorine pesticide residues in soils from six U.S. Air Force bases, 1975-76. Pestic. Monit. J. 12:230-233.

Littrell, E. E. 1986. Shell thickness and organochlorine pesticides in osprey eggs from Eagle Lake, California. Calif. Fish Game 72:182-185.

Loganathan, B. G., S. Tanabe, M. Goto, and R. Tatsukawa. 1989. Temporal trends of organochlorine residues in lizard goby *Rhinogobius flumineus* from the River Nagaragawa, Japan. Environ. Pollut. 62:237-251.

Ludke, J. L. 1976. Organochlorine pesticide residues associated with mortality: additivity of chlordane and endrin. Bull. Environ. Contam. Toxicol. 16:253- 259.

Ludke, J. L. 1977. DDE increases the toxicity of parathion to coturnix quail. Pest. Biochem. Physiol. 7:28-33.

Lundholm, C. E. 1988. The effects of DDE, PCB and chlordane on the binding of progesterone to its cytoplasmic receptor in the eggshell gland mucosa of birds and the endometrium of mammalian uterus. Comp. Biochem. Physiol. 89C:361- 368.

Magnani, B., C. D. Powers, C. E Wurster, and H. B. O'Connors, Jr. 1978. Effects of chlordane and heptachlor on the marine dinoflagellate, *Exuviella baltica*. Lohmann. Bull. Environ. Contam. Toxicol. 20:1-8.

Mayer, F. L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U.S. Environ. Prot. Agency Rep. 600/8- 87/017. 274 pp.

Mayer, F. L., Jr., and M. R. Ellersieck 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals U.S. Fish Wildl. Serv., Resour. Publ. 160. 579 pp.

McLeese, D. W., L. E. Burridge, and J. V. Dinter. 1982. Toxicities of five organochlorine compounds in water and sediments to *Nereis virens.* Bull. Environ. Contam. Toxicol. 28:216-220.

McLeese, D. W., and C. D. Metcalfe. 1980. Toxicities of eight organochlorine compounds in sediment and seawater to *Crangon septemspinosa.* Bull. Environ. Contam. Toxicol. 25:921-928.

Menzie, C. M. 1969. Metabolism of pesticides. U.S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 127. 485 pp.

Menzie, C. M. 1974. Metabolism of pesticides. An update. U.S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 184. 486 pp.

Menzie, C. M. 1978. Metabolism of pesticides. Update II. U.S. Fish Wildl. Serv., Spec. Sci. Rep. -Wildl. 212. 381 pp.

Menzie, C. M. 1980. Metabolism of pesticides. Update III. U.S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 232. 709 pp.

Mishra J., and A. K. Srivastava. 1984. Effects of chlordane on the blood and tissue chemistry of a teleost fish, *Heteropneustes fossilis.* Cell. Mol. Biol. 30:519- 523.

Miyazaki , T., K. Akiyama, S. Kaneko, S. Horii, and T Yamagishi. 1980. Identification of chlordanes and related compounds in goby-fish from Tokyo Bay. Bull. Environ. Contam. Toxicol. 24:1-8.

Moilanen, R., H. Pyysalo, K. Wickstrom, and R. Linko. 1982. Time trends of chlordane, DDT, and PCB concentrations in pike *(Esox lucius)* and Baltic herring *(Clupea harengus)* in the Turku archipelago, northern Baltic Sea for the period 1971- 1982. Bull. Environ. Contam. Toxicol. 29:334- 340.

Muir, D. C. G., R. Wagemann, N. R Grift R. J. Norstrom, M. Simon, and J. Lien. 1988. Organochlorine chemical and heavy metal contaminants in white-beaked dolphins *(Lagenorhynchus albirostris)* and pilot whales *(Globicephala melaena)* from the coast of Newfoundland Canada. Arch. Environ. Contam. Toxicol. 17:613- 629.

Nalley, L, G. Hoff, W Bigler, and N. Schneider. 1978. Pesticide levels in the omental fat of urban gray squirrels. Bull. Environ. Contam. Toxicol. 19:42- 46.

National Research Council of Canada (NRCC). 1975. Chlordane: Its effects on ecosystems and its chemistry. Nat. Res. Counc. Can. Publ. NRCC 14094. 189 pp.

Nickerson, P. R., and K. R. Barbehenn. 1975. Organochlorine residues in starlings, 1972. Pestic. Monit. J. 8:247- 254.

Nightingale, H. I. 1987. Organic pollutants in soils of retention and recharge basins receiving urban runoff water. Sod Sci. 144:373-381.

Nomeir, A. A., and N. R Hajjar. 1987. Metabolism of chlordane in mammals. Rev. Environ. Contam. Toxicol. 100: 1 - 22.

Ohlendorf, H. M., J. C. Bartonek, G. J. Divoky, E. E. Klaas, and A. J. Krynitsky. 1982. Organochlorine residues in eggs of Alaskan seabirds. U.S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 245.41 pp.

Ohno, Y., T. Kawanishi, A. Takahashi, S. Nakaura, K. Kawashima S. Tanaka, A. Y. Omori, H. Sekita, and M. Uchiyama. 1986. Comparisons of the toxicokinetic parameters in rats determined for low and high dose of -chlordane. J. Toxicol. Sci. 11:111-123.

Parrish, P. R., E. E. Dyar, J. M. Enos, and W. G. Wilson. 1978. Chronic toxicity of chlordane, trifluralin, and pentachlorophenol to sheepshead minnows *(Cyprinodon variegatus).* U.S. Environ. Prot. Agency Rep. 600/3-78-010. 53 pp.

Parrish, P. R., S. C. Schimmel, D. J. Hansen, J. M. Patrick, Jr., and J. Forester. 1976. Chlordane: effects on several estuarine organisms. J. Toxicol. Environ. Health 1:485- 494.

Passino, D. R. M., and S. B. Smith. 1987. Acute bioassays and hazard evaluation of representative contaminants detected in Great Lakes fish. Environ. Toxicol. Chem. 6:901- 907.

Peakall, D. B., R. J. Noestrom A. D. Rahimtula, and R. D. Butler. 1986. Characterization of mixed-function oxidase systems of the nestling herring gull and its implications for bioeffects monitoring. Environ. Toxicol. Chem. 5:379- 385.

Perttila M., O. Stenman, H. Pyysalo, and K. Wickstrom. 1986. Heavy metals and organochlorine compounds in seals in the Gulf of Finland. Mar. Environ. Res. 18:43- 59.

Petterson, D. S., R. H. Casey, G. F Ebell, and B. L. McIntyre. 1988. Residues in beef cattle accidentally exposed to commercial heptachlor. Aust Vet. J. 65:50-53.

Podowski, A. A., B. C. Banerjee, M. Feroz, M. A. Dudek, R. L. Willey, and M. A. Q. Khan. 1979. Photolysis of heptachlor and *cis*-chlordane and toxicity of their photoisomers to animals. Arch. Environ. Contam. Toxicol. 8:509- 518.

Prouty, R. M., and C. M. Bunck 1986. Organochlorine residues in adult mallard and black duck wings, 1981-1982. Environ. Monit. Assess. 6:49-57.

Pyysalo, H., K. Wickstrom, and R. Litmanen. 1983. A baseline study on the concentrations of chlordane-, PCB- and DDT-compounds in Finnish fish samples in the year 1982. Chemosphere 12:837-842.

Pyysalo, H., K. Wickstrom, R. Litmanen, P. L. Seppa, U. Koivusaari, and O. Hanninen. 1981. Contents of chlordane-, PCB-, and DDT-compounds and the biotransformation capacity of fishes in the lake area of eastern Finland. Chemosphere 10:865-876.

Randall, W. E., W. H. Dennis, and M. C. Warner. 1979. Acute toxicity of dechlorinated DDT, chlordane and lindane to bluegill (*Lepomis macrochirus*) *and Daphnia magna.* Bull. Environ. Contam. Toxicol. 21:849-854.

Ray, L. F., H. E. Murray, and C. S. Giam. 1983. Organic pollutants in marine samples from Portland, Maine. Chemosphere 12:1031-1038.

Reece, R. L, P. C. Scott, W M. Forsyth J. A. Gould, and D. A. Barr. 1985. Toxicity episodes involving agricultural chemicals and other substances in birds in Victoria, Australia. Vet Rec. 117:525-527.

Reichel, W L, S. K. Schmeling, E. Cromartie, T. E. Kaiser, A. J. Krynitsky, T. G. Lamont, B. M. Mulhern, R. M. Prouty, C. J. Stafford, and D. M. Swineford. 1984. Pesticide, PCB, and lead residues and necropsy data for bald eagles from 32 States--1978-81. Environ. Monit. Assess. 4:395-403.

Requejo, A. G., R. H. West, R G. Hatcher, and R A. McGillivary. 1979. Polychlorinated biphenyls and chlorinated pesticides in soils of the Everglades National Park and adjacent agricultural areas. Environ. Sci. & Technol. 13:931- 935.

Reuber, M. D., and J. M. Ward. 1979. Histopathology of liver carcinomas in (C57BL/6N x C3H/HeN/) F_1 mice ingesting chlordane. J. Natl. Cancer Inst. 63:89- 92.

Ribick, M. A., and J. Zajicek. 1983. Gas chromatographic and mass spectrometric identification of chlordane components in fish from Manoa Stream, Hawaii. Chemosphere 12:1229-1242.

Risebrough, R. W., B. W. de Lappe, W. Walker, II, B. R. T. Simoneit, J. Grimalt, J. Albaiges, J. A. G. Regueiro, A. B. Inolla, and M. M. Fernandez. 1983. Application of the mussel watch concept in studies of the distribution of hydrocarbons in the coastal zone of the Ebro Delta. Mar. Pollut. Bull. 14:181-187.

Rosales, M. T. L., A. V. Botello, H. Bravo, and E. F Mandelli. 1979. PCB's and organochlorine insecticides in oysters from coastal lagoons of the Gulf of Mexico, Mexico. Bull. Environ. Contam. Toxicol. 21:652- 656.

Saiki, M. K., and C. J. Schmitt. 1986. Organochlorine chemical residues in bluegills and common carp from the irrigated San Joaquin Valley floor, California. Arch. Environ. Contam. Toxicol. 15:357- 366.

Saxena, S. C., and A. K. Karel. 1976. On effect of chlordane on the blood glucose and of glucose administration on the acute chlordane toxicity in *Meriones hurrianae* Jerdon, the Indian desert gerbil. Bull. Environ. Contam. Toxicol. 15:593- 600.

Schick, C. T., L. A. Brennan, J. B. Buchanan, M. A. Finger, T M. Johnson, and S. G. Herman. 1987. Organochlorine contamination in shorebirds from Washington State and the significance for their falcon predators. Environ. Monit. Assess. 9:115- 131.

Schmitt, C. J., J. L. Zajicek, and R. H. Peterman 1990. National Contaminant Biomonitoring Program: residues of organochlorine chemicals in U.S. freshwater fish, 1976-1984. Arch. Environ. Contam. Toxicol. 19:748-781.

Schmitt, C. J., J. L. Zajicek, and M. A. Ribick. 1985. National Pesticide Monitoring Program: residues of organochlorine chemicals in freshwater fish. 1980-81. Arch. Environ. Contam. Toxicol. 14:225- 260.

Schwemmer, B., W P. Cochrane, and R B. Polen. 1970. Oxychlordane, animal metabolite of chlordane: isolation and synthesis. Science 169:1087.

Shaw, G. G. 1984. Organochlorine pesticide and PCB residues in eggs and nestlings of tree swallows, *Tachycineta bicolor,* in central Alberta. Can. Field-Nat. 98:258-260.

Smith, J. A., P. T. Harte, and M. A. Hardy. 1987. Trace-metal and organochlorine residues in sediments of the upper Rockaway River, New Jersey. Bull. Environ. Contam. Toxicol. 39:465-473.

Somers, J. D., B. C. Goski, and M. W. Barrett. 1987. Organochlorine residues in northeastern Alberta otters. Bull. Environ. Contam. Toxicol. 39:783-790.

Stendell, R. C., E. Cromartie, S. N. Wiemeyer, and J. R. Longcore. 1977. Organochlorine and mercury residues in canvasback duck eggs, 1972-73. J. Wildl. Manage. 41:453-457.

Stickel, L. F., W. H. Stickel, R. A. Dyrland, and D. L. Hughes. 1983. Oxychlordane, HCS-3260, and nonachlor in birds: lethal residues and loss rates. J. Toxicol. Environ. Health 12:611-622.

Stickel, L. F., W. H. Stickel, R. D. McArthur, and D. L. Hughes. 1979. Chlordane in birds: a study of lethal residues and loss rates. Pages 387- 396 *in* W B. Deichmann, ed. Toxicology and occupational medicine. Elsevier/North Holland, New York.

Stone, W B., and J. C. Okoniewski. 1988. Organochlorine pesticide-related mortalities of raptors and other birds in New York, 1982-1986. Pages 429-438 *in* T J. Cade, J. H. Enderson, C. G. Thelander, and C. M. White, eds. Peregrine falcon populations: their management and recovery. The Peregrine Fund Inc., Boise, Idaho.

Sudershan, P, and M. A. Q. Khan. 1980. Metabolism of *cis*-[^{14}C] chlordane and *cis*-[^{14}C] photochlordane in bluegill fish. J. Agric. Food Chem. 28:291-296.

Suzaki, E., B. Inoue, E. Okimasu, M. Ogata, and K. Utsumi. 1988. Stimulative effect of chlordane on the various functions of the guinea pig leukocytes. Toxicol. Appl. Pharmacol. 93:137-145.

Swackhamer, D. L., and R. A. Hites. 1988. Occurrence and bioaccumulation of organochlorine compounds in fishes from Siskiwit Lake, Isle Royale, Lake Superior. Environ. Sci. & Technol. 22:543-548.

Szaro, R. C., N. C. Coon, and E. Kolbe. 1979. Pesticide and PCB of common eider, herring gull and great black-backed gull eggs. Bull. Environ. Contam. Toxicol. 22:394-399.

Talamantes, F, and H. Jang. 1977. Effects of chlordane isomers administered to female mice during the neonatal period. J. Toxicol. Environ. Health 3:713-720.

Taylor, D. L., S. Schliebe, and H. Metsker. 1989. Contaminants in blubber, liver and kidney tissue of Pacific walruses. Mar. Pollut. Bull. 20:465-468.

Tojo, Y., M. Wariishi, Y. Suzuki, and K. Nishiyama. 1986. Quantitation of chlordane residues in mothers' milk Arch. Environ. Contam. Toxicol. 15:327-332.

Veith, G. D., D. W. Kuehl, E. N. F A. Puglisi, and A. E. Lemke. 1979. Polychlorinated biphenyls and other organic chemical residues in fish from major watersheds of the United States, 1976. Pestic. Monit. J. 13:1-11.

Veith, G. D., D. W. Kuehl, E. N. Leonard, K. Welch, and G. Pratt. 1981. Polychlorinated biphenyls and other organic chemical residues in fish from major United States watersheds near the Great Lakes, 1978. Pestic. Monit. J. 15:1-8.

Verma, S. R., S. K. Bansal, A. K. Gupta, N. Pal, A. K. Tyagi, M. C. Bhatnagar, V. Kumar, and R. C. Dalela. 1982. Bioassay with twenty-three pesticides to a fresh water teleost, *Saccobranchus fossilis.* Water Res. 16:525- 529.

Wariishi, M., and K. Nishiyama. 1989. Observations on the progress of chlordane contamination in humans by blood and serum analysis. Arch. Environ. Contam. Toxicol. 19:501-507.

Wariishi, M., Y. Suzuki, and K. Nishiyama. 1986. Chlordane residues in normal human blood. Bull. Environ. Contam. Toxicol. 36:635-643.

White, D. H. 1979. Nationwide residues of organochlorine compounds in wings of adult and black ducks, 1976-77. Pestic. Monit. J. 13:12-16.

White, D. H., K. A. King, and R. M. Prouty. 1980. Significance of organochlorine and heavy metal residues in wintering shorebirds at Corpus Christi, Texas, 1976-77. Pestic. Monit. J. 14:58-63.

White, D. H., R. C. Stendell, and B. M. Mulhern. 1979. Relations of wintering canvasbacks to environmental pollutants--Chesapeake Bay, Maryland. Wilson Bull. 91:279-287.

Wickstrom, K., H. Pyysalo, and M. Perttila. 1981. Organochlorine compounds in the liver of cod *(Gadus morhua)* in the northern Baltic. Chemosphere 10:999- 1004.

Wickstrom, K., H. Pyysalo, and M. A. Siimes. 1983. Levels of chlordane, hexachlorobenzene, PCB and DDT compounds in Finnish human milk in 1982. Bull. Environ. Contam. Toxicol. 31:251-256.

Wiemeyer, S. N., C. M. Bunck, and A. J. Krynitsky. 1988. Organochlorine pesticides, polychlorinated biphenyls, and mercury in osprey eggs--1970-79--and their relationships to shell thinning and productivity. Arch. Environ. Contam. Toxicol. 17:767-787.

Wiemeyer, S. N., S. K. Schmeling, and A. Anderson. 1987. Environmental pollutant and necropsy data for ospreys from the eastern United States, 1975-1982. J. Wildl. Dis. 23:279-291.

Williams, D. F., and C. S. Lofgren. 1983. Imported fire ant (Hymenoptera: Formicidae) control: evaluation of several chemicals for individual mound treatments. J. Econ. Entomol. 76:1201-1205.

Williams, G. M., and S. Numoto. 1984. Promotion of mouse liver neoplasms by the organochlorine pesticides chlordane and heptachlor in comparison to dichlorodiphenyltrichloroethane. Carcinogenesis 5:1689-1696.

Wood, L. W., P. A. Jones, and A. Richards. 1986. Possible sediment scavenging of chlordane and contamination of the aquatic biota in Belmont Lake, New York. Bull. Environ. Contam. Toxicol. 36:159-167.

World Health Organization (WHO). 1984. Chlordane. Environmental Health Criteria 34. World Health Organization, Geneva, Switzerland. 82 pp.

Yamagishi, T., S. Kaneko, T. Miyazaki, K. Akiyama, and S. Horri. 1981a. Oxychlordane, *trans*-nonachlor and *cis*-nonachlor residues in adipose tissues of dogs and cats collected in the Tokyo area. Bull. Environ. Contam. Toxicol. 26:407-412.

Yamagishi, T., T. Miyazaki, K. Akiyama, S. Keneko, and S. Horii. 1981b. Residues of chlordanes in fish and shellfish from Kanto area and its vicinity. J. Food Hyg. Soc. Jpn. 22:270-278.

Zitko, V. 1978. Nonachlor and chlordane in aquatic fauna. Chemosphere 1:3-7.

Zitko, V. 1979. An equation of lethality curves in tests with aquatic fauna. Chemosphere 2:47- 51.

Zitko, V., and R. L. Saunders. 1979. Effect of PCB's and other organochlorine compounds on the hatchability of Atlantic salmon *(Salmo salar)* eggs. Bull. Environ. Contam. Toxicol. 21:125-130.

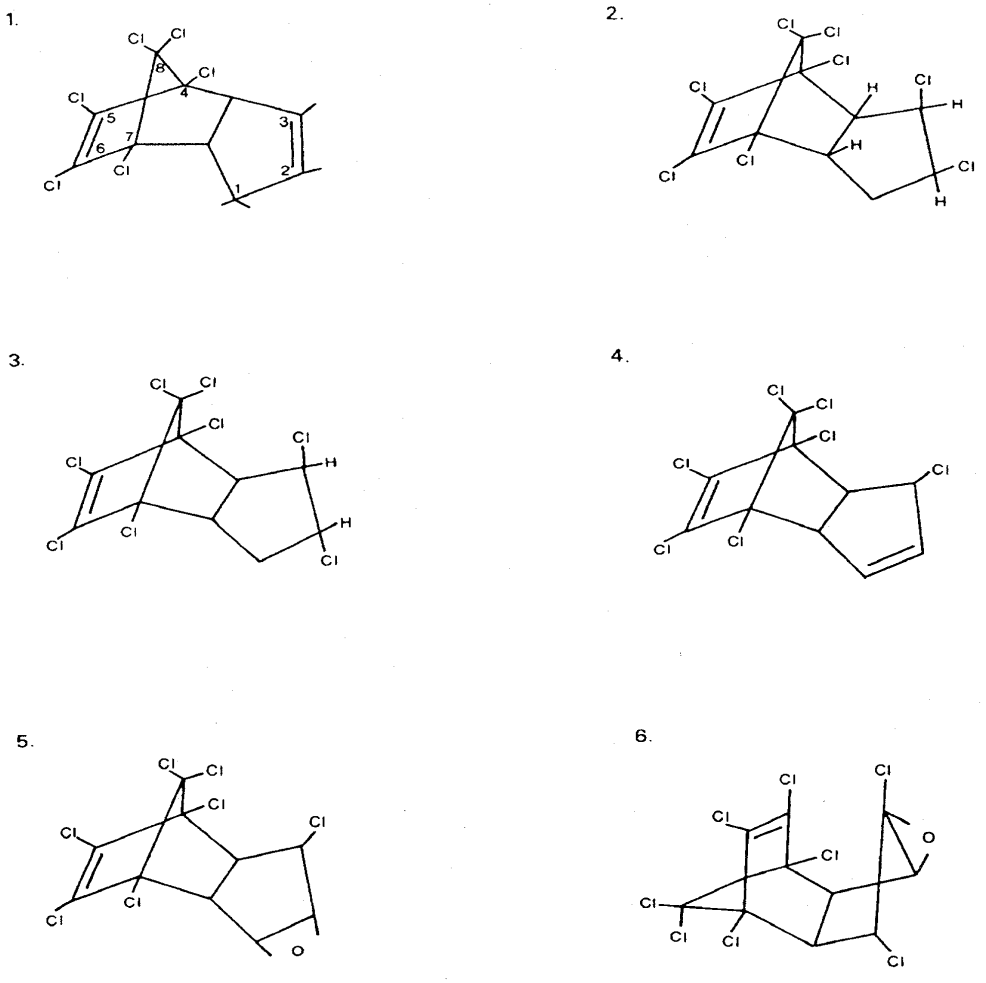


Figure. Chemical structure of chlordane-related compounds:

1. chlordene (4, 5, 6, 7, 8, 8-hexachloro-3a, 4, 7, 7a-tetrahydro-4, 7-methanoindene)

2. *cis*-chlordane, also known as *alpha*-chlordane (1-*exo*, 2-*exo*, 4, 5, 6, 7, 8, 8-octachloro-2, 3, 3a, 4, 7, 7a, hexahydro-4, 7-methanoindene)

3. *trans*-chlordane, also known as *gamma*-chlordane (1 -*exo*, 2-*endo*, 4, 5, 6, 7, 8, 8-octachloro-2, 3, 3a, 4, 7, 7a-hexahydro-4, 7-methanoindene)

4. heptachlor (1, 4, 5, 6, 7, 8, 8-heptachloro-3a, 4, 7, 7a-tetrahydro-4, 7-methanoindene)—technical heptachlor contains about 15 % *cis*-chlordane and 2.5% *trans*-chlordane

5. heptachlor epoxide (1, 4, 5, 6, 7, 8, 8-heptachloro-2, 3-epoxy-3a, 4, 7, 7a-tetrahydro-4, 7-methanoindene)

6. oxychlordane, also known as octachlor epoxide (1-*exo*, 2-*endo*, 4, 5, 6, 7, 8, 8-octachloro, 2, 3-*exo*-epoxy-2, 3, 3a, 4, 7, 7a-hexahydro-4, 7-methanoindene).

Biological Report 85(1.22)
August 1990

Contaminant Hazard Reviews
Report 22

Paraquat Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

By
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

Tables

Paraquat Hazards to Fish, Wildlife, and Invertebrates:
A Synoptic Review

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

Abstract

Paraquat (1,1' -dimethyl-4,4'-bipyridinium) and its dichloride salt (1,1', dimethyl-4, 4'-bipyridinium dichloride) are broad-spectrum contact plant killers and herbage desiccants that were introduced commercially during the past 25 years. Today, they rank among the most widely used herbicides globally and are frequently used in combination with other herbicides. The recommended paraquat field application rates for terrestrial weed control usually range between 0.28 and 1.12 kg/ha (0.25 and 1.0 lb/acre), and for aquatic weed control the range is 0.1 - 2.0 mg/L. Target plant species are unable to metabolize paraquat and tend to contain elevated residues; paraquat-resistant strains of terrestrial flora, whose numbers are increasing, require greater concentrations for control and may contain proportionately greater residues. Paraquat from decayed flora is usually adsorbed to soils and sediments. Paraquat in surface soils generally photodecomposes in several weeks, but paraquat in subsurface soils and sediments may remain bound--and biologically unavailable--for many years without significant degradation.

Paraquat is not significantly accumulated by earthworms and other species of soil invertebrates and is usually excreted rapidly by higher animals; however, delayed toxic effects--including death of birds and mammals--are common. At concentrations below the recommended application rate, paraquat is embryotoxic to developing eggs of migratory waterfowl (0.056 kg/ha) and adversely affects sensitive species of freshwater algae and macrophytes (250 µg/L), larvae of crustaceans (0.9-5.0 µg/L), and frog tadpoles and carp (500 µg/L). Sensitive species of birds are negatively affected at daily dose rates of 10 mg/kg body weight or when fed diets containing 20 mg/kg ration or drinking water containing 40 mg/L. Adverse effects in sensitive mammals were observed at dietary levels of 85 - 100 mg/kg ration and higher or 100 mg/L in drinking water. Acute oral LD50 values for sensitive species of birds were near 200 mg/kg body weight and, for mammals, 22 - 35 mg/kg body weight. Humans are among the more sensitive species, and numerous human poisonings have resulted from accidental or intentional ingestion of a concentrated paraquat formulation.

The biochemical mechanism of paraquat toxicity is due to the cyclic oxidation and reduction in tissues, leading to production of superoxide anion and other free radicals and eventually the highly destructive hydrogen peroxide. The lung is the organ most severely affected in paraquat poisoning, due largely to the preferential accumulation of paraquat in lung alveolar cells. Although many organs are affected by paraquat, death is usually due to progressive pulmonary fibrosis. At present, there is no completely successful treatment for paraquat-induced lung toxicity.

More information is needed in several areas in order to establish effective criteria for the protection of sensitive species of fish and wildlife against paraquat. These include: flux rates of paraquat from soil into terrestrial food chains; biomagnification potential of paraquat in aquatic food chains, with special reference to plants, plant detritus, amphibians, and reptiles, toxicokinetics of mixtures of paraquat and other herbicides applied concomitantly; and the implications of the high sensitivities of crustacean larvae and waterfowl embryos to paraquat. (Eisler, R. 1990. Paraquat hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.22). 28 pp.

Paraquat (1,1'-dimethyl-4,4'-bipyridinium) is one of the most widely used herbicidal chemicals in the world and is now available in more than 130 countries (Kimbrough 1974; Calderbank 1975; Dasta 1978; Haley 1979; Hughes 1988; L. Smith 1988). Its chemical structure was first described in 1882, its oxidizing and reducing properties in 1933, and its herbicidal properties in 1955. Paraquat was marketed commercially in the United Kingdom in 1962 and registered for use in the United States in 1964. As the dichloride salt, it has found wide use as a nonselective contact herbicide at application rates of 1.12 kg/ha (1 lb/acre) and lower. Useful reviews on ecological and toxicological aspects of paraquat include those by Kimbrough (1974), Smith and Heath (1976), Autor (1977), Dasta (1978), Haley (1979), Summers (1980), Bauer (1983), Onyeama and Oehme (1984), L. Smith (1985, 1988), and J. Smith (1988).

Paraquat kills plants by affecting the green parts, not the woody stems, and is usually completely and rapidly inactivated by contact with clay in the soil. In its bound form, paraquat is biologically inert and innocuous to plants and animals (Fletcher 1974).

Numerous human injuries and deaths have resulted from intentional ingestion of the concentrated commercial product (Fletcher 1974; Dasta 1978; Haley 1979; Crome 1986; J. Smith 1988; L. Smith 1988). For example, in the first 10 years following paraquat commercial use, 232 human deaths from paraquat poisoning were reported (about half were suicides), and almost all were due to the drinking of concentrated material. Most poisonings resulted from the ingestion of the 21 % cation concentrate, which had been decanted and stored in empty beer, soft drink, or lemonade bottles; paraquat is a reddish-brown liquid that resembles root beer or cola drinks. One individual sprinkled paraquat on French fried potatoes, thinking it was vinegar. He died 25 days later. Another died after applying the concentrated solution to his beard and scalp to treat a lice infestation. In Japan, more than 1,000 persons each year are reportedly poisoned by paraquat. Initially, paraquat may produce multiorgan toxicity of kidneys, liver, heart, central nervous system adrenal glands, skeletal muscle, and spleen, but the ultimate target organ is the lung, in which progressive irreversible pulmonary fibrosis develops. This effect has been described in humans, rats, mice, guinea pigs, and dogs (Kimbrough 1974; Giri et al. 1979; Hampson and Pond 1988; O'Sullivan 1989). There is no known specific antidote for paraquat poisoning.

In 1977, the discovery by narcotics authorities that some marijuana imported from Mexico had been treated with paraquat as a control agent generated much interest in the media (Dasta 1978; Haley 1979). Up to 70% of the paraquat in paraquat-treated marijuana is converted, on smoking, to bypyridine, a respiratory irritant. Frequent consumption of heavily contaminated marijuana may result in cyanosis and possibly death. The use of paraquat for this purpose has been largely discontinued.

In normal use as a spray, minor reversible injuries are reported to abraded skin, eyes, nose, and fingernails; it is not absorbed through intact skin (Kimbrough 1974; J. Smith 1988). Paraquat is fetotoxic, as judged by deliberate ingestion of concentrated solutions by nine pregnant Taiwanese women. Paraquat crosses the placenta and concentrates there to levels 4 - 6 times that of maternal blood. All fetuses died whether or not an emergency cesarean section was performed (Talbot and Fu 1988). Recent research has focused on the tendency of paraquat to accumulate in neuromelanin of mammals and amphibians and to cause lesions in the pigmented nerve cells, leading to effects very similar those of Parkinson’s disease (De Gori et al. 1988; Lindquist et al. 1988).

This report is part of a series of brief reviews on hazards of selected chemicals to fishery and wildlife resources. It was prepared in response to requests for information on paraquat from environmental specialists of the U.S. Fish and Wildlife Service.

Uses

Paraquat is a broad-spectrum contact weed killer and herbage desiccant that is used widely in agriculture and horticulture. Paraquat was formulated in 1882, but its herbicidal properties were not discovered until 1955. Since its introduction in the early 1960's, paraquat has been used extensively in about 130 countries--including Canada, the United Kingdom, and the United States--on a wide variety of agricultural crops (Fletcher 1974; Haley 1979; Kelly et al. 1979; Anonymous 1988).

Primary uses of paraquat include weed control in orchards, plantation crops, and forests; weed control before sowing or before crop emergence; pasture renovation; preharvest desiccation; and aquatic weed control, although use as an aquatic herbicide in the United States is not permitted (Anonymous 1963, 1974; Summers

1980; Dial and Bauer 1984). Paraquat is registered for preplant or preemergence use for cotton, barley, corn, lettuce, melons, peppers, potatoes, sallower, soybeans, sorghum, sugar beets, tomatoes, and wheat. It is also registered for use on noncrop areas, such as roadsides, highway margins, rights-of-way, and around commercial buildings, power plants, storage yards, fence lines, and parkways (Anonymous 1963, 1974). In Switzerland, it is used to control voles *(Arvicola terrestris)* in fruit orchards (Summers 1980).

Paraquat is available as the dichloride or dimethylsulfate salt; both compounds are extremely soluble in water (Kimbrough 1974). In the United States, paraquat dichloride is available as a 29% liquid concentrate containing 240 g/L (2 lb/gal) of paraquat cation, or as a 42 % liquid concentrate. Elsewhere, it is sold as Gramoxone liquid, containing 20-24% of paraquat dichloride (Fletcher 1974; Bauer 1983; Dial and Dial 1987a). Paraquat dichloride concentrates usually contain various wetting agents (condensation products of ethylene oxide and alkyl phenols), spreaders, humectants to promote moisture retention (calcium chloride, glycerol, polyethylene glycol), plant adhesion materials (carboxymethylcellulose, polymethacrylates), and antifoaming agents (Summers 1980).

The recommended field application rates for terrestrial weed control usually range between 0.28 and 1. 12 kg paraquat cation per hectare (0.25 and 1.0 lb/acre), or 0.56 and 2.24 kg paraquat dichloride per hectare (0.5 and 2.0 lb/acre)--both applied as an aerosol--and 0.1 and 2.0 mg/L for aquatic weed control, although sensitive aquatic plants may be affected between 0.019 and 0.372 mg/L (Ross et al. 1979; Summers 1980; Bauer 1983; Dial and Bauer 1984).

Paraquat is frequently used in combination with other herbicides (Fletcher 1974; Summers 1980). Water solutions of the dichloride salt, which usually contain 240 g/L, have been successfully mixed with 2,4-D, substituted ureas, dalapon, amitol, and various triazines (Anonymous 1963, 1974).

Background Concentrations

Data are scarce on ecosystems treated with paraquat. It is clear, however, that both terrestrial and aquatic plants accumulate paraquat, and that the compound disappears rapidly from the water column and tends to concentrate in surface muds (Table 1).

Table 1. Paraquat concentrations in field collections of selected organisms and nonbiological materials.

Sample, and other variables	Concentration (mg/kg dry weight)	Reference[a]
Treated fields		
Alfalfa, *Medicago sativa*	Up to 30	1
Grasses, various species	Up to 60	1
Mud, surface; from British lake treated with 0.5 mg/L		
Days after treatment		
1	1.2	2
2	2.4	2
8	6.7	2
32	11.2	2
197	17.7	2
364	8.0	2
Colorado farm pond treated with 1.0 mg/L		
3 h after treatment		
Water	0.6	3
Mud	1.1	3
Submerged plant, *Chara* sp.	320	3
Algae, *Spirogyra* sp.	320	3
4 days after treatment		
Water	0.2	3

Mud	0.8	3
Chara sp.	840	3
Spirogyra sp.	1,300	3
16 days after treatment		
Water	<0.1	3
Mud	16	3
Chara sp.	540	3
Spirogyra sp.	13	3

[a]1, Bauer 1983; 2, Way et al. 1971; 3, Earnest 1971.

Environmental Chemistry

General

Paraquat is a nonvolatile, ionic compound that is almost completely insoluble in organic solvents, which is typical of the bipyridyl group of chemicals. As discussed later, the biochemical mechanism of paraquat toxicity is due to the cyclic oxidation and reduction that occurs in various tissues, especially lung, leading to production of superoxide anion and other free radicals; these chemical species react with polyunsaturated free radicals, eventually forming the highly destructive hydrogen peroxide. Excretion of paraquat is rapid in living organisms, but delayed toxic effects, including death, are not unusual. No treatment or chemical has proven completely successful in protecting against paraquat-induced lung toxicity.

Paraquat is strongly adsorbed to soils and sediments and is biologically unavailable in that form; however, it is not degraded significantly for many years, except in surface soils. In surface soils, paraquat loss through photodecomposition approaches 50% in 3 weeks. In freshwater ecosystems, loss from the water column is rapid: about 50% in 36 h and 100% in 4 weeks. In marine ecosystems, 50-70% loss of paraquat from seawater was usually recorded within 24 h.

Chemical Properties

Paraquat is a nonvolatile, ionic compound that is almost completely insoluble in fat, and therefore not likely to be accumulated in food chains (Calderbank 1975). The compound belongs to the bipyridyl group of chemicals and is typical of the many hundreds that have been synthesized, variation usually being the result of introducing different quaternizing groups on the nitrogen atoms, which also shift (Fletcher 1974; Table 2). Paraquat dichloride is produced from pyridine in the presence of sodium in anhydrous ammonia by quaternizing the 4,4'-dipyridyl with methyl chloride (Haley 1979). The common paraquat salts are all fully ionized, and experiments have shown that the anions (e.g., chloride, sulfate, methyl sulfate) do not affect the toxicity of paraquat (Fletcher 1974). Chemical and other properties of paraquat are briefly summarized in Fig. 1 and Table 2.

Mode of Action

Paraquat is absorbed systematically in mammals, following different routes of exposure; absorption is greatest for the pulmonary route, followed by intragastric and dermal routes (Chui et al. 1988). Administration of paraquat by every route of entry tested frequently results in irreversible changes in the lung (Boudreau and Nadeau 1987). In the intestinal tract, where some microbial degradation occurs, most paraquat (95 - 100%) is usually excreted unchanged in feces and urine within 2 days (Summers 1980). Absorption in the gastrointestinal tract ranges from 0.26% in cows to 5% in humans, 8% in guinea pigs, 16% in cats, and up to 20% in rats; the half-time persistence (Tb 1/2) of paraquat in certain tissues is 20 - 30 min, but up to 4 days in muscle and 2 days in plasma (Bauer 1983). Delayed toxic effects of paraquat occurring after the excretion of virtually all of the material have caused it to be classified as a 'hit and run" compound--that is, a compound causing immediate damage, the consequences of which are not readily apparent (Conning et al. 1969).

Table 2. Chemical and other properties of paraquat (Anonymous 1963, 1974, 1988; Haley 1979; Kelly et al. 1979; Johnson and Finley 1980; Hudson et al. 1984; Hill and Camardese 1986; Mayer 1987).

Variable	Datum
Chemical name	
Paraquat (cation)	1,1'-dimethyl-4,4'-bipyridinium
Paraquat dichloride (salt)	1,1'-diemthyl-4,4'-bipyridinium dichloride
Molecular weight	186.2 (cation); 257.2 (salt)
CAS number	4685-14-17 (cation); $C_{12}H_4Cl_2N_2$ (salt)
Alternate names	Cekuquat, Crisquat, Dextrone, Dextrone X, Dexuron, Dual Paraquat, Esgram, Gramonol, Gramoxone, Gramuron, Herbaxon, Herboxone, Methyl Viologen, Ortho Paraquat, Orvar, Paracol, Paraquat CL, Pathclear, Pillarquat, Pillarxone, Preeglone, PP 148, PP 910, Sweep, Tenaklene Totacol, Toxer Total, Weedol
Solubility at 20º C	
Water	561 g/L
Methanol	144 g/L
Ethanol	1.7 g/L
Acetone	200 mg/L
Most organic solvents	Insoluble or sparingly soluble
Physical state	Solid; white (pure), yellow (technical)
Main uses	Herbicide, desiccant
Specific gravity	1.24–1.26
Melting point	175 C to 180 C, decomposes at 345º C
Stability	Stable on exposure to hot acids; unstable in alkalis at pH >10
Flash point	Nonexplosive, nonflammable
Volatility	Nonvolatile

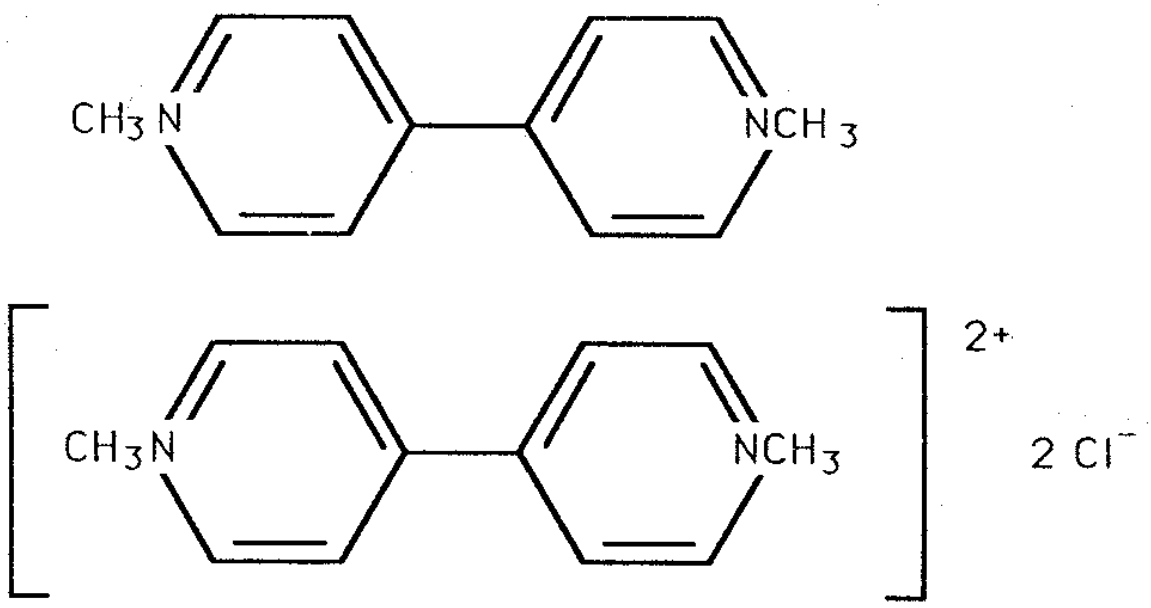


Fig. 1. Structural formula of paraquat cation (*upper*) and of paraquat dichloride salt (*lower*).

Most authorities agree that free radical pathology is the most likely mechanism by which paraquat is cytotoxic (Bus et al. 1976; Frank et al. 1982; Patterson and Rhodes 1982; Combs and Peterson 1983; Onyeama and Oehme 1984; Gabryelak and Klekot 1985; Smith 1985; Wong and Stevens 1986; Seto and Shinohara 1987; Suleiman and Stevens 1987; Darr et al. 1988; Dunbar et al. 1988a; Wegener et al. 1988; Wenning et al. 1988). The biochemical mechanism of paraquat toxicity is related to the cyclic oxidation and reduction of paraquat that occurs in lung cells, which leads to continued production of high levels of superoxide anion (0_2^-) and other cytotoxic oxygen free radicals. Superoxide anion and other oxygen free radicals initiate the peroxidation of membrane lipids, causing tissue damage and death. Paraquat oxidation is coupled with the reduction of molecular oxygen, forming superoxide anion, singlet oxygen, and hydroxyl radicals. These molecular species react with polyunsaturated fatty acid free radicals and, on further oxidation, with lipid hydroperoxide radicals. The hydroperoxide radicals then maintain the formation of new fatty acid radicals while being converted to lipid peroxides in a chain reaction. Various enzymes in the cells catabolize the superoxide radical and reduce the lipid hydroperoxides to less-toxic lipid alcohols. The superoxide anions are converted to hydrogen peroxide and oxygen; hydrogen peroxide is further inactivated to water and oxygen by catalases and peroxidases. In the presence of reduced nicotinamide adenine dinucleotide phosphate (NADPH), paraquat is reduced by microsomal NADPH-cytochrome reductase. The reduction of lipid peroxides by glutathione peroxidase requires reduced glutathione. Because the reduction of oxidized glutathione is coupled with NADPH oxidation by way of glutathione reductase, it seems that the availability of NADPH is essential for paraquat detoxification, and that the critical depletion of NADPH may render the cell more susceptible to lipid peroxidation.

The lung is the organ most severely affected in paraquat poisoning (Campbell 1968; Conning et al. 1969; Haley 1979; Aldrich et al. 1983; Bauer 1983; Combs and Peterson 1983; Christian et al. 1985; Smith 1985; Wong and Stevens 1986; Boudreau and Nadeau 1987; Baud et al. 1988; Dunbar et al. 1988a; Wegener et al. 1988). Pulmonary injury is due largely to the preferential accumulation of paraquat in the lung--mediated by an energy dependent system for uptake of endogenous polyamines--and to the continuous exposure of the lung to atmospheric oxygen. Characteristic signs of poisoning include severe anoxia, marked and widespread fibroblastic proliferation in the alveolar walls around the terminal bronchi and blood vessels, and frequently death. The specific toxicity to the lung can be explained by the accumulation of paraquat in the alveolar Type H cells. These cells are responsible for the synthesis of pulmonary surfactant, the surface-active material lining the alveolar epithelium. The pulmonary surfactant is secreted after storage in cytoplasmic organelles known as lamellar bodies. Therefore, any damage to the alveolar epithelium could alter synthesis and secretion of the pulmonary surfactant. The pulmonary effects of paraquat are probably related to the conversion of paraquat to a free radical followed by conversion to a long-lived dihydroderivative, which causes transformation of normal alveolar epithelial cells to fibroblasts. The increase in toxicity of paraquat by oxygen supports the hydroperoxide theory, in which the reversible action of the free radical's oxidation-reduction gives rise to hydrogen peroxide. Paraquat also depletes NADPH in the isolated lung to the extent of mixed function oxidation impairment. Depletion of NADPH would impair fatty acid and lipoprotein synthesis and inhibit various detoxification and biosynthetic functions.

Other organs and systems affected by paraquat include the kidney (pathology of proximal tubules), liver (hepatocellular necrosis), spleen and thymus (pathology), circulatory system (irregular and feeble heart beat, myocardial congestion, increase in erythrocytes and leucocytes, external pericarditis, myocardium edema), brain (neuronal depletion, myelin destruction), gastrointestinal tract (esophagitis; ulceration of buccal cavity, pharynx, gastric mucosa; mucosal erosion), skin (erythema, hyperkeratosis), reproductive system (degeneration), nervous system (hyperexcitability, irritability, incoordination, convulsions), various enzyme systems, and the eye (Giri et al. 1979, 1982, 1983; Summers 1980; Bauer 1983; Seto and Shinohara 1987, 1988; Hughes 1988; Takegoshi et al. 1988).

Several early indicators of paraquat-induced stress have been proposed, including alkaline phosphatase activity, fibronectin levels, and intracellular calcium uptake. Alkaline phosphatase activity is associated with the lamellar body, and changes in this variable are suggested as indicative of toxicity to Type II alveolar epithelium cells (Boudreau and Nadeau 1987). Levels of fibronectin, an extracellular matrix glycoprotein, were elevated in patients with fibrotic lung diseases and in monkeys given multiple injections of paraquat (Dubaybo et al. 1987). Lung intracellular calcium uptake was significantly disrupted, even at doses that normally produce significant increases in lung water content (Agarwal and Coleman 1988). These subjects seem to merit additional research, as does the role of polyamines in mediating fibrotic changes in the lung (Dunbar et al. 1988b);

paraquat-altered synthesis of proteins, DNA, collagen, and pentose phosphate metabolism (Simon et al. 1983); and hyperoxia--that is, increased oxygen-free radical generation (Frank et al. 1982).

Certain treatments or chemicals provide varying degrees of protection against paraquat-induced lung toxicity and lethality, although no treatment or chemical has proven completely successful. Present treatment of paraquat-poisoned animals and humans is directed to elimination of the material from the body using repeated doses of adsorbents such as Fuller's earth or bentonite; cathartics to reduce paraquat absorption; and hemodialysis, forced diuresis, and hemofiltration to enhance excretion (Fletcher 1974; Autor 1977; Haley 1979; Pond et al. 1987; Kitakouji et al. 1989). The use of 100% oxygen is contraindicated, as mortality is greatly increased (Fletcher 1974; Autor 1977; Wong and Stevens 1986). Toxicity mediated by free radicals can be moderated by several cellular defense mechanisms, including superoxide dismutase, catalase, glutathione peroxidase, vitamin E, and reduced glutathione (Gabryelak and Klekot 1985; Wenning et al. 1988). Recently, a low molecular weight superoxide dismutase mimic, based on manganese, was found to protect mammalian cells against the cytotoxic effects of the superoxide radical produced by paraquat (Darr et al. 1988). Under carefully controlled conditions of administration, certain chemicals reportedly provide limited protection to small laboratory animals: nicotinic acid (Shibata and Iwai 1988); niacin (Heitkamp and Brown 1982); cysteine (Szabo et al. 1986); N-acetylcysteine (Wegener et al. 1988); metallothionein--a metal-binding low molecular weight protein rich in cysteine (Sato et al. 1989); d-penicillamine (Szabo et al. 1986); clofibrate (Frank et al. 1982); lipid-soluble antioxidants (Kohen and Chevion 1988; Wegener et al. 1988); various amino acids (Heitkamp and Brown 1982); phenobarbitol (Bus et al. 1976; Summers 1980); methyl predinsolone (Kitazawa et al. 1988); and certain anti-inflammatory drugs (Autor 1977). In plants, the pea *(Pisum sativum)* is protected by cerium chloride--in part, through counteracting peroxide formation (Vaughn and Duke 1983).

Paraquat toxicity is increased and its effects otherwise exacerbated in organisms fed diets deficient in selenium or vitamin E, although high levels of these substances in diets did not provide protection (Autor 1977; Haley 1979; Summers 1980); by methyl prostaglandins (Williams et al. 1988) or diethyl maleate (Summers 1980); and by increased iron and copper (Kohen and Chevion 1988; Ogino and Awai 1988). Dietary changes that do not result in nutrient deficiency or toxicity may affect the biocidal properties of paraquat and other compounds. In studies with rodents subjected to paraquat insult, survival was higher in those fed cereal-based diets versus purified diets, aid higher in egg-white (protein) purified diet versus a casein diet (Tanaka et al. 1981; Evers et al. 1982), suggesting a need to use strictly defined diets in the study of paraquat toxicity to control for any paraquat- diet interactions.

Paraquat adhering to the plant surface is usually degraded photochemically (Haley 1979; Summers 1980). Paraquat is phytotoxic through inhibition of processes involving photosynthesis and respiration (Haley 1979; Christian et al. 1985; Anonymous 1988). Its mode of action in plants is similar to that in animals--that is, lipid peroxidation of membranes due to formation of the superoxide radical and related species (Summers 1980). Photosynthetic tissues reduce paraquat to stable free radicals that, on reoxidation, produce hydrogen peroxide. Unsaturated lipids in the cells are oxidized by the peroxide, and damage is dependent largely on production of hydrogen peroxide (Haley 1979; Vaughn and Duke 1983). The reaction is light- and oxygen-dependent (Conning et al. 1969; Kelly et al. 1979).

In bacteria *(Escherichia coli),* paraquat is concentrated, reduced to the monocation radical, and combined with molecular oxygen to produce the superoxide radical within the cell. Copper and iron are essential mediators in bacteriocidal effects; the cytoplasmic membrane is the target organelle in paraquat toxicity to *E. coli*, and extent of damage correlates positively with levels of these metals (Kohen and Chevion 1988).

Fate in Soils and Water

In contact with soil, paraquat is rapidly adsorbed usually in the clay mineral lattice sheets-and inactivated by base exchange; the process is facilitated by the flat and highly polarizable nature of the paraquat ion (Anonymous 1963; Conning et al. 1969; Calderbank 1975; Summers 1980; Kearney et al. 1985). The strong binding of paraquat to soil constituents reduces the mobility of the herbicide due to leaching, although paraquat is displaced from binding sites by low concentrations of ions of ammonium, potassium sodium, and calcium (Smith and Mayfield 1978). Paraquat adsorption is not significantly affected by soil pH, but is modified by soil porosity, moisture content, residence time, and adsorption capacity (Smith and Mayfield 1978; Summers 1980). Paraquat applied to a sandy loam soil at field application rates between 0.56 and 2.24 kg/ha was adsorbed by organic matter and clays, usually in the top centimeter of soil (Smith and Mayfield 1978). Typical soils contain

paraquat at about 300 mg/kg after treatment at recommended applications; however, adsorption capacity varies among soils. Clay minerals, such as kaolinite, can adsorb 2,500 - 3,500 mg/kg, whereas others, such as montmorillonite, adsorb up to 85,000 mg/kg after paraquat treatment (Summers 1980).

Paraquat is not degraded significantly in soil by chemical or microbiological vectors during incubation periods up to 16 months at 250 °C (Smith and Mayfield 1978). For example, paraquat dichloride, applied once annually at 4.48 kg/ha or 4 times annually at 1. 12 kg/ha, remained essentially undegraded in the soil for 6 years (Fryer et al. 1975; Moyer and Lindwall 1985). Massive applications to soils of 3,000 kg/ha can persist for at least 6 months without significant degradation (Moyer and Lindwall 1985). Bacterial degradation--which occurs only slowly in soils--consists of demethylation, followed by ring cleavage to eventually form the carboxylated 1-methylpyridinium ion (Fig. 2). Photochemical decomposition of paraquat is the predominant mechanism of paraquat degradation in soils (Smith and Mayfield 1978). In surface soils, paraquat loss through photodecomposition was 20-50% in 3 weeks (Christian et al. 1985). Photochemical degradation products of paraquat include 4-carboxy-1-methylpyridium ion and methylamine hydrochloride (Fig. 2). Laboratory studies have demonstrated that paraquat in soils slated for disposal can be degraded by ultraviolet (UV) irradiation in the presence of oxygen or ozone. Reaction products identified were 4-carboxy-1-methylpyridium ion, 4-picolinic acid, hydroxy-4-picolinic acid, succinic acid, N-formylglycine, malic acid and oxalic acid (as trimethylsilicon derivatives), and 4,4'-bipyridyl (Kearney et al. 1985).

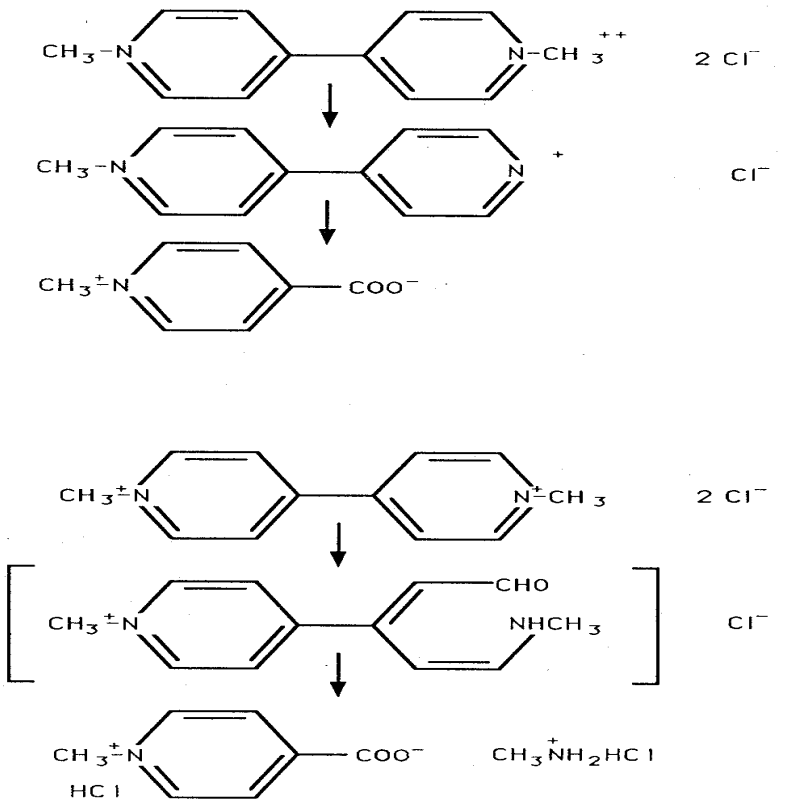


Fig. 2. Proposed pathway of paraquat degradation by a bacterial isolate (*upper*) and by ultraviolet irradiation (*lower*). Modified from Funderburk and Bozarth (1967).

Paraquat is used to control aquatic weeds. It also passes into aquatic environments through rain, where it is rapidly accumulated by aquatic organisms, especially fish (Gabryelak and Klekot 1985). Paraquat applied to control aquatic weeds is accumulated by aquatic macrophytes and algae, and it is adsorbed to sediments and suspended materials. Initial applications of 1 - 5 mg/L in the water column are usually not detectable under field conditions after 8 to 27 days (Summers 1980). The half-time persistence of paraquat in the water column at normal doses for weed control (i.e., 0.5 - 1.0 mg/L) was 36 h; less than 0.01 mg/L was detectable in 2 weeks (Calderbank 1975). In solution, paraquat was subject to photodecomposition and microbial metabolism,

degrading to methylamine and 4-carboxy-1 -methylpyridium ion (Kearney et al. 1985). In fresh water, without sediment or plants, 100% of the initial paraquat concentration of 0.5 mg/L was degraded in 35 weeks. When sediments were present, 100% loss from the water column occurred in 6-8 weeks, and when both sediment and aquatic plants were present, paraquat was not detectable in the water column in 3 - 4 weeks (Summers 1980). Mud cores taken from a paraquat-treated lake had elevated paraquat residues but showed no phytotoxic effects on barley seedlings germinated on them (Calderbank 1975).

Paraquat loss from seawater in 24 h was 70% at an initial concentration of 1 mg/L, 68% at 5 mg/L, and 76% at 10 mg/L; most of the loss occurred within the first 60 min (Fytizas 1980).

Lethal and Sublethal Effects

General

Adverse effects of paraquat (death, inhibited germination of seeds, reduced growth) in sensitive species of terrestrial plants and soil microflora have been documented at application rates of 0.28 - 0.6 kg/ha, at soil concentrations of 10 - 25 mg/kg (growth inhibition), and at soil-water concentrations as low as 1.6 mg/L (reduced growth, inhibited synthesis of protein and RNA). Among terrestrial invertebrates, certain species of mites were sensitive to paraquat at recommended rates of application, and the sensitive honeybee *(Apis mellifera)* died when its diet contained 100 mg/kg. However, paraquat in soils was not accumulated by earthworms *(Lumbricus terrestris)* and other species of soil invertebrates after applications up to 112 kg/ha. These points, and others listed in this section, are discussed in greater detail later.

Freshwater algae and macrophytes usually die at paraquat concentrations between 0.25 and 0.5 mg/L; marine algae, however, are relatively resistant and usually require 5 mg/L or higher for significant inhibition in growth to occur in 10 days. Aquatic invertebrates, especially crustaceans, seem to be the most sensitive group, with effects most pronounced at elevated temperatures in early developmental stages. Adverse effects were noted in crab larvae at nominal water concentrations between 0.9 and 5.0 µg/L, although 1,000 µg/L and higher were needed to produce similar effects in other species of aquatic invertebrates. Amphibians and fishes were usually unaffected at concentrations below 3,000 µg/L, although sensitive species such as frog tadpoles and common carp *(Cyprinus carpio)* were affected at 500 µg/L. There was little accumulation of paraquat from the medium by aquatic fauna.

Paraquat is embryotoxic to sensitive species of birds. Concentrations equivalent to 0.056 kg/ha applied in oil solution to the surface of mallard (*Anas platrhynchos*) eggs inhibited development; when applied in aqueous solution, paraquat was toxic at a dose equivalent to 0.56 kg/ha. In each case, adverse effects occurred below the recommended field application rate of about 1.0 kg/ha. The lowest doses of paraquat that produced harmful effects in sensitive birds were 10 mg/kg body weight (BW) in nestlings of the American kestrel (*Falco sparverius*), 20 mg/kg in the diet of northern bobwhite (*Colinus virginanus*), 40 mg/L in the drinking water of domestic chickens (*Gallus* sp.), and 199 mg/kg BW in mallard (acute oral LD50).

Sensitivity of mammals to paraquat was variable, due to inherent differences in interspecies resistance. Representative mammals were measurably affected at aerosol concentrations of 0.4 - 6.0 µg/L, acute oral doses of 22-35 mg/kg BW, dietary concentrations of 85 - 100 mg/kg and drinking water levels of 100 mg/L.

Terrestrial Plants and Invertebrates

In terrestrial plants, paraquat's action is at the point of local absorption (Anonymous 1963). Characteristic damage signs to susceptible species include wilting and general collapse in herbaceous plants. Regrowth may occur in some perennial plants, but in resistant species temporary scorch may be the most marked effect (Anonymous 1963). In sugarcane (*Saccharum officinarum*), paraquat application severely desiccated the plant within 72 h and disrupted activity of leaf amylase and sucrose (Haley 1979). Paraquat, once absorbed in plants, is likely to persist (Bauer 1983). The addition of cationic or nonionic surface active agents increases the phytocidal effectiveness of paraquat (Anonymous 1963), but in combination with various herbicides, paraquat was markedly less phytotoxic to certain cereal grains (O'Donovan and O'Sullivan 1986).

Paraquat adsorbed to soils is usually unavailable to crops. In wheat (*Triticum aestivum*), effects from

contaminated soils were negligible until soil residues surpassed 600- 1,000 kg/ha, causing growth reduction of 10%, or 1,650 kg/ha, causing elevated residues in leaves but not in grain (Moyer and Lindwall 1985).

Three species of grains (barley, *Hordeum vulgare;*wheat; oat, *Avena sativa)* died (>95% kill) following paraquat application of 0.28 kg/ha (O'Donovan and O'Sullivan 1986). At 0.6 kg/ha, paraquat inhibited germination and growth in seeds of six species of grasses (Kentucky bluegrass, *Poa pratensis;* perennial ryegrass, *Lolium perenne;* bentgrass, *Agrostis tenuis;* tall fescue, *Festuca arundinacea;* red fescue, *Festuca rubra;* orchard grass, *Dactylus glomerata*), but two species of legumes (alfalfa, *Medicago sativa*; red clover, *Trifolium pratense*) were comparatively resistant (Salazar and Appleby 1982). Paraquat was phytotoxic to several species of terrestrial plants (rape, *Brassica napus;* ryegrass; white clover, *Trifolium repens)* for several days following application of 1.1 - 2.2 kg/ha (Summers 1980). Transpiration rate of soybean (*Glycine max*) was lowered at 1 mg/kg (Haley 1979). Paraquat is not considered to be carcinogenic or teratogenic, but is weakly mutagenic to some plants (e.g., 4.1 % chromosomal aberrations in seeds of wheat at 9.3 mg/kg; Haley 1979). Spray solutions containing 0.6 g paraquat per liter applied to crowns of eastern redcedar (*Juniperus virginiana*) killed up to 90% of small trees and up to 30% of large trees; at 0.3 g/L, up to 60% of small trees were affected (Engle et al. 1988). Seedlings of corn (*Zea mays*) sprayed with 0.2% paraquat ion solution for 6 h had decreased rates of total protein synthesis and some polysome dissociation (Wu et al. 1988), suggesting that additional research is needed on mutagenicity of paraquat in plants.

Paraquat resistance has been documented in several genera of weeds. For example, paraquat-resistant strains of barley grass *(Hordeum glaucum)* were first noted in 1982 in Australia; resistant strains (based on chromosome counts and resistance to paraquat) were confined to a small number of alfalfa fields where paraquat had been used consistently for at least 10 years. However, the potential exists for this biotype to be transferred and established in other areas by the movement of livestock, machinery, hay, and seeds (Islam and Powles 1988; Tucker and Powles 1988). Paraquat-resistant strains of weeds have been reported in Australia, Egypt, England, and Japan (Polos et al. 1988). Paraquat-resistant strains of bacteria, ferns, and other species of flora have been documented (Carroll et al. 1988). Paraquat-tolerant ferns (*Ceratopteris richardii*) were 10 to 20 times more resistant than sensitive wild-type strains (Carroll et al. 1988). Paraquat-resistant strains of perennial rye were up to 10 times more resistant than normal susceptible strains (Faulkner and Harvey 1981). In the case of barley grass, survival was reduced 50% at 0.025 kg/ha in normal susceptible biotypes, but in resistant biotypes, 3.2 kg/ha was required (Islam and Powles 1988; Tucker and Powles 1988). Paraquat-tolerant plants may enjoy certain advantages over nonresistant plants, including resistance to various air pollutants. For example, paraquat-tolerant tobacco plants (*Nicotiana tabacum*), which had higher superoxide dismutase activity than controls, were tolerant to aerosol sprays of 2 mg SO_2/L, while controls experienced severe damage (Tanaka et al. 1988).

In every case of resistance, paraquat had been applied 2 or 3 times annually during the preceding 5 - 11 years; in some cases, a cross-resistance to atrazine was also reported (Polos et al. 1988). Paraquat-resistance mechanisms in plants include increased epicuticular wax (preventing penetration), binding of paraquat to cell walls, restricted movement into chlorplasts, and altered redox potential (Polos et al. 1988). For example, sequestration of paraquat within the apoplast of the leaf seems to be inheritable and controlled by a single nuclear gene with incomplete dominance (Islam and Powles 1988). Studies with paraquat-tolerant strains of various plants, including perennial rye and tobacco, suggest that tolerance is related to their general ability to rapidly detoxify the generated oxygen species through increased levels of superoxide dismutase, glutathione reductase, and other antioxidants (Shaaltiel et al. 1988).

At recommended field concentrations paraquat had negligible effect on soil microflora or soil fertility, although it did cause a temporary suspension of soil nitrification (Haley 1979). A concentration as low as 1.0 mg/L completely inhibited ammonium and nitrite oxidation for 40 days in a mixed culture of nitrifying bacteria isolated from soil (Gadkari 1988). Paraquat at 1.6 mg/L adversely affected *Escherichia coli* in 6 h as judged by diminished growth rate and inhibited synthesis of RNA and protein; at a higher concentration of 18.6 mg/L, interference with metabolism of glucose and DNA synthesis was observed (Davison and Papirmeister 1971). Four species of soil bacteria had 50% growth inhibition at paraquat concentrations between 93 and 18,600 mg/kg soil; moreover, the mode of action in some species of microorganisms may differ from the generally accepted mechanisms for paraquat toxicity in mammals (Carr et al. 1986). Sensitive species of soil fungi experienced marked growth inhibition between 10 and 25 mg paraquat per kilogram of soil. (Summers 1980). In

various genera of soil fungi *(Rhizopus, Ophiobolus, Helminthosporium,Fusarium, Eurotium),* paraquat concentrations up to 100 mg/L could be tolerated; at higher concentrations, spore germination was suppressed, mycelial growth was inhibited, and spore development was abnormal (Haley 1979).

Terrestrial invertebrates show varying degrees of sensitivity to paraquat. In honeybees, paraquat concentrations of 100 mg/kg syrup (diet) produced toxic signs, 4.4 kg/ha applied as a spray killed 90% in 3 days, and 1,000 mg/L in drinking water killed most in a few days and 100% within 5 weeks (Summers 1980). In soils, adsorbed paraquat may be ingested by soil invertebrates, such as earthworms, but it was not absorbed from the gut into tissues and was rapidly lost when the earthworms were transferred to clean soil (Calderbank 1975). For example, earthworms fed soil treated with 112 kg/ha had 111 mg/kg in gut contents, but <0.3 mg/kg in the carcass without gut (Summers 1980). Two species of springtails (Collembola; *Folsomia candida*, *Tullbergia granulata*) were fed diets containing 600 mg/kg for 22 weeks; they survived without measurable adverse effects. However, higher dietary levels of 1,000 and 5,000 mg/kg were associated with decreased survival, lengthier instar development, decreased egg production, and decreased egg viability (*Folsomia candida* and Tullbergia granulate (Subagja and Snider 1981). Adults and larvae of the German cockroach (*Blattella germanica*) died after consuming diets containing 1,000 mg/kg (Summers 1980). Also, paraquat was lethal to two species of mites (*Tetranychus urticae*, *Typhlodromus* sp.) at concentrations below recommended field application rates (Summers 1980).

Aquatic Organisms

In general, paraquat is more toxic to aquatic fauna in soft water than in hard water, more toxic to early developmental stages than to juveniles or adults, and more toxic in formulations containing wetting agents than in formulations without them (Summers 1980). In water, paraquat is taken up rapidly by plants or adsorbed to particulate matter in the water column; however, paraquat is not bioconcentrated by aquatic fauna (Calderbank 1975; Summers 1980). Paraquat effects on aquatic biota are summarized in Table 3, and these data suggest several trends. Early developmental stages of certain species of crustaceans are extremely sensitive, and significant adverse effects occur in the range of 0.9-100 µg/L, although most species of crustaceans and all other species of invertebrates tested were relatively unaffected at concentrations below 1,000 µg/L. Freshwater algae and macrophytes are eliminated after treatment with 250 - 500 µg/L, but marine algae are relatively resistant and require 5,000 µg/L or higher to produce significant growth inhibition. Usually, aquatic vertebrates are not adversely affected and show little accumulation at 1,000 µg/L or lower, but at 500 µg/L, frog tadpoles have low survival and a high frequency of developmental abnormalities, and carp experience biochemical upset.

Paraquat controlled *Typha* and *Phragmites* in Egyptian irrigation canals, drains, and marshes without apparent harm to fishes (Haley 1979). Paraquat residues in decomposed plants become available for adsorption to sediments and bottom muds and are not readily available for microbial degradation (Summers 1980). Indirect fish kills may occur from anoxia due, in part, to consumption of dissolved oxygen by decaying weeds (Bauer 1983). Paradoxically, it has been suggested that paraquat may be helpful in improving the oxygen status of aquatic environments at a concentration of 1 mg/L by restricting nitrate production due to inhibition of bacterial nitrification (Chan and Leung 1986; Gadkari 1988). At effective herbicidal concentrations, paraquat was also toxic to eggs-but not adults-of three species of snail vectors of bilharzias (*Bulinus truncatas, Biomphalaria alexandrina, Lymnaea calliaudi*); newly hatched snails were the most sensitive (Haley 1979).

Changes in fauna of a reservoir following use of paraquat for weed control are likely to be indirect effects caused by decomposition of angiosperms (Brooker and Edwards 1974). Planktonic invertebrates closely associated with aquatic macrophytes were either eliminated by paraquat or survived at lower densities for at least a year following treatment; analysis of content of fish stomachs showed dietary changes following weed control and reflected availability of many invertebrate species associated with aquatic plants (Brooker and Edwards 1974).

Paraquat can induce activities of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, and catalase in many species of plants, invertebrates, and vertebrates. Results of studies with ribbed mussels (*Geukensia demissa*) support the hypothesis that these bivalve mollusks can activate redox cycling compounds and demonstrate responses typical of oxidative stress observed in other species (Wenning et al. 1988). Paraquat also disrupts glucose metabolism and acetylcholinesterase activity and accumulates in melanin. Disrupted glucose metabolism in paraquat-stressed carp was attributed to a high level of circulating epinephrine (Simon et al. 1983). Paraquat-induced acetylcholinesterase inhibition in erythrocytes and electric

organs of the electric eel (*Electrophorus electricus*) was reversible (Seto and Shinohara 1987, 1988). Paraquat tended to concentrate in melanin, as judged by accumulation in neuromelanin of frogs (*Rana temporaria*) after intraperitoneal injection (Lindquist et al. 1988), with important implications for research on Parkinson's disease. It seems that paraquat has a structural similarity to a metabolite of 1-methyl -4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), which may induce a Parkinson-like condition; like paraquat, MPTP and its metabolites have melanin affinity (Lindquist et al. 1988).

Birds

Signs of oral paraquat intoxication in birds include excessive drinking and regurgitation, usually within 10 min of exposure. Other signs appeared after 3 h: diarrhea, ruffled feathers, muscular incoordination, imbalance, wing drop, hyporeactivity, slowness, weakness, running and falling, constriction of the pupil, and terminal convulsions. Additional signs reported after dermal exposure include blistering and cracking of skin, lacrimation, wing spread, and wing shivers. Death usually occurred between 3 and 20 h postexposure; remission took up to 12 days (Smalley 1973; Haley 1979; Summers 1980; Hudson et al. 1984). The blood chemistry pattern of paraquat-intoxicated Japanese quail (*Coturnix japonica*) suggested adrenal gland impairment, although recovery from hematologic effects was rapid (Clark et al. 1988). Paraquat causes pseudofeminization of male chicken and quail embryos; testes showed intersexual phenomena and Mullerian duct abnormalities; both sexes had a reduction in gonocyte number (Haley 1979; Bauer 1983).

Table 3. Effect of paraquat on selected species of aquatic plants and animals. Concentrations are milligrams of paraquat cation per liter of medium.

Taxonomic group, organism, and other variables	Concentration (ppm)	Effects	Reference[a]
Algae and macrophytes			
Lesser duckweed, *Lemna minor*	0.00074	Herbicidal	1
Submerged weeds			
4 species	0.25–0.5	Herbicidal	2
3 species	0.5–2.5	Herbicidal	2
Chara sp., *Polygonum* sp.	0.5	No adverse effects in 32 days	3
Freshwater algae			
3 species	0.25–1.0	Herbicidal	2
2 species	>5.0	Herbicidal	2
Rooted emergents			
2 species	0.25–0.5	Herbicidal	2
2 species	2.0–3.0	Herbicidal	2
1 species	>5.0	Herbicidal	2
Floating weeds			
Water weed, *Elodea canadensis*	0.5	Eradicated from British lakes in 32 days for at least 2 years	3
4 species	0.5	Herbicidal	2
Pondweed, *Potamogeton pusillus*	0.5	Residues of 36 mg/kg dry weight (DW) in 14 days	4, 5
Eurasian watermilfoil, *Myriophyllum spicatum*	1.0	Residues up to 112 mg/kg DW in 14 days	4, 5
Cattail, *Typha latifolia*	0.5	Shoreline colonies severely affected after 32-day exposure	3
Duckweed, *Spirodella oligorrhiza*	0.5	Inhibits chlorosis in 48 h	3
Marine algae			
Isochrysis galbana	5	50% growth inhibition in 10 days	6
Phaeodactylum tricornutum	10	50% growth inhibition in 10 days	6
Dunaliella tertiolecta	20	50% growth inhibition in 10 days	6
Chlorococcum sp.	50	50% growth inhibition in 10 days	6
4 species	2,500–>5,000	Respiration reduced 50% in 2 h	6
Invertebrates			
Mud crab, *Rithropanopeus harrisii*, larvae	0.00086	LC50 (19 days)	4
Rithropanopeus harrisii, larvae	0.001–0.005	50% mortality before zoeal stage	4
Isopod, *Asellus meridianus*			
15 C	0.1	LC50 (14 days)	7
15 C	0.58	LC50 (8 days)	7
5 C	0.62	LC50 (14 days)	7
5 C	6.3	LC50 (8 days)	7
Freshwater invertebrates, 3 species (*Asellus, Lymnaea, Sialis*)	0.5	No deaths in 4 days following spray application to British lake	3
Gastropod, *Murex brandaris*	1	LC50 (18 days)	8
Murex brandaris	10	LC50 (24 h)	8
Murex brandaris	1–10	Residues (in mg/kg fresh weight [FW] soft parts), after 3-day exposure ranged between 1.5 and 2.8; were dose dependent	8

Hermit crab, *Pagurus* sp.	1	LC50 (10 days)	8
Pagurus sp.	10	LC50 (36 h)	8
Pagurus sp.	1–5	Residues, in mg/kg whole body FW, after 3-day exposure ranged between 3.2 and 15; were dose dependent	8
Brown shrimp, *Penaeus aztecus*	>1	50% immobilization in 48 h	6
American oyster, *Crassostrea virginica*	>1	50% growth reduction in 96 h	6
Louisiana red crayfish, *Procambarus clarkii*			
Juvenile	1.4	LC50 (96 h)	9
Juvenile	2.4	LC50 (72 h)	9
Adult	17	LC50 (72 h)	9
All stages	Sublethal	Dose-dependent increase in hyperactivity and oxygen consumption	9
Daphnid, *Daphnia hyalina*	2.5	LC50 (14 days)	7
Daphnid, *Daphnia pulex*	2.7	50% immobilization in 48 h	10
Daphnia pulex	4	LC50 (48 h)	11
Cladoceran, *Simocephalus serrulatus*	2.8	50% immobilization in 48 h	10
Simocephalus serrulatus	3.7	LC50 (48 h)	11
Liver fluke, *Fasciola hepatica*			
Egg through miracidium	5	LC50 (20 days); effects counteracted by dinoseb	12
Egg	6	Delayed embryonic development; delayed hatch of miracidia	12
Egg	8	26% hatch	12
Egg	10	9% hatch	12
Egg	15	No hatch	12
Freshwater copepods, 2 species (*Eucyclops, Diaptomus*)	5	LC50 (48 h)	13
Freshwater copepods, 2 species	10	LC50 (24 h); effects counteracted by metribuzin, another herbicide	13
Aquatic insects, nymphs			
Corixid, *Sigara* sp.	5	LC50 (14 days)	7
Baetid, *Cloeon dipterum*	29	LC50 (14 days)	7
Daphnid, *Daphnia magna*	6	24% immobilized in 26 h; all mobile daphnids transferred to paraquat-free medium died within 24 h	14
Amphipod, *Gammarus fasciatus*	11	LC50 (96 h)	10, 11
Ribbed mussel, *Geukensia demissa*	93	Elevated catalase activity, lipid peroxidation rate, and total superoxide dismutase levels in 12–36 h	15
Geukensia demissa	744	No deaths in 7 days	15
Geukensia demissa	1,190	LC100 (7 days)	15
Chironomid, *Psectrocladius* sp., 4th instar larvae	>100	LC50 (14 days)	7
Stonefly, *Pteronarcys californica*	>100	LC50 (96 h)	10, 11
Mosquito larvae, 2 species	275–>1,000	LC50	4
Fish			
Common carp, *Cyprinus carpio*	0.5	After 6 days, 300% increase in phosphorylase and 200% increase in glucose-6-phosphatase activities in liver; increase in sugar level and serum lactic dehydrogenase activity	18
Cyprinus carpio	5	Increase in activities of various liver enzymes, and in blood sugar levels	19

		during 6-day exposure; effects enhanced by the herbicide methidathion	
Cyprinus carpio	10	During 96-h exposure, significant alterations were recorded in lipid peroxidation rate, hemoglobin concentration, and erythrocyte antioxidant enzymes--that is, catalase, superoxide dismutase, and glutathione peroxidase activities	20
Cyprinus carpio	13–214	Acetylcholinesterase activity reduced 50% after 2-h exposure in serum (13 mg/L), heart (39 mg/L), muscle (102 mg/L), and brain (214 mg/L)	21
Freshwater fish			
4 species	1	Maximum residues, in mg/kg whole body FW, during 16-day exposure, ranged between 0.6 in green sunfish (*Lepomis cyanellus*) and 1.6 in bluegill (*Lepomis macrochirus*); intermediate values recorded for rainbow trout (*Oncorhynchus mykiss*) and channel catfish (*Ictalurus punctatus*)	22
3 species	10	In 96-h exposures, paraquat caused exposure-dependent increase in lipid peroxidation rate and in activity enhancement of peroxide metabolism enzymes in erythrocytes	23
Smallmouth bass, *Micropterus dolomieui*	1	Adverse sublethal effects	22
Striped mullet, *Mugil cephalus*	1	LC50 (16 days); survivors had pronounced gill histopathology and residues (in mg/kg FW) of 0.2 in muscle, 0.2 in ovary, 4.7 in skin, and 6.1 in digestive tract	8
Mugil cephalus	10	LC50 (60 min)	8
Thai silverbarb, *Puntius gonionotus*	1	No tissue histopathology after 12-day exposure	24
Puntius gonionotus	1	No tissue histopathology after 12-day exposure; gills normal during 5-day exposure	24
Longnose killifish, *Fundulus similis*	>1	LC50 (48 h)	6
Mosquitofish, *Gambusia affinis*	3	Adverse effects	22
Gambusia affinis	604	LC50 (96 h)	5
Zebra danio, *Brachydanio rerio*	7.5–48.5	LC50 (96 h)	4
Shortfin molly, *Poecilia mexicana*	12	LC50 (24 h)	5
Medaka, *Oryzias latipes*			
Egg	12	Normal development	5
Egg	23	Abnormal development	5
Embryo	>50	100% lethal	5
Bluegill, *Lepomis macrochirus*	13	LC50 (96 h)	10, 11
Guppy, *Poecilia reticulata*	15–22	LC50 (96 h)	4
Rainbow trout, *Oncorhynchus mykiss*	15–32	LC50 (96 h)	5, 10, 11
Oncorhynchus mykiss	>100	LC50 (24 h)	10

Brown trout, *Salmo trutta*	25	LC50 (96 h)	5
Channel catfish, *Ictalurus punctatus*	>100	LC50 (96 h)	5, 10, 11
Amphibians			
Northern leopard frog, *Rana pipiens*			
Early gastrula stage	0.1	Normal growth, survival, development, and swimming behavior after 7-day exposure	16
Early gastrula stage	0.5	High mortality, high number of tail abnormalities, reduced growth rate in survivors, abnormal swimming behavior after 7-day (3 days posthatch) exposure to 0.5 mg/L and higher	16
15-day-old tadpoles	0.5	33% dead after exposure for 16 days	17
15-day-old tadpoles	2	95% dead after exposure for 16 days; growth retardation and increase in developmental abnormalities such as tail malformations and cranial defects	17
Fowler's toad, *Bufo woodhousei fowleri*, tadpole	15	LC50 (96 h)	10
Bufo woodhousei fowleri	56	LC50 (24 h)	10
Western chorus frog, *Pseudacris triseriata*, tadpole	28	LC50 (96 h)	10
Pseudacris triseriata	43	LC50 (24 h)	10
Frog, *Limondynastes peronii*, adult	100	LC50 (96 h)	5
Frog, *Adelotus brevis*, adult	262	LC50 (96 h)	5

[a]1, Ross et al. 1979; 2, Anonymous 1963; 3, Way et al. 1971; 4, Summers 1980; 5, Bauer 1983; 6, Mayer 1987; 7, Brooker and Edwards 1974; 8, Fytizas 1980; 9, Leung et al. 1980; 10, Mayer and Ellersieck 1986; 11, Johnson and Finley 1980; 12, Christian et al. 1985; 13, Naqvi et al. 1981; 14, Crosby and Tucker 1966; 15, Wenning et al. 1988; 16, Dial and Bauer 1984; 17, Dial and Dial 1987b; 18, Simon et al. 1983; 19, Asztalos et al. 1988; 20, Matkovics et al. 1987; 21, Nemcsok et al. 1984; 22, Earnest 1971; 23, Gabryelak and Klekot 1985; 24, Sinhaseni and Tesprateep 1987.

The lowest doses of paraquat causing measurable adverse effects in sensitive species of birds (Table 4) were 0.2 mg/kg BW administered by single intravenous injection to Japanese quail, causing anemia; 0.25 mg/kg applied in oil solution to the surface of mallard eggs, producing reduced survival, reduced growth, and increased frequency of developmental abnormalities; 10 mg/kg BW administered orally for 10 days to nestlings of the American kestrel, causing reduced growth; 20 mg/kg in diet of the northern bobwhite, producing a reduction in egg deposition; 40 mg/L in drinking water of the domestic chicken, causing elevated tissue residues and an increase in the number of abnormal eggs produced; and 199 mg/kg BW in mallards, producing an acute oral LD50.

Paraquat is highly toxic to avian embryos but less toxic to adult birds (Bunck et al. 1986). It is toxic by several routes of administration, including injection and topical application (Hoffman et al. 1985). Of 42 herbicides and insecticides tested, paraquat was the most toxic to mallard eggs. Paraquat applied to eggshell surfaces in nontoxic oil vehicles was significantly more embryotoxic than were aqueous paraquat solutions, presumably due to greater penetration of oil past the shell and membranes (Hoffman and Eastin 1982; Hoffman and Albers 1984; Table 4). The LC50 values for paraquat and mallard eggs were 1.68 kg/ha (1.5 lb/acre) in aqueous emulsion and 0.11 kg/ha (0.1 lb/acre) in an oil vehicle (Hoffman and Eastin 1982). The computed LC50 aqueous value was about 1.5 times that of the recommended field application rate of about 1.0 kg/ha; however, Paraquat in aqueous solution caused some deaths at only half the field level of application, and survivors showed impaired growth and some developmental abnormalities (Hoffman and Eastin 1982; Table 4).

Table 4. Effects of paraquat on selected species of birds.

Species, dose, and other variables	Effects	Reference
Mallard, *Anas platyrhynchos*		
Fertilized eggs exposed on day 3 of incubation for 0.5 min at room temperature		
Oil solutions		
0.25 mg/kg/egg, equivalent to 0.56 kg/ha or 0.05 lb/acre	17% dead, reduced growth, 16% abnormal development	Hoffman and Eastin 1982
0.5 mg/kg/egg	50% dead, some abnormal survivors	Hoffman and Albers 1984
2.5 mg/kg/egg	83% dead, 60% abnormal	Hoffman and Eastin 1982
Aqueous solutions		
2.5 mg/kg/egg, equivalent to 0.56 kg/ha or 0.5 lb/acre	23% dead, survivors stunted, 9% abnormal	Hoffman and Eastin 1982
8.3 mg/kg/egg	50% dead; computed LC50 concentration about 1.5 times the recommended field application rate; at 1.5–3.0 times the field level, paraquat produced abnormal development, including edema, stunting, and brain malformations	Hoffman and
27.7 mg/kg/egg	73% dead, 63% of survivors abnormal	Hoffman and Eastin 1982
Adults and juveniles		
199 mg/kg body weight (BW)	Acute oral LD50; deaths usually occurred 3–20 h after treatment; remission took up to 12 days	Hudson et al. 1984
600 mg/kg BW	Percutaneous LD50 for 10- to 11-month-old drakes after a 24-h dermal foot exposure; deaths occurred 6–22 h after treatment; remission took up to 5 days	Hudson et al. 1984
4,048 mg/kg diet	Fatal to 50% after 5 days on treated diet plus 3 days on untreated ration	Heath et al. 1972
Northern bobwhite, *Colinus virginianus*		
Parent generation (P_1) fed diets containing 20, 60, 180, or 360 mg/kg ration for 6 weeks; in next generation (F_1), none was administered	360 mg/kg P_1 group had reduced fertility and hatchability, significant body weight loss, reduction in ovary and oviduct weight; no histopathology or increase in chick abnormalities; the 180 mg/kg P_1 group laid significantly fewer eggs during treatment; all F_1 hens from the 20, 60, and 180 mg/kg groups started laying 1 week later than controls and produced fewer eggs; F_1 males experienced delay in maturation; F_1 chicks from the	Bauer 1983, 1985

	20 mg/kg group were significantly heavier than all other groups	
Fed diets containing 25 or 100 mg/kg food for 60 days	No signs of toxicity or impaired learning	Bunck et al. 1986
981 mg/kg diet, 2- to 3-week-old birds	Fatal to 50% after 5 days on treated diet plus 3 days on untreated diet	Heath et al. 1972; Anonymous
Japanese quail, *Coturnix japonica*		
Juveniles received a single intravenous injection of 0.2, 2, or 20 mg/kg BW	Some deaths in 20 mg/kg group; all survivors from all groups showed hemolytic anemia within 24 h postinjection, recovery beginning within 72 h; the 0.2 mg/kg birds also showed reductions in erythrocyte number, hematocrit, and hemoglobin within 24 h	Clark et al. 1988
14-day-old chicks fed treated diets for 5 days followed by 3 days of untreated food		
500 mg/kg diet	Fatal to 20%	Hill and Camardese 1986
948–970 mg/kg diet	Dietary LD50	Heath et al. 1972; Hill and Camardese 1986
1,516 mg/kg diet	Fatal to 90%	Hill and Camardese 1986
Eggs dusted with 0.4–0.8% paraquat powder	58–79% hatching rate	Bauer 1983
100 mg/L in drinking water	Lethal within 7 days	Summers 1980
American kestrel, *Falco sparverius*		
Nestlings		
Daily oral doses, for 10 days, of 10, 25, or 60 mg/kg BW	Compared to controls, all groups exhibited reduced growth rate and elevated total sulfhydryl and protein-bound sulfhydryl levels in lung; the 25 mg/kg group had reduced skeletal growth of humerus and femur; in the 60 mg/kg group, 44% died in 4 days, survivors showed abnormal blood chemistry, liver histopathology, kidney damage, reduced skeletal growth of humerus, femur, radius-ulna and tibiotarsus	Hoffman et al. 1985, 1987
Domestic chicken, *Gallus* sp.		
Egg		
>0.1 mg/kg	Hatching rate reduced after injection	Fletcher 1967; Bauer 1983
0.5 mg	Injected eggs did not hatch	Haley 1979
0.4–0.8% paraquat powder	46–77% hatching rate for eggs dusted with powder	Bauer 1983
Adult		
Single intravenous injection of 25 mg paraquat dichloride/kg BW	60% reduction in urine flow within 50 min	Prashad et al. 1981
40 mg/L drinking water for 14 days, followed by 14 days of paraquat-free water	No effect on egg production or hatchability, but 7% increase in number of abnormal eggs produced; residues in eggs rose to about	Fletcher 1967

	0.1 mg/kg, but declined to below detection limits 6 days after treatment ended; no effect on food and water consumption of hens or on number and type of abnormalities in chicks	
131 mg/kg BW	Acute oral LD50, diet deficient in vitamin E and selenium	Combs and Peterson 1983
148 mg/kg BW	Acute oral LD50, diet deficient in selenium	Combs and Peterson 1983
419 mg/kg BW	Acute oral LD50, diet deficient in vitamin E	Combs and Peterson 1983
Chicks, 8 days old, 200–380 mg/kg BW	Acute oral LD50	Haley 1979; Summers 1980; Bauer 1983
Turkey, *Meleagris gallopavo*		
20 mg/kg BW	Lethal dose, intravenous injection route	Smalley 1973
100 mg/kg BW	Lethal dose, intraperitoneal injection route	Smalley 1973
290 mg/kg BW	Lethal dose, oral administration route	Smalley 1973
500 mg/kg BW	Lethal dose, dermal route	Smalley 1973
Ring-necked pheasant, *Phasianus colchicus*		
1,468 mg/kg diet	Fatal to 50% after 5-day treated diet plus 3-day untreated diet	Heath et al. 1972

Nestlings of altricial species, such as the American kestrel, were more sensitive to paraquat exposure than were young or adults of precocial species (Hoffman et al. 1985). Several food items of kestrels (e.g., grasshoppers, small rodents, passerine birds) are readily contaminated by paraquat through direct contact during agricultural spraying or by ingestion of contaminated vegetation (Hoffman et al. 1985). From a comparative viewpoint, however, lungs of nestling kestrels were less sensitive to paraquat than were mammalian lungs (Hoffman et al. 1987).

Northern bobwhite hens immediately exposed to simulated field application rates of paraquat took longer to lay a clutch of eggs once laying had commenced; the completed clutch appeared 10 days later in the season than birds free from paraquat exposure. It is uncertain whether the paraquat-induced delay in sexual maturation produced experimentally will also be reflected in nonlaboratory situations (Bauer 1983, 1985). Turkeys (*Meleagris gallopavo*), for example, held in field plats sprayed 24 h earlier with paraquat at 100 times the recommended agricultural application rate (i.e., up to 14 kg/ha or 200 oz cation per acre) showed no signs of toxicity 30 days after spraying (Smalley 1973).

Acute toxicity of paraquat in the domestic chicken was highly responsive to nutritional selenium status and not to vitamin E status; as little as 0.01 mg Se/kg of ration protected 8-day-old chicks against acute paraquat poisoning (Combs and Peterson 1983). Paraquat administered to chickens by way of diet was less toxic than the same amount administered in drinking water (Fletcher 1967).

Mammals

Resistance to paraquat among mammals varied substantially because of inherent differences in sensitivity between species, route of administration, and reproductive state (Table 5). The lowest recorded doses of paraquat causing measurable adverse effects on growth, survival, or reproduction were aerosol concentrations of 0.4-6.0 µg/L (rat, guinea pig); 0.05 mg administered directly in the lung (rat); intravenous injection of 1-12 mg/kg BW (sheep, dog, rat); subcutaneous injection of 2.4-28 mg/kg BW (rat, mouse, monkey); intraperitoneal injection of 3-10 mg/kg BW (mouse, guinea pig, goat); acute oral dose of 22-35 mg/kg BW (dog, cat, hare, guinea pig); oral application of 70 to 90 mg/kg BW (rat); dietary levels of 85-100 mg/kg of ration (dog, mouse, rat); and drinking water concentration of 100 mg/L (mouse).

In general, intraperitoneal and intravenous injection were the most sensitive administration routes (Bauer 1983). LD50 dermal values, however, are often not true percutaneous values because of oral contamination from normal grooming (Summers 1980). Aerosol exposure to paraquat produced a concentration-dependent rapid, shallow breathing pattern in guinea pigs (*Cavia* sp.) 18 h after exposure (Burleigh-Flayer and Alarie 1988). Aerosol LC50 values in paraquat toxicity tests with mammals were directly related to the duration of exposure, paraquat concentration in spray, and particle size; particles of 3 µm (diameter) seemed most effective (Haley 1979).

Following accidental ingestion, paraquat produces rapidly progressive, fatal, interstitial inflammation and fibrosis of the lung in humans, and this has been produced experimentally in several species of laboratory animals (Butler and Kleinerman 1971; Murray and Gibson 1972). Initial symptoms of paraquat poisoning include burning of the mouth and throat followed by nausea and vomiting. After a latent period of up to several days, increasing respiratory distress develops; death is usually the result of a progressive fibrosis and epithelial proliferation that occurs in the lungs (Kirnbrough 1974). Paraquat poisoning in humans has a mortality of 30-70%, depending largely on the dose ingested. It causes multiorgan failure, including the heart, lungs, kidney, liver, and brain. Although recovery may follow mild involvement of any of these organs, many patients die from progressive untreatable pulmonary fibrosis. This illness usually succeeds renal failure and relates in part to active pulmonary uptake of paraquat (D.W. Webb 1983). In one case, a 15-year-old boy accidentally ingested a mouthful of paraquat and developed severe respiratory distress, necessitating transplantation of one lung; paraquat-induced rejection of the graft resulted in death 2 weeks after the operation (Matthew et al. 1968). Paraquat cannot be absorbed significantly through intact human skin, but in the event of broken or abraded skin brief exposure to a paraquat concentration of 5 g/L may result in death (J. Smith 1988).

Table 5. Effects of paraquat on selected species of mammals.

Species, dose, and other variables	Effect	Reference
Cow, cattle, *Bos* sp.		
Calves administered 5 mg/kg BW, intravenous injection	No effect on pulmonary function or blood gases after 7 days	Kiorpes et al. 1982
20 mg/L in drinking water for 1 month	No measurable effect	Calderbank 1975
35–75 mg/kg BW	Acute oral LD50	Fletcher 1974; Haley 1979; Summers 1980; Heitkamp and Brown 1982
200–400 mg/kg diet for 30 days	No observable effect; no measurable residues in meat or milk	Calderbank 1975
Dog, *Canis familiaris*		
25 ug/L air, 60-min exposure	No ill effects	Haley 1979
Fed diets containing 7, 34, 85, or 170 mg/kg ration for 27 months	No significant abnormalities at 7 or 34 mg/kg; toxic effects noted at 85 and 170 mg/kg diet	Anonymous 1974
12 mg/kg BW, single intravenous injection	Extensive lung damage after 7 days	Hampson and Pond 1988
25 mg/kg BW, single intravenous injection	All dead within 36 h; before death, plasma levels of glucose, cortisol, and catecholamines increased and glucose levels decreased; increases in activity of plasma lactic dehydrogenase, creatinine phosphokinase, glutamic oxaloacetic transaminase, creatinine, and rennin; residues in dead dogs (in ug/kg fresh weight [FW]) were highest in bile (41), kidney (8), lung (5), liver (5), spleen (4), heart (3), adrenal (3), pancreas (1), thymus (1), and muscle (1)	Giri et al. 1982, 1983
25–50 mg/kg BW	Acute oral LD50	Heitkamp and Brown 1982; Anonymous 1988

36 mg/kg diet for 2 years	No measurable effect	Haley 1979
Goat, *Capra* sp.		
10 mg/kg BW, intraperitoneal injection	Mild paraquat-related lung tissue changes, but toxicosis was not clinically significant after 10 days	Kiorpes et al. 1982
Guinea pig, *Cavia* sp.		
Aerosol exposure (in mg/m^3)		
0.1, 0.4, or 0.8, 6 h daily, 5 days weekly, 3-week exposure	Rapid shallow dose-dependent breathing pattern, with return to control values during first 7 days' exposure, suggesting adaptation	Burleigh-Flayer and Alarie 1988
0.7, 4-h exposure, 2-week observation	Decrease in lung volume and increase in respiratory frequency; maximum effects measured several days postexposure with return to control values	Burleigh-Flayer
0.83–2.07, 4-h exposure, flow rate 21 L/min, particles usually <0.65 u diameter	Concentration-related decrease in lung volume and twofold increase in respiratory frequency 18 days postexposure	Burleigh-Flayer and Alarie 1987
3 mg/kg BW	Acute intraperitoneal LD50	Haley 1979; Manzo et al. 1979
22–80 mg/kg BW	Acute oral LD50 in 7 days	Murray and Gibson 1972; Haley 1979; Summers 1980; Heitkamp and Brown 1982; Bauer 1983
Chinese hamster, *Cricetus* spp.		
Cultured cells subjected to 0.8 mg/L for 3 h, recovery for 21 days	50% frequency of chromosomal aberrations; higher frequency by pretreatment with diethyldithiocarbamate (an inhibitor of superoxide dismutase), or dimethyl maleate (a glutathion scavenger), or at high oxygen concentrations	Sofuni and Ishidate
Cat, *Felis domesticus*		
26–50 mg/kg BW	Acute oral LD50	Fletcher 1974; Haley 1979; Summers 1980; Heitkamp and Brown 1982; Bauer 1983
26–50 mg/kg BW	Peak concentration in blood of 13 mg/L	Conning et al. 1969
Human, *Homo sapiens*		
26–50 mg/kg BW		
Child, 6-year-old, accidentally swallowed unknown amount of Gramoxone W	Residue in urine 6 days after exposure was 3.6 mg/L; death 7 days after onset of symptoms; autopsy showed ulceration of buccal mucosa, emphysema, severe lung damage, jaundice, renal failure	Campbell 1968
Adult male, died 30 h after swallowing paraquat solution	Histopathology of lung and adrenal gland; residues (in mg/kg FW), highest in kidney (17), followed by lung (6), muscle (4.4), liver (3.8), blood (1.4), skin (0.9), and brain (0.4)	Spector et al. 1978
Ingestion--but not necessarily swallowing--of about 15 mL ("mouthful") of a 20% solution	Fatal dose	Kimbrough 1974; Spector et al. 1978
4–>40 mg/kg BW	Acute oral LD50	Manzo et al. 1979; Summers 1980
Ingestion of 30 mg/kg BW	Associated with hepatic, cardiac, or renal failure sometimes death	Dasta 1978
Total ingested dose of 3–6 g	Fatal dose	Haley 1979

Hare, *Lepus* sp.		
35 mg/kg BW	Acute oral LD50	Fletcher 1974
Japanese monkey, *Macaca fuscata*		
Adults <3.5 years old, 2 mg/kg BW every 2 days for 8 to 10 days, subcutaneous injection	After 4 injections (8 days), 63% died; after 5 injections, 75% died; all deaths occurred between days 11 and 35; at day 66, survivors had elevated lung collagen and increased ceruloplasmin	Masaoka et al. 1987
Monkey, *Macaca* sp.		
50–75 mg/kg BW	Acute oral LD50 in 7 days	Fletcher 1974; Smith and Heath 1976; Heitkamp and Brown 1982; Bauer 1983
>63 mg/kg BW, oral route	All dead within 2 days; death preceded by convulsions	Murray and Gibson 1972
Mouse, *Mus musculus*		
Fed diets containing 45, 90, or 125 mg/kg ration for two generations	At 45 mg/kg and 90 mg/kg, no significant difference from controls in reproductive organ development, fertility, mating behavior, emryotoxicity, or developmental abnormalities; at 125 mg/kg diet, survival was significantly lower, fewer pairs reproduced, females mature later; second-generation mice were more resistant than first generation	Dial and Dial 1987a
Domestic mouse, *Mus* spp.		
1.65 or 3.35 mg/kg BW intraperitoneal injection, or 20 mg/kg BW orally, daily on days 8–16 of gestation	No significant teratogenic effects; low accumulations in embryos	Bus et al. 1975
Fed diets containing 2, 10, 30, or 100 mg/kg ration for 2 years	Maximum no-effect level was 30 mg/kg diet, equivalent to 3.92 mg/kg BW daily for males and 3.82 mg/kg BW daily for females	Anonymous 1988
Single intraperitoneal injection of 8 mg/kg BW on day 9 of pregnancy, or 2 mg/kg BW on day 9, 10, 11, and 12 of pregnancy	No measurable effect on survival, reproduction, birth weight, or chromosomal aberrations; no evidence of mutagenicity to mice liver cells	Selypes et al. 1980
16–30 mg ion/kg BW	LD50, intraperitoneal injection	Manzo et al. 1979; Selypes et al. 1980; Anonymous 1988
28 mg ion/kg BW	LD50, subcutaneous injection	Anonymous 1988
38–120 mg/kg BW	Acute oral LD50	Fletcher 1974; Haley 1979
50 or 100 mg/L in drinking water	Low dose had no effect on growth or survival; high dose group showed increased postnatal moratlity after 2 generations	Bauer 1983
Rabbit, *Oryctolagus* sp.		
Single intravenous injection of 0.05 mg/kg BW	Plasma concentrations (in mg/L), 0.6 within 2 h, 0.01 at 8 h, and <0.002 at 24 h; estimated half-life (Tb 1/2) of 24.5 h	Yonemitsu 1986
Single intravenous injection of 5 mg/kg BW	Plasma concentrations (in mg/L), about 30 in 2 h, 1 in 8 h, 0.1 in 24 h, and <0.01 in 48 h; estimated Tb 1/2 of 12.8 h; kidney histopathology evident 7 days after injection but lung damage negligible	Yonemitsu 1986
Daily oral administration of 11 mg/kg BW for 30 days	No significant toxic signs	Dikshith et al. 1979

5 intraperitoneal injected doses totaling 2–100 mg/kg BW	At doses of 25 mg/kg BW and higher, rabbits usually died within 4 days posttreatment; no delayed pulmonary changes in rabbits typical of those induced in man and other animals observed in survivors up to 1 month after treatment	Butler and Kleinerman 1971
20 mg/kg BW, intravenous injection	Tended to concentrate in lung; lung histopathology and biochemical upset	Ilett et al. 1974
24 mg/kg BW, 20 dermal applications	No effect	Anonymous 1974
49–150 mg/kg BW	Acute oral LD50	Fletcher 1974; Haley 1979
Total 60-min aerosol dose of 250 mg	Significantly increased levels in serum of phospholipids, cholesterol, and triglycerides; reduced growth rate; no evidence of liver or lung damage	Seidenfeld et al. 1984
346–480 mg/kg BW	Acute dermal LD50	Anonymous 1974; Haley 1979
Sheep, *Ovis aries*		
Single intravenous injection of 1, 2, 4, or 8 mg/kg BW	Nephrotoxic, producing glemerular and tubular defects in a dose-dependent manner, including inhibited glomerular filtration rates and inhibited paraquat secretion; LD50 (6 weeks), about 1 mg/kg BW; serum levels 60 min postexposure (in mg/L), 0.07 for the 1 mg/kg group, 0.25 for the 2 mg/kg group, 1.23 for the 4 mg/kg group, 2.05 for the 8 mg/kg group	D. B. Webb 1983; D. W. Wegg 1983
50–75 mg/kg BW	Acute oral LD50	Fletcher 1974; Summers 1980; Heitkamp and Brown 1982
Rat, *Rattus* sp.		
0.000116 or 0.000232 ug/kg BW hourly for 7 days, intravenous infusion, equivalent of total dose of 0.0465 mg (low dose) or 0.093 mg (high dose)	No adverse effects evident at low dose; at high dose, survivors showed weight loss, histopathology, increased lung glutathione and glucose-6-phosphate dehydrogenase activity--reflecting paraquat-induced oxidant stress and increased demand on lung NADPH	Dunbar et al. 1988a
0.0001 or 0.0004 mg/L air, daily 6-h exposure for 3 weeks	No effect at 0.0001 mg/L; pulmonary irritation at 0.0004 mg/L	Haley 1979
0.001–1.0 mg/kg BW, entire dose in right lung	Dose-dependent lung injury and fibrosis; tissue fibronectin levels remained elevated 14 days after administration	Dubaybo et al. 1987
0.006 mg/L air, 60-min exposure	LC50; 3 um-size particle most effective	Haley 1979
0.01 or 0.05 mg, injected into brain	Intense pattern of behavioral stimulation, including increased locomotor activity, especially circling, and convulsions; abnormal brain wave patterns	De Gori et al. 1988
0.0116 mg/kg BW, single dose, various routes	Dose administered by intravenous and intragastric routes cleared rapidly; urine and feces major excretion routes; Tb 1/2 in blood	Chui et al. 1988

	about 68 min; dermal- and pulmonary-route doses tended to remain at site of injection	
0.05 mg/kg BW, entire dose in lung	Pulmonary lesions, lung congestion and collapse, edema, hemorrhage, degenerate changes, proliferative fibrosis in lung tissue	Kimbrough and Gaines 1970; Summers 1980
0.09–9.00 mg/kg BW, single subcutaneous injection	Dose-dependent avoidance of foods at >0.5 mg/kg BW; the ED50 for conditioned taste aversion was 2.4 mg/kg BW (minimum effective dose was 0.78 mg/kg BW); none of these doses produce overt clinical or histological signs of toxicity	Dey et al. 1987
0.125 or 0.25 mg/kg BW hourly, continuous intravenous infusion	After 7 days, lungs of high-dose group had elevated putrescine, spermicine, and ornithine decarboxylase activity, reflecting changes in polyamine metabolism; no measurable effects in low-dose group	Dunbar et al. 1988b
Pregnant dams given 1.5, 4.5, or 13.5 mg/kg BW daily from day 7 to day 17 of gestation	No fetal toxicity or teratogenicity in any group, although maternal survival was low in the 13.5 mg/kg group	Anonymous 1988
6 mg/kg BW, intravenous injection Fed diets containing 10, 30, 100, or 300 mg/kg for 2 years	Lung fibrosis No adverse effects in males at 30 mg/kg diet (1.06 mg/kg BW daily) and lower, or in females at 100 mg/kg diet (4.3 mg/kg BW daily) and lower; lung histopathology observed in males at 100 mg/kg diet and both sexes at 300 mg/kg; at growth, reduced food and water intake, abnormal blood chemistry, and increased frequency of cataracts; no conclusive evidence of carcinogenicity	Summers 1980 Anonymous 1988
10 or 30 mg/kg BW, intraperitoneal injection	At both doses there was a decrease in calcium uptake by lung microsomes for 3–4 days postinjection, followed by recovery during next 4 days	Agarwal and Coleman 1988
14–34 mg/kg BW, intraperitoneal injection	LD50	Haley 1979; Manzo et al. 1979; Anonymous 1988
16–18 mg/kg BW, intravenous injection	LD50	Sharp et al. 1972
18 mg/kg BW, single intraperitoneal injection	Significant increases in enzymes and compounds responsible for protecting against lipid peroxidation, including catalase, glucose-6 phosphate dehydrogenase, and nonprotein sulfhydryl	Omaye and Reddy 1980
19–26 mg/kg BW, subcutaneous injection	LD50	Haley 1979; Lock 1979; Anonymous 1988
20 mg/kg BW, intravenous injection		
Postinjection time		
5 min	Residues (in mg/kg), 90 in kidney, 30 in plasma 10–20 in lung, liver, and muscle	Summers 1980
4 h	Residues (in mg/kg), 8 in lung, 6 in kidney, 2 in liver, 0.8 in muscle, 0.3 in plasma	Summers 1980

3 days	Lung contained 3 mg/kg, kidney 0.7, muscle 0.5, liver 0.3, plasma 0.04	Summers 1980
10 days	In survivors, muscle contained 0.25 mg/kg, lung 0.1, kidney 0.06, liver 0.03, plasma 0.01	Summers 1980
Fed diets containing 20, 100, or 200 mg/kg ration for two generations	Maternal and fetal toxicity in 200 mg/kg diet	Anonymous 1988
21 mg/kg BW	90-dose oral LD50 in females	Kimbrough and Gaines 1970
27 mg/kg BW, single intravenous injection	Lung surfactant decreased 32% within 24 h, suggesting loss in alveolar stability	Haley 1979
Adult males, 30 mg/kg BW, intraperitoneal injection	No deaths 72 h after single injection; marked reduction of acid alkaline phosphatase activity in alveolar epithelium of lung	Boudreau and Nadeau 1987
45 mg/kg BW, intraperitoneal injection	After 48 h, marked increase in blood glucose, depressed plasma insulin level, marked depletion of liver glycogen, significant increase in plasma creatinine phosphokinase and glutamic oxaloacetic transaminase activity	Giri et al. 1979
Fed 8-week diets containing 50, 120, or 250 mg/kg ration	No progressive accumulations in tissues; no pulmonary lesions at 50 or 120 mg/kg diet--however, 100% of 250 mg/kg group had pulmonary lesions	Summers 1980
Fed 2-year diet containing 70 mg/kg ration	No significant toxicity	Anonymous 1974
70–90 mg/kg BW, dermal exposure	LD50	Kimbrough and Gaines 1970; Kimbrough 1974; Haley 1979; Anonymous 1988
95–174 mg/kg BW	Acute oral LD50	Kimbrough and Gaines 1970; Murray and Gibson 1972; Anonymous 1974, 1988; Kimbrough 1974; Manzo et al. 1979; Heitkamp and Brown 1982; Bauer 1983
125 mg/kg BW, oral dose	Survivors had decreased kidney glomerular filtration rate within 24 h	Lock 1979
170 mg/kg diet for 2 years	No measurable effect	Haley 1979

Paraquat tends to rapidly localize in selected tissues of injected mice, including melanin, alveolar-type cells of the lung, choroid plexus, muscle, liver, gallbladder, intestinal contents, and proximal tubules of the kidney (Waddell and Marlowe 1980). Half-time persistence of paraquat in rat tissues ranged from 20 - 30 min in plasma to about 5 days in muscle (Sharp et al. 1972).

Acute effects of paraquat poisoning in livestock and small laboratory animals are similar to those in humans (Conning et al. 1969; Murray and Gibson 1972; Rose et al. 1976; Smith and Heath 1976; Haley 1979; Kelly et al. 1979; Manzo et al. 1979; Summers 1980; Table 5). Signs of acute paraquat toxicosis included hyperexcitability leading to convulsions or incoordination, inflammation of the mouth and throat, vomiting, reluctance to eat or drink, diarrhea, tachycardia, eye irritation of the conjunctiva, corneal lesions, skin reddening, skin ulceration, skin necrosis, histopathology of liver and kidney, and respiratory failure. Paraquat was selectively accumulated in lungs of canines, primates, and rodents, regardless of route of administration. Lung pathology included congestion, hemorrhage, edema, and collapse; this was associated with degeneration of alveolar and bronchial cells. Death may occur within 10 days of acute exposure.

Chronic administration of small doses or repeated injections usually produces no clinical signs for several weeks. Generally, signs develop suddenly and include weight loss, anorexia, and death--usually within 10 days of onset of signs (Smith and Heath 1976). Decreased food consumption and consequent loss of body weight are common in paraquat-poisoned rats and dogs. The *area postrema* of the hindbrain is an important neural site for detection of blood-borne chemicals and is speculated to control paraquat-induced taste aversion formation and weight loss (Dey et al. 1987).

Rabbits are comparatively resistant to paraquat-induced lung damage, regardless of the route of administration (Dikshith et al. 1979; Summers 1980; Bauer 1983). However, the closely related hare (*Lepus europaeus*) is comparatively sensitive to paraquat. Hares--placed on alfalfa plats within a few hours after the fields were treated with paraquat at 0.6 kg/ha--experienced 50% mortality in 120 h; survivors that were killed 2 weeks later showed lung damage and ulceration of the lingual mucous membrane. Plant residues were about 30 mg/kg fresh weight for alfalfa and 60 mg/kg for weeds; residues were negligible in tissues of the hare (Lavaur et al. 1973). In a similar incident in Italy, Stracciari et al. (1980) found that only 1 of 56 hares found dead had lung damage, although all had elevated urine paraquat levels of 0.5 mg/L. It was concluded that paraquat alone was not the causative agent of death, and that paraquat interactions with other chemicals applied at the same time on other crops in the same area may have been responsible.

Paraquat applications to spruce plantations for grass control had no effect on the movement or density of field mice (*Microtus arvalis*) and voles (*Microtus agrestis*), but shrews (*Sorex* sp.) migrated from treated areas to untreated ones (Summers 1980).

Paraquat is poorly absorbed from the gut and readily excreted. Typical gut absorption rates (%) and peak concentrations in blood (mg/L) were 15-20% and 3- 4 mg/L in rats, 5- 10% and 1 mg/L in guinea pigs, 16% and 13 mg/L in cats, 0.26% in cows, and 1-5% in humans (Conning et al. 1969). Paraquat is actively secreted by a renal mechanism that is vulnerable to paraquat toxicity; poisoning of the secretory component removed a large part of the excretory capacity for paraquat (D. W. Webb 1983). In rats, a single oral LD50 dose produced a reduction in renal function within 24 h. This effect is probably secondary to a decrease in plasma volume with a consequent reduction in renal blood flow (Lock 1979). Paraquat caused mild renal tubular damage in rats; within 24 h of injection of 20 mg/kg BW, there was marked diuresis, sugar and albumin in the urine, and increased plasma urea concentrations (Lock and Ishmael 1979). Paraquat-poisoned mice showed a decreased ability to excrete organic acids and bases, probably reflecting interference with proximal tubule function because no change in glomerular filtration rate was observed (Ecker et al. 1975).

Paraquat was not mutagenic, as judged by noninterference with DNA metabolism, and had no reverse mutation-inducing capability (Anonymous 1988). Paraquat had little or no teratogenicity to mammals (Bus et al. 1975). No teratogenic effects were observed in rats fed diets containing paraquat concentrations of 400 mg/kg for 3 generations (Anonymous 1988). The most common malformations in paraquat-stressed rats were those involving costal cartilage (Bauer 1983). Recent studies demonstrated transplacental transfer of paraquat in pregnant rats and guinea pigs. High concentrations of radiolabeled paraquat were found in the placenta and throughout the fetuses within 30 min of intravenous administration; concentrations in placenta, maternal blood, and fetal blood were in the ratio of 16:4:1 (Ingebrigtsen et al. 1984), suggesting that additional research is needed on paraquat embryotoxicity.

Recommendations

Criteria have not yet been promulgated by regulatory agencies for the protection of sensitive species of fish and wildlife against paraquat.

Degradation rate of paraquat in certain soils can be slow, and the compound can persist for years--reportedly in a form that is biologically unavailable. However, data are missing or incomplete on flux rates of paraquat from soil into food webs and on interaction dynamics of paraquat with other herbicides frequently applied at the same time. It seems prudent to keep close watch on the residues of paraquat in soils in situations where repeated applications have been made over long periods (Summers 1980).

Aquatic invertebrates, especially early developmental stages of crustaceans, are unusually sensitive to paraquat; adverse effects are documented in the range of 1.0- 100 µg/L (Table 6). For this reason, paraquat should be used with caution in estuarine and marshy areas (Summers 1980). Fish seem to be "safe" against aquatic weed control concentrations of < 1.0 mg paraquat per liter (Summers 1980), but aquatic plants tend to accumulate paraquat from the medium; accordingly, more research is needed on the effects of ingestion of contaminated plants and plant detritus by amphibians, reptiles, and other aquatic fauna (Dial and Dial 1987b).

Eggs of migratory waterfowl seem to be especially sensitive to paraquat at recommended application rates in an oil vehicle, but they were significantly more resistant to the same dose applied in water (Table 6). Application of paraquat in oil solution seems contraindicated in areas containing nesting waterfowl.

Among mammals, humans are among the most sensitive to paraquat, and permissible residues in our diet are low when compared to no-observed-effect levels in other warm-blooded species (Table 6). An air concentration of 0.4 mg/m^3 may exceed a safe level for certain mammals, particularly if the size of the aerosol particle is submicroscopic and capable of penetrating the lung (Burleigh-Flayer and Alarie 1988). Accordingly, the present paraquat aerosol standard--set at 0.5 mg/m^3—may have to be lowered. Misuse of paraquat has raised the question of cancellation of its registration, cancellation of its use in homes and recreational areas, or changing its packaging to prevent people from drinking it (Haley 1979). In almost all cases of fatal human poisonings, death was due to the ingestion of a concentrated (20%) solution. More dilute formulations (5 % paraquat) are usually not fatal if swallowed accidentally, suggesting that a dilute form of paraquat should be the only formulation permitted commercially (Kimbrough 1974).

Table 6. Proposed paraquat criteria for the protection of natural resources and human health.

Resource, proposed criterion, and other variables	Concentration	Reference[a]
Aquatic organisms		
Adverse effects level, in mg/L		
Algae and macrophytes		
Freshwater	0.25	1
Marine	5.0	2
Invertebrates		
Most species	0.1	3
Sensitive species	0.001	4
Vertebrates		
Most species	1.0	5, 6
Sensitive species	0.5	7, 8, 9
Birds		
Adverse effects level		
Egg surface, in mg/kg egg		
Oil solution	0.25	10
Aqueous solution	2.8	10
Oral administration, in mg/kg body weight (BW) daily	10	11, 12
Diet, in mg/kg ration	20	13, 14
Drinking water, in mg/L	40	15
Acute oral dose, in mg/kg BW	199	16
Mammals		

No-observable-effect level		
Livestock		
Forage (alfalfa, clover, pasture, range grasses), in mg/kg	5	17
Laboratory rodents		
Diet, in mg/kg ration		
Male	30	18
Female	100	18
Diet, in mg/kg BW daily		
Male	1.1–6.6	8
Female	4.3–7.1	18
Air, in ug/L		
Adverse effects level		
Blood, in mg/L		
Guinea pig	5	20
Rat	22	20
Cat	70	20
Lung, in ug directly into lung	6	17
Lung, in mg/kg BW	0.05	4, 21
Diet in mg/kg ration	85–100	22
Air, in ug/L, particle size 2.5–5u	0.4–6	17, 23
Drinking water, in mg/L	100	13
Acute oral dose, in mg/kg BW, sensitive species	25–35	4, 13, 15, 17, 18, 24, 25
Human health		
Permissible residues (in food items), in mg/kg fresh weight		
Eggs, milk, meat, meat byproducts of domestic animals	0.01	17
Most fruits and vegetables	0.05	17
Fresh hops	0.1	17
Passion fruit	0.2	17
Almond hulls, cotton seed, beans, hop vines, potatoes, sugar beets, sugarcane	0.5	17
Sunflower seeds	2.0	17
Aerosol standard, in mg/m^3	0.5	26
Acute poisoning level		
Blood, in mg/L	7.4	20

[a]References: 1, Anonymous 1963; 2, Mayer 1987; 3, Brooker and Edwards 1974; 4, Summers 1980; 5, Earnest 1971; 6, Fytizas 1980; 7, Dial and Bauer 1984; 8, Dial and Dial 1987b; 9, Simon et al. 1983; 10, Hoffman and Eastin 1982; 11, Hoffman et al. 1985; 12, Hoffman et al. 1987; 13, Bauer 1983; 14, Bauer 1985; 15, Fletcher 1967; 16, Hudson et al. 1984; 17, Haley 1979; 18, Anonymous 1988; 19, Kimbrough 1974; 20, Seto and Shinohara 1988; 21, Kimbrough and Gaines 1970; 22, Anonymous 1974; 23, Conning et al. 1969; 24, Murray and Gibson 1972; 25, Heitkamp and Brown 1982; 26, Burleigh-Flayer and Alarie 1988.

Acknowledgments

I thank N. A. Bushby, L. J. Garrett, and P. Loreg for literature search and technical services; B. A. Roberts for secretarial help; P. H. Albers, N. C. Coon, D. J. Hoffman, J. W. Hogan, and S. N. Wiemeyer for technical and scientific review; and M.W. Nichols and J.R. Zuboy for editorial services.

References

Agarwal, A. K., and J. W Coleman. 1988. Effect of paraquat on lung calcium transport. Toxicol. Lett. 42:317 - 323.

Aldrich, T K., A. B. Fisher, and H. J. Forman. 1983. Paraquat inhibits mixed-function oxidation by rat lung. J. Appl. Physiol. Respirat. Environ. Exercise Physiol. 54:1089 - 1093.

Anonymous. 1963. Ortho paraquat. Technical information experimental data sheet. California Chemical Company, San Francisco, Calif. 6 pp.

Anonymous. 1974. Ortho paraquat. Technical information experimental data sheet. Chevron Chemical Company, Research Laboratories, Richmond, Calif. 7 pp.

Anonymous. 1988. Summary of toxicity studies on paraquat. Pestic. Sci. 13:157 - 162.

Asztalos, B., J. Nemcsok, 1. Benedeczky, R. Gabriel, and A. Szabo. 1988. Comparison of effects of paraquat and methidathion [*sic*] on enzyme activity and tissue necrosis of carp, following exposure to the pesticides singly or in combination. Environ. Pollut. 55:123 - 135.

Autor, A. P., editor. 1977. Biochemical mechanisms of paraquat toxicity. Academic Press, New York. 240 pp.

Baud, F J., R Houze, C. Bismuth, J. M. Scherrmann, A. Jaeger, and C. Keyes. 1988. Toxicokinetics of paraquat through the heart-lung block. Six cases of acute human poisoning. J. Toxicol.-Clin. Toxicol. 26:35 - 50.

Bauer, C. A. 1983. The effects of paraquat on various reproductive and growth parameters in first and second generation bobwhite quail. Ph.D. thesis, Indiana State University, Terre Haute. 70 pp.

Bauer, C. A. 1985. Effects of paraquat on reproduction and growth in northern bobwhite. J. Wildl. Manage. 49:1066-1073.

Boudreau, J., and D. Nadeau. 1987. Lung hydrolases in paraquat poisoning: early response of alkaline phosphatase. J. Toxicol. Environ. Health 22:329 - 340.

Brooker, M. R, and R. W Edwards. 1974. Effects of the herbicide paraquat on the ecology of a reservoir. III. Fauna and general discussion. Freshwater Biol. 4:311 - 335.

Bunck, C. M., T. J. Bunck, and L. Sileo. 1986. Discrimination learning in adult bobwhite quail fed paraquat. Environ. Toxicol. Chem. 5:295 - 298.

Burleigh-Flayer, H., and Y. Alarie. 1987. Concentration-dependent respiratory response of guinea pigs to paraquat aerosol. Arch. Toxicol. 59:391 - 396.

Burleigh-Flayer, H., and Y. Alarie. 1988. Pulmonary effects of repeated exposures to paraquat aerosol in guinea pigs. Fundam. Appl. Toxicol. 10:717 - 729.

Bus, J. S., S. Z. Cagen, M. Olgaard, and J. E. Gibson. 1976. A mechanism of paraquat toxicity in mice and rats. Toxicol. Appl. Pharmacol. 35:501 - 513.

Bus, J. S., M. M. Preache, S. Z. Cagen, H. S. Posner, B. C. Eliason, C. W Sharp, and J. E. Gibson. 1975. Fetal toxicity and distribution of paraquat and diquat in mice and rats. Toxicol. Appl. Pharmacol. 33:450-460.

Butler, C., II, and J. Kleinerman. 1971. Paraquat in the rabbit. Br. J. Ind. Med. 28:67 - 7 1.

Calderbank, A. 1975. Environmental effects of the herbicide, paraquat. Pages 136-139 *in* F. Coulston and F. Korte, eds. Environmental quality and safety, Vol. 4. Academic Press, New York.

Campbell, S. 1968. Paraquat poisoning. Clin. Toxicol. 1:245-249.

Carr, R. J. G., R. E Bilton, and I Atkinson. 1986. Toxicity of paraquat to microorganisms. Appl. Environ. Microbiol. 52:1112-1116.

Carroll, E. W., O. J. Schwarz, and L. G. Hickok. 1988. Biochemical studies of paraquat-tolerant mutants of the fern *Ceratopteris richardii* Plant Physiol. 87:651 - 654.

Chan, K., and S. C. Leung. 1986. Effects of paraquat and glyphosate on growth, respiration, and enzyme activity of aquatic bacteria. Bull. Environ. Contam. Toxicol. 36:52 - 59.

Christian, F A., T. Tesfamichael, and T. Tate. 1985. Long-term effects of dinoseb and paraquat, both individually and combined, on embryonic development and hatching success *of Fasciola hepatica* miracidia. Arch. Environ. Contam. Toxicol. 14:149-152.

Chui, Y. C., G. Poon, and F Law. 1988. Toxicokinetics and bioavailability of paraquat in rats following different routes of administration. Toxicol. Ind. Health 4:203 - 219.

Clark, M. W, R. R Gildersleeve, J. R Thaxton, C. R. Parkhurst, and D. I. McRee. 1988. Hematological effects of ethyl methanesulfonate, paraquat and phenylhydrazine in Japanese quail. Comp. Biochem. Physiol. 89c: 15 - 30.

Combs, G. E, and F J. Peterson. 1983. Protection against acute paraquat toxicity by dietary selenium in the chick J. Nutr. 13:538 -545.

Conning, D. M., K. Fletcher, and A. A. B. Swan. 1969. Paraquat and related bipyridyls. Br. Med. Bull. 25:245 - 249,

Crome, R 1986. Paraquat poisoning. Lancet 1:333 - 334.

Crosby, D. G., and R. K. Tucker. 1966. Toxicity of aquatic herbicides to *Daphnia magna.* Science 154:289 - 291.

Darr, D. J., S. Yanni, and S. R. Pinnell. 1988. Protection of Chinese hamster ovary cells from paraquat-mediated cytotoxicity by a low molecular weight mimic of superoxide dismutase (DF-Mn). Free Radical Biol. Med. 4:357 - 363.

Dasta, J. F. 1978. Paraquat poisoning: a review. Am. J. Hosp. Phar. 35: 1368 - 1372.

Davison, C. L., and B. Papirmeister. 1971. Bacteriostasis of *Escherichia coli* by the herbicide paraquat. Proc. Soc. Exp. Biol. Med. 136:359 - 364.

De Gori, N., F Froio, C. Strongoli, A. De Francesco, M. Calo, and G. Nistico. 1988. Behavioural and electrocortical changes induced by paraquat after injection in specific areas of the brain of the rat. Neuropharmacology 27:201 - 207.

Dey, M. S., R. I. Krieger, and R. C. Ritter. 1987. Paraquat-induced, dose-dependent conditioned taste aversions and weight loss mediated by the area postrema. Toxicol. Appl. Pharmacol. 87:212 - 22 1.

Dial, C. A. B., and N. A. Dial. 1987a. Effects of paraquat on reproduction and mortality in two generations of mice. Arch. Environ. Contam. Toxicol. 16:759 - 764.

Dial, N. A., and C. A. Bauer. 1984. Teratogenic and lethal effects of paraquat on developing frog embryos *(Rana pipiens). Bull.* Environ. Contam. Toxicol. 33:592-597.

Dial, N. A., and C. A. B. Dial. 1987b. Lethal effects of diquat and paraquat on developing frog embryos and 15-day-old tadpoles, *Rana pipiens.* Bull. Environ. Contam. Toxicol. 38:1006-1011.

Dikshith, T S. S., K. K. Datta, R. B. Raizada, and H. S. Kushwah. 1979. Effect of paraquat dichloride in male rabbits. Ind. J. Exp. Biol. 17:926 - 928.

Dubaybo. B. A., R. A. Durr, and L. A. Thet. 1987. Unilateral paraquat-induced lung fibrosis: evolution of changes in lung fibronectin and collagen after graded degrees of lung injury. J. Toxicol. Environ. Health 22:439 - 457.

Dunbar, J. R., A. J. DeLucia, R. V. Acuff, and K. E. Ferslew. 1988a. Prolonged intravenous paraquat infusion in the rat. 1. Failure of coinfused putrescine to attenuate pulmonary paraquat uptake, paraquat-induced biochemical changes, or lung injury. Toxicol. Appl. Pharmacol. 94:207 - 220.

Dunbar, J. R., A. J. DeLucia, R. V. Acuff, and K. E. Ferslew. 1988b. Prolonged intravenous paraquat infusion in the rat. II. Paraquat-induced alterations in lung polyamine metabolism. Toxicol. Appl. Pharmacol. 94:221 - 226.

Earnest, R. D. 1971. The effect of paraquat on fish in a Colorado farm pond. Prog. Fish-Cult. 33:27 - 31.

Ecker, J. L., J. B. Hook, and J. E. Gibson. 1975. Nephrotoxicity of paraquat in mice. Toxicol. Appl. Pharmacol. 34:178 - 186.

Engle, D. M., J. F Stritzke, and P L. Claypool. 1988. Effect of paraquat plus prescribed burning on eastern redcedar *(Juniperus virginiana).* Weed Technol. 2:172 - 174.

Evers, W. D., J. B. Hook, and J. T Bond. 1982. Alteration of toxicity to paraquat in mice fed a purified or cereal-based diet. Drug-Nutr. Interact. 1:237 - 248.

Faulkner, J. S., and B. M. R. Harvey. 1981. Paraquat tolerant *Lolium perenne* L.: effects of paraquat on germinating seedlings. Weed Res. 21:29 - 36.

Fletcher, K. 1967. Production and viability of eggs from hens treated with paraquat. Nature (Lond.) 215:1407 - 1408.

Fletcher, K. 1974. Paraquat poisoning. Pages 86-98 *in* B. Ballantyne, ed. Forensic toxicology. John Wright, Bristol, England.

Frank L., K. Neriishi, R. Sio, and D. Pascual. 1982. Protection from paraquat-induced lung damage and lethality in adult rats pretreated with clofibrate. Toxicol. Appl. Pharmacol. 66:269-277.

Fryer, J. D., R. J. Hance, and J. W Ludwig. 1975. Long-term persistence of paraquat in a sandy loam soil. Weed Res. 15:189-194.

Funderburk, H. H., Jr., and G. A. Bozarth. 1967. Review of the metabolism and decomposition of diquat and paraquat. J. Agric. Food Chem. 15:563 - 567.

Fytizas, R. 1980. Toxicity of paraquat to three marine organisms. Bull. Environ. Contam. Toxicol. 25:283-288.

Gabryelak, T, and J. Klekot. 1985. The effect of paraquat on the peroxide metabolism enzymes in erythrocytes of freshwater fish species. Comp. Biochem. Physiol. 81C:415 - 418.

Gadkari, D. 1988. Effects of atrazine and paraquat on nitrifying bacteria. Arch. Environ. Contam. Toxicol. 17:443 - 447.

Giri, S. N., D. L. Curry, M. A. Hollinger, and M. Freywald. 1979. Effect of paraquat on plasma enzymes, insulin, glucose, and liver glycogen in the rat. Environ. Res. 20:300 - 308.

Giri, S. N., D. L. Curry, G. Stabenfeldt, W L. Spangler, D. B. Chandler, and M. J. Schiedt. 1983. Effects of paraquat on plasma glucose, cortisol, catecholamines, and insulin in the beagle. Environ. Res. 30:80 - 88.

Giri, S. N., H. R. Parker, W L. Spangler, H. R Misra, G. Ishizaki, M. J. Schiedt, and D. B. Chandler. 1982. Pharmacokinetics of [14 Cl-paraquat and associated biochemical and pathologic changes in beagle dogs following intravenous administration. Fundam. Appl. Toxicol. 2:261 - 269.

Haley, T J. 1979. Review of the toxicology of paraquat (1, 1'-dimethyl-4, 4'-bipyridinium chloride). Clin. Toxicol. 14:1-46.

Hampson, E. C. G. M., and S. M. Pond. 1988. Ultrastructure of canine lung during the proliferative phase of paraquat toxicity. Br. J. Exp. Pathol. 69:57 - 68.

Heath, R. G., J. W Spann, E. P Hill, and J. F Kreitzer. 1972. Comparative dietary toxicities of pesticides to birds. U. S. Fish Wildl. Serv., Spec. Sci. Rep.-Wildl. 152.57 pp.

Heitkamp, M., and 0. R. Brown. 1982. Cellular mechanisms of paraquat toxicity. U.S. Fish Wildl. Serv., Tech. Pap. 107:29-36.

Hill, E. E, and M. B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to coturnix. U.S. Fish Wildl. Serv., Fish Wildl. Tech. Rep. 2. 127 pp.

Hoffman, D. J., and P H. Albers. 1984. Evaluation of potential embryotoxicity and teratogenicity of 42 herbicides, insecticides, and petroleum contaminants to mallard eggs. Arch. Environ. Contain. Toxicol. 13:15 - 27.

Hoffman, D. J., and W C. Eastin, Jr. 1982. Effects of lindane, paraquat, toxaphene, and 2,4,5-trichlorophenoxyacetic acid on mallard embryo development. Arch. Environ. Contam. Toxicol. 11:79-86.

Hoffman, D. J., J. C. Franson, 0. H. Pattee, and C. M. Bunck. 1985. Survival, growth, and histopathological effects of paraquat ingestion in nestling American kestrels (*Falco sparverius*). Arch. Environ. Contam. Toxicol. 14:495 - 500.

Hoffman, D. J., J. C. Franson, O. H. Pattee, C. M. Bunck, and H. C. Murray. 1987. Toxicity of paraquat in nestling birds: effects on plasma and tissue biochemistry in American kestrels. Arch. Environ. Contam. Toxicol. 16:177 - 183.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. Second edition. U.S. Fish Wildl. Serv., Resour. Publ. 153. 90 pp.

Hughes, J. T 1988. Brain damage due to paraquat poisoning: a fatal case with neuropathological examination of the brain. Neurotoxicology 9:243 - 248.

Ilett, K. E, B. Stripp, R. H. Menard, W. D. Reid, and J. R. Gillette. 1974. Studies on the mechanism of the lung toxicity of paraquat: comparison of tissue distribution and some biochemical parameters in rats and rabbits. Toxicol. Appl. Pharmacol. 28:216 - 226.

Ingebrigtsen, K., I. Nafstad, and R. A. Andersen. 1984. Distribution and transplacental transfer of paraquat in rats and guinea-pigs. Gen. Pharmacol. 15:201-204.

Islam, A. K. M. R., and S. B. Powles. 1988. Inheritance of resistance to paraquat in barley grass *Hordeum glaucum* Steud. Weed Res. 28:393 - 397.

Johnson, W. W, and M. T Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Fish Wildl. Serv., Resour. Publ. 137. 98 pp.

Kearney, R C., J. M. Ruth, Q. Zeng, and R Mazzocchi. 1985. UV-ozonation of paraquat. J. Agric. Food Chem. 33:953 -957.

Kelly, D. E, D. G. Morgan, and V. M. Lucke. 1979. Acute respiratory distress in dogs with paraquat poisoning. Pages 297 - 308 *in* Animals as monitors of environmental pollutants. National Academy of Sciences, Washington, D.C.

Kimbrough, R. D. 1974. Toxic effects of the herbicide paraquat. April 1974 supplement, Chest 65(4):65S-67S.

Kimbrough, R. D., and T B. Gaines. 1970. Toxicity of paraquat to rats and its effect on rat lungs. Toxicol. Appl. Pharmacol. 17:679-690.

Kiorpes, A. L., R. B. Winter, D. S. Hodgson, S. J. Galitzer, and M. C. Savides. 1982. Pathophysiological effects of paraquat intoxication in domestic ruminants: low dose studies. Vet. Hum. Toxicol. 24:81 - 85.

Kitakouji, M., T Miyoshi, S. Tanada, and T Nakamura. 1989. In vitro adsorption removal of paraquat by activated carbon and cation exchange resin. Bull. Environ. Contam. Toxicol. 42:926-930.

Kitazawa, K., T Kobayashi, T Shibamoto, and K. Hirai. 1988. Effects of methylprednisolone on acute lung paraquat toxicity in sheep. Am. Rev. Respir. Dis. 137:173 - 180.

Kohen, R., and M. Chevion. 1988. Cytoplasmic membrane is the target organelle for transition metal mediated damage induced by paraquat in *Escherichia coli.* Biochemistry 27:2597 - 2603.

Lavaur, E. D., G. Grolleau, and G. Siou. 1973. Intoxication experimentale de lievres par de la luzeme traitee au paraquat. Ann. Zool.-Ecol. Anim. 5:609 - 622.

Leung, T S., S. M. Naqvi, and N. Z. Naqvi. 1980. Paraquat toxicity to Louisiana crayfish (*Procambarus clarkii*). Bull. Environ. Contam. Toxicol. 25:465 - 469.

Lindquist, N. G., B. S. Larsson, and A. L. Sokolowsld. 1988. Autoradiography of (^{14}C) paraquat or (^{14}C) diquat in frogs and mice: accumulation in neuromelanin. Neurosci. Lett. 93:1-6.

Lock, E. A. 1979. The effect of paraquat and diquat on renal function in the rat. Toxicol. Appl. Pharmacol. 48:327 - 336.

Lock, E. A., and J. Ishmael. 1979. The acute toxic effects of paraquat and diquat on the rat kidney. Toxicol. Appl. Pharmacol. 50:67 - 76.

Manzo, L., C. Gregotti, A. Di Nucci, P Richelmi. 1979. Toxicology of paraquat and related bipyridyls: biochemical, clinical and therapeutic aspects. Vet. Hum. Toxicol. 21:404 -410.

Masaoka, T, F. Akahori, S. Arai, and K. Sakaguchi. 1987. Effect of paraquat on plasma fibronectin, serum free hydroxyproline, serum ceruloplasmin and lung collagen content in monkeys. J. Toxicol. Sci. 12:329 - 340.

Matkovics, B., H. Witas, T Gabrielak, and L. Szabo. 1987. Paraquat as an agent affecting antioxidant enzymes of common carp erythrocytes. Comp. Biochem. Physiol. 87C:217 - 219.

Matthew, H., A. Logan, M. F A. Woodruff, and B. Heard. 1968. Paraquat poisoning--lung transplantation. Br. Med. J. 3:759-763.

Mayer, F L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U.S. Environ. Prot. Agency Rep. 600/8 - 87/017. 274 pp.

Mayer, E L., Jr., and M. R. Ellersieck. 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals. U.S. Fish Wildl. Serv., Resour. Publ. 160. 579 pp.

Moyer, J. R., and C. W. Lindwall. 1985. Persistence and availability of paraquat in a Lethbridge clay loam soil. Can. J. Soil Sci. 65:523 - 529.

Murray, R. E., and J. E. Gibson. 1972. A comparative study of paraquat intoxication in rats, guinea pigs, and monkeys. Exp. Mol. Pathol. 17:317 - 325.

Naqvi, S. M., T S. Leung, and N. Z. Naqvi. 1981. Toxicities of paraquat and metribuzin (Sencor) herbicides to the freshwater copepods, *Eucyclops agilis* and *Diaptomus mississippiensis.* Environ. Pollut. 26A:275 - 280.

Nemcsok, J., A. Nemeth, Z. Buzas, and L. Boross. 1984. Effects of copper, zinc and paraquat on acetylcholinesterase activity in carp (*Cyprinus carpio* L.). Aquat. Toxicol. 5:23 - 3 1.

O'Donovan, J. T, and P. A. O'Sullivan. 1986. Annual weed control with paraquat in combination with other herbicides. Can. J. Plant Sci. 66:15 3 - 160.

Ogino, T, and M. Awai. 1988. Lipid peroxidation and tissue injury by ferric citrate in paraquat-intoxicated mice. Biochim. Biophys. Acta 958:388 - 395.

Omaye, S. T, and A. K. Reddy. 1980. Early and delayed biochemical effects of paraquat toxicity on rat lung. Exp. Mol. Pathol. 33:84 - 89.

Onyeama, H. P, and F W Oehme. 1984. A literature review of paraquat toxicity. Vet. Hum. Toxicol. 26:494 - 502.

O'Sullivan, S. P. 1989. Paraquat poisoning in the dog. J. Small Anim. Pract. 30:361 - 364.

Patterson, C. E., and M. L. Rhodes. 1982. The effect of superoxide dismutase on paraquat mortality in mice and rats. Toxicol. Appl. Pharmacol. 62:65 - 72.

Polos, E., J. Mikulas, Z. Szigeti, B. Matkovics, D. Q. Hai, A. Parducz, and E. Lehoczki. 1988. Paraquat and atrazine co-resistance in *Conyza canadensis* (L.) Cronq. Pestic. Biochem. Physiol. 30:142 - 154.

Pond, S. M., S. C. Johnston, D. D. Schoof, E. C. Hampson, M. Bowles, D. M. Wright, and J. J. Petrie. 1987. Repeated hemoperfusion and continuous arteriovenous hemofiltration in a paraquat poisoned patient. Clin. Toxicol. 25:305-316.

Prashad, D. N., D. Chambers, and D. J. Beadle. 1981. Changes in renal function associated with paraquat dichloride toxicity in the domestic fowl. Gen. Pharmacol. 12:291 - 293.

Rose, M. S., E. A. Lock, L. L. Smith, and I. Wyatt. 1976. Paraquat accumulation: tissue and species specificity. Biochem. Pharmacol. 25:419 - 423.

Ross, J. H., L. O. Lim, and R. I. Krieger. 1979. Herbicidal potency of 1, l'-alkyl-4, 4'-bipyridylium salts as a function of their physicochemical constants in duckweed. Drug Chem. Toxicol. 2:193 - 205.

Salazar, L. C., and A. P Appleby. 1982. Germination and growth of grasses and legumes from seeds treated with glyphosate and paraquat. Weed Sci. 30:235 - 237.

Sato, M., A. Ohtake, K. Takeda, H. Mizunuma, and Y. Nagai. 1989. Metallothionein-I accumulation in the rat lung following a single paraquat administration. Toxicol. Lett. 45:41-47.

Seidenfeld, J. J., C. D. Eskelson, and J. M. Toyoshima, 1984. Lipid metabolism in rabbits exposed to paraquat aerosol. Life Sci. 35:191 - 198.

Selypes, A., L. Nagymajtenyi, and G. Berencsi. 1980. Mutagenic and embryotoxic effects of paraquat and diquat. Bull. Environ. Contam. Toxicol. 25:513 - 517.

Seto, Y., and T Shinohara. 1987. Inhibitory effects of paraquat and its related compounds on the acetylcholinesterase activities of human erythrocytes and electric eel *(Electrophorus electricus).* Agric. Biol. Chem. 51:2131 - 2138.

Seto, Y., and T Shinohara. 1988. Structure-activity relationship of reversible cholinesterase inhibitors including paraquat. Arch. Toxicol. 62:37 - 40.

Shaaltiel, Y., A. Glazer, P. F Bocion, and J. Gressel. 1988. Cross tolerance to herbicidal and environmental oxidants of plant biotypes tolerant to paraquat, sulfur dioxide, and ozone. Pestic. Biochem. Physiol. 31:13 - 23.

Sharp, C. W, A. Ottolenghi, and H. S. Posner. 1972. Correlation of paraquat toxicity with tissue concentrations and weight loss of the rat. Toxicol. Appl. Pharmacol. 22:241 - 25 1.

Shibata, K., and K. Iwai. 1988. Effect of dietary paraquat on the enzymes involved in tryptophan-niacin metabolism in rats. Agric. Biol. Chem. 52:1857 - 1858.

Simon, L. M., J. Nemcsok, and L. Boross. 1983. Studies on the effect of paraquat on glycogen mobilization in liver of common carp *(Cyprinus carpio* L.). Comp. Biochem. Physiol. 75C: 167 - 169.

Sinhaseni, P., and T Tesprateep. 1987. Histopathological effects of paraquat and gill function of *Puntius gonionotus,* Bleeker. Bull. Environ. Contam. Toxicol. 38:308 - 312.

Smalley, H. E. 1973. Toxicity and hazard of the herbicide, paraquat, in turkeys. Poult. Sci. 52:1625 - 1628.

Smith, E. A., and C. 1. Mayfield. 1978. Paraquat: determination, degradation, and mobility in soil. Water Air Soil Pollut. 9:439 -452.

Smith, J. G. 1988. Paraquat poisoning by skin absorption: a review. Hum. Toxicol. 7:15 - 19.

Smith, L. L. 1985. Paraquat toxicity. Philos. Trans. R. Soc. Lond. 311 B:647 - 657.

Smith, L. L. 1988. The toxicity of paraquat. Adverse Drug React. Acute Poison Rev. 1: 1-17.

Smith, P., and D. Heath. 1976. Paraquat. Crit. Rev. Toxicol. 4:411-445.

Sofuni, T, and M. Ishidate, Jr. 1988. Induction of chromosomal aberrations in active oxygen-generating systems. 1. Effects of paraquat in Chinese hamster cells in culture. Mutation Res. 197:127- 132.

Spector, D., C. Whorton, J. Zachary, and R. Slavin. 1978. Fatal paraquat poisoning: tissue concentrations and implications for treatment. Johns Hopkins Med. J. 142:110 - 113.

Stracciari, G. L., M. Merlanti, R. Rosmini, J. M. Stracciari, and V Trocchi. 1980. Su un episodio di tossicosi ambientale da fitofarmaci in *Lepus europaeus* Pallas. Ricerch. Biol. Selvaggina 68:1 - 28. (in Italian with English summary)

Subagja, J., and R. J. Snider. 1981. The side effects of the herbicide atrazine and paraquat upon *Folsomia candida* and *Tullbergia granulata* (Insecta, Collembola). Pedobiologia 22:141-152.

Suleiman, S. A., and J. B. Stevens. 1987. Bipyridylium herbicide toxicity: effects of paraquat and diquat on isolated rat hepatocytes. J. Environ. Pathol. Toxicol. Oncol. 7:73 - 84.

Summers, L. A. 1980. The bipyridinium herbicides. Academic Press, London. 449 pp.

Szabo, L., B. Matkovics, K. Barabas, and G. Oroszlan. 1986. Effects of various thiols on paraquat toxicity. Comp. Biochem. Physiol. 83C:149-153.

Takegoshi, K., Y. Nakanuma, M. Ohta, T. Thoyama, K. Okuda, and N. Kono. 1988. Light and electron microscopic study of the liver in paraquat poisoning. Liver 8:330 - 336.

Talbot, A. R., and C. C. Fu. 1988. Paraquat intoxication during pregnancy: a report of 9 cases. Vet. Hum. Toxicol. 30:12 - 17.

Tanaka, K., I. Furusawa, N. Kondo, and K. Tanaka. 1988. SO_2 tolerance of tobacco plants regenerated from paraquat-tolerant callus. Plant Cell Physiol. 29:743 - 746.

Tanaka, R., S. Fujisawa, and K. Nakai. 1981. Study on the absorption and protein binding of carbaryl, dieldrin and paraquat in rats fed on protein diet. J. Toxicol. Sci. 6:1 - 11.

Tucker, E. S., and S. B. Powles. 1988. Occurrence and distribution in south-Eastern Australia of barley grass (*Hordeum glaucum* Steud.) resistant to paraquat. Plant Prot. Q. 3:19 - 21.

Vaughn, K. C., and S. O. Duke. 1983. In situ localization of the sites of paraquat action. Plant Cell Environ. 6:13 - 20.

Waddell, W J., and C. Marlowe. 1980. Tissue and cellular disposition of paraquat in mice. Toxicol. Appl. Pharmacol. 56:127-140.

Way, J. M., J. F. Newman, N.W. Moore, and F. W. Knaggs. 1971. Some ecological effects of the use of paraquat for the control of weeds in small lakes. J. Appl. Ecol. 8:509 - 532.

Webb, D. B. 1983. The pathophysiology of paraquat nephrotoxicity in the sheep. J. Toxicol.-Clin. Toxicol. 19:911 - 929.

Webb, D. W. 1983. Nephrotoxicity of paraquat in the sheep and the associated reduction in paraquat secretion. Toxicol. Appl. Pharmacol. 68:282 - 289.

Wegener, T, B. Sandhagen, K. W Chan, and T Saldeen. 1988. N-acetylcysteine in paraquat toxicity: toxicological and histological evaluation in rats. Upsala J. Med. Sci. 93:81 - 89.

Wenning, R. J., R. T Di Giulio, and E. R Gallagher. 1988. Oxidant-mediated biochemical effects of paraquat in the ribbed mussel, *Geukensia demissa*. Aquat. Toxicol. 12:157-170.

Williams, J. H., Jr., R. D. Fairshter, T R. Ulich, S. Crosby, M. Chen, L. Rosario, and N. D. Vaziri. 1988. Adverse effects of (15S)-15-methyl-prostaglandin E_I in normal and paraquat-exposed rats. Toxicol. Appl. Pharmacol. 92:330-334.

Wong, R. C., and J. B. Stevens. 1986. Bipyridilium herbicide toxicity in vitro: comparative study of the cytotoxicity of paraquat and diquat toward the pulmonary alveolar macrophage. J. Toxicol. Environ. Health 18:393 - 407.

Wu, C. H., H. L. Warren, K. Sitaraman , and C. Y. Tsai. 1988. Translational alterations in maize leaves responding to pathogen infection, paraquat treatment, or heat shock. Plant Physiol. 86:1323 - 1329.

Yonemitsu, K. 1986. Pharmacokinetic profile of paraquat following intravenous administration to the rabbit. Forensic Sci. Int. 32:33 - 42.

Biological Report 85(1.23)
December 1991

Contaminant Hazard Reviews
Report 23

Cyanide Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

Biological Report
This publication series of the Fish and Wildlife Service comprises reports on the results of research, developments in technology, and ecological surveys and inventories of effects of land-use changes on fishery and wildlife resources. They may include proceedings of workshops, technical conferences, or symposia; and interpretive bibliographies. ISSN 0895-1926

Copies of this publication may be purchased from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161.

This publication may be cited as:

Eisler, Ronald. 1991. **Cyanide Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review**- U.S. Fish Wildl. Serv., *Biol. Rep.* 85(1.23).

Tables

Cyanide Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

Abstract. Cyanides are used widely and extensively in the manufacture of synthetic fabrics and plastics, in electroplating baths and metal mining operations, as pesticidal agents and intermediates in agricultural chemical production, and in predator control devices. Elevated cyanide levels are normally encountered in more than 1,000 species of food plants and forage crops, and this probably represents the greatest source of cyanide exposure and toxicosis to man and to range animals. Anthropogenic sources of cyanide in the environment include certain industrial processes, laboratories, fumigation operations, cyanogenic drugs, fires, cigarette smoking, and chemical warfare. Although cyanide is ubiquitous in the environment, levels tend to be elevated in the vicinity of metal processing operations, electroplaters, gold-mining facilities, oil refineries, power plants, and solid waste combustion.

Many chemical forms of cyanide are present in the environment, including free cyanide, metallocyanide complexes, and synthetic organocyanides, also known as nitriles. But only free cyanide (i.e., the sum of molecular hydrogen cyanide, HCN, and the cyanide anion, CN^-) is the primary toxic agent, regardless of origin.

Cyanides are readily absorbed through inhalation, ingestion, or skin contact and are readily distributed throughout the body via blood. Cyanide is a potent and rapid-acting asphyxiant; it induces tissue anoxia through inactivation of cytochrome oxidase, causing cytotoxic hypoxia in the presence of normal hemoglobin oxygenation. Diagnosis of acute lethal cyanide poisoning is difficult because signs and symptoms are nonspecific, and numerous factors modify its biocidal properties, such as dietary deficiencies in vitamin B_{12}, iodine, and sulfur amino acids. Among the more consistent changes measured in acute cyanide poisoning are inhibition of brain cytochrome oxidase activity, and changes in electrical activity in heart and brain. At sublethal doses, cyanide reacts with thiosulfate in the presence of rhodanese to produce the comparatively nontoxic thiocyanate, most of which is excreted in the urine. Rapid detoxification enables animals to ingest high sublethal doses of cyanide over extended periods without harm. Antidotes in current use to counteract cyanide poisoning include a combination of sodium nitrite and sodium thiosulphate (United States), cobalt edetate (United Kingdom, Scandinavia, France), or a mixture of 4-dimethylaminophenol and sodium thiosulphate (Germany).

All available evidence suggests that cyanides are neither mutagenic, teratogenic, nor carcinogenic. Moreover, there are no reports of cyanide biomagnification or cycling in living organisms, probably owing to its rapid detoxification. Cyanide seldom persists in surface waters and soils owing to complexation or sedimentation, microbial metabolism, and loss from volatilization. More data are needed on cyanide distribution and transformation in the atmosphere.

Analytical methods for the determination of free and bound cyanides and cyanogenic compounds in biological materials are under constant revision. Further, unless tissue samples are obtained promptly after cyanide exposure and analyzed immediately, erroneous analytical values will result.

Higher plants are adversely affected by cyanide through cytochrome oxidase inhibition; the rate of production and release of cyanide by plants to the environment through death and decomposition is unknown. Nonacclimatized soil bacteria are adversely affected at 0.3 mg HCN/kg; acclimatized populations, however, can degrade wastes containing up to 60 mg total cyanide per kilogram. In some cases, soil bacteria and fungi produce cyanides as secondary metabolites, with adverse effects on certain plants. Several species of arthropods normally contain elevated whole-body cyanide concentrations, and these confer protection against predators and allow consumption of cyanogenic plants.

Fish were the most sensitive aquatic organisms tested. Adverse effects on swimming and reproduction were observed between 5 and 7.2 µg free cyanide per liter; lethal effects usually occurred between 20 and 76 µg/L. Biocidal properties of cyanide in aquatic environments were significantly modified by water pH, temperature, and oxygen content; life stage, condition, and species assayed; previous exposure to cyanides; presence of other chemicals; and initial dose tested.

Birds that feed predominantly on flesh were more sensitive to cyanide than were herbivores. Free cyanide levels associated with high avian death rates include 0.12 mg/L in air, 2.1-4.6 mg/kg body weight (BW) via acute oral exposure, and 1.3 mg/kg BW administered intravenously. Dietary levels of 135 mg total cyanide per kilogram ration resulted in growth reduction of chicks, but 103 mg total cyanide per kilogram ration had no measurable effect on domestic chickens.

Cyanogenic plants represent a problem for various range animals and wildlife, primarily among species that eat rapidly. Intakes of 4 mg HCN/kg BW are lethal to these species if it is consumed quickly. Cassava (*Manihot esculenta*) is a cyanogenic plant that accounts for up to 70% of human caloric intake in some areas, and this is associated with serious, long-term toxic effects including ataxia, optic nerve lesions, altered thyroid function, demyelination, and increases in tissue thiocyanate levels. Acute oral LD50 values for representative species of mammals ranged between 2 and 3.6 mg HCN/kg BW. Despite the high lethality of large single exposures, repeated sublethal doses--especially in diets--can be tolerated by many species for extended periods, perhaps indefinitely. Mammalian deaths were also recorded at air concentrations of 140 mg HCN/m^3 (exposure for 60 min) and 4,400 mg HCN/m^3 (exposure for 1 min), and at dermal applications between 2.3 mg HCN/kg BW for abraded skin and 100 mg HCN/kg BW for intact skin. Adverse nonlethal effects were noted at drinking water concentrations >150 mg HCN/L and at dietary concentrations >720 mg HCN/kg ration.

Free cyanide criteria currently proposed for natural resource protection include <3 µg/L medium for aquatic life, and <100 mg/kg diet for birds and livestock. For human health protection, free cyanide values are <10 µg/L drinking water, <50 mg/kg diet, and <5 mg/m^3 air.

Key words: Cyanide, toxic effects, wildlife, cyanogenic plants, aquatic organisms, criteria.

The origin of terrestrial life probably depended on the presence and reactivity of hydrogen cyanide and its derivatives; paradoxically, hydrogen cyanide is toxic to the majority of living matter (Marrs and Ballantyne 1987). Cyanide is a general respiratory poison--although uptake can also occur through ingestion or dermal absorption--producing reactions within seconds, and death within minutes (Towill et al. 1978; Environmental Protection Agency [EPA] 1980). The toxic mechanism of cyanide primarily involves the inhibition of cytochrome oxidase, the terminal oxidative enzyme of the mitochondrial electron transport chain, producing blockage of aerobic ATP synthesis (Egekeze and Oehme 1979; Younes and Strubelt 1988). Because of their highly effective lethal potency, cyanides were used for genocidal programs in Germany in World War II, in mass suicides by members of the People's Temple religious sect in Guyana, and in the substitution of medication in Tylenol capsules in drugstores in various cities in the United States. In fact, cyanides are responsible for more human deaths than any other chemicals known, owing to their deliberate use in suicide, murder, chemical warfare, genocide, and judicial execution (Way 1981, 1984; Ballantyne and Marrs 1987a; Gee 1987; Marrs and Ballantyne 1987; Yamamoto 1989). High sublethal doses of cyanide are rapidly detoxified, and accidental acute cyanide poisonings in humans are uncommon (Towill et al. 1978).

Cyanide compounds are useful to society in terms of their key role in synthetic and industrial processes, for certain fumigation and agricultural uses, and for some therapeutic applications (Ballantyne and Marrs 1987a). Cyanides are present in effluents from iron and steel processing plants, petroleum refineries, and metal-plating plants, and constitute a hazard to aquatic ecosystems in certain waste-receiving waters (Smith et al. 1979), and to livestock (EPA 1980;Towill et al. 1978). Cyanide serves no useful purpose in the human body, yet it is present in our food, air, and water (Becker 1985).

Natural sources of cyanide include various species of bacteria, algae, fungi, and higher plants that form and excrete cyanide (Way 1984). The most widely distributed major food crop with a high content of cyanogenic glycosides is cassava (*Manihot esculenta*), also known as manioc. Cassava is a staple food in human diets in over 80 countries, and it is sometimes added to animal feeds as a substitute for more expensive cereal grains (Gomez et al. 1988). In humans, chronic cyanide intoxication caused by consumption of cassava is the main etiological factor in the debilitating tropical ataxic neuropathy (Egekeze and Oehme 1980). Other plants having comparatively elevated cyanide content include fruit pits, sweet potatoes (*Ipomoea batatas*), corn (*Zea mays*), bamboo shoots (*Bambusa* spp.), linseed, (*Linum* sp.), lima beans (*Phaseolus lunatus*), and millet (*Panicum miliaceum*; Way 1984). In higher plants that contain cyanogenic glycosides, at least 20 of these compounds have been identified (EPA 1980). Amygdalin--one of the more intensively studied cyanogenic glycosides--is found in seeds of the cherry (*Prunus* spp.), plum (*Prunus* spp.), peach (*Prunus persica*), apricot (*Prunus armenaica*), apple (*Malus domestica*), pear (*Pyrus communis*), and many parts of the cherry laurel (*Prunus laurocerasus;* EPA 1980). Apricot seeds and peach kernels are food delicacies in Turkey, and have caused at least nine poisonings (two fatal) in children from that country (Gee 1987). Acute cyanide poisoning has occurred in the United States from the ingestion of almond-flavored milkshakes prepared from apricot kernels (Way 1984). Amygdalin is also the chief ingredient in laetrile, a medication prescribed by some physicians to control tumors. Both laetrile and amygdalin-containing fruit pits have been implicated as the causes of acute cyanide poisoning in humans (EPA 1980). Another naturally occurring group of organic cyanides (nitriles) is the highly toxic pseudocyanogenic glycosides, especially cycasin, and these have been implicated in a variety of tropical diseases of the nervous system, and partial or total blindness (EPA 1980). Other nitriles found in plants include the lathyrogenic compounds, glucosinolates, and the cyanopyridine alkaloids (EPA 1980).

That certain plants, such as bitter almonds *(Prunus dulcis),* cherry laurel leaves, and cassava, are poisonous if consumed in sufficient quantities has been known for at least 2,000 years. But it was not until the 1700's that cyanide was recognized as the basis for their lethal toxicity. The first account of an experimental administration of extract of bitter almonds and other poisons to dogs (*Canis familiaris*) dates from 1679, as reviewed by Sykes (1981) and Ballantyne (1987a). In 1731, two fatal cases of human poisoning in Ireland were caused by drinking cherry laurel water, in this instance used as a flavoring agent in cooking and to dilute brandy. In that same year it was shown that cherry laurel water administered to dogs by various routes proved rapidly fatal. By 1781, it was well established that mammals, birds, reptiles, amphibians, fish, and insects could all be killed with small doses of laurel water, and that death was more rapid than that produced by other poisons tested. It was also at this time that cyanide was first implicated as a homicidal agent in England. In 1782, hydrocyanic acid was isolated from Prussian blue (a dye) by the Swedish chemist Scheele. In 1786, Scheele accidentally broke a vial of the material and died from vapor poisoning. In 1787, it was determined that hydrocyanic acid contained hydrogen, carbon, and nitrogen, but did not contain oxygen, formerly believed to be an essential component of all acids. Between 1802 and 1815, hydrocyanic acid was found to be lethal in small quantities to birds and dogs, and to act rapidly when given orally, intravenously, or applied to the eye surface. By 1803, it was known that cyanide occurred naturally and could be extracted from apricots or almonds. In 1815, hydrocyanic acid was prepared in a semipure form. Between 1817 and 1948, cyanide, in appropriate doses, was used therapeutically in England for the treatment of pulmonary diseases and tuberculosis, and as a sedative. By 1830, cyanogenic glycosides containing HCN were isolated from cassava; today, more than 800 species of cyanogenic plants have been identified. In 1876, it was first demonstrated that cyanide inhibited tissue oxidation. In 1894, cobalt compounds were suggested as antidotes due to their marked cyanide-binding capacity. Studies on cyanide detoxification conducted between 1877 and 1894 showed that thiosulphate administration caused the formation of thiocyanate--a relatively harmless metabolite. By the late 1800's, cyanide was regarded as a common plant metabolite rather than as an unusual poison. In 1929, it was conclusively demonstrated that cyanide combines with the trivalent iron atom in cytochrome oxidase, a respiratory enzyme that links the tricarboxylic acid cycle and formation of metabolic water. Many reviews have been published on cyanide in the environment; particularly useful are those by Doudoroff (1976), Towill et al. (1978), Smith et al. (1979), Egekeze and Oehme (1980), EPA (1980, 1989), Vennesland et al. (1981a), Leduc et al. (1982), Leduc (1984), Way (1984), Ballantyne and Marrs (1987a), and Evered and Harnett (1988).

Cyanide hazards to fish, wildlife, and livestock are well documented. Massive kills of freshwater fish by accidental discharges of cyanide wastes are fairly common (Holden and Marsden 1964; Leduc 1978; Towill et al. 1978; EPA 1980). In one case, cyanide-containing mine effluents from a Canadian tailings pond released into a nearby creek killed more than 20,000 steelhead (Oncor*hynchus mykis;* Leduc et al. 1982). Many species

of birds were found dead near burrows of the blacktailed prairie dog (*Cynomys ludovicianus*) after the burrows had been treated with calcium cyanide to control prairie dog populations; dead birds included the burrowing owl (*Athene cunicularia*), the bald eagle (*Haliaeetus leucocephalus*), and the golden eagle (*Aquila chrysaetos;* Wiemeyer et al. 1986). An endangered California condor (*Gymnogyps californianus*) found dead in Kern County, California, in November 1983 had particles of a yellow fluorescent tracer in its mouth; these particles were similar to those mixed with sodium cyanide in M-44 spring-loaded ejector mechanism devices used in a U.S. Fish and Wildlife Service Animal Damage Control Program in that vicinity, suggesting that cyanide was a possible cause of death (Krynitsky et al. 1986). M-44 devices are known to have caused the death of magpies (*Pica* sp.), ravens and crows *(Corvus* spp.), wild turkeys *(Meleagris gallopavo),* and various unidentified species of hawks and vultures (Wiemeyer et al. 1986). Between 1980 and 1989, 519 mammals--mostly rodents (35%) and bats (34%)--were found dead at cyanide-extraction, gold-mine leach ponds in California, Nevada, and Arizona; the list included coyote *(Canis latrans),* foxes, skunks, badger *(Taxidea taxus),* weasels, rabbits, deer, and beavers (Clark and Hothem 1991). Also found dead at these same leach ponds were 38 reptiles, 55 amphibians, and 6,997 birds (Clark and Hothem 1991), including many species of waterfowl and songbirds (Allen 1990). The influence of cyanide-extraction gold-mining operations on wildlife is currently under investigation by scientists at the Patuxent Wildlife Research Center.

The major threat of cyanide poisoning to livestock and terrestrial mammalian wildlife is through ingestion of plants containing high levels of cyanogenic glycosides (Towill et al. 1978; Marrs and Ballantyne 1987). Plants implicated in cyanide poisoning of animals include the sorghums (Johnson grass, *Sorghum halepense;* Sudan grass, *Sorghum sudanense*), arrowgrass (*Triglochin* spp.), elderberry (*Sambucus* spp.), wild cherry (*Prunus* spp.), and the pits of several common fruits, such as apple, peach, and apricot; these plants and fruit pits have the potential of releasing cyanide upon ingestion (Egekeze and Oehme 1980). Domestic goats (*Capra* spp.) died of cyanide poisoning after eating leaves and fruit of the crab apple *(Malus sylvestris);* the crab apple contains cyanogenic glycosides in its leaves and fruit (Shaw 1986). Cyanide poisoning of cattle (*Bos* spp.) by forage sorghums and various hybrid cultivars has been reported in India (Bapat and Abhyankar 1984) and elsewhere (Cade and Rubira 1982; Biehl 1984). Cattle appear to be more vulnerable to cyanide poisoning than are sheep (*Ovis aries*), horses (*Equus caballus*), and pigs (*Sus* spp.; Cade and Rubira 1982). *Equine sorghum cystitis ataxia* is a condition observed in horses grazing on Sorghum or hybrid Sudan grass pastures; it is characterized by urinary incontinence, posterior incoordination, and degenerative central nervous system lesions (Egekeze and Oehme 1980). Grazing cyanogenic plants can induce sulfur deficiency in sheep, presumably because sulfur detoxifies the released cyanide (Towill et al. 1978). The increasing use of cassava and other cyanogenic plants in animal feeding portends a greater exposure to dietary cyanides (Davis 1981).

This report briefly reviews the technical literature on ecological and toxicological aspects of cyanide, with emphasis on fishery and wildlife resources, and provides recommendations for the protection of sensitive species of concern to the U.S. Fish and Wildlife Service. This account is part of a continuing series of synoptic reviews prepared in response to informational requests from Service environmental specialists.

Chemical Properties

The chemical speciation of cyanides varies according to their source. Specific terms used to describe cyanide include free cyanide, cyanide ion, simple cyanides, complex cyanides, nitriles, cyanogens, and total cyanide. The most common forms of cyanide in the environment are free cyanide, metallocyanide complexes, and synthetic nitriles. A brief description of each cyanide species follows (Smith et al. 1978, 1979; Towill et al. 1978; Egekeze and Oehme 1980; EPA 1980, 1989; Davis 1981; Leduc 1981, 1984; Leduc et al. 1982; Simovic and Snodgrass 1985; Ballantyne 1987a; Homan 1987; Marrs and Ballantyne 1987).

Free cyanide is the primary toxic agent in the aquatic environment. Free cyanide refers to the sum of molecular HCN and the cyanide anion (CN^-), regardless of origin. In aqueous solution with pH 9.2 and lower, the majority of the free cyanide is in the form of molecular HCN. The chemical names for HCN include hydrogen cyanide, hydrocyanic acid, cyanohydric acid, and prussic acid. Hydrogen cyanide (Table 1) is a colorless, flammable liquid or gas that boils at 25.7° C and freezes at -13.2° C. The gas rarely occurs in nature, is lighter than air, and diffuses rapidly; it is usually prepared commercially from ammonia and methane at elevated temperatures with a platinum catalyst. It is miscible with water and alcohol, but is only slightly soluble in ether. In water, HCN is a weak acid with the ratio of HCN to CN^- about 100 at pH 7.2, 10 at pH 8.2, and 1 at

pH 9.2. HCN can dissociate into H and CN^-. Cyanide ion, or free cyanide ion, refers to the anion CN^- derived from hydrocyanic acid in solution, in equilibrium with simple or complexed cyanide molecules. Cyanide ions resemble halide ions in several ways and are sometimes referred to as "pseudohaline" ions. For example, silver cyanide is almost insoluble in water, as are silver halides. Cyanide ions also form stable complexes with many metals.

Simple cyanides typically refer to alkali water-soluble salts, such as NaCN, KCN, $Ca(CN)_2$, and $Hg(CN)_2$, but also include several cyanide salts of alkali, alkaline earth, or heavy metals, that is, $Zn(CN)_2$, $Cd(CN)_2$, $Ni(CN)_2$, and AgCN, of varying degrees of solubility. In water, NaCN and KCN will completely dissociate to give free cyanide. All simple cyanides ionize in water to release cyanide ion which, depending on pH, will form hydrocyanic acid. For sodium cyanide, the reaction proceeds as follows:

(1) $NaCN \quad Na^+ + CN^-$

(2) $CN^- + HOH \quad HCN + OH^-$

Increased pH will maintain a larger fraction of the cyanide as CN^-, and acidification will cause the reverse. At pH 7, about 99% of the free cyanide is in the form of HCN, whereas at pH 9.3 HCN composes 50%. Since HCN is extremely water soluble and is also one of the most toxic cyanide species, it is noteworthy that the toxicity of simple cyanides will not be affected measurably below pH 8.3. Acidification of dilute (milligrams per liter) cyanide solutions will not initiate any greater release of HCN, but acidification of concentrated (grams per liter) solutions promotes HCN formation and release.

Table 1. Some properties of potassium cyanide, hydrogen cyanide, and sodium cyanide (from EPA 1989).

Property	Potassium cyanide	Hydrogen cyanide	Sodium cyanide
CAS number	151-50-8	74-90-8	143-33-9
Chemical formula	KCN	HCN	NaCN
Molecular weight	65.12	27.03	49.01
Physical state	Solid	Gas or liquid	Solid
Boiling point (º C)	--	25.7	1,496
Melting point (º C)	634.5	–13.21	563.7
Specific gravity	1.5	0.7 (liquid)	1.6
Solubility in water (g/L)	716 at 20º C	Miscible	480 at 10º C

Complex cyanides are compounds in which the cyanide anion is incorporated into a complex or complexes; these compounds are different in chemical and toxicologic properties from simple cyanides. In solution, the stability of the cyanide complex varies with the type of cation and the complex that it forms. Some of these are dissociable in weak acids to give free cyanide and a cation, while other complexes require much stronger acidic conditions for dissociation. The least-stable complex metallocyanides include $Zn(CN)_4^{2-}$, $Cd(CN)_3^-$, and $Cd(CN)_4^{2-}$; moderately stable complexes include $Cu(CN)_2^-$, $Cu(CN)_3^{2-}$, $Ni(CN)_4^{2-}$, and $Ag(CN)^{2-}$; and the most stable complexes include $Fe(CN)_6^{4-}$and $Co(CN)_6^{4-}$**.** The toxicity of complex cyanides is usually related to their ability to release cyanide ions in solution, which then enter into an equilibrium with HCN; relatively small fluctuations in pH significantly affect their biocidal properties.

Cyanogen [$(CN)_2$] is the simplest compound containing the cyanide group. Cyanogen is an extremely toxic, flammable gas that reacts slowly with water to form HCN, cyanic acid, and other compounds; it is rapidly

degraded in the environment. Cyanogen and its halide derivations are comparable in toxicity to hydrogen cyanide.

Nitriles are defined as organic compounds (RCN) containing the cyanide group. Cyanide bound to carbon as nitriles (other than as cyanogenic glycosides) are comparatively innocuous in the environment, and are low in chemical reactivity and are biodegradable. For simple mononitriles there is a clear progression, with more cyanide being released as chain length increases. A similar pattern exists in dinitriles, but corresponding compounds require a longer carbon chain than mononitriles before free cyanide is produced. Based on studies with chicken liver homogenates (Davis 1981), mononitriles were more toxic than dinitriles, and within each group the order of toxicity was $CH_3 > C_2H_5 > C_3H_7 > C_4H_9 > C_5H_{11} > C_7H_{15}$. Cyanohydrins [$R_2C(OH)CN$] and cyanogenic glycosides [$R_1R_2C(OR_3)CN$] are special classes of nitriles, in that under appropriate conditions they will decompose to HCN and cyanide ions. Cyanogens (not to be confused with cyanogen), such as acrylonitrile, propionitrile, and succinonitrile, are nitrile-containing materials of varying complexity and lability, and can liberate free and toxicologically available amounts of cyanide. But the nonnitrile portion of the cyanogen molecule may exert an independent or interactive toxicity, causing a complex response.

Cyanates contain the OCN group. Inorganic cyanates that are formed industrially by the oxidation of cyanide salts hydrolyze in water to form ammonia and bicarbonate ion. Alkyl cyanates are insoluble in water and form cyanurates. Alkyl isocyanates contain the OCN radical, are formed from cyanates, and, like cyanates, are readily hydrolyzed. Thiocyanates (SCN group) are formed from cyanides and sulfur-containing materials and are relatively stable.

Total cyanides refers to all cyanide-containing compounds, including simple and complex cyanides, cyanoglycosides, and free cyanide. Total cyanides is a chemical measurement of free cyanide present in solution or released by acidification or digestion. Only free cyanide is considered to be a biologically meaningful expression of cyanide toxicity. Under most circumstances, the concentration of total cyanide will exceed that of HCN. In some waters, however, the total cyanide concentration may consist almost entirely of free cyanide, or it may contain cyanides that readily photodecompose or dissociate to yield HCN. The relation between total cyanide and free cyanide in natural waters varies with receiving-water conditions, type of cyanide compounds present, degree of exposure to daylight, and presence of other chemical compounds.

Hydrogen cyanide has frequently been associated with the odor of bitter almonds (Ballantyne 1983; Gee 1987). The threshold odor for olfactory detection of atmospheric HCN is 1 mg/L, but the odor may not be detected for various reasons, including the presence of other odors and the fact that only 20% to 40% of those tested could detect a cyanide odor.

Analytical methods for determining free and bound cyanide and cyanogenic compounds in biological materials are under revision. Current methods include chromatography; enzymic postcolumn cleavage; electrochemical detection; and ultraviolet, infrared, proton, and carbon-13 nuclear magnetic resonance spectroscopies (Brimer 1988). Proposed newer analytical methodologies include chemiluminescence (Wu et al. 1989); deproteinization techniques (Krynitsky et al. 1986); thin film dissociation coupled with preferential ultraviolet irradiation (Kelada 1989); differential pulse polarography (Westley 1988); and modified spectrophotometric (Blago 1989; Ohno 1989), colorometric (Lundquist and Sorbo 1989), and ion chromatographic determinations (Nonomura and Hobo 1989). Analysis of cyanide and cytochrome oxidase is usually conducted with samples of whole blood, serum, plasma, brain, or ventricular myocardium tissues. Samples should be obtained as soon as possible after cyanide exposure and analyzed immediately, otherwise erroneous analytical values will result (Towill et al. 1978; Ballantyne 1983). Brain and liver are recommended for cyanide analysis if removed and analyzed within a week (Ballantyne et al. 1974). Cyanide measurements are further confounded by the presence of various antidotal agents (Ballantyne 1983); by various tissue preservatives, such as formaldoxime (Knocke 1981) and sodium fluoride (Curry et al. 1967); and by the spontaneous postmortem production of cyanide in various tissues (e.g., sterile blood, brain, liver, kidney, uterus, intestines) over time in cases of noncyanide death (Curry et al. 1967; Ballantyne et al. 1974).

Mode of Action

Cyanide is a potent and rapid-acting asphyxiant. At lethal doses, inhalation or ingestion of cyanide produces reactions within seconds and death within minutes. Cyanide's toxic effect is due to its affinity for the ferric heme form of cytochrome a_3, also known as cytochrome c oxidase, the terminal oxidase of the mitochondrial respiratory chain (Towill et al. 1978; Egekeze and Oehme 1980; Solomonson 1981; Way 1981, 1984; Leduc et al. 1982; Biehl 1984; Ballantyne 1987a; Marrs and Ballantyne 1987; Yamamoto 1989). Inhibition of the enzyme cytochrome c oxidase is thought to involve a two-step reaction--initial penetration of cyanide into a protein crevice followed by binding to heme iron. Formation of a stable cytochrome c oxidase-CN complex in the mitochondria produces a blockage of electron transfer from cytochrome oxidase to molecular oxygen and cessation of cellular respiration, causing cytotoxic hypoxia in the presence of normal hemoglobin oxygenation. Tissue anoxia induced by the activation of cytochrome oxidase causes a shift from aerobic to anaerobic metabolism, resulting in the depletion of energy-rich compounds such as glycogen, phosphocreatine, and adenosine triphosphate, and the accumulation of lactate with decreased blood pH. The combination of cytotoxic hypoxia with lactate acidosis depresses the central nervous system--the most sensitive site of anoxia--resulting in respiratory arrest and death. If the absorption rate is significantly greater than the detoxification rate, there will be a rapid accumulation of free cyanide in tissues and body fluids, resulting in the prompt onset of signs of acute cyanide poisoning. Acute cyanide poisoning is frequently encountered as a relatively massive overdose, where the amount of cyanide greatly exceeds the minimal concentration necessary to inhibit cytochrome c oxidase. In such cases, many enzymes and biological systems are disrupted, including various metalloenzymes, nitrate reductase, nitrite reductase, myoglobin, various peroxidases, catalase, and ribulose diphosphate carboxylase, resulting in severe signs of toxicity and rapid death.

The great majority of the absorbed cyanide reacts with thiosulfate in the presence of enzymes to produce thiocyanate, which is excreted in the urine over a period of several days. Owing to this rapid detoxification, animals can ingest high sublethal doses of cyanide over extended periods without harm (Towill et al. 1978; Egekeze and Oehme 1980; EPA 1980; Davis 1981; Solomonson 1981; Leduc 1984; Ballantyne 1987a; Oh et al. 1987; Marrs and Ballantyne 1987; Westley 1988; Mengel et al. 1989). Authorities are also in general agreement on several points: thiosulfate is usually low in the body, and higher levels can significantly protect against cyanide toxicity; species vary considerably in both the extent to which thiocyanate is formed and the rate at which it is eliminated from the body; thiocyanate metabolites resulting from the transulfuration process are about 120 times less toxic than the parent cyanide compound; thiocyanate may accumulate in tissues and has been associated with developmental abnormalities and other adverse effects; the two enzyme systems responsible for the transulfuration process are thiosulfate-cyanide sulfurtransferase--also known as rhodanese--and beta-mercaptopyruvate cyanide sulfurtransferase. Rhodanese is widely distributed in the body, but activity levels in mammals are highest in the mitochondrial fraction of liver. Rhodanese activity levels in catalyzing the transformation of thiosulfate to thiocyanate are limited by the availability of sulfur.

Minor detoxification pathways for cyanide include exhalation in breath as HCN and as $C0_2$ from oxidative metabolism of formic acid; conjugation with cystine to form 2-iminothiazolidene- 4-carboxylic acid or 2-aminothiazoline-4-carboxylic acid; combining with hydroxocobalamin (B_{12}) to form cyanocobalamin, which is excreted in urine and bile; and binding by methemoglobin in the blood (Towill et al. 1978; EPA 1980; Ballantyne 1987a; Marrs and Ballantyne 1987).

Absorption of hydrogen cyanide liquid or gas readily occurs through inhalation, ingestion, or skin contact (Towill et al. 1978; Egekeze and Oehme 1980; EPA 1980; Homan 1987). Inhalation and skin absorption are the primary hazardous routes in cyanide toxicity in occupational exposure. Skin absorption is most rapid when the skin is cut, abraded, or moist. Inhalation of cyanide salts is also potentially hazardous because the cyanide dissolves on contact with moist mucous membranes. Regardless of route of exposure, cyanide is readily absorbed into the bloodstream and distributed throughout the body. Cyanide concentrates in erythrocytes through binding to methemoglobin (Towill et al. 1978; EPA 1980), and free cyanide concentrations in plasma are now considered one of the better indicators of cytotoxicity (Ballantyne 1987a). Because of the affinity of cyanide for the mammalian erythrocyte, the spleen may contain elevated cyanide concentrations when compared to blood; accordingly, spleen should always be taken for analysis in cases of suspected cyanide poisoning (Ballantyne 1975). Cyanide also accumulates in various body cells through binding to metalloproteins or enzymes such as catalase and cytochrome c oxidase (EPA 1980). The brain is probably the major target organ

of cytotoxic hypoxia, and brain cytochrome oxidase may be the most active site of lethal cyanide action, as judged by distribution of cyanide, thiosulfate, and rhodanese (Solomonson 1981; Ballantyne 1987a). Significant positive correlations exist between cyanide concentrations in plasma, cerebrospinal fluid, and brain (Ballantyne 1987a); these correlations need further exploration.

Hydrogen cyanide formation may contribute to the toxicity of snake venom, owing to the high levels of L-amino acid oxidase in some snake venoms (Vennesland et al. 1981b). This enzyme is harmless on injection, but the tissue destruction caused by other venom components probably provides the required substrate and cofactor for HCN production.

Cyanide inhibits ion transport mechanisms in amphibian skin, gall bladder, and proximal renal tubules (Bello-Reuss et al. 1981). Measurable changes in cell membrane potentials of isolated gall bladder epithelium cells, for example, were induced by NaCN in a salamander (Bello-Reuss et al. 1981). Cyanide-induced hyperpolarization was caused primarily by an increase in permeability of the cell membrane to potassium, which, in turn, was mediated by an elevation of intracellular calcium ion activity, attributable to release from mitochondrial sources.

The binding rate of CN to hemeproteins, specifically hemoglobin components Ill and IV, is 370 times to 2,300 times slower in a marine polychaete annelid (*Glycera dibranchiata*), when compared to guinea pig (*Cavia* spp.), soybean (*Glycine* max), and sperm whale (*Physeter macrocephalus*); the significance of this observation is unclear but warrants further exploration (Mintorovitch et al. 1989).

Clinical Features

Accidental exposure to cyanides or cyanogens through inhalation, skin exposure, and swallowing occurs in agricultural fumigation, laboratories, industrial operations, domestic abuse, and products of combustion (Ballantyne and Marrs 1987b). Intentional exposure is reported from homicides, suicides (usually uncommon), judicial executions, chemical warfare, and covert activities (Ballantyne and Marrs 1987b).

Diagnosis of lethal cyanide poisoning is difficult because of the absence of gross pathology or histology, nonspecific congestion of viscera, and cerebral or pulmonary edema. Sometimes the blood is bright red, and sometimes the odor of bitter almonds is detected, but neither is sufficiently consistent for diagnostic purposes (Ballantyne and Marrs 1987b).

At low lethal doses of cyanide, the effects are principally on cytochrome oxidase in the central nervous system. At higher doses, cardiovascular signs and changes in electrical activity of the brain are among the most consistent changes measured (Way 1981, 1984). Acute and subacute toxic effects of poisoning with cyanide can vary from convulsions, screaming, vomiting, and bloody frothing to less dramatic events, such as a slow, quiet onset to coma and subsequent death (Way 1981). In the first stage of cyanide poisoning, victims exhibit headache, vertigo, weak and rapid pulse, nausea, and vomiting. In the second stage, there are convulsions, falling, dilated pupils, clammy skin, and a weaker and more rapid pulse. In the final stage, heartbeat becomes irregular and slow; body temperature falls; there is cyanosis of lips, face, and extremities, coma, frothy bloody saliva flow from mouth, and death (Way 1981). If acute exposure is to a sublethal dose of cyanide, this may lead to signs of toxicity, but as detoxification proceeds these signs will become less obvious and eventually vanish, and cyanide will be excreted as thiocyanate without accumulating (Ballantyne 1987a).

Chronic cyanide poisoning may develop in individuals who ingest significant quantities of cyanide or cyanide precursors in their diets; effects are exacerbated by dietary deficiencies in vitamin B_{12}, iodine, and sulfur amino acids, as well as by low levels and insufficient distribution of detoxifying enzymes such as rhodanese (Solomonson 1981). Cyanide toxicity of dietary origin has been implicated in acute animal deaths and as a major etiologic factor in toxic ataxic neuropathy in humans, and as a cause of blindness in humans suffering from tobacco amblyopia and Leber's hereditary optic atrophy (Egekeze and Oehme 1980). An increase in blood plasma cyanide is observed in healthy individuals who smoke cigarettes (Cailleux et al. 1988). An increase in blood plasma thiocyanate is also seen in smokers and in hemodialysis patients just before dialysis (Cailleux et al. 1988). Continuous intake of cyanide causes high levels of plasma thiocyanate and goiters in mammals; the antithyroid action (goiters) results from cyanide interference with iodine transport and thyroxine synthesis (Solomonson 1981; Leduc 1981, 1984). Signs of chronic cyanide poisoning include demyelination, lesions of the optic nerve, decrease in sulfur-containing amino acids, increase in thiocyanate, goiter, ataxia, hypertonia,

and depressed thyroid function (Solomonson 1981). These effects are common in areas that depend on cyanogenic plants--such as cassava--as a major dietary component (Solomonson 1981).

Biochemically, cyanide affects the citric acid cycle; strongly inhibits catalases and proteinases; induces glycolysis in protozoans, fish, and mammals; produces vitamin B_{12} deficiency; and modifies the phosphorylation mechanism of respiratory mitochondrial enzymes, causing arrested respiration due to inability to use oxygen (Leduc 1984).

Cyanide biomagnification or cycling has not been reported, probably because of cyanide's high chemical reactivity and rapid biotransformation (Towill et al. 1978; Marrs and Ballantyne 1987).

There is no evidence that chronic exposure to cyanide results in teratogenic, mutagenic, or carcinogenic effects (EPA 1980). Cyanide possibly has antineoplastic activity, as judged by a low therapeutic success against rat sarcomas (EPA 1980), but this requires additional documentation.

Confirmatory evidence of cyanide poisoning includes elevated blood thiocyanate levels--except, perhaps, when death was rapid--and reduced cytochrome oxidase activity in brain and myocardium, provided that all tissues were taken within a day or so of death, frozen quickly, and analyzed shortly thereafter (Biehl 1984; Marrs and Ballantyne 1987). Evaluation of cyanide poisoning and metabolism includes signs of toxicity, LD50 values, measurement of cyanide and thiocyanate concentrations, cytochrome c oxidase activity, metabolic modification of in vivo cyanogenesis, rate of cyanide liberation in vitro, and influence of modifying factors such as the animal species, dose, rate and frequency of administration, route of exposure, differential distribution of cyanide, detoxification rates, circadian rhythm interactions, age of the organism, and presence of antidotes (Ballantyne 1987a). For example, the concentration of cyanide measured in body fluids and tissues in humans and other animals following lethal administration of cyanide depends on several factors: route of exposure, with oral route yielding highest residues and inhalation route the lowest; amount and duration of exposure; nature of the material, with HCN and CN^- being most toxic; time to death; antidotes used; time to autopsy, with marked loss documented from simple evaporation, thiocyanate formation, hydrolysis, and polymerization; and time from autopsy to sample analysis, wherein cyanide concentrations may increase due to microbial action (Ballantyne and Marrs 1987b).

Antidotes

The antagonism of cyanide intoxication has been under investigation for at least 150 years. In 1840, cyanide lethality was reported to be antagonized by artificial respiration. In 1888, amyl nitrite was reported effective in antagonizing lethal effects of cyanide in dogs. In 1894, cobalt was shown to form a stable metal complex with cyanide and was used to antagonize cyanide. In 1933, the use of sodium thiosulfate as the sulfur donor was described (Way 1984). Many compounds are used today as cyanide antidotes including cobalt salts, rhodanese, sulfur donors, methemoglobin producers, carbohydrates, drugs used to treat acidosis, oxygen, methylene blue, 4-dimethylaminophenol, various aromatic amino- and nitro-compounds (such as aniline, p-aminopropiophenone, nitrobenzene), carbonyl compounds, and sodium pyruvate (Egekeze and Oehme 1980; EPA 1980; Solomonson 1981; Way 1981, 1984; Biehl 1984; Becker 1985; Ballantyne 1987b; Marrs 1987; Marrs and Ballantyne 1987; Way et al. 1988). Different antidotes are preferred in different countries: in the United States, a mixture of sodium nitrite and sodium thiosulfate; in France and the United Kingdom, cobalt edetate, also known as Kelocyanor; and in Germany, a mixture of 4-dimethylaminophenol and sodium thiosulfate.

The classic nitrite-thiosulfate treatment of cyanide poisoning, developed almost 60 years ago, is one of the antidotal combinations still employed (Way 1981). Excess oxygen improves this antidotal combination by potentiating the effectiveness of the nitrite-thiosulfate combination, as confirmed by studies in sheep and rats (Way 1984), even though, theoretically, oxygen should serve no useful purpose (Way et al. 1988). This therapeutic regimen protected rats against 20 LD50 doses of cyanide (Towill et al. 1978). Nitrite converts hemoglobin to methemoglobin, which has a high affinity for cyanide. The methemoglobin-HCN complex then slowly releases cyanide, which is converted to thiocyanate by way of rhodanese (Solomonson 1981). Sodium nitrite, administered intravenously, is now considered one of the more rapid therapeutic methods (Way 1984). The injection of sodium thiosulfate provides sulfur for the enzyme rhodanese to mediate the biotransformation of cyanide to the much less toxic thiocyanate (Egekeze and Oehme 1980). Multiple injections of sodium thiosulfate protected mice against death by organic cyanides and were more effective than sodium nitrite

(Willhite and Smith 1981). The nitrite-thiosulfate antidotal combination is one of the most effective treatments of cyanide poisoning, even though the specific mechanism of action of these two compounds is now being questioned, and concerns have been raised because of the toxicity of nitrite (Way 1981, 1984). One accepted therapy is an intravenous combination of sodium nitrite (1 mL of 20% solution) and sodium thiosulfate (3 mL of 20% solution), giving 4 mL of this mixture per 45 kg of body weight (Egekeze and Oehme 1980). For maximal effectiveness in treating cyanide intoxication in sheep, large doses of sodium thiosulfate (660 mg/kg BW) are given in combination with conventional doses of sodium nitrite (6.6 mg/kg BW; Egekeze and Oehme 1980). Livestock treatment in cases of suspected cyanide intoxication consists of intravenous administration of sodium nitrite at 10-20 mg/kg BW followed by sodium thiosulfate at 30-40 mg/kg BW; however, a sodium thiosulfate dose of 500 mg/kg BW, or more, may be more efficacious (Biehl 1984). Once clinical signs have abated, 1 g of activated charcoal per kilogram BW may be administered as a drench by way of a stomach tube (Biehl 1984). A 30-kg female goat *(Capra* sp.) was successfully treated after eating the leaves and fruit of the crab apple *(Malus sylvestris),* a plant that contains high levels of cyanogenic glycosides in leaves and fruits (Shaw 1986). Treatment consisted of four hourly treatments of 100 g of animal charcoal and bismuth subnitrate in water as a drench, followed by 300 mg sodium nitrite as a 1% aqueous solution, then 25 g of sodium thiosulfate. Another goat died despite identical treatment (Shaw 1986).

Cobalt compounds, such as hydroxocobalamin and its derivatives (i.e., cobalt histidine, cobalt chloride, dicobalt ethylenediamine tetracetic acid) have been used to treat cyanide poisoning for more than 100 years. Their efficacy was confirmed in pigeons (*Columba* sp.) and rabbits (*Oryctolagus sp*.), but cobalt compounds did not receive wide support as cyanide antagonists because of the inherent toxicity of cobalt ion (Way 1981, 1984). Nevertheless, proponents of the use of cobalt compounds (i.e., the United Kingdom, Scandinavia, much of Europe) stress the rapidity of action in forming a stable metal complex with cyanide, thereby preventing its toxic effect (Towill et al. 1978; Way 1984). One of the more frequently used cobalt compounds in cyanide treatment is hydroxocobalamin, which reverses cyanide toxicity by combining with cyanide to form cyanocobalamin (EPA 1980; Solomonson 1981). Hydroxocobalamin has been used in guinea pigs and baboons *(Papio anubis)* to lower blood cyanide levels, and in humans after inhalation or ingestion of cyanide compounds (Egekeze and Oehme 1980).

Dimethylaminophenol (DMAP) forms methemoglobin by setting up a catalytic cycle inside the erythrocyte, in which oxygen oxidizes the DMAP to N-N-dimethylquinoneimine, the latter oxidizing the hemoglobin to methemoglobin (Marrs 1987). Dogs poisoned with KCN and given DMAP intravenously had restored respiration and decreased plasma cyanide levels. The 4-dimethylamino-phenol induced ferrihemoglobin production, which combined with the cyanide in the red cells to form ferrihemoglobin cyanide (Christel et al. 1977).

No usable cyanide prophylactic therapy now exists for humans, although sodium thiosulfate, hydroxocobalamin, and other compounds have been used to protect against cyanide toxicity in laboratory animals (Mengel et al. 1989). For example, pyridoxal 5-phosphate, the active form of vitamin B_6, readily forms complexes with cyanides, and was effective in providing significant protection to rats (Keniston et al. 1987). Fructose fed prior to insult lessens cyanide-induced hepatotoxicity in rats (Younes and Strubelt 1988). L-ascorbic acid and dehydroascorbic acid probably act as protectants against cyanide toxicity by way of nontoxic cyanohydrin formation (Sprince et al. 1982). Carbon tetrachloride pretreatment was effective in protecting mice against death from most nitriles (Willhite and Smith 1981), and pretreatment with p-aminopropiophenone serves to protect against cyanide toxicity (D'Mello 1987).

Sources and Uses

Production of cyanides in the United States increased from about 136 million kg in 1963 to 318 million kg in 1976 (Towill et al. 1978; Way 1981; Marrs and Ballantyne 1987). Cyanide consumption in North America was 64 million kg in 1988 and 98 million kg in 1989; about 80% of these amounts was used in gold mining (Knudson 1990).

About 84% of domestic HCN production is used to produce organic cyanides, also known as nitriles, including acrylonitriles, methyl methacrylate, and adiponitrile (Towill et al. 1978). Nitriles tend to polymerize, which is the basis for their use in the manufacture of synthetic fibers, resins, plastics, dyestuffs, vitamins, solvents, elastomers, agricultural insecticides, and high pressure lubricants (Willhite and Smith 1981). The widespread usefulness of HCN is related to its strong tendency and that of its inorganic salts to form complexes

with metals. For example, sodium cyanide is used in metallurgy for the extraction of gold and silver from ores and in electroplating baths because it forms stable soluble complexes. Similar behavior makes alkali cyanide solutions excellent for cleaning silverware and other precious metals and is responsible for their general use in industry as metal cleaners (Towill et al. 1978). In Canada, more than 90% of the gold mined is extracted from ores with the cyanidation process. This process consists of leaching gold from the ore as a gold-cyanide complex, and gold being precipitated with the addition of zinc dust. A variety of cyanide compounds are produced during gold cyanidation (Simovic and Snodgrass 1985). In addition to their primary use in the metals and electroplating industries, and in the manufacture of synthetic fibers and plastics, various cyanide compounds have been used directly or as an intermediate to produce synthetic rubber, fumigants, rodenticides, insecticides, predator control agents, rocket fuels, paints and paint finishes, paper, nylon, pharmaceuticals, photographic chemicals, mirrors, cement, perfume, bleaches, soaps and detergents, riot control agents, fertilizers, and herbicides (Towill et al. 1978; Way 1981; Willhite and Smith 1981; Leduc 1984; Homan 1987).

Hydrogen cyanide vapor, because of its high and rapid acute lethal toxicity and ready diffusion, has been used widely to fumigate buildings, ships, and warehouses; to exterminate rabbits, rodents, and large predators; and in horticultural practice, to control insect pests that have developed resistance to other pesticides (Homan 1987; Ballantyne 1988). Typically, fumigation powders containing either calcium cyanide, $Ca(CN)_2$, or sodium cyanide, NaCN, are blown into burrows or scattered over the floor in greenhouses. On coming into contact with water, such powders liberate HCN vapor (Ballantyne 1988). Hydrogen cyanide released from $Ca(CN)_2$ is registered for use on almonds, dried beans, citrus, cocoa beans, grains, nuts, and spices (Towill et al. 1978). Cyanide-containing compounds are used for a variety of agricultural and pesticidal agents. These compounds include cyanogen (NCCN), as an intermediate in the production of some commercial fertilizers; cyanogen chloride (CNCl), in the manufacture of triazine herbicides; cyanogen bromide (CNBr), as a pesticidal fumigant; hydrogen cyanide, in the synthesis of methionine for animal feeds; ammonium thiocyanate (NH_4SCN), as a cotton defoliant; sodium thiocyanate (NaSCN), as a weedkiller; and calcium cyanamide (CaNCN), as a plant fertilizer, herbicide, pesticide, and defoliant of cotton and tomatoes (Homan 1987). Cyanide compounds have also been used as preservatives for raw vegetables (Towill et al. 1978).

Sodium cyanide has been used for about 50 years by the U.S. Fish and Wildlife Service against coyote in attempts to protect livestock, especially sheep. The Service has made extensive use of two NaCN ejector devices: "the coyote getter," from the late 1930's to 1970; and the M-44, from about 1968 to the present, except for the period 1972-74, when all uses of NaCN for predator control were canceled (EPA 1976a; Connolly and Simmons 1984). Although both ejectors dispense toxicant when pulled, they differ in the way ejection is achieved. In the coyote getter, the toxicant is in a 0.38-caliber cartridge case and is expelled by the explosive force of the primer plus a small powder charge. The M-44 uses a spring-driven plunger to push out its toxic contents. M-44 capsules weigh about 0.94 g, and consist of about 89% NaCN, 6% Celatom MP-78 (mostly diatomaceous silica), 5% potassium chloride, and 0.25% FP Tracerite yellow--used as a fluorescent marker (Connolly and Simmons 1984). Coyote getters and M-44's are set into the ground with only their tops protruding. Fetid scent or lure stimulates a coyote to bite and pull, whereupon a lethal dose of NaCN is ejected into its mouth; coma and death follow in 30 to 60 s. Although coyote getters were about 99% effective against coyotes, compared with 73% for M-44's, the Service decided that spring-driven plungers were less hazardous to operators than were explosive-driven plungers (Connolly and Simmons 1984). The coyote getter was generally much more selective than the trap for the capture of coyotes. It was less destructive than traps to small mammals, birds of prey, ground-nesting birds, deer, antelope, and domestic sheep, but more destructive to dogs, bears, and cattle (Robinson 1943). In a 1-year test period (1940-41) in Colorado, Wyoming, and New Mexico, the following numbers of animals were killed by the coyote getter: 1,107 coyotes, 2 bobcats (*Lynx rufus*), 24 dogs, 14 black-billed magpies (*Pica pica*), 7 foxes (*Vulpes* sp.), 8 unidentified skunks, 2 badgers, 2 unidentified eagles, 2 bears (*Ursus* sp.), and 1 each of hawk (unidentified), pika (*Ochotona* sp.), and cow (Robinson 1943).

Cyanide compounds have been used to collect various species of freshwater fish. In England and Scotland, cyanides are used legally to control rabbits, and illegally to obtain Atlantic salmon (*Salmo salar*) and brown trout (*Salmo trutta*) from rivers, leaving no visible evidence of damage to the fish (Holden and Marsden 1964). Sodium cyanide has been applied to streams in Wyoming and Utah to collect fish through anesthesia; mountain whitefish (*Prosopium williamsoni*) were sensitive to cyanide and died at concentrations that were tolerable to salmon and trout (Wiley 1984). Sodium cyanide was also used as a fish control agent in Illinois, Nebraska,

South Dakota, Missouri, and in the lower Mississippi River valley, but was never registered for this use because of human safety concerns (Lennon et al. 1970).

Cyanide compounds have been prescribed by physicians for treatment of hypertension and cancer (Sprince et al. 1982). Sodium nitroprusside ($Na_2Fe(CN)_5NO\text{-}2H_2O$) was widely used for more than 30 years to treat severe hypertension and to minimize bleeding during surgery (Solomonson 1981; Vesey 1987). Laetrile, an extract of ground apricot kernels, has been used for cancer chemotherapy and, in deliberate high intakes, as an attempted suicide vehicle (Gee 1987).

Road salt in some areas may contribute to elevated cyanide levels in adjacent surface waters (Ohno 1989). In climates with significant snowfall, road salt is applied as a deicing agent. Road salts are commonly treated with anticaking agents to ensure uniform spreading. One anticaking agent, sodium hexacyanoferrate, decomposes in sunlight to yield the highly toxic free cyanide that contaminates surface waters by runoff (Ohno 1989). Another anticaking agent, yellow prussiate of soda (sodium ferrocyanide), has been implicated in fish kills when inadvertently used by fish culturists (Barney 1989).

The military uses of HCN were first realized by Napoleon III, but it was not until World War I (WW I) that this application received widespread consideration. About 3.6 million kg of hydrogen cyanide were manufactured by France as a chemical weapon and used in WWI in various mixtures called Manganite and Bincennite, although its use was not highly successful because of limitations in projectile size and other factors. During WW II, the Japanese were armed with 50-kg HCN bombs, and the United States had 500-kg bombs. More than 500,000 kg of HCN chemical weapons were produced during WWII by Japan, the United States, and the Soviet Union, but it is not known to what extent these weapons were used in that conflict (Way 1981).

Cyanides are widely distributed among common plants in the form of cyanogenic glycosides (Egekeze and Oehme 1980; Solomonson 1981; Way 1981; Biehl 1984; Homan 1987; Marrs and Ballantyne 1987). Their toxicity following ingestion is primarily related to the hydrolytic release of HCN. Ingestion of cyanogenic plants probably has accounted for most instances of cyanide exposure and toxicosis in man and range animals. Of chief agricultural importance among plants that accumulate large quantities of cyanogenic glycosides are the sorghums, Johnson grass, Sudan grass, corn, lima beans, flax, pits of stone fruits (cherry, apricot, peach), vetch, linseed, sweet potatoes, bamboo shoots, southern mock orange, millet, almonds, and cassava. Factors favoring cyanide build-up in cyanogenic plants include high nitrogen and low phosphorus in soils (Biehl 1984); the potential for high glycoside levels is greatest in immature and rapidly growing plants (Egekeze and Oehme 1980). At present, more than 28 different cyanoglycosides have been measured in about 1,000 species of higher plants (Leduc 1984). In cassava, for example, more than 90% of the cyanide is present as linamurin, a cyanogenic glycoside, and the remainder occurs as free (nonglycoside) cyanide (Gomez et al. 1983). Laetrile, a preparation made from apricot kernels, contains high levels of amygdalin, a cyanogenic glycoside that can be degraded in the gut to cyanide and benzaldehyde. Several cases of cyanide poisoning in humans have been reported from intake of laetrile, either orally or anally (Solomonson 1981; Homan 1987). Cyanide formation in higher plants and microorganisms can also occur with compounds other than cyanogenic glycosides, such as glycine, glyoxylate plus hydroxylamine, or histidine (Solomonson 1981; Vennesland et al. 1981b). In some cases, plants may contain cyanide residues resulting from fumigation with HCN (Way 1981).

Many species of plants, including some fungi, bacteria, algae, and higher plants, produce cyanide as a metabolic product (Leduc et al. 1982; Leduc 1984). Some species of soil bacteria suppress plant diseases caused by soilborne pathogens by producing metabolites with antibiotic activity. Certain strains of *Pseudomonas fluorescens,* a soil bacterium, suppress black root rot of tobacco caused by the fungus *Thielaviopsis basicola* by excreting several metabolites, including HCN (Voisard et al. 1989). A wide variety of bacteria and fungi can degrade cyanide compounds, and may be useful in the treatment of cyanide wastes (Towill et al. 1978). For example, several species of fungi known to be pathogens of cyanogenic plants can degrade cyanide by hydration to formamide; dried mycelia of these species are now sold commercially to detoxify cyanide in industrial wastes (Knowles 1988).

Anthropogenic sources of cyanide in the environment include industrial processes, laboratories, fumigation operations, cyanogenic drugs, fires, cigarette smoking, and chemical warfare operations (Marrs and Ballantyne 1987). Cyanides are present in many industrial wastewaters, especially those of electroplaters; manufacturers of paint, aluminum, and plastics; metal finishers; metallurgists; coal gasification processes; certain mine

operations; and petroleum refiners (Towill et al. 1978; Egekeze and Oehme 1980; Way 1981, 1984). Electroplaters are a major source. In the United States alone, electroplaters discharge about 9.7 million kg of cyanide wastes annually into the environment from 2,600 electroplating plants (Marrs and Ballantyne 1987). Paint residues annually contribute an additional 141,300 kg of cyanide wastes into the environment, and paint sludges 20,400 kg (Way 1981; Marrs and Ballantyne 1987). Cyanide can also originate from natural processes, such as cyanide production by bacteria, algae, and fungi, and from many terrestrial plants that release free HCN when their cellular structure is disrupted (Leduc 1981). Hospital wastewaters usually contain no detectable cyanide, but concentrations up to 64 µg CN^-/L have been measured after alkali chlorination treatment (Tatsumoto and Hattori 1988). It seems that various compounds common in hospital wastewaters will produce 15-25 µg CN^-/L after alkali chlorination; these compounds include hydantoin (an antiepilepsy agent) and related nitrogenous compounds, such as hydantonic acid, 5,5-diphenyl hydantoin, imidazole, and 2-imidazolidinone (Tatsumoto and Hattori 1988).

Free hydrogen cyanide occurs only rarely in nature because of its high reactivity. The gas is sometimes found in the atmosphere, however, as a result of emissions from the petrochemical industry, malfunctioning catalytic converters on automobiles, fumigation of ships and warehouses, incomplete combustion of nitrogen-containing materials, and from tobacco smoke (Towill et al. 1978; Way 1981, 1984). Hydrogen cyanide is known to be produced in fires involving nitrogen-containing polymers and is probably the most important narcotic fire product other than carbon monoxide (Purser et al. 1984). Cyanide-related fire deaths and injuries, as judged by elevated blood cyanide and thiocyanate concentrations, have been documented in airplanes, jails, and high-rises (Becker 1985; Ballantyne 1987b; Lundquist and Sorbo 1989). In a study of fire victims in Scotland, elevated blood cyanide levels were found in 78% of fatalities, and 31% had blood levels considered to be toxic (Purser et al. 1984). Major factors that influence HCN release include the chemical nature of the material, temperature, oxygen availability, and burning time (Ballantyne 1987b). Substantial quantities of free HCN and organic cyanides are known to be produced in fire settings involving horsehair, tobacco, wool, silk, and many synthetic polymers, such as polyurethane and polyacrylonitriles (Egekeze and Oehme 1980; Purser et al. 1984; Becker 1985; Ballantyne 1987b). Polyacrylonitrile, for example, is used in fabrics, upholstery covers, paddings, and clothing; about 50% of the mass of the polymer is theoretically available as HCN under thermal decomposition (Purser et al. 1984; Homan 1987).

Background Concentrations

The reactivity of HCN, and its ability to condense with itself and other compounds, was probably responsible for the prebiotic formation of the majority of biochemical compounds required for life (Marrs and Ballantyne 1987). Cyanide is now known to be present in a number of foodstuff and forage plants, as a metabolite of certain drugs, and in various industrial pollutants; it also may be formed by the combustion of cyanide-releasing substances, such as plastics in airplane fires and tobacco in smoking (Robinson et al. 1985). Hydrogen cyanide production may occur in hepatopancreas of mussels, *Mytilus edulis* (Vennesland et al. 1981b), in rat liver (Solomonson 1981), and in green and blue-green algae during nitrate metabolism (Leduc et al. 1982). Except for certain naturally occurring organic cyanide compounds in plants, it is uncommon to find cyanide in foods consumed in the United States (EPA 1980).

The cyanide anion is found in a variety of naturally occurring plant compounds as cyanogenic glycosides, glycosides, lathyrogenic compounds, indoleacetonitrile, and cyanopyridine alkaloids. Plants that contain cyanogenic glycosides are potentially poisonous because bruising or incomplete cooking can result in glycoside hydrolysis and release of HCN (Towill et al. 1978). Cyanide concentrations in cyanogenic plants are usually highest in leaves of young plants; levels drop rapidly after pollination (Biehl 1984). There are about 20 major cyanogenic glycosides, of which usually only one or two occur in any plant. They are synthesized from amino acids and sugars and are found in many economically important plants, such as sorghum, flax, lima bean, cassava, and many of the stone fruits (Table 2; Towill et al. 1978; Shaw 1986). Cassava contains linamurin and lotaustralin, whereas the main cyanogenic glycoside in cereals is dhurrin; consumption of foods containing toxic cyanogens (primarily cassava) has been associated with death or morbidity--on an acute basis--or goiter and tropical ataxic neuropathy on a chronic consumption basis (Okolie and Ugochukwu 1989). Cassava is a perennial shrub, native to the neotropics, grown for its tuberous starchy roots, and a traditional dietary staple of many indigenous populations in Amazonia, especially the Tukanoan Indians in northwestern Amazonia (Dufour 1988). Cassava is one of the few food plants in which the cyanide content may create toxic problems. All

varieties of cassava contain cyanogenic glycosides capable of liberating HCN, but amounts vary greatly depending on variety and environmental conditions. Bitter cultivars of cassava provide over 70% of the Tukanoan's food energy, appearing in the diet as bread, meal, a starch drink, and boiled cassava juice. The greatly elevated total cyanide content in bitter varieties (Table 2) may contain 5.1-13.4% of the total as the toxic free cyanide (Dufour 1988).

The production of HCN by animals is almost exclusively restricted to various arthropods: 7 of about 3,000 species of centipedes; 46 of 2,500 species of polydesmid millipedes; and 10 of 750,000 species of insects, including 3 species of beetles, 4 moths, and 3 butterflies (Duffey 1981). Millipedes--which are eaten frequently by toads and starlings--secrete cyanide for defensive purposes in repelling predators; in zygaenid moths, cyanide seems to be localized in eggs (Table 2; Duffey 1981).

Cyanide concentrations in fish from streams that were deliberately poisoned with cyanide ranged between 10 and 100 µg total cyanide per kilogram whole body fresh weight (FW; Wiley 1984). Total cyanide concentrations in gill tissues of salmonids under widely varying conditions of temperature, nominal water concentrations, and duration of exposure ranged from about 30 µg/kg FW to >7,000 µg/kg (Holden and Marsden 1964). Unpoisoned fish usually contained < 1 µg/kg FW in gills, although values up to 50 µg/kg occurred occasionally. Lowest cyanide concentrations in gills occurred at elevated (summer) water temperatures; at lower temperatures, survival was greater and residues were higher (Holden and Marsden 1964). Fish retrieved from cyanide-poisoned environments, dead or alive, can probably be consumed by humans because muscle cyanide residues were considered to be low (i.e., <1,000 mg/kg FW; Leduc 1984).

Cyanide pollution is likely to occur in many places, ranging from industrialized urban areas to gold mines in the western United States and Northwest Territories of Canada (Table 2). Cyanides are ubiquitous in industrial effluents, and their increasing generation from power plants and from the combustion of solid wastes is expected to result in elevated cyanide levels in air and water (Leduc 1984). However, data are scarce on background concentrations of cyanides in various nonbiological materials. In soils, for example, high concentrations are unusual and are nearly always the result of improper waste disposal (Towill et al. 1978). Cyanides in soils are not absorbed or retained; under aerobic conditions, microbial metabolism rapidly degrades cyanides to carbon dioxide and ammonia; under anaerobic conditions, cyanides are converted by bacteria to gaseous nitrogen compounds that escape to the atmosphere (Towill et al. 1978). Heat treatment wastes from metal processing operations may contain up to 200 g CN/kg, mostly as NaCN, and are frequently hauled to landfills for disposal (Lagas et al. 1982). The presence of cyanide in landfill waste is potentially hazardous because of the possibility that cyanide may leach to soil and groundwater, release HCN, and disturb natural microbiological degradation of organic materials. Measurements at landfills in England and the Netherlands showed total cyanide levels up to 560 g/kg in soil and 12 µg/L in groundwater (Lagas et al. 1982). However, 7-month-long experimental studies of cyanide in heat treatment wastes in landfills showed that between 72 and 82% of the cyanide was converted, mostly to ammonium and organic nitrogen compounds; between 4 and 22% of the cyanide leached as free or complex cyanide; and up to 11% remained in the landfill (Lagas et al. 1982).

Table 2. Background concentrations of cyanide in selected living resources and nonbiological materials. Values are in milligrams total cyanide per kilogram fresh weight or milligrams per liter.

Environmental compartment	Concentration[a] (mg/kg or mg/L)	Reference[b]
Biological		
Cyanogenic plants		
Bamboo (*Bambusa, Arundinaria, Dendrocalamus*)		
Tip	Max. 8,000	1
Stem	Max. 3,000	1
Stargrass, *Cynodon plectostachyus*, whole	180	1
Rose family, *Malus* spp., *Pyrus* spp.	Max. 200	2
Cassava, *Manihot esculenta*		
Bitter varieties		
Leaves	347–1,000	3, 4

Roots	327–550	1, 4
Dried roots	95–2,450	1, 3, 4
Stem	1,130	1
Mash	162	5
Bark		
Total cyanide	1,351	6
Free cyanide	102	6
Peel		
Total cyanide	1,390	6
Free cyanide	255	6
Pulp		
Total cyanide	810	6
Free cyanide	53	6
Sweet varieties		
Leaves	377–500	3, 4
Roots	138	4
Dried roots	46–<100	3, 4
Mash	81	5
Lima beans, *Phaseolus lunatus*		
United States	100–170	1
Burma	2,100	1
Puerto Rico	3,000	1
Java	3,120	1
Almond, *Prunus amygdalus*, nut		
Bitter	(280–2,500)	1
Spicy	(86–98)	1
Sweet	(22–54)	1
Seeds, 4 species, Nigeria, whole, frequently consumed by humans		
Phaseolus sp.	(381–1,093)	7
Vigna sp.	(285–1,223)	7
Cajanus sp.	(208–953)	7
Canavalia sp.	(285–953)	7
Sorghum, *Sorghum spp.*, young plant, whole	Max. 2,500	1
Cyanogenic arthropods		
Millipede, *Apheloria corrugata*, whole	428	8
Millipede, *Apheloria kleinpeteri*, whole	18	8
Zygaenid moth, *Zygaena filipendulae*, whole	668	8
Mammals		
Humans, *Homo sapiens*		
Blood		
Normal	<0.2	9
Afflicted with Leber's optic atrophy	1.4	9
Plasma		
Nonsmokers	0.05; Max. 0.11	10
Smokers	0.075; Max. 0.3	10
Nonbiological		
Air		
Automobile exhaust		
Adverse conditions	Max. 10.0	1
Equipped with catalytic convertor	1.1	1
Sewage sludge		

From publicly owned treatment works, United States	749[c]	18
Water, uncontaminated		
Rural watersheds	0.003	11,12
Industrial areas	0.02	11, 12
Small watersheds, covered with grasslands and forest, uninhabited by humans	0.0007–0.002; Max. 0.005	12
Western and central Canada, 11 rivers, 1974–77	Max. 0.006	12
U.S. water supplies, 2,595 samples nationwide	0.0009; Max. 0.008	1, 13
U.K. water supplies	<0.05; Max. 0.1	1
Wastewaters/runoff		
Electroplaters		
Total cyanide	0.2; Max. 3.0	14, 15
Dissociable cyanide	0.07	15
Complex cyanide	0.2	15
Thiocyanate	0.02	15
Plating wastewater		
Before treatment with alkaline chlorination	0.18	16
After treatment	0.005	16
Road salt dock		
Total cyanide	25.6	15
Dissociable cyanide	2.9	15
Complex cyanide	23.1	15
Thiocyanate	0.0	15
Steel industry		
Plating baths	72 (9–115)	1, 14
Coke oven liquor	6 (0–8)	1
Oil refineries		
Total cyanide	0.01; Max. 4.0	14, 15
Dissociable cyanide	0.0	15
Complex cyanide	0.01	15
Thiocyanate	2.2	15
Coking operations		
Total cyanide	2.1	15
Dissociable cyanide	0.3	15
Complex cyanide	0.8	15
Thiocyanate	23.6	15
Hospital wastewaters		
Before alkaline chlorination	ND	17
After treatment	0.06	17
Gold mills, Canada	0.3–26.5	14
Gold mine cyanide extraction leach ponds, California, Nevada, and Arizona	Usually 200–300, frequently 700, occasionally 9,000	19
Wastewater treatment plants,		
Chicago		
Treated effluent		
Total cyanide	0.005–0.03	15
Dissociable cyanide	0.003–0.007	15
Complex cyanid	0.002–0.02	15
Thiocyanate	0.006–0.03	15
Untreated wastewater		
Total cyanide	0.02–0.06	15

Dissociable cyanide	0.004–0.05	15
Complex cyanide	0.02–0.08	15
Thiocyanate	0.03–0.27	15
Sludge		
Total cyanide	0.49–3.79	15
Dissociable cyanide	0.06–0.44	15
Complex cyanide	0.43–5.4	15
Thiocyanate	0.2–0.9	15

[a]Concentrations are shown as means, range (in parentheses), and maximum (Max.).

[b]1, Towill et al. 1978; 2, Shaw 1986; 3, Gomez et al. 1983; 4, Casadei et al. 1984; 5, Ukhun and Dibie 1989; 6, Dufour 1988; 7, Okolie and Ugochukwu 1989; 8, Duffey 1981; 9, Berninger et al. 1989; 10, Egekeze and Oehme 1980; 11, Leduc 1981; 12, Leduc 1984; 13, EPA 190; 14, Leduc et al. 1982; 15, Kelada 1989; 16, Nonomura and Hobo 1989; 17, Vennesland et al. 1981a; 18, Beyer 1990; 19, Clark and Hothem 1991.

[c]Concentration is in milligrams per kilogram dry weight.

Hydrogen cyanide (HCN) is a common industrial pollutant and frequently occurs in water at concentrations between 0.1 and several milligrams per liter of free HCN (Leduc 1978; Leduc et al. 1982). Total cyanides is the most often cited measurement in aqueous solutions, owing to limitations in analytical methodologies (Leduc et al. 1982). Cyanides have been identified in fresh waters of rural and wilderness areas in Canada and Germany. Concentrations ranging between 30 and 60 µg total cyanides per liter seem related to runoff, with cyanide peaks more frequent in fall and winter during periods of minimal runoff (Leduc et al. 1982). In larger rivers, cyanide was low in winter owing to dilution by high runoff, but peaked in summer because of cyanide production by plants (Leduc 1984). Cyanides do not seem to persist in aquatic environments. In small, cold oligotrophic lakes treated with 1 mg NaCN/L, acute toxicity was negligible within 40 days. In warm shallow ponds, toxicity disappeared within 4 days after application of 1 mg NaCN/L. In rivers and streams, toxicity rapidly disappeared on dilution (Leduc 1984). Cyanide was not detectable in water and sediments of Yellowknife Bay, Canada, between 1974 and 1976, although the bay receives liquid effluents containing cyanides from an operating gold mine. Nondetection was attributed to rapid oxidation (Moore 1981). Several factors contribute to the rapid disappearance of cyanide from water. Bacteria and protozoans may degrade cyanide by converting it to carbon dioxide and ammonia. Chlorination of water supplies can result in conversion to cyanate (EPA 1980). An alkaline pH favors oxidation by chlorine, and an acidic pH favors volatilization of HCN into the atmosphere (EPA 1980).

Persistence in Water, Soil, and Air

In water, cyanides occur as free hydrocyanic acid, simple cyanides, easily degradable complex cyanides such as $Zn(CN)_2$, and sparingly decomposable complex cyanides of iron and cobalt; complex nickel and copper cyanides are intermediate between the easily decomposable and sparingly degradable compounds (Towill et al. 1978). Cyanide has relatively low persistence in surface waters under normal conditions but may persist for extended periods in groundwater (Way 1981). Volatilization is the dominant mechanism for removal of free cyanide from concentrated solutions and is most effective under conditions of high temperatures, high dissolved oxygen levels, and at increased concentrations of atmospheric carbon dioxide (Leduc et al. 1982; Simovic and Snodgrass 1985). Loss of simple cyanides from the water column is primarily through sedimentation, microbial degradation, and volatilization (Leduc et al. 1982; Marrs and Ballantyne 1987). Water-soluble strong complexes, such as ferricyanides and ferrocyanides, do not release free cyanide unless exposed to ultraviolet light. Thus, sunlight may lead to cyanide formation in wastes containing iron-cyanide complexes (Towill et al. 1978; Leduc et al. 1982; Simovic and Snodgrass 1985; Marrs and Ballantyne 1987).

Alkaline chlorination of wastewaters is one of the most widely used methods of treating cyanide wastes. In this process, cyanogen chloride, (CNCl) is formed, which at alkaline pH is hydrolyzed to the cyanate ion (CNO^-). If free chlorine is present, CNO^- can be further oxidized (Way 1981; Leduc et al. 1982; Simovic and Snodgrass 1985; Marrs and Ballantyne 1987). Other methods used in cyanide waste management include lagooning for natural degradation, evaporation, exposure to ultraviolet radiation, aldehyde treatment, ozonization, acidification-volatilization-reneutralization, ion exchange, activated carbon absorption, electrolytic

decomposition, catalytic oxidation, and biological treatment with cyanide-metabolizing bacteria (Towill et al. 1978; EPA 1980; Way 1981; Marrs and Ballantyne 1987). In the case of Canadian gold-mining operations, the primary treatment for cyanide removal is to retain gold mill wastewaters in impoundments for several days to months; removal occurs through volatilization, photodegradation, chemical oxidation, and, to a lesser extent, microbial oxidation. Microbial oxidation of cyanide is not significant in mine tailing ponds, which typically have pH >10, a low number of microorganisms, low nutrient levels, large quiescent zones, and cyanide concentrations >10 mg/L (Simovic and Snodgrass 1985).

Cyanide seldom remains biologically available in soils because it is either complexed by trace metals, metabolized by various microorganisms, or lost through volatilization (Towill et al. 1978; Marrs and Ballantyne 1987). Cyanide ions are not strongly adsorbed or retained on soils, and leaching into the surrounding ground water will probably occur. Under aerobic conditions, cyanide salts in the soil are microbially degraded to nitrites or form complexes with trace metals. Under anaerobic conditions, cyanides denitrify to gaseous nitrogen compounds that enter the atmosphere.

Volatile cyanides occur only occasionally in the atmosphere, due largely to emissions from plating plants, fumigation, and other special operations (Towill et al. 1978). Under normal conditions cyanide has relatively low persistence in air, usually between 30 days and 1 year (Way 1981), although some atmospheric HCN may persist for up to 11 years (Marrs and Ballantyne 1987). Data are lacking on the distribution and transformation of cyanide in the atmosphere (Towill et al. 1978) and should be acquired.

Lethal and Sublethal Effects

Terrestrial Flora and Invertebrates

Bacteria exposed to cyanide may exhibit decreased growth, altered cell morphology, decreased motility, mutagenicity, and altered respiration (Towill et al. 1978). Mixed microbial populations capable of metabolizing cyanide and not previously exposed to cyanide were adversely affected at 0.3 mg HCN/kg; however, these populations can become acclimatized to cyanide and can then degrade wastes with higher cyanide concentrations (Towill et al. 1978). Acclimatized populations in activated sewage sludge can often completely convert nitriles to ammonia, sometimes at concentrations as high as 60 mg total cyanides per kilogram (Towill et al. 1978). Cyanide can be degraded by various pathways to yield a variety of products, including carbon dioxide, ammonia, beta-cyanoalanine, and formamide (Knowles 1988). Several species of fungi can accumulate and metabolize cyanide, but the products of cyanide metabolism vary. For example, carbon dioxide and ammonia are formed as end products by *Fusarium solani*, whereas alpha-amino butyronitrile is a major cyanide metabolite of *Rhizoctonia solani*(Towill et al. 1978). Significant amounts of cyanide are formed as secondary metabolites by many species of fungi and some bacteria by decarboxylation of glycine (Knowles 1988). Rhizobacteria may suppress plant growth in soil through cyanide production. In one case volatile metabolites--including cyanide--from fluorescent pseudomonad soil bacteria prevented root growth in seedlings of lettuce, *Lactuca sativa* (Alstrom and Burns 1989). Not all cyanogenic isolates inhibited plant growth. Some strains promoted growth in lettuce and beans by 41-64% in 4 weeks versus 49-53% growth reduction by inhibitory strains (Alstrom and Burns 1989).

In higher plants, elevated cyanide concentrations inhibited respiration (through iron complexation in cytochrome oxidase) and ATP production and other processes dependent on ATP, such as ion uptake and phloem translocation, eventually leading to death (Towill et al. 1978). Cyanide produces chromosomal aberrations in some plants, but the mode of action is unknown (Towill et al. 1978). At lower concentrations, effects include inhibition of germination and growth, but cyanide sometimes enhances seed germination by stimulating the pentose phosphate pathway and inhibiting catalase (Towill et al. 1978; Solomonson 1981). The detoxification mechanism of cyanide is mediated by rhodanese. This enzyme is widely distributed in plants (Solomonson 1981; Leduc 1984). The rate of production and release of cyanide by plants to the environment through death and decomposition is unknown (Towill et al. 1978).

Free cyanide is not found in intact plant cells. Many species of plants, such as cassava, sorghum, flax, cherries, almonds, and beans, contain cyanogenic glycosides that release HCN when hydrolyzed (Towill et al. 1978). Cyanide poisoning of livestock by forage sorghums, such as Sudan grass and various hybrid cultivars, is well known (Cade and Rubira 1982) and has led to the development of several variations of sorghums that have a reduced capability of producing cyanide poisoning (Egekeze and Oehme 1980). Cyanogenesis has an

important role in plant defense against predatory herbivores. This herbivore-plant interaction is not simple; the degree of selectivity by herbivores varies among individuals and by differences in hunger and previous diet (Jones 1988).

Cyanide metabolism in higher plants involves amino acids, N-hydroxyamino acids, aldoximes, nitriles, and cyanohydrins (Halkier et al. 1988). Cyanide is a coproduct of ethylene synthesis in higher plants. The increase in ethylene production that occurs during the senescence of certain flowers and the ripening of fruits is accompanied by a rise in beta-cyanoalanine activity; activity of this enzyme correlates closely with that of ACC (1-aminocyclopropane-l-carboxylic acid) oxidase, the last enzyme in the ethylene pathway. Manning (1988) suggested that ACC oxidase reacts with various amino acids to liberate cyanide. Cyanide added to isolated castorbean (*Ricinus communis*) mitochondria significantly enhanced the rate and amount of protein synthesis. Cyanide stimulated mitochondrial protein synthesis in a dose-dependent manner, with an optimal stimulation of over 2 times at 26 µg/L, but at this concentration mitochondrial respiration was inhibited by 90% (Kaderbhai et al. 1989). Cyanide is a weak competitive inhibitor of green bean *(Phaseolus vul*garis) lipoxygenase, an enzyme that catalyzes the formation of hydroperoxides from polyunsaturated fatty acids (Adams 1989). Because degradation of hydroperoxides causes unacceptable changes in bean flavor and color, compounds that inhibit lipoxygenase may enjoy wide application in the frozen vegetable industry (Adams 1989). Corn seedlings from cold-resistant cultivars were more resistant to 65 mg KCN/L at low temperatures (13°C) than were seedlings from cold-susceptible cultivars (25°C), as judged by respiratory activity of mitochondria (Van De Venter 1985). Results suggest that cyanide-resistant respiration may play a role in cold resistance in maize seedlings, although more evidence is needed to demonstrate that cold-resistant plants actually use their greater potential for alternative respiration at low temperatures (Van De Venter 1985).

The cyanogenic system comprising cyanogenic glycosides, cyanohydrins, betaglucosidases, and nitrile lyases is widespread in plants, but also occurs in several species of arthropods, including the tiger beetle (*Megacephala virginica*), leaf beetle (*Paropsis atomaria*), zygaenid moths, and certain butterflies (Nahrstedt 1988). In *Zygaena trifolii*, cyanide compounds seem to function as protection against predators (Nahrstedt 1988). Defensive secretions of cyanide have also been reported in polydesmid millipedes, and these organisms seem to be more tolerant than other species when placed in killing jars containing HCN (Towill et al. 1978). In a millipede (*Apheloria* sp.), cyanide is generated in a two-compartment organ by hydrolysis of mandelonitrile; cyanide generation occurs outside the gland when the components of the two compartments are mixed during ejection (Towill et al. 1978).

Highly toxic substances, such as cyanides, are sometimes feeding cues and stimulants for specialized insects. For example, instar larvae of the southern armyworm (*Spodoptera eridania*) strongly prefer cyanogenic foods, such as foliage of the lima bean, a plant with comparatively elevated cyanide content--up to 31 mg/kg in some varieties--in the form of linamurin (Brattsten et al. 1983). Feeding was stimulated in southern armyworms at dietary levels up to 508 mg KCN/kg (208 mg HCN/kg) for first to fourth instar larval stages, and between 1,000 and 10,000 mg KCN/kg diet for fifth and sixth instar larvae (Brattsten et al. 1983). Sixth instar larvae preexposed to diets containing 5,000 mg KCN/kg showed no adverse affects at dietary levels of 10,000 mg KCN/kg; however, previously unexposed larvae showed reversible signs of poisoning at 10,000 mg/kg diet, including complete inhibition of oviposition and 83% reduction in adult emergence (Brattsten et al. 1983). Experimental studies with southern armyworm larvae and thiocyanate--one of the in vivo cyanide metabolites--showed that 5,000 mg thiocyanate per kilogram diet reduced pupation by 77%, completely inhibited oviposition, and reduced adult emergence by 80% (Brattsten et al. 1983), strongly suggesting that thiocyanate poisoning is the primary effect of high dietary cyanide levels in southern armyworms.

Resistant species, such as southern armyworms, require injected doses up to 800 mg KCN/kg BW (332 mg HCN/kg BW) or diets of 3,600 mg KCN/kg for 50% mortality (Brattsten et al. 1983), but data are scarce for other terrestrial invertebrates. Exposure to 8 mg HCN/L air inhibits respiration in the granary weevil (*Sitophilus granarius*) within 15 min and kills 50% in 4 h; some weevils recover after cessation of 4-h exposure (Towill et al. 1978).

Aquatic Organisms

Numerous accidental spills of sodium cyanide or potassium cyanide into rivers and streams have resulted in massive kills of fishes, amphibians, aquatic insects, and aquatic vegetation; sources of poisonings were storage reservoirs of concentrated solutions, overturned rail tank cars, or discharge of substances generating free HCN

in the water from hydrolysis or decomposition (Leduc 1984). Data on the recovery of poisoned ecosystems are scarce. In one case, a large amount of cyanide-containing slag entered a stream from the reservoir of a Japanese gold mine as a result of an earthquake (Yasuno et al. 1981). The slag covered the streambed for about 10 km from the point of rupture, killing all stream biota; cyanide was detected in the water column for only 3 days after the spill. Within 1 month flora was established on the silt covering the above-water stones, but there was little underwater growth. After 6-7 months, populations of fish, algae, and invertebrates had recovered, although species composition of algae was altered (Yasuno et al. 1981).

Fish were the most sensitive aquatic organisms tested under controlled conditions. Significant adverse nonlethal effects, including reduced swimming performance and inhibited reproduction, were observed in the range of 5.0-7.2 µg free cyanide per liter; deaths were recorded for most species between 20 and 76 µg/L (Table 3). Among invertebrates, adverse nonlethal effects were documented between 18 and 43 µg/L, and lethal effects between 30 and 100 µg/L--although some deaths were recorded in the range 3-7 µg/L for the amphipod *Gammarus pulex* (Table 3). Algae and macrophytes were comparatively tolerant; adverse effects were reported at >160 µg free cyanide per liter (Table 3).

Table 3. Cyanide effects on selected species of aquatic organisms. All concentrations are shown as micrograms of hydrogen cyanide per liter (ppb) of medium at start unless indicated otherwise.

Species, concentration, and other variables	Effects	Reference[a]
Algae and macrophytes		
Alga, *Chlorella* sp.		
7,300	Inhibition of photosynthesis	3
30,000	Enzyme inhibition	2
Water hyacinth, *Eichhornia crassipes*		
300,000	Nonphytotoxic in 72 h; plants contained total cyanide of 6.7 g/kg dry weight (DW), equivalent to bioconcentration factor (BCF) of x22	5
Freshwater aquatic plants, nine species, 65,000, 30-min exposure	No effect on respiratory oxygen uptake in six species of angiosperms (*Myriophyllum* sp., *Potamogeton* spp., *Elodea* sp., *Ruppia* sp., *Cabomba* sp.); some effect on two species of bryophytes (*Rhynchostegium riparioides*, *Fontinalis antipyretica*) and one species of alga (*Cladophora glomerata*)	4
Alga, *Microcystis aeruginosa*		
7,990	90% kill	2
Alga, *Prototheca zopfi*		
3,000	Inhibition of respiration	2
Alga, *Scenedesmus quadricauda*		
160, as CN^-	Toxic	1
Invertebrates		
Copepod, *Acartia clausi*		
30	LC50 (96 h)	2
Isopod, *Asellus communis*		
29–40	MATC[b]	2, 8
1,834	LC50 (11 days)	
Oyster, *Crassostrea* sp.		
150	Motor activity suppressed after 10 min	2

Daphnid, *Daphnia magna*		
160	LC50 (96 h)	10
Daphnid, *Daphnia pulex*		
83	LC50 (96 h)	2
Amphipod, *Gammarus pseudolimnaeus*		
16–21	MATC[b]	8
58	LC50 (96 h) at 20º C	8
184	LC50 (96 h) at 5.2º C	8
Amphipod, *Gammarus pulex*		
3	LC50 (15 h); 50% dead in 14 days after exposure for 5 h	6
7.5	LC50 (9h); exposure for 66 min results in 50% mortality 14 days after exposure	6
15	LC50 (6 h); exposure for 45 min causes 50% mortality 14 days after exposure	6
75	LC50 (3 h); exposure for 18 min results in 50% kill 14 days after exposure	6
Mussel, *Mytilus edulis*		
18	After exposure for 14 days growth was reduced and uptake of glycine was inhibited	9
100	LC20 (14 days)	9
Mysid shrimp, *Mysidopsis bahia*		
11, 20, 43, or 70	Life-cycle (29 days) exposure produced adverse effects on survival at 70 µg/L, and on reproduction at 43 µg/L; no measurable effects at lower doses of 11 and 20 µg/L	7
93–113	LC50 (96 h)	2, 7
Snail, *Physa heterostropha*		
432	LC50 (96 h)	3, 10
Fiddler crab, *Uca tangeri*		
Isolated perfused gills subjected to 26,000 CN^-/L, as KCN	Inhibited sodium chloride absorption across gill epithelium; effect reversible if exposure <5 min and nonreversible if >30 min. Salt absorption effect regulated by $(Na^+ + K^+)$ ATPase	11
Fish		
Brown bullhead, *Ictalurus nebulosus*		
Subjected to steadily increasing concentration of waterborne cyanide over a 9-h period: 200 at 1 h, 600 at 3 h, 1,000 at 5 h, and 1,800 at 9 h	Increased heart beat rate at lower concentrations and decreased rate at higher concentrations; hyperventilation in first 3 h followed by decrease in ventilation rate; oxygen consumption paralleled changes in heart and ventilatory rates. Death in 9 h	21
Longnose gar, *Lepisosteus osseus*		
12 µg CN^-/kg BW, as sodium cyanide, equivalent to 10.7 µg CN or 20 µg NaCN, single injection	Hypoxic response and bradycardia; effects appear earlier when administered into the ventral aorta or conus than into the dorsal aorta	27
Bluegill, *Lepomis macrochirus*		
5.0	Inhibited spawning following chronic exposure	22
5.2	Complete inhibition of spawning after exposure for 57–289 days	2, 8
9.3–19.8	MATC[b]	2

19.4	Reduced survival of fry in 57-day exposure which began with eggs	8
50	Tolerated concentration at higher temperatures, but no reproduction	8
56–227	LC50 (96 h) for juveniles	8, 22
109–218	LC50 (96 h) for fry	8
232–365	LC50 (96 h) for eggs	22
535–690	LC50 (96 h) for eggs at hatching	8
Largemouth bass, *Micropterus salmoides*		
101	LC50 (96 h) for juveniles	8
Cutthroat trout, *Oncorhynchus clarki*		
1,000 for 20 min	All fish recovered within 12 min and fed and grew normally during the next 6 months	31
Coho salmon, *Oncorhynchus kisutch*		
7.0	Reduction of 50% in swimming performance during 8-day exposure	13
10	Swimming speed reduced after exposure for 2 h	2
Rainbow trout, *Oncorhynchus mykiss*		
0.1 or 1.0	No effect on sperm motility or on fertilization rate at lower dose; some effect on sperm motility at higher dose	12
5.0	Reduction of 50% in swimming performance in 20-day exposure	13
10	No effect on growth during 20-day exposure at 6º C	13
10	Increased respiration rate in 4 days, growth reduction and liver damage in 9 days, abnormal oocyte development and reduced spermatogonia production in 18–20 days	2
10, 20, or 30 for 7 days, sexually mature females	Exposure to 10 or 20 µg/L caused a reduction in serum calcium to levels insufficient for the production of exogenous yolk; this was not observed in the 30 µg/L group	14
10, 20, or 30 for 18 days, juveniles	Degenerative necrosis of liver hepatocytes at all concentrations in a dose-dependent pattern. Severe initial growth repression at all concentrations followed by a significant increase, but growth remained depressed 40% and 95% in the 20 and 30 µg/L groups, respectively, at 18 days	15
10 or 20, exposure for 20 days during midsummer, sexually maturing females	Both concentrations resulted in abnormal oocytes, delayed development, and significantly reduced the number of eggs for spawning	16
15	No effect on growth during 20-day exposure at 12º C	13
18	No deaths in 96 h at 6º C	13
20	65% reduction in weight gain after 21 days	2
28	LC50 (96 h) at 6º C	10, 13, 17
30	No effect on growth during 20-day exposure at 18º C	13
32	No deaths in 96 h at 12º C	13
42	LC50 (96 h) at 12º C	13
43	LC50 (96 h) for nonexercised juveniles	18

	during winter	
46–75	LC50 (96 h) for juveniles	8, 19
52	LC50 (96 h) for exercised juveniles during winter	18
60	No deaths in 96 h at 18º C	13
68	LC50 (96 h) at 18º C	10, 13, 17
96	LC50 (144 h)	20
Subjected to steadily increasing concentrations of waterborne cyanide: 0 at start, 200 at 1 h, 600 at 3 h, 1,000 at 5 h, and 1,800 at 9 h	Reduction in heart rate, hyperventilation, increased oxygen consumption, death in 9 h	21
Chinook salmon, *Oncorhynchus tshawytscha*		
10	After 64 days, increased growth rate and production when compared to controls	13
20	Growth reduced 27% after exposure for 64 days	2
Yellow perch, *Perca flavescens*		
76–108	LC50 (96 h) for juveniles	8, 22
288–>389	LC50 (96 h) for eggs and fry	8, 22
Fathead minnow, *Pimephales promelas*		
12.9–19.6	MATC[b]	8, 22
18–58	Reduction in RNA content in larva in 96 h at 18–36 µg HCN/L, and in DNA and protein at 18–58 µg/L	28
19	Egg reduction of 59% after exposure for 265 days at 25º C	13
35	Reduction in growth rate during chronic exposure	5
44	Hatching reduced 83% after chronic exposure	13
47	Growth reduction in 30 days	28
58	Toxicosis occurred in yolk-sac larvae within 24 h as judged by significant reductions in content of RNA and protein; however, effects were not measurable in 96 h suggesting development of partial tolerance	29
>61	Adverse effects on growth and survival during lifetime exposure	13
82–113	LC50 (96 h) for fry at 25º C	8
83–137	LC50 (96 h) for juveniles	8, 22
99	LC50 (96 h) for fry at 20º C	8
107	Reduced survival in 96 h	28
121–202	LC50 (96 h) for eggs at 25º C	8
121–352	LC50 (96 h) for eggs; more toxic at low dissolved oxygen	22
122	LC50 (96 h) for fry at 15º C	8
Mixture of NaCN plus $CdSO_4$, equivalent to 170 µg CN/L	LC50 (96 h) for adults	30
Mixture of NaCN plus $ZnSO_4$, equivalent to 180 µg CN/L	LC50 (96 h) for adults	30
230, as NaCN	LC50 (96 h) for adults	30
273	LC50 (96 h) for eggs at 20º C	8
352	LC50 (96 h) for eggs at 15º C	8
Mixture of NaCN plus $NiSO_4$, equivalent to 650 µg CN/L	LC50 (96 h) for adults	8
Black crappie, *Pomoxis nigromaculatus*		
60	Some deaths in <24 h	3

101	LC50 (96 h) for juveniles	8
Plainfin midshipman, *Porichthys notatus*		
Isolated photophores exposed to 2,600, as KCN	Maximal luminescence induced by KCN; effect inhibited by d-glucose, d-glyceraldehyde 3-phosphate, and 3-phosphoglycerate	32
Atlantic salmon, *Salmo salar*		
5.0 for 12 days, adult females	Decline in plasma and gonad vitellogenin levels	23
10	Abnormal embryonic development after 58-day exposure	2
10, 80, or 100; newly fertilized eggs continually exposed for 5 months to end of sac-fry stage	Hatching delayed 6–9 days at 80 and 100 µg/L. Hatching success reduced 15% to 40% at all test concentrations, but no measurable effects on growth or survival after hatching. Abnormalities (mostly defects of eye, mouth, vertebral column) were 6% at 10 µg/L, and 19% at 100 µg/L	24
24	LC50 (24 h) at dissolved oxygen of 3.5 mg/L	25
73	LC50 (24 h) at dissolved oxygen of 10 mg/L	25
5,000, 10,000, 25,000, 50,000, or 125,000 for 30 min	Total cyanide residues in gills ranged from 1.0 to 6.6 mg/kg fresh weight (FW) in a dose dependent manner	26
50,000 for 10, 15, 20, 25, or 30 min	Residues in gills, in mg total CN/kg FW, ranged from 1.3 (10 and 15 min) to 1.9 (15 and 20 min) to 4.5 (30 min)	26
Brown trout, *Salmo trutta*		
90	LC50 (96 h)	10
5,000, 10,000, 25,000, 50,000, 75,000, or 100,000, as CN- for 30 min	Residues in gills ranged in a dose-dependent manner from 0.6 mg CN/kg FW in the 5 mg/L group to 3.4 mg/kg FW in the 100 mg/L group	26
50,000 for 10, 15, 20, or 25 min	Residues in tissues, in mg/kg FW, ranged from 0.7 to 1.8 in gill, 0.6 to 2.3 in brain, and 1.3 to 2.5 in liver; concentrations were directly related to length of exposure	26
Brook trout, *Salvelinus fontinalis*		
5.0	Reduction of 50% in swimming performance in 29-day exposure	13
5.7–11.2	MATC[b]	8, 22
10	75% reduction in swimming endurance after exposure for 26 min	2
10–50	Swimming ability reduced 98% after exposure for 29 days	20
11	Continuous exposure of mature females for 144 days before spawning resulted in 50% reduction in number of eggs produced and 15% reduction in egg viability; however, 90 days after hatch trout were 18% heavier and 10% longer than controls	13
25	Inhibited oxygen intake after 5 h	2
33	Adverse effects on juvenile growth rate during exposure for 90 days	2, 8
56–112	LC50 (96 h) range for swimup fry and juveniles	8, 22
108–518	LC50 (96 h) for sac-fry	8, 22
>212	LC50 (96 h) for eggs	8, 22

[a]1, Towill et al. 1978; 2, EPA 1980; 3, EPA 1973; 4, Azcon-Bieto et al. 1987; 5, Low and Lee 1981; 6, Abel and Garner 1986; 7, Lussier et al. 1985; 8, Smith et al. 1979; 9, Thompson 1984; 10, Leduc et al. 1982; 11, Drews and Graszynski 1987; 12, Billard and Roubaud 1985; 13, Leduc 1984; 14, Da Costa and Ruby 1984; 15, Dixon and Leduc 1981; 16, Lesniak and Ruby 1982; 17, Kovacs and Leduc 1982b; 18, McGeachy and Leduc 1988; 19, Marking et al. 1984; 20, Ballantyne 1987a; 21, Sawyer and Heath 1988; 22, Smith et al. 1978; 23, Ruby et al. 1987; 24, Leduc 1978; 25, Alabaster et al. 1983; 26, Holden and Marsden 1964; 27, Smatresk et al. 1986; 28, Barron and Adelman 1984; 29, Barron and Adelman 1985; 30, Doudoroff 1956; 31, Wiley 1984; 32, Rees and Baguet 1989.

[b]Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Adverse effects of cyanide on aquatic plants are unlikely at concentrations that cause acute effects to most species of freshwater and marine fishes and invertebrates (EPA 1980). Water hyacinth *(Eichhornia crassipes)* can survive for at least 72 h in nutrient solution containing up to 300 mg CN/L and can accumulate up to 6.7 g/kg dry weight (DW) plant material. On this basis, 1 ha of water hyacinths has the potential to absorb 56.8 kg of cyanide in 72 h, and this property may be useful in reducing the level of CN in untreated wastewater from various electroplating factories, where concentrations generally exceed 200 mg CN/L (Low and Lee 1981). Cyanide may also affect plant community structure. Some algae, for example, metabolized CN at water concentrations <1 mg/L, but at concentrations of 1-10 mg/L, algal activity was inhibited, leaving a biota dominated by *Actinomycetes*--a filamentous bacterium (Knocke 1981).

Cyanide adversely affects fish reproduction by reducing the number of eggs spawned, and the viability of the eggs by delaying the process of secondary yolk deposition in the ovary (Lesniak and Ruby 1982; Ruby et al. 1986). Vitellogenin, a glycolipophosphoprotein present in plasma of fish during the process of yolk formation, is synthesized in liver under stimulation of estrogen and subsequently sequestered in the ovary; it is essential for normal egg development. Exposure of naturally reproducing female rainbow trout to as little as 10 µg HCN/L for 12 days during the onset of the reproductive cycle caused a reduction in plasma vitellogenin levels and a reduction in ovary weight. The loss of vitellogenin in the plasma would remove a major source of yolk (Ruby et al. 1986). Reproductive impairment in adult bluegills (*Lepomis macrochirus*) has been reported following exposure to 5.2 µg CN/L for 289 days (EPA 1980). Fertilized fish eggs are usually resistant to cyanide prior to blastula formation, but delayed effects occur at 60 to 100 µg HCN/L, including birth defects and reduced survival of embryos and newly hatched larvae (Leduc et al. 1982). Concentrations as low as 10 µg HCN/L caused developmental abnormalities in embryos of Atlantic salmon after extended exposure (Leduc 1978). These abnormalities, which were absent in controls, included yolk sac dropsy and malformations of eyes, mouth, and vertebral column (Leduc 1984).

Other adverse effects of cyanide on fish include delayed mortality, pathology, impaired swimming ability and relative performance, susceptibility to predation, disrupted respiration, osmoregulatory disturbances, and altered growth patterns. Free cyanide concentrations between 50 and 200 µg/L were fatal to the more-sensitive fish species over time, and concentrations >200 µg/L were rapidly lethal to most species of fish (EPA 1980). Cyanide- induced pathology in fish includes subcutaneous hemorrhaging, liver necrosis, and hepatic damage. Exposure of fish for 9 days to 10 µg HCN/L was sufficient to induce extensive necrosis in the liver, although gill tissue showed no damage. Intensification of liver histopathology was evident at dosages of 20 and 30 µg HCN/L and exposure periods up to 18 days (Leduc 1984). Cyanide has a strong, immediate, and long-lasting inhibitory effect on the swimming ability of fish (Leduc 1984). Free cyanide concentrations as low as 10 µg/L can rapidly and irreversibly impair the swimming ability of salmoneds in well-aerated water (Doudoroff 1976). Osmoregulatory disturbances recorded at 10 µg HCN/L may affect migratory patterns, feeding, and predator avoidance (Leduc et al. 1982; Leduc 1984). In general, fish experience a significant reduction in relative performance (based on osmoregulation, growth, swimming, and spermatogenesis) at 10 µg HCN/L, and although fish can survive indefinitely at 30 µg HCN/L in the laboratory, the different physiological requirements necessary to survive in nature could not be met (Leduc 1978, 1981; Leduc et al. 1982; Figure). Increased predation by green sunfish (*Lepomis cyanellus*) on fathead minnows *(Pimephales promelas)* was noted at sublethal concentrations of HCN, but it was uncertain if fatheads became easier prey or if green sunfish had greater appetites (Smith et al. 1979).

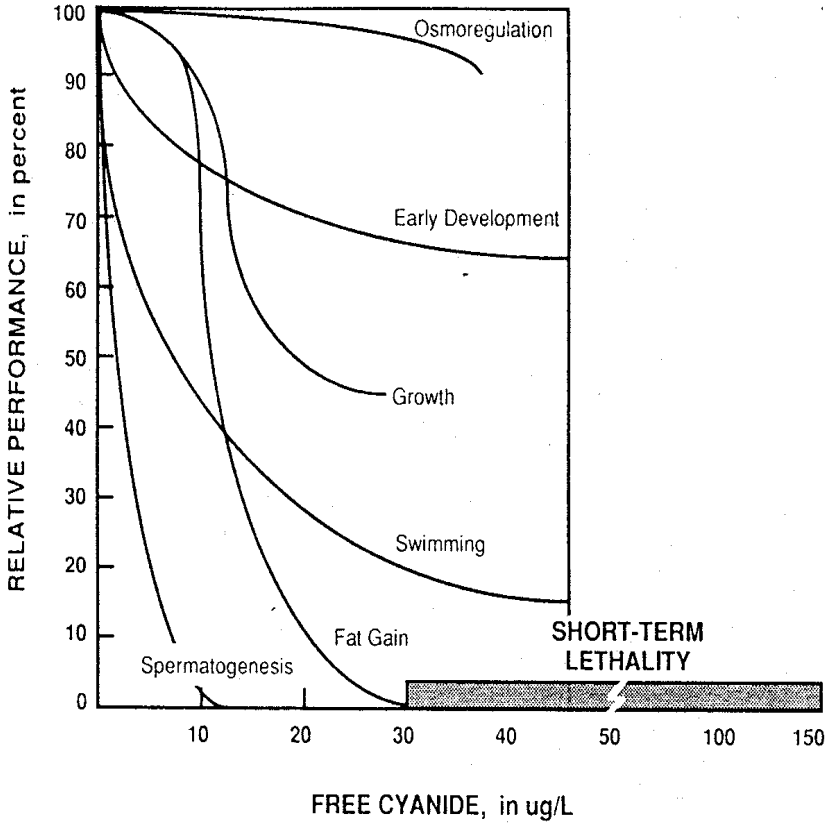


Figure. Summary of lethal and sublethal effects of free cyanide on freshwater fish. Modified from Leduc et al. (1982).

Sodium cyanide has stimulatory effects on oxygen-sensitive receptors in lungfish, amphibians, reptiles, birds, and mammals (Smatresk 1986). Facultative and aquatic air breathers appear to rely on air breathing when external chemoreceptors are stimulated, whereas obligate air-breathing fish are more responsive to internal stimuli (Smatresk 1986). Gill ventilation frequency of longnose gar (*Lepisosteus osseus*), for example, was little affected by external cyanide application, but responded strongly when cyanide was administered internally by injection (Smatresk 1986). Cyanide, like many other chemicals, can stimulate growth of fish during exposure to low sublethal levels. This phenomenon, referred to as hormesis, is little understood and warrants additional research (Leduc 1984).

The observed toxicity to aquatic life of simple and complex cyanides was attributed almost entirely to molecular (undissociated) HCN derived from ionization, dissociation, and photodecomposition of cyanide-containing compounds. The toxicity of the cyanide ion, CN^-, which is a minor component of free cyanide (HCN + CN^-) in waters that are not exceptionally alkaline is of little importance (Doudoroff 1976; Towill et al. 1978; Smith et al. 1979; EPA 1980). The acute toxicity of stable silver cyanide and cuprocyanide complex anions is much less than that of molecular HCN, but is nevertheless important; these ions can be the principal toxicants, even in some very dilute solutions. The much lower toxicities of the ferrocyanide and ferricyanide complexions--which are of high stability but subject to extensive and rapid photolysis, yielding free cyanide on direct exposure to sunlight--and the nickelocyanide ion complex are not likely to be of practical importance (Doudoroff 1976). Toxicity to aquatic organisms of organic cyanide compounds, such as lactonitrile, is similar to that of inorganic cyanides because they usually undergo rapid hydrolysis in water to free cyanide (Towill et al. 1978). There is general agreement that total cyanide concentrations in water in most cases will overestimate the actual cyanide toxicity to aquatic organisms, and that the analytically determined HCN concentration in cyanide-polluted waters

is considered to be the most reliable index of toxicity (Doudoroff 1976; Smith et al. 1979; EPA 1980; Abel and Garner 1986).

Cyanide acts rapidly in aquatic environments, does not persist for extended periods, and is highly species selective; organisms usually recover quickly on removal to clean water. The critical sites for cyanide toxicity in freshwater organisms include the gills, egg capsules, and other sites where gaseous exchange and osmoregulatory processes occur. On passing through a semipermeable membrane, the HCN molecules are usually distributed by way of the circulatory system to various receptor sites where toxic action or detoxification occurs (Leduc 1984). Once in the general circulation, cyanide rapidly inhibits the electron transport chain of vital organs. Signs of distress include increased ventilation, gulping for air at the surface, erratic swimming movements, muscular incoordination, convulsions, tremors, sinking to the bottom, and death with widely extended gill covers (Leduc 1981, 1984). The acute mode of action of HCN is limited to binding those porphyrins that contain Fe^{+3}, such as cytochrome oxidase, hydroperoxidases, and methemoglobin. At lethal levels, cyanide is primarily a respiratory poison and one of the most rapidly effective toxicants known (Leduc et al. 1982). The detoxification mechanism of cyanide is mediated by thiosulfate sulfur transferase, also known as rhodanese. This enzyme is widely distributed in animals, including fish liver, gills, and kidney. Rhodanese plays a key role in sulfur metabolism, and catalyzes the transfer of a sulfane-sulfur group to a thiophilic group (Leduc 1984). Thiosulfate administered in the water with cyanide reduced the toxicity of cyanide to fish, presumably by increasing the detoxification rate of cyanide to thiocyanate (Towill et al. 1978).

Additive or more-than-additive toxicity of free cyanide to aquatic fauna has been reported in combination with ammonia (Smith et al. 1979; Leduc et al. 1982; Alabaster et al. 1983; Leduc 1984) or arsenic (Leduc 1984). However, conflicting reports on the toxicity of mixtures of HCN with zinc or chromium (Towill et al. 1978; Smith et al. 1979; Leduc et al. 1982; Leduc 1984) require clarification. Formation of the nickelocyanide complex markedly reduces the toxicity of both cyanide and nickel at high concentrations in alkaline pH. At lower concentrations and acidic pH, solutions increase in toxicity by more than 1,000 times, owing to dissociation of the metallocyanide complex to form hydrogen cyanide (Towill et al. 1978). Mixtures of cyanide and ammonia may interfere with seaward migration of Atlantic salmon smolts under conditions of low dissolved oxygen (Alabaster et al. 1983). The 96-h toxicity of mixtures of sodium cyanide and nickel sulfate to fathead minnows is influenced by water alkalinity and pH. Toxicity decreased with increasing alkalinity and pH from 0.42 mg CN/L at 5 mg $CaCO_3$/L and pH 6.5; to 1.4 mg CN/L at 70 mg $CaCO_3$/L and pH 7.5; to 730 mg CN/L at 192 mg $CaCO_3$/L and pH 8.0 (Doudoroff 1956).

Numerous biological and abiotic factors are known to modify the biocidal properties of free cyanide, including water pH, temperature, and oxygen content; life stage, condition, and species assayed; previous exposure to cyanide compounds; presence of other chemicals; and initial dose tested. There is general agreement that cyanide is more toxic to freshwater fish under conditions of low dissolved oxygen (Doudoroff 1976; Towill et al. 1978; Smith et al. 1979; EPA 1980; Leduc 1984); that pH levels within the range 6.8-8.3 had little effect on cyanide toxicity but enhanced toxicity at acidic pH (Smith et al. 1979; EPA 1980; Leduc et al. 1982; Leduc 1984); that juveniles and adults were the most sensitive life stages tested and embryos and sac fry the most resistant (Smith et al. 1978, 1979; EPA 1980; Leduc 1984); and that substantial interspecies variability exists in sensitivity to free cyanide (Smith et al. 1979; EPA 1980). Initial dose and water temperature both modify the biocidal properties of HCN to freshwater teleosts. At slowly lethal concentrations (i.e., < 10 µg HCN/L), cyanide was more toxic at lower temperatures; at high, rapidly lethal HCN concentrations, cyanide was more toxic at elevated temperatures (Kovacs and Leduc 1982a, 1982b; Leduc et al. 1982; Leduc 1984). By contrast, aquatic invertebrates were most sensitive to HCN at elevated water temperatures, regardless of dose (Smith et al. 1979). Season and exercise modify the lethality of HCN to juvenile rainbow trout (McGeachy and Leduc 1988); higher resistance to cyanide correlated with higher activity induced by exercise and higher temperatures, suggesting a faster detoxification rate or higher oxidative and anaerobic metabolisms. Low levels of cyanide that were harmful when applied constantly may be harmless under seasonal or other variations that allow the organism to recover and detoxify (Leduc 1981). Acclimatization by fish to low sublethal levels of cyanide through continuous exposure might enhance their resistance to potentially lethal concentrations (Leduc 1981, 1984), but studies with Atlantic salmon and rainbow trout indicate otherwise. Prior acclimatization of Atlantic salmon smolts to cyanide increased their resistance only slightly to lethal concentrations (Alabaster et al. 1983). Juvenile rainbow trout previously exposed to low sublethal concentrations showed a marked reduction in fat synthesis and swimming performance when challenged with higher cyanide doses; effects were

most pronounced at low water temperatures (Kovacs and Leduc 1982a). Experimental evidence is lacking on exposure to lethal concentrations after prior exposure to high sublethal concentrations; some investigators predict decreased resistance (Leduc 1984), and others increased survival (Towill et al. 1978).

Birds

First signs of cyanide toxicosis in sensitive birds appeared between 0.5 and 5 min after exposure, and included panting, eye blinking, salivation, and lethargy (Wiemeyer et al. 1986). In more-resistant species, such as domestic chickens, signs of toxicosis began 10 min after exposure. At higher doses, breathing in all species tested became increasingly deep and labored, followed by gasping and shallow intermittent breathing. Death usually followed in 15-30 min, although birds alive at 60 min frequently recovered (Wiemeyer et al. 1986). The rapid recovery of some birds exposed to cyanide may be due to the rapid metabolism of cyanide to thiocyanate and its subsequent excretion. Species sensitivity to cyanide was not related to body size but seemed to be associated with diet (Wiemeyer et al. 1986). Birds that feed predominantly on flesh, such as vultures, kestrels, and owls, were more sensitive to cyanide than were species that feed mainly on plant material--with the possible exception of mallard (Anas *platyrhynchos*)--as judged by acute oral LD50 values (Table 4).

Table 4. Cyanide effects on selected species of birds.

Species, dose, and other variables	Effects	Reference[a]
Mallard, *Anas platyrhynchos*		
Single oral dose of NaCN		
0.53 mg CN/kg body weight (BW), equivalent to 1 mg NaCN/kg BW	No deaths	7
1.1 mg CN/kg BW (2.0 mg NaCN/kg BW)	About 6% dead	7
1.27 mg CN/kg BW (2.4 mg NaCN/kg BW)	About 33% dead	7
1.43 mg mg CN/kg BW (2.7 mg NaCN/kg BW)	LD50; 95% confidence interval (C.I.) of 2.2 and 3.2 mg NaCN/kg bW	7
Turkey vulture, *Cathartes aura*		
Single oral dose of 19.1 mg CN/kg BW, equivalent to 36 mg NaCN/kg BW	Up to 80% of the cyanide in blood was present as free cyanide and the remainder as bound cyanide	1
Single oral dose of 19.1 mg CN/kg BW, equivalent to 36 mg NaCN/kg BW	Average time to death was about 19 min and ranged between 8 and 41 min; cyanide residues postmortem, in mg CN/kg fresh weight (FW), were 6.7 in blood (Max. 21) and 0.6 in liver (Max. 2.8)	2
Rock dove, *Columba livia*		
0.12 mg CN/L air, as HCN	All dead in 10 min	2
1.6 mg CN/kg BW, equivalent to 4.0 mg KCN/kg BW	Minimum lethal dose when administered intravenously or intramuscularly	2
Black vulture, *Coragyps atratus*		
Single oral dose, as NaCN		
1.6 mg CN/kg BW	No deaths in 60 min. Mean and maximum blood CN concentrations, in mg/kg FW, were 0.7 and 0.9, respectively	2
2.4 lmg CN/kg BW	Some deaths within 30 min. Mean blood CN residues in	2

	mg/kg FW, were 0.7 in dead birds vs. 1.2 in those surviving 60 min	
2.54 mg CN/kg BW	Acute oral LD50; 95% C.I. of 2.3 and 2.8 mg CN/kg BW (4.4–5.3 mg NaCN/kg BW)	2
3.7 and 19.1 mg CN/kg BW	All dead within 16 min; maximum blood CN levels postmortem were 2.1 mg/kg FW in the low dose group and 4.2 in the high dose group	2
Japanese quail, *Coturnix japonica*		
Single oral dose, as NaCN		
4.5 mg CN/kg BW	Acute oral LD50 for adult females; 95% C.I. of 3.1 and 6.5 mg CN/kg BW	2
5.5 mg CN/kg BW	Acute oral LD50 for adult males; 95% C.I. of 4.0 and 7.5 mg CN/kg BW	2
American kestrel, *Falco sparverius*		
2.12 mg CN/kg BW, as NaCN	Acute oral LD50; 95% C.I. of 1.6 and 2.8 mg CN/kg BW	2
Domestic chicken, *Gallus domesticus*		
Intravenous route		
0.01 µg/kg BW	Most of dose recovered in urine as thiocyanate in 6 h; excretion limited by availability of transferable sulfur	3
0.6 mg CN/kg BW, equivalent to 1.5 mg KCN/kg BW	Lethal	2
0.78 mg CN/kg BW, as KCN	Sublethal; thiocyanate excretion increased 10 times after 10 min and returned to normal levels after 3.5 h; the total thiocyanate collected was equivalent to 85% of the administered dose	4
1.3 mg CN/kg BW, as KCN	Lethal	4
Inhalation route		
0.12 mg HCN/L air	All survived for at least 60 min	2
Single oral dose, as NaCN		
3.2 mg CN/kg BW, equivalent to 6.0 mg NaCN/kg BW	No deaths in 30 min; maximum CN levels, in mg/kg FW, were 1.1 in blood and 0.06 in liver	2
6.4 mg CN/kg BW	Some deaths in 30 min; maximum CN levels, in mg/kg FW were 1.6 in blood and 0.12 in liver	2
11.1 mg CN/kg BW	Acute oral LD50; 95% C.I. of 6.4 and 19.1 mg CN/kg BW	2
25.4 mg CN/kg BW	Advanced signs of acute poisoning; death probable within 30 min; maximum CN levels, in mg/kg FW, were 1.5 in blood and 0.6 in liver	2
Dietary route		
Fed cassava diets containing 4, 37, 70,	At all dietary levels, there	5

or 103 mg total cyanide per kilogram ration to day-old chicks for 8 weeks	was no significant effect on survival, growth, histology, hemoglobin, hematocrit, or lymphocyte number; however, serum thiocyanate levels increased in a dose-dependent manner	
Fed diets containing 135 mg HCN/kg Chicks, 20-day exposure	Growth and food intake significantly depressed; plasma thiocyanate concentration increased	6
Adults, 14-day exposure	Urinary excretion of thiocyanate increased 5 times in laying hens	6
California condor, *Gymnogyps californianus*		
Juvenile (8.4 kg), found dead, presumably of cyanide poisoning	No evidence of injuries or disease; yellow fluorescent particles found in mouth appeared like those placed in NaCN ejector mechanisms used in predator control. However, blood cyanide concentration was similar to that found in nonexposed vultures, including two captive California condors	2
Eastern screech-owl, *Otus asio*		
4.6 mg CN/kg BW, equivalent to 8.6 mg NaCN/kg BW	Acute oral LD50; 95% C.I. of 3.8 and 5.4 mg CN/kg BW	2
Canary, *Serinus canarius*		
0.12 mg HCN/L air	All dead in 3 min	2
European starling, *Sturnus vulgaris*		
9.0 mg CN/kg BW, as NaCN	Acute oral LD50; 95% C.I. of 4.8 and 17 mg CN/kg BW	2
Andean condor, *Vultur gryphus*		
Single oral dose of 19.1 mg CN/kg BW (36 mg NaCN/kg BW)	Blood sampled immediately after death contained 1.2 mg free CN per liter and 0.5 mg bound CN per liter	1

[a]1, Krynitsky et al. 1986; 2, Wiemeyer et al. 1986; 3, Oh et al. 1987; 4, Davis 1981; 5, Gomez et al. 1988; 6, Elzubeir and Davis 1988b; 7, Personal communication, E. F. Hill, Patuxent Wildlife Research Center.

Many species of migratory birds were found dead in the immediate vicinity of gold-mine heap-leach extraction facilities and tailings ponds, presumably as a result of drinking the cyanide-contaminated (>200 mg total cyanide per liter) waters (Clark and Hothem 1991). Migratory bird mortality from cyanide toxicosis may be eliminated at these facilities by screening birds from toxic solutions (Hallock 1990) or lowering the cyanide concentrations with hydrogen peroxide to <50 mg total cyanide per liter (Allen 1990), although the latter procedure requires verification (Clark and Hothem 1991).

Some birds may not die immediately after drinking lethal cyanide solutions. In Arizona, a red-breasted merganser *(Mergus serrator)* was found dead 20 km from the nearest known source of cyanide, and its pectoral muscle tissue tested positive for cyanide (Clark and Hothem 1991). A proposed mechanism to account for this phenomenon involves weak-acid dissociable (WAD) cyanide compounds. Cyanide bound to certain metals, usually copper, is dissociable in weak acids such as stomach acids. Clark and Hothem (1991) suggested that drinking of lethal cyanide solutions by animals may not result in immediate death if the cyanide level is

sufficiently low; these animals may die later when additional cyanide is liberated by stomach acid. More research is needed on WAD cyanide compounds.

Elevated cyanide concentrations were found in blood of chickens that died of cyanide poisoning; however, these concentrations overlapped those in survivors. Despite this variability, blood is considered more reliable than liver as an indicator of cyanide residues in exposed birds (Wiemeyer et al. 1986). No gross pathological changes in birds related to cyanide dosing were observed at necropsy (Wiemeyer et al. 1986), similar to other taxonomic groups tested.

Cyanide-nutrient interactions are reported for alanine, which appears to exacerbate cyanide toxicity, and for cystine, which seems to alleviate toxicity (Davis et al. 1988). Dietary cyanide--at levels that do not cause growth depression--alleviates selenium toxicity in chickens, but not the reverse (Davis et al. 1988; Elzubeir and Davis 1988a). For example, dietary selenium, as selenite, at 10 mg/kg for 24 days, reduced growth, food intake, and food utilization efficiency, and produced increased liver size and elevated selenium residues; the addition of 45 mg CN/kg diet (100 mg sodium nitroprusside per kilogram) eliminated all effects except elevated selenium residues in liver. The mechanism of alleviation is unknown and may involve a reduction of tissue selenium through selenocyanate formation, or increased elimination of excess selenium by increasing the amount of dimethyl selenide exhaled (Elzubeir and Davis 1988a). At dietary levels of 135 mg CN/kg plus 10 mg selenium per kilogram, chick growth was significantly decreased (Elzubeir and Davis 1988a). This interaction can be lost if there is a deficiency of certain micronutrients or an excess of vitamin K (Davis et al. 1988).

Mammals

Much of the toxicological interest in cyanide relating to mammals has focused on its rapid lethal action; however, its most widely distributed toxicologic problems are due to its toxicity from dietary, industrial, and environmental factors (Way 1981, 1984; Gee 1987; Marrs and Ballantyne 1987). Chronic exposure to cyanide is correlated with specific human diseases: Nigerian nutritional neuropathy, Leber's optical atrophy, retrobulbar neuritis, pernicious anemia, tobacco amblyopia, cretinism, and ataxic tropical neuropathy (Towill et al. 1978; Way 1981; Sprince et al. 1982; Berninger et al. 1989; Ukhun and Dibie 1989). The effects of chronic cyanide intoxication are confounded by various nutritional factors, such as dietary deficiencies of sulfur-containing amino acids, proteins, and water-soluble vitamins (Way 1981).

Most authorities now agree on five points: (1) cyanide has low persistence in the environment and is not accumulated or stored in any mammal studied; (2) cyanide biomagnification in food webs has not been reported, possibly due to rapid detoxification of sublethal doses by most species, and death at higher doses; (3) cyanide has an unusually low chronic toxicity, but chronic intoxication exists and, in some cases, can be incapacitating; (4) despite the high lethality of large single doses or acute respiratory exposures to high vapor concentrations of cyanide, repeated sublethal doses seldom result in cumulative adverse effects; and (5) cyanide, in substantial but sublethal intermittent doses can be tolerated by many species for long periods, perhaps indefinitely (Towill et al. 1978; EPA 1980; Way 1984; Ballantyne and Marrs 1987a; Table 5).

The toxicity of cyanogenic plants is a problem for both domestic and wild ungulates. Poisoning of herbivorous ungulates is more prevalent under drought conditions, when these mammals become less selective in their choice of forage; dry growing conditions also enhance cyanogenic glycoside accumulations in certain plants (Towill et al. 1978). Animals that eat rapidly are at greatest risk, and intakes of 4 mg HCN/kg BW can be lethal if consumed quickly (Egekeze and Oehme 1980). In general, cattle are most vulnerable to cyanogenic plants; sheep, horses, and pigs--in that order--are more resistant than cattle (Cade and Rubira 1982). Deer *(Odocoileus* sp.) and elk *(Cervus* sp.) have been observed to graze on forages that contain a high content of cyanogenic glycosides; however, cyanide poisoning has not been reported in these species (Towill et al. 1978).

Ruminant and nonruminant ungulate mammals that consume forage with high cyanogenic glycoside content, such as sorghums, Sudan grasses, and corn, may experience toxic signs due to microbes in the gut that hydrolyze the glycosides, releasing free hydrogen cyanide (Towill et al. 1978). Signs of acute cyanide poisoning in livestock usually occur within 10 min and include initial excitability with muscle tremors, salivation, lacrimation, defecation, urination, and labored breathing, followed by muscular incoordination, gasping, and convulsions; death can occur quickly, depending on the dose administered (Towill et al. 1978; Cade and Rubira 1982). Thyroid dysfunction has been reported in sheep grazing on stargrass *(Cynodon plectostachyus),* a plant with high cyanogenic glycoside and low iodine content. Sheep developed enlarged thyroids and gave birth to

lambs that were stillborn or died shortly after birth (Towill et al. 1978). Cyanogenic foods can exacerbate selenium deficiency, as judged by the increased incidence of nutritional myopathy in lambs on low-selenium diets (Elzubeir and Davis 1988a). A secondary effect from ingesting cyanogenic glycosides from forage is sulfur deficiency as a result of sulfur mobilization to detoxify the cyanide to thiocyanate (Towill et al. 1978).

Cyanide poisonings of livestock by forage sorghums and other cyanogenic plants are well documented (Cade and Rubira 1982). Horses in the southwestern United States grazing on Sudan grass and sorghums developed posterior muscle incoordination, urinary incontinence, and spinal cord histopathology; offspring of mares that had eaten Sudan grass during early pregnancy developed musculoskeletal deformities (Towill et al. 1978). Salt licks containing sulfur (8.5%) have been used to treat sheep after they failed to gain weight when grazing on sorghum with high HCN content (Towill et al. 1978). Sugar gum (*Eucalyptus cladocalyx*) and manna gum (*Eucalyptus viminalis*) contain high levels of cyanogenic glycosides, and both have been implicated as the source of fatal HCN poisoning in domestic sheep and goats that had eaten leaves from branches felled for drought feeding, or after grazing sucker shoots on lopped stumps (Webber et al. 1984). In one case, 10 goats died and 10 others were in distress within 2 h after eating leaves from a felled sugar gum. Dead goats had bright red blood that failed to clot and subepicardial petechial hemorrhages. Rumens of dead goats contained leaves of *Eucalyptus* spp. and smelled of bitter almonds. The 10 survivors were treated intravenously with 3 mL of a 1-L solution made to contain 20 g of sodium nitrite and 50 g of sodium thiosulphate; four recovered and six died. Of 50 afflicted goats, 24 died within 24 h and the remainder recovered (Webber et al. 1984). In rare instances HCN poisoning occurs when animals are exposed to chemicals used for fumigation or as a fertilizer (Webber et al. 1984), but there is general agreement that ingestion of plants containing high levels of cyanogenic glycosides is the most frequent cause of cyanide poisoning in livestock.

Cassava, also known as maniac, tapioca, yuca, or guacamate, is one of the very few--and, by far, the most important--food crops in which the cyanide content creates toxic problems (Cooke and Coursey 1981). Cassava is a major energy source for people and livestock in many parts of the world; it accounts for an average of 40% of the human caloric intake in Africa (Casadei et al. 1984), to more than 70% in some African diets (Way 1984). In comparison to other tropical crops it produces the highest yield per hectare (Okeke et al. 1985). Cassava is native to tropical America from southern Mexico to northern Argentina and probably has been under cultivation there for 4,000-5,000 years. It has been introduced to east Africa, Indian Ocean islands, southern India, and the Far East (Cooke and Coursey 1981). The global production of cassava roots was estimated at 50 million tons in 1950, and 100 million tons in 1980; about 44.2 million tons are grown annually in Africa, 32.7 million tons in tropical America, and 32.9 million tons in Asia (Cooke and Coursey 1981). Linamurin is the principal cyanogenic glycoside in cassava; its toxicity is due to hydrolysis by intestinal microflora releasing free cyanide (Padmaja and Panikkar 1989). Rabbits *(Oryctolagus cuniculus)* fed 1.43 mg linamurin per kilogram BW daily (10 mg/kg BW weekly) for 24 weeks showed effects similar to those of rabbits fed 0.3 mg KCN/kg BW weekly. Specific effects produced by linamurin and KCN included elevated lactic acid in heart, brain, and liver; reduced glycogen in liver and brain; and marked depletion in brain phospholipids (Padmaja and Panikkar 1989).

The use of cassava in animal feed presents two major problems: the presence of cyanogenic glycosides in the tuber, and the remarkably low protein levels in fresh and dried cassava. Pigs fed low-protein cassava diets for 8 weeks had reduced food consumption and lowered liver weight; addition of protein supplement to the diet reversed these trends (Tewe 1982b). Removal of cyanogenic glycosides from cassava tubers, mash, peels, and root meal is accomplished with several techniques. Usually, the cassava root is dried in the sun for several weeks, and this process removes most of the cyanogenic glycosides; however, under conditions of famine or food shortage, this process cannot be carried out properly (Cliff et al. 1984). Long fermentation periods, especially under conditions of high moisture content, may be effective in substantial detoxification of cassava mash (Ukhun and Dibie 1989). Cassava peels containing as much as 1,061 mg HCN/kg FW can be rendered suitable for feeding to livestock (4-625 mg/kg) by boiling for 7 min, roasting for 30 min, soaking for 15 h, or drying in the sun for 7.6 days (Okeke et al. 1985). Cassava root meal (up to 40% of cassava meal) is satisfactory as a diet supplement for domestic pigs, provided cyanide content is <100 mg/kg ration (Gomez et al. 1983).

Neuropathies associated with cassava ingestion (i.e., cyanide intoxication) can develop into a syndrome in humans and domestic animals, characterized by nerve deafness, optic atrophy, and an involvement of the sensory spinal nerve that produces ataxia. Other symptoms include stomatitis, glossitis, and scrotal dermatitis (Way 1981). Potentially more serious are long-term effects such as ataxic neuropathy, goiter, and cretinism,

which have been attributed to high cassava content in diets. Thiocyanate--one of the detoxification products--inhibits iodine absorption and promotes goiter, a common ailment in tropical countries (Cooke and Coursey 1981). At high dietary cyanide intakes there is an association with diabetes and cancer (Cliff et al. 1984), but this requires verification. The first case of cassava toxicity occurred almost 400 years ago (Cooke and Coursey 1981). The toxic principle was later identified as a cyanogenic glycoside, shown to be identical with flax linamurin (2-(beta-D-glucopyranosyloxy)-isobutyronitrile). All parts of the plant, except possibly the seeds, contain the glycoside together with the enzyme linamarase. This enzyme effects hydrolysis of the nitrile to free HCN when the tissue cellular structure is damaged (Cooke and Coursey 1981). Mantakassa disease is related to chronic cyanide intoxication associated with a diet consisting almost exclusively of cassava; in times of famine and sulfur-poor diets, Mantakassa effects were more pronounced (Casadei et al. 1984). Symptoms of Mantakassa disease include the sudden onset of difficulty in walking, increased knee and ankle reflexes, elevated serum thiocyanate levels, fever, pain, headache, slurred speech, dizziness, and vomiting. Women of reproductive age and children were the most seriously affected. Symptoms persisted for up to 4 months after treatment with hydroxycobalamin, vitamin supplements, and a high protein, energy-rich diet (Cliff et al. 1984). Mantakassa was reported in 1,102 victims in Mozambique in 1981 from a drought-stricken cassava staple area; from Zaire in 1928, 1932, 1937, and again in 1978-81; in Nigeria; and in the United Republic of Tanzania. The mean serum thiocyanate level in patients with Mantakassa is 2.6 times higher than in non-Mantakassa patients in Nigeria, and 3.5 times higher than in Tanzanian patients. Pesticides, infection, viruses, and consumption of food other than cassava were eliminated as possible causative agents in Mantakassa disease. Still unresolved is whether the disease is triggered when a threshold level of thiocyanate is reached, or when a critical combination of cyanide intoxication plus nutritional deficiency occurs (Cliff et al. 1984).

Routes of administration other than dietary ingestion should not be discounted. Livestock found dead near a cyanide disposal site had been drinking surface water runoff from the area that contained up to 365 mg HCN/L (EPA 1980). The use of cyanide fumigant powder formulations may be hazardous by contact of the powder with moist or abraded skin, contact with the eye, swallowing, and inhalation of evolved HCN (Ballantyne 1988). In rabbits, lethal systemic toxicity was produced by contamination of the eye, moist skin, or abraded skin (but not dry skin) with cyanide powder formulations (40% NaCN plus 60% kaolin) administered at 1-5 g powder per cubic meter (Ballantyne 1988). Hydrogen cyanide in the liquid state can readily penetrate the skin, and skin ulceration has been reported from splash contact with cyanides among workers in the electroplating and gold extraction industries--although effects in those instances were more likely due to the alkalinity of the aqueous solutions (Homan 1987). In one case, liquid HCN ran over the bare hand of a worker wearing a fresh air respirator; he collapsed into unconsciousness in 5 min, but ultimately recovered (EPA 1980).

Use of poisons in livestock collars is both specific and selective for animals causing depredations, as is the case for cyanide collars to protect sheep against coyotes (Sterner 1979; Table 5). These collars contain a 33% NaCN solution and are usually effective against coyotes. However, field results indicate that some coyotes kill by means other than neck attack, and some exhibit great wariness in attacking collared sheep (Savarie and Sterner 1979).

Calcium cyanide in flake form was used in the 1920's to kill black-tailed prairie dogs and pocket gophers *(Geomys bursarius)* in Kansas, and various other species of rodents in Nova Scotia (Wade 1924). For prairie dog control, the usual practice was to place 43-56 g of calcium cyanide 0.3-0.7 m below the rim of the burrow and to close the entrances. The moisture in the air liberated HCN gas, which remained in the burrow for several hours, producing 100% kill. A lower dose of 28 g per burrow was about 90% effective (Wade 1924). Control of prairie dogs with cyanide sometimes resulted in the death of burrowing owls that lived in the prairie dog burrows (Wade 1924).

Clinical signs of acute cyanide poisoning in mammals last only a few minutes after ingestion and include rapid and labored breathing, ataxia, cardiac irregularities, dilated pupils, convulsions, coma, respiratory failure, and rapid death (Egekeze and Oehme 1980; Ballantyne 1983). Cyanide poisoning causes cardiovascular changes as well as its better known effects on cellular respiration. Cyanide increases cerebral blood flow in rabbits and cats, and disrupts systemic arterial pressure in dogs (Robinson et al. 1985). Cyanide affects mammalian behavior, mostly motor functions, although these effects have not been quantified. Cyanide-induced motor alterations observed in rats and guinea pigs include muscular incoordination, increased whole-body locomotion, disrupted swimming performance, and altered conditioned avoidance responses (D'Mello 1987). As a consequence of the cytotoxic hypoxia in acute cyanide poisoning, there is a shift from aerobic to

anaerobic metabolism, and the development of lactate acidosis. A combination of rapid breathing, convulsions, and lactate acidosis is strongly suggestive of acute cyanide poisoning (Ballantyne 1983). As with other chemical asphyxiants, the critical organs that are most sensitive to oxygen depletion are the brain and heart (Egekeze and Oehme 1980). The only consistent postmortem changes found in animals poisoned by cyanide are those relating to oxygenation of the blood. Because oxygen cannot be utilized, venous blood has a bright-red color and is slow to clot (Egekeze and Oehme 1980). Bright-red venous blood is not a reliable indicator of cause of death, however, because it is also associated with chemicals other than cyanide (Ballantyne 1983).

Cyanide poisoning is associated with changes in various physiological and biochemical parameters. The earliest effect of cyanide intoxication in mice seems to be inhibition of hepatic rhodanese activity, due to either blockage by excess binding to the active site or to depletion of the sulfane-sulfur pool. These changes do not seem to occur in blood, where rhodanese functions at its maximal rate, thus preventing cyanide from reaching the target tissues and causing death (Buzaleh et al. 1989). Cyanide causes dose- and species-dependent responses on vascular smooth muscle; studies with isolated aortic strips indicate that rabbits are 80 times more sensitive than dogs or ferrets (*Mustela putorius*; Robinson et al. 1985). Rabbits killed with HCN had higher concentrations of cyanide in blood and other tissues and lower tissue cytochrome oxidase activities than did those killed with KCN (Ballantyne et al. 1972). Cyanide promotes dose- and calcium-dependent release of dopamine tissues in the domestic cat, and reductions in adenosine triphosphate (ATP) content of the carotid body (Obeso et al. 1989). Cyanide-induced hypoxia is believed to decrease ATP content of Type I glomus cells. The decrease in the phosphate transfer potential is a crucial step in the overall transduction process, that is, the activation of the transmitter release from Type I cells, with resultant release and activation of sensory nerve endings (Obeso et al. 1989). Studies with isolated heart of the domestic ferret demonstrate that cyanide affects intracellular ionic exchange of H^+, Na^+, and calcium (Fry et al. 1987); inhibits cardiac action potential (Elliott et al. 1989); and inhibits oxidative phosphorylation accompanied by an intracellular acidosis, a decrease in phosphocreatinine, and a rise in inorganic phosphate (Eisner et al. 1987). When oxidative phosphorylation is inhibited in cardiac muscle, there is a rapid decrease of developed force or pressure; most of the decrease of developed pressure produced by cyanide in ferret heart is not produced by intracellular acidosis, and may result from increased inorganic phosphate (Eisner et al. 1987). Observed changes in rat cerebral oxidative responses to cyanide may be due to redistribution of intracellular oxygen supply to mitochondria respiring in an oxygen-dependent manner or by branching effects within brain mitochondria (Lee et al. 1988). Hyperammonemia and the increase of neutral and aromatic amino acids may also be important in loss of consciousness induced by cyanide (Yamamoto 1989).

Table 5. Cyanide effects on selected species of mammals.

Species, dose, and other variables	Effects	Reference[a]
Cattle, *Bos* sp.		
Fed hybrid sorghum Sudan grass cross 988 at 15–20 kg per animal daily for 3–8 days	Of 180 cows, 21 were affected and 13 died; toxic cyanide levels were measured in fodder and in liver and ruminal contents of dead cows	44
Dog, *Canis familiaris*		
Administered doses up to 2 mg NaCN/kg body weight (BW), once or twice daily for 15 months	Acute toxic signs evident after each administration, but complete recovery within 30 min; no measurable adverse effects after 15 months	1
5.4 mg NaCN/kg BW, single subcutaneous injection	LD50	2
24 mg CN/kg BW, single oral or slow intravenous injection	Lethal; at time of respiratory arrest, blood plasma	3

route	concentration was 1 mg total CN per liter or about 0.4 mg free cyanide per liter	
Fed diets containing 150 mg NaCN/kg for 30 days	No measurable effect on food consumption, blood chemistry, behavior, or organ histology	1
Coyote, *Canis latrans*		
Single forced oral dose of NaCN, in mg/kg BW		
4	Immobilized in 13 min, but all survived for at least 30 days; some sacrificed after 30 min: NaCN residues in mg/kg fresh weight (FW) were 0.03 in blood and 0.9 in stomach	2
4.1 (2.1–8.3)	LD50	2
8	Immobilization in 9 min, death within 41 min	2
16, 32, or 64	All immobilized in less than 1 min and all died in less than 8 min. Maximum NaCN residues were 0.14 mg/L in blood and 13.0 mg/L FW in stomach	2
"Toxic" collars attached to neck of sheep and camouflaged with wool; each collar contained 50 mL of a 33% NaCN solution; toxic action commences when coyote attacks sheep and punctures collar; all coyotes tested were known to attack sheep in laboratory pens	Of three coyotes tested, one was immobilized in 1 min and died within 18 min; the other two coyotes recovered; the dead coyote had mouthed the collar for about 2 s; residues in mg NaCN/kg, were 0.26 in blood and <0.1 in stomach; the other two coyotes had mouthed the collar for 3–15 s and had NaCN levels, in mg/kg FW, of 0.014 and 0.029 in blood, and 0.6 and <0.1 in stomach	2
Toxic collar, as above; each coyote tested was known to have fatally attacked at least three domestic sheep within a 30-day period	Of the 12 coyotes that attacked the neck region of the sheep and punctured the collar, nine received lethal doses and became immobilized in 1–3 min and died 3–25 min later; the mean time to death was 11.6 min; one of the three sublethally dosed coyotes survived at last three successful attacks in which the collar was punctured, and two survived two attacks; in all cases, contact with NaCN	4

	produced shaking of the head, pawing at the mouth, rubbing the snout on the ground, and ataxia	
African giant rat, *Cricetomys gambianus*		
Weanlings fed diets for 16 weeks containing 0 mg HCN/kg (maize), 110 mg HCN/kg (cassava pulp), 150 mg HCN/kg (cassava tuber), or 597 mg HCN/kg (cassava peel)	Food consumption was similar in all diets; no pathology was observed in any organ of animals on all treatments; rats on maize and cassava pulp diets had significantly increased growth rate, feed efficiency, and protein efficiency; rats on cassava peel and tuber diets had significantly increased thiocyanate levels in serum, organs, and urine	5
Juveniles, age 10–14 weeks, fed cassava peel diets for 2 weeks containing 720 mg HCN/kg	Adverse effects on growth when cassava peel exceeds 7.8% of the ration	6
Weanlings fed 1,000 mg CN/kg diet, as KCN, for 12 weeks	Reduction in feed intake, reduced body weight, elevated thiocyante concentrations in serum (37.4 mg/L vs. 12.6), urine (341 mg/L vs. 25), liver (1.7 g/kg FW vs. 0.4), kidney (2.4 g/kg FW vs. 0.4), and spleen (2.1 g/kg FW vs. 0.3)	7
Humans, *Homo sapiens*		
Intentional oral ingestion of unknown amount of NaCN or KCN, three cases	Death between 5 and 30 min; stomach cyanide concentrations ranged between 100 and 164 mg; tissue residues postmortem in mg/kg FW, were 0.3–1.1 in blood, 0.3–1.0 in liver, and 0.2–0.3 in brain	8
Found dead, four cases, time to death unknown	Maximum cyanide concentration in stomach was 230 mg; maximum tissue residues, in mg/kg FW were 3.5 in blood, 6.3 in liver, and 0.5 in brain	8
Attempted suicide by 39-year-old-male, unknown amount of NaCN	Severe tremors and progressive loss of muscle tone--representing the first case of cyanide intoxication with delayed onset of symptoms	9
Inhalation of HCN gas, in mg/m^3, for various time intervals		

140 for 60 min	Calculated LC50	10
220 for 30 min	Calculated LC50	10
504 for 10 min	Calculated LC50	10
680 for 5 min	Calculated LC50	10
1,500 for 3 min	Calculated LC50	10
4,400 for 1 min	Calculated LC50	10
Inhalation of 2,000 mg HCN/L	First breath results in deep, rapid breathing, with collapse, convulsions, and death within 1 min	11
Inhalation of cyanogen chloride, in mg/L, for various time intervals		
1, 10 min	Irritant	1
48, 30 min	Fatal	1
159, 10 min	Fatal	1
Inhalation of cyanogen bromide, in mg/L, for various time intervals		
1.4, no time given	Irritant to eyes and nose	1
92, 10 min	Fatal	1
Single oral dose		
0.5–3.5 mg HCN/kg BW	Lethal	12, 41
0.7–3.5 mg KCN/kg BW, equivalent to 50 to 250 mg KCN/adult	Fatal	10
2 mg HCN/kg BW, or total of about 150 mg HCN	Acute LD50 for adults	13
1–5 g of NaCN or KCN, equivalent to 0.2 g/adult or 3 mg/kg BW	Minimum lethal dose	14
Tissue residues		
Whole blood, 1–2 mg free cyanide per liter	Usually lethal	42
Whole blood, 2.6–3.1 mg total CN per liter	Minimum cyanide concentration associated with death in an otherwise healthy individual	13
Whole blood, 2.6–3.1 mg total CN per liter	Minimum cyanide concentration associated with death in an otherwise healthy individual	13
Whole blood, 4–45 mg total CN per liter	Levels measured in known suicides	13
Whole body, 7 mg HCN/kg BW	Residue associated with minimum lethal dose	11
Daily dietary intake of 15–31.5 mg hydrogen cyanide from cassava	Mantakassa disease--see text for discussion	15
100 mg HCN/kg BW applied to skin surface	LD50	11
Clothing inundated with 10% NaCN solution, pH 11.4	Clinical signs of toxicity within 25 min and death in about 60 min	13
Livestock		
>200 mg HCN/kg plant materials in diet	Potentially dangerous	13

Cynomolgus monkeys, *Macaca* spp.		
Given multiple sublethal doses of KCN (5–18 mg) for 23 days	Brain histoapathology	3
Exposed to HCN gas produced from combustion of polyacrylonitrile materials at various temperatures		
300º C, 87–170 mg HCN/L air	Incapacitated in 16–30 min; blood cyanide of 4.3 mg/L	16
600º C, 120–174 mg HCN/L air	Incapacitated between 6 and 24 min, blood cyanide of 2.96 mg/L	16
900º C, 166–196 mg HCN/L air	Incapacitated between 2 and 13 min; blood cyanide concentration of 3.1 mg/L	16
Exposed to HCN gas at air concentrations of 60, 80, or 150 mg HCN/L for 30 min	At 60 mg/L, HCN had only a slight depressive effect on the central nervous system; at 80 and 150 mg/L, severe CNS depression and incapacitation occurred	17
Exposed to HCN gas at air concentrations of 100, 1092, 123, 147, or 156 mg HCN/L air	Incapacitated in 8 min at higher doses to 19 min at lowest dose tested; blood cyanide after 30 min exposure ranged between 1.7 mg/L at 100 mg HCN/L and 3.2 mg/L at 156 mg HCN/L; after recovery for 60 min, blood CN ranged between 2.0 and 2.9 mg/L	16
Domestic mouse, *Mus* spp.		
Single intraperitoneal injection		
HCN, 2.8 mg/kg BW	LD50	10
NaCN, 4.6–5.9 mg/kg BW	LD50	10
KCN, 5.3–6.7 mg/kg BW	LD50	10
Acetone cyanohydrin, $(CH_3)_2C(OH)CN$, 8.7 mg/kg BW	LD50 (7 days); first death in 5 min	18
Malonitrile, $NCCH_2CN$, 18 mg/kg BW	LD50 (7 days); first death in 4.8 h	18
Propionitrile, CH_3CH_2CN, 28 mg/kg BW	LD50 (7 days); first death in 21 h	18
N-butyronitrile, 38 mg/kg BW	LD50 (7 days); first death in 2.2 h	18
Acrylonitrile, CH_2CHCN, 46 mg/kg BW	LD50 (7 days); first death in 2.3 h	18
Succinonitrile, $NCCH_2CH_2CN$, 62 mg/kg BW	LD50 (7 days); first death in 5.1 h	18
Acetonitrile, CH_3CN, 175 mg/kg BW	LD50 (7 days); first death in 7.1 h	18
Single subcutaneous injection		
HCN, 7.8–12.0 mg/kg BW	LD50	10
KCN, 10 mg/kg BW	Loss of consciousness in 100%; blood ammonia levels increased 2.5 times; brain amino acid levels (i.e., leucine,	19

	isoleucine, tyrosine, phenylalanine) increased by 1.5–3.0 times; alpha ketoglutarate, at 500 mg/kg BW by intraperitoneal injection, completely blocked the development of cyanide-induced loss of consciousness and hyperammonemia	
Single oral dose		
8.5 mg KCN/kg BW, equivalent to 3.4 mg CN^-/kg BW	LD50	10, 20
Drinking water, 1,000 mg KCN/L, exposure for 40 days	Marked inhibition of cytochrome oxidase activity in liver, brain, and blood; increased cyanide concentrations in all tissues; inhibition of rhodanese activity; diminished labile sulfur tissue levels	43
Rabbit, *Oryctolagus* spp.		
Isolated aorta strips, 0.00014 µg NaCN/L–140 µg/L	Small contractions measured at lowest dose tested, ED50 at 70 µg/L, and maximum response at 140 µg/L; higher doses up to 14 mg/L produced relaxation	21
Single intramuscular injection, in mg/kg BW		
0.5–1.5	LD50 for HCN	10
1.6	LD50 for NaCN	10
3.1–3.3	LD50 for KCN	10
8.0		
Killed with KCN	Cyanide concentrations, in mg/kg FW, were 1.6 in serum, 5.3 in blood, and <0.4 in other tissues sampled	22
Killed with HCN	Cyanide concentrations, in mg/kg FW, were 9.3 in blood, 2.1 in brain, 2.0 in serum, 0.5 in myocardium, and <0.4 in other tissues	22
Single intravenous injection, in mg/kg BW		
0.6	LD50 for HCN	10
1.2	LD50 for NaCN	10
1.9	LD50 for KCN	10
Single dose administered to eye surface, in mg/kg BW		
1.0	LD50 for HCN	10
4.5–5.1	LD50 for NaCN	10
7.9	LD50 for KCN	10
11.2	Signs of NaCN poisoning in 3 min, death in 7 min	23
Single intraperitoneal injection, in mg/kg BW		
1.7–2.0	LD50 for HCN	10
2.8–2.9	LD50 for NaCN	10

3.6–4.0	LD50 for KCN	10
Administered as solution to skin, in mg/kg BW		
2.3	LD50 for HCN and abraded skin	10
6.9	LD50 for HCN and intact skin	10
14.3	LD50 for KCN and abraded skin	10
19.3	Abraded skin; signs of NaCN poisoning evident in 25 min, death in 41 min	23
22.3	LD50 for KCN and intact skin	10
29.5	Moist skin; signs of NaCN poisoning evident in 79 min, death in 117 min	23
>110	Dry skin; no signs of NaCN poisoning, no deaths	23
Single oral dose, in mg/kg BW		
2.5	LD50 for HCN	10
5.1	LD50 for NaCN	10
5.8	LD50 for KCN	10
12.8	Signs of NaCN poisoning in 4 min, death in 22 min	23
Single oral dose, NaCN, 10–15 mg/kg BW	All dead in 14–30 min; blood cyanide ranged between 3.7 and 5.4 mg/L	24
Inhalation of HCN from combustion of 20 g of polyacrylonitrile	All dead in 12–16 min; blood cyanide ranged between 1.6 and 3.1 mg/L	24
Interval between death and removal of tissues for analysis in rabbits killed by KCN		
Brain	Concentrations dropped from 1.6 mg/kg FW immediately after death to 1.2 in 1 day, 0.92 in 3 days, and 0.04 in 7 days	25
Blood	Residues, in mg/kg FW were 5.7 immediately after death and 2.3 after 21 days	25
Lung	Cyanide concentrations dropped from 2 mg/kg FW just after death, to 0.8 in 7 days	25
Domestic sheep, *Ovis aries*		
Intravenous or intraarterial injection, fetal lambs 80% through gestation (120 days), NaCN, 50–400 µg	Slowing of fetal heart rate, disruption of respiratory movements, significant but inconsistent changes in arterial blood pressure	26
Single intramuscular injection of 10 mg KCN/kg BW	All dead within 17 min; cyanide concentrations postmortem, in mg/kg FW, were 3.3 in blood, 1.5 in plasma, 1.6 in serum, 1.4 in cerebrospinal fluid, 0.9 in brain grey matter, and 1.0 in brain white matter	3, 10, 27
Laboratory white rat, *Rattus* spp.		
Single intraperitoneal injection		

0.1–10 mg CN/kg BW	LD50	28
5 mg NaCN or KCN/kg BW	50% decrease in brain cytochrome oxidase activity within 5–10 min	14
5 mg KCN/kg BW	Reversible intracellular metabolic changes including acidosis and increased lactate levels--typical of cellular anoxia	29
Intravenous injection, constant infusion of 0.15–0.20 mg CN/kg BW per min	LD50 in about 20 min. Rapid progressive reduction in cerebrocortical cytochrome oxidase (cytochrome aa_3) concomitant with increases up to 200% in cerebral blood flow	30
Single intracartoid artery injection of KCN		
1–2 mg/kg BW	Modest acute clinical dysfunction and incomplete suppression of brain electroencephalographic (EEG) activity	31
2.5 mg/kg BW	Some deaths; survivors showed rapid abolition of brain EEG activity, 52% reduction in brain cytochrome oxidase activity, 600% increase in lactate, 85% decrease in glycogen, 32% reduction in ATP, and 73% increase in ADP; all values returned to normal in 6–24 h, and remained normal for balance of 7-day observation period	31
3.5–5 mg/kg BW	High incidence of cardiovascular collapse and death within minutes	31
Tissue residues 2.6–2.9 mg HCN/L	Minimum lethal concentrations in rats poisoned orally with KCN	13
Inhalation exposure route, HCN vapor, in mg/m^3, for various periods		
3,778 for 10 s	LC50	10
1,128 for 1 min	LC50	10
493 for 5 min	LC50	10
151–173 for 30–60 min	LC50	10
Single oral dose		
3.4 mg KCN/kg BW	LD25	32
3.6–4.2 mg HCN/kg BW	LD50	10
5.1–5.7 mg NaCN/kg BW	LD50	10
5.7 mg KCN/kg BW	LD50	32
6, 10, or 14 mg KCN/kg BW	Some deaths in all groups; all dead at higher doses within 60 min; those killed 10 min postadministration had	13

	higer blood CN concentrations than those killed near death or at survival at 60 min	
6.4 mg NaCN/kg BW	LD50	13
7.5–10 mg KCN/kg BW	LD50	10, 13
8.6 mg KCN/kg BW	LD98	32
10 mg KCN/kg BW, equivalent to 4 mg HCN/kg BW	LD50	20
13.2 mg NaCN/kg BW or 7 mg HCN/kg BW	Dead in 10.3 min; tissue cyanide levels, in mg/kg FW, were 8.9 in liver, 5.9 in lung, 4.9 in blood, 2.1 in spleen, and 1.5 in brain	33
40 mg NaCN/kg BW, equivalent to 21 mg HCN/kg BW	Dead in 3.3 min	33
Drinking water exposure		
Equivalent to 8 mg CN/kg BW daily for 21 days	Liver normal	20
Equivalent to 21 mg CN/kg BW daily for 21 days	Significantly increased liver weight	20
200 mg CN/L for 4 weeks	Reduced growth	34
Drinking water of adults contained 150 mg CN/L, as KCN, for 2 weeks, followed by injection with radioselenium-75 and observed for 15 days	Cyanide-treated rats excreted significantly more radioselenium in urine than did controls; half-time persistence of radioselenium in treated group was 28 days vs. 38 days in controls	35
Drinking water of weanling males contained 150 mg CN/L for 9 weeks	Significant reduction in glutathion activity, and in selenium concentrations in blood kidney, liver, and muscle	35
Dietary exposure		
Fed 12 mg CN/kg BW daily for 2 years, equivalent to 300 mg HCN/kg ration	No measurable adverse effects on blood chemistry, growth, survival, or histology; elevated thiocyanate levels in liver and kidneys	1
Fed 500 mg HCN/kg ration to pregnant rats through gestation and lactation	No effect on reproduction	20
Weanlings fed diets of raw lima beans containing 727 mg CN/kg for 3 weeks, or 727 mg CN/kg diet as KCN for 3 weeks	Lima bean diet alone increased hepatic glutamate dehydrogenase (GLDH) and decreased isocitrate dehydrogenase (ICDH) activities; KCN diet had no effect on GLDH and increased ICDH activity, emphasizing the importance of dietary components when evaluating CN-containing diets	36
750 mg CN/kg diet (1,875 mg KCN/kg diet) for 8 weeks,	No measurable effect on food consumption or growth rate;	37

adequate protein	significantly increased serum and urinary thiocyanate concentrations	
As above, protein deficient diet	Reduction in body weight gain, reduction in serum thiocyanate concentration	37
Weanling males fed diets containing 1,500 mg KCN/kg, or 2,240 mg potassium thiocyanate (KSCN)/kg for 50 weeks	No deaths or clinical signs of toxicity; both groups had decreased thyroid gland activity; cyanide, but not thiocyanate, caused reduction in growth rate	38
Isolated liver segments from starved rats exposed to 100 mg KCN/L	Oxygen consumption reduced 80%, and evidence of hepatotoxicity as judged by enzyme release, glutathione depletion, and calcium accumulation in liver; hepatotoxicity prevented by feeding rats fructose	39
Domestic pig, *Sus* spp.		
Fed diet containing 96 mg CN/kg ration, as cassava peel for 72 days	No effect on food consumption or protein metabolism	40

[a]1, EPA 1980; 2, Sterner 1979; 3, Christel et al. 1977; 4, Savarie and Sterner 1979; 5, Tewe 1984; 6, Tewe 1988; 7, Tewe 1982a; 8, Curry 1963; 9, Grandas et al. 1989; 10, Ballantyne 198a; 11, Towill et al. 1978; 12, Ukhun and Dibie 1989; 13, Egekeze and Oehme 1980; 14, Way 1981; 15, Casadei et al. 1984; 16, Purser et al. 1984; 17, Purser 1984; 18, Willhite and Smith 1981; 19, Yamamoto 1989; 20, EPA 1989; 21, Robinson et al. 1985; 22, Ballantyne et al. 1972; 23, Ballantyne 1988; 24, Yamamoto et al. 1979; 25, Ballantyne et al. 1974; 26, Itskovitz and Rudolph 198; 27, Ballantyne 1975; 28, Brattsten et al. 1983; 29, Lotito et al. 1989; 30, Lee et al. 1988; 31, MacMillan 1989; 32, Keniston et al. 1987; 33, Yamamoto et al. 1982; 34, Palmer and Olson 1981; 35, Beilstein and Whanger 1984; 36, Aletor and Fetuga 1988; 37, Tewe and Maner 1985; 38, Philbrick et al. 1979; 39, Younes and Strubelt 1988; 40, Tewe and Pessu 1982; 41, Way 1984; 42, Marrs and Ballantyne 1987; 43, Buzaleh et al. 1989; 44, Bapat and Abhyankar 1984.

Organic cyanide compounds, or nitriles, have been implicated in numerous human fatalities and signs of poisoning—specially acetonitrile, acrylonitrile, acetone cyanohydrin, malonitrile, and succinonitrile. Nitriles hydrolyze to carboxylic acid and ammonia in either basic or acidic solutions. Mice *(Mus* sp.) given lethal doses of various nitriles had elevated cyanide concentrations in liver and brain; the major acute toxicity of nitriles is CN release by liver processes (Willhite and Smith 1981). In general, alkylnitriles release CN much less readily than aryl alkylnitriles, and this may account for their comparatively low toxicity (Davis 1981).

No human cases of illness or death due to cyanide in water supplies are known (EPA 1980). Accidental acute cyanide poisonings in humans are uncommon (Towill et al. 1978); however, a man accidentally splashed with molten sodium cyanide died about 10 h later (Curry 1963). Human cyanide deaths usually involve suicides, where relatively large amounts of sodium cyanide or potassium cyanide are ingested and the victims die rapidly in obvious circumstances. Recovery after oral ingestion is rare. In one case, a spouse emptied capsules containing medicine and repacked them with 40% solid NaCN. The victim took one capsule and ingested about 0.05 g, but vomited and recovered completely (Curry 1963). Human deaths are increasing from gas or smoke inhalation from urban fires, possibly owing to the increased toxicity of fire atmospheres caused by the use of organocyanide plastics in modern construction and furnishings (Egekeze and Oehme 1980). Hydrogen cyanide may be important in some fires in producing rapid incapacitation, causing the victims to remain in the fire and die from carbon monoxide or other factors, although HCN concentrations of 60 mg/L air and lower had minimal effects (Purser 1984). Exposure to the mixture of HCN and carbon monoxide, with accompanying changes in cerebral blood flow during attempts to escape from fires, may be a cause of collapse and subsequent death

(Purser 1984). For example, cynomolgus monkeys (*Macaca* spp.) exposed to pyrolysis products of polyacrylonitrile (PAN) and to low-level HCN gas had similar physiological effects in both atmospheres, specifically: hyperventilation, followed by loss of consciousness after 1-5 min; and brachycardia, with arrhythmias and T-wave abnormalities. Recovery was rapid following cessation of exposure (Purser et al. 1984). Because HCN is the major toxic product formed by the pyrolysis of PAN, Purser et al. (1984) suggested that HCN may produce rapid incapacitation at low blood levels of cyanide in fires, while death may occur later due to carbon monoxide poisoning or other factors.

Finally, cyanide does not appear to be mutagenic, teratogenic, or carcinogenic in mammals (EPA 1980; Ballantyne 1987a). In fact, there has been a long-standing hypothesis for an anticancer effect of the cyanogenic glycoside amygdalin (also called laetrile). The hypothesis is based on amygdalin's selective hydrolysis by a beta glucosidase, liberating cyanide and benzaldehyde at the neoplastic site. The cyanide then selectively attacks the cancer cell, which is presumed to be low in rhodanese, whereas normal cells are assumed to possess sufficient rhodanese and sulfur to detoxify the cyanide (Way 1981). However, many tumors are neither selectively enriched in beta glucosidase nor low in rhodanese (Way 1981).

Recommendations

Proposed free cyanide criteria suggest that sensitive species of aquatic organisms are protected at <3 µg/L, birds and livestock at <100 mg/ kg diet, and human health at concentrations of <10 µg/L drinking water, <50 mg/kg diet, and <5 mg/m^3 air (Table 6).

Analytical methodologies need to be developed that differentiate between free cyanide (HCN and CN^-) and other forms of cyanide, and that are simple, sensitive (i.e., in the µg/L range), and accurate (Smith et al. 1979; Leduc et al. 1982). Procedures need to be standardized that ensure prompt refrigeration and analysis of all samples for cyanide determination because some stored samples generate cyanide while others show decreases (Gee 1987).

Periodic monitoring of cyanide in waterways is unsatisfactory for assessing potential hazards because of cyanide's rapid action, high toxicity, and low environmental persistence. A similar case is made for cyanide in the atmosphere. Development of a continuous monitoring system of cyanides in waterways and air is recommended, with emphasis on point source dischargers, such as industrial and municipal facilities (Towill et al. 1978; Egekeze and Oehme 1980; Leduc et al. 1982). Information is needed on the fate of cyanide compounds in natural waters, relative contributions of natural and anthropogenic sources, and critical exposure routes for aquatic organisms (Leduc et al. 1982). Additional research is needed on the origin of cyanide in wilderness and rural watershed areas, specifically the roles of organic wastes and their associated bacterial flora, aquatic vegetation induced by nutrient enrichment, and terrestrial plant cover in the watershed (Leduc 1984).

Table 6. Proposed free cyanide criteria for the protection of living resources and human health.

Resource criterion, and other variables	Concentration	Reference[a]
Freshwater organisms		
Effect levels, in µg/L medium		
Minimal impairment, most species of fish	3–5	1, 2, 3, 4, 5, 6
Reduced survival, amphipods	>3–34	1, 7
Safe, most fish species	3.5 (24-h average, not to exceed 52 at any time)	7
Significant impairment, most species of fish	8–16, exposure for at least 20 days	6, 7
Hazardous		
Most fish species	>11	1, 4
Microorganisms	>300	8

Reduced survival, chronic exposure		
Bivalve molluscs, larvae	>14	1
Fish, many species	30–150	1, 5
Impaired reproduction, sensitive species of fish	>25	2
Impaired swimming ability, growth, development, and behavior	>100	3, 6
Lethal to rapidly lethal, acute exposure	300–1,000	5
Marine organisms		
Effect levels, in µg/L seawater		
Adverse effects, chronic exposure	>2	7
Minimal risk	<5	1
Hazardous	>10	1
Lethal	>30	7
Sediments, Great Lakes		
Effect level, in mg total cyanide/kg dry weight (DW)		
Nonpolluted	<0.10	20
Moderately polluted	0.1–0.25	20
Heavily polluted	>0.25	20
Birds		
Domestic chickens		
Diet, safe level, in mg total cyanide/kg ration fresh weight (FW)	90–<100	9, 10
Waterfowl		
Drinking water, safe	<50	21, 22
Livestock		
level in mg/L total cyanide		
Diet, safe level, in mg/kg FW		
Free cyanide	<100	9
Total cyanide	<625	11
Forage, hazardous level, in mg/kg FW	>200	8
Laboratory white rat		
Diet, safe level, in mg/kg ration FW	<1,000	19
Blood, in mg/L		
Normal	0.25–0.45	12
Minimum lethal concentration	2.6–2.9	12
Liver		
Minimum lethal concentration, in mg/kg FW	0.5–6.1	12
Human health		
Drinking water, in µg/L		
Recommended	<5–<10	1, 6, 8, 13
United States nationwide survey	Max. 8	7
Safe	<10	1
Goal, United States	<10	7, 14
Maximum allowable limit, United States	10	13
Goal, Canada	<20	7
Lifetime health advisory, United States and Canada	<154	14

Acceptable	<200	7
Mandatory limit	200	13
Rejected	>200	1, 8
10-day health advisory		
Child	<220	14
Adult	<770	14
Diet		
Acceptable daily intake		
Water	1.5 mg, equivalent to 0.02 mg/kg body weight (BW) daily for 70-kg adult	15
Food, in mg/kg BW	8.4	7
Food, in mg/kg FW	<50	15
Food, in mg total cyanide/kg FW	<415	11
Cassava, *Manihot esculenta*, roots, total cyanide, in mg/kg FW		
Safe	<50	16
Moderately toxic	50–100	16
Very poisonous	>100	16
Food items, in mg/kg		
Cocoa	<20 DW	13
Beans, nuts	<25 DW	1
Cereals, grains	<25 DW	13
Citrus fruits	<50 FW	1
Uncooked pork	<50 FW	13
Grains	<75 FW	1
Cereals flours	<125 DW	13
Spices	<250 FW	1, 13
Frozen meat	<950 FW	1, 13
Bakery products, yeast	<1,500 DW	13
Egg white solids	<1,000 DW	13
Tissue residues		
Blood and spleen, in µg/L or µg/kg FW		
Normal	77	17
Suspected poisoning	>1,000	17
Whole blood, in µg/L		
Usually fatal	1,000–2,000	15
Whole body, in mg/kg BW		
Fatal	4, if taken rapidly	18
Air, in mg/m^3		
Recommended safe levels		
Soviet Union, Romania, Hungary, Bulgaria, Czechoslovakia	<0.3	1
United States	<5	14
Most countries	<11	1, 15
Occupational exposure		
Proposed safe level, United States	<3	15
Safe ceiling concentration	<5	1
Hazardous levels	4.2–12.4	1
Soils in mg/kg DW		
Free cyanide		
Background	1	20
Moderate contamination	10	20
Requires cleanup	100	20
Complex cyanide		
Background	5	20

Moderate contamination	50	20
Requires cleanup	100	20

[a]1, Towill et al. 1978; 2, Smith et al. 1979; 3, Doudoroff 1976; 4, Leduc 1981; 5, Leduc 1984; 6, Leduc et al. 1982; 7, EPA 1980; 8, Egekeze and Oehme 1980; 9, Gomez et al. 1983; 10, Gomez et al. 1988; 11, Okeke et al. 1985; 12, Egekeze and Oehme 1979; 13, EPA 1973; 14, EPA 1989; 15, Marrs and Ballantyne 1987; 16, Dufour 1988; 17, Gee 1987; 18, Shaw 1986; 19, Tewe 1982; 20, Beyer 1990; 21, Allen 1990; 22, Clark and Hothem 1991.

In aquatic systems research is needed in several areas: (1) long-term effects of cyanide on life cycles, growth, survival, metabolism, and behavior of a variety of aquatic organisms and microorganisms in addition to fish (Towill et al. 1978; Leduc et al. 1982); (2) effects of seasonal pulses of cyanide on aquatic organisms in rural and wilderness areas (Leduc 1984); (3) influence of various environmental parameters (e.g., oxygen, pH, temperature), if any, on adaptive resistance to cyanide (Leduc 1981, 1984); and (4) usefulness of various biochemical indicators of cyanide poisoning, such as cytochrome oxidase inhibition (Gee 1987) and vitellogenin levels in fish plasma (*gairdneri*) (Ruby et al. 1986).

The use of M-44 sodium cyanide capsules for predator control was suspended and cancelled by the U.S. Environmental Protection Agency on 9 March 1972. M-44 use was again permitted by the U.S. Environmental Protection Agency beginning on 4 February 1976, provided that "each authorized or licensed applicator shall carry an antidote kit on his person when placing or inspecting M-44 devices. The kit shall contain at least 6 pearls of amylnitrite and instructions on their use. Each authorized or licensed applicator shall also carry on his person instructions for obtaining medical assistance in the event of accidental exposure to sodium cyanide" (EPA 1976a, 1976b).

Farmers need to be aware of factors that influence the cyanogenic potential of forage crops and to conduct regular inspections of grazing fields for cyanogenic plants. Moreover, hay and silage should be properly cured in order to minimize cyanide content before feeding to livestock (Egekeze and Oehme 1980). Selective breeding of plants with low cyanide content will help reduce livestock poisoning, but the most advisable prevention method at present is to prohibit grazing on fields where cyanogenic plants are present (Egekeze and Oehme 1980). More research seems needed on (1) effects of drought and other factors that may increase the concentration of cyanogenic glycosides in livestock forage plants, (2) mechanisms of cyanide liberation by plants, and (3) effects of cyanide on wildlife and range animals that graze on foliage with high cyanogenic glycoside content (Towill et al. 1978).

Research is needed on low-level, long-term cyanide intoxication in mammals by oral and inhalation routes in the vicinities of high cyanide concentrations, especially on the incidence of skin dermatitis, nasal lesions, and thyroid dysfunction, and on urinary thiocyanate concentrations. These types of studies may provide a more valid rationale in establishing standards and threshold limit values for HCN and inorganic cyanide (Towill et al. 1978; Egekeze and Oehme 1980).

Data are scarce on the carcinogenic, teratogenic, and mutagenic properties of cyanide, and on the distribution and transformation of cyanides in air, land, or water. Additional analysis of available information and more research in these areas is recommended. Finally, more research is needed on cyanide toxicokinetics because cyanide is a very reactive nucleophile that distributes widely through the body, is permeable to cell membranes, and may accumulate in the fetus (Towill et al. 1978).

Acknowledgments

I thank L. Garrett, N. Hestbeck, and W. Manning for literature search and retrieval services; M. Holmes and B. Roberts for secretarial assistance; D. R. Clark, Jr., C. J. Henny, J. B. Hunn, and G. C. Miller for technical review of the manuscript; and J. R. Zuboy for editorial services.

References

Abel, P. D., and S. M. Garner. 1986. Comparison of median survival times and median lethal exposure times for *Gammarus pulex* exposed to cadmium, permethrin and cyanide. Water Res. 20:579-582.

Adams, J. B. 1989. Inhibition of green bean lipoxygenase by cyanide. Food Chem. 31:243-250.

Alabaster, J. S., D. G. Shurben, and M. J. Mallett. 1983. The acute lethal toxicity of mixtures of cyanide and ammonia to smolts of salmon, *Salmo salar* L. at low concentrations of dissolved oxygen. J. Fish Biol. 22:215-222.

Aletor, V. A., and B. L. Fetuga. 1988. The interactive effects of lima bean *(Phaseolus lunatus)* trypsin inhibitor, hemagglutinin and cyanide on some hepatic dehydrogenases, ornithine carbamoyltransferase and intestinal disaccharidases in weanling rats. Vet. Hum. Toxicol. 30:540-544.

Allen, C. H. 1990. Mitigating impacts to wildlife at FMC Gold Company's Paradise Peak mine. Pages 67-71 *in* Proceedings of the Nevada wildlife/ mining workshop, 27-29 March 1990, Reno, Nev. Available from Nevada Mining Assoc., 3940 Spring Drive, Reno, Nev. 89502.

Alstrom, S., and R. G. Burns. 1989. Cyanide production by rhizobacteria as a possible mechanism of plant growth inhibition. Biol. Fert. Soils 7:232-238.

Azcon-Bieto, J., J. Murillo, and J. Penuelas. 1987. Cyanide-resistant respiration in photosynthetic organs of freshwater aquatic plants. Plant Physiol. 84:701-706.

Ballantyne, B. 1975. Blood, brain and cerebrospinal fluid cyanide concentrations in experimental acute cyanide poisoning. J. Forensic Sci. Soc. 15:51-56.

Ballantyne, B. 1983. Artifacts in the definition of toxicity by cyanides and cyanogens. Fund. Appl. Toxicol. 3:400-408.

Ballantyne, B. 1987a. Toxicology of cyanides. Pages 41-126 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Ballantyne, B. 1987b. Hydrogen cyanide as a product of combustion and a factor in morbidity and mortality from fires. Pages 248-291 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Ballantyne, B. 1988. Toxicology and hazard evaluation of cyanide fumigation powders. Clin. Toxicol. 26:325-335.

Ballantyne, B., S. P. Boardman, J. Bright, D. J. Coffee, T. D. Weber, and P. Williams. 1972. Tissue cyanide concentrations and cytochrome oxidase activities in experimental cyanide poisoning. Br. J. Pharmacol. 44(2):382P-383P.

Ballantyne, B., J. E. Bright, and P. Williams. 1974. The post-mortem rate of transformation of cyanide. Forensic Sci. 3:71-76.

Ballantyne, B., and T. C. Marrs, editors. 1987a. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England. 512 pp.

Ballantyne, B., and T. C. Marrs. 1987b. Post-mortem features and criteria for the diagnosis of acute lethal cyanide poisoning. Pages 217-247 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Bapat, J. A., and Y. N. Abhyankar. 1984. Cyanide poisoning in cattle due to feeding of sorghum. Indian J. Anim. Sci. 54:577-578.

Barney, P. J. 1989. Salt kills! Anal. Fin. 12(1):1.

Barron, M. G., and I. R. Adelman. 1984. Nucleic acid, protein content, and growth of larval fish sublethally exposed to various toxicants. Can. J. Fish. Aquat. Sci. 41:141-150.

Barron, M. G., and I. R. Adelman. 1985. Temporal characterization of growth of fathead minnow (*Pimephales promelas*) larvae during sublethal hydrogen cyanide exposure. Comp. Biochem. Physiol. 81C:341-344.

Becker, C. E. 1985. The role of cyanide in fires. Vet. Hum. Toxicol. 27:487-490.

Beilstein, M. A., and P. D. Whanger. 1984. Effects of cyanide on selenium metabolism in rats. J. Nutr. 114:929-937.

Bello-Reuss, E., T. P. Grady, and L. Reuss. 1981. Mechanism of the effect of cyanide on cell membrane potentials in *Necturus* gall-bladder epithelium. J. Physiol. 314:343-357.

Berninger, T. A., L. V. Meyer, E. Siess, O. Schon, and F. D. Goebel. 1989. Leber's hereditary optic atrophy: further evidence for a defect of cyanide metabolism? Br. J. Opthamol. 73:314-316.

Beyer, W. N. 1990. Evaluating soil contamination. U.S. Fish Wild. Serv., Biol. Rep. 90(2). 25 pp.

Biehl, M. 1984. Cyanide toxicosis. Veterinary Professional Topics, University of Illinois at Urbana, Cooperative Extension Service 10(3):5-6.

Billard, R., and P. Roubaud. 1985. The effect of metals and cyanide on fertilization in rainbow trout (*Salmo gairdneri*). Water Res. 19:209-214.

Blago, R. B. 1989. Indirect determination of free cyanide by atomic absorption spectroscopy. Atomic Spectrosc. 10:74-76.

Brattsten, L. B., J. H. Samuelian, K. Y. Long, S. A. Kincaid, and C. K. Evans. 1983. Cyanide as a feeding stimulant for the southern armyworm, *Spodoptera eridania*. Ecol. Entomol. 8:125-132.

Brimer, L. 1988. Determination of cyanide and cyanogenic compounds in biological systems. Pages 177-200 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Foundation Symposium 140. John Wiley, Chichester, England.

Buzaleh, A. M., E. S. Vazquez, and A. M. C. Batlle. 1989. Cyanide intoxication-I. An oral chronic animal model. Gen. Pharmacol. 20:323-327.

Cade, J. W., and R. J. Rubira. 1982. Cyanide poisoning of livestock by forage sorghums. Government of Victoria, Department of Agriculture, Agnote 1960/82. 2 pp.

Cailleux, A., J. F. Subra, P. Riberi, E. Tuchais, A. Premel-Cabic, and P. Allain. 1988. Cyanide and thiocyanate blood levels in patients with renal failure or respiratory disease. J. Med. 19:345-351.

Casadei, E., P. Jansen, A. Rodrigues, A. Molin, and H. gosling. 1984. Mantakassa: an epidemic of spastic paraparesis associated with chronic cyanide intoxication in a cassava staple area of Mozambique. 2. Nutritional factors and hydrocyanic acid content of cassava products. Bull. World Health Org. 62:485-492.

Christel, D., P. Eyer, M. Hegemann, M. Kiese, W. Lorcher, and N. Weger. 1977. Pharmacokinetics of cyanide in poisoning of dogs, and the effect of 4-dimethylaminophenol on thiosulfate. Arch. Toxicol. 38:177-189.

Clark, D. R., Jr., and R. L. Hothem. 1991. Mammal mortality at Arizona, California, and Nevada gold mines using cyanide extraction. Calif. Fish Game 77:61-69.

Cliff, J., A. Martelli, A. Molin, and H. Rosling. 1984. Mantakassa: an epidemic of spastic paraparesis associated with chronic cyanide intoxication in a cassava staple area of Mozambique. 1. Epidemiology and clinical and laboratory findings in patients. Bull. World Health Org. 62:477-484.

Connolly, G., and G. D. Simmons. 1984. Performance of sodium cyanide ejectors. Pages 114-121 *in* D. O. Clark, ed. Proceedings of the Eleventh Vertebrate Pest Conference. University of California Press, Davis.

Cooke, R. D., and D. G. Coursey. 1981. Cassava: a major cyanide-containing food group. Pages 93-114 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Curry, A. S. 1963. Cyanide poisoning. Acta Pharmacol. Toxicol. 20:291-294.

Curry, A. S., D. E. Price, and E. R. Rutter. 1967. The production of cyanide in post mortem material. Acta Pharmacol. Toxicol. 25:339-344.

Da Costa, H., and S. M. Ruby. 1984. The effect of sublethal cyanide on vitellogenic parameters in rainbow trout *Salmo gairdneri*. Arch. Environ. Contam. Toxicol. 13:101-104.

Davis, R. H. 1981. Cyanide detoxication in the domestic fowl. Pages 51-60 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Davis, R. H., E. A. Elzubeir, and J. S. Craston. 1988. Nutritional and biochemical factors influencing the biological effects of cyanide. Pages 219-231 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England.

Dixon, G. D., and G. Leduc. 1981. Chronic cyanide Poisoning of rainbow trout and its effects on growth, respiration, and liver histopathology. Arch. Environ. Contam. Toxicol. 10:117-131.

D'Mello, G. D. 1987. Neuropathological and behavioural sequelae of acute cyanide toxicosis in animal species. Pages 156-183 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Doudoroff, P. 1956. Some experiments on the toxicity of complex cyanides to fish. Sewage Ind. Wastes 28:1020-1040.

Doudoroff, P. 1976. Toxicity to fish of cyanides and related compounds-a review. U.S. Environ. Prot. Agency Rep. 600/3-76-038. 161 pp.

Drews, G., and K. Graszynski. 1987. The transepithelial potential difference in the gills of the fiddler crab, *Uca tangeri*: influence of some inhibitors. J. Comp. Physiol. 157B:345-353.

Duffey, S. S. 1981. Cyanide and arthropods. Pages 385-414 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Dufour, D. L. 1988. Cyanide content of cassava (*Manihot esculenta,* Euphorbiaceae) cultivars used by Tukanoan indians in northwest Amazonia. Econ. Bot. 42:255-266.

Egekeze, J. O., and R. W. Oehme. 1979. Blood and liver cyanide concentrations in rats poisoned with oral doses of potassium cyanide. Toxicol. Lett. 3:243-247.

Egekeze, J. O., and F. W. Oehme. 1980. Cyanides and their toxicity: a literature review. Vet. Q. 2:104-114.

Eisner, D. A., A. C. Elliott, and G. L. Smith. 1987. The contribution of intracellular acidosis to the decline of developed pressure in ferret hearts exposed to cyanide. J. Physiol. 391:99-108.

Elliott, A. C., G. L. Smith, and D. G. Allen. 1989. Simultaneous measurements of action potential duration and intracellular ATP in isolated ferret hearts exposed to cyanide. Circ. Res. 64:583-591.

Elzubeir, E. A., and R. H. Davis. 1988a. Effect of dietary sodium nitroprusside as a source of cyanide on the selenium status of chicks given diets of varying selenium concentration. Br. Poult. Sci. 29:769-777.

Elzubeir, E. A., and R. H. Davis. 1988b. Sodium nitroprusside, a convenient source of dietary cyanide for the study of chronic cyanide toxicity. Br. Poult. Sci. 29:779-783.

Environmental Protection Agency. 1973. Water quality criteria 1972. U.S. Environ. Prot. Agency Rep. R3-73-033. 594 pp.

Environmental Protection Agency. 1976a. M-44 sodium cyanide capsules. Approval of registration for use in device to control predators and waiver of data in support of registration and classification. Fed. Regist. 41(39):8415-8416.

Environmental Protection Agency. 1976b. Registration of M-44 sodium cyanide capsules to control predators. Modification of order. Fed. Regist. 41(56):11871-11874.

Environmental Protection Agency. 1980. Ambient water quality criteria for cyanides. U.S. Environ. Prot. Agency Rep. 440/5-80-037. 72 pp.

Environmental Protection Agency. 1989. Cyanide. Rev. Environ. Contam. Toxicol. 107:53-64.

Evered, D., and S. Harnett, editors. 1988. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England. 261 pp.

Fry, C. H., D. P. Harding, and J. P. Mounsey. 1987. The effects of cyanide on intracellular ionic exchange in ferret and rat ventricular myocardium. Proc. R. Soc. Lond. 230B:53-75.

Gee, D. J. 1987. Cyanides in murder, suicide and accident. Pages 209-216 in B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Gomez, G., M. A. Aparicio, and C. C. Willhite. 1988. Relationship between dietary cassava cyanide levels and broiler performance. Nutr. Rep. Int. 37:63-75.

Gomez, G., M. Valdivieso, J. Santos, and C. Hoyos. 1983. Evaluation of cassava root meal prepared from low- or high-cyanide containing cultivars in pig and broiler diets. Nutr. Rep. Int. 28:693-704.

Grandas, F., J. Artieds, and J. A. Obeso. 1989. Clinical and CT scan findings in a case of cyanide intoxication. Movement Disord. 4:188-193.

Halkier, B. A., H. V. Scheller, and B. L. Moller. 1988. Cyanogenic glucosides: the biosynthetic pathway and the enzyme system involved. Pages 49-66 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wile , Chichester, England.

Hallock, R. J. 1990. Elimination of migratory bird mortality at gold and silver mines using cyanide extraction. Pages 9-17 *in* Proceedings of the Nevada wildlife/mining workshop, 27-29 March 1990, Reno, Nev. Available from Nevada Mining Assoc., 3940 Spring Drive, Reno, Nev. 89502.

Holden, A.V., and K. Marsden. 1964. Cyanide in salmon and brown trout. Department of Agriculture and Fisheries of Scotland, Freshwater Salmon Fish. Res. Ser. 33. 12 pp.

Homan, E. R. 1987. Reactions, processes and materials with potential for cyanide exposure. Pages 1-21 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Itskovitz, J., and A. M. Rudolph. 1987. Cardiorespiratory response to cyanide of arterial chemoreceptors in fetal lambs. Am. J. Physiol. 252(5, Part 2):H916-H922.

Jones, D. A. 1988. Cyanogenesis in animal-plant interactions. Pages 151-170 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England.

Kaderbhai, M. A., R. B. Beechey, and N. Kaderbhai. 1989. Protein synthesis in isolated castor bean mitochondria is stimulated by cyanide. Plant Physiol. 89:669-673.

Kelada, N. P. 1989. Automated direct measurements of total cyanide species and thiocyanate and their distribution in wastewater and sludge. J. Water Pollut. Control Fed. 61:350-356.

Keniston, R. C., S. Cabellon, Jr., and K. S. Yarbrough. 1987. Pyridoxal 5'-phosphate as an antidote for cyanide, spermine, gentamicin, and dopamine toxicity: an in vivo rat study. Toxicol. Appl. Pharmacol. 88:433-441.

Knocke, W. R. 1981. Electroplating and cyanide wastes. J. Water Pollut. Control Fed. 53:847-851.

Knowles, C. J. 1988. Cyanide utilization and degradation by microorganisms. Pages 3-15 in D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England.

Knudson, T. 1990. Gold mining's deadly life blood. Sacramento (California) Bee (newspaper), 21 March 1990.

Kovacs, T. G., and G. Leduc. 1982a. Sublethal toxicity of cyanide to rainbow trout (*Salmo gairdneri*) at different temperatures. Can. J. Fish. Aquat. Sci. 39:1389-1395.

Kovacs, T. G., and G. Leduc. 1982b. Acute toxicity of cyanide to rainbow trout acclimated at different temperatures. Can. J. Fish. Aquat. Sci. 39:1426-1429.

Krynitsky, A. J., S. N. Wiemeyer, E. F. Hill, and J. W. Carpenter. 1986. Analysis of cyanide in whole blood of dosed cathartids. Environ. Toxicol. Chem. 5:787-789.

Lagas, P., J. P. G. Loch, and K. Harmsen. 1982. The behaviour of cyanide in a landfill and the soil beneath it. Pages 169-178 *in* R. Perry, ed. Effects of waste disposal on groundwater and surface water. Int. Assoc. Hydrol. Sci., Publ. 139.

Leduc, G. 1978. Deleterious effects of cyanide on early life stages of Atlantic salmon (*Salmo salar*). J. Fish. Res. Board Can. 35:166-174.

Leduc, G. 1981. Ecotoxicology of cyanides in freshwater. Pages 487-494 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Leduc, G. 1984. Cyanides in water: toxicological significance. Pages 153- 224 *in* L. J. Weber, ed. Aquatic toxicology, Vol. 2. Raven Press, New York.

Leduc, G., R. C. Pierce, and I. R. McCracken. 1982. The effects of cyanides on aquatic organisms with emphasis upon freshwater fishes. Natl. Res. Counc. Canada, Publ. NRCC 19246. 139 pp. Available from Publications, NRCC/CNRC, Ottawa, Canada KlA OR6.

Lee, P. A., A. L. Sylvia, and C. A. Piantdosi. 1988. Cyanide-related changes in cerebral O_2 delivery and metabolism in fluorocarbon-circulated rats. Toxicol. Appl. Pharmacol. 94:34-44.

Lennon, R. E., J. B. Hunn, R. A. Schnick, and R. M. Buress. 1970. Reclamation of ponds, lakes, and streams with fish toxicants: a review. Food and Agriculture Organization of the United Nations, FAO Fish. Tech. Pap. 100:57-61.

Lesniak, J. A., and S. M. Ruby. 1982. Histological and quantitative effects of sublethal cyanide exposure on oocyte development in rainbow trout. Arch. Environ. Contam. Toxicol. 11:343-352.

Lotito, S., P. Blondet, A. Francois, M. V. Kienlin, C. Remy, J. P. Albrand, M. Decorps, and A. L. Benabid. 1989. Correlation between intracellular pH and lactate levels in the rat brain during cyanide induced metabolism blockade: a combined ^{31}P-^{1}H in vivo nuclear magnetic spectroscopy study. Neurosci. Lett. 97:91-96.

Low, K. S., and C. K. Lee. 1981. Cyanide uptake by water hyacinths, *Eichhornia crassipes* (Mart). Solms. Pertanika 42:122-128.

Lundquist, P., and B. Sorbo. 1989. Rapid determination of toxic cyanide concentrations in blood. Clin. Chem. 35:617-619.

Lussier, S. M., J. H. Gentile, and J. Walker. 1985. Acute and chronic effects of heavy metals and cyanide on *Mysidopsis bahia* (Crustacea: Mysidacea). Aquat. Toxicol. 7:25-35.

MacMillan, V. H. 1989. Cerebral energy metabolism in cyanide encephalopathy. J. Cereb. Blood Flow Metab. 9:156-162.

Manning, K. 1988. Detoxification of cyanide by plants and hormone action. Pages 93-110 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England.

Marking, L. L., T. D. Bills, and J. R. Crowther. 1984. Effects of five diets on sensitivity of rainbow trout to eleven chemicals. Prog. Fish-Cult. 46:1-5.

Marrs, T. C. 1987. The choice of cyanide antidotes. Pages 383-401 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Marrs, T. C., and B. Ballantyne. 1987. Clinical and experimental toxicology of cyanides: an overview. Pages 473-495 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

McGeachy, S. M., and G. Leduc. 1988. The influence of season and exercise on the lethal toxicity of cyanide of rainbow trout (*Salmo gairdneri*). Arch. Environ. Contam. Toxicol. 17:313-318.

Mengel, K., W. Kramer, B. Isert, and K. D. Friedberg. 1989. Thiosulphate and hydroxocobalamin prophylaxis in progressive cyanide poisoning in guinea-pigs. Toxicology 54:335-342.

Mintorovitch, J., D. V. Pelt, and J. D. Satterlee. 1989. Kinetic study of the slow cyanide binding to *Glycera dibranchiata* monomer hemoglobin components III and IV. Biochemistry 28:6099-6104.

Moore, J. W. 1981. Influence of water movements and other factors on distribution and transport of heavy metals in a shallow bay (Canada). Arch. Environ. Contam. Toxicol. 10:715-724.

Nahrstedt, A. 1988. Cyanogenesis and the role of cyanogenic compounds in insects. Page 131-150 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England.

Nonomura, M., and T. Hobo. 1989. Ion chromatographic determination of cyanide compounds by chloramine-T and conductivity measurement. J. Chromatogr. 465:395-401.

Obeso, A., L. Almaraz, and C. Gonzalez. 1989. Effects of cyanide and uncouplers on chemoreceptor activity and ATP content of the cat carotoid body. Brain Res. 41:250-257.

Oh, S. Y., S. Jalaludin, R. H. Davis, and A. H. Sykes. 1987. Detoxication of cyanide in the chicken by conversion to thiocyanate, as influenced by the availability of transferable sulphur. Comp. Biochem. Physiol. 86B:129-133.

Ohno, T. 1989. Spectrophotometric determination of total cyanide in surface waters following ultraviolet induced photodecomposition. Analyst 114:857-858.

Okeke, G. C., F. C. Obioha, and A. E. Udeogu. 1985. Comparison of detoxification methods for cassava-borne cyanide. Nutr. Rep. Int. 32:139-147.

Okolie, N. P., and E. N. Ugochukwu. 1989. Cyanide contents of some Nigerian legumes and the effect of simple processing. Food Chem. 32:209-216.

Padmaja, G., and K. R. Panikkar. 1989. Intermediary metabolic changes in rabbits administered linamurin or potassium cyanide. Indian J. Exp. Biol. 27:635-639.

Palmer, I. S., and 0. E. Olson. 1981. Effect of cyanide on selenium status in rats fed low selenium diets. Nutr. Rep. Int. 24:635-641.

Philbrick, D. J., J. B. Hopkins, D. C. Hill, J. C. Alexander, and R. G. Thomson. 1979. Effects of prolonged cyanide and thiocyanate feeding in rats. J. Toxicol. Environ. Health 5:579-592.

Purser, D. A. 1984. A bioassay model for testing the incapacitating effects of exposure to combustion product atmospheres using cynomolgus monkeys. J. Fire Sci. 2:20-36.

Purser, D. A., P. Grimshaw, and K. R. Berrill. 1984. Intoxication by cyanide in fires: a study in monkeys using polyacrylonitrile. Arch. Environ. Health 39:394-400.

Rees, J. F., and F. Baguet. 1989. Metabolic control of luminescence in the luminous organs of the teleost *Porichthys:* effects of the metabolic inhibitors iodoacetic acid and potassium cyanide. J. Exp. Biol. 143:347-357.

Robinson, C. P., S. 1. Baskin, N. Visnich, Jr., and D. R. Franz. 1985. The effects of cyanide and its interactions with norepinephrine on isolated aorta strips from the rabbit, dog, and ferret. Toxicology 35:59-72.

Robinson, W. B. 1943. The "humane coyote-getter" vs. the steel trap in control of predatory animals. J. Wildl. Manage. 7:179-189.

Ruby, S. M., D. R. Idler, and Y. P. So. 1986. The effect of sublethal cyanide exposure on plasma vitellogenin levels in rainbow trout (*Salmo gairdneri*) during early vitellogenesis. Arch. Environ. Contam. Toxicol. 15:603-607.

Ruby, S. M., D. R. Idler, and Y. P. So. 1987. Changes in plasma, liver, and ovary vitellogenin in landlocked Atlantic salmon following exposure to sublethal cyanide. Arch. Environ. Contam. Toxicol. 16:507-510.

Savarie, P. J., and R. T. Sterner. 1979. Evaluation of toxic collars for selective control of coyotes that kill sheep. J. Wildl. Manage. 43:780-783.

Sawyer, P. L., and A. G. Heath. 1988. Cardiac, ventilatory and metabolic responses of two ecologically dissimilar species of fish to waterborne cyanide. Fish Physiol. Biochem. 4:203-219.

Shaw, J. M. 1986. Suspected cyanide poisoning in two goats caused by ingestion of crab apple leaves and fruits. Vet. Rec. 119:242-243.

Simovic, L., and W. J. Snodgrass. 1985. Natural removal of cyanides in gold milling effluents-evaluation of removal kinetics. Water Pollut. Res. J. Can. 20:120-135.

Smatresk, N. J. 1986. Ventilatory and cardiac reflex responses to hypoxia and NaCN in *Lepisosteus osseus,* an air-breathing fish. Physiol. Zool. 59:385-397.

Smatresk, N. J., M. L. Burleson, and S. Q. Azizi. 1986. Chemoreflexive responses to hypoxia and NaCN in longnose gar: evidence for two chemoreceptor loci. Am. J. Physiol. 251(1, Part 2):R116-R125.

Smith, L. L., S. J. Broderius, D. M. Oseid, G. L. Kimball, and W. M. Koenst. 1978. Acute toxicity of hydrogen cyanide to freshwater fishes. Arch. Environ. Contam. Toxicol. 7:325-337.

Smith, L. L., Jr., S. J. Broderius, D. M. Oseid, G. L. Kimball, W. M. Koenst, and D. T. Lind. 1979. Acute and chronic toxicity of HCN to fish and invertebrates. U.S. Environ. Prot. Agency Rep. 600/3-79-009. 129 pp.

Solomonson, L. P. 1981. Cyanide as a metabolic inhibitor. Pages 11-28 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Sprince, H., G. G. Smith, C. M. Parker, and D. A. Rinehimer. 1982. Protection against cyanide lethality in rats by L-ascorbic acid and dehydroascorbic acid. Nutr. Rep. Int. 25:463-470.

Sterner, R. T. 1979. Effects of sodium cyanide and diphacinone in coyotes (*Canis latrans*): applications as predacides in livestock toxic collars. Bull. Environ. Contam. Toxicol. 23:211-217.

Sykes, A. H. 1981. Early studies on the toxicology of cyanide. Pages 1-9 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Tatsumoto, H., and T. Hattori. 1988. Appearance of cyanide from waste solutions containing no cyanides. Environ. Tech. Lett. 9:1431-1435.

Tewe, O. O. 1982a. Effect of dietary cyanide on the performance, metabolism and pathology of the African rat (*Cricetomys gambianus* Waterhouse). Nutr. Rep. Int. 26:529-536.

Tewe, O. O. 1982b. Protein supplementation of cassava diets for growing pigs: effects on performance, nutrient utilization and cyanide metabolism. Nutr. Rep. Int. 25:451-462.

Tewe, O. O. 1984. Effect of cassava-based diets varying in cyanide content on the performance and physiopathology of the African giant rat (*Cricetomys gambianus* Waterhouse). Anim. Feed Sci. Technol. 11:1-9.

Tewe, O. O. 1988. Performance, nutrient utilization and cyanide metabolism in African giant rats (*Cricetomys gambianus* Waterhouse) fed varying dietary levels of cassava peels. Anim. Technol. 39:77-82.

Tewe, O. O., and J. H. Maner. 1985. Cyanide, protein and iodine interaction in the performance and metabolism of rats. J. Environ. Pathol. Toxicol. Oncol. 6:69-77.

Tewe, O. O., and E. Pessu. 1982. Performance and nutrient utilization in growing pigs fed cassava peel rations containing different cyanide levels. Nutr. Rep. Int. 26:51-58.

Thompson, R. S. 1984. Measurement of the inhibition of amino acid uptake. A toxicity test procedure using mussels *(Mytilus edulis).* Pages 535-545 *in* G. Persoone, E. Jaspers, and C. Claus, eds. Ecotoxicological testing for the marine environment. Proc. Int. Symp. Ecotoxicol. Test. Mar. Environ., Ghent, Belgium, 12-14 September 1983. Laboratory for Biological Research in Aquatic Pollution, State University of Ghent, Bredene, Belgium.

Towill, L. E., J. S. Drury, B. L. Whitfield, E. B. Lewis, E. L. Galyan, and A. S. Hammons. 1978. Reviews of the environmental effects of pollutants: v. cyanide. U.S. Environ. Prot. Agency Rep. 600/1-78-027. 191 pp.

Ukhun, M. E., and E. N. Dibie. 1989. Cyanide content of cassava mash and gari flour and influence of water activity (a_W) during storage. Bull. Environ. Contam. Toxicol. 42:548-552.

Van De Venter, H. A. 1985. Cyanide-resistant respiration and cold resistance in seedlings of maize (*Zea mays* L.). Ann. Bot. 56:561-563.

Vennesland, B., E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, editors. 1981a. Cyanide in biology. Academic Press, New York. 548 pp.

Vennesland, B., E. K. Pistorius, and H. S. Gewitz. 1981b. HCN production by microalgae. Pages 349-361 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Vesey, C. J. 1987. Nitroprusside cyanogenesis. Pages 184-208 *in* B. Ballantyne and T. C. Marrs, eds. Clinical and experimental toxicology of cyanides. John Wright, Bristol, England.

Voisard, C., C. Keel, D. Haas, and G. Defago. 1989. Cyanide production by *Pseudomonas fluorescens* helps suppress black root rot by tobacco under gnotobiotic conditions. Eur. Mol. Biol. Organ. J. 8:351-358.

Wade, 0. 1924. The effectiveness of calcium cyanide in the extermination of the black tail prairie dog, *Cynomys ludovicianus* (Ord.). J. Econ. Entomol. 17:339-342.

Way, J. L. 1981. Pharmacologic aspects of cyanide and its antagonism. Pages 29-40 *in* B. Vennesland, E. E. Conn, C. J. Knowles, J. Westley, and F. Wissing, eds. Cyanide in biology. Academic Press, New York.

Way, J. L. 1984. Cyanide intoxication and its mechanism of antagonism. Ann. Rev. Pharmacol. Toxicol. 24:451-481.

Way, J. L., P. Leung, E. Cannon, R. Morgan, C. Tamulinas, J. Leong-Way, L. Baxter, A. Nagi, and C. Chui. 1988. The mechanism of cyanide intoxication and its antagonism. Pages 232-243 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England.

Webber, J. J., C. R. Roycroft, and J. D. Callinan. 1984. Cyanide poisoning of goats from sugar gums (*Eucalyptus cladocalyx*). Aust. Vet. J. 62:28.

Westley, J. 1988. Mammalian cyanide detoxification with sulphane sulphur. Pages 201-218 *in* D. Evered and S. Harnett, eds. Cyanide compounds in biology. Ciba Found. Symp. 140. John Wiley, Chichester, England.

Wiemeyer, S. N., E. F. Hill, J. W. Carpenter, and A. J. Krynitsky. 1986. Acute oral toxicity of sodium cyanide in birds. J. Wildl. Dis. 22:538-546.

Wiemeyer, S. N., J. M. Scott, M. P. Anderson, P. H. Bloom, and C. J. Stafford. 1988. Environmental contaminants in California condors. J. Wildl. Manage. 52:238-247.

Wiley, R. W. 1984. A review of sodium cyanide for use in sampling stream fishes. N. Am. J. Fish. Manage. 4:249-256.

Willhite, C. C., and R. P. Smith. 1981. The role of cyanide liberation in the acute toxicity of aliphatic nitriles. Toxicol. Appl. Pharmacol. 59:589-602.

Wu, X. Z., M. Yamada, T. Hobo, and S. Suzuki. 1989. Uranine sensitized chemiluminescence for alternative determinations of copper (II) and free cyanide by the flow injection method. Anal. Chem. 61:1505-1510.

Yamamoto, H. A. 1989. Hyperammonemia, increased brain neutral and aromatic amino acid levels, and encephalopathy induced by cyanide in mice. Toxicol. Appl. Pharmacol. 99:415-420.

Yamamoto, K., Y. Yamamoto, H. Hattori, and T. Samori. 1982. Effects of routes of administration on the cyanide concentration distribution in the various organs of cyanide-intoxicated rats. Tohuku J. Exp. Med. 137:73-78.

Yamamoto, K., Y. Yamamoto, and C. Kuwahara. 1979. A blood cyanide distribution study in the rabbits intoxicated by oral route and by inhalation. Z. Rechtsmed. 83:313-317.

Yasuno, M., S. Fukushima, F. Shioyama, J. Hasegawa, and S. Kasuga. 1981. Recovery processes of benthic flora and fauna in a stream after discharge of slag containing cyanide. Verh. Int. Ver. Theor. Angew. Limnol. 21:1154-1164.

Younes, M., and 0. Strubelt. 1988. Cyanide-induced injury to the isolated perfused rat liver. Pharmacol. Toxicol. 63:382-385.

Biological Report 24
May 1992

Contaminant Hazard Reviews
Report No. 24

Fenvalerate Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

TABLES

FIGURES

Fenvalerate Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

Abstract

Synthetic pyrethroids are the newest major class of broad-spectrum organic insecticides used in agricultural, domestic, and veterinary applications, and now account for more than 30% of global insecticide use. Fenvalerate [(RS) α-cyano-3-phenoxybenzyl (RS) 2-(4-chlorophenyl)-3-methylbutyrate] is one of the newer synthetic pyrethroid insecticides and the one most widely used. Technical fenvalerate is a mixture of four optical isomers, each occurring in equal amounts, but with different efficacies against insect pests. Insecticidal properties are largely associated with the 2S, αS isomer and, to a minor extent, with the 2S, αR isomer. Isomers with a 2R configuration have negligible biocidal properties; however, tumorlike growths in rodent liver are associated with the comparatively innocuous 2R, αS isomer. Pyrethroid insecticides are potent neurotoxicants that interfere with nerve membrane function by interaction with the sodium channel. Fenvalerate is among the most effective pyrethroid neurotoxicants tested, and the 2S, αS isomer is as much as 15 times more potent than other fenvalerate isomers.

Fenvalerate persists for < 10 weeks in the environment and does not accumulate readily in the biosphere. Time for 50% loss (Tb ½) in fenvalerate-exposed amphibians, birds, and mammals is 6-14 h; for reptiles, terrestrial insects, aquatic snails, and fish it is usually > 14 h-<2 days, and for crop plants it is 2-28 days. In nonbiological compartments, Tb ½ is as long as 6 days in fresh water, 34 days in seawater, 6 weeks in estuarine sediments, and 9 weeks in soils.

At recommended application rates to control pestiferous crop insects, fenvalerate and other synthetic pyrethroids are relatively harmless to birds, mammals, and terrestrial plants; however, certain nontarget species, including bees, crustaceans, and fish, are at considerable risk, especially at low temperatures. Target insect species are usually killed at fenvalerate concentrations of 0.015 µg/insect, 0.11 kg/ha by way of aerial application, 5.4 mg/kg in soil, or 50 mg/kg in diet. Fenvalerate is especially toxic to aquatic organisms (e.g., crustaceans died at 0.003-0.03 µg/L and fish and amphibians at 0.09-1.1 µg/L), and its use in or near aquatic environments now seems contraindicated. Birds and mammals are significantly more resistant than fish and invertebrates. Adverse effects on birds occur at acute oral doses >500 mg/kg body weight (BW), and 750 mg/kg ration; <50 mg fenvalerate per kilogram of feed produced no appreciable residues in eggs and meat of exposed birds. Among sensitive mammals, adverse effects on survival occur at acute oral doses of 50—450 mg/kg BW, dietary loadings of 50-1,000 mg/kg feed, and dermal applications of 1,800 mg/kg BW.

Criteria have not yet been formulated by regulatory agencies for protection of sensitive fish and wildlife resources against fenvalerate. Current guidelines for protection of poultry, livestock, and human health include <50 mg/kg in poultry diets, <5 mg/kg in livestock diets, <3 mg/kg in human diets, and <0. 125 mg/kg BW daily in humans.

Key words: Fenvalerate, insecticide, pyrethroid, crops, aquatic life, birds, wildlife, livestock, invertebrates, ecotoxicology, criteria.

Synthetic pyrethroids, including fenvalerate [(RS) α-cyano-3-phenoxybenzyl (RS) 2-(4-chlorophenyl)-3methylbutyrate]αS isomer (A. Stavola, U.S. Environmental Protectin Agency, personal communication, 28 January 1991.[1], are now broadly recognized as a major class of synthetic organic insecticides (Gray and Soderlund 1985). Introduced commercially less than 20 years ago, synthetic pyrethroids now account for more than 30% of insecticide use worldwide (Flannigan et al. 1985; Gilbert et al. 1989) in household, agricultural, and veterinary applications (Haya 1989; Williamson et al. 1989). More than 1,000 pyrethroids have been synthesized since 1973 (Flannigan et al. 1985); they include compounds containing nitrogen, sulphur, fluorine, chlorine, and bromine, in addition to carbon, hydrogen, and oxygen (Glickman and Casida 1982). The most potent synthetic pyrethroid insecticides are the cyanophenoxybenzyl pyrethroids (Casida and Lawrence 1985); fenvalerate is the most widely used compound in this group (Clark et al. 1985).

Pyrethroid insecticides are synthetic analogs of natural pyrethrins. Natural pyrethrins were widely used in Europe during the 19th century, when few effective insecticides were available (Elliott and Janes 1978). Natural pyrethrins, which contain six insecticidally active components extracted from the dried flower heads of the pyrethrum flower (*Chrysanthemum cinariaefolium*), have high insecticidal properties and low mammalian toxicity; however, they are expensive to produce and have low photostability and high biodegradability (Wouters and Bercken 1978; Gray and Soderlund 1985; Haya 1989; Williamson et al. 1989). Modern synthetic pyrethroids have been designed to provide enhanced residual activity through greater photostability and greater resistance to chemical and biological degradation, greater insecticidal activity, diminished mammalian toxicity, and greater cost effectiveness (Elliott and Janes 1978; Vijverberg and Bercken 1982; Gray and Soderlund 1985; Smith and Stratton 1986; Coats et al. 1989; Haya 1989). The first synthetic pyrethroids, allethrin and cyclethrin, were produced around 1950 but lacked adequate photostability and were not as effective insecticidally as the natural pyrethrins. Tetramethrin was introduced in 1964, but it had inferior insecticidal activity. The first synthetic pyrethroids with greater insecticidal activity than natural pyrethrins were resmethrin and cismethrin, produced in 1968. Photostable pyrethroids were produced in the mid 1970's and included deltamethrin, cypremethrin, fenpropathrion, and fenvalerate (Smith and Stratton 1986).

Pyrethroid insecticides are generally recognized as potent neurotoxicants that interfere with nerve membrane function by interaction with the sodium channel (Elliott and Janes 1978; Vijverberg et al. 1982; Gilbert et al. 1989; Haya 1989). Synthetic pyrethroids are more toxic against insect pests, up to 10 times more potent, in some instances, than other insecticides now in general use (Bradbury and Coats 1989a). However, the stereochemical structure of pyrethroid insecticides greatly influences their toxicity to insects and mammals, and this phenomenon is especially pronounced for fenvalerate (Bradbury et al. 1987b).

As broad-spectrum insecticides, the synthetic pyrethroids are necessarily toxic to a wide range of arthropods. Most insect orders are extremely susceptible, including many types of beneficial predator and parasite species (Bradbury and Coats 1989a). Synthetic pyrethroids are also toxic to fish and nontarget aquatic insects and crustaceans (Muir et al. 1985). Fenvalerate, for example, enters freshwater aquatic environments in runoff from food crop use, in drift from forest-spray procedures, and by direct spraying of water bodies (Haya 1989). Estuarine organisms may be exposed to fenvalerate and other pyrethroids after applications to corn (*Zea mays*), cotton (*Gossypium hirsutum*), rice (*Oryza sativa*), and vegetables in coastal areas or by discharges from pyrethroid manufacturers or formulating and distribution centers (Clark et al. 1989). Fenvalerate has been implicated in kills of coastal organisms in South Carolina, primarily from agricultural runoff into estuarine tidal creeks (Scott et al. 1987).

This report was prepared in response to information requests from environmental contaminant specialists of the U.S. Fish and Wildlife Service. It is part of a continuing series of brief reviews on hazards of chemicals to fish and wildlife resources. Detailed information on ecological and toxicological aspects of fenvalerate and other synthetic pyrethroid insecticides is provided in reviews by Elliott (1977), Elliott and Janes (1978), Wouters and Bercken (1978), Glickman and Casida (1982), Vijverberg and Bercken (1982), Gray and Soderlund (1985), Leahey (1985), Smith and Stratton (1986), Coats et al. (1989), and Bradbury and Coats (1989a).

[1]The technical fenvalerate formation is no longer being manufactured by the Dupont Company, although existing stocks may be used until exhausted. The new fenvalerate formulation will be sold as Asana or Esfenvalerate, and contains only the 2*S*, α*S* isomer (A. Stavola, U. S. Environmental Protection Agency, personal communication, 28 January 1991).

Environmental Chemistry

General

Synthetic pyrethroids now account for at least 30% of the world insecticide market and are rapidly replacing other agricultural chemicals for control of insect pests. Fenvalerate is one of the more recently developed and widely used synthetic pyrethroid insecticides. It is derived from a combination of α-cyano-3-phenoxybenzyl alcohol and α-isopropyl phenylacetate ester. Technical fenvalerate is a mixture of four optical isomers, each occurring in equal amounts but with different efficacies against insect pests. Fenvalerate does not usually persist in the environment for > 10 weeks, and it does not accumulate readily in the biosphere. Time for 50% loss (Tb ½) in fenvalerate-exposed amphibians, birds, and mammals was 6-14 h; for reptiles, terrestrial insects, aquatic snails, and fish it was > 14 h-<2 days; and for various species of crop plants it was 2-28 days. Fenvalerate degradation in water is due primarily to photoactivity and, in soils, to microbial activity. Half-time persistence in nonbiological materials is variable but may last as long as 6 days in fresh water, 34 days in seawater, 6 weeks in estuarine sediments, and 9 weeks in soils.

Chemical Properties

Synthetic pyrethroid insecticides are photostable analogs of the natural pyrethrins of botanical origin; they consist of a series of related esters derived from alcohols and acids that maintain critical isosteric relations with the natural product prototype (Glickman and Casida 1982; Bradbury and Coats 1989a). Small changes in substituents and stereochemistry are sufficient to produce compounds differing in their insecticidal potency, spectrum of activity, and mammalian toxicology (Gray and Soderlund 1985). Halogenated, lipophilic, photostable compounds are exceptionally active against many species of insects; although these compounds are relatively safe to birds and mammals, they are usually extremely toxic to certain freshwater and marine groups, including fish (Leahey 1985; Coats et al. 1989).

The first significant success in creating a photostabilized pyrethroid with high insecticidal activity was achieved through use of the 3-phenoxybenzyl alcohol moiety. A further step was the finding that 2-aryl-3methylbutyric acid esters of pyrethroid alcohols were both photostable and insecticidal (Gray and Soderlund 1985).

Fenvalerate is one of the more recently developed and widely used synthetic pyrethroid insecticides, and it is a highly active phenyl acetate ester of known pyrethroid alcohols—specifically, a combination of isopropyl phenyl acetate ester and α-cyano-3-phenoxybenzyl alcohol (Wouters and Bercken 1978). The phenoxybenzyl group and the halogenated phenyl ring increase the photostability of the molecule. The cyano group, substituted on the benzylic carbon, stabilizes the ester bond against hydrolysis (Coats et al. 1989).

Fenvalerate, like most other synthetic pyrethroids, is a halogenated, lipophilic, stable compound with low solubility in water and high solubility in organic solvents (Table 1). Technical fenvalerate is a racemic mixture of four isomers, composed of equal amounts of dextrorotary and levorotary forms; however, the four optical isomers (Figure) have very different efficacies against pest species. In general, fenvalerate stereoisomers with S configurations in both the acid and alcohol moieties are more active pharmacologically and toxicologically than those with R configurations (Wouters and Bercken 1978).

Uses

Pyrethroids are used primarily for the control of household and agricultural insect pests and secondarily in industrial, stored product, and veterinary applications. They are especially advantageous for use in northern climates because their toxicity is enhanced at low temperatures (Smith and Stratton 1986). Synthetic pyrethroid insecticides, including fenvalerate, are used as alternatives to organochlorine, organophosphorus, carbamate, and natural pyrethrum insecticides because they are highly toxic to insect pests, low to intermediate in persistence, and low in toxicity to warm-blooded organisms, although extremely toxic to many aquatic organisms (Hansen et al. 1983; Coats et al. 1989). By 1982, more than 30% of the world market for insecticides consisted of synthetic pyrethroids, and this percentage is increasing (Smith and Stratton 1986).

Outside of the United States, fenvalerate is used on cotton in Australia, Greece, and South Africa and on apples (*Malus* sp.), pears (*Pyrus* sp.), and potatoes (*Solanum* sp., *Ipomoea* sp.) in Canada (Reed 1981); uses in other countries, including Mexico, are anticipated (Reed 1981), as is increased use against agricultural, poultry, dairy, and household pests (Mumtaz and Menzer 1986). In agricultural use, recommended application rates of

fenvalerate range between 0.055 and 0.224 kg/ha for control of a broad spectrum of pestiferous insects (Bennett et al. 1983).

Domestically, about 6,500 kg of fenvalerate was used in 1979; all of this amount was imported (Reed 1981). In 1980, in addition to registered use, the U.S. Environmental Protection Agency allowed an additional 80,000 kg for crisis and experimental use (Reed 1981). By 1981, fenvalerate had been registered for domestic use on apples, cotton, peanuts (*Arachis* sp.), pears, and potatoes. Additional uses were allowed under various experimental or crisis exemptions on beans (*Phaseolus* spp.); black and white pepper (*Piper* spp.); broccoli, cabbage, and cauliflower (*Brassica* spp.); celery (*Apium* sp.); corn; cucumbers (*Cucumis* sp.); eggplant (*Solanum melongena*); grapes (*Vitis* spp.); lettuce (*Lactuca* sp.); peas (*Pisum* sp.); squash (*Cucurbita* spp.); and tomatoes (*Lycopersicon esculentum*; Reed 1981). By 1989, this list was expanded to include tobacco (*Nicotiana tabacum*); soybeans (*Glycine max*); sugarcane (*Saccharum officinarum*); a wide variety of nuts, fruits, and vegetables; pine seed orchards, forest tree nurseries, mosquitos, biting insects, insect vectors of disease, mite control in poultry, and fly and tick control in cattle (Spehar et al. 1982; Akhtar 1983; Bennett et al. 1983; Hansen et al. 1983; Sine 1988; Clark et al. 1989; Smith et al. 1989).

Table 1. Chemical and other properties of fenvalerate.[a]

Variable	Datum
Chemical name	(RS)-α-cyano-3-phenoxybenzyl (RS)-2-(4-chlorophenyl)-3-methylbutyrate; cyano (3-phenoxyphenyl) methyl 4-chloro-α-(1-methylethyl) benzeneacetate; α-cyano-3-phenoxybenzyl 2-(4-chlorophenyl)-3-methylbutyrate; 4-chloro-α-(l-methyl ethyl) benzeneacetic acid cyano(3-phenoxyphenyl) methyl ester; α-cyano-3-phenoxybenzyl α-(4-chlorophenyl) isovalerate
Alternate names	Agmatrin, Belmark, Ectrin, Fenkill, Phenvalerate, Pydrin, S-5602, Sanmarton, SD 43775, Sumicidin, Sumifly, Sumipower, Sumitox, WL 43775
CAS number	51630-58-1
Chemical formula	$C_{25}H_{22}ClNO_3$
Molecular weight	419.92
Physical state	Clear yellow, viscous, liquid at 23° C
Purity	Technical grade compound is 92% pure; nature and extent of impurities unknown
Vapor pressure at 25° C	1.1×10^{-8} mm mercury
Density at 23° C	1.17 g/mL
Stability	Stable in most solvents except alcohols at ambient temperature. Unstable in alkaline media. No significant breakdown after 100 h at 75° C; gradual degradation occurred in range 150-300° C
Degradation	Cleavage of the ester linkage is the primary route
Formulations	Emulsifiable concentrate, dust, granules, wettable powder
Log octanol-water partition coefficient	6.2
Solubility at 20° C	
Acetone	>450 g/L
Chloroform	>450 g/L
Methanol	>450 g/L
Hexane	77 g/L
Water	2-85 µg/L
Seawater	24 µg/L

[a] References: Elliott 1977; Coats and O' Donnell-Jefferey 1979; Reed 1981; Tagatz and Ivey 1981; Akhtar 1983; Schimmel et al. 1983; Windholz et al. 1983; Clark et al. 1987, 1989; Crofton and Reiter 1988; Sine 1988.

The delivery vehicle of fenvalerate-containing insecticide may account for wide variations in toxic action. For example, fenvalerate microcapsules used to control caterpillar pests (*Plutella xylostella*, *Spodoptera litura*) were most effective with thin-walled capsules and small particles; however, significant protection to nontarget organisms, such as fish, occurred with thicker-walled capsules and larger particles (Ohtsubo et al. 1989). The popularity of commercial synthetic pyrethroids and their widespread replacement of older, more toxic compounds in various settings mandates a thorough understanding of the formulation used and of the active and inert components (Williamson et al. 1989).

Persistence

In nonbiological samples, half-time persistence of fenvalerate was variable but frequently ranged between 2 and 6 days in fresh water, 27 and 34 days in seawater, 3 and 9 weeks in soils, and up to 6 weeks in estuarine sediments (Table 2). Persistence was longer at higher initial application rates and under conditions of reduced light, low microbial activity, and high organic content (Table 2). Fenvalerate is not readily transported from upland field application sites into the aquatic environment. Fenvalerate that directly enters the aquatic environment by way of runoff has limited bioavailability to aquatic organisms owing to rapid adsorption onto soil particles, organic matter, or plants and to chemical hydrolysis and photodecomposition (Ohkawa et al. 1980). Under acidic conditions, fenvalerate in water is stable to hydrolysis for 100 h at 75° C; Tb ½ at elevated recommended application rates is about 21 days, primarily as a result of photodegradation (Reed 1981).

Fenvalerate is one of the more persistent synthetic pyrethroids in soils (Klaassen et al. 1986). In agricultural soils, fenvalerate is tightly adsorbed to soil particles, does not easily move laterally or to lower soil layers with groundwater, and almost always localizes in the application site because of its extremely low solubility in water (Ohkawa et al. 1980; Hill 1981; Miyamoto 1988). Fenvalerate degradation rates from mineral soil surfaces are dependent on soil type, moisture, temperature, and microbial activity. Half-time persistence in soils usually ranged between 2 and 18 days, but 3 months has also been recorded (Harris et al. 1981; Reed 1981; Bennett et al. 1986). Although fenvalerate is susceptible to chemical degradation by hydrolysis and oxidation, most authorities agree that degradation in soils is due primarily to microbial activity, that microbial degradation is most rapid under aerobic conditions, and that transformed products do not persist longer than the parent compound (Ohkawa et al. 1980; Chapman et al. 1981; Bennett et al. 1986).

In biological samples, fenvalerate neither persists for lengthy periods nor is readily accumulated (Smith and Stratton 1986). In general, fenvalerate is rapidly (i.e., Tb ½ of 6-14 h) excreted by amphibians, birds, and mammals; has low persistence in various reptiles, terrestrial insects, aquatic snails, and fish; and has moderate (i.e., Tb ½ of 2-28 days) persistence in various species of target plants (Table 3; Reed 1981; Mumtaz and Menzer 1986; Bradbury and Coats 1989a, 1989b). Animals collected after 5 days from a cotton field sprayed with 0.112 kg/ha, or from the immediate vicinity, had very low fenvalerate residues (Table 3; Bennett et al. 1983). In that study fenvalerate was detected in one of nine bird species sampled, in one of four mammals, in the western ribbon snake (*Thamnophis proximos*), in one of four amphibian species, and in fish and insects. The bird was a male dickcissel (*Spiza americana*) that had established a breeding territory within the sprayed cotton field. Carnivorous ground beetles, found moribund on the ground, contained the highest mean fenvalerate residue of 0.55 mg/kg fresh weight (FW) whole body; large numbers of dead insects were found in the fields during collection. The highest residues (0.32-0.55 mg/kg) in fish and invertebrates were in those collected from a small pool in a drainage ditch, which compares with 0.92 mg/kg found in common carp (*Cyprinus carpio*) after exposure in the laboratory for 7 days to 0.8 µg fenvalerate per liter (Bennett et al.1983).

Fenvalerate is not significantly absorbed or translocated in plants. Cotton, apples, and lettuce treated with fenvalerate contained surface residues of parent fenvalerate 8 weeks after treatment (Reed 1981). In addition to the parent compound, which accounted for 80% of all residues, identified metabolites included 3-phenoxybenzaldehyde, 3-phenoxybenzyl methylbutyric acid, and conjugates of these compounds. Half-time persistence of fenvalerate on plant surfaces is between 2 and 4 weeks, and degradation is primarily a result of weathering (Reed 1981).

Various plants sprayed with 0.25 kg fenvalerate per hectare had measurable residues 7 days after application and nondetectable residues 15-30 days after treatment (Jain et al. 1979). Washing plants in cold water to remove the pesticide was effective only on the initial day of application, removing 30-50%. Afterwards, only 3-13% could be removed by washing. Cooking removed 71-88% of the fenvalerate residues on the initial

day of treatment, but in later samplings, removal was 68-70% in spinach (*Spinacea oleracea*) and tomatoes and 38-40% in okra (*Abelmoschus esculentus*) and cauliflower (*Brassica oleracea botrytis*; Jain et al. 1979).

Adsorption and persistence in plants can be modified by other chemicals or by selected carriers, although mechanisms to account for these phenomena are unclear. The application mixture influences adsorption and persistence of fenvalerate. For example, interception and persistence in sugarcane were increased when fenvalerate was applied in a 25% water to 75% soybean oil mixture versus water or soybean oil alone (Smith et al. 1989). Also, biocidal properties of fenvalerate residues on cotton foliage were increased up to 100% due to enhanced persistence of fenvalerate in the presence of toxaphene (Brown et al. 1982).

Table 2. Fenvalerate persistence in water, sediments, and soils.

Sample and other variables	Persistence	Reference[a]
Fresh water		
Various concentrations	Half-time persistence (Tb ½) of 3.2 days (range 1.9-5.8 days); longer for higher initial doses	1
0.1 µg/L	Tb ½ of 4.1 days; 90% loss in 13.5 days	11
3.9 µg/L	Maximum concentration was 2.3 µg/L 48 h after application; at 168 h it was 0.6 µg/L	1
8.3 µg/L	Concentration declined from 5.3 µg/L at 24 h to 1.8 µg/L at 168 h	1
16.5 µg/L	Concentration declined from 17.6 µg/L at 24 h to 9.1 µg/L at 168 h	1
30.6 µg/L	Concentration declined from 54.4 µg/L at 24 h to 21.2 µg/L at 168 h	1
Seawater	Tb ½ of 8 days in light, >14 days in dark; 27-34 days under alternating light and dark	2,3
Estuarine sediments		
Sterilized	No degradation in 28 days	2
"Low" concentrations	Tb ½ of 4.5-9 days	1,3
"Various" concentrations	Tb ½ of 24-42 days	2,4,5,6
0.1-10 mg/kg dry weight (DW)	73% loss in 8 weeks at initial nominal concentration of 0.1 mg/kg DW, 78% at 1.0 mg/kg, and 96% loss in 8 weeks at 10 mg/kg DW	4
Soils		
Initial concentration of 1.0 mg/kg DW soil		
Natural mineral, pH 8.0-8.1	12% remaining after 8 weeks, about 5% after 16 weeks	7
Sterilized mineral, pH 7.7-8.1	91% remaining after 8 weeks, 87% after 16 weeks	7
Natural organic, pH 7.1-7.2	58% remaining at 8 weeks, about 32% after 16 weeks	7
Sterilized organic, pH 6.5-6.9	100% remaining after 16 weeks	7
Various (clay, silt, sand), dose unknown	Tb ½ of 22-40 h	8
Mineral soils, dose unknown	Tb ½ of 6 weeks	9
Moist sand, dose unknown	Tb ½ of 9 weeks, 88% loss in 48 weeks	9
Lethbridge surface soil, agricultural, British Columbia		

Field conditions, initial application of 150 g/ha	Tb ½ of 6 weeks, 89% loss in 45 weeks	10
Laboratory study, 70 g/ha equivalent	Tb ½ of 5.2 weeks	10

[a] 1. Coulon 1982; 2. Schimmel et al. 1983; 3. Smith and Stratton 1986; 4. Tagatz et al. 1987; 5. Tagatz and Ivey 1981; 6. Hansen et al. 1983; 7. Chapman et al. 1981; 8. Muir et al. 1985; 9. Harris et al. 1981; 10. Hill 1981; 11. Day et al. 1987.

Table 3. Fenvalerate persistence in plants and animals under field conditions.

Sample and othervariables	Persistence	Reference[a]
Alfalfa, *Medicago sativa*	Half-time persistence (Tb ½) of 9 11 days	1
Cotton *(Gossypium hirsutum)* treated with 0.224 kg/ha, residues on foliage 12 days later		
In combination with 2.24 kg/ha toxaphene	Fenvalerate residues were 11.6 mg/kg	2
Fenvalerate alone	Residues were 5.9 mg/kg	2
Cotton, foliage	Tb ½ of 2 days, 96% lost in 17 days	3,7
Cotton field sprayed with 0.112 kg/ha (0.1 pound per acre), Garland, Arkansas, July 1979. Animals collected from field 5 days later		
Mammals		
Deer mouse, *Peromyscus maniculatus*; white-footed mouse, *P. leucopus;* cotton rat, *Sigmodon hispidus*	<0.01 mg/kg whole body fresh weight (FW), less skin and GI tract	3
House mouse, *Mus musculus*	0.01 mg/kg whole body FW, less skin and GI tract	3
Birds		
Cardinal, *Richmondena cardinalis*; red-winged blackbird, *Agelaius phoeniceus*; eastern meadowlark, *Sturnella magna*; brown-headed cowbird, *Molothrus ater*; purple martin, *Progne subis subis*; horned lark, *Eremophila alpestris*; little blue heron, *Florida coerulea*; green-backed heron, *Butorides virescens virescens*	<0.01 mg/kg whole body FW, less skin and GI tract	3
Dickcissel, *Spiza americana*	0.02 mg/kg whole body FW, less skin and GI tract	3
Reptiles		
Western ribbon snake, *Thamnophis proximus*	0.12 mg/kg whole body FW, less skin and GI tract	3
Animals collected from location near cotton field 5 days later		

Insects		
Cicada, Cicadidae	<0.01 mg/kg FW whole body	3
Short-horned Acrididae	0.18-0.24 mg/kg FW whole body	3
Ground beetle, *Calosoma* sp.	0.55 mg/kg FW whole body	3
Molluscs		
Aquatic snail, unidentified	0.53 mg/kg FW soft parts	3
Fish		
Mosquitofish, *Gambusia affinis*	0.3 mg/kg FW whole body	3
Golden shiner, *Notemigonus crysoleucas*	0.47 mg/kg FW whole body	3
Amphibians		
Southern leopard frog, *Rana utricularia*; green frog, *Rana clamitans*; green treefrog, *Hyla cinerea*	<0.01 mg/kg FW whole body, less skin and GI tract	3
Fowler's toad *Bufo fowleri*	0.02 mg/kg FW whole body, less skin and GI tract	3
Old field site, Iowa, O. 112 kg/ha (0.1 pound per acre) applied on 9 June 1980, and again on 5 August 1980, 10 June 1981, and 21 July 1981		
Vegetation	Maximum immediately after each application was 12.1 mg/kg FW; residues after 24 days were always <1 mg/kg FW	1
Short-horned grasshopper, whole		
Applied 9 June 1980	Residues were 0.03 mg/kg FW after 36 days, and nondetectable (ND) in 49 days	1
Applied 5 August 1980	Residues were 0.33 mg/kg FW after 7 days, 0.19 after 14 days, and 0.12 after 21 days	1
Ground beetles, Carabidae, whole		
Applied June 1980	After 10 days, beetles contained 0.12 mg/kg FW; after 17 days residues were ND	1
Applied 5 August 1980	After 6 days, residues were O. 14 mg/kg FW and ND in 17 days	I
Applied 21 July 1981	Maximum residue after 24 days was 0.15 mg/kg FW	1
Deer mice, *Peromyscus maniculatus*, whole		
Applied 21 July 1988	Residues were 0.1 mg/kg FW after 2 days, and 0.01 after 21 days	1
Meadow vole, *Microtus pennsylvanicus*, whole		
Applied 21 July 1988	Residues were variable: 0.07 mg/kg FW after 2 days, O. 12 after 4 days, 0.46 after 8 days, and 0.04 after 21 days	1
Plants, 4 species, sprayed with 0.05% emulsifiable concentrate equivalent to 0.25 kg/ha		
Okra, *Abelmoschus esculentus*, initial	After 5 days residue was 1.6 mg/kg FW, after 7 days it was 0.8, and after 15 days it was ND	4

concentration of 4 mg/kg FW		
Cauliflower, *Brassica oleracea botrytis*, initial deposit of 0.86 mg/kg FW	Initial deposit degraded to 0.3 mg/kg in 7 days and was ND in 15 days	4
Tomato, *Lycopersicon esculentum*, initial residue of 0.85 mg/kg FW	Initial residue degraded to 0.67 mg/kg in 5 days, 0.3 in 15 days, and was ND in 30 days	4
Spinach, *Spinacea oleracea*, initial residue of 9.5 mg/kg FW	Initial residue degraded to 2.8 mg/kg in 15 days and was ND in 30 days	4
Plants, various, foliage	Mean Tb ½ of 8.2 days, range 2.8-14 days	6
Bean, *Phaseolus* sp.	Tb ½ of 14 days, essentially no translocation from leaf surface	1
Sugarcane, *Saccharum officinarum*, initial residue immediately after application was 18.8-28.2 mg/kg dry weight leaf	Residues after 7 days were 2.1-5.4 mg/kg DW; Tb ½ of 2.2-2.4 days	5

[a] 1. Bennett et al. 1986; 2. Brown et al. 1982; 3. Bennett et al. 1983; 4. Jain et al. 1979; 5. Smith et al. 1989; 6. Willis and McDowell 1987; 7. Buck et al. 1980.

Fenvalerate photoproducts merit consideration, as some may be comparatively toxic. Decarboxyfenvalerate is a major degradation product of fenvalerate that is formed by photochemical reactions in water and on plant foliage (Mikami et al. 1985). This photoproduct composes up to 10% of the total residues in forage crops that have been exposed to prolonged sunlight and drying. Decarboxyfenvalerate did not persist in tissues of hens, rats, and cows when consumed with feed for extended periods; its residue levels in ova, milk, and meat were negligible (Mikami et al. 1985).

Photolysis of fenvalerate in various solvents by sunlight yields products resulting from ester cleavage, primarily decarboxyfenvalerate, but also 15 other products. All sunlight photoproducts were relatively harmless to mice; LD50 values were >500 mg/kg body weight (BW; Holmstead et al. 1978). When photolysis was by way of ultraviolet light, however, two of the photoproducts formed (3-phenoxybenzoyl cyanide, 3-phenoxybenzyl cyanide) were considerably more toxic than fenvalerate; LD50 values for intraperitoneal injection in mice were >500 mg/kg BW for fenvalerate, 2 mg/kg BW for 3-phenoxybenzoyl cyanide, and 105 mg/kg BW for 3-phenoxybenzyl cyanide (Holmstead et al. 1978). This finding strongly suggests a need for additional research on fenvalerate photoproduct persistence and toxicity.

Mode of Action

General

Two types of synthetic pyrethroids have been identified, as judged by different behavioral, neurophysiological, chemical, and biochemical profiles: Type I, those pyrethroids lacking the α-cyano group, and Type II, those possessing the α-cyano group (i.e., fenvalerate). Induction of repetitive activity in the nervous system is the principal effect of pyrethroids. Repetitive activity originates from a prolongation of the transient increase in sodium permeability of the nerve membrane associated with excitation. All pyrethroids affect sodium channel gating in a similar manner, although Type II pyrethroids are significantly more neurotoxic than Type I pyrethroids.

Metabolism of fenvalerate proceeds by way of oxidation and hydrolysis to produce metabolites considered pharmacologically inactive or inferior to the parent compound. Insects and fish are extremely susceptible to fenvalerate when compared to mammals and birds; interspecies differences are associated with rates of metabolism, excretion, absorption, esterase activity, and neurosensitivity.

Fenvalerate is neither mutagenic nor teratogenic. Tumorlike growths in rodent tissues, however, were associated with the 2R, αS isomer (heretofore believed innocuous)--specifically, with its cholesterol conjugate.

Types of Pyrethroids

Two distinct types of synthetic pyrethroids have been identified, as judged by different behavioral, neurophysiological, chemical, and biochemical profiles in rodents: Type I, also known as Class 1 or T for tremor; and Type II, also known as Class 2 or CS for choreoathetosis-salivation (Wouters and Bercken 1978; Verschoyle and Aldridge 1980; Glickman and Casida 1982; Gray 1985; Gray and Soderlund 1985; Klaassen et al. 1986; Crofton and Reiter 1988; Bradbury and Coats 1989a; Gilbert et al. 1989; Williamson et al. 1989). In general, these authorities agree that pyrethroids containing both a halogenated acid esterified with the α-cyano-3-phenoxybenzyl alcohol--such as fenvalerate, deltamethrin, and cypermethrin--produce the Type II poisoning syndrome and that pyrethroids lacking either or both of these moieties (i.e., permethrin, resmethrin, cismethrin, allethrin, bromphenothrin, phenothrin, kadethrin, tetramethrin) tend to produce the Type I syndrome. Type I is characterized by sparring, aggressive behavior (in rats, but not mice), rapid onset of tremor in the extremities, increased body temperatures, and whole-body tremors. As toxicity progresses, mice show hyperactivity, whereas rats become prostrate and die with immediate onset of rigor mortis; in mice, death is often associated with spasmodic seizures. The Type I syndrome is very similar to that produced by p,p'-DDT. Type II is characterized by pawing and burrowing behavior, profuse salivation, a decrease in body temperature of rats (due partially to evaporation of saliva), tremors progressing to choreoathetosis (i.e., a sinuous, writhing movement), muscular contractions and seizures, and death. With repeated high doses sufficient to kill some rats, degenerative changes in sciatic and posterial tibial nerves were observed. The same two types of pyrethroid actions are also evident among insects.

Regardless of route of administration, signs of fenvalerate poisoning in rodents were similar. Doses administered by intercerebroventricular injection of comparatively low concentrations were more toxic than higher doses given orally or by intravenous or intraperitoneal injection, suggesting greater central nervous system involvement in Type II than in Type I poisoning. In fact, pyrethroids that produce the Type II syndrome--including fenvalerate--are 5 to 10 times more potent neurotoxicants than Type I pyrethroids, which suggests different sites of action in the central nervous system.

Sodium Gating Kinetics

Pyrethroids have an action at or near the sodium channel in the nerve, resulting in greatly altered ionic currents and disrupted nerve function through membrane depolarization. Based on studies with insects, crustaceans, frogs, and small mammals, there is general agreement that the sodium channel in the nerve membrane is the major target site for all synthetic pyrethroid insecticides (and many other neurotoxicants); that synthetic pyrethroids prolong the transient increase in sodium permeability of the nerve membrane during excitation, resulting in spontaneous depolarization and repetitive discharges; that persistent repetitive discharges lead to muscular fasciculations, acetylcholine depletion, and muscular weakness; that effects are enhanced at lower temperatures; and that α-cyano (Type II) pyrethroids are more potent neurotoxicants than noncyano (Type I) pyrethroids, differences in neurotoxic effects being attributed solely to the α-cyano substituent (Wouters and Bercken 1978; Gammon et al. 1981; Vijverberg and Bercken 1982; Vijverberg et al. 1982; Parker et al. 1984b; Flannigan et al. 1985; Gray and Soderlund 1985; Ruigt and Bercken 1986; Eells and Dubocovich 1988; Flodstrom et al. 1988; Clark and Brooks 1989; Gilbert et al. 1989; Holloway et al. 1989; Salgado et al. 1989). Most of these authorities agree that fenvalerate was the most effective pyrethroid tested for inducing pronounced repetitive activity in nerve fibers and that the 2S, αS isomer was up to 15 times more potent than other fenvalerate isomers. Pyrethroids induce the sodium channels to close more slowly than normal, resulting in a gradually decaying inward sodium current (called a tail current) after termination of membrane depolarization. Type I pyrethroids induce tail currents with time constants of decay in milliseconds, but Type II pyrethroids result in time constants of decay that are orders of magnitude longer and contain thousands of impulses, inducing a quickly reversible, frequency-dependent suppression of the action potential. Depolarization of axons by synthetic pyrethroids was most effective at low temperatures; the negative temperature dependence of the steady state current seems to be due to the stabilizing effect of low temperature on the open-modified channel.

Myelinated nerves of vertebrates are thought to sequester the pyrethroid molecules, known to be soluble in the myelin sheath, thereby preventing a portion of their chemical effect on the nerve axon (Flannigan et al. 1985). Fenvalerate, unlike other α-cyano pyrethroids, had little effect on the electrophysiological function of single myelinated nerve fibers in the frog (*Rana esculenta*), suggesting that additional research is needed on mechanisms other than membrane sodium transport (Tippe 1987).

The role of calcium in pyrethroid interaction with nerve tissue is under active investigation. Fenvalerate affects calcium-ATPase enzyme and calmodulin-activated enzyme activities, such as phosphodiesterase (Flodstrom et al. 1988). Fenvalerate inhibits calcium uptake by nerve cord of crayfish (*Procambarus clarki*) and axon of spiny lobster (*Panulirus japonicus*), an action that seems to be related to its lipophilic properties (Doherty et al. 1986). Fenvalerate enhances the calcium-dependent potassium-stimulated release of norepinephrine from rat brain and could lead to an overall depletion of brain stores of this neurotransmitter, producing a convulsive state typical of Type II pyrethroid poisoning (Brooks and Clark 1987; Clark and Brooks 1989). Fenvalerate evoked a calcium-dependent release of dopamine and acetylcholine from rabbit (*Oryctolagus* sp.) brain that was concentration related and specific for the 2S, αS isomer; release of dopamine and acetylcholine was antagonized completely by tetrodotoxin, a sodium channel blocker (Eells and Dubocovich 1988). The relatively low potency of fenvalerate and other Type II pyrethroids on potassiumstimulated calcium uptake in rat brain and other responses suggests that neither the sodium-calcium exchanger nor the voltage-dependent calcium channels are primary targets for pyrethroid toxicity (Ramadan et al. 1988).

Toxic isomers of Type II pyrethroids usually antagonize -aminobutyric acid (GABA) by interacting with the t-butyl bicyclophosphorothionate-picrotoxin binding site in brain; antagonism of GABA leads to a reduction in inhibition (Casida and Lawrence 1985). Fenvalerate seems to increase inhibition, however, and this may be explained by a differential effect on sodium channel kinetics (Gilbert et al. 1989). Fenvalerate also inhibits perhydrohistrionicotonin binding with electric organ membrane of the electric ray (*Torpedo* sp.; Abbassy et al. 1983) and interacts with binding sites for dihydropicrotoxinin and kainic acid in the brain (Gammon et al. 1982), but the significance of these observations is unclear.

Metabolism

The most important metabolic degradation pathways for synthetic pyrethroids are oxidation on the phenoxy ring, hydrolysis of the ester linkage, and conjugation of metabolites; rates and pathways differ among taxonomic animal groupings resulting in large differences in sensitivity (Holmstead et al. 1978; Kaneko et al. 1981; Akhtar 1983; Miyamoto 1988; Bradbury and Coats 1989a).

All metabolic degradation products of fenvalerate are pharmacologically inactive or inferior to the parent compound, implying that metabolic modifications lead to detoxication (Miyamoto 1988). Fenvalerate and other α-cyano pyrethroids, however, are consistently more resistant to oxidative attack than their noncyano analogs (Gray and Soderlund 1985). Liver is the predominant site of fenvalerate metabolism through hydrolysis by one or more hepatic microsomal esterases; inhibition of these enzymes results in enhanced toxicity (Ghiasuddin and Soderlund 1984). Hydrolysis has also been demonstrated in plasma, kidney, stomach, and brain tissues. Except for brain, however, these tissues were relatively unimportant in the detoxification process (Ghiasuddin and Soderlund 1984; Gray and Soderlund 1985).

Metabolism of the 2S isomers proceeds sequentially: hydroxylation at the phenoxy group, hydrolysis of the cyano group, and cleavage of the ester linkage (Coats et al. 1989). Fenvalerate and the 2S isomers yield two ester metabolites in feces from hydroxylation at the 4' and 2' phenoxy positions. Other significant metabolites were 3-phenoxybenzoic acid and its hydroxy derivatives from the alcohol moiety, 3-(4-chlorophenyl) isovaleric acid and its hydroxy derivatives from the acid moiety, and thiocyanate and carbon dioxide from the cyano moiety (Ohkawa et al. 1979). A slow elimination rate characterizes fenvalerate and other α-cyano pyrethroids when compared with noncyano pyrethroids; it seems to be due to the release of the cyano group during ester cleavage, which is then incorporated into the body thiocyanate pool and retained in the skin and stomach (Gray and Soderlund 1985). Decarboxyfenvalerate, a photolysis product of fenvalerate, is present in water and on plant surfaces, but it is extensively hydroxylated in mammals and excreted rapidly and completely into feces with no apparent toxic effects (Miyamoto 1988).

Signs of fenvalerate intoxication are similar in birds, fish, mammals, and insects, but insects and fish are extremely sensitive when compared with warm-blooded organisms, frequently by one to three orders of magnitude (Bradbury and Coats 1989a, 1989b). Increased resistance to fenvalerate and other synthetic pyrethroid insecticides in mammals and birds, when compared with aquatic organisms and terrestrial insects, is attributed to their higher metabolism, more rapid excretion, lower absorption from diet or the surrounding envirosphere, higher esterase activity, higher fat content, and lower neurosensitivity (Wouters and Bercken 1978; Ohkawa et al. 1979; Glickman and Casida 1982; Flannigan et al. 1985; Gray and Soderlund 1985; Klaassen et al. 1986; Bradbury and Coats 1989a, 1989b; Coats et al. 1989). For example, rainbow trout

(*Oncorhynchus mykiss*)—one of the more sensitive aquatic species—have significantly lower rates of metabolism and elimination of fenvalerate than those reported for birds and mammals (Bradbury et al. 1986; Bradbury and Coats 1989a, 1989b); show little or no esterase activity towards pyrethroids and substantially lower oxidative activity than warm-blooded animals (Bradbury and Coats 1989a, 1989b); efficiently accumulate fenvalerate from the medium (Gray and Soderlund 1985); and show greater intrinsic sensitivity of the central nervous system when compared with birds and mammals (Gray and Soderlund 1985; Bradbury and Coats 1989a).

Fenvalerate effects are antagonized or synergized by various compounds or chemicals. Dermal exposure to fenvalerate in mammals may produce a skin sensory response, most frequently on the face, characterized by itching and tingling. Administration of vitamin E up to 29 h before fenvalerate exposure partially reduced the fenvalerate-mediated skin sensation in guinea pigs (*Cavia* sp.; Malley et al. 1985). The effectiveness of vitamin E may be associated with its membrane stabilizing property, although the exact mode of action is unknown. Fenvalerate skin sensations were also reduced by piperonyl butoxide when applied directly to the skin or in conjunction with fenvalerate (Malley et al. 1985). Delayed toxic effects in rodents and insects were produced with various muscle relaxants, including propranolol and diazepam, perhaps through depolarization of nerve terminals (Gammon et al. 1982; Gray 1985; Gray and Soderlund 1985). Mice given profenofos, an esterase inhibitor, were up to 27 times more susceptible than were nontreated animals (Glickman and Casida 1982).

Mutagenicity, Teratogenicity, Carcinogenicity

Fenvalerate and other synthetic pyrethroids caused no oncogenic, reproductive, mutagenic, or teratogenic effects, as judged by results of 2-year feeding studies with rodents at 250-300 mg/kg diet, three-generation rodent reproduction studies at 250 mg/kg diet, various mutagenicity assays, bone marrow cytogenicity up to 150 mg/kg BW, the dominant lethal bioassay at 100 mg/kg, and a host-mediated bioassay in mice at 50 mg/kg BW (Reed 1981; Pluijmen et al. 1984; Flannigan et al. 1985; Gray and Soderlund 1985). Some chromosomal aberrations and alterations in the mitotic index were noted, however, in bone marrow and testis cells of rats given fenvalerate at 100 mg/kg BW orally, a dose that killed 71% of the rats (Gray and Soderlund 1985). A similar pattern was noted in mice (Flodstrom et al. 1988; Pati and Bhunya 1989), indicating that additional research is needed to establish mutagenicity of fenvalerate.

The carcinogenic potential of fenvalerate is based on negative or inconclusive evidence and centers on its ability to produce microgranulomas in various tissues, especially liver, in dogs (*Canis familiaris*) and rodents. Beagles exposed to fenvalerate at 250, 500, or 1,000 mg/kg diet for 6 months showed treatment-related microscopic effects, including histiocytic cell infiltrates in mesenteric lymph nodes and multifocal microgranulomas in liver (Parker et al. 1984b). Female rats fed a diet containing fenvalerate at 1,000 mg/kg ration for 2 years showed a statistically significant increase in the incidence of mammary tumors; however, this was judged by the authors (Parker et al. 1984a) to be of unlikely biological significance. Their unusual conclusion was based on four points: (1) none of the mammary tumor incidences exceeded those expected or reported on aged female rats of this strain, (2) time and appearance of tumors in control and treated groups were unchanged by treatment, (3) the benign-malignant ratio of mammary tumors was the same in control and treated groups, and (4) the tumors were common in this strain of rat and did not seem to be related to treatment.

Fenvalerate inhibits intercellular communication between fibroblast cells and enhances the development of hepatocyte loci in rat liver at nonheptatotoxic dose levels. Chemicals that possess these properties are likely to be tumor promoters (Flodstrom et al. 1988). Fenvalerate alone induced no hepatoxic effects in rat liver, as judged by transaminase activities and histology. However, some rats that were partially hepatectomized and insulted with nitrosodiethylamine—a carcinogen and tumor initiator—had significantly elevated numbers of liver foci after administrations of fenvalerate. This response suggested that fenvalerate is a potential tumor promoter (Flodstrom et al. 1988).

Linkage of the tumorlike formations in rodents with a specific fenvalerate stereoisomer was an important breakthrough (Kaneko et al. 1986; Okuno et al. 1986; Miyamoto et al. 1986; Miyamoto 1988). Granulatomous cells in spleen, lymph node, and liver of fenvalerate-stressed rats and mice tended to fuse, forming large multinucleated cells called giant cells. Researchers convincingly demonstrated that the 2R, αS isomer, heretofore believed innocuous, was solely responsible for the observed microgranulomas. The residual metabolite in this instance is the cholesterol conjugate [cholesterol (2R)-2-(4- chlorophenol) isovalerate] known as CPIA-cholesterol ester. This lipophilic conjugate forms rapidly, usually peaking within 60 min, and tends to

persist in tissues, especially in adrenal, spleen, liver, and mesenteric lymph node. Of the four fenvalerate isomers, only the 2R, αS isomer yielded CPIA-cholesterol ester in tissue homogenates of mice, rats, dogs, and monkeys. Mouse tissues showed relatively higher activities than those of other animals. Kidney, brain, and spleen of mice showed relatively higher capacities to form CPIA-cholesterol ester when compared with other mouse tissues; in all cases, enzyme activity localized mainly in microsomal fractions.

Researchers concluded that stereoselective formation of the CPIA-cholesterol ester resulted from the stereoselective formation of the CPIA-carboxyesterase complex only from the 2R, αS isomer, which subsequently undergoes cleavage by cholesterol to yield the CPIA-cholesterol ester that produced giant cells in mice (Kaneko et al. 1986; Miyamoto et al. 1986; Okuno et al. 1986; Miyamoto 1988). These findings strongly support the need for more research on carcinogenic potential of fenvalerate stereoisomers.

Effects

General

Fenvalerate is extremely toxic to representative nontarget aquatic organisms and to some beneficial terrestrial arthropods at concentrations substantially lower than those recommended to control pestiferous insects. Toxic effects are associated primarily with the 2S, αS isomer and are exacerbated at low temperatures. Birds, mammals, and terrestrial plants are normally tolerant.

Target insect species are usually killed at fenvalerate concentrations of 0.015 µg whole body, 0.11 kg/ha by way of aerial application, 5.4 mg/kg in the soil, or 50 mg/kg in the diet. Adverse effects on survival of sensitive aquatic organisms occur at 0.003-0.03 µg/L for crustaceans and 0.09-1.1 µg/L for fish and amphibians. Younger stages of sensitive birds had reduced survival at acute oral doses >500 mg/kg BW and reduced growth at diets containing >750 mg/kg ration; poultry diets containing fenvalerate at <50 mg/kg feed produced no appreciable residues in eggs and meat of exposed birds. Among sensitive mammals, adverse effects on survival were noted at acute oral doses of 50-450 mg/kg BW, dietary concentrations of 50-1,000 mg/kg, and dermal applications of 1,800 mg/kg BW.

Terrestrial Plants and Invertebrates

Terrestrial plants are relatively unaffected by fenvalerate at recommended application rates, as judged by negligible uptake of fenvalerate from treated soils, formation of numerous fenvalerate conjugates that are pharmacologically inactive, and metabolism of the liberated cyano group into amino acids and eventually carbohydrate and protein (Miyamoto 1988).

Adverse effects of fenvalerate on survival of terrestrial arthropods were observed at 0.002-0.015 µg whole body topical application, 0.11 kg/ha aerial application, 5.4 mg/kg in the soil, 50 mg/kg in the diet, and 1.4 g per ant mound (Table 4). Synthetic pyrethroids are more effective in biological systems at low temperatures. The relative sensitivity of insects when compared with mammals is attributed in part to this negative temperature coefficient; thus, warm-blooded animals are less affected than insects and other poikilotherms (Klaassen et al. 1986). Fenvalerate, for example, showed a negative correlation between temperature and toxicity to crickets (*Acheta pennsylvanicus*), being up to 1.9 times as toxic at 15° than at 32° C (Harris et al. 1981). A similar case is made for honeybees (Mayer et al. 1987) and for many species of aquatic invertebrates and fish (Mayer 1987).

Signs of lethal pyrethroid poisoning in insects and other arthropods generally include hyperexcitation, tremors, and convulsions, culminating in paralysis and death (Wouters and Bercken 1978). At sublethal doses equivalent to about 10% of a lethal dose, signs of poisoning in sensitive insects include cessation of feeding, wandering, hyperactivity, restlessness, and flushing out of hiding (Bradbury and Coats 1989a). The American cockroach (*Periplaneta americana*) exposed to topical lethal concentrations of fenvalerate had uncoordinated rapid movements followed by inactivity, appearance of water drops under wings and abdomen, and blackening of the abdomen (Yellamma and Reddy 1987). Signs appeared in < 1 h at lethal concentrations and < 3 h at sublethal concentrations. Roaches exposed to sublethal doses began recovery 6 h after exposure, attaining full recovery at 24 h (Yellamma and Reddy 1987).

Field application rates of fenvalerate at 0.05-0.2 kg/ha are recommended for insect control on many food crops. Under these conditions, fenvalerate remained completely effective for 5 days against adults and nymphs of aphids (*Lipaphis erysimi*), jassids (*Amrasca biguttula biguttula*), and white fly (*Bemisia tabaci*; Jain et al.

1979). Fenvalerate, applied as a drench to mounds, shows promise as an effective control agent of the fire ant, *Solenopsis invicta* (Phillips et al. 1984). Foliar applications of fenvalerate sprays at 135 mg/L effectively controlled various pests in pear orchards of northern California, including pear psylla (*Psylla pyricola*), codling moth (*Laspeyresia pomonella*), and pear rust mite (*Epitrimerus pyri*); populations of spider mites increased, especially the two-spotted spider mite, *Tetranychus urticae* (Riedl and Hoying 1980).

A concentration of 2 mg fenvalerate per liter is frequently applied to soils to control insect pests (Schreiber and Brink 1989). However, several species of soil protozoans (*Blepharisma undulans*, *Colpoda cucullus*, *Oikomonas termo*) have LC10 (9 h) values in the range of 0.1-0.18 mg/L, suggesting that some damage occurs to this group under recommended application protocols (Schreiber and Brink 1989). In fact, all fenvalerate treatments applied to control insect pests of crops also reduced populations of beneficial nontarget organisms, including spiders, ground beetles (*Calosoma* sp.), and crickets (Smith et al. 1989). For example, spiders (*Chiracanthium mildei*) exposed for 48 h to grapefruit leaves that had been dipped 1 h previously for 5 s in aqueous emulsions of fenvalerate at field-recommended application rates all died within 2 days postexposure (Mansour 1987).

Fenvalerate-tolerant strains of arthropods include insect vectors of disease, flies and cockroaches, arthropods of veterinary importance, and agricultural pests (Sawicki 1985). But serious control problems are restricted to only a few areas, such as Central America and Thailand, where insecticidal usage is often excessive (Sawicki 1985). The exact mechanisms of resistance are unknown, although tolerance to fenvalerate in the diamondback moth (*Plutella xylostella*), a worldwide pest of cabbage-type crops, is about 20% genetic, involving several genes and multiple loci (Tabashnik and Cushing 1989). Estimates of heritability in tolerance of insects to all biocides ranges between 14 and 47% (Tabashnik and Cushing 1989). Tolerant insect species, such as larvae of the common green lacewing (*Chrysopa carnea*), and resistant strains of houseflies and lepidopterous larvae may hydrolyze fenvalerate faster than sensitive species or susceptible strains (Glickman and Casida 1982). Fenvalerate-resistant strains of domestic houseflies (*Musca domestica*), for example, when compared with susceptible strains, absorbed up to one-third the fenvalerate, had a metabolic rate up to 8 times faster, began excretion of metabolites 5 times faster, and were twice as resistant to piperonyl butoxide, a synergist applied with fenvalerate (Golenda and Forgash 1989).

The alfalfa leaf cutter bee (*Megachile rotundata*) is the most important insect pollinator of alfalfa grown for seed production in France. Alfalfa is parasitized by many insects, including the flower midge (*Contarina medicaginis*). Fenvalerate, at 0.05 kg/ha, controls the flower midge without harm to alfalfa leaf cutter bees (Tasei and Debray 1985). In general, fenvalerate-treated plants were usually nontoxic to bees after 24 h (Mayer et al. 1987). Fenvalerate does not poison bees when they are in contact with contaminated (100 mg/kg) wax in combs (Stoner et al. 1985). Fenvalerate does not pose a serious threat to honeybees except when dietary levels exceed 50 mg fenvalerate per kilogram (Stoner et al. 1984). Field application of fenvalerate at 0.22 kg/ha on blooming alfalfa, pollen-shedding corn, and blooming red raspberry (*Rubus strigosus*) resulted in reduced honeybee visitation and low to moderate adult bee mortality (Mayer et al. 1987). Caged honeybees exposed to an equivalent dose of fenvalerate at 0.11 kg/ha experienced >50% mortality within 24 h (Table 4). However, field studies showed that 0.11 kg/ha caused no observable adverse effects to bee colonies located adjacent to a treated alfalfa field; researchers concluded that fenvalerate temporarily repelled bees, as judged by a 70% reduction in bee visits to the alfalfa field in the afternoon after application when compared with periods 24 h before and after application (Moffett et al. 1982). Impaired response to scent stimuli, in addition to repellency, may account for a reduction in bee visits. Recent studies by Taylor et al. (1987) suggested that bees surviving LD50 doses of fenvalerate were unable to distinguish odor-mediated learned responses for up to 6 days after treatment. This finding indicates that more research is needed on fenvalerate-associated olfactory inhibition.

Table 4. Lethal and sublethal effects of fenvalerate on terrestrial invertebrates.

Organism, dose and other variables	Effect	Reference[a]
Cricket, *Acheta pennsylvanicus*		
5.4 mg/kg mucky soil	LD50 (18 h)	1
6.5 mg/kg moist sand	LD50 (18 h)	1
Mosquito, *Anopheles stephensi*		
0.002 µg whole body	LD50	12
Indian hive bee, *Apis cerana indica*		
0.128-0.14 µg/bee	LD50, topical application	2
Honeybee, *Apis mellifera*		
0.11 kg/ha, caged bees	57% dead in 24 h	3
Bees caged with alfalfa treated previously with 0.22 kg/ha, and held under various photo-thermal regimens for 24 h	Bees held at 10° C in the dark experienced 96% mortality; bees held at 29° C in the dark had 58% dead; those held at 18-35° C with normal photo-period had 40% dead	3
0.22 kg/ha	Repelled bees for 10 h	4
0.4 kg/ha	Increased mortality for 3 days after exposure	4
0.43 kg/ha, caged bees	All dead in 24 h	3
0.9 kg/ha	Hazardous for 2 h after application	5
Fed sucrose syrup for 7-8.5 weeks containing fenvalerate at 0.1, 1, 10, 50, or 100 mg/kg	At 100 mg/kg, survival was lower and honey production declined. At 50 mg/kg diet, bees consumed less syrup, suggesting repellency. No measurable effect at 10 mg/kg diet and lower. Queens were not affected at any dose level	5
Colonies exposed for several weeks to 1, 10, 100, or 1,000 mg/kg incorporated into beeswax foundation	Adverse effects noted only at 1,000 mg/kg, namely, lower egg hatch and survival. Fenvalerate degradation in beeswax was 11% in 15 days, 21% in 75 days, and 81% in 130 days	6
Mite, *Chorioptes bovis*		
0.05% dip (500 mg/L) for 1 min	Kills all mites and their eggs on Angora goats (*Capra* sp.) within 7 days	7
Alfalfa leaf cutting bee, *Megachile rotundata*		
0.05 kg/ha	No effect on survival or reproduction	8
0.11 kg/ha	82% dead in 24 h	3
0.22 kg/ha	92% dead in 24 h	3
0.43 kg/ha	All dead within 24 h	3
Housefly, *Musca domestica*		
Susceptible strain		
0.013-0.015 µg per fly	LD5, topical dose	12,13
0.028 µg per fly	LD30, topical dose	13
Resistant strain		
0.150 µg per fly	LD5, topical dose	13
Alkali bee, *Nomia melanderi*		
0.11 kg/ha	64% dead in 24 h	3
0.43 kg/ha	All dead in 24 h	3
American cockroach, *Periplaneta americana*		
3.5 µg per roach	Nonlethal	9
10.5 µg per roach	LD50, topical	9
100 µg/kg BW	LD50, topical	12
200 µg/kg BW	LD95, topical. Diazepam delayed onset of action	10

Fire ant, *Solenopsis invicta*		
0.73-1.4 g per mound, applied as drench	All mounds viable after 4 weeks; 70-100% of mounds nonviable after 8 weeks	11
112 or 224 g/ha, aerial application	Ineffective control. After 4 weeks, population levels were 29-35% of controls	11

[a] 1. Harris et al. 1981; 2. Lingappa et al. 1985; 3. Mayer et al. 1987; 4. Moffett et al. 1982; 5. Stoner et al. 1984; 6. Stoner et al. 1985; 7. Wright et al. 1988; 8. Tasei and Debray 1985; 9. Yellamma and Reddy 1987; 10. Gammon et al. 1982; 11. Phillips et al. 1984; 12. Abbassy et al. 1983; 13. Golenda and Forgash 1989

Aquatic Organisms

"Supertoxic" compounds are those with LC50 (96 h) values < 10 µg/L (Scott et al. 1987). Fenvalerate is considered supertoxic, as judged by LC50 (96 h) values of < 1.0 µg/L for sensitive aquatic organisms, and < 10 µg/L for representative aquatic species (Table 5).

Table 5. Lethal and sublethal effects of fenvalerate on aquatic organisms.

Taxonomic group, organism, dose or concentration, and other variables	Effect	Reference[a]
Algae		
Alga, *Chlamydomonas reinhardii*		
0.109-5.17 µg/L	Up to 93% of all fenvalerate was adsorbed by algae in 48 h in a biomass-dependent manner when cells increased from 100/mL to 2 million/mL. In absence of alga, up to 33% of fenvalerate added to glass containers was adsorbed to container walls in 48 h	1
Marine algae, 4 species: *Isochrysis galbana, Skeletonema costatum, Thalassiosira pseudonana, Nitzschia angularis*		
1,000 µg/L	Insufficient to produce 50% growth inhibition in 96 h	2
Invertebrates		
Mosquito, *Aedes nigromaculis*		
Multiresistant strain, 4th stage larvae		
5.6 g/ha (0.005 pounds per acre)	58% reduction 6 h after treatment	3
11.2 g/ha (0.01 pounds per acre)	81% reduction 6 h after treatment	3
28.0 g/ha (0.025 pounds per acre)	88% reduction 6 h after treatment	3
Mosquito, *Aedes* spp.		
0.9-10.0 µg/L	LC50-LC90 range for 4th stage larvae	4
1.5-4.0 µg/L	LC50-LC90 range for 24 h stage pupae	4
Rhagionid fly, *Atherix* sp.		
0.021 µg/L	LC30 (28 days)	5
0.029 µg/L	LC50 (28 days)	5
0.032 µg/L	LC50 (96 h)	5
Cladoceran, *Ceriodaphnia lacustris*		
0.01 µg/L	Filtration rate of alga *(Chlamydomonas reinhardii)* significantly decreased after 24-h exposure	6
0.05 µg/L	Decreased food assimilation rate, 24-h exposure	6

0.21 µg/L	50% immobilization of adults in 48 h	6
Chironomids		
4.2-18.0 µg/L	LC50 (24 h), 3 species	7
4.2-80.0 g/L	LC50 (24 h), 8 species	7
Midge, *Chironomus tentans,* fourth-instar larvae		
0.015-0.93 µg/L	Normal burrowing behavior	8
Exposed for 24 h in different sediment types containing initial fenvalerate concentration of 50 µg/kg fresh weight (FW) or 48 h in water above sediment; depuration for 96 h in each case		
Sand (water column and sediment interstitial water concentrations after 24 h were 1.02 and 4.82 µg/L, respectively)	Bioconcentration factor (BCF) of x69 for those held in water column and x 102 for those held in sand	8
Silt (water column 0.17 µg/L, interstitial water 0.15 µg/L)	BCF of x74 for water column, x 116 for silt	8
Clay (water column 0.3 µg/L, interstitial water 0.34 µg/L)	BCF of x32 for water column, x 152 for clay	8
Snail, *Cipangopaludina japonica*		
0.4-0.7 µg/L	BCF of x617 in 30 days	9
Sand shrimp, *Crangon septemspinosa*		
0.04 µg/L	LC50 (96 h)	10,11
American oyster, *Crassostrea virginica*		
1.0 µg/L	BCF of x4,700 in 28 days; depuration to non-detectable levels in <7 days	12
> 1,000 µg/L	Abnormal shell growth in 50% of larvae surviving exposure for 48 h	2, 11
Mosquito, 3 species of *Culex*		
1.2-30.0 µg/L	LC50-LC90 range for 24-h stage pupae	4
4.0-10.0 µg/L	LC50-LC90 range for fourth stage larvae	4
Mosquito, *Culex pipiens pipiens*, larvae		
0.45 µg/L	LC50 (24 h), technical grade	13
30.0 µg/L	LC50 (24 h), emulsifiable formulation	13
11.0 mg/kg diet	LC50 (24 h)	13
Mosquito, *Culex quinquefasciatus*		
7-8 µg/L	LC50-LC90 range for 4th stage larvae	3
Daphnid, *Daphnia galeata mendotae*		
0.005 µg/L	Life cycle (28-day) exposure produced increased longevity but decreased production of young	1
0.01 µg/L, and higher	Decreased survival, reproduction, and generation time in lifetime exposure	1
0.042-0.084 µg/L	Whole body fenvalerate residues in presence of alga (*Chlamydomonas reinhardii*) ranged from 0.51 to 1.08 mg/kg FW after 48-h exposure	14
0.05 µg/L	Decreased filtering rate and assimilation rate of algae after exposure for 24 h; decrease in population numbers in 28-day exposure	1,6

0.051-0. 109 µg/L	In absence of algae, whole body residues ranged from 1.46 to 2.66 mg/kg FW after 48 h	14
0.16 µg/L	50% of immatures immobilized in 48 h	6, 15
0.29 µg/L	50% of adults immobilized in 48 h	6, 15
Daphnid, *Daphnia magna*		
0.25 µg/L	No measurable effect after exposure for 21 days	16, 17
0.5 µg/L	After 21 days, reduced survival and inhibited reproduction	16
0.83 µg/L	50% immobilization of immatures in 48 h	6
2.1-2.5 µg/L	50% immobilization of adults in 48 h	6,18
Daphnid, *Daphnia pulex*		
0.4-0.7 µg/L	BCF of x683 in 30 days	19
Copepod, *Diaptomus oregonensis*		
0.05 µg/L	Decreased filtration rate and food assimilation rate after 48-h exposure	6
0.12 µg/L	50% of adults immobilized in 48 h	6
Mayfly, *Ephemerella* sp.		
0.022 µg/L	LC80 (14 days)	5
0.07 µg/L	50% reduction in swimming ability in 96 h	20
0.08 µg/L	LC50 (96 h)	20
0.93 µg/L	LC50 (24 h)	5,20
Amphipod, *Gammarus pseudolimnaeus*		
0.022 µg/L	LC65 (6 days)	5
0.03 µg/L	LC50 (96 h), adults	5
0.05 µg/L	LC50 (96 h), juveniles	5
0.93 µg/L	All dead or immobilized within 5 h	5
Snail, *Helisoma trivolvis*		
0.021 µg/L	BCF of x1,167 in 28 days	5,7
0.054 µg/L	BCF of x592 in 28 days	5,7
0.79 µg/L	BCF of x386 in 28 days; no adverse effects on survival or behavior	5,7
American lobster, *Homarus americanus*		
0.14 µg/L	LC50 (96 h)	10, 11
Mosquito, 4 species, larvae		
0.9-28.0 µg/L	LC50 (24 h)	7,21
Mysid shrimp, *Mysidopsis bahia*		
0.008-0.021 µg/L	LC50 (96 h)	2,11,12,18,22
97-190 µg/kg sediment, equivalent to 0.03 µg/L water column	58% dead in 4 days, 70% dead in 10 days	23
1,200-1,600 µg/kg sediment, equivalent to 0.06-0.17 µg/L water column	All dead in 4 days	23
Copepod, *Nitocra spinipes*		
0.38 µg/L	LC50 (96 h)	23
Rusty crayfish, *Orconectes rusticus*		
20 µg/L	LC100 (96 h)	24
Grass shrimp, *Palaemonetes pugio*		
0.0016 µg/L	No deaths of larvae in 20 days; larval development prolonged by 2 days	25
0.003-0.013 µg/L	LC50 (96 h)	18,26

0.0032 µg/L	Larvae exposed for 20 days had reduced survival and inhibited metamorphosis	25
0.007 µg/L	LC50 (96 h), emulsifiable concentrate, zoeae, 10 ‰ salinity	27
0.02 µg/L	LC50 (96 h), emulsifiable concentrate, zoeae, 20 ‰ salinity	27
0.040 µg/L	LC50 (96 h), adults, emulsifiable concentrate	27
0.044 µg/L	LC50 (96 h), adults, technical grade	27
0.046 µg/L	Maximum tolerated dose in 6-h exposure, adults	27
0.1-0.15 µg/L	LC50, 90 h after 6-h exposure, adults	27
88-200 µg/kg sediment	LC50(96 h)	18,23
1,000-1,200 µg/kg sediment	LC100 (96 h)	18,23
Pink shrimp, *Penaeus duorarum*		
0.84 µg/L	LC50 (96 h)	12,22
1,200-1,600 µg/kg sediment, equivalent to 0.06-0.17 µg/L	None dead in 10 days	23
10,000-13,000 µg/kg sediment equivalent to 0.2-1.9 µg/L water column	All dead in 4 days	23
Red crayfish, *Procambarus clarkii*		
0.37 µg/L	LC50 (24 h), juveniles	28
Mosquito, *Psorophora columbiae*		
28-50 µg/L	LC50--LC90 range for fourth stage larvae	4
53-82 µg/L	LC50-LC90 range for 24-h stage pupae	4
Stonefly, *Pteronarcys dorsata*		
0.11 µg/L	38% immobilized in 72 h	5
0.13 µg/L	50% immobilized in 72 h	5
0.44 µg/L	38% immobilized in 24 h; 25% dead in 72 h	5
1.02 µg/L	All immobilized in <4 h; most dead in 72 h	
Chordates		
Amphioxus, *Branchiostoma caribaeum*		
760 µg/L	LC10 (10 days)	18
1,000 µg/L	No deaths in 96 h	18
1,600 µg/L	LC50 (96 h)	18
2,500 µg/L	LC100 (96 h)	18,23
100-1,000 µg/kg sand	Effectively colonized in 8 weeks	29
10,000 µg/kg sediments	No deaths in 10 days	18
10,000 µg/kg sand	Unable to effectively colonize during 8-week study	29
Vertebrates		
Bleak, *Alburnus alburnus*		
0.3 µg/L	LC50 (96 h)	23
Desert pupfish, *Cyprinodon macularis*		
25 µg/L	LC50 (48 h)	20
Sheepshead minnow, *Cyprinodon variegatus*		
0.3-5.0 µg/L	Whole body BCF values in fish surviving 28-day exposure were x460 (0.31 µg/L), x360 (0.62 µg/L), x500 (1.2 µg/L), x700 (2.5 µg/L), and x820 (5.0 µg/L)	22
0.56 µg/L	No effect on hatchability, survival or growth in 28-day exposure	17,22
2.2 µg/L	Growth reduction in 28-day exposure	22
4.4-5.0 µg/L	LC50 (96 h), flowthrough assay	2, 12,22,30

120 µg/L	LC50 (96 h), static assay	2
Common carp, *Cyprinus carpio*		
0.4-0.7 g/L	BCF of x69-x 117 in 30-day exposure	19
0.8 µg/L	After exposure for 7 days, 50% excreted 5 days after exposure and 87% in 25 days	19
0.9 µg/L	No deaths in 48 h	31
3.8 µg/L	LC10 (48 h)	31,32
10 µg/L	At 48 h, hypoproteinemia and altered enzyme activity in gills	31,32
21-30 µg/L	LC50 (48 h)	31,32
117 µg/L	LC90 (48 h)	31
Mummichog, *Fundulus heteroclitus*		
1.2-1.8 µg/L	LC50 (96 h)	23,26
Mosquitofish, *Gambusia affinis*		
15.0 µg/L	LC50 (48 h)	20
Channel catfish, *Ictalurus punctatus*		
1.8-1.9 µg/L	LC50 (24 h)	19,28
16.5 µg/L, equivalent to 112 g/ha	Muscle residues in dead fish ranged up to 70 µg/kg FW	28
30.6 µg/L, equivalent to 224 g/ha	Muscle residues in dead fish collected 24 h after treatment ranged up to 160 µg/kg FW	28
Bluegill, *Lepomis macrochirus*		
0.3-1.1 µg/L	LC50 (96 h)	19
0.7 µg/L	Elevated whole body calcium content after 48 h	34
0.9-1.9 µg/L	LC50 (48 h) range for water hardnesses between 6 and 309 mg $CaCO_3$/L, or between 4.2 and 13.6 ‰ salinity	35
10 µg/L	LC100 (96 h)	24
Intraperitoneal injection, in mg/kg body weight (BW)		
0.12	LD50 (48 h), 2S, αS isomer	17,36,37
0.67	LD50 (48 h), technical fenvalerate--mixture of all isomers	13,17,36,37
11.5	LD50 (48 h), 2S, αR isomer	17,36,37
216	No deaths in 48 h, 2R, αS isomer	17,36,37
264	No deaths in 48 h, 2R, αR isomer	17,36,37
California grunion, *Leuresthes* tenuis		
0.06 µg/L	No observable effect concentration in 28-day early life history exposure	23
0.3-0.6 µg/L	LC50 (96 h)	2,30
Inland silverside, *Menidia beryllina*		
1.0 µg/L	LC50 (96 h)	30
Atlantic silverside, *Menidia menidia*		
0.062 µg/L	No observable effect concentration in 28-day early life history exposure	23
0.31-0.69 µg/L	LC50 (96 h)	12, 17, 22
Tidewater silverside, *Menidia peninsulae*		
0.083 µg/L	No observable effect concentration in 28-day early life history exposure	23
1.0 µg/L	LC50 (96 h)	30

Striped mullet, *Mugil cephalus*		
0.58 µg/L	LC50 (96 h)	2, 12,22
African catfish, *Mystus vittatus*		
0.13 µg/L	Safe concentration	38
6.3 µg/L	LC50 (96 h)	38
Rainbow trout, *Oncorhynchus mykiss*		
0.00028 µg/L, exposure for 48 h followed by depuration for 48 h	Tissue residues, in µg/kg FW, were 7.06 in bile; 0.2 in fat; 0.02-0.05 in blood, brain, carcass, gill, kidney, liver, muscle, ovary, erythrocytes, and spleen; and <0.02 in heart, plasma, and testes	39
0.23-2.1 µg/L	LC50 (96 h)	17,18,19, 20,41,50
3.6 µg/L	Hyperactivity in 48 h	41
4.7-76 µg/L	LC50 (24 h)	20,42
300 µg/L	All dead in 10 h. At death, brain residues of 150-160 µg/kg FW. Similar brain residues reported through lethal intraperitoneal and intravenous injection routes	13,39,43
412 µg/L	All dead in 11 h. Before death, trout displayed elevated cough rate, tremors, seizures, elevated urine Na and K, and abnormal blood chemistry. At death, gill histopathology evident, and residues, in µg/kg FW, were 160 in brain, 250 in carcass, and 3,620 in liver	40
Steelhead trout, *Oncorhynchus mykiss*		
Steelhead embryos and larvae exposed intermittently (4.5 h daily) or continuously for 70 days after fertilization to nominal concentrations of 0.018, 0.04, 0.08, 0.135, or 0.505 µg/L		
0.018 µg/L	No deaths. Whole body BCF values at 70 days were X 400 for intermittent exposure and x4,100 for continuous exposure	40
0.04 µ g/L, tested at intermittent exposure only	No deaths; BCF of x3,200	40
0.08 µg/L	For continuous exposure, no effect on survival or growth; BCF of x3,000. For intermittent exposure 32% dead, 50% reduction in growth, BCF of x 10,700	40
0.135 µg/L, continuous exposure only	More than 90% dead, with most dying after 56 days; BCF of x 11,800	40
0.505 µg/L, continuous exposure	All dead. Most died after 49 days	40
Steelhead juveniles exposed intermittently (4.5 h daily) or continuously		
0.088 µg/L	LC50 (96 h), intermittent exposure	40
0.172 µg/L	LC50 (96 h), continuous exposure	17,40
Gulf toadfish, *Opsanus tau*		
1.2 µg/L	No observable effect concentration in 28-day	23

	early life history exposure	
2.4-5.4 µg/L	LC50 (96 h)	2,12,23
Fathead minnow, *Pimephales promelas*		
0.14-0.19 µg/L	Whole body residues of larvae in 28-day exposure ranged from 230 to 880 µg/kg FW. BCF values ranged from x 1,643 to x4,631, in a dose dependent manner	21
0.19 µg/L	No effect on larval survival or growth in 30-day exposure	45
0.33 µg/L	50% of larvae exposed for 96 h developed abnormally	45
0.34 µg/L	LC50 (48 h), adults, mixture of 2S, αS and 2S, αR isomers	36,37
0.36-0.43 µg/L	Exposure of eggs and resultant larvae for 30 days had no effect on hatchability, but adversely affected larval growth, survival, and swimming ability	21,45
0.37 µg/L	Whole body residues of survivors at 96 h contained 598 µg/kg FW, equivalent to BCF of x 1,616	46
0.49 µg/L	After 96 h, survivors contained 911 µg/kg whole body, or BCF of x 1,859	46
0.75 µg/L	After 96 h, survivors contained 1,680 µg/kg BW, or BCF of x2,240	46
0.85 µg/L	LC50 (96 h), larvae	45
1.69 µg/L	LC50 (48 h), adults, technical fenvalerate	37
2.5 µg/L	Schooling behavior absent after 48 h exposure, adults	41
2.85 µg/L	Exposure of larvae for 5 h resulted in 50% deformities 96 h later	45
3.6 µg/L	Hyperactivity after 48 h, adults	41
5.4 µg/L	LC50 (96 h), adults	17
>140 µg/L	LC50 (48 h), adults, mixture of 2R, αS and 2R, αR isomers	36,37
1.0 mg/kg FW whole body	Residue at death of fenvalerate-poisoned fish	13
Northern leopard frog, *Rana pipiens pipiens*		
3 µg/L	All dead in 72 h at 4° C	47
9 µg/L	None dead in 72 h at 20° C	47
130 µg/kg BW	LD50 (24 h), subcutaneous (sc) injection	47
1,800 µg/kg BW	LD50 (24 h). Initially pretreated with sc dose of 10 mg diazepam per kilogram BW followed by sc injection dose of fenvalerate	47
Atlantic salmon, *Salmo salar*		
0.8 µg/L	Some deaths during 96-h exposure; BCF of x200	10
1.2 µg/L	LC50 (96 h)	10
2.0-4.1 µg/L	Some deaths during 54-h exposure; BCF about x 125	10
9.3 µg/L	Some deaths during 16-h exposure; BCF of x40	10
Mozambique tilapia, *Tilapia mossambica*		
9 µg/L	No deaths in 20 days, but significant decreases in activity of catalase superoxide dismutase in liver, gill, and muscle, and significant increases in activity (and presumably metabolism) of	48,49

		fructose-1, 6-diphosphate aldolase in liver, gill, kidney, and brain	
45 µg/L		LC50 (48 h)	48,49

a 1, Day and Kaushik 1987a; 2. Mayer 1987; 3. Mulla et al. 1978; 4. Mulla et al. 1980; 5. Anderson 1982; 6. Day and Kaushik 1987c; 7. Anderson 1989; 8. Muir et al. 1985; 9. Ohkawa et al. 1980; 10. McLeese et al. 1980; 1 I. Tagatz and Ivey 1981; 12. Schimmel et al. 1983; 13. Coats et al. 1989; 14. Day and Kaushik 1987b; 15. Day 1989; 16. McKee and Knowles 1986; 17. Bradbury and Coats 1989b; 18. Clark et al. 1987; 19. Mayer and Ellersieck 1986; 20. Smith and Stratton 1986; 21. Spehar et al. 1982; 22. Hansen et al. 1983; 23. Clark et al. 1989; 24. Bills and Marking 1988; 25. McKenney and Hamaker 1984; 26. Scott et al. 1987; 27. Baughman et al. 1989; 28. Coulon 1982; 29. Tagatz et al. 1987; 30. Clark et al. 1985; 31. Jagan et al. 1989; 32. Reddy and Bashamohideen 1988; 33. Trim 1987; 34. Symonik et al. 1989; 35. Dyer et al. 1989; 36. Haya 1989; 37. Bradbury et al. 1987b; 38. Verma et al. 1981; 39. Bradbury et al. 1986; 40. Curtis et al. 1985; 41. Holcombe et al. 1982; 42. Coats and O'Donnell-Jeffery 1979; 43. Bradbury and Coats 1989a; 44. Bradbury et al. 1987a; 45. Jarvinen et al. 1988; 46. Bradbury and Coats1985; 47. Cole and Casida 1983; 48. Radhaiah and Reddy 1989; 49. Radhaiah et al. 1989.

Signs of fenvalerate poisoning in fish include loss of schooling behavior, swimming near the water surface, hyperactivity, erratic swimming, seizures, loss of buoyancy, elevated cough rate, increased gill mucus secretions, flaring of the gill arches, head shaking, and listlessness before death (Bradbury and Coats 1989a, 1989b). Fenvalerate mainly affects the teleost nervous system, as discussed earlier. It also produces osmoregulatory imbalance, as judged by altered calcium uptake (Symonik et al. 1989), abnormal sodium and potassium excretion rates, and elevated urine osmolality (Bradbury et al. 1987a; Bradbury and Coats 1989a, 1989b). Histological damage to gill surfaces by fenvalerate is attributed to high accumulations in gills, irritation due to elevated mucus secretion, increased ventilation volume, and decreased gill-oxygen uptake efficiency (Bradbury et al. 1986, 1987a; Bradbury and Coats 1989a, 1989b). In fish, as in mammals, fenvalerate toxicity is primarily dependent on the 2S, αS component of the technical mixture. Studies with individual isomers and various freshwater fishes indicate that the 2S, αS isomer is 96 times as toxic as the 2S, αR isomer, and at least 1,766 times as toxic as the 2R, αS or 2R, αR isomers (Table 5).

Laboratory studies with fenvalerate and aquatic organisms indicate marked differences in sensitivity among taxonomic groups (Table 5). Crustaceans were the most sensitive group: reduced survival was evident between 0.0032 and 0.03 µg/L, and impaired feeding and reproduction was evident between 0.0016 and 0.01 µg/L. Fish and amphibians were more tolerant to fenvalerate than were crustaceans: increased mortality was evident between 0.088 and 1.1 µg/L, and no adverse effects were demonstrated in several species between 0.062 and 0.083 µg/L, although certain salmonids showed high uptake at concentrations as low as 0.0003 µg/L. Algae, molluscs, and chordates were comparatively resistant to fenvalerate (Table 5). Survival patterns of fenvalerate-stressed aquatic organisms are significantly altered, sometimes by an order of magnitude or greater, by selected biological, chemical, and physical variables. In general, increased mortality was associated with the following: reduced metabolism and excretion (Bradbury et al. 1986; Bradbury and Coats 1989a; Coats et al. 1989; Haya 1989); depleted glycogen stores due to starvation (Haya 1989); larval and juvenile stages of development (Spehar et al. 1982; Bradbury and Coats 1989a; Haya 1989); low concentrations of humic acid and other dissolved materials (Coats et al. 1989); low particulate loadings (Coulon 1982; Coats et al. 1989); increased water hardness (Dyer et al. 1989; Coats et al. 1989); increased exposure time and bioavailability (Spehar et al. 1982; Curtis et al. 1985); emulsifiable formulations (Trim 1987; Haya 1989); low temperatures (Cole and Casida 1983; Bradbury and Coats 1989a; Coats et al. 1989); and the 2S, αS component (Ohkawa et al. 1980; Bradbury and Coats 1989a; Coats et al. 1989; Haya 1989). Fenvalerate-protective agents include diazepam and endosulfan. Diazepam provides up to 14-fold protection to frogs against toxic doses of fenvalerate (Cole and Casida 1983); endosulfan provides limited protection to estuarine fish and shrimp (Scott et al. 1987; Trim 1987).

Bioaccumulation factors for fenvalerate by representative freshwater and estuarine organisms during exposure for 28-30 days to various sublethal doses ranged from 40 to 570 times for fish, 356 to 4,700 times for invertebrates, and 477 to 933 times for algae (Smith and Stratton 1986). Because of its unusually high lipophilicity, fenvalerate is accumulated at only 30% efficiency by aquatic fauna, and uptake is not dose

dependent (Coats et al. 1989). Contamination of algal food of daphnids with fenvalerate does not seem to contribute to an increase in whole body burdens, although reduced filtration rates due to toxicity could also account for a reduced intake of fenvalerate adsorbed to algae (Table 5; Day and Kaushik 1987b, 1987c).

Fenvalerate applications of 0.055-0.220 kg/ha are recommended for control of pestiferous crop insects, but these levels are rapidly fatal to nontarget organisms if introduced accidentally into aquatic environments (Day et al. 1987). In one study, large earthen ponds containing red crayfish (*Procambarus clarki*) were treated with fenvalerate at concentrations equivalent to 28, 56, 112, or 224 g/ha. All crayfish died within 24 h at all concentrations tested (Coulon 1982). After 3 days, ponds dosed with 112 g/ha and lower were not lethal to crayfish exposed for 24 h. The 224 g/ha pond remained toxic to crayfish after 72 h (71% dead) and 120 h (32% dead); mortality was negligible (<10%) after 168 h (Coulon 1982). Fenvalerate applications of 28-112 g/ha (0.025—0.1 pounds per acre) usually control 90-100% of floodwater mosquitos and stagnant water mosquitos. But at 2 -11 g/ha equivalent, the following effects are reported: mayfly naiads are eliminated; populations of diving beetles, cladocerans, and dragonfly naiads are suppressed for up to 3 weeks; zooplankton filtration rates are reduced; colonization processes are altered; and algal and rotifer populations increase due to lack of cladoceran grazing and competition (Mulla et al. 1978, 1980; Tagatz and Ivey 1981; Anderson 1982; Spehar et al. 1982; Hansen et al. 1983; Smith and Stratton 1986; Day et al. 1987; Bradbury and Coats 1989a; Day 1989).

Sediment—water interactions are important to the understanding of fenvalerate toxicokinetics. Addition of soil to fenvalerate-treated waters reduced toxicity to channel catfish (*Ictalurus punctatus*) through adsorption of fenvalerate to clay and organic components of soil; however, crayfish were not protected (Coulon 1982). Chironomid larvae held in water on sand initially spiked with 50 µg fenvalerate per kilogram accumulated up to 15 times as much fenvalerate than did larvae held in water above spiked silt or clay; a similar pattern was evident at an initial concentration of 5 µg/kg (Muir et al. 1985). This phenomenon is attributed to the greater bioavailability of fenvalerate in sand, as judged by elevated sediment interstitial water concentrations in sand when compared with those of silt or clay (Table 5; Muir et al. 1985). Mortality was observed in systems where fenvalerate concentrations in sediments were sufficient to establish lethal concentrations in the overlying water through sediment-water partitioning; lethal effects at nominal sediment concentrations of 0.1 mg fenvalerate per kilogram were observed for mysids (*Mysidopsis bahia*) and grass shrimp (*Palaemonetes pugio*) and at 10 mg/kg for pink shrimp (*Penaeus duorarum*; Clark et al. 1989). Because fenvalerate readily sorbs and binds to organic and inorganic particulate matter, it is difficult to predict its toxic effects on aquatic biota after runoff from agricultural areas or from discharges into particulate-laden habitats (Clark et al. 1989).

Birds

Birds that died of fenvalerate poisoning contained residues of 0.1 to 1.26 mg/kg brain fresh weight (FW) and 0.74 mg/kg liver FW, based on acute oral doses of 500 to 4,000 mg/kg BW (Table 6); juveniles were more sensitive than adults (Bradbury and Coats 1989a). When compared to other synthetic pyrethroids tested in laying hens, fenvalerate provided higher, more persistent residues in tissues (Saleh et al. 1986a). Birds given single oral doses of fenvalerate as low as 250 mg/kg BW experienced significant weight loss (adults) or a reduction in the rate of weight gain (immatures); similar signs were noted at dietary levels of 15,000 mg/kg ration but not at 7,500 mg/kg feed (Bradbury and Coats 1982). Poultry diets that contain fenvalerate at <50 mg/kg feed do not produce an appreciable concentration of residues in eggs or meat of exposed birds (Akhtar et al. 1989).

Adult Japanese quail (*Coturnix japonica*) given a single oral dose of 4,000 mg/kg BW started feeding normally (Mumtaz and Menzer 1986), but in about 90 min they became hyperactive. Hyperactivity increased until 2 h postdosing, at which time feeding ceased. At 4 h, they had convulsions, irregular movements, jerking, and twitching; they became progressively ataxic and uncoordinated. One quail died at 4 h, another at 8 h. By 24 h, most of the survivors had resumed feeding, but they had an odd standing posture: head held high above the body, legs extended as far straight as possible, and wings held in an upright position close to the body. By 48 h the survivors seemed to be feeding and drinking regularly; growth was normal 14 days after exposure (Mumtaz and Menzer 1986). Signs of intoxication in fenvalerate-poisoned northern bobwhites (*Colinus virginianus*) usually appeared within 2 h and included hyperactivity, irregular locomotion, ataxia, and spastic muscle contractions (Bradbury and Coats 1982, 1989a). Bobwhites use croplands for feeding, and insects are an important dietary item of chicks and adults in summer months. Little potential exists for adverse effects of fenvalerate on bobwhite and other gallinaceous bird populations from dietary exposures, however, because

insects from sprayed fields had maximum whole body residues of only 0.5 mg/kg—a level far below that associated with adverse effects (Table 6; Bradbury and Coats 1982).

Table 6. Lethal and sublethal effects of fenvalerate on birds.

Organism, dose, and other variables	Effect	Reference[a]
Northern bobwhite, *Colinus virginianus*		
0.1-1.26 mg/kg fresh weight (FW), brain	Residues in dead birds following single oral exposure; residues increased in dose-dependent manner in dose range of 500-4,000 mg/kg body weight (BW)	1
0.74 mg/kg FW, liver	Mean residue in dead birds following single oral exposure; residue seemingly independent of dose	1
250 mg/kg BW, single oral dose, immatures, age 5 weeks	No deaths in 14 days	1
500 mg/kg BW, single oral dose, immatures	20% dead within 25 h	1
1,785 mg/kg BW, single oral dose, immatures	LD50. All deaths occurred 3 to 25 after dosing	
4,000 mg/kg BW, single oral dose, immatures	70% dead within 24 h; remainder survived at least 14 days	1
4,000 mg/kg BW, single oral dose, adults. age 19 weeks	No deaths in 14 days; all appeared normal 24 h after dosing	1
15,000 mg/kg diet, 5 days of exposure plus 3 days of clean feed	Insufficient to kill 50% of 2-week-old chicks	1
Japanese quail, *Coturnix japonica*		
4 daily treatments of 100 mg/kg BW, oral route	Maximum tissue residues 72 h after the last dose, in mg/kg FW, were 3.1 in fat, 0.9 in skin, 0.7 in liver, 0.2 in heart and kidney, 0.1 in lung, and 0.02 in brain	2
2,000 mg/kg diet, 6-week-old females, 7-day feeding	Increased liver aldrin epoxidase, intestinal cytochrome P-450, and intestinal erthoxyresorufin dealkylase	3
4.000 mg/kg BW, single oral dose. 14-day observation	75% excreted in <6 h, 90% within 24 h. Tissue residues were highest at 3 h in liver (9 mg/kg FW) and gradually declined, while in blood it peaked within 2 h and fell quickly to an equilibrium level of 1.5 mg/L	2
American kestrel, *Falco sparverius*		
Oral dose of 1,000, 2,500, or 4,000 mg/kg BW; maintained at 22° C or -5° C for 10 h after dosing	No deaths. Mild intoxication and elevated plasma alanine amino-transferase activity; holding temperature did not affect toxicity	8
Domestic chicken, *Gallus* sp.		
0.03 mg/kg diet for 32 days	No detectable residues in tissue or eggs	6
5 mg/kg BW, single	Up to 85% of administered dose eliminated	4

oral dose, residues measured in egg albumin and yolk, and various tissues during observation period of 144 h	in 24 h, 88% in 72 h. Maximum residues, in mg/kg FW, were 0.5 in kidney (24 h), 0.48 in yolk (96 h), 0.46 in liver (24 h), 0.25 in plasma (24 h), 0.19 in abdominal fat (96 h), 0.18 in albumin (24 h), 0.14 in blood cells (24 h), 0.07 in both leg muscle and heart at 144 h, and not detectable in subcutaneous fat and breast muscle	
10 mg/kg BW, single oral dose, laying hens, residues measured over 14 days	Maximum residues, in mg/kg FW, were 4.7 in blood (24 h), 4.0 in brain (7 days), 1.0 in kidney (48 h), 1.0 in heart (3 days), 0.3 in egg yolk (5 days), 0.25 in kidney (14 days), 0.23 in egg white (5 days), 0.2 in skin (5 days), 0.18 in liver (48 h), and <0.15 in fat and ovary	5
Oral doses of 1,000 mg/kg BW for 5 days, and again at 21 days	No neurotoxic effects observed in hens	6
1,500 mg/kg BW	Acute oral LD50	7

[a] 1. Bradbury and Coats 1982; 2. Mumtaz and Menzer 1986; 3. Riviere et al. 1983; 4. Akhtar et al. 1989; 5. Saleh et al. 1986a; 6. Reed 1981; 7. Smith and Stratton 1986; 8. Rattner and Franson 1984.

Birds rapidly and efficiently metabolize fenvalerate by hydrolytic cleavage of the ester bond followed by extensive hydroxylation of the acid moiety at the carbon adjacent to the carboxyl group, the methyl group, or both. Major metabolites identified in liver preparations were 2-(4-chlorophenyl)-3-methylbutyric acid, 4-hydroxyfenvalerate, 3-phenoxybenzaldehyde, and 3-phenoxybenzoic acid (Akhtar 1983; Mumtaz and Menzer 1986; Akhtar et al. 1989; Bradbury and Coats 1989a). Liver microsomal drug-metabolizing enzymes usually play an important role in pesticide metabolism; however, fenvalerate and other synthetic pyrethroids are very weak inducers of avian microsomal enzymes (Riviere et al. 1983). Birds are more resistant to fenvalerate than are mammals, as judged by studies with Japanese quail and rats. Quail excreted fenvalerate more rapidly, had lower absorption, and faster metabolism; the oral LD50 for quail was >4,000 mg/kg BW versus 450 mg/kg BW for rat, almost an order of magnitude higher (Mumtaz and Menzer 1986).

Mammals

In general, fenvalerate administered to mammals was rapidly eliminated and had little tendency to accumulate in tissues (Table 7). Fenvalerate killed sensitive species of mammals at a brain injection concentration of 1.0 mg/kg FW brain (equivalent to 14 µg/kg BW), an intraperitoneal injection concentration of 3.9 mg/kg BW, acute oral doses of 50 to 450 mg/kg BW, dietary levels of 50 to 1,000 mg/kg feed, and an acute dermal concentration of 1,800 mg/kg BW; in all cases the 2S, αS isomer was the most toxic (Table 7). Measurable residues of fenvalerate were detected in tissues of sensitive mammals at 0.15 mg/kg diet, 0.15 mg/kg BW applied dermally six times over a 3-week period, and at 2.5 mg/kg BW given orally; in all cases the 2R, αS isomer was taken up 9-16 times over other isomers (Table 7). Behavioral alterations (e. g., change in drinking water preference) occurred in mice after a single oral dose of 0.3 mg/kg BW (Table 7). No significant adverse effects were observed in dogs on diets equivalent to 12.5 mg/kg BW daily for 90 days or in rats on diets containing fenvalerate at 250 mg/kg (equivalent to 12.5 mg/kg BW) for 2 years (Table 7).

At sublethal doses in rodents (i.e., 100 mg/kg BW), fenvalerate produces neurological toxicity but no histological damage; at higher doses, pathological alterations in peripheral nerves occur (Bradbury and Coats 1989a). Rats given acutely toxic doses of fenvalerate showed histopathological changes such as axonal swelling and degeneration and myelin fragmentation of the sciatic nerve; the significance of these findings is unclear (Gray and Soderlund 1985).

Route of administration may account for wide variations in the toxic action of fenvalerate. Most authorities agree that fenvalerate is most toxic to rodents when administered by intercerebroventricular injection relative to other routes—indicating the importance of the brain in the Type II poisoning syndrome; fenvalerate was

decreasingly toxic when administered intravenously, intraperitoneally, orally, and dermally (Lawrence and Casida 1982; Flannigan et al. 1985; Grissom et al. 1985; Bradbury and Coats 1989a; Williamson et al. 1989).

Differences in fenvalerate metabolism occur, even among closely related species such as rats and mice (Kaneko et al. 1981). In both species, regardless of sex, dose level, or chiral isomer, fenvalerate is metabolized primarily by oxidation at the 2'-, 4'-phenoxy positions of the alcohol moiety and at the C-2 and C-3 positions of the acid moiety, by cleavage of the ester linkage, by conversion of the CN group to SCN^- and CO_2, and by conjugation of the resultant carboxylic acids and phenols with glucuronic acid, sulfuric acid, and amino acids. However, the taurine conjugate of 3-phenoxybenzoic acid was found in mice but not in rats; 4'-hydroxylation of the alcohol moiety and the sulfate conjugate of 3-(4'hydroxyphenoxy) benzoic acid occurred to a greater extent in rats than in mice; and more thiocyanate was excreted in mice than in rats (Kaneko et al. 1981). Dogs are remarkably different from rodents in their ability to metabolize fenvalerate (Kaneko et al. 1984). Four major differences have been observed: (1) Rats and mice show hydroxylation of the 2' position of the alcohol moiety, whereas dogs do not; (2) dogs produce 3-phenoxybenzyl alcohol and 3-(4'-hydroxyphenoxy) benzyl alcohol, whereas rodents do not; (3) the predominant conjugate of the alcohol moiety in dogs is 3-phenoxybenzoyl glycine, but this is only a minor conjugate in rodents; and (4) dogs produced more glucuronides of acid moiety and their hydroxy derivatives than did rats and mice. The proposed fenvalerate metabolic pathways in dogs (Kaneko et al. 1984) suggest that species differences and pathways are important and require more research.

Table 7. Lethal and sublethal effects of fenvalerate on mammals.

Organism, route of administration, dose, and other variables	Effect	Reference[a]
Cattle, *Bos* spp.		
Diet		
Fed 0.15 mg/kg feed for 21 days	Residues ranged up to 0.002 mg/L in milk, 0.022 mg/L in cream, 0.014 mg/kg fresh weight (FW) in fat, 0.006 mg/kg FW in liver, and <0.01 mg/kg FW in bone, brain, muscle, kidney, or lung	1
Dairy cows fed 5 or 15 mg/kg ration daily for 4 days; milk and feces collected during exposure and 6 days after exposure	Maximum concentrations of fenvalerate in milk during exposure were 48 µg/L (377 µg/kg dry weight [DW]) in the 5 mg/kg group and 250 µg/L (1,950 µg/kg DW) in the 15 mg/kg group; fenvalerate was not detectable 2 days after exposure in the low dose group and 6 days after exposure in the high dose group. In feces, the maximum concentrations ranged between 34.9 and 50.4 mg/kg DW during exposure; detectable concentrations in both groups were evident 6 days after exposure	2
Fed 10.9 mg/kg feed for 28 days	Maximum residues, in mg/kg FW, were 0.13 in whole milk, 1.0 in cream, 0.8 in fat, and 0.06 in muscle	1
Dermal		
Dairy cows of mean weight 671 kg given 0.1 g topically (0.1 mg/kg body weight [BW]) in six consecutive treatments at intervals of 3 or	After last application, no detectable fenvalerate residues were found in milk after 6 h; maximum residues in milk were 1.14 µg/L after 3 days, 0.42 in 4 days, and not detectable after 7 days	3

4 days (total 0.6 g)		
Dairy cows given three consecutive topical treatments of 0.5 g (0.5 mg/kg BW; total 1.5 g) at 2-week intervals	Maximum residues in milk, in µg/L, after last treatment were 6.8 after 6 h, 2.9 after 3 days, 2.5 at 7 days, 1.3 at 14 days, and <0.2 at 3 weeks. About 0.05% of the applied fenvalerate appears in the milk as the intact insecticide over the 59-day study	3
Dog, *Canis familiaris*		
Oral		
Male beagles, 7 months old, 1.7 mg/kg, single dose	About 84% eliminated from body within 3 days through urine and feces. Half-time persistence of 2 h in blood, and 0.7-1.0 day in whole body	4
Diet		
Fed up to 12.5 mg/kg BW equivalent for 90 days	No evidence of toxicity at any level	1
Groups of 12 beagles (6 males, 6 females 5 months old, fed fenvalerate at 250, 500, or 1,000 mg/kg feed for 6 months	For all groups, dose-dependent increase in emesis, head shaking, biting of the extremities, blood chemistry alterations, ataxia, tremors, and hepatic multifocal microgranulomas. Some males in the 1,000 mg/kg group were killed after 2 weeks while in coma. Sex-related differences were noted: increased cholesterol and alkaline phosphatase in males; poor growth and enlarged adrenals, ovaries, liver, and kidneys in females. Lymph node histopathology was observed in female 500 and 1,000 mg/kg group and in the male 1,000 mg/kg group	5
Hamster, *Cricetus* sp.		
In vitro		
5-40 mg/L	Nontoxic to isolated cells	6
Oral		
12.5 or 25 mg/kg BW for 2 days	No chromosomal aberrations in bone marrow	1
Domestic cat, *Felis domesticus*		
Dermal		
Topical aerosol treatment of fenvalerate plus Deet (N-N-diethyl-m toluamide) to control fleas and ticks	Kitten, 3 months old, died in 6 h following hypersalivation, ataxia, depression, and seizures. No histopathology at necropsy; brain AChE activity normal. Fenvalerate residues, in µg/kg, were 345,000 in skin, 230 in kidney, 150 in liver, 10 in brain. Adult (4 years old) showed signs of toxicosis 4 h after topical application; by 30 h, animal had lowered body temperature, bradycardia, and other signs of fenvalerate poisoning. At death, shortly thereafter, fenvalerate residues were 1,000 µg/kg in skin and 20 µg/kg in liver	7
Domestic mouse, *Mus* spp.		
Intercerebroventricular injection		
0.2 mg/kg BW	95% dead; 50% show signs of poisoning	8

	within 6 min of brain injection	
1.0 mg/kg FW brain, equivalent to 14 µg/kg BW	LD50; 2S, αS isomer	9
Oral, single dose		
0.3, 3, or 30 mg/kg	No deaths in any group. The 30 mg/kg group were hyperactive for 4 h after dosing. All mice preferred 0.3% saccharin solution to water	10
2.5 mg/kg BW of each of the 4 chiral isomers; tissue residues measured 6 days after administration	Residues of the 2R, αS isomer were 9-16 times as high in adrenal as that of the other 3 isomers (2S, αS; 2S, αR; 2R, αR), at least 20 times as high in heart, 6-14 times as high in kidney, 17-28 times as high in liver, at least 15 times in lung, 3-6 times in mesenteric lymph node, and >30 times as high in spleen	11
7 mg/kg BW, residues measured 6 days later	Maximum concentrations, in mg/kg FW, were 7.3 in hair, 0.9 in fat, 0.5 in skin, 0.3 in blood, and 0.08 in liver	12
8.4 mg/kg BW, residues measured 7 days later	Maximum concentrations, in mg/kg FW, were 2.3 in hair, 0.8 in fat, 0.3 in stomach contents, 0.1 in skin, and 0.05 in blood	12
50 mg/kg BW	LD50; 2S, αS isomer	13
72-845 mg/kg BW, various laboratory strains	LD50	1,13,14, 15,16
200 mg/kg BW	Slight increase in frequency of chromosome aberrations in bone marrow cells	17
>600 mg/kg BW	LD50; 2S, αR isomer	13
>5,000 mg/kg BW	LD50; 2R, αR isomer	13
Dermal		
I mg/kg BW, single application	Penetration through skin was 1.9% at 60 min, 2.2% at 6 h, and 9.1% at 24 h. Of penetrated dose, maximum percent distribution was 83% in carcass at 60 min, 1.3% in blood at 6 h, 11.5% in liver at 6 h, 2.2% in kidney at 6 h, 0.7% in fat at 6 h, and 73% in feces at 24 h	18,19
60, 600, or 1,800 mg/kg BW, single application	At 1,800 mg/kg BW, 20% died in 96 h; no deaths in other groups. Survivors in 600 and 1,800 mg/kg groups were hyperactive. All survivors preferred 0.3% saccharin solution to water	10
Intraperitoneal injection		
3.9 mg/kg BW	LD50; 2S, αS isomer	9
62 mg/kg BW	LD50	14
89 mg/kg BW	LD99	14
Diet		
Fed 5, 15, or 50 mg/kg on days 6-15 of gestation	Maternal toxicity at 50 mg/kg BW, but no effect on embryonic development	1
Fed 10, 50, 250, or 1,250 mg/kg feed for 2 years	Increased mortality, reduced growth, disrupted enzyme activity at 1,250 mg/kg. Nonneoplastic microgranulomas in lymph, liver, and spleen of 250 and 1,250 mg/kg male mice; less severe microgranu-	34

	latomous changes in mesenteric lymph node of 50 and 250 mg/kg groups; no observable effect at 10 mg/kg diet	
Fed 50, 250, or 1,250 mg/kg feed for 2 years	Nonneoplastic pathological changes diagnosed as multifocal microganulomas in lymph nodes, liver, and spleen of males at all dose levels, and in females at the 250 and 1,250 mg/kg diet level	20
Fed 100, 300, 1,000, or 3,000 mg/kg feed for 78 weeks	No evidence of carcinogenicity at any does tested. No-observable-effect-level (NOEL) was 100 mg/kg diet (equivalent to 15 mg/kg BW); dose-related effects noted in liver at 300 mg/kg diet and higher	1
125 mg/kg diet, 8 weeks, 2R, αS isomer	No deaths; 70% incidence of microgranulomas in liver	20
Fed 500 mg/kg diet of three isomers (2S, αS; 2R, αS; 2R, αR) for 2 weeks	Residues, in µg/kg FW, of the 2R, αS isomer were significantly higher than that of other isomers tested in adrenal (173 versus 10-21), heart (15 versus 2), kidney (22 versus 9-10), liver (105 versus 13), lung (31 versus 2-5), mesenteric lymph nodes (86 versus 8-12), and spleen (21 versus 1)	11
500 mg/kg diet, 13 weeks	No deaths; 100% incidence of microgranulomas or giant cell infiltration	20
500 mg/kg diet, 52 weeks, 2S, αS isomer	No microgranulomas or giant cell infiltration in liver, spleen, or lymph nodes	20
500 or 1,000 mg/kg diet, 52 weeks, 2S, αR isomer	No deaths; no microgranulomas	20
1,000 mg/kg diet, 2 weeks, 2S, αS isomer	Severe hyperexcitability and tremors and 100% kill. No microgranulomas present	20
1,000 mg/kg diet, 4 weeks, 2R, αS isomer	No deaths; 100% incidence of microgranulomas	20
1,000 mg/kg diet, 13 weeks, 2R, αR isomer	No deaths; no microgranulomas or giant cell infiltration	20
2,000 mg/kg diet, 2 weeks, 2S, αR isomer	All dead; no microgranulomas	20
Intraperitoneal (ip) injection		
40 mg/kg BW, five daily doses (total of 100 mg/kg BW)	Significant increase in frequency of chromosome aberrations induced in bone marrow cells—but frequency lower than single dose ip injection of 200 mg/kg BW	17
Subcutaneous injection		
Given five daily doses totaling 100, 150, or 200 mg/kg BW	After 35 days, incidence of sperm abnormalities was significantly increased over controls: 3.3% abnormal sperm in 100 mg/kg group, 5.9% in 150 mg/kg group, and 6.3% in 200 mg/kg group versus 2.3% in controls	17

Rabbit, *Oryctolagus* sp.		
Dermal		
0.13 mg/cm^2 skin, applied 5 days weekly for 16 weeks	Minor increases in cutaneous blood flow, skin reddening, and skin thickening	22
In vitro		
0.2-10 mg/L, liver and muscle tissues	Synthesis of protein and RNA inhibited in muscle in a dose-dependent manner; maximum inhibition was 0.2 mg/L for RNA synthesis and 10 mg/L for protein. The reverse was observed in liver; maximum stimulation was at 2 mg/L	23
Domestic sheep, *Ovis aries*		
Diet		
3-month-old lambs fed 45 mg/kg feed for 10 days, equivalent to 20 mg daily	Tissue residues, in mg/kg DW, were 3.6-4.4 in renal fat, 0.2 in leg muscle, and 0.1 in liver	24
Laboratory white rat, *Rattus* spp.		
Diet		
Fed 1, 5, 25, or 250 mg/kg ration for up to 2 years	No measurable effect on body weight, food consumption, hematology, clinical chemistry, or organ weights of any diet	25
Fed diets containing 1, 5, 25, or 250 mg/kg feed for three generations	No teratogenic or fetotoxic effects. Females in third generation fed highest dose had reduced growth	1
Fed 1, 5, 25,250, or 500 mg/kg ration for 2 years	NOEL at 250 mg/kg, equivalent to 12.5 mg/kg BW; growth suppression at 500 mg/kg diet	1
Fed 50, 150, 500, or 1,500 mg/kg feed for 15 months	NOEL at 50 mg/kg, equivalent to 2.5 mg/kg BW. Higher doses had adverse effects on growth, food consumption, and behavior	1
Fed 1,000 mg/kg ration for 2 years	Growth inhibited; organ-BW ratios increased in brain, liver, spleen, kidney, heart (females), and testes. Mammary and pituitary tumors commonly observed in treated and in control groups. No statistically significant difference in number or type of neoplasms, except for mammary tumors	25
Oral		
1.7 mg/kg BW daily for 5 consecutive days, or single dose of 8.4 mg/kg BW. Technical fenvalerate and 2S, αS isomer tested separately	No apparent differences in the nature and amount of metabolites and in the pattern of excretion and tissue residues between the racemic mixture and the 2S, αS isomer	26
Single dose, 2.5 mg/kg BW; residues, in µg/kg FW, in tissues measured 6 days after exposure		
2R, αS isomer	Residues in tissues were usually	11

	much higher than those of other isomers tested: adrenal, 371; fat, 304; heart, 40; kidney, 25; liver, 72; lung, 25; mesenteric node, 318; and spleen, 62	
2S, αS isomer	Residues were 511 in fat, 45 in mesenteric lymph node, and <22 in other tissues	11
2S, αR isomer	Fat contained 326, mesenteric lymph node 68, and other tissues <20	11
2R, αR isomer	Fat contained 756, mesenteric lymph node 94, and other tissues <23	11
Single dose of 3 mg/kg BW, individual isomers tested, fat analyzed periodically during 21 -day observation	Half-time persistence of all four isomers in fat ranged between 7 and 10 days; mean residues at 24 h and 21 days after exposure were 0.64 and 0.08 mg/kg FW, respectively	27
Decarboxyfenvalerate, single dose. 4 mg/kg BW	Almost completely eliminated in a few days, mainly by way of the feces; little translocation from GI contents and liver to other tissues; Tb ½ of 10 h in pancreas and <7 h in all other tissues	28
Single dose, 7 mg/kg BW, residues measured 6 days later	Residues, in µg/kg FW, were about 1,250 in blood, 1,200 in fat, 2,300 in hair of females, 37,000 in hair of males, 370 in liver, and 5,800 in skin	12
Single doses between 15 and 200 mg/kg BW	At 90 rain, rats showed a dosage-dependent decrease in locomotor activity and operant response rates	29
Adults given 25 or 75 mg/kg BW, 5 days a week for 10 weeks	At low dose, no signs of neurotoxicity or significant hepatotoxicity. At high dose, neurotoxicity evident only during first week; liver contained significantly elevated number of foci/cm3 and a larger percentage of liver tissue occupied by foci when compared to controls	30
450-3,000 mg/kg BW	LD50; variability due to solvent	1
451 mg/kg B W	LD50	15,21,31
Single dose of 850 mg/kg BW, observed for 7 days	Signs of toxicosis appeared in 2 h; if untreated, 80% died. Intraperitoneal injection of 400 mg/kg BW of methocarbamol followed by repeated doses of 200 mg/kg BW at every onset of signs eliminated signs of poisoning within 17 h and prevented mortality	32
Dermal		
31,155, or 310 mg/kg BW, 5 days weekly for 2 weeks; observed for 2 weeks after last treatment	No deaths. Altered blood chemistry that returned to normal during observation period, except for elevated serum alkaline phosphatase activity	33
Intravenous injection		
50-100 mg/kg BW	LD50	21

[a] 1. Reed 1981; 2. Wszolek et al. 1980; 3. Frank et al. 1984; 4. Kaneko et al. 1984; 5. Parker et al. 1984b; 6. Pluijmen et al. 1984; 7. Dorman et a1. 1990; 8. Gammon et al. 1982; 9. Lawrence and Casida 1982; 10. Mitchell et al. 1988; 11. Kaneko et al. 1986; 12. Kaneko et al. 1981; 13. Bradbury and Coats 1989a; 14. Williamson et al. 1989; 15. Bradbury and Coats 1989b; 16. El-Sewedy et al. 1982; 17. Pati and Bhunya 1989; 18. Grissom et al. 1985; 19. Grissom et al. 1987; 20. Okuno et al. 1986; 21. Gray and Soderlund 1985; 22. Flannigan et al. 1985: 23. El-Sebae et al. 1988; 24. Wszolek et al. 1981a; 25. Parker et al. 1984a; 26. Ohkawa et al. 1979; 27. Marei et al. 1982; 28. Mikami et al. 1985; 29. Crofton and Reiter 1988; 30. Flodstrom et al. 1988; 31. Smith and Stratton 1986; 32. Hiromori et al. 1986; 33. Saleh et al. 1986b; 34. Parker et al. 1983.

Cattle (*Bos* spp.) protected against various insect pests by fenvalerate-impregnated ear tags grow better than unprotected cattle. Beef cattle were protected against horn flies (*Haematobia irritans*) and other blood-sucking dipterans by fenvalerate-impregnated ear tags; during a 115-day grazing period, protected cattle had greater weight gain than unprotected cattle (Haufe 1982). This technique may have application in protecting fly-infested threatened or endangered species of mammals. Dairy cows tagged with 8% fenvalerate ear tags showed a 99.9% reduction in horn flies over a 16-week trial (Block and Lewis 1986). But other species of flies (housefly; stable fly, *Stomoxys calcitrans*; face fly, *Musca autumnalis*) were not controlled to the same extent, and they increased as horn fly populations decreased. Protected cows produced 117 kg more milk in 16 weeks than did unprotected cows; fat and protein percentages in milk were the same for both groups. The higher milk production in the fenvalerate-tagged group was attributed to more uninterrupted forage time, greater forage consumption, and more efficient energy utilization because less energy was expended on avoiding or removing flies (Block and Lewis 1986). Similar results were reported in dairy cows in a 12-week study (Harris et al. 1987). Fenvalerate was adequately distributed over the entire body and persisted for at least 80 days on the hair of cattle with one ear tag containing 10.5 g active ingredients (Yeung et al. 1989). Residues in hair were highest at 14 days (18.4 mg/kg FW) and lowest at 80 days (1.3-3.0 mg/kg FW). All four stereoisomers were present on cattle hair, and no stereoselective degradation occurred. Hair contained 14.8 mg/kg FW fenvalerate after 30 days with two ear tags (Yeung et al. 1989).

Cows fed fenvalerate in grain at 10 mg/kg diet for 4 days excreted most of the fenvalerate, essentially unchanged, in urine (Wszolek et al. 1981b). A secondary excretion route is feces, accounting for about 25% of the ingested dose; milk accounted for 0.44-0.64% of the total excreted (Wszolek et al. 1980). Half-time persistence of fenvalerate in milk of treated cows is about 6.4 days (Frank et al. 1984). Effects of low concentrations (1.14-6.8 µg/L) of fenvalerate in milk of treated cows on newborn suckling calves are unknown and merit additional research (Frank et al. 1984).

Fenvalerate toxicity is antagonized by atropine sulfate or methocarbamol, which may be effective in treating severe cases of poisoning (Hiromori et al. 1986). Conversely, some compounds exacerbate the toxicity of fenvalerate and interfere with a desired use. Domestic cats (*Felis domesticus*) treated with Fendeet (an aerosol mixture of fenvalerate and N-N-diethyl-*m*-toluamide) to control fleas and ticks sometimes show signs of toxicosis, such as tremors, hypersalivation, ataxia, vomiting, depression, and seizures. Signs usually appeared within hours of topical application, and females and juveniles seem to be the most sensitive group. The demonstrated ability of N-N-diethyl-*m*-toluamide to enhance the dermal absorption of fenvalerate is the probable cause of toxicosis (Dorman et al. 1990).

In occupational settings, fenvalerate produces temporary irritation and itching (Bradbury and Coats 1989a). Among human fenvalerate applicators, sensitive individuals complain of a burning and tingling skin sensation after using the insecticide, and sometimes they substitute an insecticide more toxic to nontarget species in order to avoid this uncomfortable sensation (Flannigan et al. 1985). This practice, if widespread, may compromise existing or proposed natural resource management practices.

Recommendations

Fenvalerate is listed under the Class IV Surveillance Index Classification, indicating a low hazard potential to humans from toxicological and exposure standpoints. This classification requires only nominal monitoring (Reed 1981). Monitoring efforts of regulatory agencies to the present, however, have been limited and of marginal worth in evaluating background concentrations of fenvalerate. Additional monitoring is recommended to measure fenvalerate residues in tissues of birds and mammals of U.S. Fish and Wildlife Service concern.

Products that contain fenvalerate and are registered for use on corn, wheat, soybeans, sorghum, oats, barley, rye, or cotton are subject to the provisions of the Endangered Species Act (Sine 1988). The Endangered Species Act requires that actions of federal agencies not jeopardize threatened or endangered species or their habitats. Specifically, the U.S. Environmental Protection Agency, in consultation with the U.S. Fish and Wildlife Service, determines whether use of fenvalerate poses a threat to listed species of animals and plants in various locations (Sine 1988). Clearly, fenvalerate and other synthetic pyrethroid insecticides should be used with extreme caution in habitats of endangered species.

No regulations exist for protection of sensitive natural resources against fenvalerate, although current application rates to control pestiferous crop insects are lethal to many species of nontarget organisms, including bees, fish, and crustaceans (Table 8). Current fenvalerate guidelines for protection of livestock, poultry, and human health are as follows: <5 mg/kg in diets of livestock, <50 mg/kg in diets of poultry, <3 mg/kg in human diets (< 1 mg/kg for vegetables, <0.5 mg/kg for meat, <0.25 mg/kg for milkfat), and <0.125 mg/kg BW for acceptable daily intake in humans (Table 8).

Despite the high toxicity of fenvalerate and other pyrethroids to aquatic organisms, few environmental problems have been documented, presumably due to the very low application levels needed to control insects, adsorption onto soil and organic matter, and comparatively rapid degradation (Gray and Soderlund 1985). Nevertheless, fenvalerate is extremely toxic to aquatic organisms (Table 8), has high bioaccumulation, and is persistent in sediments; these patterns are most pronounced in estuaries and other wetland environments. Fenvalerate use in areas adjacent to estuarine systems poses unacceptable risks to those ecosystems at concentrations not currently detectable by analytical methods (Schimmel et al. 1983). It seems reasonable to prohibit all uses of fenvalerate directly into aquatic environments and to severely restrict usage in areas adjacent to drainage systems.

Additional research is needed on sublethal effects of fenvalerate in the following areas: (1) impaired response to scent stimuli as demonstrated in bees (Taylor et al. 1987); (2) genotoxic potency as shown in positive genotoxic effects on mice bone marrow (Pati and Bhunya 1989); (3)photoproduct formation—especially those formed through ultraviolet irradiation--wherein at least two photoproducts were more toxic than the parent chemical (Holmstead et al. 1978); (4) enhanced tumor formation in rodent liver (Flodstrom et al. 1988); (5) development of analytical procedures to detect minute and short-lived reactive metabolites (Miyamoto 1988); (6) development of simplified and reliable laboratory test systems more representative of total natural ecosystems (Miyamoto 1988); and (7) interaction effects of fenvalerate degradation products with other chemicals (Smith and Stratton 1986). More research is also needed on indirect effects on wildlife due to reductions in nontarget insects and on bioavailability of fenvalerate to aquatic organisms from sediments and the sediment-water interface.

Table 8. Proposed fenvalerate criteria for the protection of natural resources and human health.

Resource and other variables	Criterion	Reference[a]
Bees (*Apis mellifera, Megachile* sp.)		
Adverse effects		
Whole body	>0.1 µg/bee	1
Diet	> 10 mg/kg fresh weight (FW)	2
Aerial application	0.05 >0.11 kg/ha	3,4
Aquatic organisms		
Crustaceans, decreased survival		
Water column	0.003-0.022 µg/L	5,6,7, 8,9,10, 11,12
Sediments	97-190 µg/kg FW	13
Fish		
Water column		
Persistent residues	>0.00028 µg/L	14
No adverse effects on growth survival, or reproduction	0.062-0.083 µg/L	13

Lethal	0.088-0.31 µg/L	5,10, 11, 13,15,16, 17,18,19,20
Brain residues at death	>0.16 mg/kg FW	20
Birds		
Acute oral exposure, single dose		
No deaths	<250 mg/kg body weight (BW)	21
Some deaths	>500 mg/kg BW	21
Persistent residues	>5 mg/kg BW	22
Tissue residues at death		
Brain	0.1-1.26 mg/kg FW	21
Liver	0.74 mg/kg FW	2 I
Dietary exposure		
Sublethal		
No residues in eggs or meat	<50 mg/kg diet	22
Biochemical upset	>2,000 mg/kg diet	24
Lethal	> 15,000 mg/kg diet	2 I
Mammals		
Dietary exposure		
Sublethal		
Persistent residues	0.15-15 mg/kg feed	23,25
Temporary tolerance level, livestock, dried apple pomace	5 mg/kg feed	23
No significant effects	12.5-15 mg/kg BW daily, 100-250 mg/kg diet	23,26
Significant adverse effects	250-1,000 mg/kg diet	27
Lethal	>50 mg/kg BW, >1,250 mg/kg diet	23,28
Single oral exposure		
Sublethal		
Behavioral changes	0.3-30 mg/kg BW	29
Persistent residues	>2.5 mg/kg BW	30
Lethal	50-450 mg/kg BW	20,23,31
Dermal exposure		
Sublethal		
Persistent residues	0.15-1.0 mg/kg BW	32,33,34
No deaths	310 mg/kg BW daily for 2 weeks	35
Lethal	1,800 mg/kg BW, single application	29
Human health		
Permanent tolerance level		
Meat and milk fat	<0.02 mg/kg FW	23
Temporary tolerance level		
Milk fat	<0.25 mg/kg FW	23
Meat	<0.5 mg/kg FW	23
Total diet	<3 mg/kg FW	23
Vegetables, "safe" level	<1 mg/kg FW	36
Acceptable daily intake (ADI), 60 kg person, 1.5 kg food daily	0.125 mg/kg BW	23
Theoretical daily exposure from diet		
Minimum	0.015 mg, 0.00025 mg/kg BW, 0.2% of AD1	23
Maximum	0.334 mg, 0.0056 mg/kg BW, 4.5% of ADI	23

[a] 1. Lingappa et al. 1985: 2. Stoner et al. 1984; 3. Tasei and Debray 1985; 4. Mayer et al. 1987; 5. Clark et al. 1987; 6. Scott et al. 1987; 7. Day and Kaushik 1987c; 8. Day and Kaushik 1987a; 9. Anderson 1982; 10.

Schimmel et al. 1983; 11. Mayer 1987; 12. Tagatz and Ivey 1981; 13. Clark et al. 1989; 14. Bradbury et al. 1986; 15. Curtis et al. 1985; 16. Mayer and Ellersieck 1986; 17. Clark et al. 1985; 18. Holcombe et al. 1982; 19. Hansen et al. 1983; 20. Bradbury and Coats 1989b; 21. Bradbury and Coats 1982; 22. Akhtar et al. 1989; 23. Reed 1981; 24. Riviere et al. 1983; 25. Wszolek et al. 1980; 26. Parker et al. 1984a; 27. Parker et al. 1984b; 28. Parker et al. 1983; 29. Mitchell et al. 1988; 30. Kaneko et al. 1986; 31. Bradbury and Coats 1989a; 32. Frank et al. 1984; 33. Grissom et al. 1985; 34. Grissom et al. 1987; 35. Saleh et al. 1986a; 36. Jain et al. 1979.

Acknowledgments

I thank L. J. Garrett, N. B. Hestbeck, and W. Manning for literature retrieval; M. G. Holmes and B. A. Roberts for secretarial help; J. R. Clark, J. F. Fairchild, M. J. Melancon, and M. W. Tome for technical and scientific review; and J. R. Zuboy for editorial services.

References

Abbassy, M. A., M. E. Eldefrawi, and A. T. Eldefrawi. 1983. Pyrethroid action on the nicotinic acetylcholine receptor / channel. Pesticide Biochemistry and Physiology 19:299-308.

Akhtar, M. H. 1983. Metabolism of fenvalerate by a chicken liver enzyme preparation. Journal of Agricultural and Food Chemistry 31:1080-1083.

Akhtar, M. H., H. L. Trenholm, and R.M.G. Hamilton. 1989. Metabolism of fenvalerate in laying hens. Journal of Agricultural and Food Chemistry 37:190-196.

Anderson, R. L. 1982. Toxicity of fenvalerate and permethrin to several nontarget aquatic invertebrates. Environmental Entomology 11:1251-1257.

Anderson, R. L. 1989. Toxicity of synthetic pyrethroids to freshwater invertebrates. Environmental Toxicology and Chemistry 8:403—410.

Baughman, D. S., D. W. Moore, and G. I. Scott. 1989. A comparison and evaluation of field and laboratory toxicity tests with fenvalerate on an estuarine crustacean. Environmental Toxicology and Chemistry 8:417-429.

Bennett, R. S., E. E. Klaas, J. R. Coats, and E. J. Kolbe. 1986. Fenvalerate concentrations in the vegetation, insects, and small mammals of an old-field ecosystem. Bulletin of Environmental Contamination and Toxicology 36:785-792.

Bennett, R. S., Jr., E. E. Klaas, J. R. Coats, M. A. Mayse, and E. J. Kolbe. 1983. Fenvalerate residues in nontarget organisms from treated cotton fields. Bulletin of Environmental Contamination and Toxicology 31:61-65.

Bills, T. D., and L. L. Marking. 1988. Control of nuisance populations of crayfish with traps and toxicants. Progressive Fish-Culturist 50:103-106.

Block, E., and D. J. Lewis. 1986. Efficacy of insecticidal ear tags on fly control and milk production of dairy cows. Canadian Journal of Animal Science 66:47-51.

Bradbury, S. P., and J. R. Coats. 1982. Toxicity of fenvalerate to bobwhite quail (*Colinus virginianus*) including brain and liver residues associated with mortality. Journal of Toxicology and Environmental Health 10:307-319.

Bradbury, S. P., and J. R. Coats. 1985. Differential toxicity and uptake of two fenvalerate formulations in fathead minnows (*Pimephales promelas*). Environmental Toxicology and Chemistry 4:533-541.

Bradbury, S. P., and J. R. Coats. 1989a. Comparative toxicology of the pyrethroid insecticides. Reviews of Environmental Contamination and Toxicology 108:133-177.

Bradbury, S. P., and J. R. Coats. 1989b. Toxicokinetics and toxicodynamics of pyrethroid insecticides in fish. Environmental Toxicology and Chemistry 8:373-380.

Bradbury, S. P.,J. R. Coats, and J. M. McKim. 1986. Toxicokinetics of fenvalerate in rainbow trout (*Salmo gairdneri*). Environmental Toxicology and Chemistry 5:567-576.

Bradbury, S. P., J. M. McKim, and J. R. Coats. 1987a. Physiological response of rainbow trout (*Salmo gairdneri*) to acute fenvalerate intoxication. Pesticide Biochemistry and Physiology 27:275-288.

Bradbury, S. P., D. M. Symonik, J. R. Coats, and G. J. Atchison. 1987b. Toxicity of fenvalerate and its constituent isomers to the fathead minnow, *Pimephales promelas*, and bluegill, *Lepomis macrochirus*. Bulletin of Environmental Contamination and Toxicology 38:727-735.

Brooks, M. W., and J. M. Clark. 1987. Enhancement of norepinephrine release from rat brain synaptosomes by alpha cyano pyrethroids. Pesticide Biochemistry and Physiology 28:127-139.

Brown, T. M., D. R. Johnson, A. R. Hopkins, J. A. Durant, and D.C. Montefiori. 1982. Interactions of pyrethroid insecticides and toxaphene in cotton. Journal of Agricultural and Food Chemistry 30:542-545.

Buck, N. A., B. J. Estesen, and G. W. Ware. 1980. Dislodgable insecticide residues on cotton foliage: fenvalerate, permethrin, sulprofos, chlorpyrifos, methyl parathion, EPN, oxamyl, and profenofos. Bulletin of Environmental Contamination and Toxicology 24:283-288.

Casida, J. E., and L. J. Lawrence. 1985. Structure-activity correlations for interactions of bicyclophosphorus esters and some polychlorocycloalkane and pyrethroid insecticides with the brain-specific t-butylcyclophosphorothionate receptor. Environmental Health Perspectives 61:123-132.

Chapman, R. A., C. M. Tu, C. R. Harris, and C. Cole. 1981. Persistence of five pyrethroid insecticides in sterile and natural, mineral and organic soil. Bulletin of Environmental Contamination and Toxicology 26:513-519.

Clark, J. M., and M. W. Brooks. 1989. Neurotoxicology of pyrethroids: single or multiple mechanisms of action? Environmental Toxicology and Chemistry 8:361-372.

Clark, J. R., L. R. Goodman, P. W. Borthwick, J. M. Patrick, Jr., G. M. Cripe, P. M. Moody, J. C. Moore, and E. M. Lores. 1989. Toxicity of pyrethroids to marine invertebrates and fish: a literature review and test results with sediment-sorbed chemicals. Environmental Toxicology and Chemistry 8:393-401.

Clark, J. R., J. M. Patrick, Jr., D. P. Middaugh, and J. C. Moore. 1985. Relative sensitivity of six estuarine fishes to carbophenothion, chlorpyrifos, and fenvalerate. Ecotoxicology and Environmental Safety 10:382-390.

Clark, J. R., M. M. Patrick, Jr., J. C. Moore, and E. M. Lores. 1987. Waterborne and sediment-source toxicities of six organic chemicals to grass shrimp (*Palaemonetes pugio*) and amphioxus (*Branchiostoma caribaeum*). Archives of Environmental Contamination and Toxicology 16:401-407.

Coats, J. R., and N. L. O'Donnell-Jeffery. 1979. Toxicity of four synthetic pyrethroid insecticides to rainbow trout. Bulletin of Environmental Contamination and Toxicology 23:250-255.

Coats, J. R., D. M. Symonik, S. P. Bradbury, S. D. Dyer, L. K. Timson, and G. J. Atchison. 1989. Toxicology of synthetic pyrethroids in aquatic organisms: an overview. Environmental Toxicology and Chemistry 8:671-679.

Cole, L. M., and J. E. Casida. 1983. Pyrethroid toxicology in the frog. Pesticide Biochemistry and Physiology 20:217-224.

Coulon, D. P. 1982. Toxicity of Ambush and Pydrin to red crawfish, *Procambarus clarkii* (Girard) and channel catfish, *Ictalurus punctatus* Rafinesque in laboratory and field studies and the accumulation and dissipation of associated residues. Ph.D. dissertation, Louisiana State University. 99 pp.

Crofton, K. M., and L. W. Reiter. 1988. The effects of Type I and II pyrethroids on motor activity and the acoustic startle response in the rat. Fundamental and Applied Toxicology 10:624-634.

Curtis, L. R., W. K. Seim, and G. A. Chapman. 1985. Toxicity of fenvalerate to developing steelhead trout following continuous or intermittent exposure. Journal of Toxicology and Environmental Health 15:445-457.

Day, K. E. 1989. Acute, chronic and sublethal effects of synthetic pyrethroids on freshwater zooplankton. Environmental Toxicology and Chemistry 8:411-416.

Day, K., and N. K. Kaushik. 1987a. An assessment of the chronic toxicity of the synthetic pyrethroid, fenvalerate, to *Daphnia galeata mendotae*, using life tables. Environmental Pollution 44:13-26.

Day, K., and N. K. Kaushik. 1987b. The adsorption of fenvalerate to laboratory glassware and the alga *Chlamydomonas reinhardii*, and its effect on uptake of the pesticide by *Daphnia galeata mendotae*. Aquatic Toxicology 10:131 - 142.

Day, K., and N. K. Kaushik. 1987c. Short-term exposure of zooplankton to the synthetic pyrethroid, fenvalerate, and its effects on rates of filtration and assimilation of the alga, *Chlamydomonas reinhardii*. Archives of Environmental Contamination and Toxicology 16:423-432.

Day, K. E., N. K. Kaushik, and K. R. Solomon. 1987. Impact of fenvalerate on enclosed freshwater planktonic communities and on in situ rates of filtration of zooplankton. Canadian Journal of Fisheries and Aquatic Sciences 44:1714-1728.

Doherty, J. D., K. Nishimura, N. Kurihara, and T. Fujita. 1986. Quantitative structure-activity studies of substituted benzyl chrysanthemates. 9. Calcium uptake inhibition in crayfish nerve cord and lobster axon homogenates in vitro by synthetic pyrethroids. Pesticide Biochemistry and Physiology 25:295-305.

Dorman, D.C., W. B. Buck, H. L. Trammel, R. D. Jones, and V. R. Beasley. 1990. Fenvalerate/N, N-diethyl-*m*-toluamide (Deet) toxicosis in two cats. Journal of the American Veterinary Medical Association 196: 100-102.

Dyer, S. D., J. R. Coats, S. P. Bradbury, G. J. Atchison, and J. M. Clark. 1989. Effects of water hardness and salinity on the acute toxicity and uptake of fenvalerate by bluegill (*Lepomis macrochirus*). Bulletin of Environmental Contamination and Toxicology 42:359-366.

Eells, J. T., and M. L. Dubocovich. 1988. Pyrethroid insecticides evoke neurotransmitter release from rabbit striatal slices. The Journal of Pharmacology and Experimental Therapeutics 246:51 4-521.

Elliott, M., editor. 1977. Synthetic pyrethroids. American Chemical Society Symposium 42. American Chemical Society, Washington, D.C. 229 pp.

Elliott, M., and N. F. Janes. 1978. Synthetic pyrethroids—a new class of insecticide. Chemical Society Reviews 7:473-505.

El-Sebae, A. H., M. H. Salem, M.R.S. El-Assar, and E. E. Enan. 1988. In vitro effects of profenofos, fenvalerate and dimilin on protein and RNA biosynthesis by rabbit liver and muscle tissues. Journal of Environmental Science and Health B23:439-451.

El-Sewedy, S. M., M. H. Mostata, E. A. El-Bassiouni, A. Abdel-Rafee, and A. H. El-Sebae. 1982. Effect of fenvalerate on kynurenine metabolizing enzymes and acid ribonuclease of mouse liver. Journal of Environmental Science and Health B17:571-579.

Flannigan, S. A., S. B. Tucker, M. M. Key, C. E. Ross, E. J. Fairchild II, B. A. Grimes, and R. B. Harrist. 1985. Primary irritant contact dermatitis from synthetic pyrethroid insecticide exposure. Archives of Toxicology 56:288-294.

Flodstrom, S., L. Warngard, S. Ljungquist, and U. G. Ahlborg. 1988. Inhibition of metabolic cooperation in vitro and enhancement of enzyme altered foci incidence in rat liver by the pyrethroid insecticide fenvalerate. Archives of Toxicology 61:218-223.

Frank, R., H. E. Braun, L. A. Miller, and G. W. Allan. 1984. Fenvalerate residues in milk following topical treatments to dairy cows. Pesticide Science 15:600-604.

Gammon, D. W., M. A. Brown, and J. E. Casida. 1981. Two classes of pyrethroid action in the cockroach. Pesticide Biochemistry and Physiology 15:181-191.

Gammon, D. W., L. J. Lawrence, and J. E. Casida. 1982. Pyrethroid toxicology: protective effects of diazepam and phenobarbital in the mouse and the cockroach. Toxicology and Applied Pharmacology 66:290-296.

Ghiasuddin, S. M., and D. M. Soderlund. 1984. Hydrolysis of pyrethroid insecticides by soluble mouse brain esterases. Toxicology and Applied Pharmacology 74:390-396.

Gilbert, M. E., C. M. Mack, and K. M. Crofton. 1989. Pyrethroids and enhanced inhibition in the hippocampus of the rat. Brain Research 477:314-321.

Glickman, A. H., and J. E. Casida. 1982. Species and structural variations affecting pyrethroid neurotoxicity. Neurobehavioral Toxicology and Teratology 4:793-799.

Golenda, C. F., and A. J. Forgash. 1989. The distribution and metabolism of fenvalerate in pyrethroid-resistant and susceptible house flies. Pesticide Biochemistry and Physiology 33:37-48.

Gray, A. J. 1985. Pyrethroid structure-toxicity relationships in mammals. Neurotoxicology 6:127-137.

Gray, A. J., and D. M. Soderlund. 1985. Mammalian toxicology of pyrethroids. Pages 193-248 *in* D. H. Hutson and T. R. Roberts, editors. Progress in pesticide biochemistry and toxicology. Vol. 5. Insecticides. John Wiley, New York.

Grissom, R. E., Jr., C. Brownie, and F. E. Guthrie. 1985. Dermal absorption of pesticides in mice. Pesticide Biochemistry and Physiology 24:119-123.

Grissom, R. E., Jr., C. Brownie, and F. E. Guthrie. 1987. In vivo and in vitro dermal penetration of lipophilic and hydrophilic pesticides in mice. Bulletin of Environmental Contamination and Toxicology 38:917-924.

Hansen, D. J., L. R. Goodman, J. C. Moore, and P. K. Higdon. 1983. Effects of the synthetic pyrethroids AC 222, 705, permethrin and fenvalerate on sheepshead minnows in early life stage toxicity tests. Environmental Toxicology and Chemistry 2:251-258.

Harris, C. R., R. A. Chapman, and C. Harris. 1981. Laboratory studies on the persistence and behaviour in soil of four pyrethroid insecticides. Canadian Entomologist 113:685-694.

Harris, J. A., J. E. Hillerton, and S. V. Morant. 1987. Effect on milk production of controlling muscid flies, and reducing fly-avoidance behaviour, by the use of fenvalerate ear tags during the dry period. Journal of Dairy Research 54:165-171.

Haufe, W. O. 1982. Growth of range cattle protected from horn flies (*Haematobia irritans*) by ear tags impregnated with fenvalerate. Canadian Journal of Animal Science 62:567-573.

Haya, K. 1989. Toxicity of pyrethroid insecticides to fish. Environmental Toxicology and Chemistry 8:381-391.

Hill, B.D. 1981. Persistence and distribution of fenvalerate residues in soil under field and laboratory conditions. Journal of Agricultural and Food Chemistry 29:107-110.

Hiromori, T., T. Nakanishi, S. Kawaguchi, H. Sako, T. Suzuki, and J. Miyamoto. 1986. Therapeutic effects of methocarbamol on acute intoxication by pyrethroids in rats. Journal of Pesticide Science 11:9-14.

Holcombe, G. W., G. L. Phipps, and D. K. Tanner. 1982. The acute toxicity of kelthane, dursban, disulfoton, pydrin, and permethrin to fathead minnows *Pimephales promelas* and rainbow trout *Salmo gairdneri*. Environmental Pollution 29A: 167-178.

Holloway, S. F., V. L. Salgado, C. H. Wu, and T. Narahashi. 1989. Kinetic properties of single sodium channels modified by fenvalerate in mouse neuroblastoma cells. Pflugers Archiv European Journal of Physiology 414:613-621.

Holmstead, R. L., D. G. Fullmer, and L. O. Ruzo. 1978. Pyrethroid photodecomposition: Pydrin. Journal of Agricultural and Food Chemistry 26:954-959.

Jagan, P., M. S. Reddy, and A. P. Rao. 1989. Effect of certain insecticides on the freshwater fish Cyprinus carpio carpio, L. Journal of Environmental Biology 10:135-138.

Jain, H. K., N. P. Agnihotri, and K. PO. Srivastava. 1979. Toxicity of fenvalerate and estimation of its residues on some vegetables. Journal of Entomological Research 3:212-216.

Jarvinen, A. W., D. K. Tanner, and E. R. Kline. 1988. Toxicity of chlorpyrifos, endrin, or fenvalerate to fathead minnows following episodic or continuous exposure. Ecotoxicology and Environmental Safety 15:78-95.

Kaneko, H., T. Izumi, M. Matsuo, and J. Miyamoto. 1984. Metabolism of fenvalerate in dogs. Journal of Pesticide Science 9:269-274.

Kaneko, H., M. Matsuo, and J. Miyamoto. 1986. Differential metabolism of fenvalerate and granuloma formation. I. Identification of a cholesterol ester derived from a specific chiral isomer of fenvalerate. Toxicology and Applied Pharmacology 83:148-156.

Kaneko, H., H. Ohkawa, and J. Miyamoto. 1981. Comparative metabolism of fenvalerate and the [2S, αS]-isomer in rats and mice. Journal of Pesticide Science 6:371-326.

Klaassen, C. D., M. O. Amdur, and J. Doull, editors. 1986. Casarett and Doull's toxicology. Third edition. Macmillan, New York. 974 pp.

Lawrence, L. J., and J. E. Casida. 1982. Pyrethroid toxicology: mouse intracerebral structure-toxicity relationships. Pesticide Biochemistry and Physiology 18:9-14.

Leahey, J. P., editor. 1985. The pyrethroid insecticides. Taylor and Francis, Philadelphia. 440 pp.

Lingappa, S., A. Jagadish, K. Shivaramu, and H. P. Prabhuswamy. 1985. Relative intrinsic toxicity of seven insecticides to foragers of the Indian hive bee, *Apis cerana indica* F. Insect Science and Its Application 6:567-568.

Malley, L. A., S. Z. Cagen, C. M. Parker, T. H. Gardiner, G. A. V. Gelder, and G. P. Rose. 1985. Effect of vitamin E and other amelioratory agents on the fenvalerate-mediated skin sensation. Toxicological Letters 29:51-58.

Mansour, F. 1987. Effect of pesticides on spiders occurring on apple and citrus in Israel. Phytoparasitica 15:43-50.

Marei, A.E.M., L. O. Ruzo, and J. E. Casida. 1982. Analysis and persistence of permethrin, cypermethrin, deltamethrin, and fenvalerate in the fat and brain of treated rats. Journal of Agricultural and Food Chemistry 30:558-562.

Mayer, D. F., C. A. Johansen, C. H. Shanks, and K. S. Pike. 1987. Effects of fenvalerate insecticide on pollinators. Journal of the Entomological Society of British Columbia 84:39-45.

Mayer, F. L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. United States Environmental Protection Agency, Report 600/8-87/017. 274 pp.

Mayer, F. L., Jr., and M. E. Ellersieck. 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals. U.S. Fish and Wildlife Service, Resource Publication 160. 579 pp.

McKee, M. J., and C. O. Knowles. 1986. Effects of fenvalerate on biochemical parameters, survival, and reproduction of *Daphnia magna*. Ecotoxicology and Environmental Safety 12:70-84.

McKenney, C. L., Jr., and D. B. Hamaker. 1984. Effects of fenvalerate on larval development of *Palaemonetes pugio* (Holthuis) and on larval metabolism during osmotic stress. Aquatic Toxicology 5:343-355.

McLeese, D. W., C. D. Metcalfe, and V. Zitko. 1980. Lethality of permethrin, cypermethrin and fenvalerate to salmon, lobster and shrimp. Bulletin of Environmental Contamination and Toxicology 25:950-955.

Mikami, N., J. Yoshimura, T. Katagi, H. Yamada, and J. Miyamoto. 1985. Metabolism of the photo-decarboxylated derivative of fenvalerate in rats. Journal of Pesticide Science 10:273-284.

Mitchell, J. A., M. C. Wilson, and M. J. Kallman. 1988. Behavioral effects of Pydrin and Ambush in male mice. Neurotoxicology and Teratology 10:113-119.

Miyamoto, J. 1988. Disposition and metabolism studies of xenobiotics in the environment: fundamentals for safety assessment. The Journal of Toxicological Sciences 13:221-246. Miyamoto, J., H. Kaneko, and Y. Takamatsu. 1986. Stereoselective formation of a cholesterol ester conjugate from fenvalerate by mouse microsomal carboxyesterase(s). Journal of Biochemical Toxicology 1:79-94.

Moffett, J. O., A. Stoner, and R. M. Ahring. 1982. Effect of fenvalerate applications on honey bees in flowering alfalfa. The Southwestern Entomologist 7:111-115.

Muir, D.C.G., G. P. Rawn, B. E. Townsend, W. L. Lockhart, and R. Greenhalgh. 1985. Bioconcentration of cypermethrin, deltamethrin, fenvalerate and permethrin by *Chironomus tentans* larvae in sediment and water. Environmental Toxicology and Chemistry 4:51-61.

Mulla, M. S., H. A. Darwazeh, and M. S. Dhillon. 1980. New pyrethroids as mosquito larvicides and their effects on non-target organisms. Mosquito News 40:6-12.

Mulla, M. S., H. A. Navvab-Gojrati, and H. A. Darwazeh. 1978. Biological activity and longevity of new synthetic pyrethroids against mosquitos and some nontarget insects. Mosquito News 38:90-96.

Mumtaz, M. M., and R. E. Menzer. 1986. Comparative metabolism and fate of fenvalerate in Japanese quail (*Coturnix coturnix japonica*) and rats (*Rattus norvegicus*). Journal of Agricultural and Food Chemistry 34:929-936.

Ohkawa, H., H. Kaneko, H. Tsuji, and J. Miyamoto. 1979. Metabolism of fenvalerate (Sumicidin) in rats. Journal of Pesticide Science 4: 143-155.

Ohkawa, H., R. Kikuchi, and J. S. Miyamoto. 1980. Bioaccumulation and biodegradation of the (S)-acid isomer of fenvalerate (Sumicidin) in an aquatic model ecosystem. Journal of Pesticide Science 5:11-22.

Ohtsubo, T., H. Takeda, S. Tsuda, M. Kagoshima, and K. Tsuji. 1989. Formulation factors of fenvalerate microcapsules influencing insecticidal efficacy and fish toxicity. Journal of Pesticide Science 14:235-239.

Okuno, Y., T. Seki, S. Ito, H. Kenoko, T. Watanabe, T. Yamada, and J. Miyamoto. 1986. Differential metabolism of fenvalerate and granuloma formation. II. Toxicological significance of a lipophilic conjugate from fenvalerate. Toxicology and Applied Pharmacology 83: 157-169.

Parker, C. M., C. B. McCullough, J. B. M. Gellatly, and C. D. Johnston. 1983. Toxicologic and carcinogenic evaluation of fenvalerate in the B6C3F1 mouse. Fundamental and Applied Toxicology 3:114-120.

Parker, C. M., D. R. Patterson, G. A. Van Gelder, E. B. Gordon, M. G. Valerio, and W. C. Hall. 1984a. Chronic toxicity and carcinogenicity evaluation of fenvalerate in rats. Journal of Toxicology and Environmental Health 13:83-97.

Parker, C. M., V. J. Piccirillo, S. L. Kurtz, F. M. Garner, T. H. Gardiner, and G. A. Van Gelder. 1984b. Six-month feeding study of fenvalerate in dogs. Fundamental and Applied Toxicology 4:577-586.

Pati, P. C., and S. P. Bhunya. 1989. Cytogenetic effects of fenvalerate in mammalian in vivo test system. Mutation Research 222:149-154.

Phillips, S. A., Jr., D. M. Claborn, and O. F. Francke. 1984. Comparison of aerial application and single-mound drenches of fenvalerate against the red imported fire ant, *Solenopsis invicta* Buren, in Texas. The Southwestern Entomologist 9:164-168.

Pluijmen, M., C. Drevon, R. Montesano, C. Malaveille, A. Hautefeuille, and H. Bartsch. 1984. Lack of mutagenicity of synthetic pyrethroids in *Salmonella typhimurium* strains and in V79 Chinese hamster cells. Mutation Research 137:7-15.

Radhaiah, V., K. V. Joseph, and K. J. Rao. 1989. Toxic effect of fenvalerate on fructose-1, 6-diphosphate aldolase activity of liver, gill, kidney, and brain of the fresh water teleost, *Tilapia mossambica*. Bulletin of Environmental Contamination and Toxicology 42:150-153.

Radhaiah, V., and S.V.K. Reddy. 1989. Toxic impact of fenvalerate on superoxide dismutase and catalase activity levels in liver, muscle and gill tissues of a freshwater fish, *Tilapia mossambica* (Peters). Biochemistry International 18:655-660.

Ramadan, A. A., N. M. Bakry, A.S .M. Marei, A. T. Eldefrawi, and M. E. Eldefrawi. 1988. Action of pyrethroids on K+-stimulated calcium uptake by, and (^{3}H)nimodipine binding to, rat brain synaptosomes. Pesticide Biochemistry and Physiology 32:114-122.

Rattner, B. A., and J. C. Franson. 1984. Methyl parathion and fenvalerate toxicity in American kestrels: acute physiological responses and effects of cold. Canadian Journal of Physiology and Pharmacology 62:787-792.

Reddy, P.M., and M. Bashamohideen. 1988. Toxic impact of fenvalerate on the protein metabolism in the branchial tissue of a fish, *Cyprinus carpio*. Current Science 57:211-212.

Reed, D. 1981. Fenvalerate insecticide. United States Food and Drug Administration, Bureau of Foods, HHF-420.8 pp. (mimeo)

Riedl, H., and S. A. Hoying. 1980. Impact of fenvalerate and diflubenzuron on target and nontarget arthropod species on Bartlett pears in northern California. Journal of Economic Entomology 73:117-122.

Riviere, J. L., J. Bach, and G. Grolleau. 1983. Effect of pyrethroid insecticides and N-(3,5-dichlorophenyl) dicarboximide fungicides on microsomal drug-metabolizing enzymes in the Japanese quail (*Coturnix coturnix*). Bulletin of Environmental Contamination and Toxicology 31:479-485.

Ruigt, G.S.F., and J. V. D. Bercken. 1986. Action of pyrethroids on a nerve-muscle preparation of the clawed frog, *Xenopus laevis*. Pesticide Biochemistry and Physiology 25:176-187.

Saleh, M. A., N. A. Ibrahim, N. Z. Soliman, and M.K.E. Sheimy. 1986a. Persistence and distribution of cypermethrin, deltamethrin, and fenvalerate in laying chickens. Journal of Agricultural and Food Chemistry 34:895-898.

Saleh, M.A.A., Z. A. Mohamed, F. A. Ahmed, and S. A. Ismail. 1986b. Comparative toxicity of flucythrinate and fenvalerate to albino rats. Egyptian Journal of Food Science 14:31-37.

Salgado, V. L., M.D. Herman, and T. Narahashi. 1989. Interactions of the pyrethroid fenvalerate with nerve membrane sodium channels: temperature dependence and mechanism of depolarization. Neurotoxicology 10:1-14.

Sawicki, R.M. 1985. Resistance to pyrethroid insecticides in arthropods. Pages 143-192 *in* D. H. Hutson and T. R. Roberts, editors. Progress in pesticide biochemistry and toxicology. Vol. 5. Insecticides. John Wiley, New York.

Schimmel, S. C., R. L. Garnas, J. M. Patrick, Jr., and J. C. Moore. 1983. Acute toxicity, bioconcentration, and persistence of AC 222,705, benthiocarb, chlorpyrifos, fenvalerate, methyl parathion, and permithrin in the estuarine environment. Journal of Agricultural and Food Chemistry 31:104113.

Schreiber, B., and N. Brink. 1989. Pesticide toxicity using protozoans as test organisms. Biology and Fertility of Soils 7:289-296.

Scott, G. I., D. S. Baughman, A. H. Trim, and J. C. Dee. 1987. Lethal and sublethal effects of insecticides commonly found in nonpoint source agricultural runoff to estuarine fish and shellfish. Pages 251-273 *in* W.B. Vernberg, A. Calabrese, F. P. Thurberg, and F. J. Vernberg, editors. Pollution physiology of estuarine organisms. University of South Carolina Press, Columbia.

Sine, C., editor. 1988. Farm chemicals handbook '88. Meister Publications, Willoughby, Ohio. 523 pp.

Smith, S., T. Reagan, G. H. Willis, J. L. Flynn, and D.C. Rester. 1989. Fenvalerate interception by and dissipation from sugarcane foliage as affected by application technology. Bulletin of Environmental Contamination and Toxicology 42:30-36.

Smith, T. M., and G. W. Stratton. 1986. Effects of synthetic pyrethroid insecticides on nontarget organisms. Residue Reviews 97:93-120.

Spehar, R. L., D. Tanner, and J. H. Gibson. 1982. Effects of kelthane and pydrin on early life stages of fathead minnows (*Pimephales promelas*) and amphipods (*Hyalella azteca*). Pages 234-244 *in* J. G. Pearson, R. B. Foster, and W. E. Bishop, editors. Aquatic toxicology and hazard assessment. Proceedings of the fifth annual symposium on aquatic toxicology. American Society for Testing and Materials Special Technical Publication 766.

Stoner, A., W. T. Wilson, and J. Harvey. 1985. Honeybee exposure to beeswax foundation impregnated with fenvalerate or carbaryl. American Bee Journal 125:513-516.

Stoner, A., W. T. Wilson, and J. O. Moffett. 1984. Effect of long-term feeding of low doses of fenvalerate or fluvalinate in sucrose syrup on honey bees in standard-size field colonies. Journal of the Georgia Entomological Society 19:490-498.

Symonik, D. M., J. R. Coats, S. P. Bradbury, G. J. Atchison, and J. M. Clark. 1989. Effect of fenvalerate on metabolic ion dynamics in the fathead minnow (*Pimephales promelas*) and bluegill (*Lepomis macrochirus*). Bulletin of Environmental Contamination and Toxicology 42:821-828.

Tabashnik, B. E., and N. L. Cushing. 1989. Quantitative genetic analysis of insecticide resistance: variation in fenvalerate tolerance in a diamondback moth (Lepidoptera: Plutellidae) population. Journal of Economic Entomology 82:5-10.

Tagatz, M. E., and J. M. Ivey. 1981. Effects of fenvalerate on field- and laboratory-developed estuarine benthic communities. Bulletin of Environmental Contamination and Toxicology 27:256-267.

Tagatz, M. E., R. S. Stanley, G. R. Plaia, and C. H. Deans. 1987. Responses of estuarine macrofauna colonizing sediments contaminated with fenvalerate. Environmental Toxicology and Chemistry 6:21-25.

Tasei, J. N., and P. Debray. 1985. The toxicity and hazard of fenvalerate to alfalfa leaf-cutter bees. Pesticide Science 16:209-210.

Taylor, K. S., G. D. Waller, and L. A. Crowder. 1987. Impairment of a classical conditioned response of the honey bee (*Apis mellifera* L.) by sublethal doses of synthetic pyrethroid insecticides. Apidologie 18:243-252.

Tippe, A. 1987. Evidence for different mechanisms of action of the three pyrethroids, deltamethrin, cypermethrin, and fenvalerate, on the excitation threshold of myelinated nerve. Pesticide Biochemistry and Physiology 28:67-74.

Trim, A. H. 1987. Acute toxicity of emulsifiable concentrations of three insecticides commonly found in nonpoint source runoff into estuarine waters to the mummichog, *Fundulus heteroclitus*. Bulletin of Environmental Contamination and Toxicology 38:681 686.

Verma, S. R., V. Kumar, and R. C. Dalela. 1981. Acute toxicity of three newly formulated pesticides to fish *Mystus vittatus*. Indian Journal of Environmental Health 23:215-221.

Verschoyle, R. D., and W. N. Aldridge. 1980. Structure-activity relationships of some pyrethroids in rats. Archives of Toxicology 45:325 329.

Vijverberg, H.P.M., and J. V. D. Bercken. 1982. Action of pyrethroid insecticides on the vertebrate nervous system. Neuropathology and Applied Neurobiology 8:421-440.

Vijverberg, H.P.M., G.S.F. Ruigt, and J. V. D. Bercken. 1982. Structure-related effects of pyrethroid insecticides on the lateral-line sense organ and on peripheral nerves of the clawed frog, *Xenopus laevis*. Pesticide Biochemistry and Physiology 18: 315-324.

Williamson, E.G., S. F. Long, M. J. Kallman, and M. C. Wilson. 1989. A comparative analysis of the acute toxicity of technical-grade pyrethroid insecticides and their commercial formulations. Ecotoxicology and Environmental Safety 18:27-34.

Willis, G. H., and L. L. McDowell. 1987. Pesticide persistence on foliage. Reviews of Environmental Contamination and Toxicology 100:23-73.

Windholz, M., S. Budavari, R.F. Blumetti, and E. S. Otterbein, editors. 1983. The Merck Index, tenth edition. Merck & Co., Rahway, New Jersey. Pages 576-577.

Wouters, W., and J. V. D. Bercken. 1978. Action of pyrethroids. General Pharmacology 9:387- 398.

Wright, F. C., F. S. Guillot, and J. E. George. 1988. Efficacy of acaricides against chorioptic mange of goats. American Journal of Veterinary Research 49:903-904.

Wszolek, P. C., D. E. Hogue, and D. J. Lisk. 1981a. Accumulation of fenvalerate insecticide in lamb tissues. Bulletin of Environmental Contamination and Toxicology 27:869-871.

Wszolek, P. C., N. A. LaFaunce, T. Wachs, and D. J. Lisk. 1981b. Studies of possible bovine urinary excretion and rumen decomposition of fenvalerate insecticide and a metabolite. Bulletin of Environmental Contamination and Toxicology 26:262-266.

Wszolek, P. C., D. H. Lein, and D. J. Lisk. 1980. Excretion of fenvalerate insecticide in the milk of dairy cows. Bulletin of Environmental Contamination and Toxicology 24:296-298.

Yellamma, K., and R. Reddy. 1987. Behavioural and physiological changes in the cockroach, *Periplaneta americana*, exposed to fenvalerate. Indian Journal of Experimental Biology 25:256-261.

Yeung, J. M., D. D. Colwell, and J. A. Shemanchuk. 1989. Fenvalerate residues on cattle hair coat from impregnated ear tags. Pesticide Science 26:21-27.

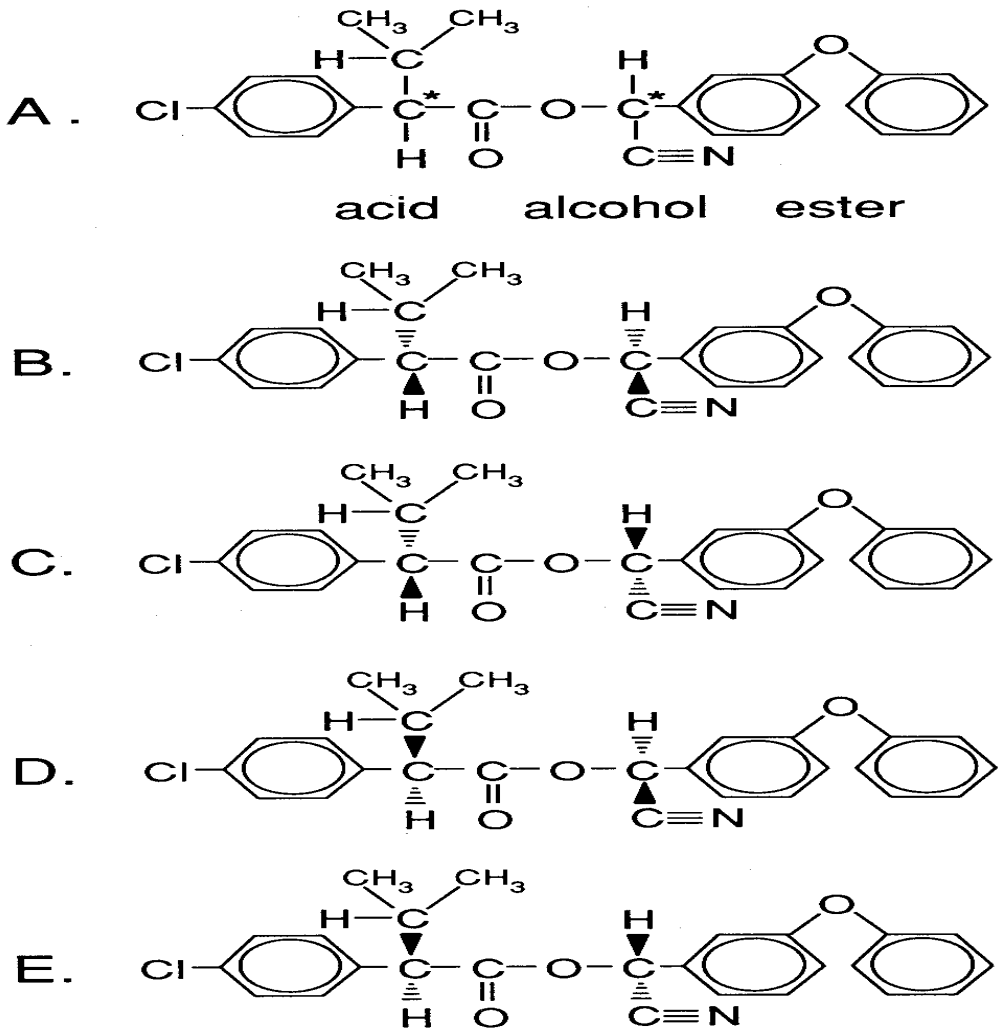


Figure. Fenvalerate and its isomers (Ohkawa et al. 1979; Hill 1981; Kaneko et al. 1981, 1986; Vijverberg and Bercken 1982; Miyamoto et al. 1986; Bradbury et al. 1987b; Bradbury and Coats 1989a, 1989b; Coats et al. 1989).

A. Chemical structure of fenvalerate denoting two asymmetric carbon atoms (*): the 2C position of the acid moiety, and the αC position of the α-cyano-3-phenoxybenzyl alcohol moiety. These two chiral centers, at the 2C and αC positions, yield a mixture of four stereoisomers, in approximately equal amounts but with greatly different biological properties.

B. (2*S*)-α-cyano-3-phenoxybenzyl (α*S*)-2-(4-chlorophenyl)-3-methylbutyrate. The 2*S*, α*S* isomer is extremely toxic to insects and is the most active form of fenvalerate.

C. (2*S*)-α-cyano-3-phenoxybenzyl (α*R*)-2-(4-chlorophenyl)-3-methylbutyrate. The 2*S*, α*R* isomer has markedly reduced insecticidal activity when compared with the 2*S*, α*S* isomer but is greatly elevated in this respect when compared with fenvalerate stereoisomers with an *R* configuration in the acid moiety, that is, the 2*R*, α*S* and the 2*R*, α*R* isomers.

D. The 2*R*, α*S* isomer is the only fenvalerate isomer that caused granulatomous changes in liver, spleen, and mesenteric lymph node in rodents.

E. The 2*R*, α*R* isomer has greatly reduced biological and toxicological properties when compared with other fenvalerate isomers. Isomers with an *R* configuration in the acid moiety degraded slightly faster than the insecticidally active 2*S*, α*S* and 2*S*, α*R* isomers.

Biological Report 4
June 1992

Contaminant Hazard Reviews
Report 25

Diflubenzuron Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U. S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

TABLES

Diflubenzuron Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U. S. Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel, Maryland 20708

Abstract. Diflubenzuron (1 -(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea), also known as dimilin, is a potent broad-spectrum insect growth regulator that interferes with chitin synthesis at time of molting and is effective in controlling immature stages of insects. Diflubenzuron was approved for domestic use in 1976 to control gypsy moth (*Lymantria dispar*), and in 1979 against the cotton boll weevil (*Anthonomus grandis*). By 1989 this compound was also registered for domestic use against mosquitos, forest Lepidoptera, mushroom flies, and leaf-eating insect pests of citrus, woody ornamentals, vegetables, and fruit.

Diflubenzuron seldom persists for more than a few days in soil and water. When used properly in forest management, it is unlikely to be leached into ground water from the application site. Degradation in water and soil is most rapid when small particle formulations are applied; microorganisms are abundant; and at elevated pH, temperature, and organic loading. Chemical and biological processes initially yield 2,6-difluorobenzoic acid and 4-chlorophenylurea. Soil degradation processes and plant and animal metabolism involve further conversion of these compounds to 2,6-difluorobenzamide and 4-chloroaniline. Ultimately, the end products are either conjugated into mostly water soluble products or biologically methylated.

Diflubenzuron applied to foliage of terrestrial plants tends to remain adsorbed for several weeks with little or no absorption or translocation from plant surfaces; loss occurs mainly from wind abrasion, rain washing, or shedding of senescent leaves. Among terrestrial insects, there is great variability in sensitivity to diflubenzuron. Sensitive pestiferous species of insects die at topical applications of 0.003-0.034 µg per larvae or after consuming diets containing 0.1 mg/kg. Some beneficial insects, such as the honey bee (*Apis mellifera*), are adversely affected at 1 mg/kg fresh weight (FW) of diet.

Diflubenzuron application rates between 28 and 56 g/ha (0.025-0.05 pounds per acre) or 2.5 to 16 µg/L are highly effective against pestiferous aquatic dipterans, including representative chaoborids, chironomids, and culicids. These same dosages temporarily suppress nontarget populations of cladocerans, copepods, mayfly nymphs, corixids, and springtails; population recovery is usually complete within 80 days. In general, crustaceans were the most sensitive nontarget aquatic organisms tested. Adverse effects on crustacean growth, survival, reproduction, and behavior occur between 0.062 and 2 µg/L. Next in sensitivity are mayflies, chironomids, caddisflies, and midges; concentrations between 0.1 and 1.9 µg/L produce low emergence and survival. Moderately resistant to diflubenzuron are larvae of diving beetles, dragonfly adults and naiads, ostracods, spiders, backswimmers, and water boatmen. Relatively tolerant of diflubenzuron (i . e., no observable adverse effects at 45 µg/L) are the algae, molluscs, fishes, and amphibians. High accumulations occur on some aquatic plants during exposure to 100 µg/L and in fish during exposure to 1 to 13 µg/L, but all species in these groups seem unaffected by elevated body burdens and grow and metabolize normally.

Birds seem comparatively resistant to diflubenzuron: acute oral LD50 doses exceed 2,000 mg/kg body weight (BW); dietary concentrations <4,640 mg/kg FW are tolerated for at least 8 days; and forest birds seem unharmed by recommended diflubenzuron application procedures to control pestiferous insects. Intraspecies differences in ability to metabolize diflubenzuron are probably large; different strains of domestic chickens show significant differences in ability to accumulate and retain this compound.

No data were found on diflubenzuron effects on mammalian wildlife. However, studies on small laboratory animals and domestic livestock indicate no observable effects in cows (*Bos bovis*) given 0.25 mg/kg BW daily for 4 months, in rabbits (*Oryctolagus cuniculus*) given 4 mg/kg BW daily on days 6 to 18 of gestation, in dogs

(*Canis familiaris*) fed diets containing 40 mg/kg for 13 weeks (equivalent to 1.6 mg/kg BW daily), in rats (*Rattus* spp.) fed diets containing 160 mg/kg for 2 years, and in rabbits and rodents given single oral or dermal doses <2,000 mg/kg BW. All experimental studies conducted with laboratory animals indicate that diflubenzuron is nonmutagenic, nonteratogenic, and noncarcinogenic. Adverse effects occur in dogs fed diets containing 160 mg/kg (6.2 mg/kg BW daily) for 13 weeks (abnormal blood chemistry), in mice (*Mus* spp.) given 125 mg/kg BW daily for 30 days (hepatocellular changes), in rabbits fed diets of 640 mg/kg for 3 weeks (abnormal hemoglobin), and in rats given 5,000 mg/kg BW daily for 13 weeks (abnormal hemoglobin). Elevated tissue residues--but no other measurable effects---occur in cows given 0.05 to 0.5 mg/kg ration for 28 days or 1 to 16 mg/kg BW for 4 months, in pigs (*Sus* spp.) given a single oral dose of 5 mg/kg BW, and in sheep (*Ovis aries*) given a single oral dose of 10 mg/kg BW.

Criteria now recommended for protection of various species include the following: dietary loadings, in mg/kg FW ration, of <0.05 for human health, <0.05 for livestock, < 1 for honey bees, and <5 for poultry; seawater concentrations <0.1 µg/L for estuarine crustacean larvae; and, for all aquatic life, restricted or prohibited use of diflubenzuron in salt-marsh mosquito breeding areas and on agricultural lands less than 5 km from coastal areas. No criteria are available or proposed for protection of avian and mammalian wildlife against diflubenzuron, probably because of an incomplete toxicological data base. (Eisler, R. 1992. Diflubenzuron hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. Fish and Wildlife Service Biological Report 4. 36 pp.).

Key words: Diflubenzuron, dimilin, benzoylphenyl urea, insecticide, ovicide, wildlife, aquatic organisms, ecotoxicology, criteria.

Compounds collectively known as insect growth regulators have been recognized, in recent years, as important new insecticides. These compounds include juvenile hormone mimics, antijuvenile hormone analogs, and chitin synthesis inhibitors. The most widely studied chitin synthesis inhibitor, and the only one currently registered for use against selected insect pests in the United States, is diflubenzuron (1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea), also known as dimilin (Christiansen 1986; Touart and Rao 1987). Chitin is a major component of the tough outer covering, or cuticle, of insects. As insects develop from immature larvae to adults, they undergo several molts, during which new cuticles are formed and old ones shed.

Diflubenzuron prevents successful development by inhibiting chitin synthetase, the final enzyme in the pathway by which chitin is synthesized from glucose (Marx 1977; Ivie 1978).

Diflubenzuron is highly effective against larval stages of many species of nuisance insects. It is used extensively to control mosquitos, midges, gnats, weevils (including the cotton boll weevil, *Anthonomus grandis*), various beetles, caterpillars of moths and butterflies (especially the gypsy moth, *Lymantria dispar*), flies, and rust mites (Marx 1977; Ivie 1978; Veech 1978; Schaefer et al. 1980; Opdycke et al. 1982a; Muzzarelli .1986). In Maryland, for example, more than 30,000 ha are sprayed annually to control gypsy moths (Swift et al. 1988a). In general, less than 140 g/ha (2 ounces per acre) of diflubenzuron is sufficient to control susceptible species, although affected larvae do not die until they molt (Marx 1977).

Most authorities agree that diflubenzuron has low mammalian toxicity, is not highly concentrated through vertebrate food chains or by absorption from water, remains stable on foliage, and seldom persists for extended periods in soil and water (Marx 1977; Ivie 1978; Schaefer et al. 1980). Chitin synthesis inhibitors, however, are not specific to insect pests. Beneficial insects also produce chitin, as do all arthropods, including spiders, crabs, crayfish, lobsters, shrimp, daphnids, mayflies, stoneflies, barnacles, copepods, and horseshoe crabs. All of these groups are adversely affected by diflubenzuron, including effects on survival, reproduction, development, limb regeneration, and population growth (Farlow 1976; Marx 1977; Christiansen 1986; Cunningham 1986; Muzzarelli 1986; Touart and Rao 1987; Weis et al. 1987).

This report was prepared in response to requests for information on diflubenzuron from environmental contaminant specialists of the U.S. Fish and Wildlife Service. It is part of a continuing series of brief reviews on chemicals in the environment, with emphasis on fishery and wildlife resources.

Environmental Chemistry

General

Diflubenzuron breakdown by hydrolysis, soil degradation, or plant and animal metabolism initially yields 2,6-difluorobenzoic acid and 4-chlorophenylurea. Ultimately, the end products are either conjugated into mostly water soluble products or are biologically acylated and methylated. At extremely low doses, diflubenzuron selectively inhibits the ability of arthropods to synthesize chitin at the time of molting, producing death of the organism from rupture of the cuticle or starvation. Other organisms that contain chitin (i.e., some species of fungi and marine diatoms), or polysaccharides similar to chitin (i.e., birds and mammals), seem unaffected.

Mobility and leachability of diflubenzuron in soils is low, and residues are usually not detectable after 7 days. Degradation is most rapid when small-particle (2-5 um) formulations are applied and soil bacteria are abundant. In water, diflubenzuron usually persists for only a few days; degradation is most rapid under conditions of high organic and sediment loadings, and elevated water pH and temperature.

Chemical and Biochemical Properties

Selected Chemical and Biochemical Properties of diflubenzuron are listed in Table 1.

Diflubenzuron degradative pathways are almost entirely through cleavage between the carbonyl and amide groups of the urea bridge. Ultimately, the end products are either conjugated into predominantly water soluble products or are acylated and methylated biologically (Metcalf et al. 1975). Hydrolysis, soil degradation, and plant and animal metabolism of diflubenzuron yield the same initial products: 2,6-difluorobenzoic acid and 4-chlorophenylurea. Soil degradation and plant and animal metabolism involve further conversion of these compounds to 2,6-difluorobenzamide and 4-chloroaniline (Schaefer et al. 1980; Gartrell 1981; Figure).

Table 1. Chemical and other properties of diflubenzuron.[a]

Variable	Data
Chemical names	1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea; N-[[(4-chlorophenyl)amino] carbonyl]-2,6-difluorobenzamide); l-(2,6-difluorobenzoyl)-3-(4-chlorophenyl) urea
Alternate names	Deflubenzon, Diflubenuron, Dimilin, DU 112307, Duphar BV, ENT-29054, Largon, Micromite, OMS 1804, PDD 6040-I, PH 60-40, TH 6040
Action	Insecticide, larvicide, ovicide; insect growth regulator acting by interference with deposition of insect chitin
CAS number	35367-38-5
Empirical formula	$C_{14}H_9ClF_2N_2O_2$
Molecular weight	310.68
Formulations	Granular, oil-dispersable concentrate; wettable powder
Manufacturing process and impurities	Produced by reaction of 2,6-difluorobenzamide with 4-chlorophenyl isocyanate. The technical product is 95% pure. Impurities are of low toxicological concern in terminal residues

Stability	Stable under sunlight and in neutral or mildly acidic solutions; unstable in strong basic solutions.
Physical state	White crystalline solid
Melting point	210—230°C (technical); 230-232°C (pure)
Solubility	
Water	0.1-0.2 mg/L at 20°C; 1.0 mg/L at 25°C
Polar organic solvents	Moderate to good
Octanol/water partition coefficient	3,500

[a] Metcalf et al. 1975; Farlow 1976; Johnson and Finley 1980; Gartrell 1981; Hudson et al. 1984; Mayer 1987; Poplyk 1989.

Interspecies variations in ability to metabolize difluobenzuron are common, as judged by metabolic patterns in rat, cow, and sheep. In all three species hydroxylation of either aromatic ring and scission of the ureido bridge constituted the main metabolic pathways. In cow and rat the prevailing route was ring hydroxylation; in sheep it was the scission reaction. In cow and sheep about half the 2,6-difluorobenzoyl moiety excreted in urine was conjugated to glycine, but in rat the acid was excreted largely unchanged. In sheep, where cleavage splitting of the diflubenzuron molecule was the primary metabolic route, there was no evidence of 4-chlorophenylurea or 4-chloroaniline in urine (Willems et al. 1980). More information on degradation and metabolic pathways of diflubenzuron is given in Metcalf et al. (1975), Schooley and Quistad (1979), Ivie et al. (1980), Willems et al. (1980), Franklin and Knowles (1981), and Jenkins et al. (1986).

Table 2. Diflubenzuron persistence in soil and water.

Sample, initial concentration, and other variables	Persistence	Reference[a]
Soil		
0.08 g/ha, aerial spray, single application	Values always <0.05 mg/kg up to 14 days after spraying	1
22.4 g/ha (0.02 pounds per acre) applied four times, one month between treatments	Residues, in mg/kg, after first treatment were 0.2 at 1 day and 0.016 at 7 days. Residues at time of fourth treatment were nondetectable (ND) at start, 0.01 at 1 h, 0.02 at 1 day, and ND between days 3 and 56	2
44.9 g/ha (0.04 pounds per acre) applied four times, 2 weeks between treatments	Maximum residues, in mg/kg, after first treatment were 0.07 at 1 day and 0.05 at 7 days. After fourth treatment, residues were 0.04 at start, 0.09 at 3 days, and ND between days 7 and 56	2
70, 210, or 630 g/ha applied once to sandy loam forest soil or clay loam forest soil, plus water equivalent to	Mobility of diflubenzuron was low and did not increase with dosage. No residues detected below 10 cm or in leachates in either soil type at all dosage levels. At 70 g/ha, all residues	3

50.8 cm of precipitation	were found in the top 2.5 cm; at 630 g/ha, 4-9% moved below 2.5 cm in sandy loam (mobility was lower in clay loam)	
Distilled water		
100 µg/L, 37°C	No degradation at pH 4 in 8 weeks; Tb 1/2 was about 7 days at pH 6 and <3 days at pH 10. Major degradation products were 4-chloro-phenylurea and 2,6-difluorobenzoic acid; small amounts of 2,6-difluorobenzamide and a quinazolinedione product were also formed	4
Pasture water		
22-45 g/ha (0.02-0.04 pounds per acre), single application	Maximum concentrations, in µg/L, were 8.8 in 1 h, 7.1 in 24 h, 3.9 in 48 h, and 2.6 in 72 h; most treatments produced ND (< 1 µg/L) residues in 24 h	5
45 g/ha (0.04 pounds per acre), single application	Concentrations, in µg/L, were 4 at start, 36 at 1 h, 9 at 24 h, and 6 at 14 days	1
45 g/ha, applied four times at 2-week intervals	Maximum concentrations, in µg/L, were 7.4 at 1 h after first treatment, 1.3 at 1 h after second application, 2.9 at 1 h after third treatment, and 6.4 at 1 h and 0.9 at 1 day after last treatment	1
80 g/ha, single application	Concentrations, in µ,g/L, of diflubenzuron declined from 20.3 at 1 h to 2.4 at 4 days; 4-chlorophenylurea increased slightly from 5.6 to 7.2 during this interval; 4-chloroaniline increased from 0.7 at 1 h to 2.6 at 4 days	6
Pond water		
2.5 µg/L	Concentration after treatment was 1.9 µg/L; after 2 weeks it was 0.5 µg/L	7
5 µg/L	Concentration immediately after treatment was 4.6 µg/L; after 2 weeks it was 0.3 µg/L	7
10 µg/L	Initial concentration in medium declined from 9.8 µg/L to 0.2 µg/L after 2 weeks	7
Seawater		
10 µg/L, sediments present	Tb 1/2 of 5.3 days; <0.7 µg/L in 19 days; <0.5 µg/L in 22 days	8
10 µg/L, sediments absent	Tb 1/2 of 17.8 days	8

100 µg/L	Tb 1/2 of 7.9 days at 38°C, and 35 days at 24°C	9
45 g/ha	Tb 1/2 of 10 days	9

[a] 1, Booth and Ferrell 1977; 2, Schaefer and Dupras 1977; 3, Sundaram and Nott 1989; 4, Ivie et al. 1980; 5, Schaefer and Dupras 1976; 6, Schaefer et al. 1980; 7, Apperson et al. 1978; 8, Cunningham et al. 1987; 9, Cunningham and Myers 1986.

The benzoylphenylureas--including diflubenzuron--control target insect populations at extremely low doses by selectively inhibiting their ability to synthesize chitin-bearing parts. Ingested diflubenzuron has no apparent adverse effects until the molting process is under way.

Diflubenzuron caused increases in cuticle chitinase and cuticle phenoloxidase activity, producing a softened endocuticle through reduction of its chitin content and a hardened exocuticle as a result of increased phenoloxidase activity (Farlow 1976). Diflubenzuron inhibits serine protease, thus blocking the conversion of chitin synthetase zymogen into. an active enzyme (Cunningham 1986; Muzzarelli 1986). Insect larvae treated with diflubenzuron develop cuticles that are unable to withstand the increased turgor occurring during ecdysis and that fail to provide sufficient muscular support during molting. These larvae are unable to cast their exuviae, resulting in death from starvation or rupture of the new, delicate, malformed cuticle (Farlow 1976). In addition to terrestrial insects, diflubenzuron is toxic to a wide variety of aquatic insects and crustaceans (Swift et al. 1988a, 1988b), but it doesn't seem to affect other organisms that contain chitin, including fungi (Muzzarelli 1986) and marine diatoms (Montgomery et al. 1990).

Chitin is a polymer of N-acetylglucosamine (AGA), and it rivals cellulose as the most abundant biopolymer in nature. Measured chitin concentrations in marine waters range between 4 and 21 µg/L, and planktonic crustaceans are the most significant source of chitin in the sea (Montgomery et al. 1990). Insect chitin is synthesized during phosphorylation by uridine disphospho N-acetyl glucosamine (UDPAGA)--the immediate precursor of chitin (Crookshank et al. 1978). Diflubenzuron inhibits the incorporation of chitin precursors into chitin, with a resultant accumulation of UDPAGA (Crookshank et al. 1978). Chitin is not found in vertebrates, although several important polysaccharides similar to chitin are found, including hyaluronic acid (HA). Hyaluronic acid is found in skin: synovial fluid, connective tissue, vitreous humor, and the covering of the ovum. Hyaluronic acid is a polysaccharide compound of alternating groups of glucuronic acid and AGA; the immediate precursor for glucuronic acid is uridine diphospho-glucuronic acid and that for AGA is UDPAGA. Because UDPAGA is used in the synthesis of chitin by insects and of HA by vertebrates, and because diflubenzuron interferes with the incorporation of UDPAGA into chitin by insects, diflubenzuron may interfere with the formation of HA in birds (Crookshank et al. 1978).

Persistence in Soil and Water

Mobility and leachability of diflubenzuron in soils is low, and residues are usually not detectable after 7 days. In water, half-time persistence (Tb 1/2) is usually less than 8 days and lowest at elevated temperatures, alkaline pH, and high sediment loadings (Table 2). Increased concentrations of diflubenzuron in soils and waters are associated with increased application frequency, flooding of treated supratidal areas, wind drift, and excessive rainfall (Cunningham 1986).

Diflubenzuron is persistent in postharvest soils during winter and spring months, especially if associated with plant litter; concentrations decline rapidly with the onset of high summer temperatures to <0.3 mg/kg DW soil in summer (Bull and Ivie 1978; Bull 1980).

Diflubenzuron particle size and soil flora may be important in the soil degradation process. Diflubenzuron adsorbed to smaller particles of 2 µm diameter had a short Tb 1/2 of 3-7 days; diflubenzuron adsorbed to larger particles (10 µm diameter) persisted for 8-16 weeks. Diflubenzuron adsorbed to particles of 2 µm diameter had a low rate of degradation in sterile soils (<6% in 4 weeks), but in nonsterile soils 98% degraded in the same period, suggesting that soil bacteria are important in the degradation process (Cunningham 1986). In Canada, data on mobility of a pesticidal chemical in forest soil must be collected before it can be registered for use under the Canadian Pest Control Products Act in order to assess its potential for groundwater contamination (Sundaram and Nott 1989). Diflubenzuron used properly in forest management is unlikely to be leached into ground water from a site of application (Sundaram and Nott 1989).

Water concentrations of diflubenzuron in treated ponds are significantly higher in surface and middle samples than in bottom samples during the first 5 h after treatment; however, after 24 h, distribution is about the same for all depths (Colwell and Schaefer 1980). Diflubenzuron persists for only a few days in pasture waters at 22-45 g/ha applied to control pasture mosquitos (*Aedes nigromaculis*, *A. melanimon*); hydrolysis and adsorption onto organic matter limit persistence in water (Schaefer and Dupras 1977). Water temperature and pH significantly affect persistence of diflubenzuron, though not always in a linear fashion. Degradation is most rapid at elevated temperatures and alkaline pH values. Half-time persistence of diflubenzuron at pH 7.7 and various thermal regimes is 8 days at 38° C, 35 days at 24°, and 29 days at 10°; at pH 10, Tb 1/2 values are 2 days at 38°, 14 days at 24°, and 32 days at 10°; degradation is negligible at pH 4, and at low temperatures regardless of pH (Cunningham 1986). In water, as in soil, small-particle (2-5 µm diameter) diflubenzuron formulations, such as WP-25%, degrade rapidly, usually in 2-8 days (Cunningham 1986). Larger-particle sand-granule formulations, developed for use in mosquito control programs wherein the compound needs to penetrate thick vegetation to reach the water, reduce drift during application, and also provide slower release of diflubenzuron into aquatic habitats (Cunningham 1986).

The presence of sediments in diflubenzuron marine microcosms results in rapid removal from seawater and ultimately a reduction in mortality of larval crustaceans (Table 2; Cunningham et al. 1987). But marine sediments that exceed 200 g diflubenzuron/kg--levels normally encountered at application rates for control of saltmarsh mosquitos--could be detrimental to juvenile and adult crustaceans that consume detritus and organic matter on the surface of the marsh or at the water-sediment interface (Cunningham and Myers 1986; Cunningham et al. 1987).

Uses

Diflubenzuron effectively inhibits molting in many species of insect pests, especially among the Lepidoptera, Coleoptera, and Diptera. In the United States diflubenzuron was approved for use by the U.S. Environmental Protection Agency (EPA) against the gypsy moth in 1976, the cotton boll weevil in 1979, and foliar feeders on soybeans in 1982. By 1989 diflubenzuron was also registered for domestic use against mosquitos, forest Lepidoptera, mushroom flies, and certain leaf-eating insect pests of citrus, woody ornamentals, vegetables, and fruits (Bull 1980; Nimmo et al. 1980; Gartrell 1981; Cunningham 1986; Muzzarelli 1986; Webb and Wildey 1986; Wilson and Costlow 1987; Martinat et al. 1988; Poplyk 1989).

In Europe and elsewhere diflubenzuron is used in a variety of ways not presently permitted in the United States. For example, diflubenzuron and other insect growth regulators are fed as admixtures to rations of chickens, cattle, and swine in order to control fly larvae breeding in their manures, and also as a spray directly on manures prior to disposal (Opdycke et al. 1982b; Opdycke and Menzer 1984; Giga 1987). Diflubenzuron has been administered orally as a bolus to beef cattle for control of face flies (*Musca autumnalis*) and horn flies (*Haematobia irritans*), two serious pests of cattle in North America; immature insects develop in fresh manure on open pasture. A single bolus released diflubenzuron into feces that killed horn and face fly larvae for 8 weeks and remained partially effective for 16 weeks (Scott et al. 1986).

Three diflubenzuron formulations are now in general use: an oil dispersable concentrate, a wettable powder (WP), and granules (Bull 1980; Cunningham 1986; Poplyk 1989). Granular formulations are produced by applying diflubenzuron to sand granules. Since technical diflubenzuron (99.5% pure) is a crystalline material that is almost insoluble in water (i.e., 0.1 mg/L at 20° C), it is usually dispersed in an organic solvent carrier. Wettable powders (25% active ingredients), however, are dispersed in water for use in many commercial applications; diflubenzuron particle size in WP-25 formulations usually ranges between 2 and 5 microns.

Lethal and Sublethal Effects

General

Diflubenzuron applied to foliage of terrestrial plants tends to remain adsorbed for several weeks with little or no absorption or translocation from plant surfaces; loss is mainly by wind abrasion, rain washing, or shedding of senescent leaves. Among insect species, there is great variability in sensitivity to diflubenzuron. In general, diflubenzuron is toxic to early life stages of insects at concentrations as low as 0.1 mg/kg diet and at topical applications between 0.003 and 0.034 µg per larvae. Among aquatic organisms, early developmental stages of crustaceans and insects are the most sensitive groups tested; adverse effects on growth, survival, reproduction, and behavior occur between 0.062 and 2.0 µg/L. Groups highly resistant to diflubenzuron include the algae,

gastropods, fishes, and amphibians. Birds are comparatively resistant: acute oral LD50 values exceed 2,000 mg diflubenzuron per kg body weight (BW), and dietary levels of 4,640 mg/kg ration are tolerated for 8 days. Also, forest birds seem unharmed by recommended diflubenzuron application procedures to control pestiferous insects. No data are available on mammalian wildlife. However, studies with small laboratory animals and domestic livestock suggest a high degree of resistance. No observable adverse effects occur in cows given 0.25 mg/kg BW daily for 4 months, in rabbits given 4 mg/kg BW daily on days 6 to 18 of gestation, in dogs fed diets containing 40 mg/kg for 13 weeks (equivalent to 1.6 mg/kg BW daily), in rats fed diets containing 160 mg/kg for 2 years, and in rabbits and rodents given single oral or dermal doses <2,000 mg/kg BW. All of these points are discussed later.

Terrestrial Plants

There is little to no absorption and translocation of diflubenzuron residues from plant surfaces (Gartrell 1981). Due to its stability and low volatility, diflubenzuron residues adhering to plant surfaces are removed primarily through physical effects such as wind abrasion, rain washing, or the loss of dead leaves (Bull 1980). A greenhouse study with corn (*Zea mays*), soybeans (*Glycine max*), cabbage (*Brassica oleracea capitata*), and apples (*Malus* sp.) showed no significant degradation of diflubenzuron residues in leaves for up to 16 weeks after treatment (Gartrell 1981). In a study with radiolabeled diflubenzuron a single dose applied to a cotton (*Gossypium hirsutum*) leaf showed <5% photodegradation in 4 weeks, <7% absorption in 7 weeks, <50% loss to weathering or volatilization in 4 weeks in samples not exposed to rain, and 77% loss in 3 weeks after a heavy rainfall (Bull and Ivie 1978; Bull 1980). Edible portions of rotational crops treated repeatedly with diflubenzuron at recommended application level shad low, but detectable, residues. Maximum concentrations, in mg/kg DW, were always <0.01 in wheat (*Triticum* spp.), <0.02 in cotton, <0.09 in collards (*Brassica* spp.), and <0.16 in radish (*Raphanus* spp.; Bull and Ivie 1978; Bull 1980).

Foliage of cotton that initially contained 100 mg/kg DW contained about 60 mg/kg after 7 weeks; leaf residues consisted entirely of the parent diflubenzuron (Gartrell 1981).

Diflubenzuron applied topically to lima bean (*Phaseolus lunatus*) foliage was not absorbed by the plant, as expected. Injected diflubenzuron, however, was metabolized, and certain of the metabolites were similar to those isolated from mites (Franklin and Knowles 1981).

Diflubenzuron mixed into compost layers of the cultivated mushroom (*Agaricus bisporus*) at 30 mg/kg compost to control dipteran pests of mushroom resulted in increased yield and size; however, at higher concentrations of 180 mg/kg and 1,080 mg/kg, mushroom yield and number were reduced, and this became more severe over time (White 1986). Frequent applications of diflubenzuron to agricultural soils are not detrimental to nitrogen-fixing bacteria (i. e., *Azotobacter vinelandii*), and high concentrations could stimulate nitrogenase activity in soils. This conclusion is based on a study by Martinez-Toledo et al. (1988) using nonsterile agricultural soils and sterilized soils inoculated with *A. vinelandii*. At diflubenzuron loadings between 100 and 500 mg/kg, all concentrations tested had a stimulatory effect on nitrogen fixation in both soils.

Terrestrial Invertebrates

Diflubenzuron is most toxic to early life stages of some insects at 0.1 mg/kg diet, 0.034 µg per larvae (about 3.1 mg/kg BW), or in combination with various chemicals (Table 3). Some beneficial insects, such as the honey bee (*Apis mellifera*), are adversely affected at dietary concentrations of 1 mg/kg for 12 weeks, 10 mg/kg for 10 weeks, or 59 mg/kg for 10 days (Table 3). At 28 to 56 g/ha (0.025 to 0.05 pounds per acre), diflubenzuron effectively controls mosquitos for 8-15 days (Booth and Ferrell 1977; Schaefer and Dupras 1977), especially organophosphorus insecticide-resistant strains of saltmarsh mosquitos in California (Lee and Scott 1989). Diflubenzuron was also effective in controlling strains of house fly (*Musca domestica*) that were resistant to organochlorine, organophosphorus, carbamate, and pyrethroid insecticides on a United Kingdom pig farm; 416 mg/m^2 to slurry pots of pig weaning rooms gave effective control 2-4 weeks after application (Webb and Wildey 1986).

Table 3. Diflubenzuron effects on selected terrestrial invertebrates.

Organism, dose, and other variables	Effect	Reference[a]
Nematode, *Acrobeloides* sp.		
Fed diet containing 100 mg/kg for 10 days	Population reduction of 97%	1
Boll weevil, *Anthonomus grandis*		
1 µg per female weevil, applied topically	After 8 days, about 62% was not absorbed, 3% was absorbed, and 35% was metabolized and excreted	2
113.4 g/ha, applied five times during winter	Reduced heavy infestations by >70% in upper Gulf coast area of Texas	3
Honey bee, *Apis mellifera*		
Fed sucrose syrup/sugar cake diets containing 0.01, 0.1, 1 or 10 mg/kg for 12 weeks	Adult colony survival reduced at 10 mg/kg; inhibited reproduction at 1 and 10 mg/kg; no measurable effect on survival or reproduction at 0.01 or 0.1 mg/kg	4
Fed diet containing 10 mg/kg for 10 weeks	No reduction in consumption of pollen or in quantity of brood reared, but >50% reduction in amount of sucrose syrup stored	5
Fed sucrose syrup containing 59 mg/kg for 10 days	Inhibited reproduction	6
Fed sucrose syrup containing 60 mg/L and drinking water containing 100 mg/L for 40 days	Treated bees consumed significantly less water and pollen and produced significantly less comb, brood, and new workers	7
German cockroach, *Blattella germanica*		
Nymphs fed diets containing 4, 20, 100, or 500 mg/kg for 4 weeks	None dead at 4 mg/kg, 15% at 20 mg/kg, 88% at 100 mg/kg, and all dead at 500 mg/kg	8
Common green lacewing *Chrysopa carnea*		
0.5 g/L spray	Reduced incubation period, reduced hatch, and reduced survival	9
2.0 g/L spray	No hatch	9
Termite, *Coptotermes heimi*		
Nymphs fed diets containing 100, 500, or 1,000 mg/kg	All dead in 24 days at 100 mg/kg, 20 days at mg/kg, or 16 days at 1,000 mg/kg. Some nymphs developed blister-like swellings on the abdomen and failed to molt into the next instar	10
Mosquito, *Culex pipiens quinquefasciatus*		

Adults fed 500 or 1,000 mg/kg diet for 2 days	At both doses, 40% of eggs failed to hatch or hatched abnormally; at the high dose, ovarian histopathology recorded	11
Cat flea, *Ctenocephalides felis*		
Larvae, held in rearing medium for 5-6 weeks		
90 µg/kg	LC 50, 1.5-day-old larvae	12
2,220 µg/kg	LC 50, 2.5-day-old larvae	12
> 100 mg/kg	LC 50, 3.5-day-old larvae	12
Termite, *Heterotermes indicola*		
Nymphs fed diets containing 100, 500, or 1,000 mg/kg feed	All dead in 14-16 days at 100-1,000 mg/kg diet	10
Gypsy moth, *Lymantria dispar*		
100 µg/kg diet	100% lethal to larvae	13
Cabbage moth, *Mamestra brassicae*		
2.2 mg/L spray	LC90, third instar larvae	14
Nematodes, various species		
Fed diet containing 1 mg/kg for 10 days	No effect on reproduction	1
Fed diet containing 10 mg/kg for 10 days	53% population reduction in *Panagrellus redvirus*, and 95% reduction in *Pelodera* sp.	1
American cockroach, *Periplaneta americana*		
Nymphs fed diets containing 100 or 800 mg/kg for 4 weeks	17% dead at low dose and 52% dead at high dose	8
Large white butterfly, *Pieris brassicae*		
0.39 mg/L spray	LC50, third instar larvae	14
Cotton leafworm, *Spodoptera littoralis*, fourth instar larvae, topical application		
3, 10, 30, or 100 ng per larva	Incorporation of N-acetyl glucosamine into chitin was inhibited by 23% at 3 ng per larva, 75% at 10 ng, 90% at 30 ng, and 98% at 100 ng	14
34 ng per larva, equivalent to 3.1 mg/kg BW	LD50, applied in combination with profenofos	15
468 ng per larva, equivalent to 42.5 mg/kg BW	LD50	15
4.3 mg/L, spray	LC90, third instar larvae	14
Termites		
Nymphs, 3 species, given 100-1,000 mg/kg diet	All dead in 14-24 days	10

Adults, 2 species, given 1,000 mg/kg diet	Fecundity reduced and eggs failed to develop	10

[a] 1, Veech 1978; 2, Bull 1980; 3, Cole 1980; 4, Stoner and Wilson 1982; 5, Nation et al. 1986; 6, Muzzarelli 1986; 7, Barker and Waller 1978; 8, Tsuji and Taneike 1988; 9, Zaki and Gesraha 1987; 10, Ahmad et al. 1986; 11, Mittal and Kohli 1988; 12, El-Gazzar et al. 1988; 13, Martinat et al. 1988; 14, Grosscurt et al. 1988; 15, El Saidy et al. 1989.

Chemical control of larvae of gypsy moth and other forest-insect defoliators may cause indiscriminate reduction of nontarget arthropods, which, in turn, may affect food resources of forest birds and small mammals. This problem is of special concern in West Virginia, where two species of endangered bats (Indiana bat, *Myotis sodalis*; eastern big-eared bat, *Plecotus phyllotis*) occur in areas threatened by gypsy moth defoliation (Martinat et al. 1988). Diflubenzuron applications, usually at 70 g/ha on 2 consecutive days, controlled gypsy moth larvae and also significantly reduced populations of canopy macrolepidoptera and nonlepidopteran mandibulate herbivores. Sucking herbivorous insects, microlepidoptera, and predaceous arthropods, however, were relatively unaffected, which suggests that although diflubenzuron can potentially affect food supply of forest birds and small mammals, these effects are probably minimal (Martinat et al. 1988).

Researchers generally agree that diflubenzuron causes incomplete ecdysis by interfering with chitin synthesis. However, diflubenzuron at lethal concentrations causes an effect in chironomid larvae (*Chironomus decorus*, *Tanypus grodhausi*) other than inhibition of chitin synthetase, as judged by histopathology of the alimentary canal--especially the ventriculus. Dysfunction of the ventriculus, an organ that normally lacks chitin, results in a general breakdown of the digestive apparatus of exposed chironomid larvae (Pelsue 1985).

Exposure of nematodes and of adults of several insect species, including boll weevil, housefly, and stable fly (*Stomoxys calcitrans*), to diflubenzuron results in deposition of eggs that appear normal but fail to hatch. This effect seems to be due to an ovicidal action and not to sterility of the treated adults, since the larvae appear to undergo normal development within the egg. Secretion of unmetabolized diflubenzuron into the eggs apparently accounts for observed ovicidal effects (Ivie and Wright 1978; Veech 1978; Ivie et al. 1980). Treated female boll weevils began to lay viable eggs 12 days after treatment and became as productive as controls in 24 days; additional treatment is required to maintain a significant suppression of egg hatch (Bull 1980).

Diflubenzuron is the most investigated benzoylphenylurea and has shown excellent potency for controlling mosquitos and certain lepidopterous and coleopterous pests. Some insect species, however, cannot be controlled efficiently by diflubenzuron. For example, the cotton leafworm (*Spodoptera littoralis*) is comparatively resistant because of reduced penetration through the exoskeleton, rapid elimination of unchanged diflubenzuron, and rapid metabolism, which occurs mainly through hydrolysis (El Saidy et al. 1989). To combat Spodoptera and other resistant pests, new benzoylphenylurea compounds have been developed, including chlorfluzuaron, teflubenzuron, and hexafluron (El Saidy et al. 1989).

Beneficial insects associated with fruit orchards show different responses to diflubenzuron treatment (Broadbent and Pree 1984). Lacewings (*Chrysopa oculata*) in contact with leaves containing 300 mg/kg DW had reduced survival and inhibited molting of first instar larvae, but the assassin bug (*Acholla multispinosa*) was not affected by contact with treated leaves. Lacewings and other beneficial predator insects fed diflubenzuron-treated twospotted spider mites (*Tetranychus urticae*) for 3 days showed no adverse effects after 14 days (Broadbent and Pree 1984). Spraying of diflubenzuron at 28 g/ha to control gypsy moth did not affect *Cotesia melanoscela*, a hymenopteran predator of the gypsy moth; however, another natural enemy, a virus, was adversely affected (Webb et al. 1989). Certain arthropod predators were unaffected by diflubenzuron at 70 mg/ha applied four times in 3 weeks to control the boll weevil; these include the convergent lady beetle (*Hippodamia convergens*), the bigeyed bug (*Geocoris punctipes*),and various species of *Coleomegilla*, *Orius*, *Nabis*, and *Chrysopa* (Deakle and Bradley 1982).

Diflubenzuron can be either hydrolyzed at the urea bridge or oxidized by ring hydroxylation followed by conjugation. Hydrolytic cleavage seems to be a major route for diflubenzuron metabolism in many insect species (El Saidy et al. 1989). Two-spotted spider mites showed <10% absorption in 96 h of topically applied diflubenzuron. Of the amount absorbed about 27% was metabolized in 96 h to 4-chlorophenyl urea, 2,6-

difluorobenzoic acid, 4'-chloroformanilide, 2,6-difluorobenzamide, and other metabolites (Franklin and Knowles 1981). Effects of diflubenzuron were synergized by profenofos (El Saidy et al. 1989) in cotton leafworm 4th instar larvae, and they were antagonized by 20-hydroxyecdysone (Soltani et al. 1987) in yellow mealworm beetle (*Tenebrio molitor*) pupae. More information is needed on interaction effects of diflubenzuron with other chemicals.

Aquatic Organisms

Laboratory Studies

Studies with diflubenzuron and representative aquatic organisms under controlled conditions (Table 4) show several trends:

1. Crustaceans are the most sensitive group of nontarget organisms tested--adverse effects on growth, survival, reproduction, and behavior of copepods, shrimp, daphnids, amphipods, and crabs occur between 0.062 and 2.0, µg/L medium, and early developmental stages were the most vulnerable;

2. Next in sensitivity are aquatic insects, including mayflies, chironomids, caddisflies, and midges--diflubenzuron concentrations between 0.1 and 1.9 µg/L medium produce low emergence and survival;

3. Other groups tested are comparatively resistant, that is, adverse effects occur at <45 µg/L -- in fish, for example, death occurred at >33,000 µg/L; and

4. Elevated accumulations occur in aquatic plants during exposure to 100 µg/L and in fish during exposure between 1 and 13 µg/L. All species in these groups, however, seemed unaffected by elevated body burdens, as judged by normal growth and metabolism.

Table 4. Diflubenzuron effects on selected aquatic organisms: laboratory studies.

Taxonomic group, organism, and concentration in medium in µg/L (ppb)	Effect	Reference[a]
Algae and macrophytes		
Diatom, *Cyclotella cryptica*		
5,000	No effect on photosynthesis during 14-day exposure	1
Bluegreen alga, *Plectonema boryanum*		
100	Residues, in µg/kg dry weight, during exposure for 4 days were 144,700 at 1 h, 85,700 at 1 day, 56,900 at 2 days, 11,700 at 3 days, and 8,300 at 4 days; *Plectonema* growth rate was unaffected	2
Alga, *Selenastrum capricornutum*		
45	No effect on growth during exposure for 120 h	3
Diatoms, 3 species (*Skeletonema costatum*, *Thalassiosira nordenskioldi*, *T. weissflogii*)		
1,000	No effect on photosynthesis during exposure for 11-14 days	1

5,000	Photosynthesis inhibited 70-80% in 11- to 14-day exposure	1
Coelenterata		
Hydra, *Hydra oligactis*		
0.1-0.12 (estimated)	After 24-h exposure, asexual budding rate significantly increased over controls during 20-day posttreatment period; some histopathology. Second generation hydras not significantly different from controls	4
Platyhelminthes		
Planarian, *Dugesia dorotocephala*		
5	No effect on survival, behavior, or asexual reproductive capacity after 24-h exposure	23
Aquatic insects		
Mosquito, *Aedes aegypti*, fourth instar larvae		
20 (equivalent to 0.056 kg/ha)	Fatal to 100% within 24 h, about 50% after 4 days, and <20% after 8 days	5
Mosquito, *Aedes albopictus*		
0.00025	LC30 (24 h), second instar larvae	6
0.0028	Adult emergence inhibited when second instar larvae exposed for 24 h	6
0.025	LC67 (24 h), second instar larvae	6
0.125	Histopathology of cuticle and anal gills in fourth instar larvae after 24-h exposure of third instar larvae	6
0.21	Adult emergence inhibited when third instar larvae exposed for 24 h	6
0.25	LC67 (24 h), third instar larvae	6
12.5	No histopathology of fourth instar larvae after 24-h exposure	6
25	LC 16 (24 h), fourth instar larvae	6
39.6	Adult emergence inhibited when fourth instar larvae exposed for 24 h	6
Mosquito, *Aedes nigromaculis*		
0.5	LC50 (48 h), larvae	7
Aquatic beetles *Hydrophilus triangularis*		
100	LC50 (48 h), larvae	7
Laccophilus spp.		
250	No deaths of adults in 216 h	7
Thermonectus basillaris		

250	No deaths of adults in 168 h	7
Tropisternus lateralis		
250	No deaths of adults in 48 h	7
Mayfly, Callibaetis sp.		
10	LC90 (168 h), nymphs	7
Chironomid, *Chironomus decorus*, fourth instar		
1.9	LC50	8
6.0	LC90	8
Midge, *Chironomus plumosus*		
560	50% of larvae immobilized in 48 h	9, 10
Caddisfly, *Clistoronia magnifica*		
0.1	Adult emergence inhibited during 4-week exposure	11
Midge, *Cricotopus* spp.		
1.6	No adult emergence in 96-h exposure	11
4.9	Molting and survival adversely affected during exposure for 96 h	11
Mosquito, *Culex pipiens* exposed as fourth instar larvae for 24 h		
8	50% reduction in adult emergence	12
100	74% reduction in adult emergence	12
1,000	No adult emergence	12
Mosquito, *Culex pipiens quinquefasciatus*		
1.0	Fourth instar larval dip had no effect on adult sterility	13
Chironomid, *Glyptotendipes paripes*, fourth instar		
1.8	LC50	8
4.1	LC90	8
Midge, *Goeldichironomus holoprasinus*		
10	LC90 (168 h), larvae	7
Dragonflies, *Orthemis* spp., *Pantala* sp.		
50	LC50 (168 h)	7
Blackfly, *Simulium vittatum*, larvae		
80 for 30 min at various water		

temperatures		
10°C	50% dead in 21 days	14
20°C	53% dead in 13 days	14
25°C	92% dead in 3 days	14
500 for 15 min	98% dead in 18 days at 10.5°C	14
1,000 for 30 min	All dead in 10 days at 15°C	14
Stonefly, *Skwala* sp.		
57,500	LC50 (96 h)	15
Midge, *Tanytarsus dissimilis*		
1.0	LC50, period between second and third instar larvae	3
4.9	Molting and survival adversely affected during 5-day exposure	11
Arachnoids		
Horseshoe crab, *Limulus polyphemus*		
5	Larvae exposed for 24 days showed slight delay in molting at 14 days; survival as in controls	6
50	Larvae exposed for 24 days showed molt rate as in controls, but high mortality immediately after ecdysis; reduced growth of survivors	16
Molluscs		
Clam, *Anodonta cygnea*		
200,000	After exposure for 3 months, all clams survived and appeared healthy. But normal calcification process disrupted on lamellar layer of the shell, producing fragile shell	17
Snail, *Juga plicifera*		
36—45	No effect on survival, growth, or reproduction during 3-week exposure	3,11
Snails, *Physa* spp.		
45	No measurable effect on growth, survival, or reproduction during 3-week exposure	3,11
Crustaceans		
Copepod, *Acartia tonsa*		
Adults exposed following terminal molt		
1	Hatch of viable nauplii reduced by 50% after 12-h exposure; no hatch after 36-h exposure. Effect not reversible for at least 30 h after exposure	18
10	Hatch of nauplii reduced by >95% after exposure for 24 h and 100% after 36 h. Effect not reversible for at least 26 h after exposure	18
100	No effect on egg production during 14-day	18

	exposure	
1,000	No adverse effect on survival during exposure for 5 days	18
Brine shrimp, *Artemia salina*		
Adults exposed to 1, 2, 5, or 10	During exposure for 80 days, there was a significant reduction in reproductive lifespan at 2, 5, and 10 µg/L. Nauplii produced viviparously by mated pairs were comparable to controls--except for the 10 µg/L group, which produced fewer nauplii. Cysts produced oviparously by treated pairs, however, had lower mean hatch-ability	19
Nauplii exposed to 1, 10, or 100	All dead within 30 days in the 100 µg/L group; survival same as controls in 12 days for the 1 and 10 µg/L groups	19
Barnacle, *Balanus eburneus*		
50	Some deaths when exposure exceeds 10 days	20
50-100	Significant acceleration of intermolt cycle at low dose, and among survivors at high dose	21
100	No deaths of adults in 28 days	21
750 or 1,000	High mortality during 10-day exposure; prolonged premolt; histopathology of cuticle-secreting epidermal cells	20
1,000 for 48 h plus clean seawater for 26 days	No deaths of adults	21
1,000 for 72 h plus clean seawater for 25 days	High mortality of adults, especially on days 7-14 postexposure	21
Copepods, 2 species		
100	Negligible mortality in 144 h	7
Blue crab, *Callinectes sapidus*		
1	High survival of megalops	22
3	Low survival of megalops	22
Ostracods, *Cypicerus* sp., *Cypridopsis* sp.		
500	Negligible mortality in 72 h	7
Daphnid, *Daphnia magna*		
0.062	Survival and reproduction adversely affected in full life cycle (21-day exposure)	3
2	All dead within 6 days	11
4.4-15	50% immobilized or dead in 48 h	3,9,10,15
Daphnids, 2 spp.		

1.5	LC50 (48 h)	7
Clam shrimp, *Eulimnadia* spp.		
0.15	LC50 (48 h)	7
Copepod, *Eurytemora affinis*		
0.75-1.00	MATC[b]	49
2.2	LC50 (48 h) for nauplii	49
Scud (amphipod), *Gammarus pseudolimnaeus*		
25-45	LC50 (96 h)	9,10,15
1,000	After exposure for 30 min, 22% dead in 55 days at 15°C	14
1,000	After 30-min exposure, 91% dead in 9 days at 25°C	14
Amphipod, *Hyalella azteca*		
1.8	LC50 (96 h)	3
2	LC60 (96 h)	11
1,000	After 30-min exposure, 3-7% dead in 19-21 days at 15°C	14
1,000	After 30-min exposure, 62-99% dead in 7-12 days at 25°C	14
Stone crab, *Menippe mercenaria*		
0.5	LC50 (48 h), larvae	22,24
Copepod, *Mesocyclops thermocyclopoides*		
1-15	Impaired fertility of ovigerous females	25
2-1,000	Prolongation of copepodite stage for 3-4 days followed by death without molting, in most cases. At 125 µg/L and higher, partial molting occurred but all died	25
500	No larval deaths in 48 h	25
1,000	LC50 (48 h) for copepodites. No effect on mating behavior of adults but abnormal ovisac development and decreased fecundity in some females	25
Mysid shrimp, *Mysidopis bahia*		
0.075	Reduction in number of young per female after exposure for 21 days	26
0.075	Reduced survival and reproductive success after exposure for 28 days	24
1.2	LC50 (21 days)	26
1.9	Exposure for 24 h resulted in 65% mortality 3 days after treatment; progeny produced before death had a significantly lower reproduction rate than	27

	controls, as did those in the next generation at nanogram/L (ppt) concentrations	
2.0-2.1	LC50 (96 h)	24,26,27,28
Grass shrimp, *Palaemonetes pugio*		
0.1-0.5	No effect on duration of molt cycle, but dose-related inhibition of regenerative limb growth noted (EC50 = 0.11 µg/L for left 5th periopod)	29
0.3-0.5	MATC[b]	30
0.3-0.5	Loss of positive phototaxis in embryos exposed for 96 h	31
0.3-1.0	Dose-dependent increase in swimming speed in light-adapted larvae	30
0.65	LC50 (7-14 days) intermolt-molt stage; deaths noted during or immediately after molting	29
<1.0	Almost all larvae that survived to day 15 eventually metamorphosed successfully to postlarvae	32
1.0 (initial), medium aged for 71 days, with or without sediments	No deaths of larvae in 22 days when sediments present; all larvae died within 22 days when sediments absent	34
1.0	Limited vertical migration of larvae	30
1.1	LC50 (96 h), early premolt stage	29
1.4	LC50 (96 h) larvae, 95% confidence interval (CI) 1.27-1.54, for wettable powder (WP-25) in water	32
1.6	LC50 (96 h), postlarvae	33
1.8	LC50 (96 h), larvae, 95% CI for technical grade in acetone is 1.64-2.08	32
2.5	All dead by day 15 regardless of formulation tested	32
2.5-5	Morphological abnormalities, both positive and negative phototaxis suppressed	29
3.4	LC50 (24-h exposure, held until molting complete in 24-48 h)	29
202	LC50 (96 h), adult males and nonovigerous females	33
2,000	Negligible mortality of late premolt stage during exposure for 96 h	29
6,985	LC50 (96 h), adult ovigerous females	33
Crab, *Rithropanopeus harrisii*		
0.05	No effect on positive phototaxis response of stage IV larvae	35
0.1	Reduced positive phototaxis of stage IV larvae	35
0.3-0.5	Increased swimming speed of stage I, II, and III larvae	35

0.5	No adverse effects on larval survival during exposure for 20 days	36
1.0	Decreased larval survival during 20-day exposure	36
10	All larvae died during 32-day exposure in containers without sediments; containers with sediments were no longer toxic after 19 days	34
Crab, *Sesarma reticulatum*		
1	No adverse effects on larval survival during 40-day exposure	36
3	Decreased larval survival during 40-day exposure	36
10	All larvae died during 40-day exposure	36
Copepod, *Tigriopus californicus*		
0.1-100	During 72-day exposure, no adverse effects were noted on adult survival and juvenile development at 0.1 µg/L. Reproduction was inhibited at 1 and 5 µg/L. Copepods exposed to 10 or 100 µg/L did not reproduce, were moribund, and had decreased survival.	1
Tadpole shrimp, *Triops longicaudatus*		
0.75	LC40 (24 h)	7
Fiddler crab, *Uca pugilator* Juveniles exposed for 24 h once a week for 10 weeks, then held in clean seawater for an additional 14 weeks		
0.2	No adverse effects on survival or ability to escape from test containers	37
2	No effect on survival, but reduced ability to escape from container	37
20	All died in 23 weeks; reduced mobility prior to death	37
200	All dead in 8 weeks; most deaths occurred in first 4 weeks	37
Adults exposed to 0.5, 5, or 50 after multiple autotomy of one chela and 5 walking legs	Continuous exposure for 18 days produced a dose-dependent retardation of regeneration and deaths during molt at 5 and 50 µg/L. The presence of sediment in test containers lessened effects, but did not eliminate them	38
Adults exposed for 13 weeks		
0.5-50	Some reduction in number of burrows dug at 15 and 60 min after exposure	39
Unknown	Burrowing activity normal on sediments	39

	containing 1 mg/kg	
Fish		
Mummichog, Fundulus *heteroclitus*		
29,800	No deaths in 96 h	40
33,000-255,000	LC50 (96 h)	5,40
Mosquitofish, *Gambusia affinis*		
Unknown	Fish exposed to radiolabeled diflubenzuron for 33 days contained about 6% of the parent diflubenzuron vs. 54% for alga (*Oedogonium cardiacum*), 82% for snail (*Physa* sp.), and 94% for larvae of mosquito (*Culex pipiens quinquefasciatus*)	42
200 for 8 days followed by 300 until day 14	Fish were 2.5 x more hyperactive than controls within 2 days, four times more during days 4-8, and no different from controls at day 14	43
1,000	No deaths in 10 days	7
Brown bullhead, *Ictalurus nebulosus*		
13.2 in pond surface layer 1 h after treatment, <0.2 after 14 days	Maximum concentrations, in µg/kg whole body fresh weight (FW), were 387 at day 1,190 at day 2, 42 at day 4, and ND at day 7	44
Channel catfish, *Ictalurus punctatus*		
Unknown	Runoff from soil containing 0.55 mg diflubenzuron/kg at start produced maximum residues during 28 days, in µg/kg FW, of 4 in muscle and 10 in viscera	2
>100,000	LC50 (96 h)	10,15
370,000	LC50 (96 h)	9
Bluegill, *Lepomis macrochirus*		
1-10	Bioconcentration factor of 13-20 times after 24-h exposure	45
10	After exposure for 24 h, residues 24 and 48 h later were 848 and 8 µg/kg FW whole fish (less tail and viscera)	45
200 (initial); diflubenzuron concentrations ranged from 1.3 to 5.1 between 3 h and 19 days; for 4-chlorophenylurea they were 0.6-3.1, and for 4-chloroaniline they were <0.1-0.4	Maximum concentrations in µg/kg whole fish FW, for diflubenzuron were 119 at 3 h, 812 at 1 day, 55 at 5 days, 196 at 12 days, and 86 at 19 days. For the metabolite 4-chlorophenylurea, these values were 1.6 at 3 h, 8 at 1 day, 40 at 50 days, and 33 at 19 days; and for 4-chloroaniline, 0.8 at 3 h, 2.1 at 1 day, and 1.1-1.3 for days 5-19	46
135,000-660,000	LC50 (96 h)	5,9
Cutthroat trout, *Oncorhynchus clarki*		
57,000-75,000	LC50 (96 h)	10,15

Coho salmon, *Oncorhynchus kisutch*		
150,000	No deaths in 96 h	47
1,000,000	No deaths in 96 h after 15-min exposure	47
Rainbow trout, *Oncorhynchus mykiss*		
29-300	No adverse effects on eyed eggs or fingerlings in 30-day flowthrough exposure	10
625-10,000	Dose-dependent decrease in serum glutamate oxalacetate transaminase (GOT) activity in 96 h, but values overlapped normal GOT range from this hatchery	50
150,000	No deaths in 96 h	47
240,000 (95% CI 201,000-286,000)	LC50 (96 h)	9, 10
1,000,000	No deaths in 96 h after 15-min exposure	47
Yellow perch, *Perca flavescens*		
>>50,000	LC50 (96 h)	15
Fathead minnow, *Pimephales promelas*		
36-45	Embryo-larval exposure for 30 days had no effect on survival, egg hatch, or growth	3,11
>100,000	LC50 (96 h)	10,15
430,000	LC50 (96 h)	9
White crappie, *Pomoxis annularis*		
5 (nominal), 3.3 (measured), 0.4 after 5 weeks	Whole body residues, in µg/kg FW, were 133 at 1 day, 355 at 4 days, 197 at 14 days, and 62 at 21 days	48
10	Fish exposed for 24 h in uncontaminated media contained 822 µg/kg FW whole fish less tail and viscera. Exposure for 48 or 72 h plus 24 h in uncontaminated media produced residues of 533 and 630 µg/kg FW	45
Atlantic salmon, *Salmo salar*		
10	Avoided medium when given choice in 10-min trials	41
>50,000	LC50 (96 h)	15
Brook trout, *Salvelinus fontinalis*		
>50,000	LC50 (96 h)	15

[a] 1, Antia et al. 1985; 2, Booth and Ferrell 1977; 3, Hansen and Garton 1982; 4, Kalafatic and Znidaric 1987; 5, Madder and Lockhart 1980; 6; Ho et al. 1987; 7, Miura and Takahashi 1974; 8, Ali and Lord 1980b; 9, Julin and Sanders 1978; 10, Johnson and Finley 1980; 11, Nebeker et al. 1983; 12, Kelada et al. 1980; 13, Mittal and Kohli 1988; 14, Rodrigues and Kaushik 1986; 15, Mayer and Ellersieck 1986; 16, Weis and Ma 1987; 17, Machado et al. 1990; 18, Tester and Costlow 1981; 19, Cunningham 1976; 20, Gulka et al. 1982; 21, Gulka et

al. 1980; 22, Costlow 1979; 23, Levy and Miller 1978; 24, Nimmo et al. 1981; 25, Rao and Paul 1988; 26, Nimmo et al. 1979; 27, Nimmo et al. 1980; 28, Mayer 1987; 29, Touart and Rao 1987; 30, Wilson et al. 1987; 31, Wilson et al. 1985; 32, Wilson and Costlow 1986; 33, Wilson and Costlow 1987, 34, Cunningham et al. 1987; 35, Forward and Costlow 1978; 36, Christiansen et al. 1978; 37, Cunningham and Myers 1987; 38, Weis et al. 1987; 39, Weis and Perlmutter 1987; 40, Lee and Scott 1989; 41, Granett et al. 1978; 42, Metcalf et al. 1975; 43, Ellgaard et al. 1979; 44, Colwell and Schaefer 1980; 45, Schaefer et al. 1979; 46, Schaefer et al. 1980; 47, McKague and Pridmore 1978; 48, Apperson et al. 1978; 49, Savitz 1991; 50, Madder and Lockhart 1978.

[b] Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

The major degradation products of diflubenzuron in water are 4-chlorophenylurea and 2,6-difluorobenzoic acid (Metcalf et al. 1975; Ivie et al. 1980); these compounds are less toxic to aquatic organisms than the parent chemical (Julin and Sanders 1978; Schaefer et al. 1979, 1980; Gattavecchia et al. 1981). A minor metabolite, 4-chloroaniline, which is classified as a mutagen by the National Cancer Institute and the Cancer Assessment group of the U.S. Environmental Protection Agency (Schaefer et al. 1980), is significantly more toxic to fish and *Euglena gracilis* than is diflubenzuron. For example, LC50 (96 h) values for 4-chloroaniline and four species of freshwater teleosts are 16 to 56 times lower than comparable data for diflubenzuron, but 4-chloroaniline is 76 times less toxic to *Chironomus* midge larvae in 48 h than diflubenzuron (Julin and Sanders 1978). There is a dose-dependent effect of 4-chloroaniline on *Euglena* growth inhibition and glycine metabolism in the range of 1-200 mg/L during exposure for 30 h (Gattavecchia et al. 1981). The most sensitive organism to 4-chloroaniline is bluegill (*Lepomis macrochirus*) with an LC50 (96 h) value of 2.3 mg/L (Julin and Sanders 1978). It is unlikely, however, that this concentration will be encountered under current diflubenzuron application practices.

Diflubenzuron inhibits several enzyme systems in crab and insect larvae, resulting in disrupted glucose metabolism, reduced N-acetylglucosamine incorporation into cuticle, and ultrastructural deformities of chitinous components of the cuticle (Christiansen and Costlow 1982; Christiansen et al. 1984; Christiansen 1986). Specifically, diflubenzuron inhibits chitin synthetase, a magnesium-requiring enzyme that catalyzes the transfer of N-acetyl-D-glucosamine to chitin; the final result is relatively large accumulations of N-acetylglucosamines (Horst 1981; Machado et al. 1990).

Diflubenzuron acts specifically on insects and crustaceans as a larvicide by interfering with chitin deposition into cuticles during juvenile development through ecdysis (Horst 1981; Antia et al. 1985; Cunningham 1986; Machado et al. 1990). The biosynthesis of chitin in arthropods is under hormonal control. Arthropods increase in size by resorbing a portion of the shell and initiating the secretion of a new exoskeleton under the old cuticle. At this time, chitin synthesis is maximal. After completion of about half the new shell, molting occurs, the old shell is discarded, and the new shell is synthesized. Diflubenzuron exposure produces disturbances in the cuticular structure, weakening the cuticle so that it fails mechanically during ecdysis of insects and crustaceans. In general, treated larvae appear healthy during the entire intermolt period until molting commences, at which time many larvae are unable to cast their molts completely and die within a few hours. Several genera of diatoms, including *Thalassiosira* and *Skeletonema*, produce up to 33% of their biomass as chitin. These diatoms synthesize chitin strands that extend outside their frustules to increase buoyancy (Montgomery et al. 1990). Chitin-producing diatoms, as well as nonchitanaceous diatoms, seem unaffected at elevated concentrations of 1 mg/L for periods up to 14 days (Antia et al. 1985). Some species of algae, especially *Plectonema boryanum*, are reported to efficiently degrade diflubenzuron (Schooley and Quistad 1979), but this requires verification.

Studies with laboratory stream communities dosed for 5 months confirm that insects and crustaceans are the most severely affected groups; adverse effects occur in the range 1.0-1.1 µg diflubenzuron per L. Fish and molluscs, however, show no adverse effects at 45 µg/L (Hansen and Garton 1982). Freshwater clams (*Anodonta cygnea*) exposed to high concentrations of diflubenzuron for lengthy periods may experience blocked polycondensation reactions to chitin chains in the outer mantle epithelium secretory cells, producing unstabilized chitin and increasing shell fragility. On this basis the comparatively resistant burrowing bivalve molluscs may be at risk if exposed over several calcification periods (Machado et al. 1990).

Fish accumulated diflubenzuron from water up to 160 times water levels, but tissue concentrations during exposure declined steadily over time (Schaefer et al. 1980).

Exposure of *Aedes albopictus*, a mosquito vector of dengue and encephalitis in Taiwan, for 24 h to 0.00025 to 25 µg/L diflubenzuron resulted in dose-dependent aberrations in larvae, pupae, and adults (Ho et al. 1987; Table 4). In general, most treated second and third instar *Aedes* larvae died during molting, while most fourth instar larvae developed abnormally (Ho et al. 1987). Unfortunately, levels of diflubenzuron used to control saltwater mosquitos and other insects are also toxic to zoeal stages of crustaceans (Costlow 1979) and adversely affect growth and reproduction of adults (Muzzarelli 1986). Treated larvae of estuarine crustaceans are characterized by the following: histological alterations in the cuticular layers of the exoskeleton at concentrations as low as 1 µg/L, higher mortality associated with molting and gross morphological deformities at concentrations as low as 0.5 µg/L, and behavioral modifications at concentrations as low as 0.1 µg/L (Cunningham 1986; Table 4). Behavioral effects in fiddler crabs (*Uca pugilator*) were the most sensitive indicator of diflubenzuron stress, and these effects may influence the ability of juvenile crabs to avoid predation, construct burrows, or feed adequately in nature (Cunningham and Myers 1987). Behavioral effects on cladocerans that may result in latent mortality include reduced filter feeding rates, reduced body movements, and inability to exhibit positive phototaxis, a characteristic of untreated individuals (Cunningham 1986; Table 4). Shrimp larvae exposed to 2.5 µg/L will not undergo daily vertical migration, and those exposed to 1 µg/L undergo only limited migration, which could affect horizontal transport and dispersal of populations and reduce recruitment to benthopelagic adult populations (Wilson et al. 1987). In addition to its inhibitory effect on cuticle synthesis diflubenzuron affects hormone balance by delaying or arresting the molt cycle, and it inhibits limb regeneration by inhibiting mitosis and differentiation (Touart and Rao 1987). Regenrated limbs of diflubenzuron-stressed crabs that survived ecdysis had lesions in the form of black areas in which the cuticle was improperly developed (Weis et al. 1987). Also, diflubenzuron caused a reduction in metabolism of betaecdysone in larval insects, leading to an excess of this molting hormone in the tissues. Treatment of decapod crustaceans with ecdysones frequently causes high mortality and molt acceleration (Gulka et al. 1982).

Toxicity and persistence of diflubenzuron in aquatic environments depend on formulation, frequency of application, quantity of organic matter, sediment type, and water pH and temperature. Biological variables are more important than physical variables in assessing diflubenzuron toxicity, especially the age of the test organism and frequency and synchrony of molting during the exposure period (Cunningham 1986). Crustaceans and other organisms that molt do not demonstrate a typical survival dose-response curve against diflubenzuron because death occurs only when molting is blocked (Nebeker et al. 1983; Cunningham 1986; Cunningham and Myers 1987; Wilson and Costlow 1987). In general, the most sensitive species had comparatively short larval or nymphal periods, and the organism molted frequently (Rodrigues and Kaushik 1986). Susceptible species include mayflies (*Leptophlebia* sp., *Baetis pygmaeus*), while more-resistant species include the stonefly (*Paragnetina media*) and caddisfly (*Hydropsyche bettani*). Amphipods were especially sensitive at 25° C, but not at 10°, 15°, or 20° C (Rodrigues and Kaushik 1986).

Mortality patterns of megalops larvae of blue crab (*Callinectes sapidus*) were elevated at higher temperatures but were seemingly unaffected by water salinity (Costlow 1979). In studies on larvae of black fly (*Simulium vittatum*), diflubenzuron was more effective against earlier larval instar stages than later ones; against rapidly growing larvae than starved, slow-growing larvae; and at 25° than at 20° C (Rodrigues and Kaushik 1986). Among diflubenzuron-stressed barnacles (*Balanus eburneus*), mortality was higher in fed groups than in starved groups, perhaps due to an increased uptake from contaminated food or to an increased molting rate due to feeding (Gulka et al. 1980). Increased fragility of cast exuviae from diflubenzuron-treated barnacles suggests mechanical weakening of the cuticle due to a decrease in chitin content (Gulka et al. 1982).

Field Studies

Field use of diflubenzuron in aquatic habitats for control of pestiferous insects also affects other species (Table 5). Diflubenzuron applications in marshes, ponds, streams, lakes, and rice fields routinely cause population reductions--sometimes irreversible--in many species of nontarget organisms, especially crustaceans and aquatic insects. Taxonomic groups that seem comparatively tolerant to diflubenzuron include algae, turbellarians, rotifers, aquatic beetles, molluscs, annelid worms, ostracods, and fish (Table 5). Following multiple applications to lake and pond ecosystems, diflubenzuron was not measurable in water, sediment, and aquatic

vegetation after several days (Booth and Ferrell 1977). Algae (*Plectonema boryanum*) reportedly degrade 80% of absorbed diflubenzuron in 1 h, primarily to 4-chlorophenylurea and 4-chloroaniline (Booth and Ferrell 1977).

Most authorities agree on four points:

1. Rates as low as 28 to 56 g diflubenzuron per surface ha (0.025 to 0.05 pounds per surface acre), or 2.5 to 16 µg/L, are highly effective against pestiferous dipterans, including many species of chaoborids, chironomids, and culicids (Mulla et al. 1975; Julin and Sanders 1978; Ali and Lord 1980a, 1980b; Cunningham 1986; Ali et al. 1988);

2. These same dosages suppress nontarget populations of cladocerans, copepods, mayfly nymphs, corixids, and springtails (Miura and Takahashi 1975; Mulla et al. 1975; Booth and Ferrell 1977; Julin and Sanders 1978; Ali and Lord 1980a; Cunningham 1986; Ali et al. 1988);

3. Moderately resistant to diflubenzuron are larvae of diving beetles, dragonfly adults and naiads, ostracods (*Cypericercus*, *Cyprinotus*), backswimmers, and water boatmen; highly resistant species include mosquitofish (*Gambusia affinis*), frogs and toads, snails, and algae (Miura and Takahashi 1974; Mulla et al. 1975; Nimmo et al. 1980); and

4. All populations of survivors begin to recover within days or weeks, and recovery is usually complete within 80 days after the last treatment (Mulla et al. 1975; Booth and Ferrell 1977; Ali and Lord 1980a; Nimmo et al. 1980; Cunningham 1986).

Unlike laboratory studies, diflubenzuron does not bioaccumulate markedly in fish or biomagnify through food chains, although altered feeding habits may occur. Under field conditions, marsh or pond sediments usually contain <50 µg/kg FW. This concentration presents negligible risk to channel catfish (*Ictalurus punctatus*) over a 28-day period, suggesting little hazard to catfish during multiple mosquito control applications of diflubenzuron (Booth and Ferrell 1977). Bioaccumulation of diflubenzuron from marsh applications are minimal, as judged by results of uptake studies using marsh sediments containing 550 µg/kg; maximum residues in fish tissues after 3 days were 4 µg/kg FW in muscle and 10 µg/kg DW in viscera (Schooley and Quistad 1979). Diflubenzuron residues are moderately persistent in algae, snails, saltmarsh caterpillars (*Estigmene acrea*), and mosquito larvae but are not biomagnified in food chains ending in fish (Schooley and Quistad 1979).

Maximum diflubenzuron concentrations range from 50 to 720 µg/kg FW in whole body of three species of freshwater teleosts exposed to water treated as many as eight times with 135 g/ha (Gartrell 1981). Feeding habits of freshwater fishes change in ponds showing marked reductions (94-99%) in copepod and cladoceran populations after diflubenzuron treatment (Colwell and Schaefer 1980), perhaps due to availability of various food items. In one study, black crappie (*Pomoxis nigromaculatus*) and brown bullhead (*Ictalurus nebulosus*) altered their diets for 1 month after treatment, eating about three times more insects and ostracods, and almost no cladocerans and copepods -- usually major items -- than before treatment (Colwell and Schaefer 1980).

Table 5. Diflubenzuron effects on selected aquatic organisms: field studies.

Ecosystem, dose, and other variables	Effect	Reference[a]
Coastal marsh, Louisiana		
6 applications, each of 28 g/ha, over 18-month period	Severe reduction in populations of amphipods, dragonfly naiads, corixid nymphs, and some adult beetles. Increased populations of snails, aquatic insect adults, and two species of fish. No change in 27 taxa. Results confounded by severe drought in experimental and control areas	1,2

Farm pond		
2.5, 5, or 10 µg/L; single application	Inhibited adult emergence by 95-100% of a gnat (*Chaoborus astictopus*), 2 to 7 days after treatment. Crustacean zooplankton suppressed at all treatment levels, especially cladocerans and copepods. Rotifers and algae were not affected. Bluegills that fed predominantly on cladocerans and copepods switched to chironomid midges and terrestrial insects after treatment, with no adverse effects.	3
Laboratory stream communities		
0.1, 1, 10, or 50 µg/L for 5 months	Aquatic insect populations were the most sensitive group, especially mayflies, stoneflies, and dipterans. These, and other invertebrates, showed rapid and permanent reductions in biomass and diversity at 1.0 µg/L and higher. Diversity showed an apparent dose-response relation, with no effect at 0.1 µg/L, intermediate reductions at 1 µg/L, and maximal reductions at 10 and 50 µg/L	4
Lake		
110 g/ha (3.7 µg/L), or 220 g/ha (7.4 µg/L); single application	At low dose, amphipods (*Hyalella azteca*) had 97% population reduction that remained depressed; temporary reduction in cladoceran and copepod populations. At high dose, marked population reductions in cladocerans, copepods, and ostracods (*Cyrinofus* sp.). Oligochaete worms were tolerant to both doses	5
110-280 g/ha	Effectively suppressed adult emergence of nuisance midges (*Tanytarsus*, *Procladius*) for up to 2 weeks; ineffective against a more pestiferous midge species (*Chironomus decorus*)	6
156 g/ha to lake surface, equivalent to 12 µg/L on April 26 and again on August 24	After first treatment, reduction within 1 week of three species of cladocerans (*Daphnia laevis*, *Ceriodaphnia* sp., *Bosmina longirostris*), and two species of copepods (*Cyclops* sp., *Diaptomus* sp.). No recovery of *Daphnia* and *Ceriodaphnia* for 6 months, but *Bosmina* reappeared 11 weeks later. *Diaptomus* was depleted for 4 months, but *Cyclops* recovered in 6-7 weeks. The amphipod	7

	Hyallela azteca was eliminated within 4 weeks, and no recolonization was evident after 6 months. No adverse effects on oligochaetes, snails (*Physa* sp.), or ostracods (*Cyprodopsis* sp.). After second treatment, temporary reduction in *Cyclops* and *Bosmina*, and no significant effects on ostracods, snails, or worms	
Pasture pond		
280 g/ha, single application	Controlled pasture mosquitos, *Aedes nigromaculis* and *A. melanimon*, and caused temporary reductions of cladoceran and mayfly nymph populations. Many cladocerans and mayflies died during the posttreatment ecdysis, characteristically with signs of incomplete cleavage of the middorsal ecdysial suture. More-tolerant groups included corixid and notonectid nymphs, and adult aquatic beetles. No effects on the most tolerant groups: turbellarians (*Mesotoma*, *Bothromestoma*), rotifers (*Asplanchna*), ostracods, algae, and spiders (*Pardosa* spp., *Lycosa* spp.)	8
Pond		
13.2 µg/L in pond surface layer 1 h after treatment; <0.2 µg/L after 14 days	Residues, in µg/kg whole body FW, in black crappie (*Pomoxis nigromaculatus*) were 426 at day 1,194 at day 2, 56 at day 4, and not detectable at day 7	9
16 µg/L (estimated from application of 56 g/ha)	Caused declines in third and fourth instar larvae *Culex tarsalis* mosquito 2-8 days after treatment, but not at 11 days	10
80 µg/L (estimated from application of 280 g/ha)	Adult *C. tarsalis* emergence from treated larvae almost completely inhibited for at least 11 days posttreatment	10
Rice field, flooded		
1.1-28 g/ha	100% control of massive rice field populations of fourth instar larvae of the mosquito *Psorophora columbiae* 3-5 days after treatment. Significant reductions in certain nontarget aquatic insect populations	11
About 1,000 µg/L (as judged by 280 g/ha in	Significant reductions in immature populations of the rice water weevil (*Lissorhopterus*	12

rice field water 10 cm deep)	*oryzophilus*) 4-5 days after rice emergence in a continuously flooded field	
About 1,500 µg/L (420 g/ha)	*Lissorhopterus* population reduced 75% when applied 7 days after rice emergence	12
River		
1,250 µg/L added for 1 h to control simuliid flies	After initial depression, target Diptera (flies), including Simuliidae, increased 4 to 40 times over pretreatment levels after 3-4 weeks, suggesting that one-time applications are useless. No adverse effects on adults and fry 3-4 weeks after exposure of dace (*Phoxinus lagowski*) and minnow (*Leuciscus hakonensis*)	13

[a] 1, Farlow 1976; 2, Farlow et al. 1978; 3, Apperson et al. 1978; 4, Hansen and Garton 1982; 5, Ali and Mulla 1978a; 6, Johnson and Mulla 1981; 7, Ali and Mulla 1978; 8, Miura and Takahashi 1975; 9, Colwell and Schaefer 1980; 10, Mulla et al. 1975; 11, Steelman et al. 1975; 12, Smith et al. 1988; 13, Satake and Yasuno 1987.

Although diflubenzuron is not sprayed directly on fresh waters in gypsy moth control, aerial spraying of large forest tracts may result in exposure of streams by way of leaf litter (Swift et al. 1988a). Residual diflubenzuron was present for at least 4 months on leaves submerged in flowing water, and it was toxic to various invertebrates. For example, treated leaves of the tulip poplar (*Liriodendron tulipifera*) that contain 10 mg diflubenzuron per m^2 after 4 months of submersion produce adverse effects on survival and growth when fed to craneflies (*Tipula abdominalis*, *Platycentropus radiatus*; Swift et al. 1988b). The effects of diflubenzuron on leaflitter processing rates in streams is unresolved and merits additional research (Swift et al. 1988a, 1988b).

Birds

Birds are comparatively resistant to diflubenzuron, as judged by the ability of the mallard (*Anas platyrhynchos*) to tolerate single oral doses up to 2,000 mg/kg BW or dietary loadings up to 4,640 mg/kg ration for 8 days (Table 6). Poisoning of insectivorous birds by diflubenzuron, after spraying in orchards as recommended, is highly improbable (Muzzarelli 1986). This conclusion is based on the maximum possible daily intake of insects by wild nestlings (15 mg/kg BW in Great tit, *Parus major*; 10 mg/kg BW in tree sparrow, *Passer montanus*), on a maximum whole body loading of 0.5 mg diflubenzuron per kg FW in insect prey, and on observations of normal growth and subsequent breeding of nestlings in orchards sprayed with diflubenzuron (Muzzarelli 1986).

Despite the apparent absence of direct effects in forest birds, the widespread use of diflubenzuron in the suppression of forest insect defoliators may lead to potentially harmful effects by reducing populations of immature lepidoptera and other mandibulate herbivorous insects upon which they feed. All field evidence collected to date, however, is either inconclusive or negative. In one study, 70.75 g diflubenzuron per ha was applied to an oak forest (*Quercus rubra*, *Q. velutina*, *Q. prinus*) in west Virginia to control first and second instars of gypsy moths (Martinat et al. 1987; Table 6). The maximum diflubenzuron residue recorded in a wide variety of canopy forager birds (blue-gray gnatcatcher, *Polioptila caerulea*; great crested flycatcher, *Myiarchus crinitus*; eastern wood-pewee, *Contopus virens*; black-capped chickadee, *Parus atricapillus*; tufted titmouse, *Parus biocolor*; red-eyed vireo, *Vireo olivaceous*; warblers, *Dendroica* spp.; scarlet tanager, *Piranga olivacea*) was 0.21 mg/kg whole body FW. A similar value, 0.20 mg/kg whole body FW, was recorded in ground or low foragers, including wood thrush (*Hylocichla mustelina*); ovenbird (*Seiurus aurocapillus*); rufous-sided towhee (*Pipilo erythrophthalmus*); indigo bunting (*Passerina cyanea*); song sparrow (*Melospiza melodia*), and chipping sparrow (*Spizella passerina*; Martinat et al. 1987).

In another study as much as 280 mg diflubenzuron per ha applied to control the Douglas-fir tussock moth (*Orgyia pseudotsugata*), an important defoliator of true firs spp.) and Douglas-fir (*Pseudotsuga menziesii*) in western North America, had no adverse effects on forest birds, as judged by population censuses, nesting studies, and bird behavior (Richmond et al. 1979; Table 6).

Domestic chickens (*Gallus* spp.) metabolize diflubenzuron to a greater extent than insects, but less than rodents and ruminants. The main pathway of diflubenzuron degradation in chickens is through cleavage of the urea bridge, whereas rats and cows tend to hydroxylate and conjugate the parent molecule (Opdycke and Menzer 1984). Metabolism studies in chickens showed that major residues in tissues and eggs were unchanged diflubenzuron and 4-chlorophenylurea; also present were 2,6-difluorobenzoic acid and 4-chloroaniline (Gartrell 1981). Metabolites in chicken excreta included 4-chlorophenylurea, 4-chloroaniline, 2,6-difluorobenzamide, 2,6-difluorobenzoic acid, and several unidentified compounds (Opdycke and Menzer 1984). At high dietary loadings of 50-500 mg/kg ration, diflubenzuron accumulates in fat, egg, and muscle tissues of chickens; however, excretion is rapid, and residues are usually negligible after 5 weeks on a clean diet (Table 6). Diflubenzuron fed at levels up to 250 mg/kg ration to male broiler chickens for 98 days had no effect on hyaluronic acid (HA) concentration in the combs and wattles (Crookshank et al. 1978). Both chitin and HA are polysaccharides and have a common biochemical precursor, uridine diphospho N-acetylglucosamine (UDPAGA; Crookshank et al. 1978), which is used in the synthesis of chitin by insects and in the production of HA by vertebrates. Since diflubenzuron interferes with the incorporation of UDPAGA into chitin by insects but not with HA production, it would seem that diflubenzuron is relatively harmless to birds; however, more research is needed for verification.

Intraspecies differences in diflubenzuron metabolism are reported for domestic chickens. The White Leghorn breed, for example, produced eggs with significantly higher residues than other breeds tested after 3 weeks on a diet containing 50 mg diflubenzuron per kg, and it had elevated concentrations in fat tissues after 15 weeks on a 10 mg/kg diet (Opdycke et al. 1982b; Opdycke and Menzer 1984). In chickens, diflubenzuron is usually eliminated more rapidly in feces than in eggs, but in the White Leghorn breed the major route of elimination is via egg production. The White Leghorn breed also differed significantly from the Rhode Island Red/Barred Plymouth Rock (RIR/BPR) breed in ability to metabolize diflubenzuron administered orally or intravenously (Table 6). White Leghorn chickens accumulated diflubenzuron to a greater extent than RIR/BPR chickens, and they retained residues for longer periods. Also, White Leghorn chickens produced a higher percentage and greater number of diflubenzuron metabolites in thir excreta than other breeds tested (Opdycke et al. 1982b).

Table 6. Diflubenzuron effects on selected birds.

Species, route of administration, dose, and other variables	Effect	Reference[a]
Mallard, *Anas platyrhynchos*		
Oral, single dose, 2,000 mg/kg body weight (BW)	Insufficient to kill 50%; anorexia observed on day after treatment	1
Dietary, 4,640 mg/kg Ration	Insufficient to kill 50% in 8 days	2
Forest birds		
From oaks (*Quercus* spp.) forest sprayed aerially with 70.75 g diflubenzuron/ha to control gypsy moth instars; samples collected 3 days prior to spraying, and up	Maximum concentrations, in mg/kg fresh weight (FW) whole body, were 0.21 in canopy birds 3 days postspray (0.09 at day 21); 0.20 in understory birds 1 day postspray, and non-detectable (ND) at day 21; 0.45 in foliage 1 day postspray (0.18 at day 21); 0.49 in foliage	3

to 21 days after spraying	arthropods at day 3, and 0.1 at day 21; ND in litter at all times; 0.11 in litter arthropods at day 10 and 0.03 at day 21. Controls, in all cases, contained <0.03, except litter arthropods, which contained 0.06 mg/kg	
Fir and Douglas-fir (*Abies* sp., *Pseudotsuga menziesii*) forest sprayed aerially with 140 or 280 mg/ha to control Douglas-fir tussock moth; effects evaluated in year of spraying and 1 year later	No significant changes in species diversity, brain cholinesterase activity, survival, morbidity, or behavior at either dose. Significant increases in total breeding pairs noted 1 year later in Townsend's warbler (*Dendroica townsendi*), MaGillivray's warbler (*Oporornis tolmiei*), and mountain chickadee (*Parus gambeli*). Some reductions in populations of warbling vireo (*Vireo gilvus*), golden-crowned kinglet (*Regulus satrapa*), and lazuli bunting (*Passerina amoena*), but all differences were attributed to biological variability rather than to insecticide effects	4
Domestic chicken, *Gallus* spp.		
Intravenous injection		
1 mg/kg BW, white leghorn breed, single dose	Half-time (Tb 1/2) persistence in blood of 14.7 h; 12% of dose excreted in 24 h	5
1 mg/kg BW, Rhode Island Red/Barred Plymouth Rock breed (RIR/BPR), single dose	Tb 1/2 of 8.4 h in blood; 29% of dose excreted in 24 h	5
Oral route		
5 mg/kg BW, white leghorn breed, single dose	Maximum residues after dosing, in mg/kg FW, were 0.25 in egg, 0.4 in eggshell, 0.19 in kidney, and 0.16 in ovary. Excretion of 50% in 8-12 h	5,6
5 mg/kg BW, RIR/BPR breed, single dose	Maximum residues after dosing were 0.14 mg/kg FW in eggs and ND in eggshell, kidney, and ovary. Excretion of 51% in 30-36 h and 82-91% in 13 days	5,6
White leghorn and RIR/BPR strains given 5 mg/kg BW daily for 11 days; residues measured in egg during dosing and for 10 days after dosing	Residues, in mg/kg FW egg, for white leghorn strain were highest at days 9 (3.5) and 11 (2.6). Values were 0.04 at day 20, and ND at day 21. Residues in RIR/BPR were lower: 1.7 at day 9, 1.1 at day 11, 0.02 at day 20, and ND at day 21. Tb 1/2 for egg residues ranged between 34 and	5

	38 h	
Dietary route		
0.05 mg/kg for 28 days	Fat contained 0.018 mg/kg FW at 28 days and <0.0006 mg/kg 7 days after withdrawal	7
0.5 mg/kg for 28 days	Fat contained 0.033 mg/kg FW at 28 days and less than 0.005 mg/kg 7 days after withdrawal	7
1.6 mg/kg for 3 weeks	Minor effects on larvae of house fly (*Musca domestica*) in manure; egg residue of 0.05 mg/kg FW	8
3.1 mg/kg for 3 weeks	Killed 85% of fly larvae in manure; egg residue of 0.25 mg/kg FW	8
5 mg/kg for 28 days	Fat contained 1.16 mg/kg FW at 28 days and <0.032 mg/kg 7-14 days after withdrawal	7
6.2 mg/kg for 3 weeks	Complete inhibition of fly larvae in manure; egg residue of 0.55 mg/kg FW	8
12.5, 25, or 50 mg/kg for 3 weeks	All diets completely inhibited fly larval development in manure; white egg residues, in mg/kg FW, were 1.0 for 12.5 mg/kg diet, 2.1 for 25 group, and 2.9 for the 50 mg/kg group; residues in brown eggs were half those of white eggs	8
Mature white leghorn hens fed diets containing 10, 50, !00, or 500 mg diflubenzuron/kg for 8 weeks	No adverse effects of any diet on feed consumption, growth, egg production, egg weight, eggshell thickness, fertility, hatchability, or progeny performance. Maximum concentrations in tissues after 8 weeks, in mg/kg FW, in the 500 mg/kg diet group, were 53 in fat, 10 in egg, 9 in liver, and 0.9 in muscle; for the 100 mg/kg group, these values were 21 in fat, 10 in liver, 3 in egg, and 0.5 in muscle; for the 50 mg/kg group, residues were 1.5 in fat, 1 in egg, 0.8 in liver, and 0.2 in muscle. Five weeks after withdrawal from all diets, diflubenzuron was <0.05 mg/kg FW in all tissues	9
Male broiler and layer breed chickens fed 205	No significant effect on body weight, food consumption, or weight of testes, liver, comb,	10

mg/kg ration for 98 days beginning at age 1 day	and feet	
Male and female layer-breed chickens were fed diets containing up to 250 mg/kg for 58 weeks, including a 26-week laying cycle. Progeny were reared to age 2 weeks.	No significant effect of any dose level on survival, egg production, egg weight, eggshell weight, fertility, hatchability or hatch weight and body weight of progeny. No gross abnormalities in progeny; growth and feathering as in controls	1 1

[a] 1, Hudson et at. 1984; 2, Farlow 1976; 3, Martinat et al. 1987; 4, Richmond et al. 1979; 5, Opdycke and Menzer 1984; 6, Opdycke et al. 1982b; 7, Gartrell 1981; 8, Miller et al. 1975; 9, Cecil et al. 1981; 10, Kubena 1981; 11, Kubena 1982.

Differences in ability to metabolize diflubenzuron between different strains of domestic chickens may be due to differences in lipid metabolism associated with egg production (Opdycke and Menzer 1984). No comparable data base exists for avian wildlife, and one should be developed through research.

Mammals

No data are available on effects of diflubenzuron on mammalian wildlife. However, results of studies on small laboratory animals and domestic livestock are available (Table 7), and these indicate several trends. Adverse effects levels occurred in dogs fed diets containing 160 mg/kg (6.2 mg/kg BW daily) for 13 weeks (abnormal blood chemistry), in mice given 125 mg/kg BW daily for 30 days (hepatocellular changes), in rabbits fed diets containing 640 mg/kg for 3 weeks (abnormal hemoglobin), and in rats given 5,000 mg/kg BW daily for 13 weeks (abnormal hemoglobin). Accumulations of diflubenzuron occurred in several species. Elevated tissue residues--but no other measurable effects---occurred in cows given 0.05-0.5 mg/kg ration for 28 days or 1-16 mg/kg BW for 4 months, in pigs given a single oral dose of 5 mg/kg BW, and in sheep given a single oral dose of 10 mg/kg BW (Table 7). No observable adverse effect levels occurred in cows given 0.25 mg/kg BW daily for 4 months, in rabbits given 4 mg/kg BW daily on dys 6 to 18 of gestation, in dogs fed diets containing 40 mg/kg for 13 weeks (equivalent to 1.6 mg/kg BW daily), in rats fed diets containing 160 mg/kg for 2 years, and in rabbits and rodents given single oral or dermal doses <2,000 mg/kg BW (Table 7).

All available data indicate that diflubenzuron is not a mutagen, teratogen, or carcinogen. Diflubenzuron is not mutagenic, as judged by the results of

1. The mouse lymphoma forward mutation test at the thymidine kinase locus (detects mutations to a nonfunctional thymidine kinase in a line of culture mouse lymphoma cells),

2. The Ames *Salmonella typhimurium* microsome reverse mutation test (ability to produce point gene mutations of a base pair),

3. The mouse micronucleus test (which detects chromosome breakage or chromosome loss from mitotic abnormalities in bone marrow erythrocytes; Mac Gregor et al. 1979), and

4. A DNA damage study with yeast, *Saccharomyces cerevisiae* (Gartrell 1981).

No teratogenicity or reproductive effects were associated with elevated doses of diflubenzuron in all species of mammals tested (Gartrell 1981). Diflubenzuron suppresses melanogenesis and uptake of nucleosides in mouse melanoma cells (Jenkins et al. 1986), and it inhibits growth of experimental tumors in mice, either alone or in combination with $CoC1_2$ (Table 7). Mixed function oxidase, induced by 3-methylcholanthrene, enhances the antitumor properties of diflubenzuron, suggesting that aromatic hydroxylation may be required for tumor growth regulation (Jenkins et al. 1986). The most likely diflubenzuron metabolite that affects tumor growth regulation is the form oxidized at the 2 carbon of the phenyl ring; other metabolites tested (i.e., 4-

chlorophenylurea, 3-OH-diflubenzuron) are only marginally effective (Jenkins et al. 1986). Diflubenzuron did not produce tumors in fetal cells of hamsters (*Cricetus* spp.) at whole body doses of 500 mg/kg, and this also suggests a relatively low oncogenic potential (Quarles et al. 1980). Diflubenzuron is not cytotoxic and does not inhibit the synthesis of complex carbohydrates in animal cells, as judged by results of studies with cultured rat glial cells, wherein diflubenzuron was not metabolized to any measurable extent, and more than 98% could be recovered from particulate fractions of whole cells (Bishai and Stoolmiller 1979).

Intestinal absorption of diflubenzuron in laboratory rats, measured as the sum of urinary and biliary excretion, decreases with increasing dose: from 50% at a single oral dose of 4 mg/kg BW to 4% at 900 mg/kg BW. Excretion is almost complete after 75 h; at that time up to 4% of the administered dose is recovered from skinned carcasses (Willems et al. 1980). About 80% of diflubenzuron metabolites excreted by rats seem to have the basic diflubenzuron structure intact. Three metabolites are largely excreted as conjugates in the bile. One metabolite, 2,6-difluorobenzoic acid, is excreted largely in urine. Its counterpart, 4-chlorophenylurea, was not present in urine or bile in appreciable quantity, nor was 4-chloroaniline detected (Willems et al. 1980). Lifetime feeding studies of 4-chloroaniline, a relatively common diflubenzuron metabolite, showed no compound-related effects in laboratory mice and rats (Gartrell 1981).

Oral treatment of sheep and cattle (*Bos* spp.) with diflubenzuron is followed by absorption of the compound through the gastrointestinal tract, metabolism, and elimination of residues through the urine, feces, and, to a limited extent, milk. Intact diflubenzuron is eliminated in the feces of orally dosed cattle and sheep (Ivie 1978). Major metabolites of diflubenzuron excreted by cattle and sheep result from hydroxylation on the difluorobenzoyl and chlorophenyl rings, and by cleavage between the carbonyl and amide groups to produce metabolites that are excreted free or as conjugates (Ivie 19.78). Cattle dosed repeatedly with diflubenzuron had detectable residues only in liver and milk. The parent compound, 4-chlorophenylurea, 2,6-difluorobenzoic acid, and 4-chloroaniline compose only 15% of the total residue in liver; the bulk of the residue is not extractable (Gartrell 1981). Dietary levels of 5 mg/kg ration produce low (13 µg/L), but detectable, diflubenzuron concentrations in milk of cattle (Gartrell 1981).

Table 7. Diflubenzuron effects on selected mammals.

Species, mode of administration, dose, and other variables	Effect	Reference[a]
Cattle, *Bos* sp.		
Dermal		
0.125 mg/cm^2 hide, single application, 1% solution to 400 cm^2 skin surface	No absorption through skin; rapid dis-appearance. Maximum residues in hair, in mg/kg fresh weight (FW), were 128 after 1 week, 19 after 2 weeks, and 4 after 4 weeks. For skin, these values were 0.4, 0.1, and <0.1	1
Diet		
0.05 mg/kg ration for 28 days	No detectable residues in milk and tissues, except liver (0.01 mg/kg FW); liver residues remained detectable after a 7-day withdrawal period	2
0.5 mg/kg ration for 28 days	No detectable residues in milk and tissues, except liver (0.08 mg/kg FW); liver residues remained detectable after a 7-day withdrawal period	2
5 mg/kg ration for 28 days	Liver residue of 0.54 mg/kg FW remained elevated after a 7-day withdrawal period; residues in milk reached 0.013 mg/L within the first few	2

	days of feeding and declined to nondetectable (ND) levels after a 4-day withdrawal period	
Fed diets equivalent to 0.25 mg/kg body weight (BW) daily for 4 months, single animal	No detectable residues in any tissue. Tb 1/2 of 4—5 days in manure; manure gave >95% control of larvae of the face fly, *Musca autumnalis*	3
Fed diet equivalent to 1 mg/kg BW daily for 4 months, single animal	No detectable residues in any tissue except omental fat (0.1 mg/kg FW). No houseflies (*Musca domestica*) or face flies developed in manure	3
Fed diet that increased from 1 mg/kg BW daily to 8 mg/kg BW over a 2-month period, then 16 mg/kg BW daily for 3 months	No detectable diflubenzuron residues in heart, muscle, or kidney; 130 µg/kg FW in liver; about 250 µg/kg FW in subcutaneous fat	3
Holstein bull calves fed diet equivalent to 2.8 mg/kg BW daily for first 7 months, then 1 mg/kg BW daily for 6-12 months	No effect on weight gain, serum testosterone at age 11 months, libido, sperm mobility, semen volume, or sperm concentration. No histo-pathology of liver, lung, kidney, or spleen. No tissue residues---except for one bull slaughtered at age 5 months: <20 µg/kg FW in muscle, 20 in liver and kidney, 40 in subcutaneous fat, and 80 in renal and omental fat	4
Fed diet equivalent to 8 mg/kg BW daily for 4-5 months, single animal	No detectable residues in milk	3
Fed diet equivalent to 16 mg/kg BW daily for 4-5 months, single animal	Maximum concentrations recorded were 20 µg/L in milk and 250 µg/kg FW in body fat. No obvious adverse effects on feeding behavior	3
Oral		
10 mg/kg BW, single-dose to a lactating cow	Extensively metabolized in 4 days; almost all totally excreted in 7 days: about 85% in feces, 15% in urine, 0.2% in milk. At 7 days, liver contained 2.9 mg/kg FW, skin 0.4, and	1

	all other tissues <0.4	
Dog, *Canis familiaris*		
Fed diets containing 10, 20, 40, or 160 mg/kg (equivalent to to 0.42, 0.84, 1.64, or 6.24 mg/kg BW daily) for 13 weeks	Abnormal hemoglobin levels in 160-mg/kg group after 6 weeks; no other abnormal findings or histopathology observed in any group at 13 weeks	2
Angora goat, *Capra* sp.		
30 mL of 2% diflubenzuron solution applied dermally 6 weeks after shearing, 25-kg females	Protected against Angora goat biting lice (*Bovicola limbatus*) for up to 18 weeks	5
Domestic mouse *Mus* sp.		
Diet		
4, 8, 16, or 50 mg/kg ration for 80 weeks	Increase in tumors in females at the 16-mg/kg level	2
Intraperitoneal injection		
3 daily injections of 1.2 mg, equivalent to 144 mg/kg BW, tumor-bearing strain	Tumors conditioned with COC12 then treated with diflubenzuron showed a 75% reduction in rate of tumor increase	6
5 daily injections of 20 mg (total of 100 mg, equivalent to 4,000 mg/kg BW), C57BL/6 strain with B 16 melanomas	Initial antitumor activity, as judged by 11-20% decrease in tumor volume, and a 2-3 day increase in tumor doubling time. But at midtreatment, tumors regained control rate of volume increase	6
2,150 mg/kg BW	Insufficient to kill 50%	7
Oral		
Adult males given 125, 500, or 2,000 mg/kg BW daily for 30 days	Hepatocellular changes at all dose levels, including histopathology and altered activities of glutathione S-transferase enzymes	8
>4,640 mg/kg BW	Acute oral LD50	2,7,8
Rabbit, *Oryctolagus* sp.		
Dermal		
2,000 mg/kg BW	Insufficient to kill 50%	7

Diet		
Males given 640 mg/kg feed for 18-21 days	Abnormal hemoglobin	2
In vitro studies		
Up to 5 mg/L	Protein and RNA synthesis rates were significantly stimulated in liver, and inhibited in muscle in a dose-dependent manner. Maximum effect in both tissues occurred at 5 mg/L for protein synthesis and 0.2 mg/L for RNA synthesis	9
Oral		
Females given 1, 2, or 4 mg/kg BW daily on days 6-18 of gestation	No compound-related maternal toxicity or birth defects	2
Sheep, *Ovis aries*		
Dermal		
Merrino sheep exposed to mass-released gravid females of the sheep blowfly (*Lucilia cuprina*)—a severe ectoparasite in Australia that may kill—in a fly-proof animal house after dermal application of 1,000, 1,500, or 2,500 mg diflubenzuron/L; sheep thoroughly wetted twice during 4 days	1,000 mg/L protected against fly strike for at least 110 days; 1,500 mg/L protected until end of trial at 170 days; 2,500 mg/L provided excellent protection against severe infestation. No resistance to diflubenzuron was acquired by blowflies	10
Oral		
Single dose of 10 mg/kg BW	Residues after 7 days, in mg/kg FW, were about 3 in liver, 0.4 in kidney, and <0.2 in all other tissues	1
Single dose of 500 mg/kg BW	In 4 days, bile accounted for 36% of diflubenzuron metabolites excreted, feces 32%, and urine 24%; in 7 days, feces were the major pathway	1
Laboratory white rat, *Rattus* sp.		
Diet		

Fed 10, 20, 40, or 160 mg/kg ration for three generations	No effect on fetotoxicity or teratogenicity	2
Fed 10, 20, 40, or 160 mg/kg ration for 2 years	No compound-related effects	2
Oral		
Females given 1, 2, or 4 mg/kg BW daily on days 6-15 of gestation	No compound-related maternal toxicity or birth defects	2
4 mg/kg BW, single dose	Intestinal absorption of 50%	11
5 mg/kg BW, single dose	72-93% excreted in 6 days, mostly in feces	11
900 mg/kg BW, single dose	Intestinal absorption of 4%	11
>4,640 mg/kg BW	Acute oral LD50	2,7
Males given 5,000 mg/kg BW daily for 13 weeks	Abnormal hemoglobin on days 1-4, and on day 8	2
Swine, *Sus* sp.		
Adult female pig given single oral dose of 5 mg/kg BW and observed for 11 days	By 11 days, 82% of dose was excreted unchanged in feces, and 5% in urine as metabolites (4-chlorophenylurea, 2, 6-difluorobenzoic acid, 4-chloroaniline, and 2,6-difluorobenzamide). Tissue residues, in mg/kg FW, ranged from ND in bone to 0.04-0.09 in stomach wall, brain, pancreas, small intestine, blood, heart, muscle, and ovary; from 0.11-0.2 for large intestine, subcutaneous fat, lymph, lung, and kidney; and from 0.23 to 0.4 in liver, omental fat, and gall bladder	12

[a] 1, Ivie 1978; 2, Gartrell 1981; 3, Miller et al. 1976; 4, Miller et al. 1979; 5, Miller et al. 1985; 6, Jenkins et al. 1986; 7, Poplyk 1989; 8, Young et al. 1986; 9, E1-Sebae et al. 1988; 10, Hughes and Levot 1987; 11, Willems et al. 1980; 12, Opdycke et al. 1982a.

The major hydroxylated diflubenzuron metabolite in cow milk (N-[[(4-chlorophenyl) amino] carbonyl] -2,6-difluoro-3-hydroxybenzamide) when fed to white rats is rapidly excreted with little biotransformation (Ivie 1978).

Metabolism of diflubenzuron by mammals and birds probably occurs by way of hydroxylation, conjugation, and cleavage of the urea moiety (Opdycke et al. 1982a); however, interspecies differences are considerable. In cows, for example, the major identified metabolic transformation is hydroxylation at the 3 position of the 2,6-difluorobenzoyl ring. In sheep, however, major metabolites arise through cleavage of the amide bond at the benzoyl carbon to produce 2,6-difluorobenzoic acid, which is excreted in the urine either free or conjugated with

glycine (Ivie 1978). The major diflubenzuron metabolite in cow urine is 2,6-difluoro-3-hydroxydiflubenzuron, accounting for 45%, and in feces 18%; unchanged diflubenzuron accounts for 43% of the administered dose in cow feces. In sheep urine, 2,6-difluorobenzoic acid and 2,6-difluorohippuric acid account for 57%; in sheep feces, unchanged diflubenzuron is 97% (Ivie 1978). In swine, the majority of the administered dose is eliminated in feces unchanged; the urine contains mostly metabolites, indicating that most of the absorbed diflubenzuron is metabolized (Opdycke et al. 1982a).

Recommendations

Since diflubenzuron toxicity seems to be similar in both insects and crustaceans, extreme care must be taken when this compound and other chitin synthesis inhibitors are used for insect control in areas where aquatic crustaceans occur. Otherwise, ecological instability may result, with consequences for feeding, metabolism, growth, reproduction, and survival of numerous nontarget organisms (Christiansen 1986). Specifically, diflubenzuron use in saltmarsh mosquito breeding areas or on agricultural lands less than 5 km from coastal areas is not recommended because of concerns that runoff may reach the adjacent estuaries, which are the primary hatcheries for many economically important species of crustaceans (Costlow 1979; Cunningham 1986; Cunningham and Myers 1986). Also, diflubenzuron concentrations in seawater should not exceed 0.1 µg/L, the minimum concentration known to produce measurable behavioral changes in estuarine crustacean larvae (Cunningham and Myers 1986).

If diflubenzuron and other insect growth regulators continue to be used near productive aquatic habitats, then food chain transfer studies are recommended. High accumulations of diflubenzuron by aquatic algae -- up to 4.5 mg/kg DW in some cases (Booth and Ferrell 1977)-- strongly implicate food chain transfer as a potential mechanism of contaminant transfer in aquatic invertebrate food webs. To protect certain fishes, diflubenzuron use to control copepod vectors of human disease--including various species of *Cyclops*--is not recommended in areas where these fishes breed or feed on *Cyclops* (Rao and Paul 1988).

For control of cotton pests, including the boll weevil, a maximum recommended treatment schedule is 421 g diflubenzuron per ha, applied six times, usually weekly, during the growing season (Bull 1980). Honey bees (*Apis mellifera*) in heavily sprayed areas, however, may experience adverse effects if their diets exceed 1 mg diflubenzuron per kg FW (Stoner and Wilson 1982). Diflubenzuron inhibits house fly development in poultry manure. A recommended cost-effective fly control program in poultry houses involves the feed-through method

(5 mg diflubenzuron per kg FW poultry diet) during hot, wet summers for 3-4 months, coupled with good sanitation and good manure management (Giga 1987).

For protection of domestic cattle, feeds should contain <0.05 mg diflubenzuron per kg FW; cottonseed may be added to cattle diets provided that diflubenzuron concentrations in the seed do not exceed 0.2 mg/kg FW and that cottonseed composes < 17% of the total diet bulk (Gartrell 1981).

Diflubenzuron causes biochemical upset, as judged by lowered testosterone levels in chickens and rats (EPA 1979), altered glutathione S-transferase activity in mouse liver (which adversely affects the ability to detoxify foreign substances by way of conjugation; Young et al. 1986), and disrupted hydroxylamine activity in human infants (EPA 1979). Additional research seems needed on biochemical alterations induced by diflubenzuron.

No diflubenzuron criteria are currently recommended for protection of avian and mammalian wildlife. All data available suggest that wildlife species are about as tolerant to diflubenzuron as are domestic poultry and livestock; however, the wildlife data base seems inadequate for practicable criteria formulation.

Anti-cancer properties of diflubenzuron require elucidation. The indication that one or more hydroxylated forms of diflubenzuron can regulate growth of mouse tumor cells provides a basis for further studies to identify and isolate the most active analog of this compound, and it suggests that other benzoylphenyl ureas may have similar properties (Jenkins et al. 1986).

Diflubenzuron has a Surveillance Index Classification of Class IV, indicating a sufficiently low hazard potential to human health from toxicological and exposure standpoints to justify only minimal monitoring efforts (Gartrell 1981). Human cancer risk of lifetime dietary exposure to diflubenzuron in a worst case scenario is

considered slight (EPA 1979). Diflubenzuron has little potential for human dietary exposure because of its limited use on cotton and the low residues measured on cottonseed, meat, milk, poultry, and eggs (Gartrell 1981). For protection of human health, tolerances of <0.05 mg/kg FW have been set for fat, meat, meat byproducts, poultry, milk, dairy products, and eggs, and <0.2 mg/kg FW for cottonseed (EPA 1979). These foods compose about 45% of the average human diet. If all of these foods bore residues at the tolerance level, they would contribute 0.035 mg daily on the basis of 1.5 kg food eaten daily. For a 60-kg adult, the theoretical maximum residue concentration would be 0.6 µg/kg BW daily. Tolerances would be approached only when maximum quantities of cottonseed fraction (i.e., hulls, meal, soapstock), all bearing tolerance-level residues, are incorporated into livestock diets. At present, however, no acceptable daily intake level in humans has been established (Gartrell 1981).

Acknowledgments

I thank L. Garrett, N. Hestbeck, and W. Manning for literature search and retrieval services; M. Holmes for secretarial assistance; W. N. Beyer, J. Clark, J. Coyle, C. J. Henny, and S. N. Wiemeyer for technical review of the manuscript; and J. D. Cox and J. R. Zuboy for editorial services.

References

Ahmad, M., Z. Salinah, N. Sultana, and S. Ahmad. 1986. Preliminary studies on the effects of diflubenzuron (dimilin) on termites (Isoptera). Pakistan Journal of Zoology 18:403-409.

Ali, A., and J. Lord. 1980a. Impact of experimental insect growth regulators on some nontarget aquatic invertebrates. Mosquito News 40:564-571.

Ali, A., and J. Lord. 1980b. Experimental insect growth regulators against some nuisance chironomid midges of central Florida. Journal of Economic Entomology 73:243-249.

Ali, A., and M. S. Mulla. 1978a. Impact of the insect growth regulator diflubenzuron on invertebrates in a residential-recreational lake. Archives of Environmental Contamination and Toxicology 7:483-491.

Ali, A., and M. S. Mulla. 1978b. Effects of chironomid larvicides and diflubenzuron on nontarget invertebrates in residential-recreational lakes. Environmental Entomology 7:21 27.

Ali, A., H. N. Nigg, J. H. Stamper, M. L. Kok-Yokomi, and M. Weaver. 1988. Diflubenzuron application to citrus and its impact on invertebrates in an adjacent pond. Bulletin of Environmental Contamination and Toxicology 41:781-790.

Antia, N. J., P. J. Harrison, D. S. Sullivan, and T. Bisalputra. 1985. Influence of the insecticide diflubenzuron (dimilin) on the growth of marine diatoms and a harpacticoid copepod in culture. Canadian Journal of Fisheries and Aquatic Sciences 42: 1272-1277.

Apperson, C. S., C. H. Schaefer, A. E. Colwell, G. H. Wemer, N. L. Anderson, E. F. Dupras, Jr., and D. R. Longanecker. 1978. Effects of diflubenzuron on *Chaoborus astictopus* and nontarget organisms and persistence of diflubenzuron in lentic habitats. Journal of Economic Entomology 71:521-527.

Barker, R. J., and G. D. Waller. 1978. Effects of diflubenzuron wettable powder on caged honey bee colonies. Environmental Entomology 7:534-535.

Bishai, W. R., and A. C. Stoolmiller. 1979. Uptake of diflubenzuron (N-[[4-chlorophenyl) amino] carbonyl]-2,6-difluorobenzamide) by rat C6 glial cells in vitro. Pesticide Biochemistry and Physiology 11:258-266.

Booth, G. M., and D. Ferrell. 1977. Degradation of dimilin by aquatic foodwebs. Pages 221-243 *in* M. A. Q. Khan, editor. Pesticides in aquatic environments. Plenum Press, New York.

Broadbent, A. B., and D. J. Pree. 1984. Effects of diflubenzuron and BAY SIR 8514 on beneficial insects associated with peach. Environmental Entomology 13:133-136.

Bull, D. L. 1980. Fate of diflubenzuron after application to cotton and the boll weevil. The Southwestern Entomologist, Supplement 1:2-7.

Bull, D. L., and G. W. Ivie. 1978. Fate of diflubenzuron in cotton, soil, and rotational crops. Journal of Agricultural and Food Chemistry 26:513-520.

Cecil, H. C., R. W. Miller, and C. Corley. 1981. Feeding three insect growth regulators to white leghorn hens: residues in eggs and tissues and effects on production and reproduction. Poultry Science 60:2017-2027.

Christiansen, M. E. 1986. Effect of diflubenzuron on the cuticle of crab larvae. Pages 175-181 *in* International conference on chitin and chitosan. Plenum Press, New York.

Christiansen, M. E., and J. D. Costlow, Jr. 1982. Ultrastructural study of the exoskeleton of the estuarine crab *Rithropanopeus harrisii*: effect of the insect growth regulator dimilin (diflubenzuron) on the formation of the larval cuticle. Marine Biology 66:217-226.

Christiansen, M. E., J. D. Costlow, Jr., and R. J. Monroe. 1978. Effects of the insect growth regulator dimilin (TH 6040) on larval development of two estuarine crabs. Marine Biology 50:29-36. TH 6040) on larval development of two estuarine crabs. Marine Biology 50:29-36.

Christiansen, M. E., E. Gosling, and M. A. Williams. 1984. Effect of the insect growth regulator diflubenzuron (dimilin) on the uptake of glucose and N-acetylglucosamine into the cuticle of crab larvae. Marine Biology 83:225-230.

Cole, C. L. 1980. Effectiveness of diflubenzuron in the upper Gulf coast of Texas. The Southwestern Entomologist, Supplement 1:22-26.

Colwell, A. E., and C. H. Schaefer. 1980. Diets of *Ictalurus nebulosus* and *Pomoxis nigromaculatus* altered by diflubenzuron. Canadian Journal of Fisheries and Aquatic Sciences 37:632-639.

Costlow, J. D. 1979. Effect of dimilin on development of larvae of the stone crab *Menippe mercenaria*, and the blue crab, *Callinectes sapidus*. Pages 355-363 *in* W. B. Vernberg, A. Calabrese, F. P. Thurberg, and F. J. Vernberg, editors. Marine pollution: functional responses. Academic Press, New York.

Crookshank, H. R., B. A. Sowa, L. Kubena, G. M. Holman, H. E. Smalley, and R. Morison. 1978. Effect of diflubenzuron (dimilin; TH-6040) on the hyaluronic acid concentration in chicken combs. Poultry Science 57:1-11.

Cunningham, P. A. 1976. Effects of dimilin (TH 6040) on reproduction in the brine shrimp, *Artemia salina*. Environmental Entomology 5:701-706.

Cunningham, P. A. 1986. A review of toxicity testing and degradation studies used to predict the effects of diflubenzuron (dimilin) on estuarine crustaceans. Environmental Pollution 40A:63-86.

Cunningham, P. A., and L. E. Myers. 1986. Dynamics of diflubenzuron (dimilin) concentrations in water and sediment of a supratidal saltmarsh site following repetitive aerial applications for mosquito control. Environmental Pollution 41A:63-88.

Cunningham, P. A., and L. E. Myers. 1987. Effects of diflubenzuron (dimilin) on survival, molting, and behavior of juvenile fiddler crabs, *Uca pugilator*. Archives of Environmental Contamination and Toxicology 16:745-752.

Cunningham, P. A., J. E. H. Wilson, D. W. Evans, and J. D. Costlow, Jr. 1987. Effects of sediment on the persistence and toxicity of diflubenzuron (dimilin) in estuarine waters: a laboratory evaluation using larvae of two estuarine crustaceans. Pages 299-331 *in* W. B. Vernberg, A. Calabrese, F. P. Thurberg, and F. J. Vernberg, editors. Pollution physiology of estuarine organsims. University of South Carolina Press, Columbia.

Deakle, J. P., and J. R. Bradley, Jr. 1982. Effects of early season applications of diflubenzuron and azinphosmethyl on population levels of certain arthropods in cottonfields. Journal of the Georgia Entomological Society 17:200-204.

El-Gazzar, L. M., R. S. Patterson, and P. G. Koehler. 1988. Activity of chitin synthesis inhibitors on the cat flea, *Ctenocephalides felis* Bouche. Journal of Agricultural Entomology 5:117-120.

Ellgaard, E. G., J. T. Barber, S. C. Tiwari, and A. L. Friend. 1979. An analysis of the swimming behavior of fish exposed to the insect growth regulators, methoprene and diflubenzuron. Mosquito News 39:311-314.

El Saidy, M. F., M. Auda, and D. Degheele. 1989. Detoxification mechanisms of diflubenzuron and teflubenzuron in the larvae of *Spodoptera littoralis* (Boisd.). Pesticide Biochemistry and Physiology 35:211-222.

El-Sebae, A. H., M. H. Salem, M.R.S. El-Assar, and E. E. Enan. 1988. In vitro effect of profenofos, fenvalerate and dimilin on protein and RNA biosynthesis by rabbit liver and muscle tissues. Journal of Environmental Science and Health B23:439-451.

Environmental Protection Agency (EPA). 1979. Tolerances and exemptions from tolerances for pesticide chemicals in or on raw agricultural commodities; diflubenzuron. Federal Register 44(85):25452-25454.

Farlow, J.E. 1976. Dimilin [1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)-urea] on the aquatic fauna of a Louisiana coastal marsh. Ph.D. thesis, Louisiana State University and Agricultural and Mechanical College, Baton Rouge. 144 pp.

Farlow, J. E., T. P. Breaud, C. C. Steelman, and P. E. Schilling. 1978. Effects of the insect growth regulator diflubenzuron on non-target aquatic populations in a Louisiana intermediate marsh. Environmental Entomology 7: 199-204.

Forward, R. B., Jr., and J. D. Costlow, Jr. 1978. Sublethal effects of insect growth regulators upon crab larval behavior. Water, Air, and Soil Pollution - 9:227-238.

Franklin, E. J., and C. O. Knowles. 1981. Metabolism of diflubenzuron by spider mites and bean plants. Pesticide Science 12: 133-141.

Gartrell, M. 1981. Diflubenzuron. U.S. Food and Drug Administration, Bureau of Foods, HFF-420.8 pp.

Gattavecchia, E., A. M. Di Pietra, D. Tonelli, and A. Borgatti. 1981. Effect of diflubenzuron and its major degradation products on the growth of *Euglena gracilis* Z. and incorporation of glycine-U-^{14}C in protein. Journal of Environmental Science and Health B16:159-166.

Giga, D. P. 1987. Evaluation of the insect growth regulators cyromazine and diflubenzuron as surface sprays and feed additives for controlling houseflies *Musca domestica* (L.) in chicken manure. International Pest Control 29:66-69.

Granett, J., S. Morang, and R. Hatch. 1978. Reduced movement of precocious male Atlantic salmon parr into sublethal dimilin-Gl and carrier concentrations. Bulletin of Environmental Contamination and Toxicology 19:462-464.

Grosscurt, A. C., M. T. Haar, B. Jongsma, and A. Stoker. 1988. PH 70-23: a new acaricide and insecticide interfering with chitin deposition. Pesticide Science 22:51-59.

Gulka, G., C. M. Doscher, and N. Watabe. 1980. Toxicity and molt-accelerating effects of diflubenzuron on the barnacle, *Balanus eburneus*. Bulletin of Environmental Contamination and Toxicology 25:477-481.

Gulka, G., C. M. Gulka, and N. Watabe. 1982. Histopathological effects of diflubenzuron on the cirripede crustacean, *Balanus eburneus*. Archives of Environmental Contamination and Toxicology 11:11-16.

Hansen, S. R., and R. R. Garton. 1982. Ability of standard toxicity tests to predict the effects of the insecticide diflubenzuron on laboratory stream communities. Canadian Journal of Fisheries and Aquatic Sciences 39:1273-1288.

Ho, C. M., T. R. Hsu, J. Y. Wu, and C. H. Wang. 1987. Effect of dimilin, a chitin synthesis inhibitor, on the growth and development of larvae of *Aedes albopictus* Skuse. Chinese Journal of Entomology 7:131-141.

Horst, M. N. 1981. The biosynthesis of crustacean chitin by a microsomal enzyme from larval brine shrimp. Journal of Biological Chemistry 256: 1412-1419.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish and Wildlife Service Resource Publication 153.90 pp.

Hughes, P. B., and G. W. Levot. 1987. Simulation of flywaves to assess the ability of diflubenzuron to protect sheep against flystrike by *Lucilia cuprina*. Veterinary Parasitology 24:275-284.

Ivie, G. W. 1978. Fate of diflubenzuron in cattle and sheep. Journal of Agricultural and Food Chemistry 26:81-89.

Ivie, G. W., D. L. Bull, and J. A. Veech. 1980. Fate of diflubenzuron in water. Journal of Agricultural and Food Chemistry 28:330-337.

Ivie, G. W., and J. E. Wright. 1978. Fate of diflubenzuron in the stable fly and house fly. Journal of Agricultural and Food Chemistry 26:90-94.

Jenkins, V. K., R. R. Perry, A. E. Ahmed, and K. Ives. 1986. Role of metabolism in effects of diflubenzuron on growth of B 16 melanomas in mice. Investigational New Drugs 4:325-335.

Johnson, G. D., and M. S. Mulla. 1981. Chemical control of aquatic nuisance midges in residential-recreational lakes. Mosquito News 41:495-501.

Johnson, W. W., and M. T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Fish and Wildlife Service Resource Publication 137.98 pp.

Julin, A. M., and H. O. Sanders. 1978. Toxicity of the IGR, diflubenzuron, to freshwater invertebrates and fishes. Mosquito News 38:256-259.

Kalafatic, M., and D. Znidaric. 1987. Effects of dimiline upon the second generation of *Hydra vulgaris*. Acta Hydrochimica et Hydrobiologica 15:647-652.

Kelada, N. L., I. A. Gaaboub, and I. A. Rawash. 1980. A comparison of the juvenilizing effect of six juvenile hormone-like activity compounds on Egyptian *Culex pipiens* L. The Journal of Agricultural Science 95:203-212.

Kubena, L. F. 1981. The influence of diflubenzuron on several weight characteristics in growing male broiler and layer chickens. Poultry Science 60:1175-1182.

Kubena, L. F. 1982. The influence of diflubenzuron on several reproductive characteristics in male and female layer-breed chickens. Poultry Science 61:268-271.

Lee, B. M., and G. I. Scott. 1989. Acute toxicity of temephos, fenoxycarb, diflubenzuron, and methoprene and *Bacillus thuringiensis* var. *israelensis* to the mummichog (*Fundulus heteroclitus*). Bulletin of Environmental Contamination and Toxicology 48:827-832.

Levy, R., and T. W. Miller, Jr. 1978. Tolerance of the planarian *Dugesia dorotocephala* to high concentrations of pesticides and growth regulators. Entomophaga 23:31-34.

Macgregor, J. T., D. H. Gould, A. D. Mitchell, and G. P. Sterling. 1979. Mutagenicity tests of diflubenzuron in the micronucleus test in mice, the L5178Y mouse forward mutation assay, and the Ames *Salmonella* reverse mutation test. Mutation Research 66:45-53.

Machado, J., J. Coimbra, F. Castilho, and C. Sa. 1990. Effects of diflubenzuron on shell formation of the freshwater clam, *Anodonta cygnea*. Archives of Environmental Contamination and Toxicology 19:35-39.

Madder, D. J., and W. L. Lockhart. 1978. A preliminary study of the effects of diflubenzuron and methoprene on rainbow trout (*Salmo gairdneri* Richardson). Bulletin of Environmental Contamination and Toxicology 20:66-70.

Madder, D. J., and W. L. Lockhart. 1980. Studies on the dissipation of diflubenzuron and methoprene from shallow prairie pools. The Canadian Entomologist 112:173-177.

Martinat, P. J., V. Christman, R. J. Cooper, K. M. Dodge, R. C. Whitmore, G. Booth, and G. Seidel. 1987. Environmental fate of dimilin 25-W in a central Appalachian forest. Bulletin of Environmental Contamination and Toxicology 39: 142-149.

Martinat, P. J., C. C. Coffman, K. Dodge, R. J. Cooper, and R. C. Whitmore. 1988. Effect of diflubenzuron on the canopy arthropod community in a central Appalachian forest. Journal of Economic Entomology 81:261-267.

Martinez-Toledo, M. V., T.D.L. Rubia, J. Moreno, and J. Gonzalez-Lopez. 1988. Effect of diflubenzuron on *Azotobacter* nitrogen fixation in soil. Chemosphere 17:829-834.

Marx, J. L. 1977. Chitin synthesis inhibitors: new class of insecticides. Science 197:1170-1172.

Mayer, F. L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U.S. Environmental Protection Agency, Report 600/8-87/017. 274 pp.

Mayer, F. L., Jr., and M. R. Ellersieck. 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals. U.S. Fish and Wildlife Service Resource Publication 160. 579 pp.

McKague, A. B., and R. B. Pridmore. 1978. Toxicity of altosid and dimilin to juvenile rainbow trout and coho salmon. Bulletin of Environmental Contamination and Toxicology 20:167-169.

Metcalf, R. L., P. Y. Lu, and S. Bowlus. 1975. Degradation and environmental fate of l-(2,6-difluorobenzoyl)-3-(4-chlorophenyl) urea. Journal of Agricultural and Food Chemistry 23:359-364.

Miller, J. A., W. F. Chamberlain, and D. D. Oehler. 1985. Methods for control of the Angora goat biting louse. The Southwestern Entomologist 10:181-184.

Miller, R. W., H. C. Cecil, A. M. Carey, C. Corley, and C. A. Kiddy. 1979. Effects of feeding diflubenzuron to young male Holstein cattle. Bulletin of Environmental Contamination and Toxicology 23:482-486.

Miller, R. W., C., Corley, and K. R. Hill. 1975. Feeding TH 6040 to chickens: effect on larval house flies in manure and determination of residues in eggs. Journal of Economic Entomology 68:181-182.

Miller, R. W., C. Corley, D. D. Oehler, and L. G. Pickens. 1976. Feeding TH 6040 to cattle: residues in tissues and milk and breakdown in manure. Journal of Agricultural and Food Chemistry 24:687-688.

Mittal, P. K., and V. K. Kohli. 1988. The effect of diflubenzuron on the egg laying and vitellogenesis in female *Culex pipiens quinquefasciatus*. Research Bulletin of the Panjab University 39:93-100.

Miura, T., and R. M. Takahashi. 1974. Insect developmental inhibitors. Effects of candidate mosquito control agents on nontarget aquatic organisms. Environmental Entomology 3:631-636.

Miura, T., and R. M. Takahashi. 1975. Effects of the IGR, TH6040, on nontarget organisms when used as a mosquito control agent. Mosquito News 35: 154-159.

Montgomery, M. T., N. A. Welschmeyer, and D. L. Kirchman. 1990. A simple assay for chitin: application to sediment trap samples from the subarctic Pacific. Marine Ecology Progress Series 64:301-308.

Mulla, M. S., G. Majori, and H. A. Darwazeh. 1975. Effects of the insect growth regulator Dimilin or TH 6040 on mosquitos and some nontarget organisms. Mosquito News 35:211-216.

Muzzarelli, R. 1986. Chitin synthesis inhibitors: effects on insects and on nontarget organisms. CRC Critical Reviews in Environmental Control 16: 141-146.

Nation, J. L., F. A. Robinson, S. J. Yu, and A. B. Bolten. 1986. Influence upon honeybees of chronic exposure to very low levels of selected insecticides in their diet. Journal of Apicultural Research 25:170-177.

Nebeker, A. V., P. McKinney, and M. A. Cairns. 1983. Acute and chronic effects of diflubenzuron (dimilin) on freshwater fish and invertebrates. Environmental Toxicology and Chemistry 2:329-336.

Nimmo, D. R., T. L. Hamaker, E. Matthews, and J. C. Moore. 1981. An overview of the acute and chronic effects of first and second generation pesticides on an estuarine mysid. Pages 3-19 *in* F. J. Vernberg, A. Calabrese, F. P. Thurberg, and W. B. Vernberg, editors. Biological monitoring of marine pollutants. Academic Press, New York.

Nimmo, D. R., T. L. Hamaker, J. C. Moore, and C. A. Sommers. 1979. Effect of diflubenzuron on an estuarine crustacean. Bulletin of Environmental Contamination and Toxicology 22:767-770.

Nimmo, D. R., T. L. Hamaker, J. C. Moore, and R. A. Wood. 1980. Acute and chronic effects of dimilin on survival and reproduction of *Mysidopsis bahia*. Pages 366-379 *in* J. G. Eaton, P. R. Parrish, and A. C. Hendricks, editors. Aquatic toxicology. ASTM STP 707. American Society for Testing and Materials, Philadelphia, Pennsylvania.

Opdycke, J. C., and R. E. Menzer. 1984. Pharmacokinetics of diflubenzuron in two types of chickens. Journal of Toxicology and Environmental Health 13:721-733.

Opdycke, J. C., R. W. Miller, and R. E. Menzer. 1982a. Metabolism and fate of diflubenzuron in swine. Journal of Agricultural and Food Chemistry 30:1223-1227.

Opdycke, J. C., R. W. Miller, and R. E. Menzer. 1982b. In vivo and liver microsomal metabolism of diflubenzuron by two breeds of chickens. Journal of Agricultural and Food Chemistry 30: 1227-1233.

Pelsue, F. W. 1985. Histopathological effects of two insect chitin inhibitors in the alimentary canal of chironomid midges (Diptera: Chironomidae). Bulletin of the Society of Vector Ecologists 10:72-79.

Poplyk, J., editor. 1989. Diflubenzuron. Page C102 *in* Farm chemicals handbook '89. Meister Publishing Company, 37841 Euclid Ave., Willoughby, Ohio.

Quarles, J. M., J. O. Norman, and L. F. Kubena. 1980. Absence of transformation by diflubenzuron in a host-mediated transplacental carcinogen assay. Bulletin of Environmental Contamination and Toxicology 25:252-256.

Rao, D. R., and G. Paul. 1988. Growth regulatory activity of dimilin against *Mesocyclops thermocyclopoides*. Current Science 57:399-400.

Richmond, M. L., C. J. Henny, R. L. Floyd, R. W. Mannan, D. M. Finch, and L. R. DeWeese. 1979. Effects of sevin-4-oil, dimilin, and orthene on forest birds in northeastern Oregon. U.S. Department of Agriculture, Pacific Southwest Forest Range Experiment Station, Research Paper PSW-148. 19 pp.

Rodrigues, C. S., and N. K. Kaushik. 1986. Laboratory evaluation of the insect growth regulator diflubenzuron against black fly (Diptera: Simuliidae) larvae and its effects on nontarget stream invertebrates. The Canadian Entomologist 118: 549-558.

Satake, K. N., and M. Yasuno. 1987. The effects of diflubenzuron on invertebrates and fishes in a river. Japanese Journal of Sanitary Zoology 38:303-316.

Savitz, J. D. 1991. Toxic effects of the insecticide diflubenzuron (dimilin) on survival and development of the estuarine copepod *Eurytemora affinis*. M. S. thesis, University of Maryland, Solomons, Maryland. 92 pp.

Schaefer, C. H., A. E. Colwell, and E. F. Dupras, Jr. 1980. The occurrence of p-chlorophenylurea from the degradation of diflubenzuron in water and fish. Proceedings of the California Mosquito Control Association 48:84-89.

Schaefer, C. H., and E. F. Dupras, Jr. 1976. Factors affecting the stability of dimilin in water and the persistence of dimilin in field waters. Journal of Agricultural and Food Chemistry 24:733-739.

Schaefer, C. H., and E. F. Dupras, Jr. 1977. Residues of diflubenzuron [1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl) urea] in pasture soil, vegetation, and water following aerial applications. Journal of Agricultural and Food Chemistry 25: 1026-1030.

Schaefer, C. H., E. F. Dupras, Jr., R. J. Stewart, L. W. Davidson, and A. E. Colwell. 1979. The accumulation and elimination of diflubenzuron by fish. Bulletin of Environmental Contamination and Toxicology 21:249-254.

Schooley, D. A., and G. B. Quistad. 1979. Metabolism of insect growth regulators in aquatic organisms. Pages 161-176 *in* M.A.Q. Khan, J. J. Lech, and J. J. Menn, editors. Pesticide and xenobiotic metabolism in aquatic organisms. American Chemical Society, Symposium Series 99, Washington, D.C.

Scott, T. W., R. W. Miller, and F. W. Knapp. 1986. Field evaluation of diflubenzuron boluses with and without flucythrinate ear tags for control of horn flies, *Haematobia irritans* and face flies, *Musca autumnalis*, on pastured cattle. Journal of Agricultural Entomology 3: 105-113.

Smith, K. A., A. A. Grigarick, and M. J. Oraze. 1988. Field evaluations of diflubenzuron and triflumuron for control of the rice water weevil in California rice fields. Journal of Agricultural Entomology 5:121-126.

Soltani, N., A. Quennedey, J. P. Delbecque, and J. Delachambre. 1987. Diflubenzuron-induced alterations during in vitro development of *Tenebrio molitor* pupal integument. Archives of Insect Biochemistry and Physiology 5:201-209.

Steelman, C. D., J. E. Farlow, T. P. Breaud, and P. E. Schilling. 1975. Effects of growth regulators on *Psorophora columbiae* (Dyar and Knab) and non-target aquatic insect species in rice fields. Mosquito News 35:67-76.

Stoner, A., and W. T. Wilson. 1982. Diflubenzuron (dimilin) effect of long-term feeding of low doses in sugar-cake or sucrose syrup on honey bees in standard-size field colonies. American Bee Journal 122:579-582.

Sundaram, K. M. S., and R. Nott. 1989. Mobility of diflubenzuron in two types of forest soils. Journal of Environmental Science and Health B24:65-86.

Swift, M. C., K. W. Cummins, and R. A. Smucker. 1988a. Effects of dimilin on stream leaf-litter processing rates. Verhandlung Internationale Vereinigung fur Theoretische und Angewandte Limnologie 23:1255-1260.

Swift, M. C., R. A. Smucker, and K. W. Cummins. 1988b. Effects of dimilin on freshwater litter decomposition. Environmental Toxicology and Chemistry 7:161-166.

Tester, P. A., and J. D. Costlow, Jr. 1981. Effect of insect growth regulator dimilin (TH 6040) on larval development of two estuarine crabs. Marine Biology 50:29-36. TH 6040) on fecundity and egg viability of the marine copepod *Acartia tonsa*. Marine Ecology Progress Series 5:297-302.

Touart, L. W., and K. R. Rao. 1987. Influence of diflubenzuron on survival, molting, and limb regeneration in the grass shrimp, *Palaemonetes pugio*. Pages 333-349 *in* W. B. Vernberg, A. Calabrese, F. P. Thurberg, and F. J. Vernberg, editors. Pollution physiology of estuarine organisms. University of South Carolina Press, Columbia.

Tsuji, H., and Y. Taneike. 1988. Insecticidal effect of diflubenzuron against cockroaches. Japanese Journal of Sanitary Zoology 39: 19-25.

Veech, J. A. 1978. The effect of diflubenzuron on the reproduction of free-living nematodes. Nematologica 24:312-320.

Webb, D. P., and K. B. Wildey. 1986. Evaluation of the larvicide diflubenzuron for the control of a multi-insecticide resistant strain of housefly (*Musca domestica*) on a UK pig farm. International Pest Control 28:64-66.

Webb, R. E., M. Shapiro, J. D. Podgwaite, R. C. Reardon, K. M. Tafman, I. Venables, and D. M. Kolodny-Hirsch. 1989. Effect of aerial spraying with dimilin, dipel, or gypehek on two natural enemies of the gypsy moth (Lepidoptera: Lymantriidae). Journal of Economic Entomology 82:1695-1701.

Weis, J. S., R. Cohen, and J. K. Kwiatkowsi. 1987. Effects of diflubenzuron on limb regeneration and molting in the fiddler crab, *Uca pugilator*. Aquatic Toxicology 10:279-290.

Weis, J. S., and A. Ma. 1987. Effects of the pesticide diflubenzuron on larval horseshoe crabs, *Limulus polyphemus*. Bulletin of Environmental Contamination and Toxicology 39:224-228.

Weis, J. S., and J. Perlmutter. 1987. Burrowing behavior by the fiddler crab *Uca pugilator*: inhibition by the insecticide diflubenzuron. Marine Ecology Progress Series 38:109-113.

White, P. F. 1986. Effects of bendiocarb and diflubenzuron on mushroom cropping. Annals of Applied Biology 108:11-20.

Willems, A.G.M., H. Overmars, P. Scherpenisse, N. D. Lange, and L. C. Post. 1980. Diflubenzuron: intestinal absorption and metabolism in the rat. Xenobiotica 10:103-112.

Wilson, J. E., R. B. Forward, Jr., and J. D. Costlow. 1985. Effects of embryonic exposure to sublethal concentrations of dimilin on the photobehavior of grass shrimp larvae. Pages 377-396 *in* F. J. Vernberg, F. P. Thurberg, S. Calabrese, and W. Vernberg, editors. Marine pollution and physiology: recent advances. University of South Carolina Press, Columbia, South Carolina.

Wilson, J. E. H., and J. D. Costlow. 1986. Comparative toxicity of two dimilin formulations to the grass shrimp, *Palaemonetes pugio*. Bulletin of Environmental Contamination and Toxicology 36:858-865.

Wilson, J. E. H., and J. D. Costlow. 1987. Acute toxicity of diflubenzuron (DFB) to various life stages of the grass shrimp, *Palaemonetes pugio*. Water, Air, and Soil Pollution 33:411-417.

Wilson, J. E. H., R. B. Forward, Jr., and J. D. Costlow. 1987. Delayed effects of diflubenzuron on the swimming and vertical distribution of *Palaemonetes pugio* larvae. Pages 351-371 *in* W. B. Vernberg, A. Calabrese, F. P. Thurberg, and F. J. Vernberg, editors. Pollution physiology of estuarine organisms. University of South Carolina Press, Columbia.

Young, M. F., L. D. Trombetta, and S. Carson. 1986. Effects of diflubenzuron on the mouse liver. Journal of Applied Toxicology 6:343-348.

Zaki, F. N., and M. A. Gesraha. 1987. Evaluation of zertel and diflubenzuron on biological aspects of the egg parasitoid, *Trichogramma evanescens* Westw. and the aphid lion *Chrysoperla carnea* Steph. Journal of Applied Entomology 104:63-69.

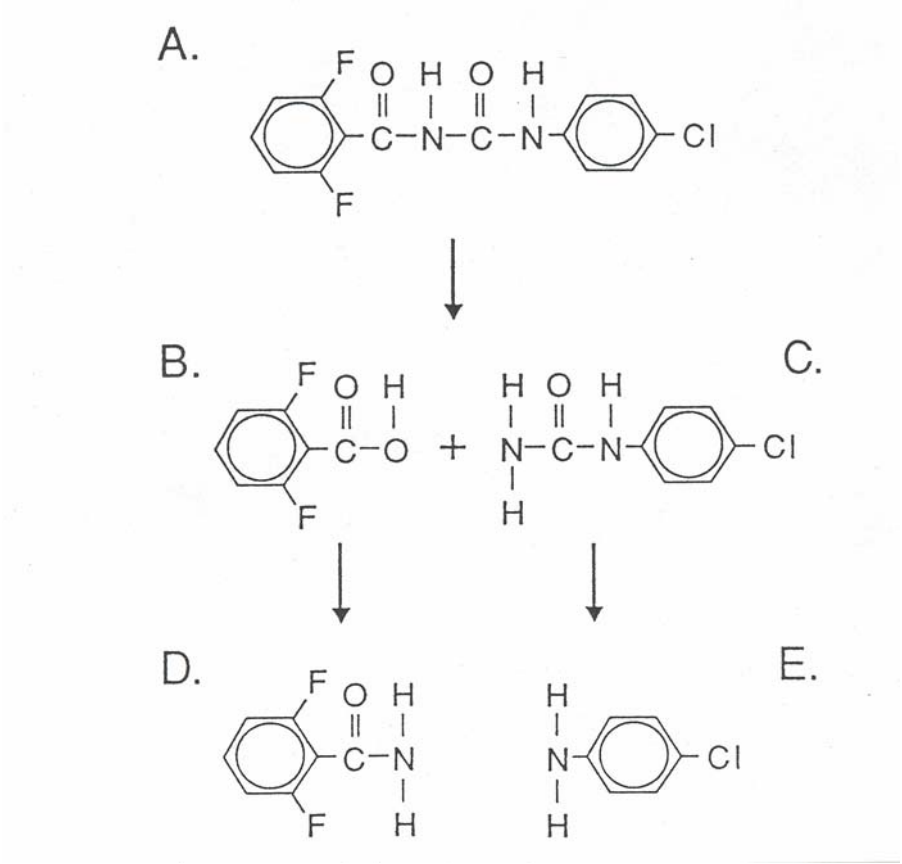


Figure. Generalized degradation pattern for diflubenzuron. Diflubenzuron (A) degrades initially to 2,6-difluorobenzoic acid (B) and 4- chlorophenylura (C). 2,6-difluorobenzoic acid degrades to 2,6-difluorbenamide (D); 4-chlorophenylurea degrades to 4-chloroaniline (E).

Biological Report 10
April 1993

Contaminant Hazard Reviews
Report 26

Zinc Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Department of the Interior
Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel Maryland 20708

TABLES

Zinc Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Department of the Interior
Fish and Wildlife Service
Patuxent Wildlife Research Center
Laurel Maryland 20708

Abstract. Ecological and toxicological aspects of zinc in the environment are reviewed with emphasis on natural resources. Subtopics include sources and uses; chemical and biochemical properties; carcinogenicity, mutagenicity, teratogenicity; background concentrations in biological and nonbiological compartments; effects of zinc deficiency; toxic and sublethal effects on terrestrial plants and invertebrates, aquatic organisms, birds, and mammals; and recommendations for the protection of sensitive resources.

The estimated world production of zinc is 7.1 million metric tons; the United States produces about 4% of the total and consumes 14%. Zinc is used primarily in the production of brass, noncorrosive alloys, and white pigments; in galvanization of iron and steel products; in agriculture as a fungicide and as a protective agent against soil zinc deficiency; and therapeutically in human medicine. Major sources of anthropogenic zinc in the environment include electroplaters, smelting and ore processors, mine drainage domestic and industrial sewage, combustion of solid wastes and fossil fuels, road surface runoff corrosion of zinc alloys and galvanized surfaces, and erosion of agricultural soils.

Zinc has its primary effect on zinc-dependent enzymes that regulate RNA and DNA. The pancreas and bone are primary targets in birds and mammals; the gill epithelium is a primary target site in fish. Dietary zinc absorption is highly variable in animals; in general, it increases with low body weight (BW) and low zinc status and decreases with excess calcium or phytate and by deficiency of pyridoxine or tryptophan. Low molecular weight proteins called metallothioneins play an important role in zinc homeostasis and in protection against zinc poisoning; zinc is a potent inducer of metallothioneins. Zinc interacts with many chemicals to produce altered patterns of accumulation, metabolism, and toxicity; some interactions are beneficial to the organism and others are not depending on the organism, its nutritional status, and other variables. Knowledge of these interactions is essential to the understanding of zinc toxicokinetics.

In natural waters, dissolved zinc speciates into the toxic aquo ion $[Zn(H_2O)_6]^{2+}$, other dissolved chemical species, and various inorganic and organic complexes zinc complexes are readily transported. Aquo ions and other toxic species are most harmful to aquatic life under conditions of low pH, low alkalinity, low dissolved oxygen, and elevated temperatures. Most of the zinc introduced into aquatic environments is eventually partitioned into the sediments. Zinc bioavailability from sediments is enhanced under conditions of high dissolved oxygen, low salinity low pH, and high levels of inorganic oxides and humic substances.

Zinc and its compounds induce testicular sarcomas in birds and rodents when injected directly into the testes; however zinc is not carcinogenic by any other route. Growth of animal tumors is stimulated by zinc and retarded by zinc deficiency. Under some conditions, excess zinc can suppress carcinoma growth, although the mechanisms are imperfectly understood. Organozinc compounds are effective mutagens when presented to susceptible cell populations in an appropriate form; the evidence for the mutagenic potential of inorganic zinc compounds is incomplete. Zinc deficiency can lead to chromosomal aberrations, but excess zinc was not mutagenic in the majority of tests. Excess zinc is teratogenic to frog and fish embryos, but conclusive evidence of teratogenicity in higher vertebrates is lacking. In mammals, excess zinc may protect against some teratogens. Zinc deficiency may exacerbate the teratogenic effects of known teratogens, especially in diabetic animals.

Background concentrations of zinc seldom exceed 40 µg/L in water 200 mg/kg in soils and sediment, or 0.5 $\mu g/m^3$ in air. Environments heavily contaminated by anthropogenic activities may contain up to 99 mg Zn/L in

water, 118 g/kg in sediments, 5 g/kg in soft, and 0.84 µg/m^3 in air. Zinc concentrations in field collections of plants and animals are extremely variable and difficult to interpret. Most authorities agree on six points: (1) elevated concentrations (i.e., >2 g Zn/kg fresh weight [FW]) are normally encountered in some species of oysters, scallops, barnacles, red and brown algae, and terrestrial arthropods; (2) concentrations are usually <700 mg Zn/kg dry weight (DW) tissue in fish, <210 mg Zn/kg DW tissue in birds, and <210 mg Zn/kg DW tissue in mammals; (3) concentrations are higher in animals and plants collected near zinc-contaminated sites than in the same species collected from more distant sites; (4) zinc content in tissue is not proportionate to that of the organism's immediate surroundings; (5) for individual species, zinc concentration varies with age, sex, season, tissue or organ, and other variables; and (6) many species contain zinc loadings far in excess of immediate needs, suggesting active zinc regulation.

The balance between excess and insufficient zinc is important. Zinc deficiency occurs in many species of plants and animals and has severe adverse effects on all stages of growth, development, reproduction, and survival. In humans, zinc deficiency is associated with delayed sexual maturation in adolescent males; poor growth in children; impaired growth of hair, skin, and bones; disrupted vitamin A metabolism; and abnormal taste acuity, hormone metabolism, and immune function. Severe zinc deficiency effects in mammals are usually prevented by diets containing >30 mg Zn/kg DW ration. Zinc deficiency effects are reported in aquatic organism at nominal concentrations between 0.65 and 6.5 µg Zn/L of medium and in piscine diets at <15 mg Zn/kg FW ration. Avian diets should contain >25 mg Zn/kg DW ration for prevention of zinc deficiency effects and <178 mg kg DW for prevention of marginal sublethal effects.

Sensitive terrestrial plants die when soil zinc levels exceed 100 mg/kg (oak and maple seedlings), and photosynthesis is inhibited in lichens at >178 mg Zn/kg DW whole plant. Sensitive terrestrial invertebrates have reduced survival when soil levels exceeded 470 mg Zn/kg (earthworms), reduced growth at >300 mg Zn/kg diet (slugs), and inhibited reproduction at >1,600 mg Zn/kg soil (woodlouse). The most sensitive aquatic species were adversely affected at nominal water concentrations between 10 and 25 µg/L, including representative species of plants, protozoans, sponges, molluscs, crustaceans, echinoderms, fish, and amphibians. Acute LC50 (96 h) values were between 32 and 40,930 µg/L for freshwater invertebrates, 66 and 40,900 µg/L for freshwater teleosts, 195 and >320,000 µg/L for marine invertebrates, and 191 and 38,000 µg/L for marine teleosts. Acute toxicity values were markedly affected by the age and nutrient status of the organism, by changes in the physicochemical regimen, and by interactions with other chemicals, especially copper salts. Pancreatic degeneration occurred in ducks fed diets containing 2,500 mg Zn/kg ration. Ducks died when fed diets containing 3,000 mg Zn/kg feed or when given single oral doses >742 mg Zn/kg BW. Domestic poultry are routinely fed extremely high dietary levels of 20 g Zn/kg ration as a commercial management technique to force the molting of laying hens and the subsequent improvement of long-term egg production that molting produces. However, poultry chicks died at 8 g Zn/kg diet, had reduced growth at 2-3 g Zn/kg diet, and experienced pancreas histopathology when fed selenium-deficient but zinc-adequate (100 mg Zn/kg) diets. Mammals are comparatively resistant to zinc, as judged by their tolerance of extended periods on diets containing >100 times the minimum daily zinc requirement. But excessive zinc through inhalation or ingestation harms mammalian survival, metabolism, and well-being. The most sensitive species of mammals were adversely affected at dietary concentrations of 90 to 300 mg Zn/kg, drinking water concentrations >300 mg Zn/L, daily intakes >9 mg Zn/kg BW, single oral doses >350 mg Zn/kg BW, and air concentrations >0.8 mg Zn/m^3. Humans are comparatively sensitive to excess zinc. Adverse effects occur in humans at >80 mg Zn/kg diet or at daily intakes >2.3 mg/kg BW.

Proposed criteria for protection of aquatic life include mean zinc concentrations of <47 to <59 µg/L in freshwater and <58 to <86 µg Zn/L in seawater. Results of recent studies, however, show significant adverse effects on a growing number of freshwater organisms in the range of 5 to 51 µg Zn/L and on saltwater biota between 9 and 50 µg Zn/L, suggesting that some downward modification in the proposed criteria is necessary.

Although tissue residues are not yet reliable indicators of zinc contamination, zinc poisoning usually occurs in birds when the liver or kidney contains >2.1 g Zn/kg DW and in mammals when concentrations exceed 274 mg Zn/kg DW in kidney, 465 mg Zn/kg DW in liver, or 752 mg Zn/kg DW in pancreas. The proposed air quality criterion for human heath protection is <5 mg Zn/m^3, but guinea pigs were more sensitive and adverse effects were evident at >0.8-4.0 mg/m^3.

Current research needs include the development of protocols to (1) separate, quantitate, and verify the different chemical species of zinc (2) identify natural from anthropogenic sources of zinc; (3) establish toxicity thresholds based on accumulation; (4) evaluate the significance of tissue concentrations in target organs as indicators of zinc stress; and (5) measure the long-term consequences of zinc interactions with other nutrients in animals of various age and nutrient status. (Eisler, R. 1993. Zinc hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. Fish and Wildlife Service Biological Report 10. 106 pp.).

Key words: Zinc, metals, toxicity, deficiency, criteria, residues, agriculture, nutrition, metallothionein, fish, invertebrates, birds, wildlife, livestock.

Zinc is an essential trace element for all living organisms. As a constituent of more than 200 metalloenzymes and other metabolic compounds, zinc assures stability of biological molecules such as DNA and of biological structures such as membranes and ribosomes (Vallee 1959; National Academy of Sciences [NAS] 1979; Casey and Hambidge 1980; Mason et al. 1988; Llobet et al. 1988b; Leonard and Gerber 1989). Plants do not grow well in zinc-depleted soils, and deficiency has resulted in large losses of citrus in California and pecans in Texas (Vallee 1959). Clinical manifestations of zinc deficiency in animals include growth retardation, testicular atrophy, skin changes, and poor appetite (Prasad 1979). The ubiquity of zinc in the environment would seem to make human deficiencies unlikely; however, reports of zinc-associated dwarfism and hypogonadism in adolescent males are now confirmed (Casey and Hambidge 1980) and reflect the fact that much of their dietary zinc is not bioavailable. Zinc deficiency was a major factor in the syndrome of nutritional dwarfism in adolescent males from rural areas of Iran and Egypt in 1961--about 3% of the population in these areas was affected--and a similar syndrome was found in Turkey, Tunisia, Morocco, Portugal, and Panama (Casey and Hambidge 1980). The use of unleavened bread as a major staple food contributed to severe zinc deficiency in the Middle East. Unleavened bread may contain adequate amounts of zinc for nutrition, and intakes may exceed recommended allowances by a wide margin; however, zinc is largely unavailable for absorption because of the high levels of fiber and phytic acid esters in unleavened bread (Casey and Hambidge 1980). Marginal deficiency of zinc in hums is probably widespread and common throughout the world, including the United States (Prasad 1979). Dietary zinc replacement usually reverses the pathologic events of zinc depletion in humans and animals (NAS 1979). But zinc repletion seems to be of little value in rat offspring with congenital malfunctions or behavioral abnormalities associated with zinc depletion (NAS 1979).

Zinc poisoning has been documented in dogs, cats, ferrets, birds, cattle, sheep, and horses, usually as a result of ingesting galvanized metal objects, certain paints and fertilizers, zinc-containing coins, and skin and sunblock preparations containing zinc oxide (Wentink et al. 1985; Ogden et al. 1988; Lu and Combs 1988a; Binnerts 1989; Robinette 1990). Signs of acute poisoning include anorexia, depression, enteritis, diarrhea, decreased milk yield, excessive eating and drinking and, in severe cases, convulsions and death (Ogden et al. 1988). Emissions from zinc smelters at Palmerton, Pennsylvania, destroyed wildlife habitat; reduced prey abundance; poisoned deer, songbirds, and shrews; and eliminated terrestrial amphibians from the mountainside at Lehigh Gap (Beyer et al. 1985; Sileo and Beyer 1985; Beyer 1988). Aquatic populations are frequently decimated in zinc-polluted waters (Solbe and Flook 1975; Everall et al. 1989b). Zinc in the aquatic environment is of particular importance because the gills of fish are physically damaged by high concentrations of zinc (NAS 1979).

Zinc toxicosis in humans is not a common medical problem, although it may appear in some metal workers and others under special conditions (NAS 1979). Industrial processes such as welding, smelting, or fabrication of molten metals can produce ultrafine metal oxides at harmful concentrations. Inhalation of these metal oxides, including oxides of zinc, causes the industrial malady known as metal fume fever (Lain et al. 1985; Lu and Combs 1988a; Llobet et al. 1988b). Symptoms occur several hours after exposure and include fever, chills, perspiration, tachycardia, dyspnea, and chest pains. Recovery is normally complete within 24 h, but susceptible workers can have persistant pulmonary impairment for several days after exposure (Lain et al. 1985). Most reports of human zinc intoxication have been in response to food poisoning from lengthy storage of acidic foods or beverages in galvanized containers (Llobet et al. 1988b; Fosmire 1990).

Historically zinc has been used by humans for industrial, ornamental, or utilitarian purposes for nearly 2,000 years and may have been used as an ointment to treat skin lesions by the ancient Egyptians and other Mediterraneans (NAS 1979). In biblical times, the Romans were known to have produced brass by mixing copper with a zinc ore (Elinder 1986). In its isolated form, zinc was not recognized until the 15th century when smelting occurred accidentally (NAS 1979). The Chinese probably were the first to extract zinc metal, although its first description in 1597 by an occidental traveler, Liborius, related that the process was observed in India (Vallee 1959). Commercial smelting began in the 18th century when it was realized that zinc could be obtained from the calamine ore used to make brass; no reports of zinc toxicosis in any form were recorded from these early accounts (NAS 1979). The first documented use of orally administered zinc was in 1826 to treat discharges from various body orifices (NAS 1979). Zinc was recognized as an essential nutrient for plants and animals in 1869. Its occurrence in biological matter, for example, human liver, was first described in 1877 (Vallee 1959). In 1934, zinc was conclusively demonstrated to be essential to normal growth and development in animals (Prasad 1979).

Zinc composes 0.004% of the earth's crust and is 25th in order of abundance of the elements (Vallee 1959). Uses of zinc include the production of noncorrosive alloys, galvanizing steel and iron products, and the therapeutic treatment of zinc deficiency (Elinder 1986). Zinc is found in coal and many manufactured products such as motor oils, lubricants, tires, and fuel oils (NAS 1979).

Ecological and toxicological aspects of zinc in the environment have been reviewed by many authorities, including Vallee (1959), Skidmore (1964), NAS (1979), Prasad (1979, 1980), U.S. Environmental Protection Agency [EPA] (1980, 1987), Nriagu (1980), Weatherley et al. (1980), Eisler (1981), Spear (1981), Apgar (1985), Elinder (1986), Vymazal (1986), Greger (1989), U.S. Public Health Service [PHS] (1989), and Sorensen (1991).

This report is part of a series of synoptic reviews on hazards of selected chemicals to plants and animals with emphasis on fishery and wildlife resources. It was prepared in response to requests for information on zinc from environmental specialists of the U.S. Fish and Wildlife Service.

Sources and Uses

World production of zinc increased from 0.5 million metric tens in 1900 to 6.1 million metric tons in 1978 (Elinder 1986) and 7.1 million metric tons in 1987 (PHS 1989). The principal ores of zinc are sulfides, such as sphalerite and wurtzite (Elinder 1986). The major world producers include Canada, the former Soviet Union, and Japan--which collectively account for about half the production--and, secondly, the United States, Australasia, Mexico, and Peru (Weatherley et al. 1980; Elinder 1986). Zinc is now available as ingots, lumps, sheets, wire, shot, strips, granules, and powder (PHS 1989). The United States produced 240,000 metric tons of zinc in 1987--mostly from Tennessee, Mississippi, and New York but also from 16 other states--and imported an additional 774,000 metric tons, thus consuming 14% of the world zinc production while producing 3.4% (PHS 1989).

Zinc is mainly used in the production of noncorrosive alloys and brass and in galvanizing steel and iron products. Zinc undergoes oxidation on the surface, thus protecting the underlying metal from degradation. Galvanized products are widely used in construction materials, automobile parts, and household appliances (Elinder 1986). Zinc oxide is used to form white pigments in rubber processing and to coat photocopy paper (EPA 1987; PHS 1989). Zinc sulfate is used as a cooperative agent in fungicides and as a protective agent against zinc deficiency in soils. When incorporated with copper compounds or arsenic-lead wettable powders and applied by spraying, it can minimize the toxic effects of these metals on fruits such as plums, apples, and peaches; in Japan alone, about 250 metric tons of zinc sulfate is sprayed in fields each year (Maita et al. 1981). Zinc is used therapeutically in human medicine in the treatment of zinc deficiency, various skin diseases, wound healing, and to reduce pain in sickle cell anemia patients (Prasad 1979; Spear 1981; EPA 1987; Warner et al. 1988).

Zinc is discharged into the global environment at an estimated yearly rate of 8.8 million metric tons; 96% of the total is a result of human activities (Leonard and Gerber 1989). Major sources of anthropogenic zinc discharges to the environment include electroplaters, smelting and ore processors, drainage from active and inactive mining operations, domestic and industrial sewage, combustion of fossil fuels and solid wastes, road surface runoff, corrosion of zinc alloys and galvanized surfaces, and erosion of agricultural soils (Weatherley et al. 1980; Spear 1981; Mirenda 1986; Llobet et al. 1988a; Buhl and Hamilton 1990). During smelting, large amounts of zinc are emitted into the atmosphere. In the United States alone during 1969, about 50,000 metric

tons of zinc were discharged into the atmosphere during smelting operations (Elinder 1986). Another 20,000 metric tons are discharged annually into U.S. estuaries (Table 1). Zinc is also dispersed from corroded galvanized electrical transmission towers for at least 10 km by runoff and by wind-driven spray and water droplets from the towers (Jones and Burgess 1984). Discharges from placer mining activities usually contain 75-165 µg Zn/L, sometimes up to 882 µg Zn/L in active mines, and these concentrations may represent acute hazards to salmonids in areas downstream of placer mine effluents (Buhl and Hamilton 1990). In Maine, galvanized culverts significantly increased zinc concentrations in stream waters, particularly in newer culverts. Zinc concentrations in culverts were highest during elevated temperatures and low flow; levels of zinc sometimes exceeded the avoidance threshold (0.05 mg/L) of Atlantic salmon (*Salmo salar*); invertebrates seemed unaffected, except for a freshwater sponge, *Spongilla* sp. (Gregory and Trial 1975). Zinc sources implicated in livestock poisonings include galvanized iron wire and troughs and zinc-containing fertilizers and fungicides (Allen et al. 1983; Reece et al. 1986). Zinc toxicosis in humans has been reported from consumption of milk stored in galvanized vessels and from food contaminated with particles of zinc from a zinc pigment plant (Zee et al. 1985). Zinc toxicity is discussed later in greater detail.

Table 1. Estimated annual zinc inputs to U.S. coastal marine ecosystems; study area comprised 116,000 km^2 (Young et al 1980).

Source	Metric tons per year
Rivers	5,950
Atmosphere	4,300
Barged wastes	3,490
Storm channels	3,060
Municipal wastewater	2,500
Direct industrial discharges	710
Vessel protection	360
Dredging release	10
Thermal discharges	2
Groundwater	1
Total	20,383

Chemical and Biochemical Properties

General

Most of the zinc introduced into aquatic environments eventually is partitioned into the sediments. Zinc release from sediments is enhanced under conditions of high dissolved oxygen, low salinity and low pH. Dissolved zinc usually consists of the toxic aquo ion ($Zn(H_2O)_6^{2+}$) and various organic and inorganic complexes. Aquo ions and other toxic species have their greatest effects on aquatic organisms under conditions of comparatively low pH, low alkalinity, low dissolved oxygen, and elevated temperatures.

Zinc has its primary metabolic effect on zinc-dependent enzymes that regulate RNA and DNA. Low molecular weight proteins, metallothioneins, play an important role in zinc homeostasis and in protection against zinc poisoning in animals; zinc is a potent inducer of metallothioneins. The pancreas and bone seem to be primary targets of zinc intoxication in birds and mammals; gill epithelium is the primary target site in fish.

Effects of excess zinc on natural resources are modified by numerous variables, especially by interactions with other chemicals. Interactions frequently produce radically altered patterns of accumulation, metabolism, and toxicity some of which are beneficial to the organism whereas others are harmful.

Chemical Properties

Zinc is a bluish-white metal that dissolves readfly in strong acids. In nature, it occurs as a sulfide, oxide, or carbonate. In solution, it is divalent and can form hydrated Zn^{2+} cations in acids, and zincated anions--probably $Zn(OH)_4^{-2}$-- in strong bases (EPA 1980, 1987). Zinc dust and powder are sold commercially under a variety of trade names: Asarco, Blue powder, CI 77949, CI pigment metal 6, Emanay zinc dust, granular zinc, JASAD Merrillite, L15, and PASCO (PHS 1989). Selected physical and chemical properties of zinc, zinc chloride, and zinc sulfate are listed in Table 2.

Because zinc ligands are soluble in neutral and acidic solutions, zinc is readily transported in most natural waters (EPA 1980, 1987). But zinc oxide, the compound most commonly used in industry, has a low solubility in most solvents (Elinder 1986). Zinc mobility in aquatic ecosystems is a function of the composition of suspended and bed sediments, dissolved and particulate iron and manganese concentrations, pH, salinity, concentrations of complexing ligands, and the concentration of zinc (EPA 1980). In freshwater, zinc is most soluble at low pH and low alkalinity: 10 mg Zn/L of solution at pH 6 that declines to 6.5 mg Zn/L at pH 7, 0.65 mg Zn/L at pH 8, and 0.01 mg/L at pH 9 (Spear 1981). Dissolved zinc rarely exceeds 40 µg/L in Canadian rivers and lakes; higher concentrations are usually associated with zinc-enriched ore deposits and anthropogenic activities. Marine waters usually contain <10 µg Zn/L, most adhering to suspended solids; however, saturated seawater may contain 1.2 - 2.5 mg Zn/L (Spear 1981).

In water the free zinc ion is thought to coordinate with six water molecules to form the octahedral aquo ion $(Zn(H_2O)_6)^{2+}$ in the absence of other complexing or adsorbing agents (Spear 1981). In freshwater zinc exists almost exclusively as the aquo ion at pH >4 and <7 (Campbell and Stokes 1985). In freshwater at pH 6, the dominant forms of dissolved zinc are the free ion (98%) and zinc sulfate (2%); at pH 9 the dominant forms are the monohydroxide ion (78%), zinc carbonate (16%), and the free ion (6%; EPA 1987). In typical river waters, 90% of the zinc is present as aquo ion and the remainder consists of $ZnHCO_3^+$, $ZnCO_3$, and $ZnSO_4$ (Spear 1981).

Table 2. Some properties of zinc, zinc chloride, and zinc sulfate (PHS 1989).

Property	Zinc	Zinc chloride	Zinc sulfate
Formula	Zn	$ZnC1_2$	$ZnSO_4$
CAS number	7440-66-6	7646-85-7	7733-02-0
Molecular weight	65.38	136.29	161.44
Melting point, ° C	419.5	290	Decomposes at 600
Boiling point, °C	908	732	
Density	7.14	2.907	3.54
Physical state	Bluish-white lustrous solid	Solid white granules	Colorless solid
Solubility	Insoluble in water, soluble in acetic acid and alkali	61.4 g/L water, 769 g/L alcohol, 500 g/L glycerol	Soluble in water, slightly soluble in alcohol

Zinc bioavailability and toxicity to aquatic organisms are highest under conditions of low pH, low alkalinity, low dissolved oxygen, and elevated temperatures (Weatherley et al. 1980). Soluble chemical species of zinc are the most bioavailable and most toxic (Spear 1981). The aquo ion predominates over other dissolved species and is suspected of being most toxic; however, aquo ion concentrations decrease under conditions of high

alkalinity, at pH >7.5, and increasing salinity (Spear 1981). Under conditions of high alkalinity and pH 6.5, the most abundant species are $ZnHCO_3^+$, Zn^{2+}, and $ZnCO_3$; at low alkalinity and an elevated pH 8.0, the descending order of abundance was Zn^{2+}, $ZnCO_3$, zinc humic acid, $ZnOH^+$, and $ZnHCO_3^+$ (Spear 1981). Water hardness is the principal modifier of acute zinc toxicity. Increased alkalinity or water hardness decreases toxicity to freshwater organism when all zinc is dissolved; this effect is associated with decreased concentration of aquo ions and is heightened by increased pH. Increased water hardness at pH <8.5 when zinc is in suspension increases toxicity associated with increased suspended $ZnCO_3$. Increased water hardness at pH >8.5 when zinc is in suspension decreases toxicity and increases suspended $Zn(OH)_2$. Suspended zinc carbonate may also be toxic, although its toxicity decreases under conditions suitable to zinc hydroxide formations; suspended $Zn(OH)_2$ is relatively nontoxic. Thus, $ZnCO_3$ composes <1% of the dissolved zinc at low pH and low alkalinity but is the predominant chemical species at high pH and high alkalinity. Organozinc complexes are not stable and under reducing conditions may dissociate, liberating Zn^{2+} (Spear 1981).

In seawater zinc exists in a dissolved state, as a solid precipitate, or adsorbed to particle surfaces. Soluable zinc in seawater exists as uncomplexed free (hydrated) ions, as inorganic complexes (the primary form in the open sea), or as organic complexes (Young et al. 1980). In seawater at pH 8.1, the dominant species of soluble zinc are zinc hydroxide (62%), the free ion (17%), the monochloride ion (6.4%), and zinc carbonate (5.8%). At pH 7, the percentage of dissolved zinc present as the free ion increases to 50% (EPA 1987). In the presence of dissolved organic materials, most of the dissolved zinc is present as organozinc complexes (EPA 1987). In estuaries and other marine environments, the relative abundance of zinc species changes with increasing salinity. At low salinities, $ZnSO_4$ and $ZnC1^+$ predominate; at higher salinities, the aquo ion predominates (Spear 1981). But as salinity decreases, the concentration of free zinc ion increases and the concentration of zinc-chloro complexes decreases, resulting in increased bioavailability of the free metal ion and increased bioconcentration by resident organisms (Nugegoda and Rainbow 1989b).

In solution, zinc is adsorbed by organic agents such as humic materials and biogenic structures (i.e., cell walls of plankton) and by inorganic adsorbing agents such as mineral particles, clays, and hydrous oxides of manganese, iron, and silicon (Spear 1981). Particulate materials in the medium may contain as little as 2% and as much as 100% of the total zinc (Sprague 1986). Formation of zinc-ligand complexes increases the solubility of zinc and probably increases the tendency for zinc to be adsorbed (EPA 1980). Sorption to particulates was lower at higher salinities because of displacement of sorbed zinc ions by alkali and alkaline earth cations (EPA 1987). Increased pH increases zinc sorption to particulates and seems to be independent of water salinity or hardhess (EPA 1987).

Most of the zinc introduced into aquatic environments is sorbed onto hydrous iron and manganese oxides, clay minerals, and organic materials and eventually is partitioned into the sediments (EPA 1987). Zinc is present in sediments as precipitated zinc hydroxide, ferric and manganic oxyhydroxide precipitates, insoluble organic complexes, insoluble sulfides, and other forms. As the sediments change from a reduced to an oxidized state, soluble zinc is mobilized and released however, the bioavailability of different forms of sediment zinc varies substantially and the mechanisms of transfer are poorly understood (EPA 1987). Sorption to sediments was complete at pH >7, but was negligible at pH <6 (EPA 1987). Zinc is dissolved from sediments at low salinities because of displacement of adsorbed zinc ions by alkali and alkaline earth cations that are abundant in brackish waters (EPA 1980). Sulfide precipitation in sediments is an important control of zinc mobility in reducing environment; precipitation of the hydroxide, carbonate, or sulfate may occur when zinc is present in high concentrations (EPA 1980).

Extractable concentrations of sediment-bound zinc positively correlated with zinc concentrations in deposit feeding clams (Luoma and Bryan 1979). Availability of sediment zinc to bivalve molluscs was higher at increased sediment concentrations of amorphous inorganic oxides or humic substances and lower at increased concentrations of organic carbon and ammonium acetatemanganese. Zinc uptake by euryhaline organisms was enhanced at low water salinity (Luoma and Bryan 1979).

Metabolism

Zinc is ubiquitous in the tissues of plants and animals (Rosser and George 1986) and is essential for normal growth, reproduction, and wound healing (Prasad 1979; Stahl et al. 1989a). More than 200 different enzymes require zinc for maximum catalytic activity, including carbonic anhydrase, alkaline phosphatase, alcohol dehydrogenase, acid phosphatase, lactic dehydrogenase, carboxypeptidase, and superoxide dismutase (Prasad 1979, 1980; Casey and Hambidge 1980; Rosser and George 1986; Blesbois and Mauger 1989; Thompson et al. 1989). Zinc has its primary effect on zinc-dependent enzymes that regulate the biosynthesis and catabolic rate of RNA and DNA (Prasad 1979; Casey and Hambidge 1980; Gipouloux et al. 1986; Sternlieb 1988). Zinc exerts a protective effect on liver by inhibiting lipid peroxidation and stabilizing lysosomal membranes (Sternlieb 1988); aids neurotransmission in the brain of fish, birds, reptiles, and mammals (Smeets et al. 1989); prolongs muscular contractions; increases oxygen affinity of myoglobin; is necessary for the growth and differentiation of muscle fiber types (Rosser and George 1986); increases numbers and birthweights of lambs of zinc-supplemented ewes; is essential for wound healing in most studied organisms (Ireland 1986); and is used therapeutically in treating patients with skin diseases, zinc deficiency and other symptoms (Mooradian et al. 1988; Sternlieb 1988).

Zinc enters the gastrointestinal tract as a component of low molecular weight proteins secreted by the salivary glands, intestinal mucosa, pancreas, and liver (Goyer 1986). Usually, only dissolved zinc is sorbed or bound. But zinc dissolution probably occurs in the alimentary tract of animals after ingestion of particulates containing undissolved zinc (EPA 1987). After ingestion, zinc is absorbed across several physiologically active membranes: gut mucosa, alveocapillary membranes, and tissue and organ membranes. The exact transport mechanism are unknown but may be associated with formation of a tetrahedral quadredentate ligand with a small organic molecule (NAS 1979). Some of the zinc taken up by the intestinal epithelial cells is rapidly transferred to the portal plasma where it associates with albumin, 2 macroglobulin, and amino acids; about 67% of the zinc in plasma is bound to albumin and about 3% is stored in the liver (Sternlieb 1988). Soluble organozinc complexes are passively absorbed across the plasma membrane of the mucosa of the intestinal villi; the soluble, nondiffusable complexes are transported in the intestinal products and excreted in feces (NAS 1979). Zinc loss from urine and sweat is usually small (Casey and Hambidge 1980). In a normal human adult about 2 g zinc is filtered by the kidneys daily and about 0.3-0.6 mg is actually excreted each day (Goyer 1986). Zinc homeostasis in rats, unlike in most mammals, is maintained by zinc secretion from the intestines rather than by regulation of zinc absorption (Elinder 1986). Initial uptake of zinc from the rat gastrointestinal tract involves binding to albumin and transport of the zinc-albumin complex from the intestines to the liver (Hoadley and Cousins 1988).

Foods rich in zinc include red meat, milk, gelatin, egg yolks, shellfish, liver, whole grain cereals, lentils, peas, beans, and rice (Sternlieb 1988). About 20-30% of zinc in the diet is absorbed, but this is highly variable and ranges from <10% to >90% (Prasad 1979; Casey and Hambidge 1980; Elinder 1986). Increased zinc absorption, for example, was associated with low body weight (BW), poor zinc status, and various prostaglandins; decreased absorption was caused by excess dietary calcium or phytate and by a deficiency of pyridoxine or tryptophan (Elinder 1986; Goyer 1986). The half-time persistence of zinc in most mammalian tissues is between 100 and 500 days; it is longer in bone and muscle and shorter in the liver (Elinder 1986).

Metallothioneins play an important role in metal homeostasis and in protection against heavy metal toxicity in vertebrates and invertebrates (Engel 1987; Overnell et al. 1987a; Andersen et al. 1989; Olsson et al. 1989; Richards 1989b; Eriksen et al. 1990). Metallothioneins are cysteine-rich (>20%), low (about 6,000) molecular weight proteins with a high affinity for copper, silver, gold, zinc, copper, and mercury. These heat-stable, metal-binding proteins are in all vertebrate tissues and are readily inducible by a variety of agents to which they bind through thiolate linkages. Zinc is a potent inducer of metallothioneins, and a redistribution of zinc from enzymes to metallothioneins is one way to maintain low intracellular zinc concentrations. Metallothioneins also serve as temporary storage proteins for zinc and other metals during early development and may function by maintaining the pool of available zinc at an appropriate concentration. Metallothioneins are quite similar among organisms, that is, all metallothioneins are small proteins of molecular weight 6,000-10,000, rich in sulfur and cysteine, and lack aromatic amino acids (Sprague 1986). Metallothioneins isolated from cattle, sheep, horses, pigs, and other livestock contain 61 amino acids; thioneine, the metal-free protein, is a single chain polypeptide with a molecular weight of about 6,000 (Richards 1989b). Chicken thioneine consists of 63 amino acids, including histidine, an

amino acid not present in mammalian metallothioneins. The unusually high cysteine content enables metallothioneins to selectively bind up to 7 zinc and 12 copper atoms per mole of protein (Richards 1989a).

Metallothioneins are involved in zinc homeostasis in the chick, rat, and calf. When zinc is present at high dietary concentrations, a temporary zinc storage protein aids in counteracting zinc toxicity (Oh et al. 1979). Zinc absorption in mice is directly proportional to intestinal metallothionein levels and implies a significant role of metallothionein in zinc absorption (Starcher et al. 1980). Chick embryo hepatic metallothionein is highly responsive to exogenous zinc introduced into the yolk and increases in a dose-dependent manner; a similar pattern is evident in turkey development (Fleet and McCormick 1988). Zinc protects against subsequent exposure to zinc insult, and protection is believed to be mediated by metallothioneins (Woodall et al. 1988). For example, preexposure of South African clawed frog (*Xenopus laevis*) tadpoles to 5 mg $ZnSO_4$ ($7H_2O$)/L for 96 h resulted in no deaths during subsequent exposure to 15 mg Zn/L for 90 h but in 45% deaths in the nontreated group; at 20 mg Zn/L, 15% died in the pretreated group versus 50% in the nontreated group (Woodall et al. 1988). Metallothioneins are an important factor in zinc regulation during the period of exogenous vitellogenesis in rainbow trout (*Oncorhynchus mykiss*). In female rainbow trout, for example, metallothioneins maintain homeostasis of hepatic zinc during egg formation (Olsson et al. 1989). In plaice (*Pleuronectes platessa*), a marine fish, intraperitoneal injection of zinc raised hepatic metallothionein-ike species by a factor of 15; metallothionein levels remained elevated for the next 4 weeks (Overnell et al. 1987a).

In marine molluscs and crustaceans, excess zinc is usually sequestered by metal-binding proteins and subsequently transported to storage or detoxification sites; soluble proteins and amino acids may contain 20-70% zinc (Sprague 1986). Metallothioneins are actively involved in zinc regulation during normal growth processes in the blue crab (*Callinectes sapidus*), as judged by a decrease in zinc content in the hemolymph and the digestive gland during molting (Engel 1987).

Elevated metallothionein levels are not necessarily indicative of heavy metal insult. Starcher et al. (1980) show that liver metallothionein levels in mice are elevated after acute stress or starvation and that this effect is blocked by actinomycin D, a protein synthesis inhibitor. It is further emphasized that not all zinc-binding proteins are metallothioneins (Webb et al. 1985; Andersen et al. 1989; Richards 1989a; Eriksen et al. 1990). Low molecular weight metal-binding proteins---not metallothioneins--were induced in snails and polychaete annelids in metals-contaminated environments (Andersen et al. 1989). A high molecular weight protein fraction was detected in the plasma of laying turkey (*Meleagris gallopavo*) hens that bound significant amounts of zinc and that coeluted with vitellogenin; vitellogenin, a metalloprotein, from laying hens contained 0.54 mg Zn/kg protein (Richards 1989a). In rock oysters (*Saccostrea cucullata*) collected near an iron-ore shipping terminal, some of the tissue zinc was bound to a high molecular weight (around 550,000), iron-binding protein called ferritin (Webb et al. 1985). Ferritin accounts for about 40% of the protein-bound zinc in rock oysters and most probably in other bivalves containing elevated tissue levels of zinc (Webb et al. 1985); however, this requires verification. In four species of sediment-feeding marine polychaete annelids, zinc was mainly associated with high molecular weight proteins, suggesting that metallothionein-like proteins may not be satisfactory for monitoring purposes and that other cytosolic components should be studied (Eriksen et al. 1990).

High zinc levels induce copper deficiency in rats and interfere with metabolism of calcium and iron (Goyer 1986). Excess zinc interferes with normal metabolism of the pancreas, bone, gall bladder and kidney in mammals and gill in fish. The pancreas is a target organ for zinc toxicity in birds and mammals. Pancreatic alterations are documented from experimentally produced zinc toxicosis in cats, sheep, dogs, calves, chickens, and ducklings and naturally in sheep and calves. Pancreatic changes were limited to acinar cells, specifically cytoplasmic vacuolation, cellular atrophy, and eventually cell death (Lu and Combs 1988a; Kazacos and Van Vleet 1989). Excess zinc may cause stimulation of bone resorption and inhibition of bone formation in chicks, dogs, monkeys, and rats (Kaji et al. 1988). By preferentially accumulating in bone, zinc induces osteomalacia--a softening of the bone caused by deficiency of calcium, phosphorus, and other minerals (Kaji et al. 1988). Zinc plays a role in bone metabolism of aging rats (Yamaguchi et al. 1989b). Normally, the femoral zinc diaphysis content in rats increases from 50 to 150 mg/kg fresh weight (FW) during the first 3 weeks of life and remains constant thereafter. Oral administration of zinc (5-20 mg/kg BW daily for 3-day-old to 28-week-old rats) increased alkaline phosphatase activity and calcium content in the femur and delayed bone deterioration in aging rats (Yamaguchi et al. 1989b). Its high affinity for electrons causes zinc to bind covalently to proteins, mostly at imidazole and cysteine residues. In the mud puppy (*Necturus maculosus*), zinc blocks apical membrane anion exchange in gallbladder epithelium and blocks chloride channels in nerve and muscle cells.

The slow onset and reversal of the effects suggest a covalent modification of the exchanger or an effect requiring Zn^{2+} transport to the cell interior (Kitchens et al. 1990).

Zinc toxicity to aquatic organisms is dependent on the physical and chemical forms of zinc, the toxicity of each form, and the degree of interconversion among the various forms. Aquatic plants and fish are relatively unaffected by suspended zinc, but many aquatic invertebrates and some fish may be adversely affected from ingesting enough zinc-containing particulates (EPA 1987). Zinc toxicosis affects freshwater fish by destruction of gill epithelium and consequent tissue hypoxia. Signs of acute zinc toxicosis in freshwater fish includes osmoregulatory failure, acidosis and low oxygen tensions in arterial blood, and disrupted gas exchange at the gill surface and at internal tissue sites (Spear 1981). Zinc exerts a critical influence on mammalian and piscine immune systems (Ghanmi et al. 1989). Lymphocytes from the pronephros of common carp (*Cyprinus carpio*) were transformed by various mitogenetic agents; zinc added to lymphocyte cultures enhanced thymidine incorporation and inhibited the response of the mitogenetic agents--although Zn^{2+} itself was toxic at these concentrations (650 µgZn^{2+}/L; Ghanmi et al. 1989).

Interactions

Zinc interacts with numerous chemicals. The patterns of accumulation, metabolism, and toxicity from these interactions sometimes greatly differ from those produced by zinc alone. Recognition of these interactions is essential to the understanding of zinc kinetics in the environment.

Cadmium

Calcium-zinc interactions are typical because sometimes they act to the organism's advantage and sometimes not, depending on the organism, its nutritional status, and other variables.

Dietary cadmium accentuates signs of zinc deficiency in turkeys, chicks, rodents, and pigs (NAS 1979). Chicks on a zinc-deficient diet showed an increased frequency of muscle and feather abnormalities when 40 mg Cd/kg diet was added; however, supplementation of the diet with 200 mg Zn/kg for 14-15 days lessened or reversed the adverse effects of cadmium (Supplee 1963). But cadmium promotes the growth of zinc-limited phytoplankton (Price and Morel 1990). Substitution of trace metals or metalloenzymes could be a common strategy for phytoplankton in trace-metal impoverished environments such as the ocean and could result in an effective colimitation of phytoplankton growth by several bioactive elements (Price and Morel 1990). Zinc-deficient marine diatoms (*Thalassiosira weissflogii*), for example, can grow at 90% of their maximum rate when supplied with cadmium (which substitutes for zinc in certain macromolecules); cobalt can also substitute for zinc, although less efficiently than cadmium (Price and Morel 1990).

Zinc diminishes or negates the toxic effects of cadmium. Specifically, zinc protected embryos of the toad (*Bufo arenarum*) and other amphibian embryos against cadmium-induced developmental malformations (Herkovits et al. 1989; Herkovits and Perez-Coll 1990; Rivera et al. 1990). Zinc counteracted adverse effects of cadmium on limb regeneration and on the growth of the fiddler crab (*Uca pugilator*; Weis 1980). Preexposure of a freshwater amphipod (*Gammarus pulex*) to 10 µg Zn/L for 2 weeks increased whole body zinc content from 74 to 142 mg/kg dry weight (DW) and protected against the toxic effects of subsequent cadmium exposure of 500 µg Cd/L for 96 h (Howell 1985). In crickets (*Acheta domesticus*), excess zinc in diets of larvae protected against cadmium toxicity (Migula et al. 1989). Zinc protected rats (*Rattus* sp.) against the toxic effects of cadmium such as testicular lesions, reduced sperm counts, hepatotoxicity, and lung damage (Sato and Nagai 1989; Saxena et al. 1989a). Zinc protected mouse (*Mus* sp.) embryos against cadmium toxicity (Yu and Chan 1988. An effective protection ratio of cadmium to zinc was 1:1 for mouse embryos, but for free living embryos of the toads, this ratio of cadmium to zinc was 1:8 (Belmonte et al. 1989). Zinc reversed the toxic action of cadmium on natural killer cells of mice: 500 mg Zn/L drinking water negated the toxic action of 50 mg Cd/L (Chowdhury and Chandra 1989). The mechanisms of zinc protection against cadmium were variously attributed to metallothionein induction (Sato and Nagai 1989), enhanced detoxification rates of cadmium (Rivera et al. 1990), and competition with cadmium for the same metalloenzyme sites (Yu and Chan 1988; Rivera et al. 1990).

Waterborne solutions of zinc-cadmium mixhires were usually additive in toxicity to aquatic organisms, including freshwater fish (Skidmore 1964) and amphipods (de March B. G. E. 1988), and to marine fish (Eisler and Gardner 1973), copepods (Verriopoulos and Dimas 1988), and amphipods (Ahsanullah et al. 1988).

However, mixtures of zinc and cadmium were less toxic than expected to *Daphnia magna*, as judged by acute lethality studies (Attar and Maly 1982).

Zinc exerted antagonistic effects on uptake of cadmium by gills of the freshwater clam (*Anodonta cygea*) but accelerated cadmium transport from gills towards internal organs (Hemelraad et al. 1987). Cadmium uptake in tissues of *Anodonta* was reduced by about 50% during exposure for 16 weeks to water containing 25 µg Cd/L and 2.5 mg Zn/L (Hemelraad et al. 1987). In a marine prawn (*Pandalus montagui*), cadmium exposure had no effect on tissue zinc levels, but zinc enhanced cadmium uptake in hepatopancreas at the expense of the carcass (Ray et al. 1980). In marine fish, cadmium was taken up more rapidly at elevated seawater zinc levels; however, zinc concentrations in fish tissues decreased with increasing tissue cadmium burdens, suggesting competition between these two metals for the same physiologically active site (Eisler 1981). Zinc concentrations in larval shrimp (*Palaemon serratus*) within its threshold regulation range of 75-525 µg Zn/L were not affected by the addition of 100 µg Cd/L (Devineau and Amiard Triquet 1985). In zebrafish (*Brachydanio rerio*), zinc did not affect cadmium uptake by the whole body or gills but inhibited intestinal uptake and tended to increase gill cadmium elimination rates (Wicklund et al. 1988). Among marine vertebrates, cadmium is selectively accumulated over zinc (Eisler 1984). In ducks, zinc selectively competes with cadmium on high and low molecular weight protein pools in the kidney and liver. Once the high molecular weight protein pool is zinc-saturated excess zinc is stored on metal binding proteins with serious implications for waterfowl stressed simultaneously with cadmium and zinc (Brown et al. 1977). On the other hand, a cadmium-induced disease in bone collagen of chicks was prevented by zinc because of preferential accumulation of zinc (Kaji et al. 1988).

Copper

Mixtures of zinc and copper are generally acknowledged to be more-than-additive in toxicity to a wide variety of aquatic organisms, including oyster larvae (Sprague 1986), marine fish (Eisler and Gardner 1973; Eisler 1984), freshwater fish (Skidmore 1964; Hilmy et al. 1987a) and amphipods (de March 1988), and marine copepods (Sunda et al. 1987; Verriopoulos and Dimas 1988). But zinc-copper mixtures were less-than-additive in toxicity to marine amphipods (*Allorchestes compressa*; Ahsanullah et al. 1988).

Zinc added to the ambient water depressed copper accumulations in tissues of juvenile catfish (*Clarias lazera*), but copper added to the medium depressed zinc uptake Hilmy et al. 1987a). A similar situation was reported in barnacles (*Elminius modestus*); however, simultaneous exposure to copper and zinc resulted in enhanced uptake of both metals (Elliott et al. 1985).

In higher organisms, zinc is a copper antagonist and potentiates the effects of nutritional copper deficiency in rats and chicks. This effect only occurs at extremely high zinc to copper dietary ratios. The addition of copper to the diet of chicks or rats in physiological amounts counteracted all observed signs of zinc intoxication (Tom et al. 1977). No antagonism was evident between dietary copper and zinc fed to channel catfish (*Ictalurus punctatus*) fingerlings; therefore, the high levels of supplemental zinc required in practical feeds should not impair copper status if normal dietary copper levels are present (Gatlin et al. 1989).

High levels of administered zinc limit copper uptake in humans and certain animals (Samman and Roberts 1988) and provides protection against toxicosis produced by copper in pigs and sheep (Allen et al. 1983). Excessive zinc in humans interferes with copper absorption from the intestine, resulting in copper deficiency and eventually in cardiovascular diseases; high zinc intakes also decrease iron bioavailability, leading to a reduction of erythrocyte life span by 67% (Saxena et al. 1989b). Copper deficiency induced by excess dietary zinc is associated with lameness in horses, donkeys, and mules (NAS 1979; Bridges 1990; Ostrowski et al. 1990).

Lead

Lead-zinc mixtures were more-than-additive in toxicity to marine copepods (Verriopoulos and Dimas 1988) and significantly delayed development of mud crab (*Rithropanopeus harrisii*) larvae (EPA 1987). Lead is accumulated up to 10 times more rapidly by marine fish at elevated zinc concentrations in seawater (Eisler 1981).

Among terrestrial animals, zinc protects against lead toxicosis. Dietary zinc reduced the toxic effects of dietary lead to larvae of the house cricket (Migula et al. 1989). Zinc at 100-200 µg/egg (1 mg Zn/kg egg) significantly protected developing white leghorn chicks against lead-induced 50 µg/egg) deformities and death

when injected into the yolk sac on day 7 of incubation (Anwer et al. 1988). Zinc also protects against lead toxicity in horses (Anwer et al. 1988) and against testicular injury induced by lead in rats (Saxena et al. 1989a).

Nickel

Nickel-zinc mixtures were additive in toxicity to marine copepods (Verriopoulos and Dimas 1988) and to the three-spined stickleback (Skidmore 1964).

Oral nickel toxicity in chicks was prevented by increased dietary zinc (Warner et al. 1988). Nickel is a leading cause of allergic contact dermatitis in many industrial nations; about 6% of the general public and about 11% of dermatology clinic patients are sensitive to nickel (Warner et al. 1988). Zinc prevents nickel sulfate-induced allergic contact dermatitis in guinea pigs (*Cavia* spp.) through addition of 100-200 mg Zn/L drinking water for 4 weeks before nickel insult (Warner et al. 1988). Nickel and other metals that cause allergic contact dermatitis penetrate the skin, complex with selected ligands, and stimulate a delayed hypersensitivity. Zinc is thought to block the sites where nickel complexes to the protein (Warner et al. 1988).

Other Chemicals

Zinc interacts with a wide variety of inorganic, organic, and biological agents, but in most cases the available information is fragmentary and the mechanisms of action are unknown. Mice pretreated with zinc at 6.5 mg Zn/kg BW for 9 days showed increased resistance to arsenic toxicosis during a 30-day observation period (Kreppel et al. 1988). Oral zinc therapy was effective in treating biological agents such as infectious pododermatitis in cattle; ovine foot rot in sheep; sporidesmin in sheep, cattle, and rodents; and the toxins of the fungus *Phomopsis leptostromiformis* in sheep (Allen et al. 1983). Calcium modifies zinc toxicity to freshwater aquatic organisms, and increased calcium is associated with decreased acute toxicity (Everall et al. 1989b; Handy et al. 1989). Zinc absorption in the rat gut is decreased after ingestion of phosphorus as polyphosphate or as orthophosphate and high levels of calcium (Greger 1989). Zinc cytotoxicity is blocked by increased calcium or iron but not by magnesium (Borovansky and Riley 1989). Zinc reportedly protects rats against carbon tetrachloride poisoning (Allen et al. 1983).

Various cheating agents, including disodium ethylene diamine tetraacetic acid (EDTA), disodium calcium cyclohexanediamine tetraacetate, D-penicillamine, 2,3-dimercapto-l-propane sulfonic acid, and 2,3-dimercaptosuccinic acid protect mice against zinc acetate poisoning (Llobet et al. 1988b). Zinc protects toad embryos against agents known to produce malformations, including excess Vitamin A, acetazolamide, calcium-EDTA, and acetaminophen (Herkovits et al. 1989). Venom of the jararaca (*Bothrops jararaca*), a venomous Brazilian serpent, contains a zinc metalloprotease called J protease; the proteolytic activity of J protease is inactivated by EDTA and other sequestering agents (Tanizaki et al. 1989).

Chromium-zinc mixtures were more than additive in toxicity to *Tisbe holothuriae*, a marine copepod. Zinc in combination with chromium was more toxic to copepods than mixtures of zinc with copper, lead, nickel, or cadmium (Verriopoulos and Dimas 1988).

Renal tubular absorption of zinc in mice was impaired by certain diuretics and was further influenced by dietary proteins (Goyer 1986).

Zinc absorption in rats was depressed after consumption of high levels of inorganic iron; absorption was normal with organoirons (Greger 1989).

Mercury-zinc mixtures were more-than-additive in toxicity to oyster larvae (Sprague 1986). Preexposure of common mussels (*Mytilus edulis*) to 50 µg Zn/L for 28 days conferred increased tolerance to 75 µg Hg/L (Roesijadi and Fellingham 1987). Zinc inhibited the accumulation of mercury in marine snails and crustaceans (Andersen et al. 1989).

Zinc deficiency places an increased demand on selenium pools in daphnids. As little as 5 µg Se/L in zinc-free water eliminated overt cuticle damage and substantially increased reproduction but did not alter the shortened life span. Cladocerans at the threshold of selenium deficiency become overly selenium-deficient when zinc supplies are lacking (Keating and Caffrey 1989). Insufficient copper introduces cuticle problems in daphnids similar to those introduced by insufficient zinc or selenium, increasing the likelihood of a proposed

relation between glutathione peroxidase (which contains selenium) and copper-zinc superoxide dismutase (Keating and Caffrey 1989).

High levels of dietary tin increased zinc loss from rats (Greger 1989). Zinc prevented toxic effects of vanadium (10 mg/kg BW) on bone metabolism of weanling rats (Yamaguchi et al. 1989a).

Carcinogenicity, Mutagenicity, Teratogenicity

General

When injected directly into the testes, zinc can induce testicular sarcomas in birds and rats but has not been shown to be tumorogenic by any other route. Zinc promotes tumor growth after conditions of zinc deficiency but excess zinc may suppress or inhibit tumor proliferation, although the mechanisms of the action are imperfectly understood. Chromosomal aberrations were observed under conditions of zinc deficiency, but excess zinc was not mutagenic in most tests. Organozinc compounds are effective mutagens when presented to susceptible cell populations in an appropriate form, but the evidence for inorganic zinc is incomplete. Zinc is teratogenic to frog and fish embryos, but conclusive evidence of teratogenicity in mammals is lacking. Zinc may protect against the effects of some mammalian teratogens. Under conditions of mild zinc deficiency, however, diabetes and effects of various teratogens are exacerbated.

Carcinogenicity

Carbamate esters of zinc, zineb, and ziram are carcinogenic and teratogenic in animals, which is, however, attributed to the action of the carbamate esters and not to zinc (Elinder 1986). Results of studies with small mammals showed zinc to be cocarcinogenic with 4-nitroquinoline-N-oxide on oral cancer and with N-ethyl-N-nitrosourea on brain cancer (Leonard and Gerber 1989).

There is conclusive evidence that repeated intratesticular injections of zinc salts can induce testicular sarcomas in birds and rats (NAS 1979; Elinder 1986; Goyer 1986; PHS 1989). Testicular teratomas in roosters were first produced experimentally in 1926 when zinc salts were injected into the testes as a method of practical castration; tumors could be induced only by intratesticular injection during the spring period of gonadal growth (Guthrie 1971). Teratomas of the testes were observed in fowl given testicular injections of 2 mL of 10% $ZnSO_4$ solution (PHS 1989). Teratomas were induced in Japanese quails (*Coturnix coturnix japonica*) by intratesticular injections of 3% zinc chloride solutions during a period of testicular growth stimulated by increased photoperiod; tumors were similar to those of domestic fowl and have histological features in common with spontaneous testicular teratomas in humans (Guthrie 1971). Testicular tumors in rats were produced by direct intratesticular injection of zinc; no other carcinogenic effects were produced by any other route regardless of dose (Goyer 1986). It is emphasized that zinc and zinc compounds are not conclusively carcinogenic except when injected directly into the testes; no field or experimental evidence exists showing zinc to be tumorogenic through any other route (NAS 1979; Phillips and Kindred 1980; Elinder 1986; Leonard and Gerber 1989; PHS 1989).

Zinc is essential for the growth of rapidly proliferating cells such as tumors. The high zinc requirements of these cells in tumor disease can result in latent zinc deficiency. Accordingly, growth of animal tumors is stimulated by zinc and retarded by zinc deficiency (Prasad 1979; Leonard and Gerber 1989). In mouse fibrosarcoma cells, zinc inhibits endonucleases, subsequently blocking DNA fragmentation and tumor cell lysis, allowing tumors to grow (Flieger et al. 1989). There is no evidence that zinc deficiency causes cancer (NAS 1979), although deficiency was associated with decreasing tumor growth (Prasad 1979; Phillips and Kindred 1980). Malignant human tissues, for example, frequently contained less zinc than normal tissue, that is, 78 mg/kg FW in a normal liver versus 18 mg/kg FW in a cancerous liver (Phillips and Kindred 1980).

Zinc can also inhibit tumor growth (NAS 1979), although the mechanisms of zinc suppression of carcinomas are imperfectly understood (Phillips and Kindred 1980). Zinc inhibits the growth of mouse melanoma cells at concentrations between 8.2 and 9.9 mg Zn/L culture medium (Borovansky and Riley 1989). The addition of 100 mg $ZnSO_4$/L to drinking water of hamsters inhibited formation of dimethylbenzanthracene-induced carcinomas (Phillips and Kindred 1980). High zinc diets of 500 mg/kg ration reduced growth of a chemically induced hepatoma in rats (Phillips and Kindred 1980). Intramuscular injections of zinc oxide or zinc acetate administered together with nickel sulfide--a potent muscle carcinogen--delayed but did not prevent 100% tumor incidence in rats during a 66-week observation period (Kasprzak et al. 1988). Administration of zinc slows the carcinogenic

process induced by nickel from the production of water-soluble and water-insoluble zinc compounds, despite markedly different retention times in muscle of zinc compounds (Tb½ ZnO = 24 days, zinc acetate = 2.5 days, Ni_3S_2 = 21 days). Zinc in either form exerted no measurable influence on nickel retention at the injection site or early local cellular reactions to nickel (Kasprzak et al. 1988). Testicular tumors in rats caused by injection of cadmium were suppressed by zinc injection (Leonard and Gerber 1989) when the zinc to cadmium molar ratio was about 100:1 (Phillips and Kindred 1980). Inhibition of cadmium carcinogenesis by zinc is a complex phenomenon, depending on dose, route, and target site (Waalkes et al. 1989). For example, the number of cadmium-induced testicular tumors in rats was reduced by 50% during a 2-year period after three subcutaneous injections of 65.4 mg Zn/kg BW given within 18 h of the initial cadmium insult, although unlike controls, this group had a marked elevation in prostatic tumors; tumor number was reduced by 92% when rats were given 100 mg Zn/L in drinking water (Waalkes et al. 1989).

Mutagenicity

Results of mutagenicity studies with whole organisms were usually negative because homeostatic controls of absorption and protein binding preclude the likelihood of zinc being genotoxic under standard feeding conditions (Thompson et al. 1989). However, zinc is an effective mutagen and clastogen when presented to a susceptible cell population in an appropriate form (Thompson et al. 1989). Zinc acetate produced dose-related positive responses in the mouse lymphoma assay and also in a cytogenetic assay with Chinese hamster ovary cells; however, results of mutagenicity assays with inorganic zinc were negative in the *Salmonella* mutation assay and in unscheduled DNA synthesis on primary cultures of rat hepatocytes (Thompson et al. 1989). Organozinc compounds have mutagenic potential, as judged by the positive responses with zinc 2,4-pentanedione and *Salmonella* (Thompson et al. 1989).

Structural chromosome aberrations, particularly chromatid gaps and increased frequency of fragment exchange, were observed in rat bone marrow cells after 14 days of exposure to 240 mg Zn/L drinking water (Kowalska-Wochna et al. 1988). Chromosomal aberrations were observed in bone marrow cells of mice fed diets equivalent to 650 mg Zn/kg BW daily in mice exposed to zinc oxide by inhalation, and in mice maintained on a low calcium diet (PHS 1989). Aberrations in bone marrow of mice given 5,000 mg Zn/kg diet may be associated with calcium deficiency (Leonard and Gerber 1989). Calcium is displaced by zinc in calcium-depleted conditions, leading to chromosomal breaks and interference in the repair process (PHS 1989).

Zinc chloride induces chromosomal aberrations in human lymphocytes in vitro (Elinder 1986). A higher incidence of chromosome anomalies in leukocytes occurs among workers exposed to zinc (Elinder 1986), but these aberrations are probably due to other (unspecified) mutagenic factors in the work environment (Leonard and Gerber 1989).

Zinc inhibits the mutagenic action of some carcinogens because it is a constituent of mutagen detoxifying enzymes or because it acts directly on the microsomal monooxygenases forming the ultimate carcinogen (Leonard and Gerber 1989). Zinc significantly reduced a genotoxic effect of lead in rat bone marrow cells (500 mg Pb/L drinking water followed by 240 mg Zn/L for 2 weeks) and also protected against lead accumulations in erythrocytes and lead-induced inhibition of delta-amino levulinic acid dehydratase (Kowalska-Wochna et al. 1988). Zinc deficiency can lead to chromosomal aberrations, but excess zinc was not mutagenic in the majority of tests for DNA damage--except for zinc-containing fungicides wherein the organic dithiocarbamate constituents were the mutagenic agents and for zinc chromate wherein the chromate ion was the active agent (Leonard and Gerber 1989). Frequencies of sister chromatid exchanges in calves with hereditary zinc deficiency, also known as Lethal Trait A46, are lower than in healthy normal cows, suggesting a fundamental association between disturbed zinc metabolism and the low incidence of sister chromatid exchanges in A46 cattle (Bosma et al. 1988).

Teratogenicity

Excess zinc is teratogenic to frog and fish embryos, possibly by inhibition of DNA synthesis (Dawson et al. 1988; Fort et al. 1989). Zinc at 150 mg/kg in rat diets was associated with inhibited fetal implantation but this needs confirmation (Elinder 1986). No conclusive evidence now exists demonstrating that excessive zinc produces any teratogenic effect in mammals (NAS 1979; Dawson et al. 1988; Leonard and Gerber 1989).

Excess zinc may protect against some teratogens, such as calcium EDTA (Leonard and Gerber 1989). Also, teratogenic effects of cadmium salts in golden hamsters was reduced by simultaneous administration of zinc salts (NAS 1979).

Zinc deficiency is clearly teratogenic in mammals (Dawson et al. 1988; Leonard and Gerber 1989). Severe maternal zinc deficiency is known to be teratogenic in rats. Fetal malformations--especially calcification defects--from maternal zinc deficiency affect almost every tissue (Ferreira et al. 1989). Skeletal malformations are most common, possibly because of a reduction in cellular proliferation and in activity of bone alkaline phosphatase (Leonard and Gerber 1989). Human zinc deficiency may act teratogenically, either directly or indirectly through other toxic agents (Jameson 1980). Zinc deficiency may exacerbate effects of several teratogenic agents such as thalidomide; there is also the possibility that zinc deficiency may increase the incidence of spina bifida and anencephaly, but this needs verification (Leonard and Gerber 1989). Diabetes during pregnancy can amplify the effects of a mild maternal zinc deficiency. In one study, diabetic and nondiabetic rat strains were fed a low zinc diet (4.5 mg Zn/kg diet), an adequate zinc diet (24.5 mg/kg), or a high zinc diet (500 mg/kg) throughout gestation. Fetuses from diabetic dams were smaller, weighed less, and had less calcified skeletons and more malformations than fetuses from control dams. In controls, maternal dietary zinc had a minor effect on fetal malformation frequency. In diabetic strains, however, the low zinc diet had a strong teratogenic effect (Uriu-Hare et al. 1989).

Background Concentrations

General

Total zinc concentrations in nonbiological samples seldom exceed 40 µg/L in water, 200 mg/kg in soils and sediments, or 0.5 µg/m^3 in air. Environments heavily contaminated by anthropogenic activities may contain up to 99 mg Zn/L in water 118 g/kg in sediments, 5 g/kg in soil, and 0.84 µg/m^3 in the atmosphere. Zinc was detectable in all samples of plants and animals measured. Grossly-elevated (i.e., >4 g/kg DW) concentrations were normally encountered in selected tissues of marine bivalve molluscs, barnacles, and polychaete annelids. In general, zinc concentrations were elevated in organisms collected near anthropogenic point sources of zinc contamination but were modified substantially by the organism's diet, age, reproductive state, and zinc-specific sites of accumulation as well as by inherent interspecies differences.

Nonbiological

Zinc concentrations in freshwater, seawater, groundwater, sewage sludge, sediments, and soils are listed in Table 3. These data are considered reliable, although newer clean laboratory techniques suggest that dissolved zinc concentrations in nonpolluted rivers may be 10 to 100 times lower than previously reported (Shiller and Boyle 1985).

Zinc concentrations in water seldom exceed 40 µg/L except near mining, electroplating and similar activities--where concentrations between 260 and 954 µg/L were frequently recorded. Drinking water usually contains <10 µg Zn/L, although concentrations >2 mg/L may occur after passage through galvanized pipes (Goyer 1986). Zinc-contaminated streams in the Platte River Basin sometimes contain up to 99 mg Zn/L and in Arkansas up to 79 mg/L (Mirenda 1986). Zinc concentrations in water downstream of placer mining activities in Alaska sometimes exceed the concentrations that are toxic to the Arctic grayling, *Thymallus arcticus* (Buhl and Hamilton 1990). The disappearance of the stone loach (*Noemacheilus barbatulus*) in the United Kingdom from streams receiving industrial wastes was attributed directly to zinc concentrations in the stream rising from 1 mg/L to a lethal 5 mg/L (Solbe and Flook 1975).

Table 3. Zinc concentrations (milligrams of zinc per kilogram fresh weight [FW] or dry weight [DW] in representative nonbiological materials.

Material	Concentration[a] (mg/kg or mg/L)	Reference[b]
Earth's crust	40 DW	11
Freshwater		
Canada		
Normal	<0.04 FW	1
Acidic mine tailings	0.9 FW, Max. 3.3 FW	2
wastes, Sudbury, Ontario		
United States		
Alaska		
Contaminated streams	0.029-0.882 FW	3
Downstream of placer	0.125 (0.075-0.165) FW	3
mining activities		
Nationwide	0.0005-0.010 FW	4
Worldwide, rivers	0.021 FW	2,5
Groundwater, near Lake Erie	Max 0.954 FW	1
Seawater		
Australia (polluted)	0.134 FW	6
Canada	0.01-0.04 FW	1
Irish Sea		
Coastal	0.007 FW	6
Near shore	0.003 FW	6
Offshore	0.003 FW	6
Open ocean		
Deep water	0.0006 FW	6
Surface	0.000002-0.0001 FW	4
United Kingdom		
Clyde estuary	0.006 FW	7
Heavily polluted	0.026 FW	6
Polluted	0.007-0.012 FW	6
Severn estuary	0.022 FW	7
United States, San Diego		
Coastal	0.0005 FW	6
Harbor	0.0026 FW	6
Western Mediterranean		
Coastal	0.0015-0.002 FW	6
Estuary	Max 0.010 FW	6
Near Shore	0.0036 FW	6

Sediments		
Australia	35 DW; Max. 280	8
Canada		
Lakes	55-160 DW	1
Marine	64-180 DW	1
Streams and rivers	50-138 DW	1
Mediterranean	5-20 DW	S
Sweden and Norway	Usually <130 DW; Max. 118,000	8
United Kingdom	70-245 DW; Max. 825 DW	8
United States		
Corpus Christi, Texas		
Bay	10-229 DW	9
Harbor	229-11,000 DW	9
New York Bight		
Uncontaminated site	18 DW	9
Sewage dump site	252 (54-416) DW	9
Northeast	15-20 DW; Max. 1,500 DW	8
Puget Sound	65 DW; Max. 185 DW	8
Rhode Island, near electroplaters		
Narragansett Bay	110 (53-168) DW	9
Providence River	490 DW	9
Southern California Bight	55-75 DW; Max. 2,800	8
Sewage Sludge		
United Kingdom, Glasgow	1,125 DW	7
United States		
Average	1,409 DW	10
Missouri	1,200 (170-13,000) DW	10
Soils		
United States	54 (<25-2,000) DW	10
Uncontaminated	10-300 DW	11
Near smelters	5,000 DW	11

[a]Concentrations are shown as means, range (in parentheses), and maximum (Max.).

[b] 1. Spear 1981; 2. Mann et al. 1989; 3. Buhl and Hamilton 1990; 4. EPA 1987; 5. Mann and Fyfe 1988; 6. Sprague 1986; 7. Nugegoda and Rainbow 1988b; 8. Young et al. 1980; 9. Eisler et al. 1977; 10. Beyer 1990; 11. Elinder 1986.

Concentrations of zinc in sediments and soils usually do not exceed 200 mg/kg but can range between 3 and 118 g/kg as a result of human activities (Table 3). Atmospheric zinc levels were almost always <1 µg/m^3, although they tended to be higher over industrialized areas (Goyer 1986). Average zinc concentrations were <0.001 µg/m^3 atmosphere at the South Pole, 0.01-0.02 µg,/m^3 atmosphere in rural areas of the United States, <0.01-0.84 µg/m^3 atmosphere in U.S. cities, and 0.06-0.35 µg/m^3 atmosphere at various locations in the United Kingdom (Elinder 1986).

Biological

Zinc measurements in field collections of plants and animals (Table 4) show several trends. (1) Zinc is present in all tissues of all organisms measured. (2) Concentrations are elevated in organisms near anthropogenic point sources of zinc contamination. (3) Concentrations are normally grossly elevated (>4 g/kg FW soft parts) in bivalve molluscs and barnacles. (4) Zinc-specific sites of accumulation include the frond in algae; the kidney in molluscs; the hepatopancreas in crustaceans; the jaws in polychaete annelids; the viscera, gonad, and brain in fish; the liver, kidney, and bone in birds; and the serum, pancreas, feces, liver, kidney, and bone in mammals. (5) Interspecies variations in zinc content are considerable, even among taxonomically closely-related species. (6) Intraspecies differences in zinc content vary with age, size, sex, season, and other modifiers. (7) Many species regulate zinc within a threshold range of concentrations.

Additional information on background concentrations of zinc is given in Vallee (1959), NAS (1979), Young et al. (1980), and Eisler (1980, 1981).

Terrestrial Plants and Invertebrates

Zinc concentrations in forest plants vary considerably. Some species of oaks (*Quercus* spp.), for example, are accumulators whereas others may be termed discriminators. In descending order of concentration zinc is in the roots, foliage, branches, and trunk of individual species (Van Hook et al. 1980). Small lateral roots accumulate zinc to much greater levels than other vegetation components and are probably most sensitive to changes in zinc inputs. Half-time persistence of zinc in forest ecosystems varies from about 3 years in organic matter components to >200 years in large soil pools (Van Hook et al. 1980).

Table 4. Effects of zinc on representative terrestrial plants and invertebrates.

Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
Aquatic plants		
Euglena sp., from acidic mine tailings waste discharges (0.9 mg Zn/L, Max. 3.3 mg/L)	143 DW; Max. 410 DW	1
Aquatic moss, *Fontinalis squamosa*		
Contaminated river, Wales, 1985	Max. 2,810 DW	2
Uncontaminated site	<400 DW	2
Marine plants		
Phytoplankton	38 DW	3
Seaweeds	90 DW	3
Eelgrass, *Zostera marina*		
Leaf	Max. 195 DW	4
Rhizome	Max. 70 DW	4
Root	Max. 155 DW	4
Stem	Max. 85 DW	4
Terrestrial plants and invertebrates		
Honey bee, *Apis mellifera*, Czechoslovakia, 1986-87		
Drones	77-89 DW	5

Honey	0.6-4.5 DW	5
Pollen in combs	39-55 DW	5
Wax	11-249 DW	5
Workers, whole		
Foragers, spring	116-204 DW	5
Dead overwintering	8-13 DW	5
Young	83-160 DW	5
Grey field slug, *Deraceras reticulatum*, near lead-zinc mine		
Digestive gland	3,968 DW	6
Foot-head	308 DW	6
Gonads	118 DW	6
Intestine	380 DW	6
Whole	800 DW	7
Earthworms, north-eastern United States, whole		
From uncontaminated soils (23-200 mg Zn/kg DW), 6 species	120-650 DW	8
From mining sites (100-2,500 mg Zn/kg DW), 5 species	200-950 DW	8
From industrial sites (24-320 mg Zn/kg DW soil), 6 species	320-1,600 DW	8
Near galvanized towers (28-270 mg Zn/kg DW soil), 1 species	340-690 DW	8
Earthworms, whole, gut empty		
Dendrodrilus rubidus	(308-1,683) DW	9
Lumbricus rubellus	(394-3,873) DW	9
Gastropods, whole, near abandoned mine, soil contained 1,377 mg Zn/kg DW		
Arion ater	900 DW	7
Arion hortensis	600 DW	7
Arion subfuscus	1,200 DW	7
Derocerus caruanae	1,000 DW	7
Lichen, *Lasallia papulosa*		
Near zinc smelter	2,560 DW	10

Control population	214 DW	10
Isopod, *Oniscus asellus*, whole, from soil containing various concentrations of zinc (mg Zn/kg soil DW)		
<0.3Max. 150 DW		11
1-10	Max. 350 DW	11
>50	Max. >500 DW	11
Plants, terrestrial	Average 100 DW	114
Woodlouse, *Porcellio scaber*		
Near metal smelter of maximum soil zinc of 24,900 mg/kg DW, and soil litter of 4,150 mg/kg DW		
Hepatopancreas	Max. 13,500 DW	12
Whole	Max. 1,500 DW	12
From soil containing various concentrations of zinc (mg Zn/kg soil DW), whole organism		
<0.3	Max. 350 DW	11
1-10	Max. 550 DW	11
>50	Max. >1,000 DW	11
Protozoans, marine	63-279 DW	13
Coelenterates		
Soft coral, *Alcyonia alcyonium*, whole	9.6 FW	14
Plumose anemone, *Metridium senile*, whole	18 FW	14
Various species, whole		
Uncontaminated areas	50 DW	3
Noncontaminated areas	<80 FW; <120 DW	13
Contaminated areas	Max. 603 DW	13
Molluscs, aquatic		
Abalones, soft parts	55 (38-100) DW	17
Bivalves		
Kidney granules	10,000-43,320 DW	15
Soft parts	91-660 DW	16
Cephalopods		

Soft parts	81-150 DW; Max. 580 DW	16,17
Whole	250 DW	3
Chitons, soft parts	290-700 DW	17
Clams, soft parts	81-115 DW; Max. 510 DW	17
Sydney rock oyster, *Crassostrea commercialis*, soft parts, Southeast Asia	800 (64-1,920) DW	18
American oyster, *Crassostrea virginica*, soft parts		
Chesapeake Bay	3,975 (60-12,800) DW	18
Gulf of Mexico	2,150 (485-10,000) DW	18
South Carolina	2,410 (280-6,305) DW	18
United States	1,018-1,641 (204-4,000) FW	19
Drills, soft parts	536-3,470 DW	17
Gastropods, soft parts	84-763 DW	16
Limpets, soft parts		
18 species	112 (14-760) DW	17
7 species	196 (86-430) DW	17
Clam, *Macoma balthica*, adults, San Francisco Bay, soft parts	200-600 DW	20
Mussels, soft parts	109-267 DW; Max. 7,700 DW	17
Common mussel, *Mytilus edulis*		
Soft parts, 0.43 g DW		
Visceral mass	34-100 DW	21
Gills and palps	47-94 DW	21
Remainder	48-110 DW	21
Soft parts, 0.22 g DW		
Visceral mass	28-112 DW	21
Gills and palps	38-158 DW	21
Remainder	40-130 DW	21
Kidney, Newfoundland		
October 1984	144 (50-427) DW	22
April 1985	828 (94-3,410) DW	22
Oyster drill, *Ocenebra erinacea*, soft parts	1,451-2,169 DW	23
European flat oyster, *Ostrea edulis*, soft parts		
Contaminated site	10,560 (4,700-12,640) DW	24
Clean site	98 DW	24
Oysters		
Sort parts	1,960-7,270 DW; Max. 49,000 DW	17
Soft parts	100-271 FW	19

Scallop, *Pecten* sp.		
Kidney	32,000 DW	17
Kidney granules	120,000 DW	17
Soft parts	200 DW	17
Scallops, soft parts	105-212 DW; Max. 462 DW	
Green-lipped mussel,		
Perna viridis, Hong Kong		
Soft parts, 1986-87	56-134 DW	25
Soft parts, 1986		
March	63-150 DW	26
May	77-94 DW	26
Clam, *Pitar morrhuana*, soft parts, near electroplating plant, Rhode Island, 1973	Max. 276 DW	27
Rock oyster, *Saccostrea cucullata*, soft parts, Hong Kong, 1986		
March	2,082-3,275 DW	26
May	2,210-2,863 DW	26
Whelks, soft parts	198 (13-650) DW	17
Crustaceans		
Amphipods, marine, whole, western British coastal waters		
Orchestia gammarellus	104-392 DW	28
Orchestia mediterranea	120-506 DW	28
Talitrus saltator	178-306 DW	28
Talorchestia deshayesii	199-208 DW	28
Amphipods, *Themisto* spp., whole	76 (72-81) DW	29
Barnacle, *Balanus amphitrite*, soft parts	Max. 1,937 DW	30
Barnacle, *Balanus balanoides*, soft parts	1,028-3,438 FW	31
Crustaceans, marine		
Northeast Atlantic ocean, July 1985, whole		
Decapods	35-57 DW	32
Euphausids	44-96 DW	32
Mysids	24-44 DW	32
Soft parts		
Amphipods	73-109 DW	16
Barnacles	690-27,837 DW	16
Barnacles	1,050-5,140 DW; Max. 113,000 DW	17

Copepods	60-170 DW	16
Copepods	164-177 DW; Max. 1,300 DW	17
Crabs	68-102 DW; Max. 340 DW	17
Euphausids	53-83 DW	16
Isopods	94 DW	16
Shrimps	14-69 DW; Max. 150 DW	17
Various species		
Blood	0.2-87 FW	19
Excretory organs	Max. 29 FW	19
External eggs	24-107 FW	19
Gills	8-69 FW	19
Hepatopancreas	34-169 FW	19
Muscle		
Leg	15-68 FW	19
Abdominal	10-24 FW	19
Shell	5-17 FW	19
Stomach fluid	1-92 FW	19
Ovary	26-82 FW	19
Vas deferens	13-30 FW	19
Urine	Max. 2.2 FW	19
Whole	18-54 FW	19
Hermit crab, *Eupagurus bernhardus*, whole	282 FW	19
Euphausid, *Euphausia superba*, whole	68 (42-75) DW	29
Euphausid, *Meganyctiphanes norvegica*, whole		
Firth of Clyde	43 (27-62) DW	29
Northeast Atlantic Ocean	102 (40-281) DW	29
Euphausids, whole	13 FW	33
American lobster, *Homarus americanus*		
Gill	102-126 DW	34
Green gland	114-148 DW	34
Hepatopancreas	70-135 DW	34
Muscle		
Pincer	100-127 DW	34
Tail	80 DW	34
Crayfish, *Orconectes virilis*, collected 12-150 km from metal smelter		
Hepatopancreas		
12 km	190 DW	35
30 km	166 DW	35
150 km	92 DW	35
Digestive tract		
12 km	154 DW	35

30 km	100 DW	35
150 km	111 DW	35
Muscle		
12 km	93 DW	35
30 km	97 DW	35
150 km	80 DW	35
Grass shrimp, *Palaemonetes pugio*		
From sediments containing 627 mg Zn/kg DW		
Exoskeleton	58 FW	36
Muscle	55 FW	36
From sediments containing 8 mg Zn/kg DW		
Exoskeleton	18 FW	36
Muscle	30 FW	36
Prawn, *Pandalus montagui*		
Cuticle	57 DW	37
Eye	70 DW	37
Gill	106 DW	37
Hepatopancreas	30 DW	37
Muscle	57 DW	37
Whole	58 DW	37
Pink shrimp, *Penaeus brasiliensis*, adults, whole	(47-75) DW; (181-290) FW	38
Insects, marine, whole	110-197 DW	13
Chaetognaths, whole	76-90 DW	13
Annelids, aquatic		
Annelids, marine		
Jaws		
Total	5,000-24,000 DW	13
Basal section	1,790 DW	13
Distal section	34,950 DW	13
Whole body	22-1,564 DW	13
Lugworm, *Arenicola*, *marina*, whole	1.8 FW	14
Freshwater leech, *Erpobdella octoculata*, adults, whole body	Upstream (18 µg Zn/L) from zinc-polluted mine waste discharge, whole body content of 1,439-1,559 DW; reproduction normal. Downstream (180 µg Zn/L), concentration after 19-month exposure was 1,932-2,432 DW; reproduction impaired	116
Sandworm, *Nereis diversicolor*		

Head	843-995 DW	39
Parapodia	216-418 DW	39
Trunk	158-218 DW	39
Echinoderms, various species, **whole**	Usually 100 DW or lower, frequently >100 DW; Max. 245 FW, 1,500 DW	3,13
Tunicates, whole	200 DW; Max. 64 FW, 370 DW	3, 13
Fish		
Catostomids, 3 species, Missouri, blood		
Site contaminated with mine tailings	10.9-13.4 FW, 94-119 DW	40
Uncontaminated site	8.7-11.2 FW, 76-86 DW	40
White sucker, *Catostomus commersoni*		
From metals-contaminated lake (400 µg Zn/L)		
Eggs	83-158 DW	41
Larvae	511 DW	41
Ovaries		
Prespawning	114 DW	41
Postspawning	290 DW	41
Testes, postspawning	89 DW	41
From control lake (2.7 µg Zn/L)		
Eggs	69-108 DW	41
Larvae	163 DW	41
Ovaries		
Prespawning	84 DW	41
Postspawning	317 DW	41
Testes, postspawning	163 DW	41
New Brunswick, whole	92-93 DW	42
Nova Scotia, whole	98-122 DW	42
African sharptooth catfish, *Clarias gariepinus*, age 4-8 years, South Africa, 1988-89, lake sediments contained 1,104 mg Zn/kg DW (595-2,189)		
Brain	335 DW	43
Fat	5O DW	43
Gill	177 DW	43
Gonad	126 DW	43
Heart	196 DW	43
Intestine	143 DW	43
Kidney	143 DW	43
Liver	143 DW	43
Muscle	59 DW	43
Spleen	163 DW	43

Vertebrae	75 DW	43
Baltic herring, *Clupea harengus*, liver	23 FW	14
Freshwater fish, various species		
Great Lakes		
Whole, less intestines, 4 species	12-20 FW	19
Liver, 10 species	11-48 FW	19
Greece, 1987-88, muscle, 11 species	7 (3-37) FW	44
United States, nationwide, whole		
1978-79	25 (8-168) FW	45
1980-81	24 (9-109) FW	45
1984		
Geometric mean	21.7 FW	121
85th percentile	34.2 FW	121
Maximum	118.4 FW	121
From metals-contaminated (636 µg dissolved Zn/L) lake, Indiana, whole		
Bowfin, *Amia calva*	93 DW	46
White sucker, *Catostomus commersoni*	102 DW; Max. 152 DW	46
Brown bullhead, *Ictalurus nebulosus*	127 DW; Max. 139 DW	46
Warmouth, *Lepomis gulosus*	140 DW; Max. 166 DW	46
Orangespot sunfish, *Lepomis humilis*	248 DW	46
Redear sunfish, *Lepomis microlophus*	477 DW; Max. 820 DW	46
Largemouth bass, *Micropterus salmoides*	119 DW; Max. 207 DW	46
Golden shiner, *Notemigonus crysoleucas*	160 DW; Max. 171 DW	46
Yellow perch, *Perca flavescens*	160 DW; Max. 171 DW	46
Black crappie, *Pomoxis nigromaculatus*	123 DW	46
From metals-contaminated stream, Missouri, muscle, 5 species	3.1-24 FW	47,115
Shortfin mako, *Isurus oxyrinchus*, vertebrae	36 (5-127) DW	48
Marine fish, various species		
Muscle		
54 species	0-5 FW	19
32 species	5.1-10 FW	19
7 species	10.1-15 FW	19
4 species	15.1-20 FW	19

2 species	20.1-25 FW	19
Whole	80 DW	3
Red Sea, 1980-82		
Triggerfish, *Balistoides viridiscens*		
Muscle	66 DW	49
Liver	154 (81-227) DW	49
Ovaries	291 (287-792) DW	49
Surgeonfish, *Ctenochaetus strigosus*, muscle	29 (11-43) DW	49
Halfbeak, *Hemiramphus marginatus*, muscle	32 DW	49
Labrids, 3 species, muscle	33 (19-51) DW	49
Lethrinids *Lethrinus* spp.		
Muscle	33 (13-112) DW	49
Liver	95 (43-146) DW	49
Ovaries	146 (72-259) DW	49
Testes	152 (141-164) DW	49
Snapper, *Lutianus fulviflamma*, muscle	48 (25-70) DW	49
Parrotfish, *Scarys gyttatus*		
Liver	17 DW	49
Muscle	62 DW	49
Serranids, 4 species		
Muscle	51 (8-112) DW	49
Liver	130 (78-183) DW	49
Rabbitfish, *Siganus oramin*		
Muscle	55 (18-195) DW	49
Liver	179 (68-611) DW	49
Sparids, 2 species, muscle	56 (34-76) DW	49
Goatfish, *Upeneus tragula*, muscle	51 (37-68) DW	49
Pacific hake, Merluccius productus		
Muscle	4 (3-6) FW	33
Whole	12 FW	33
Catfish, *Mystus gulio*, juveniles, whole, India		
From contaminated estuary (100-120 µg Zn/L, 120-145 mg Zn/kg sediment DW)	160-180 DW	50
From uncontaminated estuary (10 µg Zn/L, 30 mg Zn/kg sediment)	15 DW	50
Yellow perch, *Perca flavescens*, whole		

New Brunswick	81-103 DW	42
Nova Scotia	68-85 DW	42
Blue shark, *Prionace glauca*, vertebrae	95 (32-210) DW	45
Atlantic salmon, *Salmo salar*		
Eggs		
Hatchery	20-35 FW	51
Native	19-28 FW	51
Liver, juveniles		
Hatchery	29-41 FW	51
Native	34 FW	51
Muscle	13 DW	52
Ovaries	166 DW	52
Spines	79-219 DW	52
Stomach contents	78 DW	52
Brook trout, *Salvelinus fontinalis*, whole		
New Brunswick	87-158 DW	42
Nova Scotia	90-110	42
Atlantic mackerel, *Scomber scombrus*, liver	31 FW	14
King mackerel, *Scomberomorus cavalla*, otolith		
Age <1 year	16 DW; Max. 50 DW	53
Age 2 years	11 DW	53
Age 10 years	8 DW	53
Lesser spotted dogfish, *Scyliorhinus caniculus*, liver	8.7 FW	14
Monkfish, *Squatina squatina*, liver	8 FW	14
Reptiles		
American alligator, *Alligator mississippiensis*, eggs (less shell), Florida, 1984	4.9-9.2 FW	54
Birds		
Blue-winged teal, *Arias discors*, Texas, 1983		
Muscle		
Males	13.8 FW	55
Females	11.3 FW	55
Liver		
Autumn	41.4 FW	55
Spring	33.7 FW	55
Mallard, *Anas platyrhynchos*, liver	54 FW	56
Canvasback, *Aythya valisineria*, Chesapeake Bay liver	41 FW	56

Nicobar pigeon, *Caloenas nicobarica*, zinc-poisoned		
Kidney	2,107 DW	57
Liver	3,575 DW	57
Ovary	654 DW	57
Turkey vulture, *Cathartes aura*, California, 1980-81		
Liver	21-44 FW	58
Kidney	16-24 FW	58
Feather	81-110 DW	58
Common raven, *Corvus corax*, California, 1980-81		
Liver	14-45 FW	58
Kidney	17-33 FW	58
Feather	110-160 DW	58
Trumpeter swan, *Cygnus buccinator*, USA, 7 western states, 1976-87, found dead		
Liver, kidney, femur	96 (61-160) FW	118
Blood	5.2 (3.7-8.8) FW	118
Dutch Wadden Sea		
Knots, 3 species, recently-formed primary feathers		
Juveniles	100-400 DW	59
Adults	Max. 977 DW	59
Geese, 3 species, feather vane	93-164 DW; Max. 330 DW	59
Little egret, *Egretta garzetta*, France, found dead		
Bone	100 DW	60
Feather	80 DW	60
Gizzard	140 DW	60
Kidney	70 DW	60
Liver	120 DW	60
Lung	50 DW	60
Muscle	70 DW	60
Stomach	65 DW	60
Chicken, *Gallus* sp.		
Egg yolk	64 DW	61
Kidney	70 DW	61
Liver	69 DW	61
Liver	32 (25-56) FW	62
Pancreas	88 DW	61
Seminal plasma		

Age 30 weeks	9.8 FW	63
Age 60 weeks	9.8-25 FW	63
California condor, *Gymnogyps californianus*, dead on collection, 1980-86		
Nestlings (died from handling shock)		
Liver	22 FW	64
Kidney	17 FW	64
Juveniles (died from cyanide poisoning)		
Liver	33 FW	64
Feather	99-100 DW	64
Subadults (died from lead poisoning)		
Liver	30 FW	64
Kidney	33 FW	64
Feather	85 DW	64
Adults (died from lead poisoning), liver	27-250 FW	64
California, 1980-81, feather	46-130 DW	58
Kern County, California, 1976		
Liver	49 FW	65
Kidney	16 FW	65
White-tailed eagle, *Haliaeetus albicilla*		
Blood, clotted	7.5 FW	66
Brain	20 FW	66
Feather	88 DW	66
Femur	284 (175-390) DW	66
Heart	28 (21-39) FW	
Intestine	50 (27-76) FW	66
Kidney	43 (35-60) FW	66
Liver	68 (38-100) FW	66
Lung	14 (11-17) FW	66
Muscle	55 (42-80) FW	66
Stomach	25 (20-30) FW	66
Bald eagle, *Haliaeetus leucocephalus*, egg, 1968		
Wisconsin	30-56 DW; 4-8 FW	67
Maine	32-52 DW; 4-7 FW	67
Florida	36-65 DW; 5-8 FW	67
Glaucous gull, *Larus hyperboreus*		
Liver	32 (26-47) FW	68
Kidney	46 (37-57) FW	68
Turkey, *Meleagris gallopavo*		
Laying hens		
Serum	6.9 FW	117

Liver	75 DW	117
Nonlaying hens		
Serum	1.6 FW	117
Liver	39 DW	117
Red-breasted merganser, *Mergus serrator*, egg, Lake Michigan, 1978	15 (12-20) FW	69
Black-crowned night-heron, *Nycticorax nycticorax*, liver, prefledglings, 1979		
Massachusetts	602 (482-784) DW	70
North Carolina	649 (479-857) DW	70
Rhode Island	503 (246-885) DW	70
Osprey, *Pandion haliaetus*		
Eastern United States, 1975-82, liver		
Iowa	98 FW	71
Maryland	19-34 FW	71
Massachusetts	89 FW	71
New Jersey	63-120 FW	71
North Carolina	69 FW	71
South Carolina	73 FW	71
Wisconsin	59 FW	71
Virginia	27-150 FW	71
Eastern United States, 1964-73, liver		
Florida	27-36 FW	56
Maryland	18-93 FW	56
New Jersey	22 FW	56
Ohio	60-80 FW	56
All ospreys, liver		
Immatures	67 FW	56
Adults	38 FW	56
Brown pelican, *Pelecanus occidentalis*		
Egg contents		
South Carolina, 1971-72	6.4 (5.5-8.0) FW	119
Florida, 1969-70	6.4 (4.3-8.3) FW	119
Liver		
Found dead		
South Carolina, 1973	26 FW	119
Florida, 1972-73	41-50 FW	119
Georgia, 1972	33 FW	119
Shot		
Florida, 1970	32-55 FW	119

South Carolina, 1973	31-38 FW	119
Greater flamingo, *Phoenicopterus ruber*		
Bone	123 (103-145) DW	60,72
Feather		
Inner barbs	66 (38-105) DW	60,72
Outer barbs	101 (45-190) DW	60,72
Kidney	115 (90-167) DW	60,72
Liver	758 (525-963) DW	60,72,73
Lung	43 (33-56) DW	60,72
Muscle	53 (38-78) DW	60,72
Seabirds		
Albatrosses, 3 species		
Liver	(29-86) FW	68
Kidney	(31-65) FW	68
Fulmars, 2 species		
Liver	36-95 FW	68
Kidney	32-96 FW	
Penguins, 4 species		
Liver	(27-73) FW	68
Kidney	(25 -71) FW	68
Petrels, 7 species		
Liver	(28-81) FW	68
Kidney	(15-78) FW	68
Shearwaters, 2 species		
Liver	(28-54) FW	68
Kidney	(27-88) FW	68
Skuas, 3 species		
Liver	(21-51) FW	68
Kidney	(22-53) FW	68
South Atlantic Ocean, adults, 15 species		
Kidney	28-63 (15-88) FW	74
Liver	22-67 (18-86) FW	74
Spain, infertile eggs, 1985-86		
Golden eagle, *Aquila chrysaetos*	8.4 (5.5-11.9) FW	75
Buzzard, *Buteo buteo*	14 FW	75
White stork, *Ciconia ciconia*	9.8 (6.2-19.2) FW	75
Peregrine, *Falco peregrinus*	11.8 (8.8-16.7) FW	75
Booted eagle, *Hieraetus pennatus*	9.4 (7.7-13.0) FW	75
Black kite, *Milvus migrans*	12.6 (6.4-29.4) FW	75
Common blackbird, *Turdus merula*, from metals-contaminated area (1,750 mg Zn/kg DW soil), feathers of various age (days), feathers washed or unwashed before analysis		

4, unwashed	(100) DW	76
400, unwashed	(546) DW	76
26, washed	(90) DW	76
150, washed	(100) DW	76
400, washed	(162) DW	76
Hoopoe, *Upupa epops*, nestling feathers, age (days)		
7	(200) DW	77
21	(600) DW	77
35	(1,000) DW	77
Mammals		
Antelopes, zoo animals, 7 species, blood serum	4.6-9.4 (1.9-12.9) FW	78
Cattle, cow, *Bos* spp.		
Brain, fetus	50-86 DW	79
Feces		
Normal	220 DW	57
Zinc-poisoned	8,740 DW	57
Food items		
Cereal grains, normal	20-30 DW	80
Grasses, normal	25-60 DW	80
Turnips, beets, chicory roots, potatoes	67-390 DW	80
Hair, distance from Czechoslovakian power plant		
6 km	167 (114-199) FW	81
26 km	32 (21-43) FW	81
Heart, fetus	78-160 DW	79
Kidney		
Adult	92-133 DW	79
Age 2+ years	16 (13-17) FW	82
Fetus	83-251 DW	79
Normal	18 (11-56) FW; 80 DW	57, 82
Zinc-poisoned	670 DW	57
Liver		
Adult	116-150 DW	79
Age 2+ years	40 (27-49) FW	82
Fetus	548-703 DW	79
Normal	135 DW	57
Zinc-poisoned	2,000 DW	57
Milk, days postpartum		
0	21 FW	83
1	12 FW	83
30	6 FW	83

150	4 FW	83
Muscle, Age 2+ years	49 (28-80) FW	82
Dog, *Canis familiaris*		
Serum		
Normal	1.7 (0.6-2.0) FW	84
Zinc-poisoned	29 FW	84
Seminal plasma	1,750 DW	85
Spermatozoa		
Ejaculated	1,040 DW	85
Nonejaculated	150-180 DW	85
Goat, *Capra* sp., milk, days postpartum		
0	17-25 FW	83
1	8-15 FW	83
90	5-6 FW	83
150	3-5 FW	83
Red deer, *Cervus elaphus*, Germany		
Kidney	131 DW	86
Kidney cortex	33 (20-184) FW	87
Liver	111 DW	86
Bank vole, *Clethrionomys glareolus*		
Diet		
Spring	56-70 DW	88
July-December	37-43 DW	88
Bone	145-199 DW	88
Heart	69-74 DW	88
Kidney	79-91 DW	88
Liver	78-103 DW	
Muscle	44-51 DW	
Testes		
December-September	126-163 DW	88
October-November	ND	88
Hooded seal, *Cystophora cristata*, liver	57 FW	89
Indian elephant, *Elephas maximas*, serum		
Young, age <15 years	2.0 FW	90
Adult females	2.8 FW	90
Big brown bat, *Eptesicus fuscus*, captive colony, guano	340 DW	91
Horse, *Equus caballus*, near zinc smelter versus control location		
Kidney	150 DW vs. 17 DW	92
Liver	402 DW vs. 23 DW	92

Pancreas	788 DW vs. 7 DW	92
Serum	2.65 FW vs. 0.8-1.2 FW	92
Kidney cortex	41 FW	87
Plasma, mares, Australia		
All	0.5-1.2 FW	93
Thoroughbreds	0.47 FW	94
Farm horses		
Pregnant	0.52 FW	94
Lactating	0.44 FW	94
Northern sea lion, *Eumetopias jubata*		
Brain	(33-51) DW	95
Heart	(94-101) DW	9'5
Kidney	(99-202) DW	95
Liver	(102-247) DW	95
Lung	(42-69) DW	95
Muscle	(90-140) DW	95
Pancreas	(78-262) DW	95
Spleen	(56-117) DW	95
Long-finned pilot whale, *Globicephala melaena*, Newfoundland, Canada, stranded, 1980-82		
Blubber	1.5 (0.6-3.0) DW	96
Kidney	99 (58-139) DW	96
Liver	234 (68-716) DW	96
Muscle	62 (38-80) DW	96
Gorilla, *Gorilla gorilla gorilla*, captives, plasma	2.4 (0.9-7.3) FW	97
Gray seal, *Halichoerus grypus*		
Blubber	5 FW	14
Kidney	37 FW	14
Liver	84 FW	14
Muscle	43 FW	14
Human, *Homo sapiens*		
Diet		
Protein-rich foods (meat, seafood)	10-50 FW	113
Grains	10-100 FW	113
Vegetables, fruits	<5 FW	113
Erythrocytes	10. 1 - 13.4 FW	98
Hair	>105 FW	98
Milk	3 FW	113
Plasma	0.7-1.6 FW	97,98
Prostate	100 FW	113
Semen	100-350 FW	19
Skin	20-1,000 DW	19

White-beaked dolphin, *Lagenorhynchus albirostris*, Newfoundland, Canada, ice-entrapped, 1980-82, 2-6 years old		
Kidney	85 (68-112) DW	96
Liver	100 (43-136) DW	96
Muscle	53 (36-89) DW	96
Rhesus monkey, *Macaca mulatta*, plasma	0.66-0.98 FW	99
Marine mammals		
Pinnipeds, 9 species		
Liver	(27-97) FW; (123-406) DW	68
Kidney	(11-78) FW; (146-353) DW	68
Muscle	(14-49) FW	68
Cetaceans, 9 species		
Liver	(18-109) FW	68
Kidney	(4-86) FW	68
Muscle	(7-51) FW	68
Sirenians		
Liver	(58-1,101) FW	68
Kidney	(14-54) FW	68
Muscle	(8-28) FW	68
Southeastern bat, *Myotis austroriparius*, Florida, 1981-83, liver		
Near battery salvage plant	31 (27-35) FW	91
Noncontaminated site	28 (26-30) FW	91
Gray bat, *Myotis grisescens*, Florida, 1981-83, guano		
Near battery salvage plant	640 DW	91
Distant sites	390-530 DW	91
Mule deer, *Odocoileus hemionus*, Montana		
Kidney	97 FW	86
Liver	113 FW	86
White-tailed deer, *Odocoileus virginianus*		
Illinois, liver	70 DW	86
Pennsylvania, various distances from zinc smelter		
< 8 km		
Feces	577 (185-1,797) DW	86
Kidney	310 (211-454) DW	86
Liver	167 (137-205) DW	86

10-20 km		
Feces	574 (1,384) DW	86
Kidney	274 (212-355) DW	86
Liver	167 (137-205) DW	86
>100 km		
Feces	185 (77-445) DW	86
Kidney	145 (103-205) DW	86
Liver	132 (95-182) DW	86
Sheep, *Ovis* sp., kidney	22 (14-38) FW	62
Ringed seal, *Phoca hispida*.		
Liver	176 (121-576) DW	100
Kidney	209 (104-441) DW	100
Muscle	79 (52-135) DW	100
Harbor porpoise, *Phocoena phocoena*		
Blubber	4 FW	14
Liver	37 FW	14
Muscle	22 FW	14
Dall's porpoise, *Phocoenoides dalli*		
Adults		
Bone, skin	270-296 FW	101
Heart, liver, pancreas, kidney, whole body	25-51 FW	101
Brain, lung, testes	11-20 FW	101
Blubber, blood, muscle	4-9 FW	101
Fetus		
Liver	82 FW	101
Other tissues	<6 FW	101
Rat, *Rattus* sp., spermatozoa		
Ejaculated	890 DW	85
Nonejaculated	860 DW	85
Striped dolphin, *Stenella coeruleoalba*		
Blubber	16 FW	14
Muscle	11 FW	14
Pig, *Sus* spp., adults		
Kidney	22 (16-33) FW	62,82
Liver	74 (28-160) FW	82
Muscle	24 (8-53) FW	82
Bottle-nosed dolphin, *Tursiops truncatus*		
Blubber	20 FW	14
Muscle	11 FW	14
Polar bear, *Ursus maritimus*		
Kidney	33 (20-49) FW	120
Liver	58-63 (33-100) FW	58,120

Integrated studies		
Electrical transmission towers		
(corroded, galvanized), Ontario, Canada		
Soils		
Near towers	11,480 DW	102
1 km	10,431 DW	102
2 km	10,869 DW	102
5 km	362 DW	102
10 km	160 DW	102
25-50 km	54-70 DW	102
Plants, 5 species, roots and shoots		
Near towers	Max. 1,535 DW	102
1-5 km	Max. 297 DW	102
12-25 km	Max. 55 DW	102
Estuary, Calcasieu River, Louisiana		
Invertebrates		
Periphyton, whole	264 (49-1,300) DW	103
Zooplankton, whole	330 (31-3,550) DW	103
Ctenophores, whole	31-64 DW	103
Hooked mussel,	61 (39-86) DW	103
Brachidontes exustus, soft parts		
American oyster,	3,300 (1,000-7,794) DW	103
Crassostrea virginica, soft parts		
Blue crab, *Callinectes sapidus*, muscle	112 (106-213) DW	103
Brown shrimp, *Penaeus aztecus*, whole	46-61 DW	103
White shrimp, *Penaeus setiferus*, whole	44-62 DW	103
Fish, muscle		
Gulf menhaden, *Brevoortia patronus*	115 DW	103
Gizzard shad, *Dorosoma cepedianum*	25 DW	103
Threadfin shad, *Dorosoma petenense*	29 DW	103
Blue catfish, *Ictalurus furcatus*	35 (16-61) DW	103
Spot, *Leiostomus xanthurus*	22 (217-31) DW	103
Spotted gar, *Lepisosteus oculatus*	(22-239) DW	103
Atlantic croaker, *Micropogonias undulatus*	31 (15-95) DW	103
White mullet, *Mugil curema*	86 DW	103
Southern flounder, *Paralichthys lethostigma*	24 DW	103
Flotation mill (lead-zinc),		
Greenland		
Near outfall		
Suspended particulates	11,600 (1,058-25,700) FW	104
Sediments	Max. 6,799 FW	104
Water	0.035 FW	104

Mussel, *Mytilus edulis*, soft parts	502 (340-813) FW	104
Seaweed, *Fucus disticus*	300 FW	104
Control site		
Suspended particulates	123 FW	104
Sediments	129 FW	104
Water	0.0002 FW	104
Mussel	100 FW	104
Seaweed	8 FW	104
Freshwater lake, India		
Water	0.2 FW	105
Sediment	540 FW	105
Phytoplankton	11-15 FW	105
Zooplankton	60 FW	105
Fish, whole	10 FW	105
Grassland ecosystem		
On a revegetated mine tailings dam		
Soil (1-8 cm depth)	1,915-2,160 DW	106
Vegetation		
Live	157-201 DW	106
Dead	303-646 DW	106
Invertebrates, whole		
Herbivores	355-746 DW	106
Carnivores	403-515 DW	106
Detritivores	769-1,275 DW	106
Field vole, *Microtus agrestis*		
Bony tissues	183-226 DW	106
Soft tissues	160-281 DW	
Common shrew, *Sorex araneus*		
Bony tissues	438-547 DW	
Soft tissues	160-281 DW	106
Control grassland ecosystem		
Soil (1-8 cm depth)	52-62 DW	106
Vegetation		
Live	23-41 DW	106
Dead	24-56 DW	196
Invertebrates, whole		
Herbivores	133-299 DW	106
Carnivores	277-372 DW	106
Detritivores	248-1,095 DW	106
Field vole		
Bony tissues	178-249 DW	106
Soft tissues	53-121 DW	106

Common shrew		
Bony tissues	847-420 DW	106
Soft tissues	145-204 DW	106
Lead smelter, South Australia, marine outfall, whole organisms		
Samples collected 2.5-5.2 km from source		
Sediments	1,270 DW; Max. 16,700 DW	107
Seagrasses, 5 species	823 DW; Max. 3,540 DW	107
Crustaceans, 5 species	148 DW; Max. 767 DW	107
Tunicate, *Polycarpa pediculata*	153 DW; Max. 345 DW	107
Bivalve molluscs, 5 species	4,880 DW; Max. 20,300 DW	107
Carnivorous fish, 8 species	163 DW; Max. 440 DW	107
Omnivorous fish, 3 species	222 DW; Max. 619 DW	107
Herbivorous fish, six-lined trumpeter, *Siphamia cephalotes*	310 DW; Max. 480 DW	107
Samples collected 18-18.8 km from outfall		
Sediments	21 DW	107.
Seagrasses	72 DW	107
Crustaceans	68 DW	107
Tunicate	98 DW	107
Bivalve molluscs	2,590 DW	107
Carnivorous fish	78 DW	107
Omnivorous fish	105 DW	107
Herbivorous fish	97 DW	107
Metals-contaminated forest versus control location, Poland		
Yellow-necked field mouse, *Apodemus flavicollis*		
Liver	119 DW vs. 109 DW	108
Kidney	220 DW vs. 87 DW	108
Hair	179 DW vs. 122 DW	108
Carcass	109 DW vs. 98 DW	108
Bank vole, *Clethrionomys glareolus*		
Liver	120 DW vs. 116 DW	108
Kidney	156 DW vs. 143 DW	108
Hair	243 DW vs. 169 DW	108
Carcass	148 DW vs. 153 DW	108
Old-field community, Ohio, treated with sewage sludge for 10 consecutive years		
Treated area		
Sludge	866 DW	109
Soil	107 DW	109
Perennial plant, *Rubus frondosus*	41 DW	109
Giant foxtail, *Setaria faberii*	97 DW	109

Earthworm, *Lumbricus rubellus*	615 DW	169
Bluegrass, *Poa* spp.	85 DW	109
Japanese brome, *Bromus japonicum*	80 DW	109
Control area		
Perennial plant	14 DW	109
Bluegrass	35 DW	109
Japanese brome	35 DW	109
Zinc smelter, Palmerton, Pennsylvania		
Site 2 km downwind of smelter		
Soil	24,000 DW	110
Foliage, 8 species	660 DW	110
Acorns and berries, 4 species	59 DW	110
Fungi, 4 species	320 DW	110
Moths, 6 species	250-480 DW	110
Beetle, *Dendroides* sp.	1,450 DW	110
Caterpillar, *Porthetria dispar*	280 DW	110
Birds, 10 species, carcasses	140 (93-210) DW	110
White-footed mouse, *Peromyscus leucopus*, carcass	192 DW	110
Short-tailed shrew, *Blarina brevicauda*, carcass	377 DW	110
Site 10 km upwind of smelter		
Soil	960 DW	110
Foliage	118 DW	110
Acorns and berries	27 DW	110
Fungi	120 DW	110
Moths, 9 species	140-340 DW	110
Beetles, 2 species	470 DW	110
Caterpillar, *P. dispar*	170 DW	110
Birds, 10 species, carcasses	120 (78-170) DW	110
White-footed mouse, carcass	145 DW	110
Short-tailed shrew, carcass	201 DW	110
Zinc smelter, Peru, South America, 1980-84		
Soil, kilometers from smelter		
1	575 DW	111
13	183 DW	11]
27	154 DW	111
33	52 DW	111
35-55	16-29 DW	111
Domestic sheep, *Ovis aries*, liver, kilometers from smelter		
13	305 DW	111
29	165 DW	111

>100	77 DW	111
Zinc smelters, various		
Soils	Max. 80,000 DW	112
Trees, foliage	Max. 4,500 DW	112

[a] Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

[b] 1. Mann et al. 1989; 2. Mason and Macdonald 1988; 3. Young et al. 1980; 4. Brix and Lyngby 1982; 5. Veleminsky et al. 1990; 6. Greville and Morgan 1989a; 7. Greville and Morgan 1989; 8. Beyer and Cromartie 1987; 9. Morgan and Morgan 1988; 10. Nash 1975; 11. Hopkin et al. 1989; 12. Hopkin et al. 1986; 13. Eisler 1981; 14. Morris et al. 1989; 15. Sullivan et al. 1988; 16. White and Rainbow 1985; 17. Sprague 1986; 18. Prestey et al. 1990; 19. NAS 1979; 20. Cain and Luoma 1986; 21. Amiard et al. 1986; 22. Lobel 1986; 23. Amiard-Triquet et al. 1988; 24. Bryan et al. 1987; 25. Chan 1988a; 26. Chu et al. 1990; 27. Eisler et al. 1978; 28. Weeks and Moore 1991; 29. Rainbow 1989; 30. Anil and Wagh 1988; 31. Walker et al. 1975; 32. Ridout et al. 1989; 33. Cutshall et al. 1977; 34. Waiwood et al. 1987; 35. Bagatto and Alikhan 1987; 36. Khan et al. 1989; 37. Nugegoda and Rainbow 1998b; 38. Shrestha and Morales 1987; 39. Fernandez and Jones 1989; 40. Schmitt et al. 1984; 41. Munkittrick and Dixon 1989; 42. Peterson et al. 1989; 43. Bezuidenhout et al. 1990; 44. Lazos et al. 1989; 45. Lowe et al. 1985; 46. Murphy et al. 1978; 47. Schmitt and Finger 1987; 48. Vas et al. 1990; 49. Hanna 1989; 50. Joseph 1989; 51. Craik and Harvey 1988; 52. Poston and Ketola 1989; 53. Grady et al. 1989; 54. Heinz et al. 1991; 55. Warren et al. 1990; 56. Wiemeyer et al. 1980; 57. Zee et al. 1985; 58. Wiemeyer et al. 1986; 59. Goede 1985; 60. Cosson et al. 1988; 61. Williams et al. 1989; 62, Ellen et al. 1989; 63. Blesbois and Mauger 1989; 64. Wiemeyer et al. 1988; 65. Wiemeyer et al. 1983; 66. Falandysz et al. 1988; 67. Krantz et al, 1970; 08. Thompson 1990; 69. Haseltine et al. 1981; 70. Custer and Mudhern 1983; 71. Wiemeyer et al. 1987; 72. Cosson et al. 1988a; 73. Cosson 1989; 74. Muirhead and Furness 1988; 75. Hernandez et al. 1988; 76. Weyers et al. 1988; 77. Kaur 1989; 78. Vahala et al. 1989; 79. Gooneratne and Christensen 1989; 80. Binnerts 1989; 81. Pisa and Cibulka 1989; 82. Jorhem et al. 1989; 83. Park and Chukwu 1989; 84. Latimer et al. 1989; 85. Saito et al. 1967; 86. Sileo and Beyer 1985; 87. Holterman et al. 1984; 88. Wlostowski et al. 1988; 89. Nielsen and Dietz 1990; 943. Sreekumar and Nirmalan 1989; 91. Clark et al. 1986; 92. Gunson et al. 1982; 93. Auer et al. 1988b; 94. Auer et al. 1988a; 95. Hamanaka et al. 1982; 96. Muir et al. 1988; 97. McGuire et al. 1989; 98. Casey and Hambidge 1980; 99. Keen et al. 1989; 100. Wagemann 1989; 101. Fujise et al. 1988; 102. Jones and Burgess 1984; 103. Ramelow et al. 1989; 104. Loring and Astound 1989; 105. Prahalad and Seenayya 1989; 106. Andrews et al. 1989; 107. Ward et al. 1986; 108. Sawicka-Kapusta et al. 1987; 109. Levine et al. 1989; 110 Beyer et al. 1985; 111. Reif et al. 1989; 112. Buchauer 1971; 113. Elinder 1986; 114. Vymazal 1986; 115. Dwyer et al. 1988; 116. Willis 1985a; 117. Richards 1989; 118. Blus et al. 1989; 119. Blus et al. 1977; 120. Norheim et al. 1992; 121. Schmitt and Brumbaugh 1990.

Terrestrial plants growing beneath corroded galvanized fencing have been poisoned by zinc (Jones and Burgess 1984). Vegetables are relatively low in zinc, but growing plants can accumulate zinc applied to soils (Geyer 1986). High soil level of zinc is the primary cause of vegetation damage near zinc smelters (Buchauer 1971; Leonard and Gerber 1989). Elevated zinc concentrations in soils near zinc smelters inhibit seedling root elongation and probably prevent establishment of invader species in denuded areas (Buchauer 1971). Lichen species richness and abundance were reduced by about 90% in lichen communities near a Pennsylvania zinc smelter; elevated zinc concentrations were the probable cause of the impoverished lichen flora (Nash 1975). Soils and vegetation surrounding zinc smelters in Palmerton, Pennsylvania were grossly contaminated with zinc, cadmium, and lead. Zinc was primarily responsible for the destruction of trees and subsequent erosion of the soil, reductions in moss and lichen flora, reductions in litter arthropod populations, and reductions in species diversity of soil fungi and bacteria; zinc residues were elevated in slugs and millipedes (Sileo and Beyer 1985; Beyer 1988). Soil litter invertebrates were rare or absent 2 km downwind of the smelter; unlike soil litter invertebrates from more distant sites, invertebrates collected up to 10 km upwind of the smelters had significantly elevated zinc concentrations (Beyer et al. 1985).

The maximum zinc concentration in earthworms collected from a contaminated site was 1,600 mg/kg DW whole animal; for uncontaminated sites it was 650 mg/kg (Beyer and Cromartie 1987). Whole body zinc concentrations in earthworms (*Dendrodrilus rubidus*, *Lumbricus rubellus*) tended to reflect zinc concentrations in

soil, although zinc accumulations in both species seem to be physiologically regulated when soil zinc values exceeded 1,000 mg/kg DW (Morgan and Morgan 1988).

Whole body zinc content of terrestrial isopods seems to reflect soil zinc levels and may be a useful indicator of soil contamination (Hopkin et al. 1989). *Porcellio scaber*, a terrestrial isopod known as a woodlouse, is recommended as a biological indicator of zinc contamination because of the positive correlation between zinc content in soil or leaf litter and woodlouse hepatopancreas. Zinc content in *Porcellio*, litter, and soil near a zinc smelter was >1,000 mg/kg DW in whole isopod, >9,000 mg/kg DW in hepatopancreas, > 10,000 mg/kg DW in litter, and >50,000 mg/kg DW in soil (Hopkin et al. 1986).

Interspecies variability in zinc content of terrestrial invertebrates is large and governed by numerous modifiers. For example, whole body zinc content in closely-related species of terrestrial gastropods collected from a single contaminated site was between 600 and 1,200 mg/kg DW (Greville and Morgan 1989a). In grey field slugs (*Deroceras reticulatum*), zinc was highest in late spring and lowest in summer and positively correlated with tissue cadmium concentrations; starvation for 16 days had no effect on body zinc concentrations (Greville and Morgan 1989b). Zinc tends to concentrate in mechanical structures of various invertebrates, such as mandibular teeth. High concentrations of zinc are reported in jaws of polychaete worms, cutting edges of the mandibles of herbivorous insects, mandibles of various species of beetles, copepod mandibles, chaetognath teeth and spines, mandibular teeth of ants, and fangs of spiders (Schofield and Lefevre 1989). Honey bees (*Apis mellifera*) collected near a lead smelting complex at East Helena, Montana, had depressed whole body zinc concentrations despite increased ambient air zinc values; however, whole body burdens of arsenic, cadmium, copper, and lead were significantly elevated and may have influenced zinc kinetics (Bromenshenk et al. 1988). Also, pollen was usually the most indicative source of zinc and other heavy metals in bees (Veleminsky et al. 1990).

Aquatic Organisms

Concentrations of zinc in tissues of aquatic organisms are usually far in excess of that required for normal metabolism. Much of the excess zinc is bound to macromolecules or present as insoluble metal inclusions in tissues (Eisler 1981, 1984; EPA 1987). Diet is the most significant source of zinc to aquatic organisms and is substantially more important than uptake from seawater (Eisler 1981, 1984). In general, zinc concentrations in sediments and tissues of aquatic organisms are elevated in the vicinity of smelters and other point sources of zinc and decrease with increasing distance (Ward et al. 1986; Table 4).

Freshwater algae in Canadian mine tailing environments heavily concentrate zinc and other metals and may retard metal dispersion through the water column (Mann and Fyfe 1988). Zinc levels in field collections of marine algae and macrophytes are usually at least several orders of magnitude higher than zinc concentrations in the surrounding seawater (Eisler 1981). In general, concentrations in marine aquatic flora were high when seawater zinc concentrations were elevated, although the relation was not linear. Marine flora, especially red and brown algae, are among the most effective marine zinc accumulators. Increasing accumulations of zinc in marine algae were associated with decreasing light intensity, decreasing pH, increasing temperature, decreasing levels of DDT, and increasing oxygen. Ionic zinc was accumulated more rapidly than other forms of zinc (Eisler 1981). Many species of marine algae had zinc concentrations >1 g/kg DW (Eisler 1980). These grossly elevated levels were usually associated with nearby industrial or domestic outfalls containing substantial amounts of zinc (Eisler 1981). In eelgrass (*Zostera marina*), zinc concentrations increased with age of leaf (Brix and Lyngby 1982).

In the Fal estuary, England, long-term metal pollution during the past 120 years resulted in zinc sediment levels between 679 and 1,780 mg/kg DW, producing benthic communities that favor zinc-tolerant organisms, such as oysters and nereid polychaetes, and a general impoverishment of mussels, cockles, non-nereid polychaetes, and gastropods (Bryan et al. 1987).

Zinc in molluscs is usually associated with high molecular weight proteins, with diet (as opposed to ambient water zinc concentrations), from collection locales with elevated sediment zinc burdens, and with particulate matter from dredging and storm perturbations (Eisler 1981). Zinc levels in molluscs were highest in animals collected near anthropogenic point sources of zinc. Excess zinc accumulations do not seem to affect normal molluscan life processes, and zinc is frequently accumulated far in excess of the organism's immediate needs (Eisler 1981). American oysters (*Crassostrea virginica*), for example, may naturally contain up to 4 g Zn/kg FW

soft parts; this is comparable to accumulations observed in oysters exposed to 0.2 mg Zn/L for 20 weeks (NAS 1979). Zinc tends to accumulate in the molluscan digestive gland and stomach as excretory granules and in the kidney as concretions (Eisler 1981; Sprague 1986; Sullivan et al. 1988). The preferred storage site in mussels and scallops is the kidney and in oysters, the digestive gland (Sprague 1986). In oysters, granules may contain up to 60% of the total body zinc, explaining, in part, how some shellfish can exist with such high body burdens (Sprague 1986).

Zinc in molluscan tissues is usually elevated under conditions of increasing water temperature and pH and decreasing salinity (Eisler 1981); however, zinc accumulation kinetics in molluscs vary considerably among species (Chu et al. 1990). Variations in zinc content of clam tissues were associated with seasonal changes in tissue weights (Cain and Luoma 1986). Unlike conspecifics collected at more distant sites, gastropods nearest a ferronickel smelter had elevated zinc concentrations in the hepatopancreas; however, there were no consistent seasonal variations (Nicolaidu and Nott 1990). Fluctuations in zinc content of common mussels (*Mytilus edulis*) related to size or season of collection were sufficient to conceal low chronic or short-term pollution (Amiard et al. 1986). Diet, which is the primary route of zinc accumulation in most molluscs, had no significant effect on whole body zinc content of certain predatory marine gastropods. Whole body zinc concentrations of gastropod oyster drills (*Ocenebra erinacea*) were between 1,451 and 2,169 mg/kg DW and remained unchanged after feeding for 6 weeks on Pacific oysters (*Crassostrea gigas*) containing 1,577 mg Zn/kg DW or common mussels (*Mytilus edulis*) containing 63 mg Zn/kg DW (Amiard-Triquet et al. 1988).

High zinc concentrations in crustaceans are usually associated with industrial contamination. In barnacles (*Balanus* spp.), high (>3.3 g/kg DW soft parts) levels are attributed to inorganic granules that contain up to 38% zinc and that accumulate in tissue surrounding the midgut (Eisler 1980, 1981). In descending order of chemical abundance, the granules consist of phosphorus, zinc, potassium, sulfur, and chlorine (Thomas and Ritz 1986). These insoluble, membrane-limited spheres form in response to high zinc levels in the ambient seawater within 12 days of exposure and concentrate in specified cells around the gut: the stratum perintestinale (Walker et al. 1975; Sprague 1986; Thomas and Ritz 1986). Zinc granules in barnacles represent a detoxification mechanism for surplus zinc (Thomas and Ritz 1986). Older barnacles have greater whole body zinc accumulations than younger stages, and accumulations change seasonally (Anil and Wagh 1988). Zinc concentrations in marine crustacean tissues are usually <75 mg/kg FW or <100 mg/kg DW; exceptions include hepatopancreas, molts, eggs, fecal pellets, and barnacles (Table 4). In crustaceans, zinc is slightly elevated in hepatopancreas but in most tissues only 2 to 3 times higher than in muscle (Sprague 1986). For marine crustaceans, the highest concentration recorded in muscle was 57 mg Zn/kg FW in the king crab, *Paralithodes camtschatika* (NAS 1979), and was associated with two metal binding proteins of molecular weight 11,500 and 27,000 (Eisler 1981). In crustacean tissues, zinc levels were higher in summer at lower salinities and in young animals (Eisler 1981), although young amphipods had higher zinc residues than older stages (Rainbow 1989). Seasonal accumulations of whole body zinc in the shrimp (*Palaemon serratus*) during spring and summer and loss in winter seem to reflect water zinc concentrations in the range of 0.0 to 9.0 µg/L (Alliot and Frenet-Piron 1990). Zinc is present in crustacean serum at concentrations >1,000 times greater than in ambient seawater in serum, it serves primarily as a cofactor of carbonic anhydrase--the principal enzyme involved in calcification. Serum zinc concentrations in crustaceans seem to be independent of season and water temperature or salinity (Sprague 1986).

Molting results in a 33-50% loss of total zinc in marine crustaceans; molts, together with fecal pellets, constitute an important vehicle of zinc transfer in marine ecosystems (Eisler 1981). The freshwater opossum shrimp (*Mysis relicta*) can transport zinc from sediments into the water column and in the reverse during their migratory cycle. *Mysis relicta* and other benthic invertebrates play an important role in determining the concentration of zinc and other metals in lake sediments (Van Duyn-Henderson and Lasenby 1986). Unlike decapod crustaceans, marine amphipods do not regulate body zinc concentrations; amphipod body burdens of zinc may reflect sediment total zinc levels and suggest that certain groups may be suitable bioindicators (Rainbow et al. 1989). Molting had no effect on body zinc concentration in four species of adult marine amphipods (Weeks and Moore 1991), and this forces a reexamination of the role of cast exuviae in zinc transport.

In annelids, zinc content was highest in nonselective deposit feeders, omnivores, and carnivores and from animals collected from sediments with elevated zinc levels (Eisler 1981). Freshwater tubificid worms have the potential to increase zinc concentrations in the water column, particularly during short episodes of high

burrowing activity (Krantzberg and Stokes 1985). A high zinc content seems to be a structural characteristic of jaws of marine nereid worms (Table 4). In the marine polychaete worm *Nereis diversicolor*, zinc is localized in the gut wall, epidermis, nephridia, and blood vessels; most of the body zinc is present in wandering amoebocytic cells of excretory organs. Zinc in *Nereis* may be present as insoluble granules in membrane bound vesicles; excretion is through exocytosis with the aid of amoebocytes (Fernandez and Jones 1989). Unlike the insoluble zinc phosphate granules of molluscs and crustaceans, zinc granules in *Nereis* were very soluble and retained only by sulfide precipitation (Pirie et al. 1985).

Marine vertebrates, including fish and elasmobranchs, have lower zinc concentrations in tisues (6-400 mg/kg DW) than marine plants and invertebrates (Eisler 1980, 1981, 1984). Highest concentrations in muscle of marine fish (20.1-25.0 mg/kg FW) were recorded in the northern anchovy (*Engraulis mordax*) and the Atlantic menhaden (*Brevoortia tyrannus*; NAS 1979). The highest zinc concentrations measured in whole freshwater fish in the conterminous United States in 1978-79 were in common carp (*Cyprinus carpio*) from Utah; concentrations in carp from Utah were between 70 and 168 mg Zn/kg FW versus an average of 63 mg Zn/kg FW for this species collected elsewhere (Lowe et al. 1985). Zinc concentrations in fish tend to be higher near urban areas (Peterson et al. 1989); highest in eggs, viscera and liver (Eisler and LaRoche 1972; Eisler 1981); lowest in muscle (Eisler 1981); positively correlated with metallothionein concentrations (Overnell et al. 1987b); lower in all tissues with increasing age and growth (Eisler and LaRoche 1972; Eisler 1981, 1984; Grady et al. 1989); and relatively unaffected by water salinity, temperature, or copper concentrations (Eisler and LaRoche 1972; Eisler 1981). Zinc residue data from marine fish that were dead on collection are of limited worth because dead fish accumulate zinc from seawater at a substantially higher rate than living teleosts (Eisler 1981).

Zinc concentrations in fish and other aquatic vertebrates are modified by diet, age of the organism, reproductive state, and other variables. In fish, diet is the major route of zinc uptake and juveniles accumulate zinc from the medium more rapidly than embryos or larvae (Cutshall et al. 1977; Eisler 1981). Because the diet of many teleost carnivores changes drastically with age and because upper trophic level vertebrates are frequently used as indicators of water quality, more research into zinc burdens in prey organisms is needed (Eisler 1984). A reduction in serum zinc during egg formation in a flatfish (*Pleuronectes platessa*) may represent a transfer of zinc to eggs (Overnell et al. 1987b). High (>35 mg/kg FW) zinc concentrations in eggs of Atlantic salmon are sometimes associated with increasing mortality, although low (14 mg/kg FW) concentrations seem to have no adverse effect on survival (Craik and Harvey 1988). Zinc concentrations in Atlantic salmon milt ranged from 0.5 to 5.5 mg Zn/kg and was linearly proportional to spermatozoan abundance (Poston and Ketola 1989). In lakes containing 1,150 mg Zn/kg sediment and 209-253 µg Zn/L water column, white sucker (*Catostomus commersoni*) females did not grow after sexual maturity and had increased incidences of spawning failure. Alterations in growth and reproduction were related, in part, to nutritional deficiencies as a result of chronic effects of elevated sediment zinc on the food base of the sucker, that is, invertebrate fauna were absent in the uppermost 7 m (Munkittrick and Dixon 1988). Eggs of the white sucker incubated at a metals-contaminated site (400 µg Zn/L), but not eggs of conspecifics, at a noncontaminated (2.7 µg Zn/L) site, produced larvae with a decreased tolerance to copper and with elevated zinc body burdens; larval size and fertilization rate were the same at both sites (Munkittrick and Dixon 1989).

Birds

Zinc residues were elevated in birds collected near zinc smelters (Beyer 1988). In general, the highest concentrations of zinc in birds are in the liver and kidney and the lowest in muscle (Eisler 1981, 1984). In giant Canada geese (*Branta canadensis maxima*), more zinc is contained in red muscle than in white muscle and more in slow contracting muscle than in fast muscle (Rosser and George 1986). Zinc concentrations in marine birds normally are between 12 mg/kg FW in eggs and 88 mg/kg FW in the liver. The highest recorded concentration of zinc in a marine bird was 541 mg/kg DW in the liver of a booby (*Sula* sp.) that died from polychlorinated biphenyl poisoning. Elevated zinc levels in these birds may have been a manifestation of toxicant-induced stress (i.e., breakdown in osmoregulatory processes), as in other taxonomic groups (Eisler 1981). Seabirds with high zinc concentrations in the liver and kidney tend to have high cadmium levels in these tissues (Muirhead and Furness 1988). In flamingos, zinc in the liver positively correlated with copper levels in the liver and kidney and with metallothionein levels in the kidney (Cosson 1989). In egrets, zinc positively correlated with metallothionein protein levels in the liver (Cosson 1989). In blue-winged teals (*Anas discors*), zinc concentrations were higher in the liver than in muscle, higher in males than in females, and higher in

autumn than in spring (Warren et al. 1990). Zinc concentrations in the liver of black-crowned night-herons (*Nycticorax nycticorax*) were usually higher in younger birds, although weight and sex had no direct effect on zinc content (Custer and Mulhern 1983). Zinc concentrations in tissues and feathers of dead California condors (*Gymnogyps californianus*) that had died from a variety of causes (Table 4) were similar to those in turkey vultures (*Cathartes aura*), common ravens (*Corvus corax*), and ospreys (*Pandion haliaetus*) and are considered normal (Wiemeyer et al. 1988). The highest recorded concentration in condor liver of 250 mg/kg FW approaches those in livers of mallards (*Anas platyrhynchos*) that died from high dietary loadings of zinc (Wiemeyer et al. 1988). Zinc concentrations in the liver of ospreys were similar between age groups and sexes (Wiemeyer et al. 1987). With the onset of egg production in turkeys (*Meleagris gallopavo*), serum zinc in hens increased from 1.6 to 6.9 mg/L and remained significant elevated throughout egg laying; during this same period, zinc concentration in the liver declined from 75 to 39 mg/kg DW, although total zinc in the liver increased because of an increase in liver weight (Richards 1989a).

Zinc concentrations in the sediments of the Rhine River increased about 6 times between 1900 and 1950 and have remained stable since then. But migratory waterfowl from this collection locale do not have elevated zinc concentrations in their primary feathers (Goede 1985). Zinc content in feathers of the hoopoe (*Upupa epops*) increased from 200 mg/kg DW at age 7 days to 1,000 mg/kg DW at age 35 days (Kaur 1989). Hoopoe populations are declining in India and this decline is said to be associated with increasing zinc concentrations in feathers (Kaur 1989). Feathers of the greater flamingo (*Phoenicopterus ruber*) are proposed indicators of atmospheric zinc contamination: the average zinc content was 53% more in outer barbs of the black primary feathers exposed to air pollution than in inner barbs (Cosson et al. 1988a). More research into the use of feathers as indicators of zinc contamination is needed.

Zinc concentrations in seminal plasma are about 100 times lower in domestic chickens (*Gallus* sp.) than in humans and most other mammals, except sheep. Concentrations of zinc in fowl seminal plasma after in vivo storage of spermatozoa for 24 h at 4°C were near the threshold values toxic to spermatozoa (Blesbois and Mauger 1989), suggesting that poultry spermatozoa normally function near their lower lethal zinc threshold.

Mammals

White-tailed deer (*Odocoileus virginianus*) collected near a zinc smelter, but not conspecifics from more distant sites, had elevated tissue zinc concentrations. Deer with zinc concentrations of 150 mg/kg FW (750 mg/kg DW) in the renal cortex potion of the kidney had swollen joints, lameness, and joint lesions similar to those of zinc-posioned horses from the same area (Sileo and Beyer 1985). Zinc was elevated in the kidney cortex of red deer (*Cervus elaphus*) and older deer tended to have higher concentrations (as high as 184 mg/kg DW) than younger deer (as low as 20 mg/kg FW); in older deer, zinc was associated with the metallothionein fraction (Holterman et al. 1984). Zinc residues were usually elevated in rodents near smelters (Beyer et al. 1988). Rodents from metals-contaminated forests had zinc loadings in tissues similar to those from control locations, although lead and cadmium were significantly elevated in the contaminated zone (Sawicka-Kapusta et al. 1987). Elevated zinc concentrations in mine tailings reportedly do not represent a notable contamination hazard to the invading mammalian fauna, although zinc concentrations in invertebrates, especially earthworms, and vegetation were elevated (Andrews et al. 1989; Table 4).

Otters (*Lutra lutra*) were found only on a single unpolluted tributary of a river system contaminated by zinc mine drainage waste, suggesting that a contaminated food supply may be responsible for the avoidance by otters of otherwise suitable habitat (Mason and Macdonald 1988).

Marine mammals collected near heavily urbanized or industrialized areas or near zinc pollution point sources, but not individuals of the same species and of similar age from relatively pristine environments, usually had elevated zinc concentrations (Eisler 1984). Zinc concentrations in tissues of the ringed seal (*Phoca hispida*) were essentially the same in animals near a lead-zinc mine and in animals in a distant reference site, although lead and selenium burdens were elevated in the vicinity of the mine site (Wagemann 1989). Concentrations of zinc in tissues of the Northern sea lion (*Eumetopias jubata*) were highest in the liver and pancreas and next highest in descending order in the kidney, muscle, heart, spleen, and lung; this rank order is comparable to that in human tissues (Hamanaka et al. 1982). There is considerable variation among species in tissue zinc concentrations; threefold differences are not uncommon for the same tissue in different species of marine mammals (Muir et al. 1988). Marine mammals contained the lowest zinc concentrations (2-505 mg/kg DW, elevated in the liver) of all groups of marine organisms examined. Because zinc is usually available in sufficient

quantity in the marine environment and is usually accumulated in excess of the organism's immediate needs, it remains unclear why zinc is comparatively depressed in tissues of marine mammals (Eisler 1981).

Zinc toxicosis in horses near a zinc smelter was characterized by lameness, swollen joints, and unkempt appearance, particularly in foals. Zinc concentrations in afflicted foals, but not in foals at more distant sites, were elevated in the pancreas, liver, kidney, and serum (Gunson et al. 1982). Foals born near the smelter had joint swellings that were attributable to generalized osteochondrosis; lesions were similar to those induced experimentally in animals fed high zinc diets and may have been the result of a zinc-induced abnormal copper metabolism (Gunson et al. 1982). Concentration of zinc in tissues of horses from farms near the Palmerton smelter were extremely high and approaching lethal thresholds in some cases; zinc poisoning was a cause of debility and death of foals (Sileo and Beyer 1985). Grazing mares managed with standard husbandry had significant monthly variations in plasma zinc because, in part, of dietary factors such as nutritional supplementation and seasonal variations in the quality of grazing pasture (Auer et al. 1988b). Peak plasma zinc levels in horses positively relate to age (in weanlings age 22-52 weeks) and to summer diets (Cymbaluk and Christison 1989).

Dairy cattle near a lead and zinc ore processing facility did not have elevated blood or hair zinc levels, although daily zinc intake was 5.6 mg/kg BW versus 1.2 mg/kg BW daily by cattle in a control area (Milhaud and Mehannaoui 1988). In cattle, proximity to zinc refineries did not result in significant elevation of zinc concentrations in the liver and kidney (Spierenburg et al. 1988). However, cows living within 6 km of a power plant in Czechoslovakia, but not a herd at a 26-km distance, had elevated zinc loadings in hair and poor reproduction (Pisa and Cibulka 1989). In adult bovines, zinc reserves are usually small and located primarily in the skeleton and muscle, although appreciable hepatic accumulations can occur in the fetus. At 270 days of gestation, for example, 30% of zinc in fetal cattle is in the liver; zinc concentration is about 4 times higher in the fetal than in the maternal liver (Gooneratne and Christensen 1989). Liver concentrations >120 mg Zn/kg DW in cattle are frequently associated with elevated dietary zinc loadings (Binnerts 1989). Concentrations of zinc in milk of cows and goats varied significantly between breeds and with zinc level in diet and declined markedly after parturition (Park and Chukwu 1989).

A normal 70-kg human male contains 1.5-2.0 g zinc or about 21-29 mg Zn/kg BW; normal zinc uptake is 12-15 mg daily, equivalent to 0.17-0.21 mg/kg BW (Prasad 1979). Foods rich in zinc are seafoods, meats, grains, dairy products, nuts, and legumes (Goyer 1986). About 90% of the total body zinc is in the musculoskeletal system (Rosser and George 1986). Highest zinc concentrations of 100-200 mg/kg occur in the prostate, eye, brain, hair, bone, and reproductive organs; intermediate concentrations of 40-50 mg/kg occur in the liver, kidney, and muscle (NAS 1979; Casey and Hambidge 1980). In blood, about 80% of the total zinc is in red cells where it is associated with carbonic anhydrase. The mean plasma zinc level is about 0.9 mg/L; about half is in a freely-exchangeable form loosely bound to albumin; most of the remainder is tightly bound to macroglobulins and amino acids, especially histidine and cysteine (Casey and Hambidge 1980; Goyer 1986). The greatest zinc concentration in the human body is in the prostate and may be related to the elevated levels of acid phosphatase, a zinc-containing enzyme in that organ (Goyer 1986). The prostate gland contributes zinc to spermatozoa in dogs--a necessary process for canine fertility and fecundity; in rats, however, the prostate does not contribute to zinc in spermatozoa, and its function is not essential for reproduction in rats (Saito et al. 1967).

Zinc Deficiency Effects

General

Zinc is important in the metabolism of proteins and nucleic acids and is essential for the synthesis of DNA and RNA. Zinc deficiency has been reported in humans and a wide variety of plants and animals--with severe effects on all stages of reproduction, growth, and tissue proliferation in the young. In early gestation, zinc deficiency may cause severe congenital abnormalities. Later in gestation, deficiency can cause growth inhibition and brain growth impairment, leading to altered behavioral development after birth. Feeding a low zinc diet to lactating dams produces signs of zinc deficiency in suckling pups. In humans, zinc deficiency is associated with delayed sexual maturation in adolescent males; poor growth in young children; impaired growth of hair, skin, and bone; disrupted Vitamin A metabolism; and abnormal taste acuity, hormone metabolism, and immune function.

Terrestrial Plants

Zinc deficiencies in citrus groves in California, pecan trees in Texas, and various crops in Australia resulted in large crop losses (Vallee 1959). Applications of zinc salts were effective under acidic soil conditions. But neutral or alkaline soils rendered zinc salts insoluble and zinc therapy ineffective. Zinc salts sprayed on leaves or injected into tree trunks overcame the problems of soil solubility and have generally been successful (Vallee 1959). Zinc is usually bound strongly in plants, particularly in grains, markedly decreasing its availability to animal consumers. Binding is attributed mainly to high content of phytate and also to high levels of fiber hemicelluloses, and amino acid-carbohydrate complexes (Casey and Hambidge 1980). Whole-grain cereals and legumes are considered rich sources of zinc (Casey and Hambidge 1980).

Aquatic Organisms

Nutritional zinc deficiency is rare in aquatic organisms (Spear 1981), although reports are available of experimentally-induced zinc deficiency in algae, sponges, daphnids, echinoderms, fish, and amphibians.

Experimental zinc deficiency in euglenoids (*Euglena gracilis*) was associated with arrested growth and abnormal cell differentiation and development, leading to extensive teratological abnormalities. Zinc-deprived *Euglena* survived for extended periods through decreased metabolism (Falchuk et al. 1985; Falchuk 1988). Marine algae stopped growing when ambient zinc concentrations fell below 0.7 µg/L, and zinc-deficient cultures of freshwater algae were unable to metabolize silicon (Vymazal 1986).

A freshwater sponge (*Ephydatia fluviatilis*) grew normally at a concentration of 0.65 µg Zn/L, but growth was reduced at lower concentrations (Francis and Harrison 1988).

Daphnids (*Daphnia pulex*, *Daphnia magna*) reared for six brood cycles in zinc-free water showed reduced survival, inhibited reproduction, and cuticle damage (Keating and Caffrey 1989).

Zinc is important in pH regulation of sperm of marine invertebrates. Zinc reduction in semen to <6.5 µg/L adversely affected sperm pH and motility in sea urchins (*Strongylocentrotus purpuratus*, *Lytechnicus pictus*), horseshoe crab (*Limulus polyphemus*), and starfish (Clapper et al. 1985a, 1985b).

Rainbow trout fry fed diets containing 1-4 mg Zn/kg ration had poor growth, increased morality, cataracts, and fin erosion; supplementing the diet to 15-30 mg Zn/kg alleviate these signs (Spry et al. 1988). Spry et al. (1988) also fed rainbow trout fry diets containing 1, 90, or 590 mg Zn/kg ration and simultaneously exposed them to a range of waterborne zinc concentrations of 7, 39, 148, or 529 µg Zn/L. After 16 weeks, the 7 µg Zn/L plus 1 mg/kg diet group showed clear signs of deficiency including a significantly reduced plasma zinc concentration (which was evident as early as the first week of exposure), reduced growth (with no growth after week 12), decreased hematocrit, and reduced plasma protein and whole body zinc concentration. Elevating waterbone zinc to 39 or 148 µg Zn/L partially corrected the deficiency but did not restore plasma or whole body zinc to initial levels or in fish raised for 16 weeks on a zinc-adequate diet of 90 mg Zn/kg ration. There were no toxic effects at any other dietary-waterborne zinc mixture. It was concluded that zinc uptake from water was independent of uptake from diet because at any dietary zinc level, an increase in the waterborne zinc resulted in an increase in whole body zinc. In freshwater, where waterborne concentrations of <10 µg Zn/L are most commonly encountered, waterborne zinc contributions to whole body zinc loadings are probably insignificant. When dietary zinc was adequate (i.e., 90 mg Zn/kg ration), the contribution of waterborne zinc was significant in the case of rainbow trout (Spry et al. 1988). In marine teleosts, diet is the major zinc source when seawater contained <15 µg Zn/L; at higher ambient concentrations of 600 µg Zn/L, waterborne zinc contributed up to 50% of the total body zinc burden (Spry et al. 1988).

Experimentally-produced zinc deficiency in toad embryos resulted in adults with abnormal ovarian development, altered meiotic and ovulation processes, and embryos with a high incidence of congenital malformations (Herkovits et al. 1989).

Birds

Zinc deficiency in the chicken, turkey, and Japanese quail is characterized by low survival, reduced growth rate and food intake, poor feathering, shortening and thickening of long bones of legs and wings, reduced egg production and hatchability, skeletal deformities in embryos, an uncoordinated gait, reduced bone alkaline

phosphatase activity, and increased susceptibility to infection (Blamberg et al. 1960; NAS 1979; Prasad 1979; Apgar 1985; O'Dell et al. 1989); Stahl et al. 1989a).

Laying hens (*Gallus* sp.) had low egg hatchability on diets that contained 6 mg Zn/kg and produced chicks that were weak and poorly feathered; these chicks usually died within a few days on 8-9-mg Zn/kg diets (Blamberg et al. 1960). Zinc-deficient chicks (13-16 mg Zn/kg DW diet for 4 weeks) had pathological defects in epiphyseal cartilage; no interference with calcification was noted in controls fed diets containing 93-96 mg Zn/kg feed (Westmoreland and Hoekstra 1969). Pullets fed diets containing 28 mg Zn/kg for 4 months and then 4 mg Zn/kg ration for 4.5 months produced few hatchable eggs after 4 months; prevalent malformations included faulty trunk and limb development, missing vertebrae, missing limbs and toes, abnormal brain morphology, small eyes, and skeletal malformations (Blamberg et al. 1960). Most zinc deficiency effects were reversed by increasing dietary zinc concentrations to 96-120 mg/kg (Blamberg et al. 1960).

Chicks of the Japanese quail fed an excess of zinc (25-30 mg Zn/kg diet) during their first week of life were protected during a subsequent period of zinc deprivation (1 mg Zn/kg diet for 1 week). Birds that received an initial intake of zinc in excess of requirements grew significantly better than birds on a minimal amount of zinc. Japanese quails may store excess zinc in bones; this zinc store may become available during a subsequent period of zinc deprivation, especially during a period of rapid bone growth (Harland et al. 1975); but this requires verification.

Egg production constitutes a major loss of zinc and other trace metals by the laying hen. Vitellogenin mediates the transfer of zinc from the liver to the maturing oocyte, ultimately resulting in deposition into yolk of the newly formed egg (Richards 1989a). More research into the role of zinc in avian reproduction seems needed.

Mammals

Compared with zinc toxicity, zinc deficiency is a much more frequent risk to mammals (Leonard and Gerber 1989). Zinc is required in all stages of the cell cycle, and deficiency adversely affects metabolism of DNA, RNA, proteins, and activity of carbonic anhydrase, lactic dehydrogenase, mannosidase, and other enzymes (NAS 1979; Prasad 1979, 1980; Apgar and Everett 1988). In zinc deficiency, the activity of various zinc-dependent enzymes are reduced in testes, bone, esophagus, and kidney of rats, and alkaline phosphatase activity is reduced in bone and plasma of zinc-deficient rats, pigs, and cows (Prasad 1979; Vergnes et al. 1990). Deficiency leads to loss of appetite and taste, skin disturbances, slow wound healing, impaired brain development, deficient immune system, and disrupted water metabolism (Binnerts 1989). Zinc deficiency adversely affected testicular function in humans and animals and seems to be essential for spermatogenesis and testosterone metabolism (Prasad 1980). Zinc deficiency in young men with very low zinc intakes resulted in testicular lesions and reduced accessory gland weights, primarily from reduced food intake and growth (Apgar 1985). Zinc deficiency during pregnancy produced low birth weight, malformations, and poor survival in rats, lambs, and pigs; the role of zinc in human reproductive problems is still unclear (Apgar 1985). Zinc-deficient diets for ruminants and small laboratory animals usually contain <1 mg Zn/kg ration, although rats show deficiency at <12 mg Zn/kg ration (Elinder 1986). Zinc deficiency has been documented in humans, small laboratory animals, domestic livestock, minks, and monkeys; signs of severe zinc deficiency in mammals include decreased food intake, growth cessation, fetal malformations, testicular atrophy, swelling of feet, excessive salivation, dermal lesions, parakeratosis of the esophagus, impaired reproduction, hair loss; unkempt appearance, stiffness, abnormal gait, skin and organ histopathology, and hypersensitivity to touch (NAS 1979; Jameson 1980; Elinder 1986; Gupta et al. 1988; O'Dell et al. 1989). Selected examples of zinc deficiency in various species follow.

Zinc deficiency in humans is rare and usually associated with severe malabsorption, parenteral alimentation lacking zinc, or geophagia (Sternlieb 1988). Symptoms of zinc deficiency depend in part on age, acuteness of onset, duration and severity of the zinc depletion, and the circumstances in which deficiency occurs. Many of the features of zinc deficiency observed in humans are similar to those in zinc-deficient animals (Casey and Hambidge 1980). Simple nutritional deficiency from marginal zinc intake may be common even in the United States (Casey and Hambidge 1980). Factors of zinc deficiency include inadequate dietary intake (protein-calorie malnutrition), decreased availability (high fiber-phytate diets), decreased absorption, excessive losses (increased sweating, burns), increased requirements (rapid growth, pregnancy, lactation), as well as old age, alcoholism, and possible genetic defects (Casey and Hambidge 1980). Zinc deficiency may also occur as a

result of liver or kidney disease, gastrointestinal disorders, skin disorders, parasitic infections, diabetes, and genetic disorders, such as sickle cell disease (Prasad 1979). Clinical disorders aggravated by zinc deficiency include ulcerative colitis, chronic renal disease, and hemolytic anemia (Goyer 1986). In the 40 years since human zinc deficiency was demonstrated, it has been observed in a wide variety of geographic areas and economic circumstances. Severe zinc deficiency occurs in some areas of the Middle East and North Africa and is frequently associated with the consumption of unrefined cereals as a major part of the diet (Casey and Hambidge 1980). Chronic zinc deficiency in humans is associated with dwarfism, infantile testes, delayed sexual maturity, birth defects, poor appetite, mental lethargy, immunodeficiency, skin disorders, night blindness, impotence, spleen and liver enlargement, defective mobilization of vitamin A, delayed wound healing, impaired taste acuity, abnormal glucose tolerance, impaired secretion of luteinizing hormone, and iron and folate deficiency (Prasad 1979, 1980; Casey and Hambidge 1980; Elinder 1986; Goyer 1986; Sternlieb 1988; Mackay-Sim and Dreosti 1989). A deficiency of zinc in the growing age period results in growth retardation; a severe zinc deficiency may be fatal if untreated (Prasad 1980). Zinc-deficient humans excrete <100 µg zinc daily in urine rather than a normal daily >300 µg zinc (Goyer 1986). Zinc deficiency may exacerbate impaired copper nutrition; interactions with cadmium and lead may modify the toxicity of these metals (Goyer 1986). Acrodermatitis enterohepatica is a disease characterized by skin eruptions, gastrointestinal disorders, and low serum zinc levels. One causative factor is poor intestinal absorption of zinc; a complete cure was accomplished by oral administration of 135 mg zinc daily as 600 mg zinc sulfate (Elinder 1986). Using radiozinc-65, it was shown that afflicted individuals had a greater turnover of plasma zinc, a smaller pool of exchangeable zinc, and a reduced excretion of zinc in stool and urine (Prasad 1979). Zinc deficiency in humans is usually treated by oral administration of 1 mg Zn/kg BW daily (Casey and Hambidge 1980). However, zinc-deficient humans given daily intravenous injections of 23 mg zinc experienced profuse sweating blurred vision, and hypothermia (Saxena et al. 1989b). An endemic zinc deficiency syndrome among young men has been reported from Iran and Egypt and is characterized by retarded growth, infantile testes, delayed sexual maturation, mental lethargy, anemia, reduced concentration of zinc in plasma and red cells, enlarged liver and spleen, and hyperpigmentation; oral supplementation of 30 mg zinc daily had a prompt beneficial effect (Prasad 1979; Elder 1986). A zinc deficiency syndrome during human pregnancy includes increased maternal morbidity, abnormal taste sensations, prolonged gestation, inefficient labor, atonic bleeding, and increased risks to the fetus (Jameson 1980). Pregnant women with initially low and subsequently decreasing serum zinc levels had a high frequency of complications at delivery, including congenital malformations in infants. (Jameson 1980). Multiple severe skeletal abnormalities and organ malformations in human fetuses have been attributed to zinc deficiency (Casey and Hambidge 1980). In newborns, zinc deficiency is manifested by growth retardation, dermatitis, hair loss, impaired healing, susceptibility to infections, and neuropsychologic abnormalities (Casey and Hambidge 1980; Goyer 1986).

Hereditary zinc deficiency occurs in certain strains of cattle (*Bos* spp.) and affects the skin and mucous membranes of the gastrointestinal tract. The disease, Lethal Trait A46, is caused by failure of a single autosomal recessive gene regulating zinc absorption from the intestine. Affected animals die within a few months from secondary bacterial infections unless treated daily with high oral doses of zinc compounds (Bosma et al. 1988). Certain imported breeds of cattle in the western Sudan with low zinc serum levels (i.e., <0.6 mg/L) showed signs of zinc deficiency, including stunted growth, weakness, skin lesions, and loss of hair pigment (Damir et al. 1988). Cows fed a low (25 mg/kg ration) but adequate zinc diet had liver zinc concentrations below the expected 125 mg Zn/kg DW; increasing the total zinc dietary loading to 45 or 50 mg/kg DW is recommended for counteracting reduced zinc absorption in diets with soybean products (Binnerts 1989). Cows and calves fed low zinc diets of 25 mg Zn/kg ration showed a decrease in plasma zinc from 1.02 mg/L at start to 0.66 mg/L at day 90; cows fed 65 mg Zn/kg diet had a significantly elevated (1.5 mg Zn/L) plasma zinc level and increased blood urea and plasma proteins (Ramachandra and Prasad 1989). Biomarkers to identify zinc deficiency in bovines include zinc concentrations in plasma, unsaturated zinc-binding capacity, ratio of copper to zinc in plasma, and zinc concentrations in other blood factors; indirect biomarkers include enzyme activities, red cell uptake, and metallothionein content in the plasma and liver (Binnerts 1989).

Domestic goats (*Capra* sp.) fed a zinc-deficient diet (15 mg Zn/kg developed skin histopathology and alopecia (hair loss) after 177 days; zinc-deficient diets lacking vitamin A hastened the process, and signs were evident between 46 and 68 days (Chhabra and Arora 1989). No signs were evident in goats fed vitamin A-adequate diets containing 80 mg Zn/kg ration (Chhabra and Arora 1989).

Guinea pigs (*Cavia* spp.) fed a zinc-deficient diet (1.25 mg Zn/kg FW) for 60 days had significant reductions in zinc concentration in the serum (0.5 mg/L), kidney (10 mg/kg FW), testes (9.5 mg/kg FW), and liver (9.4 mg/kg FW). Guinea pigs fed 1.25 mg Zn/kg FW diet for 45 days followed by a zinc-replete diet of 100 mg/kg FW for 15 days had normal concentrations of zinc in serum (1.6-2.0 mg/kg FW), kidney (18-20 mg/kg FW), testes (19-27 mg/kg FW), and liver (15-17 mg/kg FW; Gupta et al. 1988). Zinc-deficient guinea pigs (<3 mg Zn/kg diet, 1 mg Zn/L drinking water), but not zinc-adequate animals (<3 mg Zn/kg diet, 15 mg Zn/L), exposed from day 30 of gestation to term on day 68 produced young with a low birth weight and severe skin lesions, were sensitive to handing and slow in recovering balance when turned on side, and had a peculiar stance; fetal zinc concentrations were depressed 15-33% in the liver and placenta (Apgar and Everett 1988). Disrupted immunocompetence responses and disordered protein metabolism were found in guinea pigs fed a zinc-deficient diet of 1.25 mg/kg FW ration for 45 days; marked, although incomplete, restoration occurred when this group was switched to 100 mg Zn/kg ration for 15 days (Verma et al. 1988). Neuromuscular pathology was evident in weanling guinea pigs fed a zinc-deficient diet (<1 mg Zn/kg) for 4 weeks, as judged by abnormal posture, skin lesions, and disrupted vocalizations; signs became severe after 5-6 weeks, but a single intraperitoneal injection of 1.3 mg Zn/kg BW (as $ZnSO_4$) caused remission within 7 days (O'Dell et al. 1989). Acute experimental allergic encephalomyelitis was induced in guinea pigs maintained on low (6 mg/kg), normal (20 mg/kg), and high (200 mg/kg) levels of zinc in the diet. Acute experimental allergic encephalomyelitis is usually a fatal disease of the central nervous system induced by inoculation with protein found in myelin of the central nervous system. Those on the zinc-deficient diet exhibited the expected signs of zinc deficiency but, unlike other groups, did not develop neurological signs of acute experimental allergic encephalomyelitis (Scelsi et al. 1989). Experimental allergic encephalomyelitis suppression in the zinc-deficient guinea pigs is ascribed to the influence of zinc deficiency of the T-cell function. A model of autoimmune central nervous system disease such as experimental allergic encephalomyelitis that requires a prominent T-lymphocyte sensitization can be altered or suppressed when the immunoregulatory mechanisms are impaired by zinc deficiency (Scelsi et al. 1989).

Unlike conspecifics on diets containing 100 mg Zn/kg, rhesus monkeys (*Macaca mulatta*) fed a marginally deficient zinc diet (4 mg Zn/kg diet) between age 5.5 and 30.0 months had lower plasma zinc levels, delayed onset of accelerated weight gain and linear growth, and no loss of subcutaneous fat--typical of early adolescence (Golub et al. 1988). Marginal dietary zinc deprivation also depressed immune function in rhesus monkeys by about 30% and impaired both learning and reversal of a visual discrimination task by 33-66% (Golub et al. 1988). When pregnant rhesus monkeys are fed a diet marginally deficient in zinc (4 mg/kg), perturbations in the mother's immune system can occur. Their infants, but not controls (100 mg Zn/kg diet), had reduced immune responsiveness despite the absence of marked differences in plasma or soft tissue zinc concentrations (Keen et al. 1989). Infant rhesus monkeys from zinc-deprived (4 mg Zn/kg ration) pregnant dams and subsequently fed the same low zinc diet showed delayed skeletal maturation during their first year. The condition was most severe at age 6 months but began to return to normal despite continuation of the marginally zinc-deficient diet (Leek et al. 1988).

Mice (*Mus* sp.) fed a zinc-deficient diet of 0.7 mg Zn/kg ration for 40 days, unlike mice fed a zinc-adequate diet of 36.5 mg Zn/kg, had a reduced growth rate, impaired phagocytic function, increased susceptibility to lead poisoning, and reduced zinc content in the blood (0.7 mg/L vs. 1.0-1.1 mg/L) and liver (12 mg Zn/kg FW vs. 17-19 mg Zn/kg FW; Tone et al. 1988). Zinc deficiency during early development affects neural tube development through arrested cell growth (Mackay-Sim and Dreosti 1989). Zinc deficiency in mice may disrupt olfactory function through interference with zinc-containing neurons in higher olfactory centers. Adult mice fed a zinc-deficient diet of 5 mg Zn/kg ration for 42 days, unlike mice given 100 mg Zn/kg diet, could not distinguish odors, although olfactory epithelia seemed normal (Mackay-Sim and Dreosti 1989).

Mink (*Mustela vison*) kits fed a zinc-deficient diet of 4.1 mg Zn/kg FW ration for 4 days retained 0.49 mg Zn/kit and lost weight. Kits fed a zinc-adequate diet (35-45 mg Zn/kg FW, 100-150 mg/kg DW) retained 2.5 mg Zn/kit, and those fed 83 mg Zn/kg FW diet retained 7.8 mg Zn/kit. Kits on low doses ate less than other groups. The most important excretory route was urine in the zinc-deficient group and feces in higher dose groups (Mejborn 1989).

Domestic sheep (*Ovis aries*) fed a low zinc diet (2.2 mg Zn/kg DW diet) for 50 days, unlike sheep fed a zinc-adequate diet (33 mg Zn/kg DW diet), excreted less zinc (<4 mg daily vs. 23-25 mg), consumed less food (409 g daily vs. 898 g), and had lower plasma zinc concentrations (0.18 mg/L vs. 0.53-0.58 mg/L); a reduction in

plasma alkaline phosphatase activity and an increase in plasma zinc binding capacity were also noted (Khandaker and Telfer 1990). Sensitive indicators of zinc deficiency in lambs include significant reductions in plasma alkaline phosphatase activity and plasma zinc concentrations; signs were clearly evident in lambs fed 10.8 mg Zn/kg DW diet for 50 to 180 days (Vergnes et al. 1990). A normal diet for lambs contains 124-130 mg Zn/kg DW ration and 33 for adults (Vergnes et al. 1990). One recommended treatment for zinc-deficient sheep is ruminal insertion of zinc-containing boluses every 40 days; bolus zinc release is about 107 mg daily (Khandaker and Telfer 1990).

Zinc-deficient pregnant laboratory white rats (*Rattus* sp.) have reduced litter size, a high frequency of fetal deformities, low birth weight, and a prolonged parturition; dams are inactive and seem indifferent toward young (Harland et al. 1975). Fetal skeletal defects are prominent in rats fed zinc-deficient diets of 10 mg/kg ration during a 21-day gestation period. About 91% of zinc-deficient fetuses had multiple skeletal malformations, but controls fed 76 mg Zn/kg diet had none (Ferreira et al. 1989). Zinc-deficient (1.5 mg Zn/kg diet) pregnant rats also had increased iron levels in the liver, kidney, and spleen; depleted liver glycogen: and reduced levels of zinc in the pancreas and duodenum (Mamba et al. 1989). Zinc deficiency causes testicular atrophy and hypogonadism in rats; the effects include spermatic arrest, histopathology of seminiferous tubules and interstitial cells, reduced serum testicular testosterone levels, and reduced testicular zinc concentrations (Hafiez et al. 1990). Zinc is required in Leydig cells for normal testosterone activity. Calcitonin inhibits transmembrane influx of zinc in the isolated rat Leydig cell, but these effects usually take >2 days and are critical only in states of borderline zinc deficiency (Chausmer et al. 1989). Zinc deficiency during pubertal development of rats depresses the activity of dipeptidyl carboxypeptidase in the testes and epididymis; this enzyme is required for maturation and development of sperm cells and reduced activity may cause suppression of sexual maturity (Reeves 1990). Laboratory white rats fed zinc-deficient diets for 20 days show an aversion to the zinc-deficient diet. They readily consumed a familiar zinc-adequate diet for 15 days, but the previously deficient animals continued to avoid zinc-deficient diets when given a choice (Cannon et al. 1988). Zinc deficiency in rats (<1 mg Zn/kg diet for 26 days) significantly reduced blood pressure and this correlated positively with serum angiotensin converting enzyme activity; increasing the dietary intake of calcium had no effect on these responses (Reeves and O'Dell 1988). During zinc deficiency, zinc is mobilized from bone in young immature animals and may be available for metabolic processes including growth (Calhoun et al. 1978). Diabetic rats are at risk of developing zinc deficiency because of zinc's role in modulating immune system dysfunction in diabetes mellitus (Mooradian et al. 1988). Cadmium toxicity is related to the zinc status of the body. Zinc-deficient rats (<1 mg Zn/kg diet) and zinc-adequate rats (40 mg/kg) were both challenged with cadmium. The zinc-deficient group had accelerated zinc loss from the kidneys; enlarged liver, kidneys, spleen and lungs; and increased distribution of cadmium in tissues (Sato and Nagai 1989). Other signs in zinc-deficient laboratory white rats included decreased food intake and loss of body weight (Vallee 1959; Cannon et al. 1988; Reeves and O'Dell 1988; Dib et al. 1989; Ferreira et al. 1989; Mamba et al. 1989; Mansour et al. 1989; Sato and Nagai 1989); reduced serum zinc (Calhoun et al. 1978; Reeves and O'Dell 1988); altered cholesterol metabolism (Samman and Roberts 1988); increased serum magnesium (Reeves and O'Dell 1988); lowered bone (femur) zinc concentrations (Calhoun et al. 1978); degenerated olfactory epithelium (Mackay-Sim and Dreosti 1989); reduced serum total proteins (Mansour et al. 1989); decreased activity of glutamate, glycine, methionine, arginine, lysine, and proline (Bettger 1989); and increased dental caries (Goldberg et al. 1990).

Zinc deficiency in domestic pigs (*Sus* sp.) is associated with a condition known as porcine parakeratosis, characterized by dermatitis, diarrhea, vomiting, anorexia, severe weight loss, and eventually death; the condition is exacerbated by high calcium levels (Vallee 1959).

Lethal and Sublethal Effects

General

Significant adverse effects on growth, reproduction, and survival are documented for sensitive marine and freshwater species of aquatic plants, invertebrates, and vertebrates at nominal water concentrations between 10 and 25 µg Zn/L. Sensitive terrestrial plants died when soil zinc concentrations were >100 mg/kg and showed decreased photosynthesis when total plant contained >178 mg Zn/kg DW. Representative soil invertebrates showed reduced growth at 300-1,000 mg Zn/kg diet and reduced survival at 470-6,400 mg Zn/kg soil. Domestic poultry and avian wildlife had reduced growth at >2,000 mg Zn/kg diet, and reduced survival at >3,000 mg Zn/kg diet or at a single oral dose >742 mg Zn/kg BW; younger stages (i.e., chicks, ducklings) were least resistant.

Sensitive species of livestock and small laboratory animals were adversely affected at >0.8 mg Zn/m^3 air, 90-300 mg Zn/kg diet, >90 mg Zn/kg BW daily, >300 mg Zn/L drinking water, and >350 mg Zn/kg BW single oral dose.

Terrestrial Plants and Invertebrates

Sensitive terrestrial plants die when soil zinc levels exceed 100 mg/kg or when plant zinc content exceeds 178 mg/kg DW (Table 5). The phytotoxic zinc level for barley (*Hordeum vulgare*) is not known, but zinc content of barley leaf rarely exceeds 100 mg/kg DW (Chang et al. 1983). Uptake of zinc from soils by plants is dependent on soil type; for example, uptake is lower in coarse loamy soils than in fine loamy soils (Chang et al. 1983). Zinc uptake by barley leaf is greater with increasing rate of sludge application, but the relation is not proportional (Table 5).

Among terrestrial invertebrates, adverse effects on earthworm survival were documented at 470-662 mg/kg soil, slugs had reduced food consumption at 300 mg Zn/kg diet and reduced growth at 1,000 mg Zn/kg diet, and woodlice had impaired reproduction at 1,600 mg Zn/kg soil and reduced survival at 5,000 mg Zn/kg diet or 6,400 mg Zn/kg soil (Table 5).

High zinc concentrations in soils are responsible for reductions in populations of soil invertebrates near brass mills and zinc smelters (Beyer 1990). Soils in the vicinity of zinc smelters contained up to 35 g Zn/kg and had decreased populations of arthropods; experimentally, 20 g of total zinc per kilogram of soil could account for the decreased survival (Beyer et al. 1984). Zinc concentrations exceeding 1,600 mg/kg soil litter are associated with reduced natural populations of decomposer organisms in contaminated forest soil litter, and this has been verified experimentally (Beyer and Anderson 1985). Poisoning of decomposer organisms, such as the woodlouse (*Porcellio scaber*), may disrupt nutrient cycling and reduce the number of invertebrates available as wildlife food (Beyer and Anderson 1985). The woodlouse contains higher concentrations of zinc than other terrestrial invertebrates: up to 152 mg Zn/kg DW whole organism (Hopkin and Martin 1985). It is speculated that the large zinc stores in *P. scaber* repels predators that find zinc distasteful (Hopkin and Martin 1985).

Table 5. Effects of zinc on representative terrestrial plants and invertebrates.

Organism, dose, and other variables	Effect	Reference[a]
Plants		
Fir, *Abies pindrow,* wooden stakes coated with 10% zinc oxide	Protects wood against termite damage for 5 years compared with 4 years for copper sulfate, 2 years for calcium carbonate, and <6 months for untreated wood	1
Red maple, *Acer rubrum*, 100 mg Zn/kg culture medium	Lethal to seedlings	2
Lichen, *Cladonia uncialis*, whole plant zinc content	Depressed photosynthesis when whole lichen burden is >178 mg Zn/kg DW; decreased respiration at >3,550 mg Zn/kg DW	3
Barley, *Hordeum vulgare*, leaf, from soil treated with sludge for 3 years		
No sludge	21-25 mg/kg DW	4
80 kg Zn/ha/year	26-47 mg/kg DW	4
160 kg Zn/ha/year	29-56 mg/kg DW	4
320 kg Zn/ha/year	41-57 mg/kg DW	4

Lichen, *Lasallia papulosa*, whole plant zinc content	Significant depression in photosynthesis at >308 mg Zn/kg DW and in respiration at >3,300 mg Zn/kg DW	3
Oak, *Quercus rubra*, culture medium contained 100 mg Zn/kg	Lethal to seedlings	2
Corn, *Zea mays*, grown on sludge amended loam plots; soil contains a maximum of 460 mg Zn/kg DW	Leaf contains a maximum of 293 mg Zn/kg DW (60 mg Zn/kg for controls); grain contains a maximum of 65 mg Zn/kg DW (32 mg Zn/kg for controls)	5
Invertebrates		
Earthworm, *Aporrectodea tuberculata*; concentrations of zinc in soil ranged from 28 mg/kg DW to 470 mg/kg DW versus concentrations in whole worms (less gut contents)	At soil zinc concentration of 28 mg/kg DW (control), worms contained 320 mg Zn/kg DW. At soil zinc levels of 97, 110, 190, and 320 mg/kg DW, whole worms contained 810, 1,300, 1,100, and 650 mg Zn/kg DW, respectively. No worms were found at soil zinc levels of 470 mg/kg DW	6
Slug, *Arion ater*, fed diets containing 10, 25, 50, 100, 300, or 1,000 mg Zn/kg ration for 27 days	No deaths in any group. Significantly reduced food consumption in 300 and 1,000 mg/kg diets. All groups weighed less than controls at day 27, but growth was statistically impaired only in the 1,000 mg/kg group	7
Slug, *Arion ater*, fed diets containing up to 1,000 mg/kg feed for 30 days	No adverse effects except for glycogen depression at 1,000 mg/kg diet	8,9
Spider, *Dysdera crocata*, fed woodlice (*Porcellio scaber*) at rate of one every 3 days for 36 days		
Woodlice from uncontaminated site (87 mg Zn/kg DW whole organism)	Whole spider contains 182 mg Zn/kg DW	10
Woodlice from contaminated site (152 mg Zn/kg DW whole organism)	Whole spider contains 118 mg Zn/kg DW (116 mg Zn/kg DW in starved spiders)	10
Earthworm, *Eisenia foetida*		
10-12 µg Zn/cm^2 applied to epidermis	LC50 (48 h)	11
662 mg Zn/kg artificial soil (95% C.I. 574-674)	LC50 (2 weeks)	11
Woodlice, *Porcellio scaber*, fed soil litter containing up to 12,800 mg Zn/kg for 64 weeks	Soil litter containing ≥1,600 mg Zn/kg had adverse effects on reproduction; adult survival was reduced at >6,400 mg Zn/kg litter	12

Woodlice, *Porcellio scaber*, fed diets containing up to 20,000 mg Zn/kg feed for 8 weeks		Decreased survival at ≥5,000 mg/kg	13

[a] 1. Roomi et al. 1990; 2. Buchauer 1971; 3. Nash 1975; 4. Chang et al. 1983; 5. Hinesly et al. 1977; 6. Beyer et al. 1987; 7. Marigomez et al. 1986; 8. Recio et al. 1988a; 9. Recio et al. 1988b; 10. Hopkin and Martin 1985; 11. Neuhauser et al. 1985; 12. Beyer and Anderson 1985; 13. Beyer et al. 1984.

Slugs (*Arion ater*) are resistant to high dietary zinc intakes (1,000 mg/kg feed) for 30 days, although zinc accumulations occur in excretory and calcium cells of the digestive gland (Recio et al. 1988a, 1988b). Histochemical detection of zinc in digestive glands of *Arion* is an indication of high levels of zinc in the environment (Recio et al. 1988a). Zinc elimination in *Arion* occurs directly from lipofuscin material of excretory cells and from spherules of calcium cells; excretion of lipofuscin material through feces is the major excretory route (Recio et al. 1988a).

Zinc normally aids wound healing in terrestrial invertebrates. Wounding of the optic tentacle, foot tissue, and partial shell removal in *Helix aspersa*, a terrestrial gastropod, resulted in deposition of zinc in the wound area after 2 to 5 days. Increased zinc in *Helix* wound areas may be necessary to promote protein synthesis, collagen, formation, and mitotic cell division (Ireland 1986).

Aquatic Organisms

Significant adverse effects of zinc on growth, survival, and reproduction occur in representative sensitive species of aquatic plants, protozoans, sponges, molluscs, crustaceans, echinoderms, fish, and amphibians at nominal water concentrations between 10 and 25 µg Zn/L (Table 6).

Table 6. Effects of zinc on representative aquatic plants and animals. Concentrations are in micrograms of zinc per liter of medium.

Taxonomic group, organism, and other variables	Concentration (ppb)	Effects	Reference[a]
Plants			
Alga, *Amphidinium carteri*	400	Growth inhibition	1
Aquatic plants, various	30->200,000	Adverse effects	2
Brown alga, *Ascophyllum nodosum*	100	No effect on growth in 10 days	2
Ascophyllum nodosum	250	Decreased growth in 10 days	2
Coccolithophorid, *Cricosphaera carterae*	77	Growth reduced 50% in 4 days	2
Freshwater algae, 11 species	140-800	Growth inhibition	3
Freshwater algae, most species	>1,000	Growth inhibition	1
Brown macroalgae, *Fucus serratus*	9.5	Bioconcentration Factor (BCF) of x10,770 in 140 days	2
Fucus serratus	8.8	Altered lipid metabolism	2
Marine macroalgae, *Fucus vesiculosus*	3,500	No adverse effects	2
Fucus *vesiculosus*	7,000	Growth retardation	2
Dinoflagellate, *Glenodinium halli*	20	Chlorophyll reduced 65% in 2 days	2
Dinoflagellate, *Gymnodinium*	110-392	Chlorophyll reduced about 65%	2

splendens		in 2 days in temperature range 16-30° C	
Gymnodinium *splendens*	100	Growth inhibition in 38 days	3
Alga, *Isochrysis galbana*	74	Chlorophyll reduced 65% in 48 h at 16 ppt salinity, 20° C	2
I. galbana	430	Chlorophyll reduced 65% in 48 h at 16° C, 16 ppt salinity	2
Kelp, *Laminaria digitata*	100	Growth inhibition in 24 days	1
Brown macroalga, *Laminaria hyperborea*	250 8-10 days	Reduced growth of sperophytes in	2
Marine algae, 4 species	50-500	Decrease in cell numbers	1
Marine algae, 5 species	100	Growth inhibited in 48 h	2
Marine macroalgae, 4 species	100	No adverse effects	2
Marine macroalgae, 4 species	1,400	Growth reduction	2
Diatom, *Nitzschia closterium*	271-300	50% growth inhibition in 4 days	2
Diatom, *Nitzschia longissima*	100	Growth stimulated during exposure for 1-5 days	2
Dinoflagellate, *Procentrum micans*	319	50% growth inhibition in 4 days	2
Diatom, *Phaeodactylum tricornutum*	250	BCF of x1,800 in 3 days	2
P. tricornutum	4,800	6.7% increase in growth during 12-day exposure	2
Phytoplankton	15	Primary productivity reduced in 14 days	2
Marine alga, *Rhizosolenia* sp.	15-25	Photosynthesis reduction	3
Alga, *Scenedesmus quadricauda*	2	Adverse effects	4
S. quadricauda	64	Growth inhibition in 14 days	2
S. quadricauda	300	Lethal	4
Diatom, *Schroederella schroederi*	19	Growth inhibited 50% in 48-96 h	2
Freshwater alga, *Selenastrum capricornutum*	30	Some growth inhibition in 7 days	1
S. cupricornutum	40-68	95% growth inhibition in 14 days	1
S. capricornutum	100	100% growth inhibition in 7 days	1
Diatom, *Skeletonema costatum*	19.6	Adverse effects	4
S. costatum	50-100	Growth reduced 20-23% in 10-15 days	2
S. costatum	200	Growth stimulated in 1-5 days	2
S. costatum	265	Metabolic disruption in 3 days	2
Diatom, *Thalassiosira pseudonana*	65	Adverse effects	4
T. pseudonana	500	Growth reduced 41% in 11-15 days	2
T. pseudonana	823	Growth reduced 50% in 72 h	2
Green macroalga, *Ulva lactuca*	65	BCF of x255 in 6 days	2
Protists			
Protozoan, *Cristigera* sp.	50-125	Growth reduced in 5-h exposure	1,2
Bacterium, *Escherichia coli*	650-1,400	Growth inhibition	3
Microorganisms, various	650-1,100	Growth inhibition, usually	3

Paramecium, *Paramecium multi-micronucleatum*	560-10,000	LC50 (3 h)	3
Bacterium, *Pseudomonas* sp.	1,000-10,000	Growth inhibition	3
Protozoan, *Vorticella convallaria*	50	LC50 (48 h)	3
Porifera			
Freshwater sponge, *Ephydatia fluviatilis*			
Adults	6.5	No effect on growth; no tolerance developed with long-term exposure	5
Adults	26	After exposure for 10 days, tissue deterioration and death during 3-week postexposure period	5
Rotifers			
Rotifer, *Philodena acutiformis*			
Adults	500	LC50 (48 h), 25° C	
Adults	1,550	LC50 (48 h), 5° C	2
Molluscs			
Freshwater snail, *Ancylus fluviatilis*			
Juvenile	80	LC50 (100 days), shell length <2 mm	6
Adult	100	No adverse effect on reproduction in 100 days	6
Juvenile	130	LC50 (100 days), shell length >3 mm	6
Adult	180	Reproduction reduced in 100 days	6
Bay scallop, *Argopecten irradians*			
Larvae	50	Growth rate reduced 22% in 9 days	7
Larvae	109	Growth reduced 50% in 9 days	7
Larvae	120	LC50 (9 days), increased shell deformities	7
Larvae	150-200	All dead at metamorphosis	7
Juvenile	2,250	LC50 (96 h)	8
Freshwater snail, *Biomphalaria glabrata*	500	By day 33 of exposure, embryo survival was reduced 50% and adult growth and reproduction inhibited	9
Asiatic clam, *Corbicula fluminea*	<20	Residues were 169 mg/kg dry weight (DW) parts after feeding on periphyton containing 393-1,327 mg/kg DW for 30 days	11
C. fluminea	25	Normal growth during exposure for 30 days	10
C. fluminea	34	Residues were 433 mg/kg DW soil parts in 30 days after feeding on periphyton containing 956-4,369 mg Zn/kg DW;	11

		growth reduced; cellulase enzyme activity reduced	
C. fluminea	50-500	Growth inhibited between days 20 and 30 of exposure	10
C. fluminea	218	BCF of x126 in 28 days	2
C. fluminea	1,000	After exposure for 30 days, about 30% died. Survivors had osmoregulatory impairment and residues of 2,000 mg Zn/kg DW soft parts (200 mg Zn/kg DW soft parts in controls). Depuration complete by day 17 postexposure, and growth rate returns to normal	10
Pacific oyster, *Crassostrea gigas*			
Larvae	10-20	Reduced larval settlement in 20 days	1
Larvae	30-35	Reduced larval settlement in 6 days	2
Larvae	50	Normal growth and development in 5 days	12
Larvae	70	Abnormal shell development in 48 h	1
Larvae	75	No deaths in 48 h	1
Larvae	80-95	Growth reduced 50% in 4 days	2
Larvae	119-310	LC50 (48 h)	1,13
Larvae	125	Substrate attachment inhibited in 5 days	1,2
Larvae	200	No growth in 5 days	12
Embryo	233	LC50 (96 h)	2
Larvae	250	Increasing incidence of abnormal development and mortality	12
Sperm	444	Fertilization success reduced 50% in 60 min	2
Larvae	500	All died in 48 h	1
American oyster, *Crassostrea virginica*			
Adult	100	Whole body concentration of 2,560-2,708 mg Zn/kg fresh weight (FW) soil parts after 20-week exposure (1,036-1,708 mg Zn/kg FW soil parts in controls)	14
Adult	200	After exposure for 20 weeks, residues were 3,185-3,813 mg Zn/kg FW soft parts	14
Embryo	230	LC50 (96 h)	2
Larvae	340	LC50 (48 h)	13
Red abalone, *Haliotis rufescens*			

Larvae	19	No adverse affects after 9-day exposure	13
Larvae	41	Normal development during 48-h	13
Larvae	50	50% abnormal development during exposure for 9 days	13
Larvae	68	50% abnormal development in 48-h exposure	13
Marine gastropod, *Littorina littorea*			
Adult	0.2 (controls)	Zinc concentrations in all tissues were <185 mg/kg DW, except kidney, which was 372 mg/kg DW	15
Adult	10	After exposure for 42 days, tissue zinc residues were: head-foot 120 mg/kg DW, gills 255 mg/kg DW, whole soft parts 605 mg/kg DW, viscera 1,322 mg/kg DW, stomach 1,918 mg/kg DW, and kidney 2,153 mg/kg DW	15
Freshwater pond snail, *Lymnaea luteola*, adult	1,680	LC50 (96h)	85
Hard shell clam, *Mercenaria mercenaria*			
Larvae	50	5% died in 12 days	1
Larvae	168	50% dead or abnormal in 48 h	1
Embryo	195	LC50 (96 h)	2
Larvae	195-341	LC50 (10-12 days)	1
Larvae	279	All died in 48 h	1
Softshell clam, *Mya arenaria*			
Adult	10	Soft parts contained 9.5 mg Zn/kg FW after 16 weeks at 0-10° C, and 11 mg/kg after 2 weeks at 16-22° C	14
Adult	200	BCF of x85-135 in 50 days	2
Adult	500	Soft parts contained 31-48 mg Zn/kg FW after exposure for 6-16 weeks at 0-10° C, and 59-82 mg/kg after 1-2 weeks exposure at 16-22° C	14
Adult	900	No deaths in 7 days at 22° C	16
Adult	1,550	LC50 (7 days) at 22° C	16
Adult	25,000	All dead after 70-day exposure at 0-10° C; at exposure temperature of 16-22° C, all dead by day 14	17
Common mussel, *Mytilus edulis*			
Adult	25	Maximum kidney zinc residue after 18 days was 14.1 g/kg DW (4.9 g/kg in controls)	18

Adult	60	Shell growth rate reduced 50% in 2-6 days of exposure	2
Embryo	96-314	Development inhibited 50% in 72 h	2
Adult	100	No accumulations in tissues after 4-day exposure	19
Adult	230-860	In 7-h exposure, pumping rate decreased with increasing zinc, and was completely stopped at >470 µg/L; recovery on return to background levels	20
Adult	1,000	After exposure for 24 h, zinc concentration in soil parts rose from 150 mg/kg DW to 252 mg/kg DW and remained elevated for at least 6 weeks postexposure	21
Larvae	1,752	LC50 (48 h)	13
Adult	1,800	Reduced byssal thread production	2
Adult	5,000	LC50 (7 days)	2
Adult	5,000	LC100 (16 days)	19
Adult	20,800	LC50 (24-h exposure plus 6 weeks postexposure); none dead during exposure	22
Sperm	65,400	Respiration inhibited 50% in 20 min	23
Mud snail, *Nassarius obsoletus*			
Adult	200	Decreased oxygen consumption in 72 h	1
Egg	650	Abnormal veliger development	24
Adult	5,000	No deaths in 168 h	25
Green-lipped mussel, *Perna virdis*			
Adult	<178-362	Maintains constant body concentration over 21-day exposure period	26
Adult	>362	Accumulation in tissue	26
Adult	6,090	LC50 (96 h)	26
Freshwater snail, *Physa heterostropha*, juvenile	241	LC50 (96 h)	2
Surf clam, *Spisula solidissima*, juvenile	2,950	LC50 (96 h)	8
Bryozoans			
Bryozoan, *Bugula neritina*, larvae	200	LC50 (5 h)	3
Bryozoan, *Watersipora cucullata*, larvae	650	LC50 (5 h)	3
Crustaceans			

Copepod, *Acartia tonsa*	290	50% immobilized in 48 h	
A. tonsa	294	LC50 (96 h)	2
Amphipod, *Allorchestes compressa*	580-2,000	LC50 (96 h)	3,27
Brine shrimp, *Artemia* sp.	14-1,360	Egg hatching significantly reduced in dose-dependent manner; no effect on survival of prenauplii larvae	28
Cladoceran, *Ceriodaphnia reticulata*	51	LC50 (96 h)	2
Hermit crab, *Clibanarius olivaceous*			
Larvae	1-90	Molting delayed in dose-dependent manner	29
Larvae	100	LC50 (96 h)	29
Larvae	125	LC100 (96 h)	29
Daphnid, *Daphnia galeata mendotae*	15	BCF of x9,400 in 2 weeks	2
D. g. mendotae	30	BCF of x5,833 in 2 weeks	2
D. g. mendotae	60	BCF of x6,333 in 2 weeks	2
Daphnid, *Daphnia magna*	5-14	LC50 (72 h) at 30° C	2
D. magna	25	No effect in soft water (50 mg $CaCO_3$/L) in 50 days	30
D. magna	42-52	MATC [b]; water contains 104-211 mg $CaCO_3$/L	1,2
D. magna	68-655	LC50 (96 h)	31
D. magna	70	Reproduction reduced 16% in 21 days	2
D. magna	100	LC50 (48 h), starved	84
D. magna	250	Nonlethal in 6 weeks when sediments present in test container. Final sediment value of 13,400 mg/kg DW (600 mg/kg DW in controls). Organisms had whole body residues of 450 mg/kg DW	32
	"		
D. magna	280	LC50 (48 h), fed	3
D. magna	560	LC50 (24 h) at 25° C	84
D. magna	560	50% immobilized in 48 h	33
D. magna	2,300	LC50 (24 h) at 5° C	3
Daphnid, *Daphnia pulex*	253	LC50 (96 h)	2
D. pulex	280	LC50 (48 h)	
D. pulex	500	LC50 (24 h) at 25° C	3
D. pulex	1,550	LC50 (24 h) at 5° C	3
Copepod, *Eudiaptomus padanus*	500	LC50 (48 h)	
Amphipod, *Gammarus duebeni*			
Natural population	>100	Survival reduced in 7 days	34
Natural population	1,000	All dead in 7 days at 10 ppt	

		salinity, 84% dead at 30 ppt	34
Zinc-tolerant population	1,000	50% dead in 14 days at 10 ppt salinity, 33% dead at 30 ppt	34
American Lobster, *Homarus americanus*			
Larvae	130	LC50 (17 days)	3
Larvae	381	LC50 (96 h)	2
Adult	13,000	LC50 (11 days)	3
Mysid, *Mysidopis bahia*	120-230	MATC[b]	1,2
M. bahia	499	LC50 (96 h)	2,13
Crayfish, *Orcenectes virilis*	130,000	No deaths in 10 days	35
Hermit crab, *Pagurus longicarpus*			
Adult	200	LC50 (168 h)	25
Adult	400	LC50 (96 h)	1,2
Prawn, *Palaemon elegans*	562	LC67 (21 days)	36
Shrimp, *Pandalus montagui*	65	BCF of x 3.7 in 14 days	2
Mysid, *Praunus flexuosus*	2,000	LC50 (192 h), 5^{o}C, 4.5 ppt salinity	37
Mudcrab, *Rithropanopeus harrisii*, larvae	50	Delayed development in 16-days exposure	1
Copepod, *Tisbe holothuriae*			
Life Cycle	7	No effect on population size after exposure for 4 generations	38
Life Cycle	10	Some deaths in fourth generation	38
Life Cycle	70	All dead by end of first generation	38
Copepodid	421	LC50 (48 h)	39
Adults	620-700	LC50 (48 h)	38,40
Females with egg sacs	713	LC50 (48 h)	39
Copepod, *Tropocyclops praisinus mexicanus*, Quebec lakes, uncontaminated	52-26	LC50 (48 h) in soft water	41
T.P. mexicanus, Quebec lakes, contaminated	2,934	LC50 (48 h) in hard water lake; metal preexposure protective effect hypothesized	41
Aquatic insects			
Mayfly, *Epeorus latifolium*			
Larvae	30	Gradual decrease in growth rate in 4-week exposure; some deaths before emergence	42
Larvae	100-300	Growth inhibited after 2 weeks; all dead before emergence	42
Midge, *Tanytarsus dissimilis*, embryo through third instar	37	LC50 (10 days)	1,2

Annelids			
Polychaete worm, *Capitella capitata*			
Larvae	50-100	Abnormal development during 16 day exposure	2
Adult	1,250	LC50 (28 days)	2
Adult	10,700	LC50 (48 days)	13
Leech, *Erpobdella octoculata*			
Juveniles	60	LC50 (70 days)	43
Adults	100	LC50(70 days)	43
Adults	180	High frequency of abnormal eggs produced in 60-day exposure	43
Adults	320	Inhibited reproduction in 60-day exposure	43
Juveniles	390	LC50 (40 days)	43
Juveniles	2,100	LC50 (96 h)	43
Adults	4,800	LC50 (40 days)	43
Adults	8,800	LC50 (96 h)	43
Polychaete, *Neanthes arenaceodentata*, juveniles	900	LC50 (28 days)	3
Sandworm, *Nereis diversicolor*			
Adults	1,500	No deaths in 168 h	25
Adults	2,600	LC50 (168 h)	25
Adults	10,000	Whole body zinc concentration in survivors after exposure for 34 days was 2,500 mg/kg DW (180 mg/kg DW in controls)	14
Adults	10,000	After 96-h exposure at; 6° C, zinc residues were 1,031 mg/kg DW in head (843 mg/kg DW in controls), 366 mg/kg DW in trunk (158 mg/kg DW in controls), and 455 mg/kg DW in parapodia (275 mg/kg DW in controls); uptake was higher at 12° and 20° C	44
Adults	20,000	No death in 96 h	44
Adults	40,000	LC50 (47 h) for nontolerant strains; LC50 (70 h) for zinc-tolerant strains	45
Worm, *Spirorbis lamellora*, larvae	350	LC50 (3 h)	3
Echinoderms			
Sea urchin, *Anthocidarius crassispina*			
Egg	65	No effect on fertilization membrane formation or development in eggs transferred 1 min after insemination	46
Egg	326	Irreversible inhibition of	

		fertilization membrane formation in eggs transferred 10 s after insemination	46
Starfish, *Asterias rubens*			
Adult females	240	Increased steroid metabolism in pyloric caeca after 21 days	47
Adults	1,000	No deaths in 168 h	25
Adults	2,300	LC50 (168 h)	25
Sand dollar, *Dendraster excentricus*, sperm	28	Fertilization success reduced 50% in 60 min	2
Echinoderms, 3 species, embryos	60-200	Embryonic development inhibited	46
Red sea urchin, *Strongylocentrotus franciscanus*, sperm	313	Fertilization success reduced 50%	2
Purple sea urchin, *Strongylocentrotus purpuratus*, embryos	23	Development inhibited 50% in 5 days	2
Fish			
Longfin dace, *Agosia chrysogaster*,	228	LC50 (96 h)	2
Murrel, *Channa punctatus*, fingerlings, 31-day exposure	12,000	Growth rate reduced by day 19; liver RNA and proteins decreased by day 20; muscle RNA and proteins reduced by day 30	49,50
Texas cichlid, *Cichlasoma cyanoguttatum*, adults, exposure for 4 weeks	40 (control), 65, or 90	Residues were 0.8, 28, and 34 mg Zn/kg FW in muscle; 6, 56, and 25 mg Zn/kg FW in viscera; 6, 59, and 98 mg Zn/kg FW in gills; and 12, 66, and 92 mg Zn/kg FW in bone	51
Air-breathing catfish, *Clarias lazera*, juveniles	26,000-52,000	LC50 (96 h) at 25.1° C (26,000) through 9.3° C (52,000); at 88,000 µg/L and 18.5° C, 50% died and survivors had BCF of x544 in gill, x425 in liver, and x250 in muscle	52
Baltic herring, *Clupea harengus*, eggs exposed from fertiliza-tion through hatching	500, 2,000, 6,000, or 12,000	Histopathology of epidermis and kidney in larvae at >6,000 µg/L; no measurable effects at < 2,000 µg/L	53,54
Atlantic herring, *Clupea harengus harengus*, embryos and larvae	50	Significant increase in incidence of jaw and branchial abnormalities	2
Freshwater fish, 4 species, adults	4,600-17,300	LC50 (5 days)	55
Mummichog, *Fundulus heteroclitus*			
Adults	810	BCF of x16 in whole fish after 56 days	2
Adults	10,000	Zinc concentration in scale, rose from 229 mg/kg DW at start to 746 mg/kg DW	56

		after 45 days and to 1,608 mg/kg DW after 94 days	
Adults	10,000	Zinc content in scale after 45 days exposure and 21 to 49 days in uncontaminated water fell from 746 mg/kg DW to 422-498 mg/kg DW	56
Adults	43,000	No deaths in 8 days; no significant increase in tissue zinc levels	57
Adults	52,000-66,000	LC50 (8 days)	25,57
Adults	71,000-153,000	LC50 (48 h)	58
Mosquitofish, *Gambusia affinis*, adults, muscle	18,000	After 24 h, zinc increased from 82 to 134 µg/kg FW; significant increases in glycogen, total lipids, phospholipids, and cholesterol; decreases in RNA and proteins	59
Flagfish, *Jordanella floridae*			
Life cycle	26-51	MATC [b]	2
Larvae	85	LC80 (30 days)	3
Adults	139	BCF of x417 in whole fish in 100 days	2
Cypriniform freshwater fish, *Labeo rohita*			
Juveniles and adults	20,000	No deaths in 96 h	60
Juveniles	65,000	LC50 (96 h); liver glycogen reduced; BCF of x22 in whole fish	60
Adults	77,000	LC50 (96 h); survivors had disrupted respiration and decreased liver glycogen	60
Spangled perch, *Leiopotherapon unicolor*, adults, exposed for 2 h	5,000, 10,000, or 20,000	Temporary decrease in ventilation rate at 5 mg/L; significant increase in ventilation rate at 10 and 20 mg/L; bradycardia at 20 mg/L	61
Spot, *Leiostomus xanthurus*	38,000	LC50 (96 h)	62
Bluegill, *Lepomis macrochirus*			
Adults	76-235	Reproduction inhibition	3
Adults	100	Hyperactivity	3
Fry	235	Lethal in 3 days	1,2
Adults, exposed for 7 days, then placed in a lethal NaC1 salinity (1.46%) for 60 h	2,350	Exposed fish all dead in 60 h (8 h for controls); plasma chloride declined in zinc-exposed fish, suggesting that zinc reduces permeability of gills to chloride	63
Adults	5,400	LC50 (96 h) at 20 mg $CaCO_3$/L	3
Adults	40,900	LC50 (96 h) at 360 mg $CaCO_3$/L	3

Marine fish, most species	>1,000	LC50 (96 h)	1
Tidewater silverside, *Menidia peninsulae*	5,600	LC50 (96 h)	62
Striped bass, *Morone saxatilis*			
Larvae	100-119	LC50 (96 h)	1,2
Fry	430-1,180	LC50 (96 h)	1,2
Adults	6,700	LC50 (96 h)	1
Stone loach, *Noemacheilus barbatulus*, adults	1,900-2,000	LC50 (25 days)	3,55
N. barbatulus	3,500	LC50 (96 h)	55
Loach, *Noemacheilus* sp.	25,000	LC50 (96 h)	64
Cutthroat trout, *Oncorhynchus clarki*	61-600	LC50 (96 h)	1,65
O. clarki	360	None dead in 14 days	66
O. clarki	670	LC50 (14 days)	3,66
Coho salmon, *Oncorhynchus kisutch*			
Water hardness <50 mg $CaCO_3$/L	280	LC50 (96 h)	3
Juveniles	500-10,700	Decreased white blood cell count in 24h	3
0.5-0.9 g BW	820-1,810	LC50 (96 h)	67
Rainbow trout, *Oncorhynchus mykiss*			
Immatures	5.6	Avoidance, 10- to 20-rain tests	1,2
Larvae and alevins	10	LC54 (28 days)	3
Immatures	47	94% avoidance, 40-rain tests	2
Early life stages	70-140	LC50 (25 days)	3
Juveniles	81	Hyperglycemia in 24 h	3
Fry	90-93	LC50 (96 h)	1,2
Life cycle	140-547	MATC [b]	1,2
Weight 0.6 g	169	LC50 (96 h)	67
Juveniles	210-1,120	Increased blood glucose in 7-63 days	3
Parr	240-830	LC50 (96 h) at 30 mg CaCO3/L	1
Juveniles	310	LC20 (14 days)	66
Immatures	352	Hyperglycemia in 9 days	2
Larvae and alevins	400-2,800	LC50 (120 h)	3
Juveniles	410	LC50 (14 days)	66
Juveniles	430	LC59 (96 h) at 26 mg CaCO3/L	3
Juveniles	520	LC50 (96 h) at 47 mg CaCO3/L	3
Fry	689	LC50 (96 h)	2
Juveniles	690	Increased respiration in 24 h	3
Immatures	1,030	LC50 (96 h) value for group acclimatized to 80 µg Zn/L for 28 days (469 µg Zn/L in nonacclimatized group)	68

Adults	1,120	Reduced growth in 85 days	3
Parr	1,190-4,520	LC50 (96 h) at 350 mg CaCO3/L	1
Juveniles	2,960	LC50 (96 h) at 179 mg CaCO3/L	3
Parr	4,700	LC50 (96 h) at 500 mg CaCO3/L	1
Juveniles	4,800-7,200	LC50 (96 h) at 333-504 mg CaCO3/L	3
Fry	10,000	16°/o dead in 90 h versus none dead in group pretreated with 5 mg Zn/L for 96 h	69
Fry	15,000	79% dead in 90 h versus 20% dead in group pretreated with 5 mg Zn/L for 96 h	69
Sockeye salmon, *Oncorhynchus nerka*			
Embryo through smolt	242	No measurable effects in 18-month exposure	1
Immatures	447	LC50 (115 h)	1
Immatures	750	LC50 (96 h)	3
Chinook salmon, *Oncorhynchus tshawytscha*			
Swim up	97	LC50 (96 h)	1
Chronic exposure	270-510	MATC [b]	1,2
Smolts	446	LC50 (96 h)	2
Minnow, *Phoxinus phoxinus*			
Yearlings	50-130	Reduced growth during exposure for 150 days; no deaths	70
Larvae	60	Decreased swimming ability after exposure for 108 days	3
Larvae	80	LC37 (40 days)	3
Adults	130	Reduced growth during 150-day exposure; some deaths	70
Juveniles	160	Decreased swimming ability after 109 days	3
Adults	200	Decreased swimming ability after 100 days	3
Adults	200	Reduced growth during 30-day exposure; some deaths	70
Adults	250	LC50 (150 days)	3
Fathead minnow, *Pimephales promelas*			
Life cycle	78-145	MATC [b]	1,2
Juveniles	125	Reduced growth in 7 days	2
Larvae	152-294	LC84 (8 weeks)	3
Adults	180	65 to 83% reduction in fecundity in 10-month exposure	1,2
Adults	480	Reduced growth in 30 days	3

Embryo-larvae	500-1,400	50% developmental malformations in 96h	71
Larvae	600	LC50 (96 h)	3
Adults	600	Preexposure for 14 days increased resistance 28% over controls in 96-h zinc toxicity assays	72
Adults	800	LC50 (30 days)	3
Adults	870	LC50 (96 h) at 20 mg $CaCO_3$/L,	3
Adults	1,800	Exposure for 7 days decreased tolerance 63% in 96-h zinc toxicity assays; tolerance decreased 74% after exposure for 14 days	72
Adults	2,800	LC15 (10 months), no eggs deposited	73
Embryo-larvae	3,600	LC50 (6 days)	71
Adults	4,700-6,100	LC50 (96 h) at 50 mg $CaCO_3$/L	3
Adults	6,400-10,900	LC50 (96 h) at 100 mg $CaCO_3$/L	3
Adults	7,100	LC50 (96 h) at 166 mg $CaCO_3$/L	3
Adults	8,200-21,000	LC50 (96 h) at 200 mg $CaCO_3$/L	3
Adults	33,400	LC50 (96 h) at 360 mg $CaCO_3$/L	3
Guppy, *Poecilia reticulata*			
Age 5 days	128	After 134 days, whole body zinc content of 0.6 mg/kg DW (0.3 mg/kg DW in controls); growth reduced	74
Adults	173	Whole body BCF of x466-965 in 30 days	2
Age 5 days	250	Delayed sexual maturation after 134 days	74
Age 5 days	500	Reproduction inhibited	74
Age 5 days	1,350-1,500	LC50 (96 h)	74
Adult males	4,400-5,700	LC50 (96 h)	74
Adult females	5,600-7,300	LC50 (96 h)	74
Atlantic salmon, *Salmo salar*			
Parr	50	50% avoidance in 4 h	2
Parr	100	Avoidance within 20 rain	3
Immatures, Water hardness	100-500	LC50 (21 days)	1
14 mg $CaCO_3$/L	420	LC50 (96 h)	1
20 mg $CaCO_3$/L	600	LC50 (96 h)	1
Brown trout, *Salmo trutta*			
Yolk-sac fry	4.9	40% with noncalcified vertebrae center; all dead in 18 days at pH 4.5 and soft water	75

Yolk-sac fry	9.8-19.6	60% to 75% dead in 20-30 days; 6% to 21% with abnormal vertebrae in pH 4.5 and soft water	75
Yearlings	<140	LC50 (96 h) at pH 8, 10 mg CaCO3/L	76
Adults	570	LC17 (14 days)	66
Adults	640	LC50 (14 days)	66
Yearlings	3,200	LC50 (96 h) at pH 5, 204 mg CaCO3/L	76
Brook trout, *Salvelinus fontinalis*			
Chronic exposure	534-1,360	MATC [b]	1,2
Adults	630	LC17 (14 days)	
Adults	960	LC50 (14 days)	3,66
Cabezon, *Scorpaenichthys marmoratus*, larvae	192	LC50 (96 h)	2
Dogfish, *Scyliorhinus* sp., exposure for 25 days	15,000	No significant accumulations in kidney and muscle, but elevated levels, as judged by BCF values in gill filament (x1.6), spleen (x1.7), pancreas (x2.7), and liver (x5.2)	77,78
Arctic grayling, *Thymallus arcticus*			
BW 0.2-1.8 g	112-168	LC50 (96 h)	67
Fry	315	LC50 (96 h)	67
Alevins	1,580-2,920	LC50 (96 h)	67
Tilapia, *Tilapia sparrmanii*, adults, exposure for 72 h	98,000	Decreased oxygen consumption, mucous precipitation on gills, histopathology of gill epithelium	79
Bolti, *Tilapia zilli*			
Adults	13,000	LC50 (96 h) at 25° C	52
Adults	21,000	LC50 (96 h) at 21° C; residues in survivors were 38,000 mg/kg DW in gill (70 mg/kg DW in controls); 23,000 mg/kg DW in liver (50 mg/kg DW controls); and 2,000 mg/kg DW in muscle, blood, serum, and liver chemistry (10 mg/kg DW in controls)	58,80
Adults	27,000	LC50 (96 h) at 15.3° C	52
Adults	33,000	LC50 (96 h) at 9.3° C	52
Amphibians			
Marbled salamander, *Ambystoma opacum*, embryos	2,380	50% dead or deformed in 8 days	2
Narrow-mouthed toad, *Gastrophryne*	10	50% dead or deformed in 7 days	2

carolinensis, embryos			
Leapfrog; *Rana dalmutina*, larvae, exposed during formation of gonadal structures	9,000	Toxic effect on larval gonad, especially on germ cells of ovarian structure	S1
Newt, *Triturus cristatus*, adults, held in tank with a zinc-plated base	200 to 3,000 over a 7-day period	Zinc-poisoned newts were lethargic, ate poorly, and has skin darkening before death. Zinc residues were elevated in kidney, brain, liver, and intestine, when compared to controls. The hippocampus region of the brain of poisoned newts contained zinc-rich cells	82
South African clawed frog, *Xenopus laevis*			
Embryos	>1,500	At 96 h, some midgut malformations and pericardial edema	83
Embryos	2,700	50% malformations in 96 h	83
Embryos	3,600	50% developmental malformations in 6 days	71
Embryos	>4,000	Severe edema of the pericardium and eye, gut miscoiling, and head and mouth malformations. At high sub-lethal concentrations, severe skeletal kinking, micropthalamia, and microencephaly	83
Tadpoles, pretreated with 5 mg Zn/L for 96 h	15,000-20,000	At 15 mg/L, none died in pretreated group versus 45% dead in controls at 90 h; at 20 mg/L, 15% died in pretreated group versus 50% in untreated controls	69
Embryos	34,500	LC50 (96 h)	71,83

[a]l. EPA 1980; 2. EPA 1987; 3. Spear 1981; 4. Vymazal 1986; 5. Francis and Harrison 1988; 6. Willis 1988; 7. Yantian 1989; 8. Nelson et al. 1988; 9. Munzinger and Guarducci 1988; 10. Belanger et al. 1986; 11. Farris et al. 1989; 12. Brereton et al. 1973; 13. Hunt and Anderson 1989; 14. Eisler 1980; 15. Mason 1988; 16. Eisler 1977a; 17. Eisler 1977b; 18. Lobel and Marshall 1988; 19. Amiard-Triquet et al. 1986; 20. Redpath and Davenport; 1988; 21. Hietanen et al. 1988b; 22. Hietanen et al. 1988a; 23. Akberali et al. 1985; 24. Conrad 1988; 25. Eisler and Hennekey 1977; 26. Chan 1988a; 27. Ahsanullah et al. 1988; 28. Bagshaw et al. 1986; 29. Ajmalkhan et al. 1986; 30. Paulauskis and Winner 1988; 31. Attar and Maly 1982; 32. Memmert 1987; 33. Khangarot and Ray 1989; 34. Johnson and Jones 1989; 35. Mirenda 1986; 36. Nugegoda and Rainbow 1989c; 37. McLusky and Hagerman 1987; 38. Verriopoulos and Hardouvelis 1988; 39. Verriopoulos and Moraitou-Apostolopoulou 1989; 40. Verriopoulos and Dim as 1988; 41. Lalande and Pinel-Alloul 1986; 42. Hatakeyama 1989; 43. Willis 1989; 44. Fernandez and Jones 1989; 45. Grant, et al. 1989; 46. Nakamura et al. 1989; 47. Voogt et al. 1987; 48. Eisler 1981; 49. Shukla and Pandey 1986b; 50. Shukla and Pandey 1986a; 51. Villegas-Navarro and Villarreal-Trevino 1989; 52. Hilmy et al. 1987c; 53. Somasundaram 1985; 54. Somasundaram et

al. 1985; 55. Solbe and Flook 1975; 56. Sauer and Warabe 1989a; 57. Eisler 1967; 58. Burton and Fisher 1990; 59. Taneja et al. 1958; 60. Bengeri and Patil 1986; 61. Gehrke 1988; 62. Mayer 1987; 63. Heath 1987; 64. Pundir 1989; 65. Mayer and Ellersieck 1986; 66. Nehring and Goettl 1974; 67. Buhl and Hamilton 1990; 68. Anadu et al. 1989; 69. Woodall et al. 1988; 70. Bengtsson 1974; 71. Dawson et al. 1988; 72. Hobson and Birge 1989; 73. Brungs 1969; 74. Pierson 1981; 75. Sayer et al. 1989; 76. Everall et al. 1989b; 77. Floe et al. 1979; 78. Crespo et al. 1979; 79. Grobler et al. 1989; 80. Hilmy et al. 1987c; 81. Gipouloux et al. 1986; 82. Taban et al. 1982; 83. Fort et al. 1989; 84.. NAS 1979; 85. Khangarot and Ray 1988.

[b]MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Acute LC50 (96 h) values for freshwater invertebrates were between 32 and 40,930 µg Zn/L; in fish, this range was 66 to 40,900 µg/L (EPA 1987). For marine invertebrates the LC50 (96 h) range was 195 µg/L for embryos of the hard-shelled clam (*Mercenaria mercenaria*) to >320 mg/L for adults of the Baltic clam (*Macoma balthica*). For marine telcosts LC50 (96 h) values were between 191 µg/L for larvae of the cabezon (*Scorpaenichthys marmoratus*) to 38 mg/L for juvenile spot, (*Leiostomus xanthurus*; EPA 1987). Many factors are known to modify the biocidal properties of zinc in aquatic environment. In general, zinc was more toxic to embryos and juveniles than to adult, to starved animals, at elevated temperatures, in the presence of cadmium and mercury, in the absence of chelating agent, at reduced salinities, under conditions of marked oscillations in ambient zinc concentrations, at decreased water hardness and alkalinity, and at low dissolved oxygen concentrations (Skidmore 1964; Weatherley et al. 1980; Spear 1981; EPA 1987; Paulauskis and Winner 1988; Table 6).

Bioconcentration factors (BCF) for zinc accumulation from the medium varied widely between and within species of aquatic organisms. For representative freshwater organisms, BCF values ranged from 107 to 1,130 for insects and from 51 to 432 for fish (EPA 1980). In marine environments, the most effective zinc accumulators included red and brown algae, ostreid and crassostreid oysters, and scallops. The ranges of BCF values for representative marine groups were 370 to 64,000 for algae, 85 to 1,500,000 for crustaceans, 15 to 500 for echinoderms, as much as 4 million for scallop kidneys, and 1,900 to 6,900 for fish (Eisler 1980). Significant zinc accumulations were reported after death in algae and fish, suggesting that residue data from these and other organisms found dead on collection are of limited worth (Eisler 1980). Maximum net daily accumulation rates by various whole marine organisms were 1.3 mg Zn/kg FW for the alga *Ascophyllum nodosum*, 7.7 mg Zn/kg FW for the common mussel *Mytilus edulis*, 19.8 mg Zn/kg FW for the oyster *Crassostrea virginica*, 32 mg Zn/k FW for the killifish *Fundulus heteroclitus*, 32 mg Zn/kg FW for the softshell clam *Mya arenaria*, and 223 mg Zn/kg FW for the sandworm *Nereis diversicolor*; in general, accumulation rates and total accumulations were higher at elevated water temperatures and at higher ambient zinc water concentrations (Eisler 1980).

Algae and Macrophytes

Blue green algae are among the most zinc-resistant aquatic plants (Vymazal 1986). Algae are classified by Vymazal (1986) as very resistant (>10 mg Zn/L), resistant (2-10 mg/L), moderately resistant (0.5-2 mg/L), low resistant (0.1-0.5 mg/L; *Navicula*, *Synedra*), and very low resistant (<0.1 mg Zn/L; *Diatoma*, *Tabellaria*, *Microspora*, *Ulothrix*).

The most sensitive aquatic plant was *Schroederella schroederi*, a diatom; 19 µg Zn/L was sufficient to inhibit growth by 50% in 48 h (EPA 1987). Freshwater aquatic plants are usually absent from areas containing >2.0 mg Zn/L; in hard waters of artificial streams containing 170 mg $CaCO_3$/L, a water concentration of 1.1 mg Zn/L caused a 50% decrease in the number of algal species (Spear 1981). Most freshwater diatom populations decreased in the range of 175-380 µg Zn/L; this sensitivity may be useful as an indicator of zinc contamination (Spear 1981). Zinc and cadmium are strongly synergistic in their toxic action to plants. Any level of cadmium >10 µg/L should be suspected of producing a significant increase in the toxicity of available zinc to freshwater plants (Whitton 1980).

In heavily-contaminated zinc environments (130-6,500 µg Zn/L), zinc-tolerant species are dominant (Spear 1981). Highly-tolerant strains of algae require 1.5-1.65 mg Zn/L for normal growth; at least three species of

some tolerant strains can live in water containing 3 g Zn/L (Vymazal 1986). Highly tolerant mutant strains of *Anacystis nidulans* required 1.5-16.5 mg Zn/L. In France, at least 17 species of freshwater algae seemed to be flourishing at 42.5 mg Zn/L and pH 4.2 (Vymazal 1986). Zinc-tolerant strains of aquatic algae tolerate high zinc concentrations with little bioconcentration. A zinc-tolerant strain of *Euglena gracilis*, for example, tolerates >700 mg Zn/L but contains <500 mg Zn/kg DW whole organism versus 50 mg Zn/L and 5,000 mg/kg DW for nontolerant strains (Fukami et al. 1988a). Another zinc-tolerant strain of *Euglena* had normal growth at 300 mg Zn/L and residues of about 7,000 mg Zn/kg DW versus the population decline of nontolerant strains at 300 mg Zn/L (Fukami et al. 1988b).

Algae are effective accumulators of zinc. Three species of marine algae had a mean BCF of 1,530 in 12 days, 4,680 in 34 days, and 16,600 in 140 days (EPA 1980). Bioconcentration factors for zinc and various species of algae are quite variable and usually range from 76 to 163,750 (Vymazal 1986; EPA 1987). Many species of aquatic plants contain ≥150 mg Zn/kg DW. In one case, algae (*Mougeotia* spp.) from northern England in zinc-contaminated waters contained a spectacular 219 g Zn/kg DW (Vymazal 1986); it is probable that most of the zinc in *Mougeotia* was not biologically incorporated. Algal accumulations of zinc are modified significantly by physiochemical variables. Zinc concentrations in algae were higher under conditions of decreasing light intensity, water pH, DDT levels, copper, cadmium, phosphate, suspended sediments, organic chelators and other complexing agents, calcium, and magnesium and under conditions of increasing water temperature, dissolved oxygen, duration of exposure, and ambient zinc concentrations (Eisler 1980; Whitton 1980; Vymazal 1986).

Unlike algae, submerged aquatic macrophytes play a minor role in cycling of zinc (Lyngby et al. 1982). Rooted aquatic macrophytes may participate in heavy metal cycling in the aquatic environment either as a source or as a sink. But studies with eelgrass (*Zostera marina*) show that zinc exchange between the sediment and the water is insignificant (Lyngby et al. 1982).

Molluscs

Zinc was most toxic to representative molluscs at elevated temperatures (Eisler 1977a; Sprague 1986; Khangarot and Ray 1987), in comparatively soft water or to marine molluscs in low salinity (Sprague 1986; Khangarot and Ray 1987), at earlier developmental stages (Munzinger and Guarducci 1988), at low dissolved oxygen concentrations (Khangarot and Ray 1987), and with increasing exposure to high zinc concentrations (Amiard-Triquet et al. 1986).

High zinc accumulations in molluscs are usually linked to high levels of calcium in tissues, low ambient concentrations of iron or cobalt, exposure to organochlorine or organophosphorus insecticides, low salinity, elevated temperatures, increased particulate loadings in medium, increasing length of exposure to higher doses of zinc, increasing age of the organism, and especially to proximity of heavily carbonized and industrialized areas (Eisler 1980). Radiozinc-65 was rapidly accumulated in southern quahogs (*Mercenaria campechiensis*) during a 10-day period; accumulation in the kidney was linear over time and enhanced at elevated phosphate loadings in the medium (Miller et al. 1985).

Large variations in daily zinc accumulation rates by marine bivalve molluscs are typical. For example, softshell clams (*Mya arenaria*) immersed in 500 µg Zn/L at 16-22° C had daily accumulation rates of 2 mg/kg FW soft parts on day 1 of exposure, 7.7 mg Zn/kg FW soft parts between days 1 and 7, and 3.3 mg Zn/kg FW soft parts between days 7 and 14. At a lower temperature regimen of 0-10° C, immersion in 500 µg/L produced daily accumulation rates of 9.9 mg/kg FW soft parts for the first 42 days, but clams lost zinc at a rate of 0.24 mg/kg daily between days 42 and 112 (Eisler 1981). At 2,500 µg/L and 16-22° C, daily accumulation rates in surviving *Mya* were 32.0 mg Zn/kg FW soft parts on day 1 of exposure and 11.7 between days 1 and 7. Changes in accumulation rates of zinc by *Mya* reflect, at least partially, complex interactions between water temperature, ambient zinc concentrations, duration and season of exposure, and physiological saturation and detoxification mechanisms (Eisler 1977a, 1977b).

The half-time persistence (Tb½) of zinc in whole molluscs is extremely variable and reported to range from 4 days in the common mussel (*Mytilus edulis*) to 650 days in the duck mussel (*Anodonta nutalliana*); intermediate values were 23-40 days in the limpet (*Littorina irroratea*), 76 days in the California mussel (*Mytilus californianus*), and 300 days in the Pacific oyster (NAS 1979). Zinc persistence in selected organs also shows considerable variability and may be significantly different from Tb½ values in the whole animal. For example, the

Tb½ of zinc in the *Mytilus edulis* kidney was estimated at 2 to 3 months (Lobel and Marshall 1988) versus 4 days for whole animal (NAS 1979).

Mytilus edulis has been used extensively as a model for molluscan zinc kinetics. Results of selected studies follow. In mussels, zinc is taken up by the digestive gland, gills, and mantle and rapidly transported by hemolymph to the kidney where it is stored in insoluble granules (Lobel and Marshall 1988). There is a high degree of variability in soft tissues of *M. edulis* that is due entirely to an unusually high degree of variability in zinc of 97 to 7,864 mg/kg DW in the kidney (Lobel 1987). This variability in zinc content of the kidney is due largely to a low molecular weight zinc complex (700-1,300) that showed a high degree of variability and a positive correlation with zinc concentration in the kidney (Lobel and Marshall 1988). But at low ambient concentrations of 50 µg Zn/L, the most sensitive bioindicators of zinc exposure were gills and labial palps (Amiard-Triquet et al. 1986). Food composition had little effect on tissue distribution of radiozinc-65 in mussels as judged by 5-day feeding studies of radiolabeled diatoms (*Thalassiosira pseudonana*), green alga (*Dunaliella tertiolecta*), glass beads, and egg albumin particles (Fisher and Teyssie 1986). Soft part BCF values ranged from 12 to 35 times and was probably due to a rapid desorption of radiozinc from the food particles into the acidic gut, followed by binding to specific ligands or molecules. The Tb½ in mussel soft parts ranged from 42 to 80 days for all food items--including glass beads--and about 20 days in shell (Fisher and Teyssie 1986). Elevated temperatures in the range 10° to 25° C were associated with increased uptake rates of zinc from seawater by mussels (Watkins and Simkiss 1988). If the temperature is oscillated through this range during a 6-h period, there is a further enhancement of zinc uptake. This effect parallels decreases in zinc content of cytosol fractions and increases in granular fractions (Watkins and Simkiss 1988). Mussels were more sensitive to zinc than other tested bivalve molluscs. The pumping rate of mussels completely stopped for as long as 7 h on exposure to 470 to 860 µg Zn/L; however, other tested bivalves showed only a 50% reduction in filtration rates in the range of 750 to 2,000 µg Zn/L (Redpath and Davenport 1988). *Mytilus edulis* accumulates zinc under natural conditions but does not depurate under some conditions (Luten et al. 1986). This conclusion was based on results of a study of mussels that were transferred from a pristine environment in the Netherlands to a polluted estuary for 70 days and then returned for 77 days. At the start, zinc concentration was 106 mg/kg DW soft parts. By day 70, it had risen to 265 mg/kg DW at a linear daily uptake of 0.47 mg/kg. But mussels contained 248 mg/kg DW on day 147, indicating that elimination was negligible (Luten et al. 1986). In another study, zinc depressed sperm motility through respiratory inhibition at 6.5 mg/L, a concentration much higher than that normally found environmentally (Earnshaw et al. 1986). In mussel spermatozoa, zinc caused reductions of bound calcium and phosphorus in both acrosomes and mitochondria, suggesting increased permeability of organelle membranes to both elements (Earnshaw et al. 1986).

Arthropods

Arthropods were the most zinc-sensitive group of tested invertebrates (Table 6). Toxicity was usually greatest to marine crustaceans (Eisler 1981), to larvae (Eisler 1980), at elevated temperatures (Spear 1981; Sprague 1986; McLusky and Hagerman 1987), during extended exposures (EPA 1980, 1987), in soft water (Winner and Gauss 1986; Paulauskis and Winner 1988), under condition of starvation (NAS 1979; Verriopoulos and Moraitou-Apostolopoulou 1989), at salinity extremes above and below the isosmotic point (McLusky and Hagerman 1987), in summer (Eisler 1980), at low concentrations of humic acid (Winner and Gauss 1986; Paulauskis and Winner 1988), in proximity to anthropogenic discharges (Eisler 1980), and at low sediment particulate loadings (Memmert 1987). Acquired zinc tolerance is reported in amphipods collected from zinc-contaminated sewage wastes (Johnson and Jones 1989) and in fiddler crabs (*Uca* spp.) from a metals-contaminated area. *Uca* from zinc-contaminated areas were more resistant to zinc than crabs from pristine areas, as judged by increased survival and lower tissue zinc concentrations (Devi 1987; Devi and Rao 1989a, 1989b). More research into acquired zinc tolerance seems warranted.

Adverse effects of zinc insult to crustaceans include gill histopathology in prawns, *Macrobrachium hendersodyanum* (Patel and Kaliwal 1989); increased tissue total proteins, decreased glycogen, and decreased acid phosphatase activity in crabs, *Portunus pelagicus* (Hilmy et al. 1988); retardation of limb regeneration of fiddler crabs, *Uca pugilator* (Weis 1980); Waiwood et al. 1987). For example, tissue zinc residues in Homarus americanus exposed for 4 days to 25 mg Zn/L were especially high in gills (2,570 mg Zn/kg DW vs. 126 mg Zn/kg DW at start), hepatopancreas (734 mg Zn/kg DW vs. 135 mg Zn/kg DW), and green gland (1,032 mg Zn/kg DW vs. 148 mg Zn/kg DW). After 7 days in uncontaminated media tissue zinc residues remained elevated in gills (675 mg Zn/kg DW), hepatopancreas (603 mg Zn/kg DW), green gland (286 mg Zn/kg DW), and other

tissues (Waiwood et al. 1987). Zinc concentrations in crustacean soft tissues usually are between 50 and 208 mg/kg DW and exceed soft tissue zinc enzymatic requirements by factors of 1.4 to 6.0 (Depledge 1989).

Half-time persistence of zinc is about 17 days in the prawn (*Palaemon elegans*; Nugegoda and Rainbow 1988b) and between 30 and 270 days in five other crustacean species (NAS 1979). Differences in half-time persistence are linked to differences in excretion rates of ionic zinc and complexed zinc. In general, crustaceans excrete ionic zinc first and complexed zinc next; surface-adsorbed zinc is turned over faster than internally-adsorbed zinc; molting accounts for a 33-50% loss of the total body burden in crabs (Eisler 1981).

Crustaceans can accumulate zinc from both water and food (EPA 1987). In uncontaminated waters, the diet is probably the major source of zinc. Absorption from the stomach is efficient and occurs in part through the hepatopancreas. When a large pulse of zinc reaches the blood from the stomach, some is excreted, but much is resorbed and stored in the hepatopancreas in a relatively nonlabile form. Ultimately, stored zinc is also excreted, although removal through the gut is unimportant (Bryan et al. 1986). Zinc absorption is initially at the gill surface, is followed by transport on a saturable carrier in the cell wall, and is most efficient at low dissolved ambient zinc concentrations. Urinary excretion is an important body removal pathway, especially at high dissolved ambient concentrations when it can account for 70-80% of the total zinc excretion (Bryan et al. 1986).

Barnacles (*Elminius modestus*) usually accumulate zinc to high body concentrations without significant excretion. Barnacle detoxification mechanisms of the stored zinc includes production of metabolically inert zinc phosphate granules (Rainbow and White 1989). However, *Elminius modestus* transplanted from an area of high ambient zinc (101 µg/L) to an environment of low ambient zinc (4 µg/L) lost zinc slowly (0.3% body burden daily) during an 11-week period. Whole body zinc burdens declined from 1,554 to 125 mg/kg DW or at about 4.1 mg/kg DW daily (Thomas and Ritz 1986). In the case of *Balanus balanoides*, another barnacle, high BCF values were attributed to inorganic granules that contained as much as 38% zinc and accumulated in tissues surrounding the midgut (Eisler 1980).

Crustaceans--and other groups--can regulate body concentration of zinc against fluctuations in intake, although the ways in which regulation is achieved vary among species (Bryan et al. 1986). Regulation of whole body zinc to a constant level is reported for many crustaceans, including intertidal prawns (*Palaemon* spp.), sublittoral prawns (*Pandalus montagui*), green crabs (*Carcinus maenus*), lobsters (*Homarus gammarus*), amphipods (*Gammarus duebeni*), isopods (*Asellus communis*), and crayfish (*Austropotamobius pallipes*; Devineau and Amiard-Triquet 1985; Bryan et al. 1986; Lewis and McIntosh 1986; Nugegoda and Rainbow 1988b; Johnson and Jones 1989; Rainbow and White 1989). The body zinc concentration at which zinc is regulated in crustaceans usually increases with increasing temperature, salinity, molting frequency, bioavailability of the uncomplexed free metal ions, and chelators in the medium (Nugegoda and Rainbow 1987, 1988a, 1989a, 1989b). Lobsters (*Homarus gammarus*) are able to equilibrate over a 30-day period in seawater containing between 2 and 505 µg/L. In response to a 100-fold rise in seawater concentrations (from 5 to 500 µg/L), zinc levels in whole body, blood, hepatopancreas, excretory organs, and gills almost doubled but changed little in muscle. Zinc concentrations in shells increased about 12 times, largely through adsorption (Bryan et al. 1986). Regulation of zinc in lobster blood is achieved by balancing uptake through the gills against urinary excretion and loss over the body surface including the gills (Bryan et al. 1986). The sublittoral prawn (*Pandalus montagui*) can regulate total body zinc concentration to a constant level (75 mg/kg DW) in dissolved zinc concentrations up to 22 µg/L, beyond which there is net accumulation of body zinc. This threshold of zinc regulation breakdown is lower than that in *Palaemon elegans* (93 µg Zn/L) and *Palaemonetes varians* (190 µg Zn/L) under the same physiochemical conditions (Nugegoda and Rainbow 1987, 1988a, 1988b, 1989a, 1989b, 1989c; Rainbow and White 1989). The authors conclude that regulation of body zinc concentration is most efficient in decapods adapted to the fluctuating environments of littoral habitats, possibly, as a result of changes in permeability of uptake surfaces in combination with improved zinc excretion systems.

Freshwater crayfish (*Orconectes virilis*) are among the more resistant crustaceans (LC50 value of 84 mg Zn/L in 2 weeks) and can easily tolerate the recommended water quality criteria of 50-180 µg/L; nevertheless, some streams in Arkansas and Colorado contain 79-99 mg Zn/L (Mirenda 1986). *Orconectes virilis* exposed to extremely high sublethal ambient zinc concentrations of 63 mg/L for 2 weeks show whole body BCF values of only 2; a similar pattern was observed at other concentrations. In all cases, zinc tended to concentrate in gills and hepatopancreas at the expense of muscle, carapace, and intestine (Mirenda 1986). In freshwater crayfish (*Procambarus acutus acutus*), the major uptake route was the ambient medium and not diet, although retention

time of dietary zinc was greater (Giesy et al. 1980). When dietary zinc was the only zinc source, crayfish rapidly reached a steady state; when water was the only zinc source, crayfish did not reach a steady state (Giesy et al. 1980). Freshwater mysidaceans and their particulate wastes may play an important role in zinc cycling. The freshwater opossum shrimp (*Mysis relicta*) feeding on sediments ingested 2 to 4 times more zinc than mysids feeding on zooplankton. However, sediment-feeding mysids excreted 3 to 5 times more zinc than zooplankton consumers; zinc concentrations were up to 24 times higher in fecal pellets of sediment feeders than in food (Van Duyn-Henderson and Lasenby 1986). In the freshwater crayfish *Austropotamobius pallipes*, fecal excretion is a major zinc removal pathway; a similar case is made for the green crab (*Carcinus maenus*; Bryan et al. 1986).

Marine copepods (*Anomalocera*, *Acartia*, *Temora*) excreted 52% of the ingested zinc in fecal pellets that subsequently leached all zinc to seawater within 24 h (Fisher et al. 1991).

Freshwater insects, including many species of mayflies, damselflies, stoneflies, and caddisflies, are relatively tolerant to zinc, with LC50 values usually >1.33 mg/L--although some species were adversely affected at concentrations between 30 and 37 µg Zn/L (EPA 1987; Table 6). Mayfly (*Epeorus latifolium*) larvae were adversely affected at ambient water concentrations of 30 µg Zn/L but could tolerate dietary loadings of 600 mg Zn/kg DW ration without measurable effects on growth or emergence (Hatakeyama 1989). Chironomid insect populations were reduced or missing immediately downstream from coal mine drainage containing 5-10 mg Zn/L; populations further downstream recovered numerically but in comparison with upstream communities, their diversity was reduced (Wilson 1988).

Annelids

Populations of freshwater oligochaetes and leeches were reduced in numbers of individuals and number of taxa in mine tailing effluents containing 146-213 µg Zn/L or sediments containing >20 g Zn/kg DW (Willis 1985b). Leeches (*Erpobdella octoculata*) experienced a reduction in density and reproductive capacity in streams containing 25 to 310 µg Zn/L from mine wastes and did not avoid these harmful concentrations (Willis 1989).

The highest rate of net zinc absorption reported for any group of invertebrates was 2,230 mg Zn/kg BW daily in sandworms (*Nereis diversicolor*) from sediments with low zinc levels during exposure for 34 days in 250 mg Zn/L. At 10 mg Zn/L, the rate decreased to 55 mg Zn/kg BW daily (Eisler 1981). Zinc uptake in *Nereis* increased with increasing sediment zinc levels, at lower salinities (Eisler 1980), and at elevated temperatures (Fernandez and Jones 1987, 1989). Zinc had no significant effect on burrowing behavior of *Nereis*, even at acutely lethal concentrations (Fernandez and Jones 1987). Sandworms from zinc-contaminated sediments were more resistant to waterborne zinc insult by 10-100 times than sandworms from clean sediments (EPA 1987). Tolerance to zinc in sandworms may be a result of acclimatization or genetic adaption. In either event, the degree of metal tolerance decreases rapidly as the level of zinc contamination declines, suggesting that some zinc-tolerant worms may be competitively inferior to normal individuals in clean environments (Grant et al. 1989). More research on zinc-tolerant populations seems merited.

Unlike other major groups of marine benthic organisms, the polychaete *Neanthes arenaceodentata* has a limited capacity to regulate zinc (Mason et al. 1988). Uptake in *Neanthes* occurs from the free ionic pool of zinc whereas EDTA complexes and EDTA-zinc complexes are largely excluded. Zinc accumulates linearly over time (350 h) and the rate decreases with increasing temperature in the range 4-21° C. Mason et al. (1988) concluded that uptake and accumulation of zinc is passive in *Neanthes* and does not require metabolic energy. Zinc transfer across the plasma membrane is by way of diffusion. Inside the cell, zinc binds to a variety of existing ligands that maintain an inwardly directed diffusion gradient, preventing zinc efflux. Accumulation rats is determined by the number and binding characteristics of the available ligands and their accessibility to zinc. After 50 h of exposure, worms selectively accumulate zinc over cadmium from the medium by a process requiring metabolic energy, and this is attributed to a change in the turnover rate and to the size and nature of the pool of zinc-binding ligands (Mason et al. 1988).

Echinoderms

In echinoderms, zinc concentrations are usually higher in detrital feeders than in carnivores, higher in surface feeders than in sediment feeders, and higher in specimens collected inshore than those collected offshore in deeper waters (Eisler 1980). Sea cucumbers (*Stichopus tremulus*) accumulate radiozinc-65 from

seawater by a factor of 1,400; however, radiozinc accumulation data should be viewed with caution because addition of stable zinc can reduce radiozinc-65 accumulations in echinoderm viscera up to 10-fold (Eisler 1981). Zinc inhibits the formation of the fertilization membrane in sea urchin eggs, possibly by interfering with cortical granule-derived proteases and proteins (Nakamura et al. 1989).

Fish

Several trends are evident (Table 6): (1) freshwater fish are more sensitive to zinc than marine species; (2) embryos and larvae are the most sensitive developmental stages; (3) effects are lethal or sublethal for most species in the range 50-235 µg Zn/L and at 4.9-9.8 µg Zn/L for the brown trout (*Salmo trutta*); and (4) behavioral modifications, such as avoidance, occur at concentrations as low as 5.6 µg Zn/L. Signs of zinc poisoning in fish included hyperactivity followed by sluggishness before death, fish swam at the surface, were lethargic and uncoordinated, showed hemorrhaging at gills and base of fins, shed scales, and had extensive body and gill mucous (Bengeri and Patil 1986). Zinc is most toxic to yearlings of brown trout in soft water at pH 4-6 and pH 8-9; toxicity at alkaline pH is attributed to the formation of ZnOH+, $Zn(OH)_2$, and $ZnCO_3$ in both hard and soft water--suggesting increased entrapment of metal precipitates within mucous and epithelial layers of the gill (Everall et al. 1989a). Acute zinc poisoning in fish is generally attributed to blockade of gas exchange across the gills, causing hypoxia at the tissue level. Tissue hypoxia in fish is a major physiological change before death once the gas exchange process at the gills is no longer sufficient to meet its oxygen requirements (Burton et al. 1972; NAS 1979; Everall et al. 1989a; Grobler et al. 1989). Cardiorespiratory responses to zinc in the spangled perch (*Leiopotherapon unicolor*) are similar to those induced by hypoxia; zinc-poisoned perch had damaged gill epithelia, resulting in impaired gas exchange and lowered oxygen tension in arterial blood (Gehrke 1988). Acute exposures to high lethal concentrations of zinc also caused histopathology of epithelia lining the oral capacity (Eisler and Gardner 1973).

Many factors modify the lethal properties of zinc to fish. Zinc is more toxic under conditions of comparatively low dissolved oxygen concentrations, high sodium concentrations, decreased loadings of organic complexing agents (Spear 1981), and low pH (NAS 1979). In guppies (*Poecilia reticulata*), females were more resistant than males to acute zinc insult; adults of both sexes were more resistant than 5-day-old fry (Pierson 1981). Dominant bluegills (*Lepomis macrochirus*) survived exposure to 32 mg Zn/L longer than submissive fish (NAS 1979). Water temperature is also an important modifier and it is generally agreed that zinc is more toxic at elevated temperatures (NAS 1979; Spear 1981; Hilmy et al. 1987c) when acclimatization temperature is considered. For example, cold-acclimatized (3° C) Atlantic salmon survived longer than warm-acclimatized (19° C) salmon when exposed to lethal concentrations of zinc at their respective acclimatization temperatures. However, at test temperatures lower than their former acclimatization temperatures, salmon were less tolerant of zinc (Hodson and Sprague 1975).

Fish surviving high sublethal concentrations of zinc had significant alterations in blood and serum chemistry, liver enzyme activity (Hilmy et al. 1987b), muscle glycogen, total lipids, phospholipids, cholesterol, RNA, and proteins (Taneja et al. 1988).

Reproductive impairment seems to be one of the more sensitive indicators of zinc stress in freshwater teleosts, and effects are evident in the 50-340 µg Zn/L range (Spear 1981). In some cases, reproduction was almost totally inhibited at zinc concentrations that had no effect on survival, growth, or maturation of these same fish (Brungs 1969). Zinc-induced developmental abnormalities were documented in marine teleosts, but concentrations were grossly elevated. Eggs of the Baltic herring (*Clupea harengus*), for example, exposed to >6 mg Zn/L had an altered rate of development and produced deformed larvae with cellular disruptions in the brain, muscle, and epidermis (Somasundaram 1985; Somasundaram et al. 1985).

Avoidance tests with fathead minnows (*Pimephales promelas*) showed that almost all except males with established territories avoid 284 µg Zn/L when given a choice; avoidance thresholds were 6.4 times higher for established males (Korver and Sprague 1989).

Limited tolerance to zinc was observed in freshwater fish preexposed to sublethal levels of zinc (Spear 1981; Heath 1987; Woodall et al. 1988; Anadu et al. 1989; Hobson and Birge 1989). In one case, rainbow trout acclimatized to 50 µg Zn/L for 21 days were as much as 5 times more tolerant to subsequent zinc exposures than nonacclimatized trout; this was not evident at 100 µg Zn/L; also, acclimatization to zinc produced tolerances to copper and cadmium in trout (Anadu et al. 1989). The mechanisms to account for this

phenomenon are unknown, but several theories are proposed: increased metallothionein synthesis (Woodall et al. 1988), although this is disputed by Hobson and Birge (1989); high mortality during preexposure may have caused the selection of more zinc-tolerant individuals (Spear 1981); and tolerance may be limited to strains capable of increased zinc excretion, although no evidence now exists linking genetic mechanisms to zinc resistance (Spear 1981).

The estimated half-time persistence (Tb½) of zinc in whole mosquitofish (*Gambusia affinis*) was 215 days (Newman and Mitz 1988). The half-time persistence of zinc in whole marine fish ranged from 35 to 75 days in the mummichog (*Fundulus heteroclitus*) to 295-313 days in a flatfish (*Pleuronectes platessa*); Tb½ in mummichogs was shortest at 30° C, longest at 10° C, and intermediate at 20° C (NAS 1979).

Fish can accumulate zinc from both the surrounding medium and from their diet (EPA 1987). The freshwater zebra danio (*Brachydanio rerio*) accumulated zinc from the medium, but there was no additional zinc enrichment from a *Daphnia* diet (Memmert 1987). In marine fish, however, diet was considered the major route of zinc intake and significantly more important than water zinc levels (Eisler 1980).

In freshwater fish, BCF values for whole individuals were between 51 and 500 times (EPA 1987) but are strongly influenced by dose, duration of exposure, water chemistry, and other variables. In mosquitofish, uptake rate from water and zinc elimination rate decreased with increasing age of the fish (Newman and Mitz 1988). In the three-spined stickleback (*Gasterosteus aculeatus*), uptake was greater in hard water than in soft water and greater in larger fish, suggesting a surface adsorption mechanism (Matthiessen and Brafield 1977). In brown trout, however, uptake was lower and excretion greater in hard water of 220 mg $CaCO_3$/L than in soft water of 9 mg $CaCO_3$/L, thereby reducing tissue burdens (Everall et al. 1989a). Starved rainbow trout accumulated zinc more rapidly than fed fish because of an increased contribution of waterborne zinc to total body zinc levels (Handy and Eddy 1990). Rapidly growing chinook salmon (*Oncorhynchus tshawytscha*) fingerlings removed radiozinc-65 from the medium and retained nearly all of it for 63 days after transfer to uncontaminated media. Most of the radiozinc-65 was translocated to vertebral column, head, and visceral mass (Joyner and Eisler 1961). The outer surface of the bone seems to be an ion-exchange medium capable of taking up large quantities of metal ions whether natural or foreign to the system. Metals thus exchanged from serum proteins may be prevented from undergoing further exchange by the overlayering action of growing bone (Joyner and Eisler 1961). Channel catfish (*Ictalurus punctatus*) fingerlings fed diets containing up to 200 mg Zn/kg FW ration for 12 weeks had elevated bone zinc levels (359 mg/kg DW vs. 254 mg/kg DW in controls) and reduced hematocrit, but survival and feed conversion efficiency was the same as by controls (Gatlin et al. 1989). Plasma zinc levels in four species of freshwater fish on diets containing 100-200 mg Zn/kg ration ranged between 9.3 and 15.1 mg Zn/L FW; in rainbow trout, zinc tended to concentrate in the erythrocyte membrane (Bettger et al. 1987).

In marine fish, zinc residues were usually higher in dead than in live or moribund animals, higher in smaller fish, higher in liver and viscera, and higher with decreasing water cadmium levels (Eisler 1980). Uptake from the medium by adult mummichogs was inversely related to zinc concentration in the water (EPA 1987). In mummichogs, zinc accumulates in scales during exposure to 10 mg Zn/L, significantly elevating the zinc to calcium ratio; ratios remained elevated for at least 4 months after transfer to low zinc media, and this phenomenon may have application for environmental monitoring (Sauer and Watabe 1989a).

Scale osteoblasts of zinc-exposed mummichogs showed an increase in the number of lysosome-like structures contained by cytoplasm and suggests that osteoblast lysosomes are involved in zinc accumulation in fish scales by enzymatic degradation of metallothioneins or other metal-binding proteins (Sauer and Watabe 1989). Dietary zinc is not well assimilated in marine flatfish. Turbot (*Scopthalmus maximus*) fed diets containing 100 (control) or 1,000 mg Zn/kg DW for 200 days were not different in renal and hepatic metallothionein levels or in zinc concentrations in the liver, kidney, muscle, skin, or bone; a similar case is made for other marine flatfish (Overnell et al. 1988). However, intraperitoneally injected (2 mg Zn/kg BW) turbots had an 18-fold increase in liver metallothionein constant and a 3-fold increase in liver zinc, confirming the ability of this species to synthesize metallothionein rapidly to a high concentration (Overnell et al. 1988).

Amphibians

Amphibian embryos are more sensitive to zinc than older stages; developmental abnormalities were evident in most species at concentrations >1.5 mg Zn/L (Table 6). Embryos of the narrowmouthed toad (*Gastrophryne carolinensis*) seem to be especially sensitive; adverse effects were reported at 10 µg Zn/L (EPA 1987), but this requires verification. Amphibians and other taxonomic groups were rare or absent in the vicinity of zinc smelters but not in more distant sites (Beyer et al. 1985).

In tests with isolated skin of frogs (*Rana* spp.), Zn^{2+} stimulates sodium transport and inhibits chloride-related tissue conductance; however, the skin of toads is relatively insensitive to zinc (Nagel et al. 1988). In early stages of embryonic development, Zn^{2+} stimulates multiplication of germ cells, but long-term treatment with $ZnSO_4$ has a toxic effect on the larval gonad and especially on the germ cells of the ovarian structure that is developed in frog larvae (Gipouloux et al. 1986).

Birds

Ducks (*Anas* spp.) had reduced survival when fed diets containing 2,500-3,000 mg Zn/kg ration or when force-fed zinc metal shot equivalent to 742 mg Zn/kg BW (Table 7). Domestic chickens (*Gallus* sp.) were more resistant: 8,000 mg Zn/kg ration was fatal to chicks, although higher doses were routinely fed to laying hens to induce molting; 2,000-3,000 mg Zn/kg ration inhibited chick growth; 178 mg Zn/kg feed caused immunosuppression in chicks; and dietary concentrations as low as 100 mg Zn/kg caused pancreas histopathology in chicks under conditions of selenium deficiency (Table 7). Excessive zinc (2,000 mg/kg diet for 21 days) fed to chicks (*Gallus* sp.) caused zinc accumulations in tissues, reduced tissue turnover of zinc, reduced liver turnover of iron, and reduced copper content of the liver and pancreas and iron in the tibia (Stahl et al. 1989b). However, hens were less sensitive and, when fed diets containing 2,000 mg Zn/kg for 44 weeks, produced chicks that had no apparent alteration in tissue zinc, copper, or iron metabolism (Stahl et al. 1990).

Table 7. Effects of zinc on representative birds.

Species, dose, and other variables	Effects	Reference[a]
Mallard, *Anas platyrhynchos*		
Fed diets containing 3,000 mg Zn/kg feed, and higher, for 30 days	At 3,000 mg/kg ration, ducks had leg paralysis and decreased food consumption; at >3,000 mg/kg diet, many deaths occurred	1
Age 7 weeks. Fed diets containing 3,000, 6,000, 9,000, or 12,000 mg Zn/kg dry weight (DW) diet for 60 days; zinc in form of zinc carbonate	Food intake reduced for all groups; the 9,000 and 12,000 mg/kg groups had almost zero intake. High mortality after 30 days in all groups; only 17% of 3,000 mg/kg group alive at day 60. Zinc residues at time of death or at day 60 for the 3,000 mg/kg group were 89 mg/kg fresh weight (FW) in pancreas (1,252 mg/kg FW in controls); 401 mg/kg FW in liver (54 mg/kg FW); 88 mg/kg FW in adrenals (45 mg/kg FW); 413 mg/kg FW in kidney (27 mg/kg FW); 32 mg/kg FW in muscle (14 mg/kg FW); 78 mg/kg FW in testes (17 mg/kg FW); and 71 mg/kg FW in ovary (31 mg/kg FW)	2
Age 1 year. Single oral dose of five number 6 zinc shot in gelatin capsules,	All shot retained in gizzard after 14 days; no adverse effects after 28 days. Residues at	3

equivalent to 0.40 g zinc or 495 mg Zn/kg body weight (BW)	28 days were 217 mg/kg DW in liver, 79 mg/kg DW in kidney, and 126 mg/kg DW in feather	
Drakes, 18 months old, force-fed eight number 6 zinc shot pellets	By day 30 posttreatment, 20% had died. The mean weight loss was 33% in dead birds and 22% in survivors. About 83% of survivors developed signs of zinc poisoning	4
Age 1 year. Single oral dose of ten number 6 zinc shot in gelatin capsules, equivalent to 0.80 g zinc or 990 mg Zn/kg BW	Two to 4 shot voided in first 48 h, but no further loss for 28 days. Residues at 28 days were 211 mg Zn/kg DW in liver (171 mg Zn/kg DW in control birds), 72 mg Zn/kg DW in kidney (61 mg Zn/kg DW), 143 mg Zn/kg DW in feather (128 mg Zn/kg DW)	3
Pekin duck, *Anas platyrhynchos*		
3-day-old male white ducklings fed diet containing 2,500 mg Zn/kg, as $ZnSO_4.H_2O$, for 56 days	Progressive ultrastructural degeneration of pancreatic acinar cells evident as early as day 5	5
Japanese quail, *Coturnix coturnix japonica*		
Intratesticular injection of 3% zinc chloride equivalent to 1 mg Zn/kg testes or 0.02 mg/kg BW	Testicular teratomas produced during a period of testicular growth stimulated by increased photoperiod	6
Hens fed diet containing 15,000 mg Zn/kg ration, as zinc oxide, for 7 days	Significant reduction in body weight, egg production approached zero at day 3, eggshell breaking strength reduced, molting induced	7
14-day-old quail fed diets containing various concentrations of zinc, as zinc phosphide (a rodenticide) for 5 days followed by 3 days of untreated feed	At 600 mg Zn/kg ration, 7% died and all had reduced food intake. At 990 mg Zn/kg diet, 53% died; at 1,634 mg/kg died, 93% died	8
Domestic chicken, *Gallus* sp.		
Developing embryos, 1 day old, with 0.76 mg Zn/yolk at start, supplemented with 0.2, 0.4, or 0.6 mg zinc	Hepatic metallothionein levels increased by factors of 3.9 (0.2 mg), 4.7 (0.4 mg), and 7.1 (0.6 mg)	9
Femurs from 9-day-old chick embryos cultivated for 6 days at 3.26 mg Zn/L	Inhibited calcium accumulations in bone and increased alkaline phosphatase activity of medium	10
As above, 6.5 mg Zn/L	Decrease in calcified tissues	10
Domestic breeding hens fed diets containing 28, 38, 48, 68, 94, or 178 mg Zn/kg ration for up to 9 months	Progeny growth after 3 weeks was not affected by maternal zinc feeding levels. A minimum of 38 mg Zn/kg diet was considered necessary for minimal feather fraying and maximal immune response in chicks. Diets containing 178 mg Zn/kg may be excessive and cause	11

	immunosuppression of young progeny without affecting growth	
Fed 28 (control), 48, 228, or 2,028 mg Zn/kg diets for 12 or 44 weeks. Hens were 56 weeks old at start of short-term study and 24 weeks old at start of long-tern study	Zinc treatments had no effect on overall egg production, feed conversion, feed consumption, hatchability, or progeny growth to age 3 weeks. Zinc was elevated in eggs from hens fed the 2,028 mg/kg diet, but chick performance and tissue zinc content were unaffected by maternal zinc nutritional status	12
Chicks fed diets containing 37 (control), 100, or 2,000 mg Zn/kg feed for 21 days	No accumulations in 100 mg/kg group; zinc excretion rate about x2 controls. No deaths in 2,000 mg/kg group, but growth rate was decreased, anemia evident, tissue copper and iron decreased, and tissue zinc increased	13
Day-old chicks fed selenium-deficient diets plus 100 mg Zn/kg FW, as zinc oxide, purified ration for 9 days	Elevated zinc concentrations in pancreas, and pancreas histopathology	14
Hens fed diets containing 218, 257, 1,762, or 1,861 mg Zn/kg diet for up to 40 weeks	Eggs from hens fed 218 or 257 mg Zn/kg diet contained a maximum of 14 mg/kg FW, equivalent to about 25% more zinc than eggs produced by control hens. Eggs from the two higher-dose diets had a maximum of 19 mg/kg FW or 57-90% more zinc than eggs produced by hens fed a control diet of 26-28 mg Zn/kg.	15
9-day-old chicks fed purified diet containing 500 mg Zn/kg ration for 2 weeks	Plasma alpha-tocopherol reduced 64%; plasma and pancreas zinc concentrations elevated	16
Day-old chicks fed selenium-adequate diet plus 2,000 mg Zn/kg FW, as zinc oxide, nonpurified ration for 9 days	Negligible effects on pancreas zinc concentration and on pancreas exocrine function	14
9-day-old chicks fed nonpurified diet containing 2,000 mg Zn/kg ration for 80 days.	No effect on plasma alpha-tocopherol or plasma and pancreas zinc content	16
Chicks fed diets containing 2,000 or 3,000 mg Zn/kg ration for 30 clays	Slight reduction in growth at 2,000 mg/kg; significant growth reduction at 3,000 mg/kg	1
Day-old chicks fed diets containing up to 4,000 mg Zn/kg ration for 4 weeks	No effect on growth, survival, or feed conversion. Zinc accumulated in tissue metallothioneins, especially in liver and kidney; levels normal after 5 days on zinc-deficient diet	17
Day-old chicks fed diets containing 4,000, 8,000, or 16,000 mg Zn/kg for 5 weeks	All dead at 16,000 mg/kg diet. The 8,000 mg/kg group had 80% mortality; survivors had signifi-cantly reduced growth and feed conversion. At 4,000 mg/kg, no significant effect on growth or	17

	survival; zinc concentrations elevated in kidney, liver, intestinal mucosa, and pancreas--but values normal after 10 days on basal diet	
Age 71 weeks, laying hens. Fed diet containing 10,000 mg Zn/kg feed for 2 days, then 5,000 mg/kg diet for 4 days	Hens started to molt and ceased laying. Feed intake decreased about 90%. Zinc concentrations increased in pancreas 7 times, in liver 6 times, in kidney 3 times, and were elevated in shell gland and yolk. High zinc levels in kidney reflect high zinc excretion rates; high pancreatic zinc (410 mg Zn/kg FW) may suppress the release of insulin by calmodulin inhibition, and could account for the rapid cessation of lay	18
White leghorns and brown layers were fed diets containing 10,000, 20,000, or 30,000 mg Zn/kg feed, as zinc oxide, for up to 3 weeks to induce molting	Cessation of egg laying in all treatments. On resumption of egg production, zinc levels in albumin or eggshell were not affected by the treatment or strain; zinc levels in yolk increased and depended on feed intake rather than dose. No increase in zinc content in eggs laid after egg production resumed, regardless of dose or duration of zinc treatment	19
White leghorn laying pullets and hens fed diet containing 20,000 mg Zn/kg feed for 5 days	Reduced body weight on day 5, and significantly lowered egg production for 4 weeks. Eggs collected 14-28 days after the 5-day study period had reduced fertility and hatchability. Normal growth, egg production, fertility, and hatch-ability during weeks 4-12 posttreatment	20
Laying hens fed diet containing 20,000 mg Zn/kg, as zinc oxide, for 4 days followed by 18 days on basal (35 mg Zn/kg) diet	At day 4, liver zinc concentrations increased 10 times, kidney 3 times, egg yolk 3 times, and pancreas 25 times; liver and kidney values returned to normal by day 22, but pancreas concentration (1,673 mg/kg DW) remained elevated when compared to controls (88 mg/kg DW). At day 10, reduced weight of ovary and oviduct	21
Turkey, *Meleagris gallopavo*		
Zinc concentration of sperm storage medium increased from 25 to 90 mg/L.	Fertilizing ability of stored sperm significantly reduced	22

[a] 1. NAS 1979; 2. Gasaway and Buss 1972; 3. French et al. 1987; 4. Grandy et al. 1968; 5. Kazacos and Van Vleet 1989; 6, Guthrie 1971; 7. Hussein et al. 1988; 8. Hill and Camardese 1986; 9. Fleet and McCormick 1988; 10. Kaji et al, 1988; 11. Stahl et al. 1989a; 12. Stahl et al. 1990; 13. Stahl et al. 1989b; 14. Lu and Combs 1988a; 15. Stahl et al. 1988; 16. Lu and Combs 1988b; 17. Oh et al 1979; 18. Veheyen et al. 1990; 19. Decuypere et al. 1988; 20. Palafox and Ho-A 1988; 21. Williams et al. 1989;p 22. Blesbois and Mauger 1989.

Zinc-poisoned mallards (*Anas platyrhynchos*) force fed zinc shot pellets developed ataxia, paresis, and total loss of muscular control of legs, including the ability to swim (Wobeser 1981). The muscular, weakness associated with zinc intoxication would probably make ducks highly susceptible to predation and argues against the use of zinc shot as a substitute for lead shot (Grandy et al. 1968). Mallards fed 3,000 mg Zn/kg DW ration for 60 days had diarrhea after 15 days; leg paralysis in 20 days; high mortality after 30 days; and zinc residues that were 14 times higher in pancreas than in controls, 7 times higher in liver, 15 times higher in kidney; and 2 to 4 times higher in the adrenals, muscle, testes, and ovary at day 60 (Gasaway and Buss 1972).

In Australia, almost all aviary birds are held in cages of galvanized wire mesh, resulting in sporadic cases of "new wire disease" caused by the ingestion of galvanized metal. In one case, peachfaced lovebirds (*Agapornis roseicollis*) died within 5 weeks of placement in a newly erected wire cage; dead birds had elevated liver zinc concentrations of 75-156 mg/kg DW versus normal values of 21-33 mg/kg DW (Reece et al. 1986). Zinc poisoning in a captive Nicobar pigeon (*Caloenas nicobarica*) was attributed to plated zinc metal fragments found in the gizzard--presumably ingested from the galvanized cage bars. In addition to elevated tissue zinc concentrations, this pigeon had a swollen liver and kidneys and extensive kidney histopathology (Zee et al. 1985). A zinc-poisoned blue and gold macaw (*Ara ararauna*) showed weakness, ataxia, extreme thirst, diarrhea, cyanosis, and a plasma zinc concentration of 15.5 mg/L after ingesting galvanized hardware cloth that was 24% zinc by weight and 0.2% lead. The bird was treated with 35 mg/kg BW calcium versanate intramuscularly and 30 mg thiamine hydrochloride per kilogram of BW; recovery following chelation therapy took 2 months, at which time plasma zinc was 0.6-0.8 mg/L versus 1.3-2.0 mg/L for normal birds (Morris et al. 1986). New galvanized wire used in aviary construction should weather for 1 to 2 months and then be scrubbed with a mild acidic solution such as vinegar and rinsed; flakes of galvanized metal--which contain up to 2.4 g Zn/kg--should be removed before birds are put in cages (Reece et al. 1986).

Zinc toxicosis was diagnosed in a gray-headed chachalaca (*Ortalis cinereiceps*) after it ingested a copper-plated zinc penny; necropsy showed pancreas histopathology and severe gizzard erosion; liver contained 1,910 mg Zn/kg FW (Droual et al. 1991).

Large amounts of zinc are crucial for new feather growth. Zinc deficiency during this period results in stunted, frayed, easily-broken feathers. Studies with the giant Canada goose (*Branta canadensis maxima*) showed that zinc was released from the pectoralis muscle during molt-induced atrophy and used for growth of feathers and leg muscles during this period (Rosser and George 1986).

Zinc phosphide--a rodenticide--is relatively toxic in comparison with elemental zinc or zinc oxide; most of the biocidal action is attributed to the phosphide fraction. Acute oral LD50 values for zinc phosphide were between 16 and 47 mg/kg BW in the ring-necked pheasant (*Phasianus colchicus*), golden eagle (*Aquila chrysaetos*), mallard, and horned lark (*Eremophila alpestris*; Hudson et al. 1984). Signs of zinc phosphide poisoning include excessive drinking, regurgitation, muscular incoordination, appetite loss, sluggishness, rapid breathing, and eyelid droop. Signs appeared as soon as 15 min after dosing, and death usually occurred between 2 and 21 h; remission took up to 1 month (Hudson et al. 1984).

High dietary levels of zinc are frequently fed to poultry to force molting and reduce egg deposition (Decuypere et al. 1988; Hussein et al. 1988). Extremely high dietary levels of 20 g Zn/kg ration have been used as a commercial management technique to force the molting of laying hens .and the subsequent improvement of long-term egg production that molting produces (Lu and Combs 1988a). Laying hens given high zinc diets increased their zinc uptakes 5-40 times in a dose-dependent pattern despite the decreased food intake associated with high zinc dietary levels. Zinc preferentially accumulated in chicken kidney, liver, pancreas, and gizzard; significant increases in egg zinc occurred at dietary levels of 10 and 20 g Zn/kg (Verheyen et al. 1990). Unlike adults, high dietary levels of zinc adversely affected pancreatic exocrine function in the chick; effects were exacerbated under conditions of selenium deficiency and feeding of purified diets (Lu and Combs 1988a). Impaired enteric absorption and transport of vitamin E as a consequence of zinc-induced pancreatic insufficiency is a major cause of reduced tissue concentrations of alpha-tocopherol produced in chicks by excess dietary zinc; these effects were magnified by diets low in corn, soybean meals, and other materials known to chelate zinc and thus reduce its biological availability (Lu and Combs 1988b). Excess dietary zinc causes pancreatic damage in the chick, including reduced activities of major digestive enzymes, elevated plasma amylase activities, reduced digestibility of starch, and reduced vitamin A activity; these changes were associated directly with elevated tissue zinc concentrations, especially in the pancreas (Lu et al. 1990).

Mammals

Livestock and small laboratory animals are comparatively resistant to zinc, as judged by their tolerance for extended periods to dietary loadings >100 times the minimum recommended daily zinc requirement (Table 8). Nevertheless, excessive zinc intake through inhalation or oral exposure can have drastic effects on survival, metabolism, and well being. Sensitive species mammals were affected at 90-300 mg Zn/kg diet, >300 mg Zn/L drinking water, > 90 mg/kg BW daily, > 350 mg Zn/kg BW as a single oral dose, and > 0.8 mg Zn/m^3 air (Table 8).

Zinc is relatively nontoxic in mammals. A wide margin of safety exists between normal intakes and those producing deleterious effects. In most cases, dietary levels up to 100 times the daily requirement for extended periods show no discernable effects (NAS 1979; Wentink et al. 1985; Goyer 1986; Leonard and Gerber 1989). The possibility of oral zinc intoxification in adult humans is unusually low, as judged by the low (40%) bioavailability of zinc from the gastrointestinal tract and the high tolerances to zinc reported in domestic livestock and small laboratory animals (Llobet et al. 1988a, 1988b). Humans ingesting up to 12 g of elemental zinc, equivalent to 33 mg/kg BW for a 60-kg adult, during a 2-day period show no evidence of hematologic, hepatic, or renal toxicity (Goyer 1986).

Excessive zinc intake adversely affects survival of all tested mammals --including humans--and produces a wide variety of neurological, hematological, immunological, hepatic renal, cardiovascular, developmental, and genotoxic effects (PHS 1989). The most sensitive species of mammals showed adverse effects at dietary levels of 80-90 mg Zn/kg in humans, 300 mg Zn/kg ration in domestic cats, and 500 mg Zn/kg feed in rats; drinking water concentrations of 300 mg/L in domestic mice and 800 mg Zn/L in laboratory white rats; daily whole body intakes >90 mg Zn/kg in horses; acute oral LD50 doses of 350-800 mg Zn/kg BW in rats; intraperitoneal injections of 13 mg Zn/kg BW in mice; and 0.8 mg Zn/m^3 air in guinea pigs (Table 8).

Metal fume fever is commonly encountered by industrial workers exposed to zinc fumes and is characterized by pulmonary irritation, fever, chills, and gastroenteritis (Saxena et al. 1989b). Attacks begin 4-8 h after exposure and recovery, in 24-48 h. The pathogenesis of metal fume fever is unknown but may be associated with endogenous pyrogens released by cell lysis (Goyer 1986). Rabbits, rats, and cats exposed to zinc oxide fumes for 3.5 h at concentrations of 110-600 mg/m^3 reacted with a transient fall in body temperature followed by leucocytosis; heavily-exposed animals had signs of bronchopneumonia (Elinder 1986). The current atmospheric threshold limit value for zinc is 5 mg/m^3; however, results of studies with guinea pigs suggest that the current threshold limit value for zinc oxide should be lowered (Lam et al. 1985; Table 8).

Excessive zinc uptake is associated with lameness, unthrifty appearance, and osteochondrosis in foals and pigs, nephrosis in ferrets, and pancreatic fibrosis in sheep (Gunson et al. 1982). Zinc-poisoned mammals are usually characterized by a decreased growth rate, subcutaneous hematomas, ulcerative gastritis, hemorrhagic enteritis, lesions of major limb joints, renal lesions, elevated serum and tissue zinc concentrations, acute diarrhea, copper deficiency, impaired reproduction, and decreased activity of cardiac and hepatic cytochrome oxidase (Saxena et al. 1989b). In severe cases, histopathological changes in the liver and especially in the pancreas, and degenerative changes in the kidney and gastrointestinal tract are evident and are followed by life-threatening hemolytic anemia (Straube et al. 1980; Allen et al. 1983; Robinette 1990). The pancreas is the key to the diagnosis of zinc toxicity and in estimation of the period of exposure; in sheep, it takes about 4 weeks of continued ingestion of toxic amounts of zinc before the pancreas is affected (Allen et al. 1983). More research into the role of the pancreas in zinc toxicokinetics is needed.

Zinc is important to the normal functioning of the central nervous system. At low concentrations, zinc protects mammalian brain neurons by blocking N-methyl-D-aspartate receptor-mediated toxicity. At high concentrations, zinc is a potent, rapidly acting neurotoxicant in the mammalian brain, as judged by zinc-induced neuronal injury of in vitro mature cortical cell cultures (Choi et al. 1988). Increased brain levels of zinc are associated with Pick's disease in certain strains of rodents with inherited epileptic seizures. Intravenous injection of zinc in rats with genetically inherited epilepsy produces seizures; a similar response occurs with intracranial injection of zinc in rabbits with inherited audiogenic seizures (Choi et al. 1988).

Table 8. Effects of zinc on representative mammals.

Organism, route of administration, dose, and other variables	Effects	Reference[a]
Cows, cattle, *Bos* spp.		
Dairy cows fed control diet (310 mg Zn/kg dry weight [DW] feed) or control diet supplemented with 1,000 or 2,000 mg Zn/kg DW ration (as $ZnSO_4 \cdot H_2O$)	The 1,000 mg/kg supplement has no adverse effects on milk production, feed intake, body weight, general health, or reproduction; there was a moderate increase in zinc content of plasma and milk. Cows fed the 2,000 mg Zn/kg diet, however, had decreased milk yield and feed intake after several weeks; calf weights were lower; adverse effects reversed when excess zinc was removed from diet	1
Calves fed diets containing 600 mg Zn/kg for 21 days	Appeared normal, although zinc levels were elevated in pancreas, liver, and kidney	2
Lactating dairy cows fed diets containing 700 or 1,000 mg Zn/kg feed for 6 weeks	No change in general health or milk production; no increase in milk zinc content	2
Lactating cows fed diets containing up to 1,386 mg Zn/kg feed for 5 weeks	No significant change in food intake, weight gain, milk production or in zinc concentrations in plasma (1.15-1.3 mg/kg fresh weight [FW]) or milk (3.7-4.3 mg/kg FW)	3
Calves and young female cattle fed roughage harvested in vicinity of a factory galvanizing steel tubes, and containing 3,000-7,300 mg Zn/kg DW roughage	Signs of chronic zinc poisoning evident after 12-14 months. Signs included reduced appetite, emaciation, submandibular edema, diarrhea, moderate anemia, elevated serum zinc (4.3-6.0 mg/L versus normal 1.8-2.1 mg/L), liver zinc (420-1,600 mg/kg DW versus normal 72-248 mg/kg DW), kidney zinc (910-1,680 mg/kg DW versus normal 40-114 mg/kg DW), and low serum calcium and magnesium	4

Dog, *Canis familiaris*		
Fed diets containing up to 1,000 mg Zn/kg ration for up to 1 year	No measurable signs of damage	2
Pomeranian, 2.2 kg, 4 months old, ingested four copper-clad zinc pennies	Hemolytic anemia, vomiting, salivation, serum zinc dropped from 29 mg/L to 4.4 mg/L 15 days after coins were surgically removed (normal dog serum zinc values range between 0.6 and 2.0 mg/L)	5
Zinc-poisoned oral route, (lethal) dose unspecified	Tissue zinc concentrations (in mg/L or mg/kg FW) were 32 in serum, 16-32 in plasma, 20-25 in urine, 369 in liver, and 295 in kidney. Normal values were 0.7-1.1 in serum, 0.6-1.0 in plasma, 1.3-2.0 in urine, 17-32 in liver, and 9-23 in kidney	6 ..
Died from ingestion of 34 copper-clad zinc pennies	Elevated zinc levels in serum, liver, and kidney; jaundice, anoxeria, anemia, vomitation, dark red urine	7
Guinea pig, *Cavia* sp.		
Inhalation of 0.8 mg Zn/m^3 for 1 h	Difficulty in breathing	8
Inhalation of 4 mg Zn/m^3, 3 h daily for 6 days	Temporary lung damage	8
Inhalation of 5 mg Zn/m^3, as ultrafine zinc oxide, 3 h daily for 6 days	Decrease in lung capacity, alveolar volume, and diffusing capacity for carbon monoxide; values remained depressed for at least 72 h after last exposure. Persistent inflammation of proximal portion of alveolar ducts and adjacent alveoli	9, 10
Horse, *Equus caballus*		
Weanling foals, age 3 months, fed diets containing 7.7 mg Cu/kg plus 29, 250, 1,000, or 2,000 mg Zn/kg ration for 15 weeks. At start, serum zinc level was 0.6 mg/L and serum copper level 1.4 mg/L	Foals fed 29 or 250 mg Zn/kg diets had normal serum copper and zinc concentrations. Those fed 1,000 or 2,000 mg kg diet became hypocupremic in 5 to 6 weeks and developed lameness owing to cartilaginous disease similar to osteochondritis dessicous. Foals fed high zinc diets became lame when serum copper fell to 0.3 mg/L for >1 week; at end of study, arthritic foals had <0.2 mg Cu/L serum. Serum zinc	11

	concentrations rose to >2 mg/L within 2 weeks at 1,000 or 2,000 mg Zn/kg diet; liver zinc was <333 mg/kg DW at diets of 250 mg Zn/kg, 2,728-3,511 mg/kg DW at 1,000 mg Zn/kg diet, and 4,364-4,524 mg/kg DW at the highest dietary loading of 2,000 Zn/kg in 15 weeks	
Adults, vicinity of lead-zinc smelter, ingesting >90 mg Zn/kg body weight (BW) daily	Decreased growth, lameness, bone deformities, death.	2
Cat, *Felis domesticus*		
Fed diet containing 300 mg Zn/kg ration for 16 weeks	Weight loss and pancreas histopathology	2
Fed diets containing >600 mg Zn/kg ration	Diets rejected	2
Fed diet containing 9,000 mg Zn/kg ration for 3-53 weeks	Pancreas histopathology	8
Human, *Homo sapiens*		
Dietary route		
80 mg/kg ration for 6 weeks	Digestive problems	8
90 mg Zn/kg ration for 5 weeks	Decreased serum cholesterol levels	8
153 mg Zn/kg ration for 6 weeks	Altered immune system	8
<150 mg zinc daily	No effect on male plasma cholesterol; females have decreased cholesterol	12
160 mg zinc daily	Increased plasma cholesterol level in both sexes; increased risk of heart disease in males	12
Inhalation route, 600 mg Zn/m^3 for 10 min	Metal fume fever, that is, difficulty in breathing, flu-like symptoms	8
Oral route		
15-year-old girl who consumed 220 mg zinc sulfate twice daily "for some time"	Acute gastrointestinal bleeding ulcers	13
Boy who consumed 12 g of elemental zinc	Headache and lethargy	13
Single oral dose of 45 g zinc as $ZnS0_4$ (normal is 15-20 mg daily)	Death, preceded by dehydration, electrolyte imbalance, abdominal pain, nausea, vomiting, dizziness, muscular incoordination, and acute renal failure	14
Domestic mouse, *Mus* sp.		
Dietary route		
68, 682, or 6,820 mg Zn/kg ration for 13 weeks (fed as 300, 3,000, or	No observed effects at 682 mg/kg diet (and lower), equivalent to 104-109 mg Zn/kg BW daily. At	15

30,000 mg $ZnSO_4 \cdot 7H_2O$/kg ration)	6,820 mg Zn/kg ration, however, adverse effects were documented on survival, growth, food and water intake, and blood chemistry; lesions noted in pancreas, stomach, intestine, spleen, and kidney	
500 mg/kg for 3 months	Anemia	8
30,000 mg/kg ration for 13 weeks	Some deaths, liver and kidney histopathology	8
Drinking water, 300 mg/L, for 5-14 months	Pancreas histopathology	8
Intraperitoneal injection, four injections over 9-day period totaling 13 mg Zn/kg BW	Toxic. Severe weight loss and some deaths	23
European ferret, *Mustela putorius furo*		
Fed basal diet (27 mg Zn/kg feed) or basal diet plus 500, 1,500, or 3,000 mg Zn/kg ration for up to 197 days; four animals per group	Ferrets fed 500 mg/kg all survived with no significant histopathology; zinc concentrations were 148 mg/kg DW in liver (115 mg/kg DW in controls) and 383 mg/kg DW in kidney (180 mg/kg DW). At 1,500 mg/kg, all four ferrets were in extremis or dead by day 21. At death, liver zinc was 859 mg/kg DW and kidney zinc 1,000 mg/kg DW; ferrets had 40-50% loss in body weight; food intake had decreased 80%; and erythrocyte number, hemoglobin, and hematocrit had significantly decreased. Ferrets fed the 3,000 mg/kg diet died between days 9 and 13, lost up to 40% of initial BW, and food intake decreased 77%; postmortem examination showed blood in intestine, orange-colored liver, and kidney histopathology. Elevated zinc content in liver of 1,273 mg/kg DW and in kidney of 1,138 mg/kg DW	8,16,17
Rabbit, *Oryctolagus* sp.		
Single oral dose of 65 mg Zn/kg BW, as $ZnSO_4$	Half-time persistence of 713 min	8
Intravenous injection of 0.325 mg Zn/kg BW, as $ZnSO_4$	Half-time persistence of 268 min	8
Intraperitoneal injection of 3.4 mg zinc daily	Associated with lowered plasma cholesterol levels	12
Domestic sheep, *Ovis aries*		
Domestic ewe, age 5 years, found moribund, suspected zinc poisoning	Elevated zinc levels were 650 mg/kg DW in liver (144 mg/kg DW in controls) and 760 mg/kg DW in kidney (84 mg/kg DW); muscle residues same	18

	as controls, that is, 154 mg/kg DW (158 mg/kg DW); generalized jaundice; liver degeneration and blockage of bile ducts	
Found dead, zinc-poisoned naturally	Zinc concentrations were 463 mg/kg DW in liver (165 mg/kg DW in controls), 274 mg/kg DW in kidney (150 mg/kg DW), and 752 mg/kg DW in pancreas (88 mg/kg DW)	19
Zinc-poisoned experimentally, oral route	Zinc concentrations were 1,125-1,671 mg/kg DW in liver, 2,130-2,442 mg/kg DW in kidney, 1,440-1,932 mg/kg DW in pancreas, and 4,900 mg/kg DW in feces (158 mg/kg DW feces in controls)	19
Lambs fed diets containing 1,000 mg Zn/kg	Food intake reduced; approaching toxic level	2,7
Laboratory white rat, *Rattus* sp.		
Dietary route		
Adult males given 500 mg Zn/kg ration, as $ZnSO_4$, for 6 weeks	After 3 weeks, spermatogenesis was arrested at the primary spermatocyte stage. After 4 weeks, food consumption declined, forelimb lameness, and swelling in cervical lymph nodes. At 6 weeks, testes showed enlarged lumen and abnormal germinal epithelium	20
682 mg Zn/kg ration, as $ZnSO_4.7H_2O$, for 13 weeks	No observable effect level, equivalent to 53-55 mg Zn/kg BW daily	15
2,000 mg Zn/kg ration, chronic exposure	Tolerated	2
4,000-5,000 Zn/kg ration for 18 days	Fetotoxic dose, poor reproduction	2,8
5,000-10,000 mg Zn/kg ration	Reduced growth, anemia, poor reproduction, disrupted liver catalase and cytochrome oxidase activity, copper deficiency	14
6,820 mg Zn/kg ration for 13 weeks	Retarded growth, low food intake, abnormal blood chemistry, regressive changes in pancreas	15
Drinking water route		
Doses equivalent to 0, 160, 320, and 640 mg Zn/kg BW daily for 3 months	No significant effect of any dose on organ weight, hematocrit, hemoglobin, glucose, and enzyme activity. Effects noted only at 640 mg kg BW daily: some deaths, less drinking water ingested, decreased volume of urine, significant increase in urea, and	21

	decrease in creatinine. Tissue residues were significantly elevated over controls in high dose group at 3 months: 60 mg Zn/kg FW in liver (20 mg Zn/kg FW in controls), 38 mg Zn/kg FW in kidney (16 mg Zn/kg FW), 330 mg Zn/kg FW in bone (92 mg Zn/kg FW), 21 mg Zn/kg FW in blood (3 mg Zn/kg FW), and 36 mg Zn/kg FW in spleen (16 mg Zn/kg FW). Residues were the same as controls in brain, lung, and muscle	
800 mg Zn/L for 30 days	Liver alterations	8
Intragastric administration		
180 g adults given single dose of 500 mg, equivalent to 2,777 mg/kg BW	Serum zinc reached a maximum of 3.5 mg Zn/L after 60 min and returned to normal (1.6 mg/L) within 24 h	22
165 g adults given 500 mg daily for up to 30 days, equivalent to 3,030 mg Zn/kg BW daily	Serum zinc after 7, 14, or 80 days was 1.9, 2.2, and 2.1 mg/L, respectively; 10 days after last dose, serum zinc was normal	22
Single oral dose, 350-800 mg Zn/kg BW	Acute oral LD50	2,21
Domestic pig, *Sus* sp.		
Weanlings fed diet containing 1,000 mg Zn/kg feed for 30 days	Decreased growth rate and food intake, arthritis, lameness, and inflammation of the gastrointestinal tract	13

[a] 1. Miller et al. 1989; 2. NAS 1979; 3. Gaynor et al. 1988; 4. Wentink et al. 1985; 5. Latimer et al. 1989; 6. Robinette 1990; 7. Ogden et al. 1988; 8. PHS 1989; 9. Lain et al. 1985; 10. Goyer 1986; 11. Bridges 1990; 12. Sammon and Roberts 1988; 13. Elinder 1986; 14. Prasad 1979; 15. Malta et al. 1981; 16. Straube et al. 1980; 17. Reece et al. 1986; 18. Schlosberg 1976; 19. Allen et al. 1983; 20. Saxena et al. 1989b; 21. Llobet et al. 1988a; 22. Castellano et al. 1988; 23. Kreppel et al. 1988.

Zinc fed to adult male rats at 500 mg/kg diet for 3 weeks or longer harms the testes and other male accessory organs; effects are a direct result of zinc cytotoxicity from transfer across the blood-testes barrier (Saxena et al. 1989a). Elevated dietary zinc also depresses bone calcium levels and increases fecal calcium loss in rats (Greger 1989). Increases in serum zinc levels of rats after acute zinc overload is due mainly to increases in the zinc bound to the albumin fraction and secondarily to that bound to the globulin fraction (Castellano et al. 1988). Albumin may play a new physiological role by fitting its binding capacity to serum zinc levels, essentially binding all excess zinc that arrives in the blood (Castellano et al. 1988).

Zinc toxicosis has been observed in humans and livestock after ingestion of acidic foods or drink prepared and stored in galvanized containers (Latimer et al. 1989). Symptoms occur within 24 h and include nausea, vomiting, diarrhea and abdominal cramps. The emetic dose for zinc in humans was estimated at 225-450 mg (3.2-6.4 mg Zn/kg BW), equivalent to 1-2 g zinc sulfate (Elinder 1986). Zinc poisoning in dogs is well documented as a result of ingestion of galvanized metal objects, calamine lotion, skin and sunblock preparations containing zinc oxide, staples, nails, fertilizers, some paints, products containing zinc undecylenate, metallic hardware items with a high zinc content, nuts on certain types of animal transport cages, and pennies (Latimer et al. 1989; Robinette 1990). The propensity of some individuals to throw pennies (U.S. coinage) into animal cages while visiting zoos and animal parks should be considered a potential source of zinc poisoning in captive animals. Pennies minted before 1982 contain 95% copper and 5% zinc; however, copper-clad pennies minted after 1981 contain 97.6% zinc and 2.4% copper (Ogden et al. 1988).

Humans given zinc supplements should be aware of possible complications attendant to their use (Fosmire 1990). Low intakes of 100-300 mg zinc daily in excess of the recommended dietary allowance of 15 mg zinc daily may produce induced copper deficiency, impaired immune function, and disrupted blood lipid profiles. Patients treated with zinc supplements (150 mg daily) to control sickle cell anemia and nonresponsive celiac disease developed a severe copper deficiency in 13 to 23 months; normal copper status was restored by cessation of zinc supplements and increased dietary copper (Fosmire 1990).

Because of false positives, zinc may confound interpretation of the paralytic shellfish poisoning mouse bioassay, one of the routine tests used to measure shellfish safety for human consumption. For example, mice injected intraperitoneally with extracts of healthy oyster tissues showed extreme weakness, a drop in body temperature, cyanosis, and some deaths (McCulloch et al. 1989). The threshold for a toxic paralytic shellfish poisoning response corresponds to a drained tissue zinc level >900 mg/kg FW, and this overlaps the zinc concentration range of 230-1,650 mg/kg FW (1,900-9,400 mg/kg DW) recorded in healthy oyster soft tissues (McCulloch et al. 1989).

Recommendations

For growing agricultural crops: (1) sewage sludge may be applied to soils if total zinc content does not exceed 150 to 560 kg/ surface hectare (Table 9); (2) a maximum permissible extractable soil zinc concentration of 23 mg/kg DW is recommended, according to Soviet agronomists (Beyer 1990); and (3) seedlings of oak (*Quercus* spp.) and red maple (*Acer rubrum*) will eventually die in culture medium containing >100 mg Zn/kg (Buchauer 1971), although total zinc concentrations for global crop production routinely exceed 100 mg/kg DW soil (Table 9). Research is needed in standardized methodology for measurement of bioavailable (i.e., extractable) soil zinc and on its relation to other soil measurements such as total zinc and depth of cultivation in the case of surface application.

Table 9. Proposed zinc criteria for the protection of natural resources and human health.

Resource, criterion, and other variables	Effective zinc concentration	Reference[a]
Crop plants		
Sewage sludge applied to agricultural soils		
Europe, acceptable	150-<300 kg/ha at pH 6.0-7.0	1
Florida		
Maximum permissible	205 kg/ha	1
Unacceptable	>10,000 mg/kg dry weight (DW)	1
Oregon[b], Wisconsin[b], acceptable	250 - < 1,000 kg/ha	1
Vermont[b], acceptable	280 - < 1,120 kg/ha	1
Maryland[b], Massachusetts[b], acceptable	280-<560 kg/hg	1
Minnesota[b], Missouri[b], acceptable	280-<1,120 kg/ha	1
Illinois, maximum	560 kg/ha	1
Soils		
Soviet Union, maximum permissible	23 mg/kg DW, extractable by ammonium acetate buffer at pH 4.8	1
Alberta, Canada, for growing livestock forage	<100 mg/kg DW	1
Quebec, Canada		

Background	200 mg/kg DW	1
Marginal	500 mg/kg DW	1
Unacceptable	>3,000 mg/kg DW	1
Netherlands		
Background	200 mg/kg DW	1
Marginal	500 mg/kg DW	1
Unacceptable	>3,000 mg/kg DW	1
Ontario, Canada, acceptable	<220 mg/kg DW	1
Germany, acceptable	<300 mg/kg DW	2
New Jersey, goal	<350 mg/kg BW	1
New York, acceptable		
Agricultural soils	168-<250 kg/ha DW	1
Forest soils	<560 kg/ha DW	1
Terrestrial Invertebrates		
Earthworms		
High accumulations, but otherwise safe	97 mg/kg DW soil	3
Adverse effects	>400 mg/kg DW soil	3
Slugs, diet, adverse effects	>300 mg/kg DW	4
Freshwater aquatic life		
Water		
Total recoverable zinc		
60 mg $CaCO_3$/L	47 µg/L, 24 h average; not to exceed 180 µg/L at any time	5
100 mg $CaCO_3$/L	47 µg/L, 24 h average; not to exceed 320 µg/L at any time	5
200 mg $CaCO_3$/L	47 µg/L, 24 h average; not to exceed 570 µg/L at any time	5
Acid-soluble zinc[c]	4-day average concentration not to exceed the numerical value e ((0.8473 [ln] hardness)+ 0.7614) more than once every 3 years on average; 1-h concentration not to exceed e((0.8473 [ln] hardness)+ 0.8604) more than once every 3 years on average. See below for examples	6
50 mg $CaCO_3$/L	4-day average not to exceed 59 µg/L; 1-h average not to exceed 65 µg/L	6
100 mg $CaCO_3$/L	4-day average not to exceed 110 µg/L; 1-h average not to exceed 120 µg/L	6
200 mg $CaCO_3$/L	4-day average not to exceed 190 µg/L; 1-h average not to exceed 210 µg/L	6
Adverse effects, most sensitive species		
Brown trout, *Salmo trutta*, embryos and fry	4.9-19.6 µg/L	7

Daphnid, *Daphnia magna*	5-14 µg/L	6
Rainbow trout, *Oncorhynchus mykiss*	5.6-10 µg/L	5,6,8
Narrow-mouthed toad, *Gastrophryne carolinensis*, embryos	10 µg/L	6
Daphnid, *Daphnia galeata mendotae*	15-30 µg/L	6
Freshwater sponge, *Ephydatia fluviatilis*	26 µg/L	9
Mayfly, *Epeorus latifolium*	30 µg/L	10
Midge, *Tanytarsus dissimilis*	37 µg/L	5,6
Atlantic salmon, *Salmo salar*	50 µg/L	6
Cladoceran, *Ceriodaphnia reticulata*	51 µg/L	6
Flagfish, *Jordanella floridae*	51 µg/L	6
Diet		
Channel catfish, *Ictalurus punctatus*		
Minimum	20 mg/kg DW	11
Recommended	150-200 mg/kg DW	11
Rainbow trout, *Oncorhynchus mykiss*		
Minimum	10-30 mg/kg DW; 15-30 mg/kg fresh weight (FW)	12,13
Adequate	90 mg/kg FW	13
Sediments		
Great Lakes		
Safe	<90 mg/kg DW	1
Marginal	90-200 mg/kg DW	1
Unacceptable	>200 mg/kg DW	1
Wisconsin and Ontario, for Great Lakes sediments dredged from harbors and for disposal in water	<100 mg/kg DW	1
Marine aquatic life		
Seawater		
Total recoverable zinc	58 µg/L, 24-h average; not to exceed 170 µg/L at any time	5
Acid-soluble zinc[c] (20)	4-day average concentration does not exceed 86 µg/L more than once every 3 years on average; 1-h average concentration does not exceed 95 µg/L more than once every 3 years on average	6
No adverse effect, most species		
Algae	<1,400 µg/L	14
Molluscs	<54 µg/L	15
Crustaceans	<230 µg/L	15
Adverse effects, most sensitive species		
Brown algae, *Fucus serratus*	8.8-9.5 µg/L	6

Copepod, *Tisbe holothuriae*	10 µg/L	16
Pacific oyster, *Crassostrea gigas*, larvae	10-20 µg/L	6
Alga, *Rhizosolenia* spp.	15-25 µg,/L	8
Diatom, *Schroederella schroederi*	19 µg/L	6
Diatom, *Skeletonema costatum*	19.6 µg/L	17
Dinoflagellate, *Glenodinium halli*	20 µg/L	6
Purple sea urchin, *Strongylocentrotus purpuratus,* embryos	23 µg/L	6
Sand dollar, *Dendraster excentricus*	28 µg/L	6
Atlantic herring, *Clupea harengus*, embryos	50 µg,/L	6
Mud crab, *Rithropanopeus harrisii,* larvae	50 µg/L	5
Diet, fish, adequate	90 mg/kg FW	13
Tissue residues, minimum theoretical requirement for whole molluscs and crustaceans	34.5 mg/kg DW	18
Birds		
Mallard, *Anas platyrhynchos*		
Zinc-poisoned		
Diet	2,500-3,000 mg/kg DW ration	19,20,21
Single oral dose	0.64; , 517-742 mg/kg body weight (BW)	22
Birds, various, tissue concentrations		
Normal		
Liver	21-33 mg/kg DW	23
Plasma	1.3-2.0 µg/L	24
Zinc-poisoned		
Liver	75-156 mg/kg DW	23
Plasma	15.5 mg/L	24
Japanese quail, *Coturnix coturnix japonica*, safe level	25-30 mg/kg DW diet	25
Chicken, *Gallus* sp.		
Recommended daily intake	>31 mg	26
Diet		
Adverse effects, zinc deficiency	<38 mg/kg DW ration	27,28,29
Adequate	93-120 mg/kg DW ration	28,29
Excessive	>178 mg/kg DW ration	27
Toxic	>2,000 mg/kg DW ration	20,30,31
Mammals		
Cattle, *Bos* spp.		
Diet		
Soluble zinc, recommended level		

Calves	>8 mg/kg DW	20
Adults		
Beef cattle	10-30 mg/kg DW	20
Dairy cattle	40 mg/kg DW	20
Total zinc		
Marginal	25 mg/kg DW	32
Recommended	45-60 mg/kg DW	32,33
Maximum tolerated		
Calves	500 mg/kg DW	35
Adults	1,000 mg/kg DW	34,35
Toxic	>900-2,000 mg/kg DW	34,35
Tissue residues		
Liver		
Zinc-deficient	<10 mg/kg DW	32
Suboptimal	10-30 mg/kg DW	32
Optimal	30-120 mg/kg DW	32
Excessive	>120 mg/kg DW	32
Lethal	>500 mg/kg DW	34
Plasma		
Zinc-deficient	<0.66 mg/L	33
Normal	1.02 mg/L	33
Elevated	1.5 mg/L	33
Serum, zinc-deficient	<0.6 mg/L	36
Recommended daily intake		
Calves		
5 months old	3 g (25-35 mg/kg BW)	34
14-18 months old	16 g (50-80 mg/kg BW)	34
Cows	55 g (110-140 mg/kg BW)	34
Dog, *Canis familiaris*, tissue concentrations, normal versus zinc-poisoned		
Serum	0.7-1.1 versus 33 mg/L	37
Plasma	0.6-1.0 versus 16-32 mg/L	37
Urine	1.3-2.0 versus 20-25 mg/L	37
Liver	17-32 versus 369 mg/kg FW	37
Kidney	9-23 versus 295 mg/kg FW	37
Guinea pig, *Cavia* spp.		
Air, adverse effects	0.8-4.0 mg Zn/m^3	38
Diet		
Deficient	3 mg/kg DW plus 1 mg/L drinking water	39
Adequate	3 mg/kg DW plus 15 mg/L drinking water	40
Normal	20 mg/kg DW	41

Adequate	100 mg/kg FW	39
High	200 mg/kg DW	41
Tissue concentrations, zinc deficient versus normal		
Serum	0.5 versus 1.6-2.0 mg/L	39
Liver	9.4 versus 15-17 mg/kg FW	39
Testes	9.5 versus 19-27 mg/kg FW	39
Kidney	10 versus 16-20 mg/kg FW	39
Domestic goat, *Capra* sp., diet		
Soluble zinc, recommended		
Adults	>4 mg/kg DW	20
Kids	>7 mg/kg DW	20
Total zinc		
Deficient	<15 mg/kg DW	42
Recommended	80 mg/kg DW	42
Bank vole, *Clethrionomys glareolus*, diet, recommended	30 mg/kg DW	43
Horse, *Equus caballus*		
Diet		
No adverse effects	250 mg/kg DW	44
Adverse effects	1,000 mg/kg DW	44
Daily intake, adverse effects	>90 mg/kg BW	20
Domestic cat, *Felis domesticus*, diet, adverse effects	300 mg/kg DW	20
Humans, *Homo sapiens*		
Air		
Safe levels		
Zinc chloride, fumes	<1 mg/m^3	20,38
Zinc oxide, fumes	<5 mg/m^3	28,38,45,46
Zinc and zinc oxides	5-10 mg/m^3	38
Zinc oxide, total dust	10 mg/m^3	38
Zinc oxide, fume and dust, ceiling limit	15 mg/m^3	38
Adverse effects, zinc oxides	600 mg/m^3 for 10 min	38
Daily intake		
Recommended dietary intake, assuming availability of 20%		
Children		
To age 1 year	3-6 mg	48
1-10 years	8-10 mg	48
No age specified	10 mg	2,20,26,47,49,50
Males		

Age 11-17	14-15 mg	48
Age 18+	11-15 mg	48
No age specified	15 mg	2,20,26, 47,49,50
Females		
Age 10-13	13-15 mg	48
Age 14+	11-15 mg	48
No age specified	12 mg	48
Pregnant	15-20 mg	48
Lactating	25-27 mg	47,48
Maximum safe total, adults		
Not zinc deficient	0.3-1.0 mg/kg BW	2
Zinc deficient	1 mg Zn/kg BW, oral administration	48
Adverse effects level	>160 mg (>2.3 mg/kg BW)	51
Diet		
Seafoods, safe level, Australia,	<40 mg/kg FW	14
Adverse effects		
Gastrointestinal disorders	>80 mg/kg DW diet for 6 weeks	38
Severe copper deficiency	150 mg zinc daily for 13-23 months	49
Vomiting	Single dose of 225-450 mg zinc or 1-2 g of $ZnSO_4$	49
Drinking water		
Safe level	5 mg/L	2,20,38
Adverse effects, acute GI distress	>280 mg/L	20
Intravenous injection, adverse effects	23 mg/kg BW daily	52
Soils, Canada, nonhazardous to human health		
Ontario, residential, parkland, commercial, industrial	<800 mg/kg DW	1
Alberta, noncrop uses	<700 mg/kg DW	1
Tissue residues		
Serum		
Normal	0.5-1.29 mg/L	38
No toxic effects	1.92 mg/L	38
Plasma		
Zinc-deficient	0.4-0.6 mg/L	45
Normal	0.7-1.1 mg/L	48
GI disturbances	1.51 mg/L	38
Rhesus monkey, *Macaca mulatta,* diet		
Deficient	4 mg/kg DW	52
Adequate	100 mg/kg DW	53
Mouse, *Mus* spp.		

Diet		
Zinc-deficient	<5 mg/kg DW	54
Zinc-adequate	36.5 mg/kg DW	54
Tolerated	100 mg/kg DW	54
Tolerated	682 mg/kg DW for 13 weeks (107 mg/kg BW)	55
Harmful	500 mg/kg DW for 3 months	38
Harmful	6,820 mg/kg DW	55
Fatal	30,000 mg/kg DW for 13 weeks	38
Drinking water, adverse effects	300 mg/L	38
Tissue residues		
Blood		
Deficient	0.7 mg/L	56
Normal	1.0-1.1 mg/L	56
Liver		
Deficient	12 mg/kg FW	56
Normal	17-19 mg/kg FW	56
European ferret, *Mustela putorius furo*, diet		
Tolerated	500 mg/kg DW	57
Fatal	1,500 mg/kg DW	38
Mink, *Mustela vison*, diet		
Zinc-deficient	4.1 mg/kg FW	58
Adequate	35-45 mg/kg FW; 100-150 mg/kg DW	58
Domestic sheep, *Ovis aries*		
Diet		
Soluble zinc, adequate		
Adults	>4 mg/kg DW	20
Lambs	>7 mg/kg DW	20
Total zinc		
Adults, adequate	33 mg/kg DW	59,60
Lambs		
Adequate	124-130 mg/kg DW	59
Harmful	>1,000 mg/kg DW	20,61,62
Recommended daily intake	>18 mg	26
Tissue residues		
Feces		
Normal	158 mg/kg DW	61
Zinc-poisoned	4,900 mg/kg DW	61
Kidney		
Normal	84-150 mg/kg DW	61,63
Elevated	>180 mg/kg DW	61
Zinc-poisoned	274-760 mg/kg DW	61,63
Liver		

Normal	144-165 mg/kg DW	61,63
Elevated	>250 mg/kg DW	61
Zinc-poisoned	463-650 mg/kg DW	61,63
Pancreas		
Normal	88 mg/kg DW	61
Zinc-poisoned	752 mg/kg DW	61
Laboratory white rat, *Rattus* sp.		
Diet		
Soluble zinc, recommended	15 mg/kgDW	20
Total zinc		
Zinc-deficient	<12 mg/kg DW	47
Adequate	76 mg/kg DW	64
Adverse effects	>500 mg/kg DW	52
Fetotoxic	>4,000 mg/kg DW	20,38
Daily intake		
Tolerated	320 mg/kg BW	65
Harmful	640 mg/kg BW	65
Single oral dose, harmful	>350 mg/kg BW	20,65
Domestic pig, *Sus* sp.		
Diet		
Soluble zinc, safe levels		
Normal	14-20 mg/kg DW	20
Cassava-rice-bran	>40 mg/kg DW	20
Soy base	50 mg/kg DW	20
Total zinc, harmful	1,000 mg/kg DW	47
Recommended daily intake	>20 mg	26

[a] 1. Beyer, 1990; 2. Leonard and Gerber 1989; 3. Beyer et al. 1987; 4. Marigomez et al. 1986; 5. EPA 1980; 6. EPA 1987; 7. Sayer et al. 1989; 8. Spear 1981; 9. Francis and Harrison 1988; 10. Hatakeyama 1989; 11. Gatlin et al. 1989; 12. Bettger et al. 1987; 13. Spry et al. 1988; 14. Eisler 1981; 15. Sprague 1986; 16. Verrioposulos and Hardouvelis 1988; 17. Vymazal 1986; 18. White and Rainbow 1985; 19. Kazacos and Van Vleet 1989; 20. NAS 1979; 21. Gasaway and Buss 1972; 22. Grandy et al. 1968; 23. Reece et al. 1986; 24. Morris et al. 1986; 25. Harland et al. 1975; 26. Ellen et al. 1989; 27. Stahl et al. 1989a; 28. Blamberg et al. 1960; 29. Westmoreland and Hoekstra 1969; 30. Stahl et al. 1990; 31. Oh et al. 1979; 32. Binnerts 1989; 3,3. Ramachandra and Prasad 1989; 34. Wentink et al. 1985; 35. Miller et al. 1989; 36. Damir et al. 1988; 37. Robinette 1990; 38. PHS 1989; 39. Gupta et al.. 1988; 40. Apgar and Everett 1988; 41. Scelsi et al. 1989; 42. Chhabra and Arora 1989; 43. Wlostowski et al. 1988; 44. Bridges 1990; 45. Goyer 1986; 46. Lain et al. 1985; 47. Elinder 1986; 48. Casoy and Hambidge 1980; 49. Fosmire 1990; 50. Sternlieb 1988; 51. Sammon and Roberts 1988; 52. Saxena et al. 1989b; 53. Golub et al. 1988; 54. Mackay-Sire and Dreosti 1989; 55. Malta et al. 1981; 56. Tone et al. 1988; 57. Straube et al. 1980; 58. Mejborn 1989; 59. Vergnes et al. 1990; 60. Khandaker and Telfer 1990; 61. Allen et al. 1983; 62. Ogden et al. 1988; 63. Schlosberg 1976; 64. Ferreira et al. 1989; 65. Llobet et al. 1988a.

[b] Higher values permissible for soils with higher cation exchange capacity (Beyer 1990).

[c] Zinc that passes through a 0.45 µm membrane filter after acidification to pH 1.5-2.0 with nitric acid (EPA 1987).

[d] Higher concentrations recommended to compensate for reduced bioavailability caused by excess calcium and phytate in diet (Gatlin et al. 1989).

Data on zinc hazards to terrestrial invertebrates are limited; however, sensitive species are adversely affected at dietary concentrations >300 mg Zn/kg or at soil concentrations >400 mg/kg (Table 9).

Water quality criteria protection of aquatic life should include both total recoverable zinc and acid-soluble zinc (EPA 1980, 1987). For example, if total recoverable zinc is substantially above the proposed criteria and acid-soluble zinc is below the limit, there is cause for concern (EPA 1987). To protect about 95% of freshwater animal genera, EPA recommends water concentrations that average <47 µg total recoverable zinc per liter, not to exceed 180 µg/L at any time in soft water (i.e., <50 mg $CaCO_3$/L), or a mean concentration of 59 µg acid soluable zinc per liter, not to exceed 65 µg/L at any time in soft water (Table 9). These criteria are unsatisfactory because lower ambient zinc concentrations between 5 and 51 µg/L clearly have significant negative effects on growth, survival, and reproduction of important species of freshwater fish, amphibians, insects, sponges, and crustaceans (Table 9). Some downward modification seems necessary in the current proposed zinc criteria for freshwater aquatic life protection.

To protect important species of marine animals, EPA recommends that total recoverable zinc in seawater should average <58 µg/L and never exceed 170 µg/L; for acid-soluble zinc, these values are <86 and 95 µg/L (Table 9). As was the case for freshwater biota, there is a growing body of evidence (Table 9) demonstrating that many species of marine plants, crustaceans, molluscs, echinoderms, and fish are adversely affected at ambient zinc concentrations between 9 and 50 µg/L or significantly below the current proposed criteria for marine life protection.

Effects of zinc deficiency were produced experimentally in freshwater sponges at <0.65 µg Zn/L (Francis and Harrison 1988), in rainbow trout fed diets containing <15 mg Zn/kg FW (Spry et al. 1988), in certain species of marine algae at <0.7 µg Zn/L (Vymazal 1986), and in certain species of marine invertebrates at <6.5 µg Zn/L (Clapper et al. 1985a, 1985b) or <34 mg Zn/kg DW whole organism (White and Rainbow 1985). Zinc deficiency in natural aquatic ecosystems has not yet been credibly documented.

In aquatic environments, Spear (1981) spotlights three research needs: (1) development of analytical procedures for measurement of individual dissolved zinc species, notably the aquo ion and zinc chloride, and for nondissolved species that occur in natural waters; (2) separation of natural from anthropogenic influences of sediment-water interactions on flux rates with an emphasis on anoxic conditions, the role of microorganisms, and the stability of organozinc complexes; and (3) establishment of toxicity thresholds for aquatic organisms based on bioaccumulation and survival to determine the critical dose and the critical dose rate with an emphasis on aquatic communities inhabiting locales where zinc is deposited in sediments. These research needs are still valid.

Bird diets should contain 25-38 mg Zn/kg DW feed to prevent zinc deficiency effects, 93-120 mg Zn/kg DW feed for adequate to optimal growth, <178 mg Zn/kg DW feed to prevent marginal sublethal effects, and <2,000 mg Zn/kg DW feed to prevent the death of chicks and ducklings (Table 9). Extremely high dietary levels of 20 g Zn/kg ration are fed routinely to laying hens by poultry managers to force molting and to improve long-term egg preduction (Lu and Combs 1988a); in these cases, zinc preferentially accumulates in the kidney, liver, pancreas, and eggs (Verheyen et al. 1990). Much additional work now seems warranted on the role of zinc in avian nutrition and on the significance of tissue concentrations as an indicator of zinc stress.

The normal daily intake for all human age groups ranges between 8 and 14 mg (Casey and Hambidge 1980), but pregnant women require an additional 350-375 mg zinc during their pregnancy (Jameson 1980). Zinc used therapeutically in humans at >160 mg daily may have deleterious effects on copper status (Samman and Roberts 1988). Lower levels--close to the recommended daily allowance of 15 mg--are reported to interfere with iron metabolism and with high density lipoprotein cholesterol concentrations (Fosmire 1990) but this requires verification. The proposed air quality criterion for human health protection is 5 mg Zn/m^3, although this is demonstrably harmful to guinea pigs (Table 9). It is not yet known whether guinea pigs are more sensitive than humans to atmospheric zinc or if some downward modification is needed in the current zinc air quality criterion for protection of human health and presumably wildlife.

Single oral doses >350 mg Zn/kg BW were fatal to rats, although doses of 320 mg/kg BW were tolerated (Table 9), suggesting a rapid breakdown in ability to regulate zinc in a relatively narrow critical threshold range. More research into zinc regulation of massive doses seems needed.

Data that link zinc concentrations in tissues with environmental zinc perturbations in mammals are rare. For example, elevated zinc concentrations were >120 mg Zn/kg DW tissue in cattle liver, >180 mg Zn/kg DW tissue in sheep kidney, and >250 mg Zn/kg DW tissue in sheep liver (Table 9). The significance of zinc residues in animal tissues is unclear. No international regulations or guidelines applicable to zinc are available (PHS 1989). No U.S. Food and Drug Administration action level or other maximum acceptable concentration exists for zinc, and therefore no Final Residue Value can be calculated (EPA 1987). This seems to be a research need of high priority.

Eating seafoods that contain high concentrations of zinc does not seem to present a threat to human health. However, oysters from Tasmania allegedly caused nausea and vomiting in some people who ate them; these oysters contained about 20 g Zn/kg FW soft parts or about 500 times more than the Australian food regulation of 40 mg/kg FW (Eisler 1981).

In mammals, large differences are evident between and within species in resistance to zinc poisoning and in sensitivity to zinc nutritional needs (Table 9). Adverse effects of excess dietary zinc occurred in sensitive species at 80 mg Zn/kg DW (in humans) and 300 mg Zn/kg DW (in cats); other tested species were significantly more resistant. Daily intake rates considered harmful over long periods ranged from about 2.3 mg/kg BW in humans to >90 mg/kg BW in horses. Dietary loadings that optimally prevented zinc deficiency were 30 mg Zn/kg DW diet for bank voles, 33 mg Zn/kg DW diet for adult sheep (124-130 mg Zn/kg DW diet for lambs), 37 mg Zn/kg DW diet for mice, 45-60 mg Zn/kg DW diet for cattle, 76 mg Zn/kg DW diet for rats, 80 mg Zn/kg DW diet for goats, 100 mg Zn/kg DW diet for monkeys, and 150 mg Zn/kg DW diet for minks; recommended daily intake ranged from about 0.2 mg/kg BW in humans to 110-140 mg/kg BW in cattle (Table 9). More research with animals of various age and nutrient status is needed to determine the interaction effects of zinc with proteins, calcium, chloride, and other trace elements and on the long-term consequences of nutrient interactions (Gregor 1989).

Acknowledgments

I thank L. Garrett and W. Manning for literature search and retrieval services; M. Holmes for secretarial assistance; W. N. Beyer, D. R. Buckler, S. N. Wiemeyer, and two anonymous referees for technical review of the manuscript.

References

Ahsanullah, M., M. C. Mobley, and P. Rankin. 1988. Individual and combined effects of zinc, cadmium and copper on the marine amphipod *Allorchestes compressa*. Australian Journal of Marine and Freshwater Research 39:33-37.

Ajmalkhan, S., K. Rajendran, and R. Natarajan. 1986. Effect of zinc on zoeal development of the estuarine hermit crab *Clibanarius olivaceous* (Henderson). Proceedings of the Indian Academy of Sciences 95:515-524.

Akberali, H. B., M. J. Earnshaw, and K. R. M. Marriott. 1985. The action of heavy metals on the gametes of the marine mussel, *Mytilus edulis* (L)--II. Uptake of copper and zinc and their effect on respiration in the sperm and unfertilized egg. Marine Environmental Research 16:37-59.

Allen, J. G., H. G. Master, R. L. Peet, K. R. Mullins, R. D. Lewis, S. Z. Skirrow, and J. Fry. 1983. Zinc toxicity in ruminants. Journal of Comparative Pathology 93:363-377.

Alliot, A., and M. Frenet-Piron. 1990. Relationship between metals in sea-water and metal accumulation in shrimps. Marine Pollution Bulletin 21:30-33.

Amiard, J. C., C. Amiard-Triquet, B. Berthet, and C. Metayer. 1986. Contribution to the ecotoxicological study of cadmium, lead, copper and zinc in the mussel *Mytilus edulis*. I. Field study. Marine Biology 90:425-431.

Amiard-Triquet, C., J. C. Amiard, B. Berthet, and C. Metayer. 1988. Field and experimental study of the bioaccumulation of some trace metals in a coastal food chain: seston, oyster (*Crassostrea gigas*), drill (*Ocenebra erinacea*). Water Science and Technology 20:13-21.

Amiard-Triquet, C., B. Berthet, C. Metayer, and J. C. Amiard. 1986. Contribution to the ecotoxicological study of cadmium, copper and zinc in the mussel *Mytilus edulis*. II. Experimental study. Marine Biology 92:7-13.

Anadu, D. I., G. A. Chapman, L. R. Curtis, and R. A. Tubb. 1989. Effect of zinc exposure on subsequent acute tolerance to heavy metals in rainbow trout. Bulletin of Environmental Contamination and Toxicology 43:329-336.

Andersen, R. A., K. D. H. Eriksen, and T. Bakke. 1989. Evidence of presence of a low molecular weight, nonmetallothionein-like metal-binding protein in the marine gastropod *Nassarius reticulatus* L. Comparative Biochemistry and Physiology 94B:285-291.

Andrews, S. M., M. S. Johnson, and J. A. Cooke. 1989. Distribution of trace element pollutants in a contaminated grassland ecosystem established on metalliferous fluorspar tailings. 2: zinc. Environmental Pollution 59A:241-252.

Anil, A. C., and A. B. Wagh. 1988. Accumulation of copper and zinc by *Balanus amphitrite* in a tropical estuary. Marine Pollution Bulletin 19:177-180.

Anwer, J., S. Ali, and N. K. Mehrota. 1988. Antagonistic effect of zinc in lead treated developing chick embryos. Drug and Chemical Toxicology 11:85-95.

Apgar, J. 1985. Zinc and reproduction. Annual Review of Nutrition 5:43-68.

Apgar, J., and G. A. Everett. 1988. Effect of zinc deficiency on the guinea pig during pregnancy Pages 576-580 *in* Trace element analytical chemistry in medicine and biology. Walter de Gruyter, Berlin.

Attar, E. N., and E. J. Maly. 1982. Acute toxicity of cadmium, zinc, and cadmium-zinc mixtures to *Daphnia magna*. Archives of Environmental Contamination and Toxicology 11:291-296. .

Auer, D. E., J. C. Ng, and A. A. Seawright. 1988a. Assessment of copper and zinc status of farm horses and training thoroughbreds in south-east Queensland. Australian Veterinary Journal 65:317-320.

Auer, D. E., J. C. Ng, D. P. Steele, and A. A. Seawright. 1988b. Monthly variation in the plasma copper and zinc concentration of pregnant and non-pregnant mares. Australian Veterinary Journal 65:61-62.

Bagatto, G., and M. Alikhan. 1987. Zinc, iron, manganese, and magnesium accumulated in crayfish populations near copper-nickel smelters at Sudbury, Ontario, Canada. Bulletin of Environmental Contamination and Toxicology 38:1076-1081.

Bagshaw, J. C., P. Rafiee, C. O. Matthews, and T. H. MacRae. 1986. Cadmium and zinc reversibly arrest development of *Artemia* larvae. Bulletin of Environmental Contamination and Toxicology 37:289-296.

Belanger, S. E., J. L. Farris, D. S. Cherry, and J. Cairns, Jr. 1986. Growth of Asiatic clams (*Corbicula* sp.) during and after long-term zinc exposure in field-located and laboratory artificial streams. Archives of Environmental Contamination and Toxicology 15:427-434.

Belmonte, N. M., O. E. Rivera, and J. Herkovits. 1989. Zinc protection against cadmium effects on preimplantation mouse embryos. Bulletin of Environmental Contamination and Toxicology 43: 107-110.

Bengeri, K. V., and H. S. Patil. 1986. Respiration, liver glycogen and bioaccumulation in *Labeo rohita* exposed to zinc. Indian Journal of Comparative Animal Physiology 4:79-84.

Bengtsson, B. E. 1974. Effect of zinc on growth of the minnow *Phoxinus phoxinus*. Oikos 25:370-373.

Bettger, W. J. 1989. The effect of dietary zinc deficiency on erythrocyte-free and membrane-bound amino acids in the rats. Nutrition Research 9:911-919.

Bettger, W. J., D. J. Spry, K. A. Cockell, C. Y. Cho, and J. W. Hilton. 1987. The distribution of zinc and copper in plasma erythrocytes and erythrocyte membranes of rainbow trout (*Salmo gairdneri*). Comparative Biochemistry and Physiology 87C:445-451.

Beyer, W. N. 1988. Damage to the forest ecosystem on Blue Mountain from zinc smelting. Pages 249-262 *in* D. D. Hemphill, editor. Trace substances in environmental health--XXII. A symposium. University of Missouri Press, Columbia.

Beyer, W. N. 1990. Evaluating soil contamination. U.S. Fish and Wildlife Service Biological Report 90(2). 25 pp.

Beyer, W. N., and A. Anderson. 1985. Toxicity to woodlice of zinc and lead oxides added to soil litter. Ambio 14:173-174.

Beyer, W. N., and E. J. Cromartie. 1987. A survey of Pb, Cu, Zn, Cd, As, and Se in earthworms and soil from diverse sites. Environmental Monitoring and Assessment 8:27-36.

Beyer, W. N., G. Hensler, and J. Moore. 1987. Relation of pH and other soil variables to concentrations of Pb, Cu, Zn, Cd, and Se in earthworms. Pedobiologia 30:167-172.

Beyer, W. N., G. W. Miller, and E. J. Cromartie. 1984. Contamination of the 02 soil horizon by zinc smelting and its effect on woodlouse survival. Journal of Environmental Quality 13:247-251.

Beyer, W. N., O. H. Pattee, L. Sileo, D. J. Hoffman, and B. M, Mulhern. 1985. Metal contamination in wildlife living near two zinc smelters. Environmental Pollution 38A:63-86.

Bezuidenhout, L. M. H. J. Schoonbee, and L. P. D. de Wet. 1990. Heavy metal content in organs of the African sharptooth catfish, *Clarias gariepinus* (Burchell), from a Transvaal lake affected by mine and industrial effluents. Part 1. Zinc and copper. Water S A 16:125-129.

Binnerts, W. 1989. Zinc status of cows as deduced from the liver zinc content. Netherlands Journal of Agricultural Science 37: 107-117.

Blamberg, D. L, U. B. Blackwood, W. C. Supplee, and G. E Combs. 1960. Effect of zinc deficiency in hens on hatchability and embryonic development. Proceedings of the Society of Experimental Biology and Medicine 104:217-220.

Blesbois, E., and I. Mauger. 1989. Zinc content of fowl seminal plasma and its effects on spermatozoa after storage at 4° C. British Poultry Science 39:677-685.

Blus, L. J., B. S. Neely, Jr., T. G. Lamont, and B. Mulhern. 1977. Residues of organochlorines and heavy metals in tissues and eggs of brown pelicans, 1969-73. Pesticides Monitoring Journal 11:40-53.

Blus, L. J., R. K. Stroud, B. Reiswig, and T. McEneaney. 1989. Lead poisoning and other mortality factors in trumpeter swans. Environmental Toxicology and Chemistry 8:263-267.

Borovansky, J., and P. A. Riley. 1989. Cytotoxicity of zinc in vitro. Chemical-Biological Interactions 69:279-291.

Bosma, A. A, B. M. J. L. Mannaerts, N. A. de Haan, and J. Kroneman. 1988. Sister chromatid exchanges in calves with hereditary zinc deficiency (Lethal Trait A46). Veterinary Quarterly 10:230-233.

Brereton, A. H. Lord, I. Thornton, and J. S. Webb. 1973. Effect of zinc on growth and development of larvae of the Pacific oyster *Crassostrea gigas*. Marine Biology 19:96-101.

Bridges, C. H. 1990. Influence of variable content of dietary zinc on copper metabolism of weanling foals. American Journal of Veterinary Research 51:275 -280.

Brix, H., and J. E. Lyngby 1982. The distribution of cadmium, copper, lead, and zinc in eelgrass (*Zostera marina* L.). Science of the Total Environment 24:51-68.

Bromenshenk, J. J., J. L. Gudatis, R. C. Cronn, and G. J. Olbu. 1988. Uptake and impact of heavy metals to honey bees. American Bee Journal 128:800-801.

Brown, D. A., C. A. Bawden, K. W. Chatel, and T. R. Parsons. 1977. The wildlife community of Iona Island jetty, Vancouver B.C., and heavy-metal pollution effects. Environmental Conservation 4:213-216.

Brungs, W. A. 1969. Chronic toxicity of zinc to the fathead minnow, *Pimephales promelas* Rafinesque. Transactions of the American Fisheries Society 98:272-279.

Bryan, G. W., P. E. Gibbs, L. G. Hummerstone, and G. R. Burt. 1987. Copper, zinc, and organotin as longterm factors governing the distribution of organisms in the Fal estuary in southwest England Estuaries 10:208-219.

Bryan, G. W., L. W. Hummerstone, and E. Ward. 1986. Zinc regulation in the lobster *Homarus gammarus*: importance of different pathways and excretion. Journal of the Marine Biological Association of the United Kingdom 66: 175-199.

Buchauer, M. J. 1971. Effects of zinc and cadmium pollution on vegetation and soils. Ph.D. thesis, Rutgers University, New Brunswick, N.J. 329 pp.

Buhl, K. J., and S. J. Hamilton. 1990. Comparative toxicity of inorganic contaminants related by placer mining to early life stages of salmonids. Ecotoxicology and Environmental Safety 20:325-342.

Burton, D. J., and D. J. Fisher. 1990. Acute toxicity of cadmium, copper, zinc, ammonia, 3,3'-dichlorobenzidine, 2,6-dichloro-4 -nitroaniline, methylene chloride, and 2,4,6-trichlorophenol to juvenile grass shrimp and killifish. Bulletin of Environmental Contamination and Toxicology 44:776-783.

Burton, D. T,, A. H. Jones, and J. Cairns, Jn. 1972. Acute zinc toxicity to rainbow trout (*Salmo gairdneri*): confirmation of the hypothesis that death is related to tissue hypoxia. Journal of the Fisheries Research Board of Canada 29:1463-1466.

Cain, D. J., and S. N. Luoma. 1986. Effect of seasonally changing tissue weight on trace metal concentrations in the bivalve *Macoma balthica* in San Francisco Bay. Marine Ecology Progress Series 28:209-217.

Calhoun, R., E.G. McDaniel, al. M. P. Howard, and J. C. Smith, Jr. 1978. Loss of zinc from bone during deficiency state. Nutrition Reports International 17:299-306.

Campbell, P. G. C., and P. M. Stokes. 1985. Acidification and toxicity of metals to aquatic biota. Canadian Journal of Fisheries and Aquatic Sciences 42:2034-2049.

Cannon, D. S., I. L. Crawford, and L. E. Carrell. 1988. Zinc deficiency conditions food aversions in rats. Physiological Behavior 42:245-247.

Casey, C. E., and K. M. Hambidge. 1980. Epidemiological aspects of human zinc deficiency. Pages 1-27 *in* J. O. Nriagu, editor. Zinc in the environment. Part II: health effects. John Wiley, New York

Castellano, M. C., F. Soteras, A. Cordova, L. M. Elosegui, and J. F. Escanero. 1988. Zinc distribution between serum ligands in rats: acute and chronic overload of zinc. Medical Science Research 16:1229-1230.

Chan, H. M. 1988a. A survey of trace metals in *Perna viridis* (L.) (Bivalvia: Mytilacea) from the coastal waters of Hong Kong. Asian Marine Biology 5:89-102.

Chan, H. M. 1988b. Accumulation and tolerance to cadmium, copper, lead and zinc by the green mussel *Perna viridis*. Marine Ecology Progress Series 48:295-303.

Chang, A. C., A. L. Page, J. E. Warneke, M. R. Resketo, and T. E. Jones. 1983. Accumulation of cadmium and zinc in barley grown on sludge-treated soils: a longterm field study. Journal of Environmental Quality 12:391-397.

Chausmer, A. B., C. Chavez, R. M. Wain, and Y. Daaka. 1989. Calcitonin, zinc, and testicular function. Metabolismo 38;714-717.

Chhabra, A., and S. P. Arora. 1989. Histological alterations in certain tissues of goats fed zinc- and vitamin A-deficient diets. Indian Journal of Animal Sciences 59:1045-1048.

Choi, D. W., M. Yokoyama, and J. Koh. 1988. Zinc neurotoxicity in cortical cell culture. Neuroscience 24:67-79.

Chowdhury, B. A., and R. K. Chandra. 1989. Effect of zinc administration on cadmium-induced suppression of natural killer cell activity in mice. Immunology Letters 22:287-292.

Chu, K. H., W. M. Cheung, and S. K. Lau. 1990. Trace metals in bivalves and sediments from Tolo Harbour, Hong Kong. Environment International 16:31-36.

Clapper, D. L, J. A. Davis, P. J. Lamothe, C. Patton, and D. Epel. 1985a. Involvement of zinc in the regulation of pH, motility, and acrosome reactions in sea urchin sperm. Journal of Cell Biology 100::1817-1824.

Clapper, D. L, P. L Lamothe, J. A. Davis, and D. Epel. 1985b. Sperm motility in the horseshoe crab. V: zinc removal mediates chelator initiation of motility. Journal of Experimental Zoology 236:83-91.

Clark, D. R., Jr., A. S. Wenner, and J. F. Moore. 1986. Metal residues in bat colonies, Jackson County, Florida, 1981-1983. Florida Field Naturlist 14:38-45.

Conrad, G. W. 1988. Heavy metal effects on cellular shape changes, cleavage, and larval development of the marine gastropod mollusk, (*Ilyanassa obsoleta* Say). Bulletin of Environmental Contamination and Toxicology 41:79-85.

Cosson, R. P. 1989. Relationships between heavy metal and metallothionein-like protein levels in the liver and kidney of two birds: the greater flamingo and the little egret. Comparative Biochemistry and Physiology 94C:243-248.

Cosson, R. P., J. C. Amiard, and C. Amiard-Triquet. 1988a. Trace elements in little egrets and flamingos of Camargue, France. Ecotoxicology and Environmental Safety 15:107-116.

Cosson, R. P., C. Amiard-Triquet, and J. C. Amiard. 1988b. Utilization des plumes dans le recherche des sources de contamination des oiseaux. par les elements traces: Cd, Cu, Hg, Pb, Se, et Zn chez les flamants de Camargue, France. Water, Air, and Soil Pollution 42:103-115.

Craik, J. C. A., and S. M. Harvey. 1988. A preliminary account of metal levels in eggs of farmed and wild Atlantic salmon and their relation to egg viability. Aquaculture 73:309-321.

Crespo, S., R. Flos, J. Balasch and G. Alonso. 1979. Zinc in the gills of dogfish (*Scyliorhinus canicula* L.) related to experimental aquatic zinc pollution. Comparative Biochemistry and Physiology 63C:261-266.

Custer, T. W, and B. M. Mulhern. 1983. Heavy metal residues in prefledging black-crowned night-herons from three Atlantic coast colonies. Bulletin of Environmental Contamination and Toxicology 30:178-185.

Cutshall, N. H. J. R. Naidu, and W. G. Pearcy. 1977. Zinc and cadmium in the Pacific hake *Merluccius productus* of the western U.S. coast. Marine Biology 44:195-201.

Cymbaluk, N. E, and G. I. Christison. 1989. Effects of dietary energy and phosphorus content on blood chemistry and development of growing horses. Journal of Animal Science 67:951-958.

Damir, H. A., M. E. S. Barri, S. M. El Hassan, M. H. Tageldin, A. A. Wahbi, and O. F. Idris. 1988. Clinical zinc and copper deficiencies in cattle of western Sudan. Tropical Animal Health and Production 20:52-56.

Dawson, D. A., E. E Stebber, S. L. Burks, and J. A. Bantle. 1988. Evaluation of the developmental toxicity of metal-contaminated sediments using short-term fathead minnow and frog embryo-larval assays. Environmental Toxicology and Chemistry 7:2744.

Decuypere, E., J. Helsen, S. V. Gorp, and G. Verheyen. 1988. The use of high zinc diets as forced molting method: effect on Zn uptake and egg Zn content. Archives fur Gefluegelkunde 52:245-251.

de March B. G. E. 1988. Acute toxicity of binary mixtures of five cations (Cu^{2+}, Cd^{2+}, Zn^{2+}, Mg^{2+}, and K^{+}) to the freshwater amphipod *Gammarus lacustris* (Sars): alternative descriptive models. Canadian Journal of Fisheries and Aquatic Sciences 45:625-633.

Depledge, M. H. 1989. Re-evaluation of metabolic requirements for copper and zinc in decapod crustaceans. Marine Environmental Research 27:115-126.

Devi, V. U. 1987. Heavy metal toxicity to fiddler crabs, *Ucu annulipes* Latreille and *Uca triangularis* (Milne Edwards): tolerance to copper, mercury, cadmium, and zinc. Bulletin of Environmental Contamination and Toxicology 39:1020-1027.

Devi, V. U., and Y. P. Rao. 1989a. Heavy metal toxicity to fiddler crabs, *Uca annulipes* Latreille and *Uca triangularis* (Milne Edwards): respiration on exposure to copper, mercury, cadmium, and zinc. Bulletin of Environmental Contamination and Toxicology 43:165-172.

Devi, V. U., and Y. P. Rao. 1989b. Zinc accumulation in fiddler crabs *Uca annulipes* Latreille and *Uca triangularis* (Milne Edwards). Ecotoxicology and Environmental Safety 18:129-140.

Devineau, J., and C. Amiard-Triquet 1985. Patterns of bioaccumulation of an essential trace element (zinc) and a pollutant metal (cadmium) in larvae of the prawn *Palaemon serratus*. Marine Biology 86:189-148.

Dib, A., J. P. Clavel, and J. P. Carreau. 1989. Effects of gamma-linolenic acid supplementation on lipid composition of liver microsomal membranes. I. Pregnant rats fed a zinc-deficient diet and those fed a balanced one. Journal of Clinical Biochemistry and Nutrition 6:95-102.

Droual, R., C. U. Meteyer, and E D. Galey. 1991. Zinc toxicosis due to ingestion of a penny in a gray-headed chachalaca (*Ortalis cinereiceps*). Avian Diseases 35:1007-1011.

Dwyer, F. J., C. J. Schmit, S. E. Finger, and P.M. Mehrle. 1988. Biochemical changes in longear sunfish, *Lepomis megalotis*, associated with lead, cadmium and zinc from mine railings. Journal of Fish Biology 33:307-317.

Earnshaw, M. J., S. Wilson, H. B. Akberali, R. D. Butler, and K. R. M Marriott. 1986. The action of heavy metals on the gametes of the marine mussel, *Mytilus edulis* (L.)--III. The effect of applied copper and zinc on sperm motility in relation to ultrastructural damage and intracellular metal localization. Marine Environmental Research 20:261-278.

Eisler, R. 1967. Acute toxicity of zinc to the killifish, *Fundulus heteroclitus*. Chesapeake Science 8:262-264.

Eisler, R. 1977a. Acute toxicities of selected heavy metals to the softshell clam, *Mya arenaria*. Bulletin of Environmental Contamination and Toxicology 17:137-145.

Eisler, R. 1977b. Toxicity evaluation of a complex metal mixture to the softshell clam *Mya arenaria*. Marine Biology 43:265-276.

Eisler, R. 1980. Accumulation of zinc by marine biota. Pages 259-351 *in* J. O. Nriagu, editor. Zinc in the environment. Part II: health effects. John Wiley & Sons, Inc., New York.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. Biological Trace Element Research 6:165-180.

Eisler, R., M. M. Barry, R. L. Lapan, Jr., G. Telek, E. W. Davey, and A. E. Soper. 1978. Metal survey of the marine clam *Pitar morrhuana* collected near a Rhode Island (USA) electroplating plant. Marine Biology 45:311-317.

Eisler, R., and G. R. Gardner. 1973. Acute toxicology to an estuarine teleost of mixtures of cadmium, copper and zinc salts. Journal of Fish Biology 5:131-142.

Eisler R. and R. J. Hennekey. 1977. Acute toxicities of Cd^{2+}, Cr^{+6}, Hg^{2+}, Ni^{2+}, and Zn^{2+} to estuarine macrofauna. Archives of Environmental Contamination and Toxicology 6:315-323.

Eisler, R., R. L. Lapan, Jr., G. Telek E. W. Davey A. E. Soper, and M. Barry. 1977. Survey of metals in sediments near Quonset Point, Rhode Island. Marine Pollution Bulletin 8:260-264.

Eisler, R, and G. LaRoche. 1972. Elemental composition of the estuarine teleost *Fundulus heteroclitus* (L). Journal of Experimental Marine Biology and Ecology 9:29-42.

Elinder, C. G. 1986. Zinc. Pages 664-679 *in* L. Friberg, G. E Nordberg, and V. B. Vouk, editors. Handbook on the toxicology of metals, second edition. Volume II: specific metals. Elsevier, New York.

Ellen, G., J. W. van Loon, and K. Tolsma. 1989. Copper, chromium, manganese, nickel and zinc in kidneys of cattle, pigs and sheep and in chicken livers in the Netherlands. Zeitschrift für Lebensmittel-Untersuchung und-Forschung 189:534-537.

Elliott, N. G., D. A. Ritz, and R. Swain. 1985. Interaction between copper and zinc accumulation in the barnacle *Elminius modestus* Darwin. Marine Environmental Research 17:13-17.

Engel, D. W. 1987. Metal regulation and molting in the blue crab, *Callinectes sapidus*: copper, zinc, and metallothionein. Biological Bulletin 172:69-82.

Eriksen, K. D. H., T. Andersen, J. Stenersen, and R. A. Andersen. 1990. Cytosolic binding of Cd, Cu, Zn and Ni in four polychaete species. Comparative Biochemistry and Physiology 95C:111-115.

Everall, N. C., N. A. A. Macfarlane, and R. W. Sedgwick. 1989a. The effects of water hardness upon the uptake, accumulation and excretion of zinc in the brown trout, *Salmo trutta* L. Journal of Fish Biology 35:881-892.

Everall, N. C., N. A. A. Macfarlane, and R. W. Sedgwick. 1989b. The interactions of water hardness and pH with the acute toxicity of zinc to the brown trout, *Salmo trutta* L. Journal of Fish Biology 35:27-36.

Falandysz, J., B. Jakuczun, and T. Mizera. 1988. Metals and organochlorines in four female white-tailed eagles. Marine Pollution Bulletin 19:521-526.

Falchuk, K. 1988. Zinc deficiency and the *E. gracilis* chromatin. Pages 75-91 *in* A. S. Prasad, editor. Essential and toxic trace metals in human health and disease. Alan R. Liss, New York.

Falchuk, K. H., B. Mazus, E. Ber, L. Ulpino-Lobb, and B. L. Vallee. 1985. Zinc deficiency and the *Euglena gracilis* chromatin: formation of an -amanitin-resistant RNA polymerase II. Biochemistry 24:2576-2580.

Farris, J. L, S. E. Belanger, D. S. Cherry, and J. Cairns, Jr. 1989. Cellulolytic activity as a novel approach to assess long-term zinc stress to *Corbicula*. Water Research 23: 1275-1283.

Fernandez, T. V., and N. V. Jones. 1987. Some studies on the effect of zinc on *Nereis diversicolor* (Polychaete-Annelida). Tropical Ecology 28:9-21.

Fernandez, T. V., and N. V. Jones. 1989. The distribution of zinc in the body of *Nereis diversicolor*. Tropical Ecology 30:285-293.

Ferreira, R. M. C. d. C., I. M. Marquiegui, and I. V. Elizaga. 1989. Teratogenicity of zinc deficiency in the rat: study of the fetal skeleton. Teratology 39:181-194.

Fisher, N. S., C. V. Nolan, and S. W. Fowler. 1991. Assimilation of metals in marine copepods and its biogeochemical implications. Marine Ecology Progress Series 71:37-43.

Fisher, N. S., and J. L. Teyssie. 1986. Influence of food composition on the biokinetics and tissue distribution of zinc and americium in mussels. Marine Ecology Progress Series 28:197-207.

Fleet, J. C., and C. C. McCormick. 1988. The ontogeny and induction of zinc by hepatic chick embryo metallothionein. Proceedings of the Society for Experimental Biology and Medicine 188:52-60.

Flieger, D. G. Reithmuller, and H. W. L. Ziwgler-Heitbrock. 1989. Zn^{++} inhibits both tumor necrosis factor-mediated DNA fragmentation and cytolysis. International Journal of Cancer 44:315-319.

Flos, R., A. Caritat, and J. Balasch. 1979. Zinc content in organs of dogfish (*Scyliorhinus canicula* L.) subject to sublethal aquatic zinc pollution. Comparative Biochemistry and Physiology 64C:77-81.

Fort, D. J., B. L. James, and J. A. Bantle. 1989. Evaluation of the developmental toxicity of five compounds with the frog embryo teratogenesis assay. *Xenopus* (FETAX) and a metabolic activation system. Journal of Applied Toxicology 9:377-388.

Fosmire, G. J. 1990. Zinc toxicity. The American Journal of Clinical Nutrition 51:225-227.

Francis, J. C., and E W. Harrison. 1988 Copper and zinc toxicity in *Ephydatia fluviatilis* (Porifera: Spongillidae). Transactions of the American Microscopical Society 107:67-78.

French, M. C., C. W. Haines, and J. Cooper. 1987. Investigation into the effects of ingestion of zinc shot by mallard ducks (*Anas platyrhynchos*). Environmental Pollution 47:305-314.

Fujise, Y., K. Honda, R. Tatsukawa, and S. Mishima. 1988. Tissue distribution of heavy metals in Dall's porpoise in the northwestern Pacific. Marine Pollution Bulletin 19:226-230.

Fukami, M., H. Obayashi, E. Yoshimura, S. Yamazaki, and S. Toda. 1968a. Effects of zinc on metal metabolism of the zinc tolerant chlorotic mutant of *Euglena gracilis* Z. Agricultural and Biological Chemistry 52:2343-2344.

Fukami, M., H. Obayashi, Y. Yoshioka, M. Kuroishi, S. Yamazaki, and S. Toda. 1988b. A zinc tolerant chlorotic mutant strain of *Euglena gracilis* Z. induced by zinc. Agricultural and Biological Chemistry 52:601-604.

Gasaway, W. C., and I. O. Buss. 1972. Zinc toxicity in the mallard duck. Journal of Wildlife Management 36:1107-1117.

Gatlin, D. M., III, H. F. Phillips, and E. L. Torrans. 1989. Effects of various levels of dietary copper and zinc on channel catfish. Aquaculture 76:127-134.

Gaynor, P. J., M. J. Montgomery, and C. R. Holmes. 1988. Effect of zinc chloride or zinc sulfate treatment of protein supplement on milk production. Journal of Dairy Science 71:2175-2180.

Gehrke, P. C. 1988. Acute cardio-respiratory responses of spangled perch, *Leiopotherapon unicolor* (Gunther 1859), to sublethal concentrations of zinc, temephos and 2,4-D. Australian Journal of Marine and Freshwater Research 39:767-774.

Ghanmi, Z., M. Rouabhia, O. Othmane, and P. A. Deschaux. 1989. Effects of metal ions on cyprinid fish immune response: in vitro effects of Zn^{2+} and Mn^{2+} on the mitogenetic response of carp pronephros lymphocytes. Ecotoxicology and Environmental Safety 17:183-189

Giesy, J. P., J. W. Bowling, and H. J. Kania. 1980. Cadmium and zinc accumulation and elimination by freshwater crayfish. Archives of Environmental Contamination and Toxicology 9:683-697.

Gipouloux, J. D., C. Girard, and S. Gipouloux. 1986. Number of somatic and germ cells during early stages of gonadal development in frog larvae treated with zinc sulphate. Roux's Archives of Developmental Biology 195:193-196.

Goede, A. A. 1985. Mercury, selenium, arsenic and zinc in waders from the Dutch Wadden Sea. Environmental Pollution 37A:287-309.

Goldberg, M., J. R Carreau, F. C. M. Driessens, and D. Septier. 1990. Zinc deficiency-induced changes in the lipid composition and ultrastructure of rat incisor teeth. Archives of Oral Biology 35:255-264.

Golub, M. S., M. E. Gershwin, L. S. Hurley, and A. G. Hendrickx. 1988. Studies of marginal zinc deprivation in rhesus monkeys. VIII. Effects in early adolescence. American Journal of Clinical Nutrition 47:1046-1051.

Gooneratne, S. K, and D. A. Christensen. 1989. A survey of maternal and fetal tissue zinc, iron, manganese and selenium concentrations in bovine. Canadian Journal of Animal Science 69:151-159.

Goyer, R. A. 1986. Toxic effects of metals. Pages 582-635 *in* C. D. Klaassen, M. O. Amdur, and J. Doull, editors. Casarett and Doull's toxicology. Third edition. Macmillan, New York.

Grady, J. R., A. G. Johnson, and M. Sanders. 1989. Heavy metal content in otoliths of king mackerel (*Scomberomorus cavalla*) in relation to body length and age. Contributions in Marine Science 81:17-23.

Grandy, J. W., IV, L. N. Locke, and G. E. Bagley. 1968. Relative toxicity of lead and five proposed substitute shot types to pen-reared mallards. Journal of Wildlife Management 32:483-488.

Grant, A., J. G. Hateley, and N. V. Jones. 1989. Mapping the ecological impact of heavy metals on the estuarine polychaete *Nereis diversicolor* using inherited metal tolerance. Marine Pollution Bulletin 20:235-238.

Greger, J. L. 1989. Effect of dietary protein and minerals on calcium and zinc utilization. Critical Reviews in Food Science and Nutrition 28:249-271.

Gregory, R. W., and J. Trial. 1975. Effect of zinc-coated culverts on vertebrate and invertebrate fauna in selected Maine streams. Land and Water Resources Institute, University of Maine at Orono, Completion Report A-033-ME. 18 pp.

Greville, R. W.., and A. J. Morgan. 1989a. Concentrations of metals (Cu, Pb, Cd, Zn, Ca) in six species of British terrestrial gastropods near a disused lead and zinc mine. Journal of Molluscan Studies 55:31-38.

Greville, R. W., and A. J. Morgan 1989b, Seasonal changes in metal levels (Cu, Pb, Cd, Zn and Ca) within the grey field slug, *Deroceras reticulatum*, living in a highly polluted habitat. Environmental Pollution 59A:287-303.

Grobler, E., H. H. Du Preez, and J. H. J. van Vuren. 1989. Toxic effects of zinc and iron on the routine oxygen consumption of *Tilapia sparrmanii* (Cichlidae). Comparative Biochemistry and Physiology 94C:207-214.

Gunson, D. E., D. E Kowalczyk, C. R. Shoop, and C. E Ramberg, Jr. 1982. Environmental zinc and cadmium pollution associated with generalized osteochondrosis, osteoporosis, and nephrocalcinosis in horses. Journal of the American Veterinary Medical Association 180:295-299.

Gupta, R. P., P. C. Verma, J. R. Sadana, and R. K. P. Gupta. 1988. Studies on the pathology of experimental zinc deficiency in guinea-pigs. Journal of Comparative Pathology 98:405-413.

Guthrie, J. 1971. Zinc induction of testicular teratomas in Japanese quail (*Coturnix coturnix japonica*) after photo-periodic stimulation of testis. British Journal of Cancer 25:311-314.

Hafiez, A. A., Z. H. M. El-Kirdassy, N. M. El-Malkh, and E. M. I. El-Zayat. 1990. Role of zinc in regulating the testicular function. Part 3. Histopathological changes induced by dietary zinc deficiency in testes of male albino rats. Die Nabrung 34:65-73.

Hamanaka, T., T. Itoo, and S. Mishima. 1982. Age-related change and distribution of cadmium and zinc concentrations in the Steller sea lion (*Eumetopias jubata*) from the coast of Hokkaido, Japan. Marine Pollution Bulletin 13:57-61.

Handy, R. D., and E B. Eddy. 1990. The influence of starvation on waterborne zinc accumulation by rainbow trout, *Salmo gairdneri*, at the onset of episodic exposure in neutral soft water. Water Research 24:521-527.

Handy, R. D., E B. Eddy, and G. Romain. 1989. In vitro evidence for the ionoregulatory role of rainbow trout mucous in acid, acid/aluminum and zinc toxicity. Journal of Fish Biology 35:737-747.

Hanna, R. G. M. 1989. Levels of heavy metals in some Red Sea fish before hot brine pools mining. Marine Pollution Bulletin 20:631-635.

Harland, B. F, M. R. S. Fox, and B. E. Fry, Jr. 1975. Protection against zinc deficiency by prior excess dietary zinc in young Japanese quail. Journal of Nutrition 105:1509-1518.

Haseltine, S. D., G. H. Heinz, W. L. Reichel, and J. E Moore. 1981. Organochlorine and metal residues in eggs of waterfowl nesting on islands in Lake Michigan off Door County, Wisconsin, 1977-78. Pesticides Monitoring Journal 15:90-97.

Hatakeyama, S. 1989. Effect of copper and zinc on the growth and emergence of *Epeorus latifolium* (Ephemeroptera) in an indoor model stream. Hydrobiologia 174:17-27.

Heath, A. G. 1987. Effects of waterborne copper or zinc on the osmoregulatory response of bluegill to a hypertonic NaCl challenge. Comparative Biochemistry and Physiology 88C:307-311.

Heinz, G. H., H. E Percival, and M. L. Jennings. 1991. Contaminants in American alligator eggs from Lake Apopka, Lake Griffin, and Lake Okeechobee, Florida. Environmental Monitoring and Assessment 16:277-285.

Hemelraad, J., H. A. Kleinveld, A. M. de Roos, D. A. Holwerda, and D. I. Zandee. 1987. Cadmium kinetics in freshwater clams. III. Effects of zinc on uptake and distribution of cadmium in *Anodonta cygnea*. Archives of Environmental Contamination and Toxicology 16:95-101.

Herkovits, J., and C. S. Perez-Coll. 1990. Zinc protection against delayed development produced by cadmium. Biological Trace Element Research 24:217-221.

Herkovits, J., C. S. Perez-Coll, and S. Zeni. 1989. Protective effect of zinc against spontaneous malformations and lethality in *Bufo arenarum* embryos. Biological Trace Element Research 22:247-250.

Hernandez, L. M., M. J. Gonzalez, M. C. Rico, M. A. Fernandez, and A. Aranda. 1988. Organochlorine and heavy metal residues in falconiforme and ciconiforme eggs (Spain). Bulletin of Environmental Contamination and Toxicology 40:86-93.

Hietanen, B., I. Sunila, and R. Kristoffersson. 1988a. Toxic effects of zinc on the common mussel *Mytilus edulis* L. (Bivalvia) in brackish water. I. Physiological and histopathological studies. Annales Zoologici Fennici 25:341-347.

Hietanen, B., I. Sunila, and R. Kristoffersson. 1988b. Toxic effects of zinc on the common mussel *Mytilus edulis* L. (Bivalvia) in brackish water. II. Accumulation studies. Annales Zoologici Fennici 25:349-352.

Hill, E. E, and M. B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to coturnix. U.S. Fish and Wildlife Service Technical Report 2. 147 pp.

Hilmy, A. M., N. A. El-Domiaty, A. Y. Daabees, and A. Alsarha. 1987a. The toxicity to *Clarias lazera* of copper and zinc applied jointly. Comparative Biochemistry and Physiology 87C:309-314.

Hilmy, A. M., N. A. El-Domiaty, A. Y Daabees, and H. A. A. Latife. 1987b. Some physiological and biochemical indices of zinc toxicity in two freshwater fishes, *Clarias lazera* and *Tilapia zilli*. Comparative Biochemistry and Physiology 87C:297-301.

Hilmy, A. M., N. A. El-Domiaty, A. Y. Dadbees, and H. A. A. Latife. 1987c. Toxicity in *Tilapia zilli* and *Clarias lazera* (Pisces) induced by zinc, seasonally. Comparative Biochemistry and Physiology 86C:263-265.

Hilmy, A. M., N. E A. El-Hamid, and K. S. Ghazaly. 1988. Biochemical and physiological changes in the tissues and serum of both sexes in *Portunus pelagicus* (L.) following acute exposures to zinc and copper. Folia Morphologica 36:79-94.

Hinesly, T. D., R. L Jones, E. L. Ziegler, and J. J. Tyler. 1977. Effects of annual and accumulative applications of sewage sludge on assimilation of zinc and cadmium by corn (*Zea mays* L.). Environmental Science & Technology 11:182-188.

Hoadley, J. E., and R. J. Cousins. 1988. Regulatory mechanisms for intestinal transport of zinc and copper. Pages 141-155 *in* A. S. Prasad, editor. Essential and toxic trace elements in human health and disease. Alan R. Liss, New York.

Hobson, J. E, and W. J. Birge. 1989. Acclimation-induced changes in toxicity and induction of metallothionein-like proteins in the fathead minnow following sublethal exposure to zinc. Environmental Toxicology and Chemistry 8:157-169.

Hodson, P. V., and J. B. Sprague. 1975. Temperature-induced changes in acute toxicity of zinc to Atlantic salmon (*Salmo salar*). Journal of the Fisheries Research Board of Canada 32:1-10.

Holterman, W. E M. O., P. de Voogt, and J. H. J. C. Peereboom-Stegeman. 1984. Cadmium/zinc relationships in kidney cortex and metallothionein of horse and red deer: histopathological observations on horse kidneys. Environmental Research 35:466-481.

Hopkin, S. P., C. A. C. Haines, and S. Bragg. 1989. Terrestrial isopods as biological indicators of zinc pollution in the Reading area, south east England. Monitors Zoologico Italiano Monografia 4:477-488.

Hopkin, S. P., G. N. Hardisty, and M. H. Martin. 1986. The woodlouse *Porcellio scaber* as a biological indicator of zinc, cadmium, lead and copper pollution. Environmental Pollution 11B:271-290.

Hopkin, S. P., and M. H. Martin. 1985. Assimilation of zinc, cadmium, lead, copper, and iron by the spider *Dysdera crocata*, a predator of woodlice. Bulletin of Environmental Contamination and Toxicology 34:183-187.

Howell, R. 1985. Effect of zinc on cadmium toxicity to the amphipod *Gammarus pulex*. Hydrobiologia 123:245-249.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. Second edition. U.S. Fish and Wildlife Service Resource Publication 153. 90 pp.

Hunt, J. W., and B. S. Anderson. 1989. Sublethal effects of zinc and municipal effluents on larvae of the red abalone *Haliotis rufescens*. Marine Biology 101:545-552.

Hussein, A. S., A. H. Cantor, and T. H. Johnson. 1988. Use of high levels of dietary aluminum and zinc for inducing pauses in egg production of Japanese quail. Poultry Science 67:1157-1165.

Ireland, M. 1986. Effects of wound healing on zinc distribution and alkaline phosphatase activity of *Helix aspersa* (Gastropoda: Pulmonata). Journal of Molluscan Studies 52:169-173.

Jameson, S. 1980. Zinc and pregnancy. Pages 183-197 *in* J. O. Nriagu, editor. Zinc in the environment. Part II: health effects. John Wiley, New York,

Johnson, I., and M. B. Jones. 1989. Effects of zinc/salinity combinations on zinc regulation in *Gammarus duebeni* from the estuary and the sewage treatment works at Looe, Cornwall. Journal of the Marine Biological Association of the United Kingdom 69:249-260.

Jones, R., and M. S. E. Burgess. 1984. Zinc and cadmium in soils and plants near electrical transmission (hydro) towers. Environmental Science & Technology 18:731-734.

Jorhem, L., B. Sundstrom, C. Astrand, and G. Haegglund. 1989. The levels of zinc, copper, manganese, selenium, chromium, nickel, cobalt, and aluminum in the meat, liver and kidney of Swedish pigs and cattle. Zeitschrift for Lebensmittel-Untersuchung und-Forschung 188:39-44.

Joseph, K. O. 1989. Heavy metal contamination of fish of the estuarine environment in Madras region. Proceedings of the National Academy of Science of India 59B:45-50.

Joyner, T., and R. Eisler. 1961. Retention and translocation of radioactive zinc by salmon fingerlings. Growth 25:151-156.

Kaji, T., R. Kawatani, M. Takata, T. Hoshino, T. Miyahara, H. Konzuka, and F. Koizumi. 1988. The effects of cadmium, copper or zinc on formation of embryonic chick bone in tissue culture. Toxicology 50:303-316.

Kasprzak, K. S., R. M. Kovatch, and L. A. Poirier. 1988. Inhibitory effect of zinc on nickel subsulfide carcinogenesis in Fischer rats. Toxicology 52:253-262.

Kaur, S. 1989. Accumulation of lead, zinc and cadmium in the nestling feathers of hoopoe *Upupa epops*. Journal of the Bombay Natural History Society 86:244-245.

Kazacos, E. A., and J. E Van Vleet. 1989. Sequential ultrastructural changes of the pancreas in zinc toxicosis in ducklings. American Journal of Pathology 134:581-595.

Keating, K. I., and P. B. Caffrey. 1989. Selenium deficiency induced by zinc deprivation in a crustacean. Proceedings of the National Academy of Sciences of the United States of America 86:6436-6440.

Keen, C. L, B. Lonnerdal, M. S. Golub, J. Y. Uriu-Hare, K. L. Olin, A. G. Hendrickx, and M. E. Gershwin. 1989. Influence of marginal maternal zinc deficiency on pregnancy outcome and infant status in rhesus monkeys. Pediatric Research 26:470-477.

Khan, A. T., J. S. Weis, and L. D'Andrea. 1989. Bioaccumulation of four heavy metals in two populations of grass shrimp, *Palaemonetes pugio*. Bulletin of Environmental Contamination and Toxicology 42:339-343.

Khandaker, Z. H., and S. B. TeLler. 1990. Treatment of zinc deficiency in sheep by zinc containing boluses. Asian-Australasian Journal of Animal Sciences 3:53-59.

Khangarot, B. S., and P. K. Ray. 1987. Zinc sensitivity of a freshwater snail, *Lymnaea luteola* L., in relation to seasonal variations in temperature. Bulletin of Environmental Contamination and Toxicology 39:45-49.

Khangarot, B. S., and P. K. Ray. 1988. Sensitivity of freshwater pulmonate snails, *Lymnaea luteola* L. to heavy metals. Bulletin of Environmental Contamination and Toxicology 41:208-213.

Khangarot, B. S., and P. K. Ray. 1989. Investigation of correlation between physicochemical properties metals and their toxicity to the water flea *Daphnia magna* Straus. Ecotoxicology and Environmental Safety 18:109-120.

Kitchens, D. L, K. Dawson, and L Reuss. 1990. Zinc blocks apical membrane anion exchange in gallbladder epithelium. American Journal of Physiology 258:G745-G752.

Korver, R. M., and J. B. Sprague. 1989. Zinc avoidance by fathead minnows (*Pimephales promelas*): computerized tracking and greater ecological relevance. Canadian Journal of Fisheries and Aquatic Sciences 46:494-502.

Kowalska-Wochna, E., J. Moniuszko-Jakoniuk, E. Kulikowska, and K. Miniuk. 1988. The effect of orally applied aqueous solutions of lead and zinc on chromosome aberrations and induction of sister chromatid exchanges in the rat (*Rattus* sp.). Genetica Polonica 29:181-189.

Krantz, W. C., B. M. Mulhern, G. E. Bagley, A. Sprunt, IV,, E J. Ligas, and W.. B. Robertson, Jr. 1970. Organochlorine and heavy metal residues in bald eagle eggs. Pesticides Monitoring Journal 4:136-140.

Krantzberg, G., and P.M. Stokes. 1985. Benthic macroinvertebrates modify copper and zinc partitioning in freshwater-sediment microcosms. Canadian Journal of Fisheries and Aquatic Sciences 42:1465-1473.

Kreppel, H., K. Kolb, F. X. Reichl, B. Fichtl, and W. Forth. 1988. Pretreatment with low doses of cadmium or zink decreases lethality in mice acutely poisoned with arsenic. Pages 594-600 *in* Trace element analytical chemistry in medicine and biology. Walter de Gruyter, Berlin.

Lalande, M., and B. Pinel-Alloul. 1986. Acute toxicity of cadmium, copper, mercury and zinc to *Tropocyclops prasinus mexicanus* (Cyclopoida, Copepoda) from the Quebec lakes. Environmental Toxicology and Chemistry 5:95-102.

Lain, H. F., M. W. Conner, A. E. Rogers, S. Fitzgerald, and M. O. Amdur. 1985. Functional and morphologic changes in the lungs of guinea pigs exposed to freshly generated ultrafine zinc oxide. Toxicology and Applied Pharmacology 78:29-38.

Latimer, K. S., A. V. Jain, H. B. Inglesby, W. D. Clarkson, and G. B. Johnson. 1989. Zinc-induced hemolytic anemia caused by ingestion of pennies by a pup. Journal of the American Veterinary Medical Association 195:77-80.

Lazos, E. S., G. Aggelousis, and A. Alexakis. 1989. Metal and proximate composition of the edible portion of 11 freshwater fish species. Journal of Food Composition and Analysis 2:371-381.

Leek, J. C., C. L. Keen, J. B. Vogler, M. S. Golub, L. S. Hurley, A. G. Hendrickx, and M. E. Gershwin 1988. Long-term marginal zinc deprivation in rhesus monkeys. IV. Effects on skeletal growth and mineralization. American Journal of Clinical Nutrition 47:889-895.

Leonard, A., and G. B. Gerber. 1989. Zinc toxicity: does it exist? Journal of the American College of Toxicology 8:1285-1290.

Levine, M. B., A. T. Hall, G. W. Barrett, and D. H. Taylor. 1989. Heavy metal concentrations during ten years of sludge treatment in an old-field community. Journal of Environmental Quality 18:411-418.

Lewis, T. E., and A. W. McIntosh. 1986. Uptake of sediment-bound lead and zinc by the freshwater isopod *Asellus communis* at three different pH levels. Archives of Environmental Contamination and Toxicology 15:495-504.

Llobet, J. M., J. L. Domingo, M. T. Colomina, E. Mayayo, and J. Corbella. 1988a. Subchronic oral toxicity of zinc in rats. Bulletin of Environmental Contamination and Toxicology 41:36-43.

Llobet, J. M., J. L. Domingo, and J. Corbella. 1988b. Antidotes for zinc intoxication in mice. Archives of Toxicology 61:321-323.

Lobel, P. B. 1986. Role of the kidney in determining the whole soft tissue zinc concentration of individual mussels (*Mytilus edulis*). Marine Biology 92:355-359.

Lobel, P. B. 1987. Short-term and long-term uptake of zinc by the mussel, *Mytilus edulis*: a study in individual variability. Archives of Environmental Contamination and Toxicology 16:723-732.

Lobel, P. B., and H. D. Marshall. 1988. A unique low molecular weight zinc-binding ligand in the kidney cytosol of the mussel *Mytilus edulis*, and its relationship to the inherent variability of zinc accumulation in this organism. Marine Biology 99:101-105.

Loring, D. H., and G. Asmund. 1989. Heavy metal contamination of a Greenland fjord system by mine wastes. Environmental Geology and Water Sciences 14:61-71.

Lowe, T. P., T. W. May, W. G. Brumbaugh, and D. A. Kane. 1985. National Contaminant Biomonitoring Program: concentrations of seven elements in freshwater fish, 1978-1981. Archives of Environmental Contamination and Toxicology 14:363-388.

Lu, J., and G. E Combs, Jr. 1988a. Effects of excess dietary zinc on pancreatic exocrine function in the chick. Journal of Nutrition 118:681-689.

Lu, J., and G. E Combs, Jr. 1988b. Excess dietary zinc decreases tissue -tocopherol in chicks. Journal of Nutrition 118:1349-1359.

Lu, J., G. E Combs, Jr., and J. C. Fleet. 1990. Time-course studies of pancreatic damage induced by excess dietary zinc in the chick. Journal of Nutrition 120:389-397.

Luoma, S. N., and G. W. Bryan. 1979. Trace metal bioavailability: modeling chemical and biological interactions of sediment-bound zinc. Pages 577-609 *in* E. A, Jenne, editor. Chemical modeling in aqueous systems. American Chemical Society Symposium Series 93.

Luten, J. B., W. Bouquet, M. M. Burggraf, and J. Rus. 1986. Accumulation, elimination, and speciation of cadmium and zinc in mussels, *Mytilus edulis*, in the natural environment. Bulletin of Environmental Contamination and Toxicology 37:579-586.

Lyngby, J. E., H. Brix, and H. I-L Schierup. 1982. Absorption and translocation of zinc in eelgrass (*Zostera marina* L.). Journal of Experimental Marine Biology and Ecology 58:259-270.

Mackay-Sim, A., and I.E. Dreosti. 1989. Olfactory function in zinc-deficient adult mice. Experimental Brain Research 76:207-212.

Maita, K., M. Hirano, K. Mitsumori, K. Takahashi, and Y. Shirasu. 1981. Subacute toxicity studies with zinc sulfate in mice and rats. Journal of Pesticide Science 6:327-336.

Mamba, K, K. Taniguchi, S. Kagabu, and T. Makita. 1989. Quantitative and morphological studies on the influence of zinc deficiency on the liver of pregnant rats. Japanese Journal of Veterinary Science 51:566-573.

Mann, H., and W. S. Fyfe. 1988. Biogeochemical cycling of the elements in some fresh water algae from gold and uranium mining districts. Biorecovery 1:3-26.

Mann, H., W. S. Fyfe, R. Kerrich, and M. Wiseman. 1989. Retardation of toxic heavy metal dispersion from nickel-copper mine tailings, Sudbury district, Ontario: role of acidophilic microorganisms. I. Biological pathway of metal retardation. Biorecovery 1:155-172.

Mansour, M. M. S., N. M. El-Malkh, and E. M. I. ElZayat. 1989. Effect of dietary zinc deficiency on serum and testicular total protein contents in male albino rats. Journal of Drug Research (Cairo) 18:131-142.

Marigomez, J. A., E. Angulo, and V. Saez. 1986. Feeding and growth responses to copper, zinc, mercury and lead in the terrestrial gastropod *Arion ater* (Linné). Journal of Molluscan Studies 52:68-78.

Mason, A. Z. 1968. The kinetics of zinc accumulation by the marine prosobranch gastropod *Littorina littorea*. Marine Environmental Research 24:135-139.

Mason, A. Z., K. D. Jenkins, and P. A. Sullivan. 1988. Mechanisms of trace metal accumulation in the polychaete *Neanthes arenaceodentata*. Journal of the Marine Biological Association of the United Kingdom 68:61-80.

Mason, C. F., and S. M. Macdonald. 1988. Metal contamination in mosses and otter distribution in a rural Welsh river receiving mine drainage. Chemosphere 17:1159-1166.

Matthiessen, P., and A. E. Brafield. 1977. Uptake and loss of dissolved zinc by the stickleback *Gasterosteus aculeatus* L. Journal of Fish Biology 10:399-410.

Mayer, E L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U.S. Environmental Protection Agency Report 600/8-87/017. 274 pp.

Mayer, E L., Jr., and M. R. Ellersieck. 1986. Manual of acute toxicity: interpretation and data base for 410 chemicals and 66 species of freshwater animals. U.S. Fish and Wildlife Service Resource Publication 160. 579 pp.

McCulloch, A. W., R. K. Boyd, A. S. W. de Freitas, R. A. Foxall, W. D. Jamieson, M. V. Laycock, M. A. Quilliam, J. C. Wright, V. J. Boyko, J. W. McLaren, M. R. Miedema, R. Pocklington, E. Arsenault, and D. J. A. Richard. 1989. Zinc from oyster tissue as causative factor in mouse deaths in official bioassay for paralytic shellfish poisoning. Journal of the Association of Official Analytical Chemists 72:384-386.

McGuire, J. T., E. S. Dierenfeld, R. H.. Poppenga, and W. E. Brazelton. 1989. Plasma alpha-tocopherol, retinol, cholesterol, and mineral concentrations in captive gorillas. Journal of Medical Primatology 18: 155-161.

McLusky, D. S., and L. Hagerman. 1987. The toxicity of chromium, nickel and zinc: effects of salinity and temperature, and the osmoregulatory consequences in the mysid *Praunus flexuosus*. Aquatic Toxicology 10:225-238.

Mejborn, H. 1989. Zinc balances in young and adult mink (*Mustela vison*) in relation to dietary zinc intake. Journal of Animal Physiology and Animal Nutrition 61:187-192.

Memmert, U. 1987. Bioaccumulation of zinc in two freshwater organisms (*Daphnia magna*, Crustacea and *Brachydanio* rerio, Pisces). Water Research 21:99-106.

Migula, P., A. Kafel, A. Kedziorski, and M. Nakonieczny. 1989. Combined and separate effects of cadmium, lead and zinc on growth and feeding in the house cricket (*Acheta domesticus*). Biologia Bratislava 44:911-921.

Milhaud, G. E., and S. Mehannaoui. 1988. Indicators of lead, zinc and cadmium exposure in cattle: I. Results in a polluted area. Veterinary and Human Toxicology 30:513-517.

Miller, W. J., H. E. Amos, R. P. Gentry, D. M. Blackman, R. M. Durrance, C. T. Crowe, A. S. Fielding, and M. W. Neathery. 1989. Long-term feeding of high zinc sulfate diets to lactating and gestating dairy cows. Journal of Dairy Science 72:1499-1508.

Miller W. L, N.J. Blake, and R. H. Byrne. 1985. Uptake of Zn^{65} and Mn^{54} into body tissues and renal concretions by the southern quahog, *Mercenaria campechiensis* (Gmelin): effects of elevated phosphate and metal concentrations. Marine Environmental Research 17:167-171.

Mirenda, R. J. 1986. Acute toxicity and accumulation of zinc in the crayfish, *Orconectes virilis* (Hagen). Bulletin of Environmental Contamination and Toxicology 37:387-394.

Mooradian, A. D., D.C. Norman, and J. E. Morley. 1988. The effect of zinc status on the immune function of diabetic rats. Diabetologia 31:703-707.

Morgan, J. E., and A. J. Morgan. 1988. Earthworms as biological monitors of cadmium, copper, lead and zinc in metalliferous soils. Environmental Pollution 54A:123-138.

Morris, P. J., J. Jensen, and E Applehans. 1986. Lead and zinc toxicosis in a blue and gold macaw (*Ara ararauna*) caused by ingestion of hardware cloth. Annual Proceedings of the American Association of Zoo Veterinarians 1985:13-17.

Morris, R. J., R. J. Law, C. R. Allchin, C. A. Kelly, and C. E Fileman. 1989. Metals and organochlorines in dolphins and porpoises of Cardigan Bay, West Wales. Marine Pollution Bulletin 20:512-523.

Muir, D. G. G., R. Wagemann, N. P. Grift, R. J. Norstrom, M. Simon, and J. Lien. 1988. Organochlorine chemical and heavy metal contaminants in whitebeaked dolphins (*Lagenorhynchus albirostris*) and pilot whales (*Globicephala melaena*) from the coast of Newfoundland, Canada. Archives of Environmental Contamination and Toxicology 17:613-629.

Muirhead, S. J., and R. W. Furness. 1988. Heavy metal concentrations in the tissues of seabirds from Gough Island, South Atlantic Ocean. Marine Pollution Bulletin 19:278-283.

Munkittrick, K. R., and D. G. Dixon. 1988. Growth, fecundity, and energy stores of white sucker (*Catostomus commersoni*) from lakes containing elevated levels of copper and zinc. Canadian Journal of Fisheries and Aquatic Sciences 45:1355-1365.

Munkittrick, K. R., and D. G. Dixon. 1989. Effects of natural exposure to copper and zinc on egg size and larval copper tolerance in white sucker (*Catostomus commersoni*). Ecotoxicology and Environmental Safety 18:15-28.

Munzinger, A., and M. L. Guarducci. 1988. The effect of low zinc concentrations on some demographic parameters of *Biomphalaria glabrata* (Say), Mollusca: Gastropoda. Aquatic Toxicology 12:51-61.

Murphy, B. R., G. J. Atchison, A. W.. McIntosh, and D. J. Kolar. 1978. Cadmium and zinc content of fish from an industrially contaminated lake. Journal of Fish Biology 13:327-335.

Nagel, W, Y. Natochin, and J. Crabbe. 1988. Effects of divalent cations on chloride movement across amphibian skin. Pfluegers Archiv European Journal of Physiology 411:540-545.

Nakamura, S., C. Ohrni, and M. K. Kojima. 1989. Effect of zinc ion on formation of the fertilization membrane in sea urchin eggs. Zoological Science (Tokyo) 6:329-333.

Nash, T. H., III. 1975. Influence of effluents from a zinc factory on lichens. Ecological Monograph 4,5: 183-198.

National Academy of Sciences (NAS). 1979. Zinc. United States National Academy of Sciences, National search Council, Subcommittee on Zinc. University Park Press, Baltimore, Md. 471 pp.

Nehring, R. B., and J. R Goettl, Jr. 1974. Acute toxicity of a zinc-polluted stream to four species of salmonids. Bulletin of Environmental Contamination and Toxicology 12:464-469.

Nelson, D. A., J. E. Miller, and A. Calabrese. 1988. Effect of heavy metals on bay scallops, surf clams, and blue mussels in acute and long-term exposures. Archives of Environmental Contamination and Toxicology 17:595-600.

Neuhauser, E. F., R. C. Loehr, D. L. Milligan, and M. R. Malecki. 1985. Toxicity of metals to the earthworm *Eisenia fetida*. Biology and Fertility of Soils 1:149-152.

Newman, M. C., and S. V. Mitz. 1988. Size dependence of zinc elimination and uptake from water by mosquitofish *Gambusia affinis* (Baird and Girard). Aquatic Toxicology 12:17-32.

Nicolaidu, A., and J. A. Nott. 1990. Mediterranean pollution from a ferro-nickel smelter: differential uptake by some gastropods. Marine Pollution Bulletin 21:137-143.

Nielsen, C. O., and R. Dietz. 1990. Distributional pattern of zinc, cadmium, mercury, and selenium in livers of hooded seal (*Cystophora cristata*). Biological Trace Element Research 24:61-71.

Norheim, G., J. U. Share, and O. Wiig. 1992. Some heavy metals, essential elements, and chlorinated hydrocarbons in polar bear (*Ursus maritimus*) at Svalbard. Environmental Pollution 77:51-57.

Nriagu, J. O., editor. 1980. Zinc in the environment. Part I: ecological cycling;, Part II: health effects. John Wiley, New York.

Nugegoda, D., and P. s. Rainbow. 1987. The effect of temperature on zinc regulation by the decapod crustacean *Palaemon elegans* Rathke. Ophelia 27:17-30.

Nugegoda, D., and P. S. Rainbow. 1988a. Effect of a chelating agent (EDTA) on zinc uptake and regulation by *Palaemon elegans* (Crustacea: Decapoda). Journal of the Marine Biological Association of the United Kingdom 68:25-40.

Nugegoda, D., and P. S. Rainbow. 1988b. Zinc uptake and regulation by the sublittoral prawn *Pandalus montagui* (Crustacea: Decapoda). Estuarine Coastal and Shelf Science 26:619-632.

Nugegoda, D., and P. S. Rainbow. 1989a. Effects of salinity changes on zinc uptake and regulation by the decapod crustaceans *Palaemon elegans* and *Palaemonetes varians*. Marine Ecology Progress Series 51:57-75.

Nugegoda, D., and P. S. Rainbow. 1989b. Salinity, osmolality, and zinc uptake in *Palaemon elegans* (Crustacea: Decapoda). Marine Ecology Progress Series 55:149-157.

Nugegoda, D., and P. S. Rainbow. 1989c. Zinc uptake and regulation breakdown in the decapod crustacean *Palaemon elegans* Rathke. Ophelia 30:199-212.

O'Dell, B. L., J. K. Becket, M. P. Emery, and J. D. Browning. 1989. Production and reversal of the neuromuscular pathology and related signs of zinc deficiency in guinea pigs. Journal of Nutrition 119:196-201.

Ogden, L., W. C. Edwards, and N. A. Nail. 1988. Zinc intoxication in a dog from the ingestion of copper clad zinc pennies. Veterinary and Human Toxicology 30:577-578.

Oh, S. H., H. Nakaue, J. T. Deagen, P. D. Whanger, and G. H. Arscott. 1979. Accumulation and depletion of zinc in chick tissue metallothioneins. Journal of Nutrition 109: 1720-1729.

Olsson, P. E., M. Zafarullah, and L. Gedamu. 1989. A role of metallothionein in zinc regulation after oestradiol induction of vitellogenin synthesis in rainbow trout, *Salmo gairdneri*. Biochemical Journal 257:555-559.

Ostrowski, S. R., E. W. Gunter, and T. D. Matte. 1990. Blood lead and zinc protoporphyrin levels in donkeys and mules near a secondary lead smelter in Jamaica, 1987-88. Veterinary and Human Toxicology 32:53-56.

Overnell, J., T. C. Fletcher, and R. McIntosh. 1988. The apparent lack of effect of supplementary dietary zinc on zinc metabolism and metallothionein concentrations in the turbot, *Scopthalmus maximus* (Linnaeus). Journal of Fish Biology 33:563-570.

Overnell, J., R. McIntosh, and T. C. Fletcher. 1987a. The enhanced induction of metallothionein by zinc, its half-life in the marine fish *Pleuronectes platessa*, and the influence of stress factors on metallothionein levels. Experientia 43: 178-181.

Overnell, J., R. McIntosh, and T. C. Fletcher. 1987b. The levels of liver metallothionein and zinc in plaice, *Pleuronectes platessa* L., during the breeding season, and the effect of oestradiol injection. Journal of Fish Biology 30:539-546.

Palafox, A. L., and E. Ho-A. 1980. Effect of zinc toxicity in laying white leghorn pullets and hens. Poultry Science 59:2024-2028.

Park, Y. W., and H. L. Chukwu. 1989. Trace mineral concentrations in goat milk from French-Alpine and Anglo-Nubian breeds during the first 5 months of lactation. Journal of Food Composition and Analysis 2:161-169.

Patel, H. S., and M. B. Kaliwal. 1989. Histopathological effects of zinc on the gills of prawn *Macrobrachium hendersodyanum*. Zeitschrift fün Angewandte Zoologie 76:505-509.

Paulauskis, J. D., and R. W. Winner. 1988. Effects of water hardness and humic acid on zinc toxicity to *Daphnia magna* Straus. Aquatic Toxicology 12:273-290.

Peterson, R. H., A. Sreedharan, and S. Ray. 1989. Accumulation of trace metals in three species of fish from lakes in New Brunswick and Nova Scotia (Canada): influence of pH and other chemical parameters. Water Pollution Research Journal of Canada 24:101-117.

Phillips, J. L., and M. K. Kindred. 1980. Tumorogenesis and zinc. Pages 199-213 *in* J. O. Nriagu, editor. Zinc in the environment. Part II: health effects. John Wiley, New York.

Pierson, K. B. 1981. Effects of chronic zinc exposure on the growth, sexual maturity, reproduction, and bioaccumulation of the guppy, *Poecilia reticulata*. Canadian Journal of Fisheries and Aquatic Sciences 38:23-31.

Pirie, B., L. Fayi, and S. George. 1985. Ultrastructural localization of copper and zinc in the polychaete, *Nereis diversicolor*, from a highly contaminated estuary. Marine Environmental Research 17:197-198.

Pisa, J., and J. Cibulka. 1989. Cd, Pb, Hg, Cu, and Zn content in hair and cervical mucous in cattle kept in industrial area in Czechoslovakia. Ekologia-CSSR 8:421-432.

Poston, H. A., and H. G. Ketola. 1989. Chemical composition of maturing and spawning Atlantic salmon from different locations. Progressive Fish-Culturist 51:133-139.

Prahalad, A. K., and G. Seenayya. 1989. Physico-chemical interactions and bioconcentration of zinc and lead in the industrially polluted Husainsager Lake, Hyderabad, India. Environmental Pollution 58A:139-154.

Prasad, A. S. 1979. Clinical, biochemical, and pharmacological role of zinc. Annual Review of Pharmacology and Toxicology 20:393-426.

Prasad, A. S. 1980. Manifestations of zinc abnormalities in hums beings. Pages 29-59 *in* J. O. Nriagu, editor. Zinc in the environment, Part II: health effects. John Wiley, New York,

Presley, B. J., R. J. Taylor, and P. N. Boothe. 1990. Trace metals in Gulf of Mexico oysters. Science of the Total Environment 97/98:551-593.

Price, N. M., and F. M. Morel. 1990. Cadmium and cobalt substitution for zinc in a marine diatom. Nature 344:658-660.

Pundir, R. 1989. Acute toxicity levels of cadmium, lead, zinc and molybdenum to the stone loach, *Nemacheilus botia*. Journal of Hydrobiology 5:23-27.

Rainbow, R S. 1989. Copper, cadmium and zinc concentrations in oceanic amphipod and euphausiid crustaceans, as a source of heavy metals to pelagic seabirds. Marine Biology 103:513-518.

Rainbow, R S., P. G. Moore, and D. Watson. 1989. Talitrid amphipods (Crustacea) as biomonitors for copper and zinc. Estuarine Coastal and Shelf Science 28:567-582.

Rainbow, R S., and S. L White. 1989. Comparative strategies of heavy metal accumulation by crustaceans: zinc, copper and cadmium in a decapod, an amphipod and a barnacle. Hydrobiologia 174:245-267,

Ramachandra, K. S., and J. Prasad 1989. Influence of supplemental zinc on hemato-biochemical indices in growing calves. Indian Journal of Animal Science 59:1120-1122.

Ramelow, G. J., C. L Webre, C. S. Mueller, J. N. Beck, J. C. Young, and M. R Langley. 1989. Variations of heavy metals and arsenic in fish and other organisms from the Calcasieu River and Lake, Louisiana. Archives of Environmental Contamination and Toxicology 18:804-818.

Ray, S., D. W. McLeese, B. A. Waiwood, and D. Pozzack. 1980. The disposition of cadmium and zinc in *Pandalus montagui*. Archives of Environmental Contamination and Toxicology 9:675-681.

Recio, A., J. A. Marigomez, E. Angulo, and J. Moya. 1988a. Zinc treatment of the digestive gland of the slug *Arion ater* L. 1. Cellular distribution of zinc and calcium. Bulletin of Environmental Contamination and Toxicology 41:858-864.

Recio, A., J. A. Marigomez, E. Angulo, and J. Moya. 1988b. Zinc treatment of the digestive gland of the slug *Arion ater* L. 2. Sublethal effects at the histological level. Bulletin of Environmental Contamination and Toxicology 41:865-871.

Redpath, K. J., and J. Davenport. 1988. The effect of copper, zinc and cadmium on the pumping rate of *Mytilus edulis* L. Aquatic Toxicology 13:217-226.

Reece, P,. L, D. B. Dickson, and P. J. Bunowes. 1986. Zinc toxicity (new wire disease) in aviary birds. Australian Veterinary Journal 63:199.

Reeves, P. G. 1990. Zinc deficiency and dipeptidyl carboxypeptidase activity. Comparative effects on epididymis and testis of rats. Biological Trace Element Research 24:1-11.

Reeves, P. G., and B. L. O'Dell. 1988. Effect of zinc deficiency on blood pressure in rats fed normal and high levels of dietary calcium. Nutrition Research 8:1143-1150.

Reif, J. S., E. Ameghino, and M. J. Aaronson. 1989. Chronic exposure of sheep to a zinc smelter in Pont. Environmental Research 49:40-49.

Richards, M. P. 1989a. Influence of egg production on zinc, copper and iron metabolism in the turkey hen (*Meleagris gallopavo*). Comparative Biochemistry and Physiology 93A:811-817.

Richards, M. P. 1989b. Recent developments in trace element metabolism and function: role of metallothionein in copper and zinc metabolism. Journal of Nutrition 119: 1062-1070.

Ridout, R S., P. S. Rainbow, H. S. J. Roe, and H. R. Jones. 1989. Concentrations of V, Cr, Mn, Fe, Ni, Co, Cu, Zn, As and Cd in mesopelagic crustaceans from the north east Atlantic Ocean. Marine Biology 100:465-471.

Rivera, O. E., N. Belmonte, and J. Herkovits. 1990. Zinc protection against cadmium effect on estrual cycle of Wistar rat. Biological Trace Element Research 25:35-38.

Robinette, C. L. 1990. Zinc. Veterinary Clinics of North America Small Animal Practice 20:539-544.

Roesijadi, G., and G. W. Fellingham. 1987. Influence of Cu, Cd, and Zn preexposure on Hg toxicity in the mussel *Mytilus edulis*. Canadian Journal of Fisheries and Aquatic Sciences 44:680-684.

Roomi, M. W., A. H. Shah, M. Anwarullah, and M. Hussain. 1990. Studies on the control of subterranean termites by inorganic pesticides. Anzeiger Schaedlingskunde Pflanzenschutz Umweltschutz 63:50-52.

Rosser, B. W. C., and J. C. George. 1986. Molt-induced muscle atrophy decreases the zinc content of the pectoralis of the giant Canada goose (*Branta canadensis maxima*). Experientia 42:549-550.

Saito, S., L. Zeitz, I. M. Bush, R. Lee, and W. E Whirmore, Jr. 1967. Zinc content of spermatozoa from various levels of canine and rat reproductive tracts. American Journal of Physiology 213:749-752.

Samman, S., and D.C. K. Roberts. 1988. Zinc and cholesterol metabolism. Nutrition Research 8:559-570.

Sato, M., and Y. Nagai. 1989. Effect of zinc deficiency on the accumulation of metallothionein and cadmium in the rat liver and kidney. Archives of Environmental Contamination and Toxicology 18:587-593.

Sauer, G. R., and N. Watabe. 1989a. Temporal and metal-specific patterns in the accumulation of heavy metals by the scales of *Fundulus heteroclitus*. Aquatic Toxicology 14:233-248.

Sauer, G. R., and N. Watabe. 1989b. Ultrastructural and histochemical aspects of zinc accumulation by fish scales. Tissue & Cell 21:935-943.

Sawicka-Kapusta, K., A. Gorecki, and R. Lange. 1987. Heavy metals in rodents from polluted forests in southern Poland. Ekologia Polska 35:345-354.

Saxena, D. K., R. C. Murthy, C. Singh, and S. V. Chandra. 1989a. Zinc protects testicular injury induced by concurrent exposure to cadmium and lead in rats. Research Communications in Chemical Pathology and Pharmacology 64:317-329.

Saxena, R., R. S. Bedwal, and R.S. Mathur. 1989b. Zinc toxicity and male reproduction in rats: a histological and biochemical study. Trace Elements in Medicine 6:119-133.

Sayer, M. D. J., J. P. Reader, and R. Morris. 1989. The effect of calcium concentration on the toxicity of copper, lead and zinc to yolk-sac fry of brown trout, *Salmo trutta* L., in soft, acid water. Journal of Fish Biology 35:323-332.

Scelsi, R., D. M. Franciotta, C. Camana, E Savoldi, and M. Allegrini. 1989. Suppression of experimental allergic encephalomyelitis after dietary zinc deprivation in guinea pigs. Nutrition Research 9:1345-1354.

Schlosberg, A. 1976. Suspected poisoning of sheep associated with high tissue zinc levels. Refuah Veterinarith 33:77-78.

Schmitt, C. J., and W. G. Brumbaugh. 1990. National Biocontaminant Monitoring Program: concentrations of arsenic, cadmium, copper, lead, mercury, selenium, and zinc in U.S. freshwater fish, 1976-1984. Archives of Environmental Contamination and Toxicology 19:731-747.

Schmitt, C. J., E J. Dwyer, and S. E. Finger. 1984. Bioavailability of Pb and Zn from mine tailings as indicated by erythrocyte aminolevulinic acid dehydratase (ALA-D) activity in suckers (Pisces: Catostomidae). Canadian Journal of Fisheries and Aquatic Sciences 41:1030-1040.

Schmitt, C. J., and S. E. Finger. 1987. The effects of sample preparation on measured concentrations of eight elements in edible tissues of fish from streams contaminated by lead mining. Archives of Environmental Contamination and Toxicology 16:185-207.

Schofield, R., and H. Lefevre. 1989. High concentrations of zinc in the fangs and manganese in the teeth of spiders. Journal of Experimental Biology 144:577-581.

Shiller, A. M., and E. Boyle. 1985. Dissolved zinc in rivers. Nature 317:49-52.

Shrestha, K. P., and E. Morales. 1987. Seasonal variations of iron, copper and zinc in *Penaeus brasiliensis* from two areas of the Caribbean Sea. Science of the Total Environment 65: 175-180.

Shukla, J. P., and K. Pandey. 1986a. Effect of a sublethal concentration of zinc sulphate on the growth rate of fingerlings of *Channa punctata* (Bloch), a freshwater murrel. Acta Hydrochimica et Hydrobiologia 14:677-680.

Shukla, J. P., and K. Pandey. 1986b. Zinc induced changes in the nucleic acids and protein metabolism in the fingerlings of a freshwater murrel, *Channa punctatus*. Acta Hydrochimica et Hydrobiologia 14:195-197.

Sileo, L., and W. N. Beyer. 1985. Heavy metals in white-tailed deer living near a zinc smelter in Pennsylvania, Journal of Wildlife Diseases 21:289-296.

Skidmore, J. E 1964. Toxicity of zinc compounds to aquatic animals, with special reference to fish. Quarterly Review of Biology 39:227-248.

Smeets, W. J. A. J., J. Perez-Clausell, and F. A. Geneser. 1989. The distribution of zinc in the forebrain and midbrain of the lizard *Gekko gecko*. Anatomy and Embryology 180:45-56.

Solbe, J. F. D. L. G., and V. A. Flook. 1975. Studies on the toxicity of zinc sulphate and of cadmium sulphate to stone loach *Noemacheilus barbatulus* (L) in hard water. Journal of Fish Biology 7:631-637.

Somasundaram, B. 1985. Effects of zinc on epidermal ultrastructure in the larva of *Clupea harengus*. Marine Biology 85:199-207.

Somasundaram, B., P. E. King, and S. E. Shackley. 1985. The effect of zinc on the ultrastructure of the posterior gut and pronephric ducts of the larva of *Clupea harengus* L. Comparative Biochemistry and Physiology 81C:29-37.

Sorensen, E. M. B. 1991. Zinc. Pages 119-174 *in* Metal poisoning in fish. CRC Press, Boca Raton, Fla.

Spear, P. A. 1981. Zinc in the aquatic environment: chemistry, distribution, and toxicology. National Research Council of Canada Publication NRCC 17589. 145 pp.

Spierenburg, T. J., G. J. De Graaf, and A. J. Baars. 1988: Cadmium, zinc, lead, and copper in livers and kidneys of cattle in the neighbourhood of zinc refineries. Environmental Monitoring and Assessment 11:107-114.

Sprague, J. B. 1986. Toxicity and tissue concentrations of lead, zinc, and cadmium for marine mollusks and crustaceans. International Lead Zinc Research Organization, Research Triangle Park, N.C. 215 pp.

Spry, D. J., P. V. Hodson, and C. M. Wood. 1988. Relative contributions of dietary and waterborne zinc in the rainbow trout, *Salmo gairdneri*. Canadian Journal of Fisheries and Aquatic Sciences 45:32-41.

Sreekumar, K. R, and G. Nirmalan. 1989. Mineral status in the blood of Indian elephants. Indian Journal of Animal Sciences 59:1253-1258.

Stahl, J. L, M. E. Cook, and J. L. Greger. 1988. Zinc, iron, and copper contents of eggs from hens fed varying levels of zinc. Journal of Food Composition and Analysis 1:309-315.

Stahl, J. L., M. E. Cook, M. L. Sunde, and J. L. Greger. 1989a. Enhanced humoral immunity in progeny chicks fed practical diets supplemented with zinc. Applied Agricultural Research 4:86-89.

Stahl, J. L., J. L. Greger, and M. E. Cook. 1989b. Zinc, copper and iron utilization by chicks fed various concentrations of zinc. British Poultry Science 30:123-134.

Stahl, J. L., J. L. Greger, and M. E. Cook. 1990. Breeding-hen and progeny performance when hens are fed excessive dietary zinc. Poultry Science 69:259-263.

Starcher, B.C., J. G. Glauber, and J. G. Madaras. 1980. Zinc absorption and its relationship to intestinal metallothionein. Journal of Nutrition 110:1391-1397.

Sternlieb, I. 1988. Copper and zinc. Pages 525-533 *in* I. M. Arias, W. B. Jakoby, H. Popper, D. Schachter, and D. A, Shafritz, editors. The liver: biology and pathobiology. Second edition, Raven Press, New York.

Straube, E. F., N. H. Schuster, and A. J. Sinclair. 1980. Zinc toxicity in the ferret. Journal of Comparative Pathology 90:355-361.

Sullivan, R A., W. E. Robinson, and M. R Morse. 1988. Isolation and characterization of granules from the kidney of the bivalve *Mercenaria mercenaria*. Marine Biology 99:359-368.

Sunda, W. G., P. A. Tester, and S. A. Huntsman 1987. Effects of cupric and zinc ion activities on the survival and reproduction of marine copepods. Marine Biology 94:203-210.

Supplee, W. C. 1963. Antagonistic relationship between dietary cadmium and zinc. Science 139:119-120.

Taban, C. H., M. Cathieni, and R Burkard. 1982. Changes in newt brain caused by zinc water-pollution. Experientia 38:683-685.

Taneja, S. K., P. Arya, and U. Bains. 1988. Effects of $ZnSO_4$ toxicity on the skeletal muscles of the mosquitofish, *Gambusia affinis*. Research Bulletin of the Panjab University Science 39:207-211.

Tanizaki, M. M., R. B. Zimgali, H. Kawazaki, S. Imajoh, S. Yamazaki, and K. Suzuki. 1989. Purification and some characteristics of a zinc metalloprotease from the venom of *Bothrops jararaca* (jararaca). Toxicon 27:747-755.

Thomas, P. G., and D. A. Ritz. 1986. Growth of zinc granules in the barnacle *Elminius modestus*. Marine Biology 90:255-260.

Thompson, D. R. 1990. Metal levels in marine vertebrates. Pages 143-182 *in* R. W. Furness and P. S. Rainbow, editors. Heavy metals in the marine environment, CRC Press, Boca Raton, Fla.

Thompson, E. D., J. A. McDermott, T. B. Zerkle, J. A. Skare, B. L. B. Evans, and D. B. Cody. 1989. Genotoxicity of zinc in 4 short-term mutagenicity says. Mutation Research 223:267-272.

Tom, K., M. Chen, W. Goettlich-Riemann, J. Tanimoto, S. Grey, D. Wake, and R. E. Rucker. 1977. Collagen and elastin metabolism in relation to dietary zinc and copper in the chick and rat. Nutrition Reports International 15:191-198.

Tone, K., T. Suzuki, and T. Todoroki. 1988. Influence of zinc deficiency on the phagocytosis in mice. Asia-Pacific Symposium on Environmental and Occupational Toxicology, 4-7 October 1987, Singapore: Proceedings 8:301-305.

U.S. Environmental Protection Agency (EPA). 1980. Ambient water quality criteria for zinc. U.S. Environmental Protection Agency Report 440/5-80-079. 158 pp.

U.S. Environmental Protection Agency (EPA). 1987. Ambient water quality criteria for zinc--1987. U.S. Environmental Protection Agency Report 440/5-87-003. 207 pp.

U.S. Public Health Service (PHS). 1989. Toxicological profile for zinc. U.S. Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, Ga. 121 pp.

Uriu-Hare, J. Y., J. S. Stern, and C. L. Keen. 1989. Influence of maternal dietary Zn intake on expression of diabetes-induced teratogenicity in rats. Diabetes 38:1282-1290.

Vahala, J., J. Pospisil, P. Spala, and F. Kase. 1989. Biochemical blood serum values of healthy antelopes kept in the East-Bohemian zoological garden at Dvur Kvalove Nad Labem--I. The Tragelaphinae, the Hippotraginae and the Aepycerotinae. Acta Veterinaria BRNO 58:17-29.

Vallee, B. L. 1959. Biochemistry, physiology and pathology of zinc. Physiological Reviews 39:443-490.

Van Duyn-Henderson, J., and D.C. Lasenby. 1986. Zinc and cadmium transport by the vertically migrating opossum shrimp, *Mysis relicta*. Canadian Journal of Fisheries and Aquatic Sciences 43:1726-1732.

Van Hook, R. I., D. W. Johnson, and B. R Spalding. 1980. Zinc distribution and cycling in forest ecosystems. Pages 419-437 *in* J. O. Nriagu, editor. Zinc in the environment, Part I: ecological cycling. John Wiley, New York.

Vas, P., J. D. Stevens, G. A. Bonwick, and O. A. Tizini. 1990. Cd, Mn, and Zn concentrations in vertebrae of blue shark and shortfin mako in Australian coastal waters. Marine Pollution Bulletin 21:203-206.

Veleminsky, M., P. Laznicka, and P. Stary. 1990. Honeybees (*Apis mellifera*) as environmental monitors in Czechoslovakia. Acta Entomologica Bohemoslovaca 87:37-44.

Vergnes, H. A., M. K. Courdouhji, J. F. Guelfi, J. S. Grozeda, and M. Lamand. 1990. Effect of zinc deficiency in lambs on plasma and neutrophil alkaline phosphatase. Small Ruminant Research 3:167-177.

Verheyen, G., J. Helsen, and E. Decuypere. 1990. Accumulation of zinc in egg yolk ovarian follicles and organs after forced resting by high dietary zinc. British Poultry Science 31:147-154.

Verma, P. C., R. P. Gupta, J. R. Sadand, and R. K. P. Gupta. 1988. Effect of experimental zinc deficiency and repletion on some immunological variables in guinea pigs. British Journal of Nutrition 59:149-154.

Verriopoulos, G., and S. Dimas. 1988. Combined toxicity of copper, cadmium, zinc, lead, nickel, and chrome to the copepod *Tisbe holothuriae*. Bulletin of Environmental Contamination and Toxicology 41:378-384.

Verriopoulos, G., and D. Hardouvelis. 1988. Effects of sublethal concentrations of zinc on survival and fertility in four successive generations of *Tisbe*. Marine Pollution Bulletin 19: 162-166.

Verriopoulos, G., and M. Moraitou-Apostolopoulou. 1989. Toxicity of zinc to the marine copepod *Tisbe holothuriae*; the importance of the food factor. Archiv für Hydrobiologie 114:457-463.

Villegas-Navarro, A., and C. M. Villarreal-Trevino. 1989. Differential uptake of zinc, copper, and lead in Texas cichlid (*Cichlasoma cyanoguttatum*). Bulletin of Environmental Contamination and Toxicology 42:761-768.

Voogt, P A., P. J. D. Besten, G. C. M. Kusters, and M. W. J. Messing. 1987. Effects of cadmium and zinc on steroid metabolism and steroid level in the sea star *Asterias rubens* L. Comparative Biochemistry and Physiology 86C:83-89.

Vymazal, J. 1986. Occurrence and chemistry of zinc in freshwaters--its toxicity and bioaccumulation with respect to algae: a review. Part 2: toxicity and bioaccumulation with respect to algae. Acta Hydrochimica et Hydrobiologia 14:83-102.

Waalkes, M. P., S. Rehm, C. W. Riggs, R. M. Bare, D. E. Devor, L. A. Poirier, M. L. Wenk, and J. R. Henneman. 1989. Cadmium carcinogenesis in male wistar [Crl:(WI)BR] rats: dose-response analysis of effects of zinc on tumor induction in the prostate, in the testes, and at the injection site. Cancer Research 42:4282-4288.

Wagemann, R. 1989. Comparison of heavy metals in two groups of ringed seals (*Phoca hispida*) from the Canadian Arctic. Canadian Journal of Fisheries and Aquatic Sciences 46:1558-1563.

Waiwood, B. A., V. Zitko, K. Haya, L. E. Burridge, and D. W. McLeese. 1987. Uptake and excretion of zinc by several tissues of the lobster (*Homarus americanus*). Environmental Toxicology and Chemistry 6:27-32.

Walker, G., R S. Rainbow, R Foster, and D. J. Crisp. 1975. Barnacles: possible indicators of zinc pollution? Marine Biology 30:57-65.

Ward, T. J., R. L Correll, and R. B. Anderson. 1986. Distribution of cadmium, lead and zinc amongst the marine sediments, sea grasses and fauna, and the selection of sentinel accumulators, near a lead smelter in South Australia. Australian Journal of Marine and Freshwater Research 37:567-585.

Warner, R. D., C. R. Dorn, J. R. Blakeslee, D. E Gerken, J. C. Gordon, and E. J. Angrick. 1988. Zinc effects on nickel dermatitis in the guinea pig. Contact Dermatitis 19:98-108.

Warren, R. J., B. M. Wallace, and P. B. Bush. 1990. Trace elements in migrating blue-winged teal: seasonal-, sex-, and age-class variations. Environmental Toxicology and Chemistry 9:521-528.

Watkins, B., and K. Simkiss. 1988. The effect of oscillating temperatures on the metal ion metabolism of *Mytilus edulis*. Journal of the Marine Biological Association of the United Kingdom 68:93-100.

Weatherley, A. H., P. S. Lake, and S.C. Rogers. 1980. Zinc pollution and the ecology of the freshwater environment. Pages 337-417 *in* J. O. Nriagu, editor. Zinc in the environment. Part I: ecological cycling. John Wiley, New York.

Webb, J., D. J. Macey, and V. Talbot. 1985. Identification of ferritin as a major high molecular weight zinc-binding protein in the tropical rock oyster, *Saccostrea cucullata*. Archives of Environmental Contamination and Toxicology 14:403-407.

Weeks, J. M., and P. G. Moore. 1991. The effect of synchronous moulting on body copper and zinc concentrations in four species of talitrid amphipods (Crustacea). Journal of the Marine Biological Association of the United Kingdom 71:481-488.

Weis, J. S. 1980. Effect of zinc on regeneration in the fiddler crab *Uca pugilator* and its interactions with methylmercury and cadmium. Marine Environmental Research 3:249-255.

Wentink, G. H., T. J. Spierenburg, G. J. de Graaf, and A. C. A. van Exsel. 1985. A case of chronic zinc poisorting in calves fed with zinc-contaminated roughage. Veterinary Quarterly 7:153-157.

Westmoreland, N., and W. G. Hoekstra. 1969. Pathological defects in the epiphyseal cartilage of zinc-deficient chicks. Journal of Nutrition 98:76-82.

Weyers, B., E. Gluck, and M. Stoeppler. 1968. Investigation of the significance of heavy metal contents of blackbird feathers. Science of the Total Environment 77:61-67.

White, S. L., and P. S. Rainbow. 1985. On the metabolic requirements for copper and zinc in molluscs and crustaceans. Marine Environmental Research 16:215-229.

Whitton, B. A. 1980. Zinc and plants in rivers and streams. Pages 363-400 *in* J. O. Nriagu, editor. Zinc in the environment. Part II: health effects. John Wiley, New York.

Wicklund, A., P. Runn, and L. Norrgren. 1988. Cadmium and zinc interactions in fish: effects of zinc on the uptake, organ distribution, and elimination of ^{109}Cd in the zebrafish, *Brachydanio rerio*. Archives of Environmental Contamination and Toxicology 17:345-354.

Wiemeyer, S. N., R. M. Jurek, and J. E Moore. 1986. Environmental contaminants in surrogates, foods, and feathers of California condors (*Gymnogyps californianus*). Environmental Monitoring and Assessment 6:91-111.

Wiemeyer, S. N., A. J. Krynitsky, and S. R. Wilbur. 1983. Environmental contaminants in tissues, foods, and feces of California condors. Pages 427-439 *in* S. R. Wilbur and J. A. Jackson, editors. Vulture biology and management. University of California Press, Berkeley.

Wiemeyer, S. N., T. G. Lamont, and L. N. Locke. 1980. Residues of environmental pollutants and necropsy data for eastern United States ospreys, 1964-1973. Estuaries 3:155-167.

Wiemeyer, S. N., S. K. Schmeling, and A. Anderson. 1987. Environmental pollutant and necropsy data for ospreys from the eastern United States, 1975-1982. Journal of Wildlife Diseases 23:279-291.

Wiemeyer, S. N., J. M. Scott, M. P. Anderson, P. H. Bloom, and C. J. Stafford. 1988. Environmental contaminants in California condors. Journal of Wildlife Management 52:238-247.

Williams, S. N., R. D. Miles, M. D. Ouart, and D. R. Campbell. 1989. Short-term high level zinc feeding and tissue zinc concentration in mature laying hens. Poultry Science 68:539-545.

Willis, M. 1985a. A comparative survey of the *Erpobdella octoculata* (L.) populations in the Afon Crafnant, N. Wales, above and below an input of zinc from mine-waste. Hydrobiologia 120:107-118.

Willis, M. 1985b. Analysis of the effects of zinc pollution on the macroinvertebrate populations of the Afon Crafnant, North Wales. Environmental Geochemistry and Health 7:98-109.

Willis, M. 1988. Experimental studies on the effects of zinc on *Ancylus fluviatilis* (Muller) (Mollusca; Gastropoda) from the Afon Crafnant, N. Wales. Archiv fur Hydrobiologie 112:299-316.

Willis, M. 1989. Experimental studies on the effects of zinc on *Erpobdella octoculata* (L.) (Annelida: Hirudinea) from the Afon Crafnant, N. Wales. Archiv für Hydrobiologie 116:449-469.

Wilson, R. S. 1988. A survey of the zinc-polluted River Nent (Cumbria) and the East and West Allen (Northumberland), England, using chironomid pupal exuviae. Spixiana Supplement 14:167-174.

Winner, R. W., and J. D. Gauss. 1986. Relationship between chronic toxicity and bioaccumulation of copper, cadmium and zinc as affected by water hardness and humic acid. Aquatic Toxicology 8:149-161.

Wlostowski, T., W. Chetnicki, W. Gierlachowska-Baldyga, and B. Chycak. 1988. Zinc, iron, copper, manganese, calcium and magnesium supply status of free-living bank voles. Acta Theriologica 33:555-573.

Wobeser, G. A. 1981. Diseases of wild waterfowl. Plenum Press, New York. 163 pp.

Woodall, C., N. Maclean, and E Crossley. 1988. Responses of trout fry (*Salmo gairdneri*) and *Xenopus laevis* tadpoles to cadmium and zinc. Comparative Biochemistry and Physiology 89C:93-99.

Yamaguchi, M., H. Oishi, and Y. Suketa. 1989a. Effect of vanadium on bone metabolism in weanling rats: zinc prevents the toxic effect of vanadium. Research in Experimental Medicine 189:47-53.

Yamaguchi, M., K. Ozaka, and Y. Suketa. 1989b. Alteration in bone metabolism with increasing age: effects of zinc and vitamin D_3 in aged rats. Journal of Pharmacobio-Dynamics 12:67-73.

Yantian, L. 1989. Effect of zinc on the growth and development of larvae of bay scallop *Argopecten irradians*. Chinese Journal of Oceanology and Limnology 7:318-326.

Young, D. R., T. K. Jan, and G. P. Hershelman. 1980. Cycling of zinc in the nearshore marine environment. Pages 297-335 *in* J. O. Nriagu, editor. Zinc in the environment. Part I: ecological cycling. John Willey, New York.

Yu, H. S., and S. T.. H. Chan. 1988. Zinc amelioration of cadmium toxicity on preimplantation mouse zygotes in vitro. Teratology 37:13-19.

Zee, J. V. D., P. Swart, and A. J. H. Schotman. 1985. Zinc poisoning in a Nicobar pigeon. Journal of Zoo Animal Medicine 16:68-69.

Biological Report 20
February 1994

Contaminant Hazard Reviews
Report 27

Famphur Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

By
Ronald Eisler

U.S. Department of the Interior
National Biological Survey
Washington, D.C. 20240

TABLES

FIGURE

Suggested citation:

Eisler, R. 1994. Famphur hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. National Biological Survey Biological Report 20.

Famphur Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Department of the Interior
National Biological Survey
Washington, D.C. 20240

Abstract

Famphur (phosphorothioic acid, O-[(dimethylamino)sulfonyl], phenyl] O, O-dimethyl ester), also known as Warbex, is a systemic organophosphorus insecticide used almost exclusively as a veterinary chemical to control parasites in livestock. Only famphur and its oxygen analog, famoxon, were of toxicological significance; other famphur metabolites were 31 to 237 times less toxic, as judged by acute oral-toxicity tests in the mouse (*Mus* sp.). Famphur is administered to livestock by intramuscular or subcutaneous injection, through the diet, as a dermal pour-on, or as an oral bolus. In mammals, famphur induced mortality at concentrations as low as 11.6 mg/kg body weight (BW) in intraperitoneal injection (mouse), 27 mg/ kg BW in a single oral exposure (mouse), greater than 33.3 mg/kg BW in an intramuscular injection (Brahman cattle, Bos *indicus*), and 400 mg/ kg BW in a dermal application (rat, *Rattus* sp.). Latent effects of famphur exposure were reported in reindeer (*Rangifer tarandus*) hinds one year posttreatment (altered blood chemistry). Famphur is rapidly metabolized by mammals, the half-time persistence of famphur and famoxon in subcutaneous fat of cattle after a single pour-on application is 0.9 days. Famphur has been used illegally by U.S. farmers to kill feral birds--including migratory waterfowl--thought to be depredating crops. Pour-on applications of famphur to cattle at recommended doses are sometimes associated with bird die-offs, especially the black-billed magpie (*Pica pica*). Magpie mortality was probably associated with the lengthy persistence (>90 days) of famphur on cattle hair and the ingestion of cattle hair by magpies. Cattle hair composed as much as 12% of gizzard contents of dead magpies, and hair in the gizzards of dead magpies averaged 4,600 mg famphur and famoxon / kg. Secondary poisoning of eagles and hawks foraging on famphur-killed vertebrates and tertiary poisoning of a great horned owl (*Bubo virginianus*) feeding on a famphur-poisoned hawk are documented. In the laboratory, sensitive species of birds died after single oral doses of 1.8-3.0 mg famphur/kg BW or when fed diets containing 35-49 mg famphur/kg ration. Depressed cholinesterase activity in the brain and in plasma occurred in nestlings at daily oral concentrations as low as 0.3 mg famphur/kg BW. No published data were available on the fate or effects of famphur in aquatic ecosystems. In the absence of aquatic toxicity data on famphur, it is recommended that famphur and famoxon concentrations do not exceed the analytical detection limits of these compounds in water (0.005 mg/ L) or in tissues of aquatic organisms (<0.01 mg/kg fresh weight). Current recommendations include the discontinuance of topical applications of famphur to cattle because of its association with primary and secondary poisoning of birds, and more research on famphur in the three areas of latent effects on treated livestock, fate and effects in aquatic ecosystems, and carcinogenicity evaluation.

Key words: Famphur, Warbex, organophosphorus insecticide, livestock, fish, wildlife, invertebrates, ecotoxicology.

Famphur (phosphorothioic acid, O,-[4-[(dimethylamino)sulfonyl], phenyl] O, O-dimethyl ester), also known as Warbex, is a systemic organophosphorus insecticide found effective against lice, grubs, flies, and gastrointestinal nematodes of ruminants. Introduced commercially in 1961, the compound is especially effective against cattle grubs (*Hypoderma* spp.) when fed in the diet, injected subcutaneously or intramuscularly, or applied as a pour-on and oral drench treatment (Gatterdam et al. 1967; Kaemmerer and Buntenkotter 1973; Black et al. 1979; Felton et al. 1981; Gallo and Lawryk 1991).

Many dead birds, including robins, hawks, and magpies were found after cattle were treated with pour-on applications of famphur (Henny et al. 1985; Smith 1987). The black-billed magpie (*Pica pica*) was especially sensitive; ranchers reported observations of magpies dying after famphur use on cattle as early as 1973 (Henny et al. 1985). Dead magpies usually had famphur in the gizzard contents and severely depressed brain cholinesterase activity--a characteristic of organophosphorus poisoning. Populations of the black-billed magpie in western states declined between 1968 and 1979, which coincides with widespread use of famphur in that region; however, factors other than famphur may have caused the decline (Henny et al. 1985).

This report was prepared in response to requests for information on famphur from environmental contaminant specialists of the U.S. Fish and Wildlife Service. It is part of a continuing series of brief reviews of chemicals in the environment with emphasis on fishery and wildlife resources.

Uses

The cholinesterase-inhibiting and intoxicating properties of organophosphorus compounds have been known since these products were first synthesized about 60 years ago (Randell and Bradley 1980). During World War II, the more toxic organophosphorus compounds--such as soman, tabun, and sarin--were stockpiled for use as potential chemical warfare agents. More than 50,000 organophosphorus compounds have been synthesized and screened for possible insecticidal and antihelminthic activity and several dozen, including famphur, are now available commercially (Randell and Bradley 1980). During the 1970's, most organochlorine insecticides were removed from common use in North America, Europe, and most developed countries, and the removal increased reliance on carbamate and organophosphorus compounds, the two major classes of cholinesterase-inhibiting pesticides (Mineau 1991). The relative lack of target specificity of these compounds and their high acute toxicity to many nontarget organisms were ignored in favor of their short-term environmental persistence and lack of accumulation in organisms. The anticholinesterase insecticides now account for the majority of globally registered insecticides (Mineau 1991).

Famphur is not now applied to forests or crops but is used almost exclusively as a veterinary chemical (Smith 1987). A single treatment controls cattle grubs and reduces cattle lice infestations (American Cyanamid Company 1984). Famphur is especially effective against maggots of the botfly and warble fly (*Hypoderma* spp.) and of other oestrid flies (Seel 1985). Eggs from this group of insects are laid on the feet and legs of cattle and other mammals and licked off by the host and hatch in the mouth or esophagus. The resultant larvae burrow through the tissues to the skin of the animal's back where they live until ready to pupate and cause warbles or swellings (Seel 1985; Tarry 1986). When applied carelessly, famphur and other systemic insecticides are highly toxic and frequently produce acute poisonings in ruminants (Ballantyne and Marrs 1992). Famphur is not now registered or regulated by the U.S. Environmental Protection Agency.

Cholinesterase-inhibiting agents such as famphur vary widely in their effectiveness of controlling target pests and depend on the route of administration, dose rate, formulation, and timing and frequency of applications (Mineau 1991). Famphur can be administered to livestock by intramuscular injection, orally in the diet, as a dermal pour-on, or as a bolus. Intramuscular injections of 35% famphur concentrate are usually given in the gluteal muscle (Loomis and Schock 1978). When fed in the diet, famphur is formulated as a 33.3% liquid feed premix (Pasarela et al. 1967; Smith 1987). The topical use of famphur as a systemic insecticide was recommended in 1970. At dosages between 15 and 35 mg/kg body weight (BW), 12.5-13.2% w/v famphur as a pour-on over part of the backline of cattle in fall controls warbles before they develop into grubs the following year (Henny et al. 1985) and controls various species of lice (Annand et al. 1976). When used as a pour-on for cattle-tick control, famphur may be transferred from treated cattle to untreated animals (Annand et al. 1976), presumably through body contact. The solvent used in preparing dermal formulations of famphur significantly affects absorption hazards. In the case of the laboratory white rat (*Rattus* sp.), corn oil proved to be the least hazardous solvent and acetone the most hazardous; benzene was intermediate (Durham 1967). Famphur can also be administered in a rumen bolus as a systemic insecticide against ticks in cattle. Boluses have been

designed to release 200 mg famphur/bolus daily over a 65-75 day post-ingestion period; actual release rates range from 207 to 308 mg daily (Hair et al. 1979).

Technical information by the American Cyanamid Company (1984) lists five precautions and warnings for the use of famphur: 1. Famphur is "Toxic to fish, birds, and other wildlife. Keep out of lakes, ponds, and streams. Do not apply to areas where run-off occurs. Do not contaminate water by cleaning of equipment or disposal of wastes." 2. After use, all containers should be drained and rinsed several times with a solution of water, detergent, and lye ("bury rinse solution deeply in an isolated location with 18 inches [7 cm] of cover"); the empty container should be punctured and crushed to prevent reuse. 3. Famphur should not be used in combination with any compound having cholinesterase-inhibiting activity either simultaneously or within a few days before or after treatment. 4. Famphur use on livestock is contraindicated for less than 3-months old calves; animals stressed from castration, dehorning, or overexcitement; and sick or convalescent animals. Brahman and Brahman crossbreeds are less tolerant of cholinesterase-inhibiting insecticides than other breeds, and Brahman bulls are especially sensitive and should not be treated with famphur. Cattle should not be slaughtered for at least 35 days after treatment with famphur. 5. For humans, famphur is considered harmful or fatal if swallowed or absorbed through the skin, especially by children. If poisoning should occur, physicians are advised that atropine is antidotal and that pralidoxime chloride may be effective as an adjunct to atropine. Pour-on formulations are flammable, and users should keep them away from heat, sparks, and open flames including hot branding irons and cautery dehorning devices (American Cyanamid Company 1984).

Chemistry and Metabolism

Some physical and chemical properties of famphur are listed in Table 1. Gas chromatography is used to measure famphur and its oxygen analog famoxon in bovine milk, blood, and edible tissues; detection limits are 0.005 mg/L milk and <0.01 mg/kg tissue (Pasarela et al. 1967; Annand et al. 1976). The main degradation routes of famphur in mammals occur through hydrolysis of the P-O phenyl, P-O methyl, and N-methyl bonds; oxidative desulfuration and N-demethylation take place to a small extent (Figure; Kaemmerer and Buntenkotter 1973; Eto 1974). In the metabolic scheme for famphur in mammals (Figure), only famphur and its oxygen analog, famoxon, were of toxicological significance, as judged by acute oral toxicity in mice (Gatterdam et al. 1967). In studies with mice, acute oral LD50 values in mg/kg BW were 27 for famphur; 18 for famoxon; 2,270 for O-desmethylfamphur; 860 for O, N-bisdesmethylfamphur; 2,290 for p-(N, N-dimethylsulfamoyl)phenol; 2,500 for p-(N-methylsulfamoyl)phenol; 6,400 for p-hydroxybenzenesulfonic acid; and greater than 5,000 for p(N,N-dimethylsulfamoyl)phenyl glucuronide.

Famphur residues of 1 to 3 mg/kg fresh weight (FW) are common in cattle tissues after normal pour-on applications of the chemical (Annand et al. 1976). The half-time persistence of famphur in subcutaneous fat of cattle after a single pour-on application was 0.9 days and was independent of dose within the range of 25 to 150 mg/kg BW or initial tissue residues between 1.8 and 12.3 mg/kg FW; fat residues were less than 0.08 mg/kg FW 5 days after treatment and less than 0.01 mg/ kg FW after 11 days. These observations suggest that famphur tissue residues are near or below detection levels within 1 week after treatment, even with gross misuse of the chemical (Annand et al. 1976). However, famphur at concentrations greater than 1,000 mg/ kg persists on cattle hair for greater than 90 days, and this persistence has serious implications for local bird populations (Henny et al. 1985).

Famphur and other organophosphorus compounds are metabolized and excreted with greater efficiency by mammals than by the target pests before these compounds can bind to and ultimately inhibit the cholinesterase enzyme (Randell and Bradley 1980). Mice, for example, degrade famphur rapidly. Less than 1 h after an intraperitoneal injection of 1 mg famphur / kg BW, only 8.34% of the original administered dose remained in the mouse: 8.11% as the parent famphur, 0.22% as famoxon, and 0.01% as desmethylfamphur (Kaemmerer and Buntenkotter 1973). Famphur's biocidal properties are associated with its ability to inhibit cholinesterase activity, blocking synapses at the neuromuscular junction. Useful and recent reviews of ecological and toxicological properties of cholinesterase inhibiting agents in the environment--including organophosphorus insecticides--are given by Gallo and Lawryk (199 1), Mineau (1991), and Ballantyne and Marrs (1992). Brain cholinesterase inhibition is often used to diagnose death of wildlife after exposure to famphur and other organophosphorus insecticides (Mineau 1991). It is emphasized that the type and number of cholinesterase compounds and cholinesterase activities vary widely between species and tissues, and activities are further modified by

metabolic factors, age, genotype, circadian rhythms, sex, reproductive status, nutritional status, ambient temperature, and disease (Mineau 1991).

Table 1. Chemical and other properties of famphur.[a]

Variable	Datum
Chemical names	Phosphorothioic acid 0-[4- [(dimethylamino) sulfonyl], phenyl] O, O-dimethyl ester; Phosphorothioic acid, O, O-dimethyl-, O-ester with p hydroxy-N, N-dimethylbenzene sulfonamide; Phosphorothioic acid, O, O-dimethyl O-p-(dimethylsulfamoyl) phenyl ester; 0 0-Dimethyl hydrogen phosphorothioate, O-ester with p-hydroxy-N, N-dimethylbenzenesulfonamide; 0-[4-1 (Dimethylamino) sulfonyl] phenyl phosphorothioic acid O, O-dimethyl ester; O, O-Dimethyl O, p-(N, N-dimethylsulfamoyl) phenyl phosphorothioate; O, p-(Dimethylsulfamoyl) phenyl O, O-dimethyl phosphorothioate; p-(Dimethylsulfamoyl)phenyl dimethyl phosphorothioate; O, O-dimethyl O-[p-(dimethylsulfamoyl)-phenyl] phosphorothioate; Dimethyl p-(dimethylsulfamoyl) phenyl phosphorothionate; O, O-dimethyl-O, p-(dimethylsulfamoyl) phenyl phosphorothionate
Alternate names	AC 38023, American Cyanamid 38023, Bo-Ana, CL 38023, Cyflee, Dovip, ENT 25644, Famaphos, Famfos, Famophos, Famphos, Fanfos, Warbex, 38023
Primary use	Systemic livestock insecticide
CAS number	52-85-7
Empirical formula	$C_{10}H_{16}NO_5PS_2$
Molelcular weight	325.36
Melting point, crystals vs. powder	52.5-53.5° C vs. 55° C
Solubility	
Chlorinated hydrocarbons	Highly soluble
Water	-100 mg/L
Polar solvents	Slightly soluble
Aliphatic hydrocarbons	Insoluble

[a] O'Brien et al. 1965; Gatterdam et al. 1967; Pasarela et al. 1967; Tucker and Crabtree 1970; Schafer 1972; Kaemmerer and Buntenkotter 1973; Eto 1974; Black et al. 1979; Ryan and McLeod 1979; Hudson et al. 1984; Hill and Camardese 1986; Smith 1987; Gallo and Lawryk 1991.

Lethal and Sublethal Effects

General

Famphur controls many species of pestiferous insects that afflict poultry and livestock. The LD50 values for target insects ranged from 2.4-4.1 mg/kg BW from a dermal route and 8.0-11.8 mg/kg BW from abdominal injection. Toxicity of famphur is often associated with differential degradation and cholinesterase sensitivity among various species of target pests. Famoxon is more effective than famphur in producing cholinesterase inhibition and death, and this confirms the generalization that the corresponding oxons are the more potent anticholinesterase agents.

No published data were available on famphur toxicity to aquatic life. Other data, however, suggest that acute famphur toxicity to fishes may be comparable to that of other phosphorothioate insecticides. Among birds, sensitive species had reduced survival after single oral doses of 1.8 to 3.0 mg famphur/kg BW or when fed diets containing 35-49 mg famphur/kg ration. Daily oral doses as low as 0.3 mg famphur/kg BW caused depressed cholinesterase activity in the brain and in plasma. Secondary poisoning of eagles and hawks foraging on famphur-killed vertebrates and tertiary poisoning of a great horned owl (*Bubo virginianus*) feeding on a famphur-poisoned hawk are documented. Famphur has also been used illegally to kill feral birds--including migratory waterfowl and other federally protected species--thought to be depredating crops. Famphur-induced mortality in mammals was documented at concentrations as low as 11.6 mg/ kg BW in intraperitoneal injection (mouse), 27 mg/kg BW in oral exposure (mouse), >33.3 mg/kg BW in intramuscular injection (Brahman cattle), and 400 mg/kg BW in dermal application (rat). In reindeer, altered blood chemistry was evident one year after famphur exposure. Famphur is metabolized rapidly by mammals; residues in animal tissues and milk--regardless of mode of administration, length of exposure, or dose--were usually not detectable within 4 days of final exposure.

Terrestrial Invertebrates

Famphur controls many species of pestiferous insects that afflict poultry and livestock, especially warble flies (*Hypoderma* spp.). Famphur is one of the most toxic compounds for the control of adults and late instars of the lesser mealworm (*Alphitobius diaperinus*), the most abundant beetle inhabiting poultry litter and manure (Vaughan and Turner 1984). *Alphitobius diaperinus* can transmit several diseases to poultry, including avian leukosis--one of the most costly diseases for the poultry industry. By tunnelling, *A. diaperinus* can destroy polyurethane and polystyrene panels adjacent to manure. Famphur also controls the lesser mealworm in nests of birds and in bat roosts (Vaughan and Turner 1984). The northern fowl mites (*Ornithonyssus sylviarum*) is the most important ectoparasite of commercial breeders and laying hens in the United States. However, attempts to control northern fowl mites with famphur were ineffective regardless of tested mode of administration (De Vaney and Ivie 1980).

Cattle lice (*Haematopinus* spp.)were controlled when the equivalent of 2.5 mg famphur/kg BW in diets was fed to cattle for at least 30 days (Ivey et al. 1976) or 40.5 mg/kg BW were applied as a topical pour-on (Randell and Bradley 1980). Famphur was used in 1971 to control cattle lice with pour-on applications equivalent to 15-35 mg/kg BW (Annand et al. 1976). Pour-on treatments of Australian yearling heifers were especially effective in controlling the long-nosed sucking louse (*Linognathus vituli*) and the short-nosed sucking louse (*Haematopinus eurysternus*); untreated heifers grew more slowly than famphur-treated heifers (Bailey et al. 1984). Larvae of the hornfly (*Haematobia irritans*) were controlled in manure of cattle fed famphur at 2.5-5.0 mg/kg BW daily (Ivey et al. 1976). Manure of treated cows contained low concentrations of famphur (as much as 0.14 mg/kg FW) 1 day after diet cessation, but residues were nondetectable thereafter (Henny et al. 1985).

In Alaska, reindeer (*Rangifer tarandus*) infested with reindeer warble flies (*Oedemagena tarandi*) produced hides of little value and low quality meat. Reindeer warble flies were not controlled by pour-on applications of famphur because the product was unable to penetrate the hair coat of reindeer; however, intramuscular injections were effective (Ivey et al. 1976). In Norway, Sweden, and Finland, famphur was the most promising control agent against reindeer warble flies and reindeer nostril flies (*Cephenomyis trompe*)--two parasites that together caused a 15 to 20% annual loss of total yield in reindeer husbandry (Nieminen et al. 1980).

Famphur was not very effective in the control of ticks. The tropical horse tick (*Anocentor nitens*) is a species of serious concern to horse breeders in Florida mainly because it transmits *Babesia caballi*, the causative agent of equine piroplasmosis. A secondary concern is that heavy tick infestations may cause injury to the ears of the

horse (Gladney et al. 1972). Data were unavailable on famphur control of ticks in horses; however, famphur was 99.9-100% effective in controlling *A. nitens* in Hereford steers and heifers when fed in the diet at 5 mg/kg BW for 14 to 21 days. Famphur at 2.5 mg/kg BW in cattle diets for 7 days was only partially effective (39-87.5%) in controlling horse ticks (Gladney et al. 1972). Famphur--despite multiple treatments--was not effective in controlling cattle ticks (*Haemaphysalis longicornis*) when used as a pour-on at recommended application rates in weaned Hereford calves (Heath et al. 1980).

Results of selected studies of famphur and insects indicate several trends: males are more sensitive than females; the oxygen analog, famoxon, is more toxic than the parent chemical; dermal LD50 values range from 2.4 to 4.1 mg/kg BW; abdominal injection LD50's range from 8.0 to 11.8 mg/kg BW; and metabolic degradation rates vary widely among species (Table 2). Famoxon is about 100 times more effective than famphur in controlling house flies (*Musca domestica*), which confirms the generalization that the corresponding oxons are the most effective anticholinesterase agents and are, in fact, the actual toxicants (O'Brien et al. 1965).

Differences in toxicity of organophosphorus compounds among species is often associated with differential degradation rates, pathways, and metabolites. Although injections of famphur were equally toxic to mice (*Mus* sp.), the American cockroach (*Periplaneta americana*), and the milkweed bug (*Oncopeltus fasciatus*), famphur was rapidly degraded by mice (91.7% degraded within 1 h after injection) and the cockroach (81.5% in 1 h); however, the milkweed bug degraded only 15.4% during a similar period (O'Brien et al. 1965). The variations in degradation rate among mice and cockroaches were relatively small, about 1.9 times. Despite the great similarity in famphur toxicity to mice and cockroaches, net famoxon production-like famphur persistence--was very low in the mouse but 10 times higher in the milkweed bug. The cholinesterase activity in the milkweed bug was 32 times more resistant to inhibition by famoxon than either mouse or cockroach cholinesterase, and this could account for the comparatively slow breakdown of famphur by the milkweed bug (O'Brien et al. 1965).

There is a correlation among cholinesterase-activity depression in rabbit blood, depression of cholinesterase activity in ectoparasites feeding on the blood of the host, and mortality of ectoparasites (Smith and Goulding 1970). In one case, rabbits (*Oryctolagus* sp.) parasitized by the yellow fever mosquito (*Aedes aegypti*)and Rocky mountain wood tick (*Dermacentor andersoni*) were treated with 5 to 50 mg of famphur/kg BW administered orally, subcutaneously, or intravenously. Regardless of dose or route of administration, tick and mosquito mortality was related to cholinesterase activity levels in rabbit plasma and erythrocytes. Some ectoparasite deaths were noted when cholinesterase levels in rabbits were depressed 32%; ectoparasite mortality increased to 90% at 33% depression and to 100% at 68% cholinesterase inhibition. In general, wood ticks and mosquitos reflected cholinesterase-activity levels of the host rabbit. Surviving female ticks that fed on dosed hosts laid no eggs during a 32-day post-removal observation period. Mosquitos that had fed on famphur-dosed hosts were more susceptible to cold than those that fed on control hosts (Smith and Goulding 1970).

Table 2. Famphur effects on selected terrestrial invertebrates.

Organism, dose, and other variables	Effect	Reference[a]
Lesser mealworm, *Alphitobius diaperinus*, topically applied		
3.44 mg/kg body weight (BW), 95% confidence interval (CI) 2.4-3.8 mg/kg BW	LD50 (24 h), adults	1
3.61 (95% CI of 3.32-4.08) mg/kg BW	LD50 (24 h), late instars	1
Milkweed bug, *Oncopeltus fasciatus*		
Abdominal injection, various doses		
Famoxon, 3.0 mg/kg BW	LD50	2

Famphur, 8.0 mg/kg BW	LD50	2
Single abdominal injection of 1 mg famphur/kg BW; whole body residues of famphur, famoxon, and N-desmethyl famphur measured 1 h after injection	Of total amount injected, 84.6% remained after 1 h: 79.4% famphur, 2.2% famoxon, and 3.1% N-desmethyl-famphur	2
American cockroach, *Periplaneta americana*		
Abdominal injection, various doses		
Famoxon, 4.6 (males) or 8.6 (females) mg/kg BW	LD50	2
Famphur, 9.0 (males) or 11.8 (females) mg/kg BW	LD50	2
Single abdominal injection of i mg famphur/kg BW; whole body residues of famphur, famoxon, and N-desmethylfamphur measured 1 h after injection	Of total amount injected, 18.5% remained after 1 h: 16.8% famphur, 0.5% famoxon, and 1.2% N-desmethyl-famphur	2

[a] 1, Vaughan and Turner 1984; 2, O'Brien et al. 1965.

Aquatic Organisms

An extensive literature search revealed no published data on famphur toxicity to aquatic animals. Unpublished studies of acute lethality were, however, conducted with bluegills (*Lepomis macrochirus*) and rainbow trout (*Oncorhynchus mykiss*). In those studies, the range in LC50 values at 96 h was 18 to 21 mg/L in bluegills and 4.9 to 5.3 mg/L in rainbow trout; the no-observable-effect concentration at 96 h ranged from 14 to 18 mg/ L in bluegills and was 2.1 mg/L in rainbow trout (U.S. Environmental Protection Agency, OPPTS/OPP / EFED / EEB, personal communication, 30 June 1993).

Although no data were available on effects of famphur in aquatic ecosystems, there is a substantial data base on other organophosphorus insecticides. For example, methyl parathion (O, O-dimethyl O-[p-nitrophenyl] phosphorothioate), another phosphorothioate organophosphorus insecticide, had LC50 (96 h) values for the bluegill (5.7 mg/L) and the rainbow trout (2.7 mg/L) that were similar to those of famphur (Khan 1977). But exposure for 96 h is not sufficient to satisfactorily evaluate the aquatic toxicity of organophosphorus insecticides. The mortality of adult northern puffers (*Sphoeroides maculatus*) continuously exposed to 20.2 mg/L of methyl parathion was less than 5% in 96 h but 100% in 40 days. Puffers refused to eat during exposure, and survivors between days 10 and 40 showed complete inhibition of serum esterase activity, zinc-depleted liver and gills, and altered blood chemistry (Eisler 1967, 1972). In another study, male guppies (*Poecilia reticulata*) held in sublethal concentrations (0.01-1.0 mg/L) of methyl parathion for 40 days or longer showed a dose-dependent decrease in spermatogenesis (Billard and de Kinkelin 1970). Pesticide-induced mortality patterns of representative organophophorus compounds are also modified by water temperature, pH, and salinity. The mummichog (*Fundulus heteroclitus*), an estuarine cyprinodontiform teleost, was most sensitive to organophosphorus compounds at elevated temperatures, reduced salinities, and low pH (Eisler 1970b). Duration of exposure to organophosphorus compounds also affects mummichog survival: fishes exposed to high (LC75, 24-h) concentrations of representative insecticides for more than 30 min died by day 21 postexposure; some insecticides were as much as 8.3 times more toxic after exposure for 240 h than 96 h, as judged by LC50 values (Eisler 1970b). In general, crustaceans were more sensitive than teleosts--sometimes by several orders of magnitude--to organophosphorus insecticides in 96-h tests; assayed grass shrimp (*Palaemonetes vulgaris*) and

fishes were most sensitive to organophosphorus insecticides at high salinities in the 1.2-3.6% test range and high temperatures in the 10-30° C test range (Eisler 1969; 1970c, 1972). Marine clams and gastropods were comparatively resistant to organophosphorus insecticides; none died in 96-h exposure to 25 mg/L of five organophosphorus insecticides, including methyl parathion. But during a postexposure of 133 days, some bivalves and gastropods died (Eisler 1970a), and these deaths are similar to the delayed mortality of some species of mammals and invertebrates after exposure to certain organophosphorus insecticides (Negherbon 1959).

The expected continued use of famphur in the environment and its vehicular transport along roads that border navigable waters suggest a need for aquatic toxicity data. Famphur data--like those on other organophosphorus insecticides-should reflect the influence of dose, exposure duration, formulation, and other biological and abiotic variables on growth, survival, and metabolism of representative species of aquatic organisms.

Birds

The avian acute oral LD50 of famphur is usually between 1 and 9.5 mg/kg BW (Schafer 1972; Hill and Mendenhall 1980). Laboratory studies with sensitive species of birds revealed reduced survival after a 5-day consumption of diets containing 35 to 49 mg famphur/kg ration (Hill et al. 1975; Table 3). Depressed cholinesterase activity in the brain and in plasma of European starling (*Sturnus vulgaris*) nestlings occurred after 15 daily oral exposures of concentrations as low as 0.3 mg famphur/kg BW (Powell and Gray 1980; Table 3). Signs suggesting famphur poisoning in mallards (Anas *platyrhynchos*) included regurgitation, goose-stepping, ataxia, wing drop, tremors, and tonic seizures (Tucker and Crabtree 1970; Hudson et al. 1984).

Famphur is considered a Class-II-toxic compound to the Japanese quail (*Coturnix japonica*) according to the classification of Hill and Camardese (1986). Class-II compounds (very toxic) kill 50% of the test organisms on diets containing 40 to 200 mg chemical/kg ration for 5 days. By comparison, the 50% kill in other classes (in mg/kg diet) is less than 40 in Class I (highly toxic), greater than 200-1,000 in Class III (moderately toxic), greater than 1,000-less than 5,000 in Class IV (slightly toxic), and greater than 5,000 in Class V (practically nontoxic; Hill and Camardese 1986). Smith (1987) rates famphur as a Class-I-toxic compound, as judged by results of dietary tests with mallards.

Birds killed by organophosphorus compounds in the wild consistently show 80 to 95% depression of brain-cholinesterase activity (Hill 1992). Depression of brain-cholinesterase activity by greater than 20% in birds has been used as a conservative criterion to indicate significant exposure to organophosphorus chemicals. Depression of brain-cholinesterase activity by greater than 50% and confirmation of suspected organophosphorus chemical residues in tissues or ingesta are criteria for cause-effect diagnosis of death in birds exposed to cholinesterase-inhibiting chemicals (Henny et al. 1985; Hill 1992). Death occurs in many avian species when brain-cholinesterase inhibition is 60 to 90%; however, no common barn-owls (*Tyto alba*) died or showed signs of intoxication after consuming famphur-poisoned Japanese quail, although 70% of the owls had brain-cholinesterase inhibition within these lethal bounds (Hill and Mendenhall 1980). Common barn-owls fed famphur-poisoned quail, the digestive tracts of which had been removed, showed significant but lesser brain-cholinesterase-activity inhibition than barn-owls fed intact poisoned quail, indicating that famphur or cholinesterase-inhibiting metabolites were most heavily concentrated in digestive tracts (Table 3).

The black-billed magpie seems unusually sensitive to famphur. Dead famphur-poisoned magpies contained as much as 290 mg famphur/kg liver FW, 4,770 mg/kg gizzard FW, and less than 0.2 mg/kg muscle or fat (Hill and Mendenhall 1980). There is a growing body of literature on adverse effects on magpies from pour-on (13.2% famphur) applications along the backline of cattle to control cattle warbles at the recommended rate of 0.326 mL/kg BW, not to exceed 118 mL/animal--equivalent to 43 mg/kg BW, not to exceed 15.6 g/animal (Felton et al. 1981; Henny et al. 1985; Seel 1985; Smith 1987). Felton et al. (1981) documented three occasions when dead birds were found after pour-on-famphur treatment of cattle against warble flies: (1) 12 black-billed magpies in a nearby field 2 to 3 days after cattle were treated; (2) 6 magpies during a 14-day period (although other species of corvids were present, only magpies were affected); and (3) 8 European robins (*Erithacus rubecula*) and a single dunnock (*Prunella modularis*) near a cattle crush a few days after famphur treatment. The dead birds had no measurable brain cholinesterase activity, and famphur was detected in the gizzards of birds in all 3 incidents (Felton et al. 1981). Partially paralyzed magpies containing as many as 3,500 mg famphur/kg gizzard contents were found in the vicinity of cattle recently treated with a pour-on formulation of famphur to control an

infestation by warble-flies; another 20 to 30 dead magpies were found in the immediate area (Seel 1985). Magpies and one red-tailed hawk (*Buteo jamaicensis*) were the only dead species found where cattle had been topically treated with famphur, although several other species including killdeers (*Charadrius vociferus*) and European starlings (Henny et al. 1985) were common in these pastures. Famphur residues were detected in all dead magpies and hawks, and brain-cholinesterase-activity depression ranged from 70 to 92%. Based on residue concentrations in the gizzards, dead magpies contained 5.2-6.1 mg famphur/kg whole body; these values were above the acute oral LD50 values for several species of birds (Henny et al. 1985; Table 3). The most probable explanation for the sensitivity of magpies to famphur is associated with the contents of the poisoned magpies that consisted of as much as 12% cattle hair (Henny et al. 1985). Although most organophosphorus compounds degrade rapidly, famphur persists for greater than 90 days on hair of Hereford bulls and steers and Angus yearlings. Famphur concentration in hair of a Hereford bull averaged 38,000 mg/kg FW one week after a single pour-on treatment and a maximum of 12,000 mg/kg FW 60 days posttreatment. High concentrations of famphur in the gizzards of magpies indicated that the material was ingested and not from dermal contact or inhalation. Tissue residues in mg famphur/kg FW in famphur-poisoned magpies were as much as 550 in the upper GI tract, 4.3 in the lower GI tract, and 3 in the whole body. Cow hair from gizzards of dead magpies averaged 4,600 mg famphur and famoxon/kg FW; other animal matter in the gizzard contained 620 mg famphur and famoxon/kg FW and plant matter 340 mg famphur and famoxon/kg FW. A potentially lethal dose to magpies would be 8-19 mg of treated hair at day 7 and 26-60 mg of treated hair after 60 days. Coincidentally, magpie mortality persisted for more than 3 months; most deaths occurred 5 to 13 days after cattle were treated (Henny et al. 1985). The manure-insect-bird pathway of famphur translocation is untenable because of extremely low (<0.14 mg/ kg FW) concentrations of famphur in cow manure (Henny et al. 1985).

Table 3. Famphur effects on birds.

Route of administration, organism, dose, and other variables	Effect	Reference[a]
Dietary exposure		
Treated feed for 5 days, then untreated feed for 3 days Mallard, *Anas platyrhynchos* 35 mg/kg diet	About 50% survived; ducklings age 10 days	1
Japanese quail, *Coturnix japonica*; 69 mg/kg diet, 95% confidence interval (CI) of 49-97 mg/kg diet	50% dead; 14-day-old quail	2
Ring-necked pheasant, *Phasianus colchicus*; 49 mg/kg diet, 95% CI of 40-61 mg/kg diet	50% dead; 10-day-old chicks	1
Domestic chicken, *Gallus* sp. Fed 50 mg/kg ration for 10 days (in attempt to control northern fowl mite, *Ornithonyssus sylviarum*) Common barn-owl, *Tyto alba*, adults, 475 g body weight (BW)	Ineffective in controlling mites. Feed consumption, body weight, and egg production significantly decreased	3

Barn-owls were fed whole famphur-poisoned Japanese quail. Quail received multiple doses of famphur (a total of 1 mg over a 3-day period). One poisoned *Coturnix* was fed daily for 10 days. If no famphur was lost or metabolized by *Coturnix* prior to death, then barn-owls received a maximum of 21 mg/kg BW for the 10-day period or 2.1 mg famphur/kg	Barn-owls did not avoid famphur-poisoned *Coturnix*, fed normally, and did not lose weight. By the tenth day, plasma-cholinesterase activities in barn-owls were depressed 45-81%, and brain-cholinesterase activities were depressed 32-73%	4
As above, except digestive tract was removed from famphur-poisoned Coturnix before presentation to barn-owls	Barn owls had brain-cholinesterase activity values intermediate between controls and those fed poisoned whole *Coturnix*	4
Multiple oral doses		
Japanese quail; dosing by gavage over 3 days: 300 µg on days 1 and 2 and 400 µg on day 3; mean weight of 120 g	Some deaths; cumulative dose received at day 3 = 8.33 mg/kg BW	4
Domestic chicken; 2.5 mg/kg BW once daily for 8 days; observed for 10 days posttreatment	Egg production, body weight, and feed consumption decreased significantly; ineffective in controlling northern fowl mite	3
European starling, *Sturnus vulgaris*, free-living nestlings, age 4 days. Dosed perorally with famphur dissolved in corn oil at 0.3, 1.0, or 3.0 mg famphur/kg BW daily for 15 days, then killed at age 19 days	At 0.3 mg/kg BW, 1 nestling died after the second dose (age 6 days) and another after the fifth dose vs. no deaths in controls; at day 19, brain-cholinesterase activity was depressed 51% and plasma activity 49%. At 1.0 mg/kg BW, 1 died after the third dose; at day 19, brain-cholinesterase activity level was depressed 75% and plasma cholinesterase 25%. At 3.0 mg/kg BW, 9 of 11 tested nestlings died within 8 h of the first dose, another within 8 h of the second dose, and the last was killed by a predator after the second dose. The 2 nestlings that survived a single dose were moribund and their brain-cholinesterase activity was depressed 85%	5

Single oral dose		
Red-winged blackbird, *Agelaius phoeniceus;* 1.8 mg/kg BW, 95% CI of 1.0-3.2 mg/kg BW	LD50	6, 9
Mallard; 9.87 mg/kg BW, 95% CI of 5.88-16.6 mg/kg BW	LD50 for 3-4 months old hens	7, 8
Domestic chicken; 10 mg/kg BW in gelatin capsule to control northern fowl mite; observed for 10 days posttreatment	Ineffective in controlling mites. On day 2 posttreatment, 1 of 12 chickens had died and 9 others showed muscular incoordination, especially in the legs. By day 3 posttreatment, most of the 9 were again standing and feeding and feces had reverted from a greenish diarrheic discharge to the normal consistency. By day 10 posttreatment, body weight and egg production was significantly decreased, although egg weight was unaffected	3
European starling; 4.2 mg/kg BW, 95% CI of 1.99-9.50 mg/kg BW	LD50	6, 9

[a] 1, Hill et al. 1975; 2, ill and Camardese 1986; 3, DeVaney and Ivie 1980; 4, Hill and Mendenhall 1980; 5, Powell and Gray 1980; 6, Smith 1987; 7, Tucker and Crabtree 1970; 8, Hudson et al. 1984; 9, Schafer 1972.

Secondary poisoning of flesh-eating birds foraging on famphur-killed vertebrates is well-documented; the degree of hazard to the predator related to the amount and type of consumed tissues and famphur concentrations in the prey tissues (Heinz et al. 1979; Hill and Mendenhall 1980; Henny et al. 1985, 1987; Hill 1992). Secondary poisoning of raptors killed by famphur that was topically applied to livestock include the bald eagle (*Haliaeetus leucocephalus*)--after eating cattle that died within 100 days of famphur treatment or famphur-poisoned brown-headed cowbirds (*Molothrus ater*) and European starlings-and a red-tailed hawk after eating famphur-poisoned black-billed magpies or European starlings (Henny et al. 1987). In one case, an adult-female bald eagle that was unable to fly near Lewes, Delaware, was brought to a national wildlife refuge where it died after a few days (Franson et al. 1985). Stomach contents included one lead shot and remains of brown-headed cowbirds and European starlings. A necropsy revealed no signs of lead poisoning. Clinical signs, physical examination, and presence of a full crop suggested acute poisoning. Crop and stomach contents were analyzed for a variety of pesticides, metals, and herbicides, but only famphur was elevated at 1.9 mg/ kg FW. As judged by famphur residues in the GI tract and by brain-cholinesterase-activity inhibition of 85%, the authors concluded that famphur was the probable cause of death (Franson et al. 1985). There is also a case of tertiary poisoning in which a great horned owl (*Bubo virginianus*) died after consuming a dead famphur-poisoned red-tailed hawk. In all of these cases brain-cholinesterase activity of poisoned birds was depressed greater than 50% and undigested remains contained famphur (Henny et al. 1987).

Famphur has also been used to intentionally kill birds, including migratory waterfowl and other protected species, and should be added to the list of other toxic organophosphorus insecticides such as monocrotophos, dicrotophos, and parathion that have been used for this purpose (White et al. 1989). In 1988, for example, famphur was used illegally by farmers in Georgia and West Virginia to kill birds thought to be depredating crops. Corn and grain at the mortality sites contained between 4,240 and 8,500 mg famphur/kg. Dead birds at these locations included Canada geese (*Branta canadensis*), mallards, American black ducks (*Anas rubripes*), American crows (*Corvus brachyrhynchos),* common grackles (*Quiscalus quiscula*), red-winged blackbirds (*Agelaius phoeniceus*), sandhill cranes (*Grus canadensis*), and a single red-tailed hawk. Most of the poisoned waterfowl, cranes, raptors, corvids, and songbirds from the 5 sites had severely depressed brain-cholinesterase activity (i.e., >50%), poisoned bait in the gizzards, and famphur concentrations in the gastrointestinal tracts ranging from 5 mg/kg FW in the red-tailed hawk to 1,480 mg/ kg FW in Canada geese. It was concluded that all birds died from direct ingestion of the poisoned bait, except the red-tailed hawk that had eaten one or more famphur-poisoned crows (White et al. 1989).

Mammals

Famphur is a group-D compound that is not classifiable as a human carcinogen (Sine 1991). However, a study of leukemia risk among males in Iowa and Minnesota indicated a slight but significant elevation in risk--especially chronic lymphocyte leukemias--for farmers but not for nonfarmers. Moreover, a significantly elevated leukemia risk was seen from exposure to specific animal insecticides including famphur (Brown et al. 1990). It is clear that more research is needed on the potential carcinogenicity of famphur.

Signs of famphur toxicosis in cattle include ataxia, muscular fasciculations, general weakness, lacrimation, salivation, and diarrhea (Randell and Bradley 1980). In comparison with European breeds of cattle (*Bos taurus*), the Brahman (*Bos indicus*) and European X Brahman hybrids are more sensitive to famphur, and Brahman bulls are more sensitive than cows (Johnson et al. 1972; Randell and Bradley 1980; Table 4). At a comparatively low dose of 16.6 mg famphur/kg BW, both *B. taurus* and *B. indicus* are tolerant of intramuscular injectable famphur; however, *B. indicus* is more sensitive and bulls sometimes died when treatment levels exceeded 33.3 mg/kg BW (Randell and Bradley 1980; Table 4). In addition to cattle, famphur-induced mortality in other species of mammals was documented (Table 4). Single exposures of famphur in mg/ kg BW killed rabbits (*Oryctolagus* sp.) at 2,730 in dermal exposure; mice (*Mus* sp.) at 27 in oral dose or 11.6 by intraperitoneal injection; domestic sheep (*Ovis aries*) at 400 in oral dose; and laboratory white rats (*Rattus* sp.) at 400 dermal exposure or greater than 28 in oral dose (Table 4). Mice receiving fatal or near-fatal intraperitoneal injections of famphur or famoxon began to convulse 10-20 min postinjection; death came within 45 min postinjection, usually from respiratory failure. Mice remaining alive at 60 min postinjection usually recovered (O'Brien et al. 1965).

Table 4. Famphur effects on mammals.

Organism, route of administration, dose, and other variables	Effect	Reference[a]
Cattle, *Bos* spp.		
Bolus		
Given to 180-kg calves 12 days before infestation by 30-60 day-old larvae of ticks. Sustained release equivalent to 3, 5, or 6.8-10.1 mg famphur/kg body weight (BW) daily	Ineffective at 3 mg/kg BW against fever ticks (*Boophilus annulatus*, *B. microlopus*) and the American dog tick (*Dermacentor variabilis*). At 5 mg/kg BW, famphur was effective (87-97%) against fever ticks but ineffective against the dog tick. At the highest daily release rate, famphur was 100% effective against fever ticks between	1

	days 12 and 41 but remained ineffective against the dog tick	
7 mg/kg BW daily (range 4.5-11.5 mg/kg BW daily)	Bolus was 99-100% effective against Gulf Coast tick (*Amblyomma maculatum*) and 60-86% effective against the lone star tick (*A. americanum*). Heifers showed no signs of organophosphorus insecticide poisoning but had slight reduction in erythrocyte-cholinesterase activity	2
Diet		
Lactating cows fed diets equivalent to 3.3 mg famphur/kg BW for 90 days	Concentrations in milk on day of withdrawal were 0.025 mg famphur/L and 0.023 mg famoxon / L. During the next four milkings (i.e., through day 8 posttreatment), famphur and famoxon residues in milk were always <0.005 mg/L	3
Calves fed rations equivalent to 3.3 or 9.9 mg famphur/kg BW for 90 days	Within 2 days of cessation of the low-dose-contaminated diet all calf tissues were free of famphur and famoxon; this value was 4 days for the 9.9 mg/kg BW group. Concentrations of famphur (famoxon) in mg/kg FW in the high-dose group at the end of the 90-day feeding study were 0.31 (0.03) in muscle, 1.6 (0.23) in fat, 5.6 (0.5) in liver, and 0.49 (0.19) in kidney	3
Adult rations contained equivalent of 5 mg famphur/kg BW daily	99.5-100% effective in control of Gulf Coast tick and lone star tick; ineffective against the American dog tick	1
Adults given equivalent of 5 mg famphur/kg BW daily	Effective against tropical horse tick (*Anocentor nitens)* but not completely effective against 3 other species of ticks	2
Adults given equivalent of 5 mg/kg BW daily for 10 days,	>90% control of cattle grubs (*Hypoderma* spp.). Manure from treated cattle	4

administered as a 33%-feed premix	controlled larvae of horn fly (*Haematobia irritans*) but was ineffective against larvae of the house fly (*Musca domestica*)	
Intramuscular injection		
15 mg/kg BW; Hereford steers	97% grub reduction in calves, 93% in cows, and calves, Angus cows; to 94% in steers control cattle grubs (*Hypoderma lineatum, H. bovis*)	5
16.6, 33.3, or 49.9 mg/kg BW, single injection; Brahman bulls, steers, and heifers 6-8 months old, 169-200 kg BW. Observed for 28 days posttreatment	All doses inhibited erythrocyte-cholinesterase levels by 45-95%. All groups tolerated 16.6 mg/kg BW. Severe toxicosis in the two high-dose groups (9 of 20) in bulls but not in heifers and steers; 7 of the 9 bulls died or had to be euthanized; necropsy showed severe pulmonary edema	6
18 mg/kg BW, single injection	Residues <0.7 mg/L in blood 2 h postinjection	7
36 mg/kg BW, single injection	Residues in blood >0.7 mg/L 2 h postinjection, but <0.7 mg/ L after 4 h	7
54 mg/kg BW, single injection	Residues in blood >0.7 mg/L 1-2 h postinjection, but <0.7 mg/L after 4 h	7
60.7 mg/kg BW, single injection of radiolabeled famphur	Blood plasma levels in mg/kg fresh weight (FW) were 0.4 after 4 h and 0.18 after 72 h; for famoxon, these values were not detectable at 4 h and 0.05 at 72 h. Plasma and urine radioactivity levels reached maxima after 24 h	7, 8
83.2 mg/kg BW; Brahman bulls and Angus bulls, 7-9 months old, 174-184 kg BW	5 of 6 injected Brahman bulls showed severe signs of toxicosis and 4 died within 48 h; recovery of the 5th bull took 10 days. Only 1 of 5 Angus bulls showed clinical signs of toxicosis, but it recovered	6
Oral		
9.9 mg/kg BW; single application, residues measured 24 h posttreatment; control values always <0.05 mg / kg FW of famphur and famoxon		
Fat; famphur vs. famoxon (mg / kg FW)	0.14 vs. <0.05	3

Kidney; famphur vs. famoxon (mg / kg FW)	<0.05 vs. <0.05	3
Liver; famphur vs. famoxon (mg / kg FW)	0.08 vs. 0.05	3
Muscle; famphur vs. famoxon (mg/kg FW)	<0.05 vs. <0.05	7
18 mg/kg BW	Residues in blood >0.7 mg/L 18-24 h after ingestion	7
20, 30, or 40 mg/kg BW, each with 8 mg levamisole / kg BW; administered as a paste to cattle yearlings in California, Nebraska, and Kentucky	As much as 85% reduction in cattle grubs and nematode gastrointestinal worms at 20 mg / kg BW + levamisole; as much as 98.2% reduction in 30 or 40 mg/kg BW groups	9
36 mg/kg BW, single dose	Residues in blood >0.7 mg/L 6-72 h after intake, but <0.7 mg/L after 96 h	7
Pour-on		
15 to 35 mg/kg BW, cows	Controls cattle-biting lice (*Damalina bovis*), long-nosed cattle lice (*Linognathus vituli*), and short-nosed cattle lice (*Haematopinus eurysternus*)	10
20.25, 40.5, or 60.75 mg/kg BW; Holstein Friesian calves; blood-cholinesterase-activity levels measured up to 49 days posttreatment	At the 2 lowest doses, significant depression from day 2 through day 14; blood cholinesterase normal at day 21. At 60.75 mg/kg, blood cholinesterase decreased for entire 49-day posttreatment. No outward signs of organophosphate intoxication and normal food intake and demeanor	11
23 mg/kg BW, cows	At 24 h whole milk had 0.24 mg famphur/L of which 76% was in the butterfat fraction; after 72 h residues in milk were <0.008 mg/L	10
25 mg/kg BW, cows	After 24 h, mean residue of famphur in subcutaneous fat was 1.8 mg/kg FW, maximum was 2.46 mg/kg FW	10
40 mg/kg BW; Hereford	87% effective in controlling cattle	5

steers and calves, Angus cows	grubs in calves; 100% effective in cows and steers	
40 mg/kg BW, cattle yearlings	100% effective in controlling cattle grubs and nematode gastrointestinal worms	9
40 or 50 mg/kg BW; yearling steers; Canada, late autumn; single treatment	Although not completely satisfactory for control of *Hypoderma* spp. (52-68% reduction in grubs)--possibly because of low absorption associated with low ambient temperatures at time of treatment--and some inhibition in blood-cholinesterase activity (maximum inhibition of 31-38% reached 15 days after treatment), both groups of treated steers gained significantly more weight than a control group during the posttreatment of 181 days and were otherwise normal	12
40, 80, or 209 mg/kg BW; Brahman bulls, steers, and heifers; mean weight of 117 kg		
40 mg / kg BW	Erythrocyte cholinesterase depression after 24 h was 43% in bulls and 33-34% in steers and heifers	13
80 mg/kg BW	After 5 h, 1 of 13 bulls was anorexic and salivating	13
209 mg/kg BW	After 48 h, erythrocyte-cholinesterase depression was 56% in bulls, 55% in steers, and 51% in heifers.	13
40.5 mg/kg BW, Brahman bull calves	2 of 3 famphur-treated calves died	11
45 mg/kg BW, cows	Famphur concentrations in mg/kg FW after 24 h were <0.05 in liver and kidney, 1.25 in fat, and 1.41 in muscle. After 7 days, these values were 0.53 in fat and 0.71 in muscle. By day 14, maximum values were 0.11 mg / kg FW in fat and <0.02 in other tissues	10
50 mg/kg BW, cows	After 24 h, mean residue of famphur in subcutaneous fat was 2.08 mg/kg	10

	FW, maximum was 3.00 mg/kg FW	
150 mg/kg BW, cows	After 24 h, famphur concentrations in subcutaneous fat ranged from 6.3 to 12.3 mg/kg FW	10
Angora goat, *Capra* sp.; pour-on, 4.1-4.8 mg/kg BW; nannies 27-41 kg; single application	100% effective in 14-day control of Angora goat biting louse (*Bovicola limbatus*) and hairy goat louse (*B. crassipes*); significant protection after 45 days	14
Laboratory mouse, *Mus* sp.		
Dermal; mice infected nasally or orally with rodent botfly (*Cuterebra* sp.) were dipped 48 h post-infestation for 30 sec in 25% emulsifiable famphur solutions (0.001-10%) and examined 1 week later. Entire body was submersed except head	50% kill of larvae after immersion in 0.0072% solution (18 mg famphur / L); 90% control in 0.051% solution (127.5 mg/L)	16
Oral		
Male mice, 8-12 weeks old, orally and nasally infected with 1st-stage larvae of rodent botfly. Two days after infection, mice were given single doses of 1.46 or 3.38 mg famphur / kg BW	Low dose killed 50% of larvae; high dose killed 90%	17
As above, except that mice were given 1.5 mg famphur/kg BW at 1, 2, or 3 days after infestation	Most effective control (71% dead larvae) when administered at 3 days	17
18 mg/kg BW	Acute LD50, famoxon	7
27-30 mg/kg BW	Acute LD50, famphur	7, 15
Intraperitoneal injection		
Single injection of 1 mg famphur/kg BW; residues of famphur, famoxon, and N-desmethylfamphur measured 1 h post-injection	Only 8.3% of the injected dose was measurable 1 h post-injection: 8.1% as the parent famphur, 0.2% as famoxon, and 0.01% as N-desmethylfamphur	18
5.8 mg famoxon/kg BW	LD50	18
11.6 mg famphur/kg BW	LD50	18
Rabbit, *Oryctolagus* sp.		
50 mg/kg BW; oral, subcutaneous, or	No effect on reproduction	25

intravenous route		
2,730 mg/kg BW, dermal route	LD50	15
Domestic sheep, *Ovis aries*		
Bolus; sustained release of 7 mg famphur/kg BW daily	Completely effective against Gulf Coast tick, partial control of lone star tick,	2
Intravenous injection	ineffective against American dog tick	
Single injection of radiolabeled famphur equivalent to 22.3 mg famphur/kg BW. Sheep killed at 96 h and tissues analyzed for residual radioactivity	More than 50% of the administered dose was excreted within 6 h and 98% within 48 h. About 97% was excreted in urine and <3% in feces. Residues, in mg/kg FW, were 1.4 in blood; 0.3 to 0.6 in kidney, liver, spleen, lung, and cerebrospinal fluid; and <0.1 in bile, fat, brain, and muscle	7, 8
Single injection, 22.3 mg/kg BW	Famphur (famoxon) residues in blood plasma, in mg/kg FW, were 0.6 (5.6) at 2 h, and nondetectable (0.01) at 24 h	7
Intravenous or intramuscular injection; urine collected over 24-h period after single application of radiolabeled famphur	Urinary radioactivity was due to the unchanged O-desmethyl compound (13-24%); N, N-dimethyl sulfamoylphenyl glucuronide (32-33%); O, N-bisdesmethylfamphur 31-34%); and N-methyl sulfamoylphenyl glucuronide (8-15%)	8
Intramuscular injection		
Single injection of radiolabeled famphur, equivalent to 55.1 mg/kg BW. Sheep killed at 72 h and tissues analyzed for residual radioactivity	About 64% of the administered dose was recovered in excreta after 72 h. Residues in mg/kg FW were 15 at the muscle injection site; 5-8 in kidney, bile, and fat; 1.6-2.3 in liver, spleen, lung, and blood; and 0.7-0.9 in brain, muscle, and cerebrospinal fluid	7, 8
Single injection, 55.1 mg/kg BW	Famphur (famoxon) residues in blood plasma, in mg/kg FW, were 0.9 (0.1)	7, 8
Oral, single dose; 400 mg/kg BW	LD50	15, 19, 20
Rumen infusion; peroral administration by cannulation for 72 h of ewes given doses equivalent to 5 or 7 mg	At 5 mg/kg BW, famphur caused a significant increase in mortality and decrease in percent egg hatch of adult Gulf Coast ticks and complete control	21

famphur/kg BW daily. After infusion for 72 h sheep were challenged by various blood-sucking arthropods	of the bedbug (*Cimex lectularius*) At 7 mg/kg BW daily, Gulf Coast ticks were completely controlled, but dose was ineffective against the lone star tick and the American dog tick	
Reindeer, *Rangifer tarandus*; intramuscular injection		
15 mg/kg BW, single injection	At 24 h residues were highest (8.1-9.1 mg/kg FW) in fatty tissues; at muscle injection site, residues ranged up to 635 mg/kg vs. 0.6 mg/kg FW in normal muscle. At 7 days post-treatment, residues in mg/kg FW, were 0.03-0.19 in fat, 0.03 in injection-site muscle, and 0.03 in liver. At 5 weeks, famphur was detectable only in fat; by 7 weeks, no famphur was detectable in any tissue. Famoxon was not found in any tissue at any time	22
30 mg/kg BW, single injection	Residues at 24 h in mg/kg FW were as high as 38 in fat, 8 in muscle, 5 in liver and 2.5 in kidney	22
30 mg/kg BW, single injection	90-95% reduction in larvae of warble fly (*Oedemagena tarandi*) and nostril fly *(Cephenomyia trompe*)	23
Accidental overdose (usually double-dosed), 60 mg/kg BW	Atropine sulfate is recommended antidote	23
Laboratory white rat, *Rattus* sp.		
Dermal, single application, mg/kg BW		
400	LD50, adult males	19
533	LD50, adult females	19
Diet containing 1, 3, or 25 mg famphur/kg for as many as 90 days	At 90 days all groups had depressed plasma cholinesterase, although growth and appetite seemed normal. Whole blood cholinesterase was depressed in the 3 and 25 mg/kg group; brain cholinesterase was significantly reduced in the 25 mg/kg group	24
Diet containing 25 mg famphur/kg for 90 days,	Blood chemistry and histology normal at necropsy on day 132. Rats avoided diets	24

then famphur-free diet for 42 days	during famphur-free phase	
Oral, single dose, in mg/kg BW		
28	LD50, adult males	19
35	LD50	7, 20
36-62	LD50	15
51	LD50, adult females	19
73	LD50, weanling males	19
Subcutaneous injection; urine collected during 24 h period after single application of radiolabeled famphur	Urinary radioactivity was due to the unchanged O-desmethyl compound (>50%); N,N-dimethyl sulfamoylphenyl glucoronide (30%); O,N-bisdesmethylfamphur (12%), and N-methyl sulfamoylphenyl glucuronide (7%)	8

[a] 1, Hair et al. 1979; 2, Teel et al. 1979; 3, Pasarela et al. 1967; 4, Drummond 1968; 5, Loomis and Schock 1978; 6, Randell and Bradley 1980; 7, Kaemmerer and Buntenkotter 1973; 8, Gatterdam et al. 1967; 9, Campbell et al. 1987; 10, Annand et al. 1976; 11, Watson and Black 1981; 12, Khan and Kozub 1981; 13, Johnson et al. 1972; 14, Fuchs and Shelton 1985; 15, Smith 1987; 16, Drummond and Gingrich 1972; 17, Gingrich et al. 1972; 18, O'Brien et al. 1965; 19, Gallo and Lawryk 1991; 20, Eto 1974; 21, Teel et al. 1977; 22, Ivey et al. 1976; 23, Nordkvist 1975; 24, Black et al. 1979; 25, Smith and Goulding 1970.

Latent effects of famphur exposure in reindeer hinds (Nieminen et al. 1980) strongly indicated a need for additional studies in this subject area. Intramuscular injections of reindeer hinds and their 4-week-old calves controlled warble-fly infection in treated animals. Treated calves did not differ significantly from controls during the following year in body weight, body temperature, or blood chemistry. Treated hinds, however, had significantly lower erythrocyte sedimentation rates and serum-gamma-globulin concentrations and significantly higher hemoglobin, serum calcium, serum inorganic phosphorus, and serum magnesium than untreated hinds 1 year after treatment (Nieminen et al. 1980).

Reduced brain-cholinesterase activity in avian and mammalian wildlife is associated with adverse effects on metabolism, reproduction, sensory behavior, motor activity, food and water intake, learning, and memory (Mineau 1991). Cholinesterase activity in mammals regenerates rapidly after a cessation from treatment with famphur (Kaemmerer and Buntenkotter 1973). In humans, typical symptoms of organophosphorus-induced cholinesterase inhibition include headache, giddiness, nervousness, blurred vision, weakness, nausea, cramps, diarrhea, chest discomfort, sweating, salivation, vomiting, and tremors (Gallo and Lawryk 1991). In severe cases, victims show muscular weakness, convulsions, coma, loss of reflexes, loss of sphincter control, and eventually death. Effects of cholinesterase-inhibiting agents in humans are usually counteracted with repeated intravenous injections of atropine sulfate (2-4 mg), intravenous injections of pralidoxime chloride (1 g), and oxygen (Gallo and Lawryk 1991). Rats had depressed plasma-cholinesterase activity when fed diets containing as little as 1 mg famphur / kg for as many as 90 days, although growth and appetite seemed normal (Black et al. 1979). Brahman bulls had maximum erythrocyte-cholinesterase inhibition 14 days after intramuscular injection of famphur; cholinesterase-activity levels recovered towards normal during the next 14 days, and recovery correlated with the formation of new erythrocytes (Randell and Bradley 1980). Except for cholinesterase-activity inhibition, there were no signs of organophosphate intoxication in Brahman heifers and steers given single dermal doses of 20 to 61 mg famphur/kg BW. Cholinesterase activity was inhibited for as many as 14 days posttreatment at the lower (20-41 mg/kg BW) doses and for at least 7 weeks at 61 mg/ kg BW (Table 4).

Famphur is metabolized rapidly in mammals. In cattle, famphur controlled target insect pests when administered as a bolus, in the diet, as an oral paste, by intramuscular injection, or by pour-on. Regardless of mode of administration, length of exposure, or dose, famphur residues in tissues and milk were usually nondetectable within 4 days of final exposure. A similar pattern was evident in other species of mammals (Table

4). Rats and sheep metabolize famphur differently. During the first 24-h postdosing period, urine of rats contained as much as 2 times more of the unchanged O-desmethyl compound than urine of sheep, about the same amount of dimethylsulfamoylphenyl glucoronide, about 0.3 times as much O, N-bisdesmethylfamphur, and about 0.5 times less methylsulfamoylphenyl glucoronide (Gatterdam et al. 1967). With the exception of the oxon, metabolites of famphur were considerably less toxic to mammals than the parent chemical. In general, famoxon was 100 times more effective than famphur in depressing erythrocyte-cholinesterase activity (Kaemmerer and Buntenkotter 1973).

Famphur in pour-on applications penetrates skin at different rates depending on the solvent. In rat skin, penetration was most rapid when the solvent was acetone and least rapid in corn oil and benzene; the percent of remaining famphur in rat skin 3 h after a single dermal application was 38% from the acetone mixture and 67% from both benzene and corn oil solvents (O'Brien and Dannelley 1965). The penetrability of famphur pour-on formulations used in lice control on Angora goats was enhanced when applied in combination with a liquid-detergent wetting agent (Fuchs and Shelton 1985). Laboratory screening tests in which small mammals are treated with chemicals and parasitized by insects are now used to predict the effectiveness of systemic insecticides. Tests with mice and rodent botfly (*Cuterebra* sp.) were useful in predicting the effectiveness of famphur against larvae of the common cattle grub (*Hypoderma lineatum*) in cattle (Gingrich et al. 1972; Table 4), and show promise for screening additional chemicals.

Recommendations

The four primary areas of concern about famphur use are (1) mortality of birds associated with topical applications to cattle; (2) latent effects on domestic livestock; (3) the absence of aquatic toxicity data; and (4) potential carcinogenicity.

Because of its high toxicity to birds and field and experimental evidence of primary and secondary poisoning of birds, famphur is considered hazardous to feral birds--especially magpies-where cattle are topically treated with this insecticide (Felton et al. 1981; Henny et al. 1985, 1987). The pour-on application for cattle is now preferred to systematic dipping or intramuscular injection; dipping is reportedly labor intensive and costly (Hair et al. 1979). Intramuscular injection is more labor intensive, causes greater tissue damage and higher famphur absorption at the injection site, and produces a greater depression in blood-cholinesterase levels and a lower rate of weight gain in cattle than pour-on application (Loomis and Schock 1978). Nevertheless, famphur-induced mortality of magpies and other birds can be significantly reduced or eliminated by changing the insecticide application from the present pour-on method to other, now available modes of administration such as by diet, bolus, and intramuscular injection (Henny et al. 1985, 1987). Furthermore, a warning should be added to famphur labels stating that livestock dying within 3 months of famphur treatment should be removed from the range or farmland; this would offer partial protection to carrion-eating raptors such as eagles and vultures (Henny et al. 1987).

Reindeer are considered safe for human consumption 6 to 7 weeks after famphur treatment by intramuscular injection (dermal applications of famphur seldom penetrate the thick hair coat of reindeer). Treated reindeer had no detectable residues in liver, kidney, and muscle after 3 weeks (Ivey et al. 1976) and none in fat and other tissues after 6 to 7 weeks (Nordkvist 1975; Ivey et al. 1976). However, treated hinds during the following year had a significantly greater altered blood-chemistry profile than untreated hinds (Nieminen et al. 1980), suggesting a need for additional research on latent effects of famphur exposure. A safe dosage for cattle (*Bos* spp.) is 7 to 25 mg/kg BW by intramuscular injection or 40-55 mg/ kg BW by pour-on (Loomis and Schock 1978). The maximum concentration of famphur and famoxon allowed in cattle meat, fat, and meat by-products in the United States is 0.1 mg/ kg (Kaemmerer and Buntenkotter 1973; Ryan and McLeod 1979). In Australia, the maximum value is 0.05 mg/kg FW (Annand et al. 1976). The recommended minimum time between famphur treatment and slaughter of Australian cattle is 14 days. The half-time persistence of famphur in cattle tissues is 0.9 days, implying that even with gross misuse of the chemical, residues fall to low levels within a week (Annand et al. 1976). At present, no published studies were available on latent effects of famphur to cattle. Evidence of latent effects of famphur in reindeer (Nieminen et al. 1980) strongly suggest initiation of research into this subject area with cattle and other treated livestock.

No published data were available on effects and fate of famphur in aquatic ecosystems. This seems to be a high-priority research need in view of the increasing and illegal use of famphur to kill migratory waterfowl (White et al. 1989). In the absence of these data, it is recommended that concentrations of famphur and famoxon in

water and in tissues of aquatic organisms not exceed current analytical detection limits of 0.005 mg/L in water or 0.01 mg/kg FW tissue.

The carcinogenicity of famphur has not been satisfactorily resolved. Recent studies indicate a significantly elevated risk for leukemias among farmers handling famphur (Brown et al. 1990), but this needs verification.

Acknowledgments

I thank L. Garrett and W. Manning for literature search and retrieval services; M. G. Holmes for secretarial assistance; and A. J. DeLonay, C. J. Henny, P. F. P. Henry, E. F. Hill, and three anonymous referees for technical review of the manuscript.

Cited Literature

American Cyanamid Company. 1984. Warbex (famphur) pour-on for cattle 13.2%. American Cyanamid Company, ANH-19002, 4/87, TCEM. 2 pp.

Annand, A. M., J. H. P. Dingle, A. B. Heath, and W. A. Palmer. 1976. Residues of famphur in bovine tissues and milk following its application as a pour-on insecticide. Australian Journal of Experimental Agriculture and Animal Husbandry 16:82-87.

Bailey, P. J., W. A. D. Carroll, and B. Knee. 1984. Effects of lice infestation on the growth of beef heifers in Victoria. Australian Journal of Experimental Agriculture and Animal Husbandry 24:140-143.

Ballantyne, B., and T. C. Marrs, editors. 1992. Clinical and experimental toxicology of organophosphates and carbamates. Butterworth-Heinemann, Oxford, England. 641 pp.

Billard, R., and P. de Kinkelin. 1970. Sterilisation des testicules de guppies par des doses non letales de parathion. Annales d'Hydrobiologie 1:91-99.

Black, W. D., V. E. Valli, M. J. Claxton, and M. L. Marceau-Day. 1979. The effects of the subchronic feeding of the organophosphate famphur to rats. Toxicology and Applied Pharmacology 50:167-170.

Brown, L. M., A. Blair, R. Gibson, G. D. Everett, K. P. Cantor, L. M. Schuman, L. F. Burmeister, S. F. Van Lier, and F. Dick. 1990. Pesticide exposures and other agricultural risk factors for leukemia among men in Iowa and Minnesota. Cancer Research 50:6585-6591.

Campbell, J. B., F. W. Knapp, E. C. Loomis, D. J. Boxler, F. Herald, and L. L. Dunning. 1987. Efficacy of levamisole/famphur paste for control of cattle grubs (Diptera: Oestridae) and gastrointestinal worms (Nematoda: Trichostrongylidae). Journal of Economic Entomology 80:1028-1030.

De Vaney, J. A., and G. W. Ivie. 1980. Systemic activity of coumaphos, famphur, crufomate, ronnel, and phosmet given orally to hens for control of the northern fowl mite, *Ornithonyssus sylviarum* (Canestrini and Fanzago). Poultry Science 59:1208-1210.

Drummond, R. O. 1968. Further evaluation of animal systemic insecticides, 1967. Journal of Economic Entomology 61:1261-1264.

Drummond, R. O., and R. E. Gingrich. 1972. Detection of systemic activity of insecticides applied dermally to white mice infested with larvae of Cuterebra sp. Journal of Economic Entomology 65:1211-1212.

Durham, W. F. 1967. The interaction of pesticides with other factors. Residue Reviews 18:21-103.

Eisler, R. 1967. Tissue changes in puffers exposed to methoxychlor and methyl parathion. U.S. Bureau of Sport Fisheries and Wildlife Technical Paper 17. 15 pp.

Eisler, R. 1969. Acute toxicities of insecticides to marine decapod crustaceans. Crustaceana 16:302-310.

Eisler, R. 1970a. Latent effects of insecticide intoxication to marine molluscs. Hydrobiologia 36:345-352.

Eisler, R. 1970b. Factors affecting pesticide-induced toxicity in an estuarine fish. U.S. Bureau of Sport Fisheries and Wildlife Technical Paper 45. 20 pp.

Eisler, R. 1970c. Acute toxicities of organochlorine and organophosphorus insecticides to estuarine fishes. U.S. Bureau of Sport Fisheries and Wildlife Technical Paper 46. 12 pp.

Eisler, R. 1972. Pesticide-induced stress profiles. Pages 229-233 *in* M. Ruivo, editor. Marine pollution and sea life. Fishing News (Books), London.

Eto, M. 1974. Organophosphorus pesticides: organic and biological chemistry. CRC Press, Cleveland, Ohio.

Felton, C. L., P.M. Brown, M. R. Fletcher, and P. I. Stanley. 1981. Bird poisoning following the use of warble fly treatments containing famphur. Veterinary Record 108:440.

Franson, J. C., E. J. Kolbe, and J. W. Carpenter. 1985. Famphur toxicosis in a bald eagle. Journal of Wildlife Diseases 21:3 18-320.

Fuchs, T. W., and M. Shelton. 1985. Effectiveness of new methods of biting lice control on Angora goats. The Southwestern Entomologist 10:15-19.

Gallo, M. A., and N.J. Lawryk. 1991. Organic phosphorus pesticides. Pages 917-1123 *in* W. J. Hayes, Jr., and E. R. Laws, Jr., editors. Handbook of pesticide toxicology. Volume 2. Classes of pesticides. Academic Press, New York.

Gatterdam, P. E., L. A. Wozniak, M. W. Bullock, G. L. Parks, and J. E. Boyd. 1967. Absorption, metabolism, and excretion of tritium-labeled famphur in the sheep and calf. Journal of Agricultural and Food Chemistry 15:845-853.

Gingrich, R. E., O. Drummond, and W. J. Gladney. 1972. Use of white mice experimentally infested with larvae of a rodent botfly for screening systemic insecticides. Journal of Economic Entomology 65:742-745.

Gladney, W. J., S. E. Ernst, C. C. Dawkins, R. O. Drummond, and O. H. Graham. 1972. Feeding systemic insecticides to cattle for control of the tropical horse tick. Journal of Medical Entomology 9:439-442.

Hair, J. A., W. J. Gladhey, R. B. Davey, R. O. Drummond, and P. D. Teel. 1979. Sustained-release famphur bolus for control of *Boophilus* ticks. Journal of Economic Entomology 72:135-138.

Heath, A. C. G. J. D. Tenquist, and D. M. Bishop. 1980. Effects of pour-on organophosphate insecticides and a diamidide acaricide on the cattle tick, *Haemaphysalis longicornis*. New Zealand Journal of Experimental Agriculture 8:79-81.

Heinz, G. H., E. F. Hill, W. H. Stickel, and L. F. Stickel. 1979. Environmental contaminant studies by the Patuxent Wildlife Research Center. Pages 9-35 *in* E. E. Kenaga, editor. Avian and mammalian wildlife toxicology. American Society for Testing and Materials Special Technical Publication 693, Philadelphia, Pa.

Henny, C. J., L. J. Blus, E. J. Kolbe, and R. E. Fitzner. 1985. Organophosphate insecticide (famphur) topically applied to cattle kills magpies and hawks. Journal of Wildlife Management 49:648-658.

Henny, C. J., E. J. Kolbe, E. F. Hill, and L. J. Blus. 1987. Case histories of bald eagles and other raptors killed by organophosphorus insecticides topically applied to livestock. Journal of Wildlife Diseases 23:292-295.

Hill, E. F. 1992. Avian toxicology of anticholinesterases. Pages 272-294 *in* B. Ballantyne and T. C. Marrs, editors. Clinical and experimental toxicology of organophosphates and carbamates. Butterworth-Heinemann, Oxford, England.

Hill, E. F., and M. B. Camardese. 1986. Lethal dietary toxicities of environmental contaminants and pesticides to coturnix. U.S. Fish and Wildlife Service Technical Report 2. 147 pp.

Hill, E. F., R. G. Heath, J. W. Spann, and J. D. Williams. 1975. Lethal dietary toxicities of environmental pollutants to birds. U.S. Fish and Wildlife Service Special Scientific Report--Wildlife 191. 61 pp.

Hill, E. F., and V. M. Mendenhall. 1980. Secondary poisoning of barn owls with famphur, an organophosphate insecticide. Journal of Wildlife Management 44:676-681.

Hudson, R. H., R.K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. Second edition. U.S. Fish and Wildlife Service Resource Publication 153.90 pp.

Ivey, M. C. J. S. Palmer, and R. H. Washburn. 1976. Famphur and its oxygen analogue: residues in the body tissues of reindeer. Journal of Economic Entomology 69:260-262.

Johnson, W. P., B. T. Alford, and J. J. Drain. 1972. Safety of famphur to young Brahman heifers, bulls and steers. Veterinary Medicine, Small Animal Clinician 67:686.

Kaemmerer, K., and S. Buntenkotter. 1973. The problem of residues in meat of edible domestic animals after application or intake of organophosphate esters. Residue Reviews 46:1-240.

Khan, M. A., and G. C. Kozub. 1981. Systemic control of cattle grubs (*Hypoderma* spp.) in steers treated with Warbex and weight gains associated with grub control. Canadian Journal of Comparative Medicine 45:15-19.

Khan, M. A. Q., editor. 1977. Pesticides in aquatic environments. Plenum Press, New York. 257 pp.

Loomis, E. C., and R. C. Schock. 1978. Comparison of famphur (warbex) pour-on and intramuscular injectable formulations for cattle grub control, California, 1975-1976. Journal of Medical Entomology 14:649-651.

Mineau, P., editor. 1991. Cholinesterase-inhibiting insecticides. Their impact on wildlife and the environment. Chemicals in agriculture. Volume 2. Elsevier Science Publishers, Amsterdam, The Netherlands. 348 pp.

Negherbon, W. O. 1959. Organic phosphates. Pages 536-576 *in* W. O. Negherbon, editor. Handbook of toxicology. Volume III. Insecticides. A compendium. WADC Technical Report 55-16. Aero Medical Laboratory, Wright Air Development Center, Air Research and Development Command, U.S. Air Force, Wright-Patterson Air Force Base, Ohio. Armed Services Technical Information Agency. Arlington Hall Station, Va.

Nieminen, M., J. Timisjarvi, and M. Laitinen. 1980. The effects of antiparasitic treatment on the condition of semi-domestic reindeer (*Rangifer tarandus*). Reports from the Kevo Subarctic Research Station (Finland) 16:23-26.

Nordkvist, M. 1975. Large scale field trials against larvae of *Oedemagena tarandi* and *Cephenomyia trompe* in Swedish reindeer. Biological Papers of the University of Alaska 1 :518-522.

O'Brien, R. D., and C. E. Dannelley. 1965. Penetration of insecticides through rat skin. Journal of Agricultural and Food Chemistry 13:245-247.

O'Brien, R. D., E. C. Kimmel, and P. R. Sferra. 1965. Toxicity and metabolism of famphur in insects and mice. Journal of Agricultural and Food Chemistry 13:366-369.

Pasarela, N. R., R. E. Tondreau, W. R. Bohn, and G. O. Gale. 1967. Gas chromatographic determination of famphur and its oxygen analog residues in bovine milk, blood, and edible tissues. Journal of Agricultural and Food Chemistry 15:920-926.

Powell, G. V. N., and D.C. Gray. 1980. Dosing free-living nestling starlings with an organophosphate pesticide, famphur. Journal of Wildlife Management 44:918-921.

Randell, W. F., and R. E. Bradley. 1980. Effects of injectable famphur on young Brahman and Angus cattle. American Journal of Veterinary Research 44:1423-1426.

Ryan, J. J., and H. A. McLeod. 1979. Chemical methods for the analysis of veterinary drug residues in foods. Part I. Residue Reviews 71:1-82.

Schafer, E. W. 1972. The acute oral toxicity of 369 pesticidal, pharmaceutical and other chemicals to wild birds. Toxicology and Applied Pharmacology 21:315-330.

Seel, D.C. 1985. Magpie containing warble-fly insecticide. British Birds 78:302-303.

Sine, C., editor. 1991. Farm Chemicals Handbook '91. Meister Publishing Company, Willoughby, Ohio.

Smith, G. J. 1987. Pesticide use and toxicology in relation to wildlife: organophosphorus and carbamate compounds. U.S. Fish and Wildlife Service Resource Publication 170. 171 pp.

Smith, H. G, Jr., and R. L. Goulding. 1970. Toxicological aspects of three organophosphorus compounds (cythioate, famphur, and fenthion) in the host-ectoparasite system. Journal of Economic Entomology 63:1640-1646.

Tarry, D. W. 1986. Progress in warble fly eradication. Parasitology Today 2:111-116.

Teel, P. D., J. A. Hair, and T. C. Randolph, Jr. 1977. Continuous administration of famphur for control of ticks and bed bugs feeding on ruminants. Journal of Economic Entomology 70:664-666.

Teel, P. D., J. A. Hair, and L. G. Stratton. 1979. Laboratory evaluation of a sustained-release famphur bolus against Gulf coast and lone star ticks feeding on Hereford heifers. Journal of Economic Entomology 72:230-233.

Tucker, R. K., and D. G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. U.S. Fish and Wild-life Service Resource Publication 84. 131 pp.

Vaughan, J., and E. C. Turner, Jr. 1984. Residual and topical toxicity of various insecticides to the lesser mealworm (Coleoptera:Tenebrionidae). Journal of Economic Entomology 77:216-220.

Watson, K., and W. D. Black. 1981. Whole blood cholinesterase activity in calves after topical treatment with famphur. Canadian Veterinary Journal 22:179-181.

White, D. H., L. E. Hayes, and P. B. Bush. 1989. Case histories of wild birds killed intentionally with famphur in Georgia and West Virginia. Journal of Wildlife Diseases 25: 184-188.

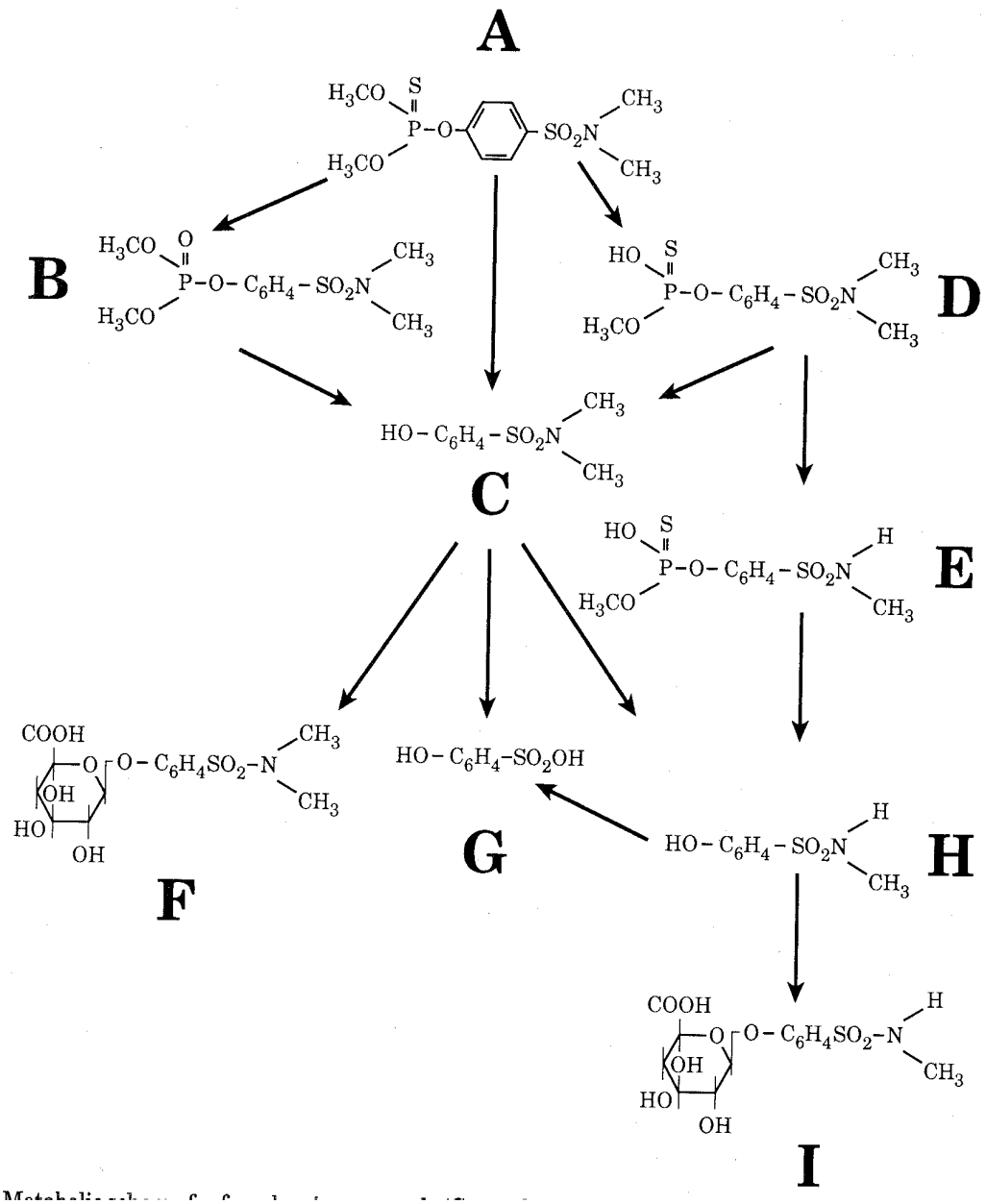


Figure. Metabolic scheme for famphur in mammals (Gatterdam et al. 1967). Major metabolic routes are indicated by an asterisk (*). A, famphur; B, famoxon; C, *p*-(N,N-dimethylsulfamoyl)phenol; D, *O*-desmethylfamphur; E, *O*, N-bisdesmethylfamphur; F, *p*-(N,N-dimethylsulfamoyl)phenyl glucuronide; G, *p*-hydroxybenzene sulfonic acid; H, *p*-(N-methylsulfamoyl)phenol; and I, *p*-(N-methylsulfamoyl)phenyl glucuronide. According to this scheme, famphur (A) initially undergoes oxidation at the P=S bond to yield famoxon (B), or hydrolysis at the P-*O*-phenyl bond to yield the transitory *p*-(N,N-dimethylsulfamoyl)phenol (C)*, or hydrolysis at one of the P-*O*-methyl bonds to yield *O*-desmethylfamphur (D)*. *p*, N,N-dimethylsulfamoyl)phenol (C) may also arise by hydrolysis of famoxon (B) or *O*-desmethylfamphur (D)*. p-(N,N-dimethylsulfamoyl)phenol (C) is immediately conjugated to fore *p*-(N,N-dimethylsulfamoyl)phenyl glucoronide (F)*, or transformed to *p*-hydroxybenzene sulfonic acid (G) or *p*-(N-methylsulfamoyl)phenol (H). *O*-desmethylfamphur (D) can also give rise to *O*, N-bisdesmethylfamphur (E)* by removal of one of the methyl groups of the sulfonamide moiety. *O*, N-bisdesmethylfamphur (E) is hydrolyzed to the corresponding transitory *p*-(N-methylsulfamoylphenol) (H)* which is immediately conjugated to yield the corresponding glucoronide, *p*-(N-methylsulfamoyl)phenyl glucuronide (I)*.

Biological Report 23
June 1994

Contaminant Hazard Reviews
Report 28

Acrolein Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

By
Ronald Eisler

U.S. Department of the Interior
National Biological Survey
Patuxent Environmental Science Center
Washington, D.C. 20240

TABLES

FIGURE

Suggested citation:

Eisler, R. 1994. Acrolein hazards to fish, wildlife, and invertebrates: a synoptic review. U. S. National Biological Survey Biological Report 23.

Acrolein Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by
Ronald Eisler

U.S. Department of the Interior
National Biological Survey
Patuxent Environmental Science Center
Washington, D.C. 20240

Abstract. Acrolein (CH_2=CHCHO) is the simplest member of the unsaturated aldehydes and enters the environment from incomplete combustion of fossil fuels, industrial discharges, herbicides, chemical control agents of fouling organisms, and normal metabolic processes of animals. Acrolein is volatile, flammable, and explosive. Biochemical and toxic effects of acrolein are caused by its reaction with sulfhydryl compounds to form a stable thiol ether. Acrolein metabolites under certain conditions are reportedly mutagenic, teratogenic, or carcinogenic. Acrolein degrades quickly in soils and in plant tissues; in water the half-time persistence is usually less than 50 h and in the atmosphere, less than 3 h. In treated irrigation canals, acrolein probably eliminates or seriously depletes all populations of aquatic fauna. Recommended herbicidal concentrations of acrolein for the control of submerged aquatic weeds usually exceed 1,000 µg/L; however, short-term tests with various species show that frog tadpoles die at 7 µg/L, representative fish are killed at 14 to 62 µg/L, and sensitive crustaceans are immobilized or die at 34 to 80 µg/L. Terrestrial plants and insects are comparatively resistant to acrolein; terrestrial plants tolerated 500 µg acrolein/L air and 25,000 µg/L in irrigation water, and adult fruitflies (*Drosophila melanogaster*), 3,700,000 µg acrolein/L culture medium. Birds are adversely affected by concentrations greater than 51 µg acrolein/kg whole egg by injection of eggs, greater than 9,100 µg/kg body weight (BW) by single oral doses, and greater than 50,000 µg/L (greater than 113 mg/m^3) by air concentrations. Mammals were affected by 50 µg acrolein/L air for 1 min, by 300 µg/L air for 10 min, and by intravenous injections of 850-6,000 µg/kg BW. Acrolein was fatal to mammals after exposure to 660 µg/L air for 24 days, 8,000-11,000 µg/L air for 4 h, 875,000 µg/L air for 1 min, and 4,000-28,000 µg/kg BW by single oral doses, or when fed diets equivalent to 500 µg/kg BW for 102 weeks. Proposed acrolein criteria for the protection of various resources include less than 15,000 µg/L in irrigation water of agricultural crops, less than 68 µg/L for aquatic fauna in acute exposures and less than 21 µg/L in chronic exposures, and less than 44 µg/L (less than 0.1 mg/m^3) in air for rats. No acrolein criteria are now available for the protection of avian and terrestrial wildlife. Acrolein criteria for the protection of human health include less than 320 µg/L in drinking water, less than 110 µg/L in air (less than 0.25 mg/m^3), and less than 0.68 µg/kg BW daily intake from all sources. More research is needed on acrolein and its metabolites.

Key words: Acrolein, aldehyde, herbicide, ecotoxicology, fish, aquatic plants, invertebrates, criteria.

Acrolein (CH_2=CHCHO) is an aldehyde that was first isolated in 1843 from the dry distillation of fats and glycerol (Beauchamp et al. 1985). It is now known that acrolein is ubiquitous in the environment; it is often present in trace amounts in foods and as a component of smog, fuel combustion products such as wood smoke, exhaust emissions from internal combustion engines, and cigarette smoke (Smith 1962; U.S. Environmental Protection Agency [EPA] 1980; Beauchamp et al. 1985). Atmospheric concentrations of acrolein over urban areas are between 2 and 7 µg/L; cigarette smoke, however contains about 10,000 µg of acrolein/L (Beauchamp et al. 1985). Acrolein is classified as a hazardous chemical because of its reactivity and flammability (EPA 1980). At low sublethal concentrations, acrolein is widely known for its acrid pungent odor and strong irritating effects on mucous membranes of the eyes and of the upper respiratory tract, its toxicity to cilia in all organisms, and its interference with nucleic acid synthesis in bacteria (Marano and Puiseux-Dao 1982; Beauchamp et al. 1985). In bulk, acrolein during storage or transfer is potentially hazardous if it becomes overheated or contaminated with water. For example, in 1982, 17,000 residents from Toft, Louisiana, were evacuated when two large tanks of acrolein began to burn (Bowmer and Smith 1984).

Acrolein enters the aquatic environment from its use as an aquatic herbicide, from industrial discharges, and as a byproduct of the chlorination of organic compounds in wastewater and drinking water treatment (EPA 1980). Dilute solutions of acrolein kill undesirable plant life in irrigation streams and ditches (National Research Council [NRC] 1977) and have been used routinely in about 4,000 km of irrigation canals in southeastern Australia to control submerged weeds, including *Potamogeton tricarinatus, Elodea canadensis,* and *Vallisneria gigantea* (Bowmer and Smith 1984). Acrolein has also been used for many years in channel maintenance in the United States (especially in western states), Canada, Egypt, Argentina, Mexico, and Turkey (Bowmer and Smith 1984). Unlike most other aquatic herbicides, acrolein rapidly dissipates from the water by volatilization and degradation without leaving phytotoxic residues (Bowmer and Smith 1984; Parent et al. 1992). However, acrolein provides only temporary control of submerged weeds and also kills fish and other aquatic life at recommended treatment concentrations (Bowmer and Smith 1984). In one Montana stream, acrolein killed all fish in a 4-km stretch after application to control submerged weeds; some fish deaths were recorded as far as 6.4 km downstream (Fritz-Sheridan 1982). Useful reviews on ecological and toxicological aspects of acrolein are presented by Smith (1962), EPA (1980), Beauchamp et al. (1985), and the Agency for Toxic Substances and Disease Registry [ATSDR] (1990).

This report is part of a continuing series of brief reviews of environmental contaminants and their effects on living organisms with special emphasis on fishery and wildlife resources. It was prepared in response to requests for information on acrolein from environmental specialists of the U.S. Fish and Wildlife Service.

Sources and Uses

General

Acrolein enters the environment as a result of normal metabolic processes; incomplete combustion of coal, wood, plastics, tobacco, and oil fuels; and industrial emissions. Acrolein has been detected in smog, foods, and water. It is used extensively in chemical manufacture, for control of fouling organisms, and as an herbicide to control submerged weeds in irrigation canals.

Sources

Acrolein is ubiquitous in the environment as a result of natural and anthropogenic sources. Sources of atmospheric acrolein include smog; incomplete combustion of coal, wood, gasoline, plastics and fats; tobacco smoke; and industrial emissions. The total amount of acrolein released into the atmosphere is unknown. In 1978, production losses of acrolein by emission from the four main U.S. plant locations were estimated at 34,682 kg; however, the gaseous emission streams are now either burned on emergence from the exhaust stack or sent to a furnace to destroy residual material (Beauchamp et al. 1985). Acrolein is found in photochemical smog and contributes to the smog's irritant capacity to the eye and respiratory pathways (Beauchamp et al. 1985; Leikauf et al. 1989). Recorded maximum acrolein concentrations in smog ranged from 12 to 14 µg/L (0.025 to 0.032 mg/m^3) in Los Angeles between 1961 and 1963 and were 13 µg/L in Hudson County, New Jersey (EPA 1980). For humans, exposure to atmospheric acrolein is greatest in the vicinity of incompletely combusted organic materials such as coal, wood, and petrol; highest acrolein concentrations are reported near forest fires and urban area fires (Beauchamp et al. 1985; Srivastava et al. 1992). The burning of southern pine (*Pinus* sp.), for example, generates 22 to 121 mg of acrolein/kg of burned wood (EPA 1980).

Acrolein is also in the smoke of burning plastic materials. Air samples from more than 200 fires in Boston, Massachusetts, contained greater than 3,000 µg acrolein/L (greater than 6.8 mg/m^3) in more than 10% of all samples; greater than 3,000 µg acrolein/L air is an immediately hazardous concentration for human life and health (Beauchamp et al. 1985). Cigarette smoke in some enclosed areas may account for as much as 12,400 µg of acrolein/L air (Feron et al. 1978; Astry and Jakab 1983; Beauchamp et al. 1985; Leikauf et al. 1989; Cohen et al. 1992). In the case of an enclosed room of 30 m^3 capacity, smoking 5 cigarettes raises the air concentration to about 50 µg acrolein/L and smoking 30 cigarettes, to 380 µg/L (EPA 1980).

Acrolein is also generated when animal or vegetable fats are subjected to high temperatures (Feron et al. 1978; EPA 1980). Acrolein was detected aboard submarines in trace concentrations as a degradation product during the heating of lubrication oils and edible fats (Lyon et al. 1970). Large amounts of acrolein are generated from exhausts of internal combustion engines (Astry and Jakab 1983; Heck et al. 1986; Ballantyne et al. 1989). Acrolein concentrations of 10,000 µg/L (23 mg/m^3) have been measured in nondiesel automobile exhausts, 2,900 µg/L in diesel engine emissions, and 2,600-9,600 µg/L in other internal combustion engines (EPA 1980). Acrolein concentrations in air from several urban areas in the United States ranged from a maximum of 10 µg/L in 1960 to 1.8-3.4 µg/L in 1968; air in Tokyo during this period had an average acrolein concentration of 7.2 µg/L (Beauchamp et al. 1985). Urban acrolein pollution is derived mainly from automobile exhaust and incomplete burning of refuse (Beauchamp et al. 1985). Acrolein is formed during normal metabolic degradation of spermine and spermidine, glycerol, allyl formate, allyl alcohol, and cyclophosphamide (EPA 1980; Marano and Puiseux-Dao 1982; Leach et al. 1987). Acrolein was also in spores from the wheat stem fungus (*Puccinia graminis*) of infected wheat (*Triticum aestivum*); acrolein was the major chemical factor that normally induced infection structure formation in Puccinia (Macko et al. 1978).

Acrolein has been detected in effluent-water streams from industrial and municipal sources. Municipal effluents from Dayton, Ohio, for example, contained between 20 and 200 µg acrolein/L in 6 of 11 analyzed samples (EPA 1980; Beauchamp et al. 1985). Acrolein is also a component of many foods, and processing may increase the acrolein content (EPA 1980). Acrolein has been identified in raw turkey, potatoes, onions, coffee grounds, raw cocoa beans, alcoholic beverages, hops (EPA 1980), white bread, sugarcane molasses, souring salted pork, and cooked bluefin tuna (*Thunnus thynnus*; Beauchamp et al. 1985).

Occupational exposure to acrolein may occur during its production and isolation as a chemical intermediate or during the manufacture of acrylic acid, acrylic acid esters, and methionine (Beauchamp et al. 1985). Other sources of acrolein in the workplace include emissions from rubber vulcanization plants, from welding of metals treated with anticorrosion primers, and from pitch-cooking plants and skin contact with herbicides during applications for aquatic weed control and with paper and paperboard, the manufacture of which includes acrolein as a slimicide. Acute acrolein poisoning from occupational exposure is improbable. However, the risks of poisoning are significant in certain industries including welding of fat and oil cauldrons, smelting work and foundry operations, printing plants, linoleum and oil cloth factories, manufacture of insulators, tin plating of sheet iron, and processing of linseed oil (Beauchamp et al. 1985).

Uses

Since its discovery in 1843, acrolein has been known to polymerize readily in the presence of many chemicals, and since 1947 it has been used safely in a wide variety of commercial applications (Albin 1962; Fischer 1962). Acrolein is presently produced by the catalytic oxidation of propylene for the manufacture of methionine, glutaraldehyde, 1,2,6-hexane thiol, and other chemicals. The largest quantity of acrolein produced by this process is converted directly to acrylic acid and acrylic acid esters (Beauchamp et al. 1985). In 1975, global production of acrolein was 59,000 metric tons; in 1980, this value was 102,000 tons--including 47,600 tons produced by the United States (EPA 1980). In 1983, about 250,000 tons (about 550 million pounds) of acrolein were produced; 92% was converted to acrylic acid and 5% to methionine; 3% was used as an aquatic herbicide (Beauchamp et al. 1985; Heck et al. 1986). Acrolein copolymers are used in photography, in textile treatment, in the paper industry, as builders in laundry and dishwater detergents, and as coatings for aluminum and steel panels (EPA 1980). Acrolein is used to scavenge sulfides from oil-field floodwater systems (Kissel et al. 1981), to crosslink protein collagen in the leather tanning industry, and to fixate tissue of histological samples (EPA 1980). The use of acrolein as a military poison gas has been advocated because of its lacrimatory and blistering properties; during World War I the French used acrolein under the name of Papite in hand grenades because of its irritating effect on the respiratory airways and the ocular mucosa (Beauchamp et al. 1985).

Acrolein has been used since 1960 to control submerged aquatic weeds in irrigation systems in the United States, Australia, and other countries where open channels distribute water for crop production (Hill 1960; Bartley and Hattrup 1975; Bowmer and Higgins 1976; EPA 1980; Reinert and Rodgers 1987). Acrolein is preferable to sodium arsenite for herbicidal control of submerged weeds because arsenicals are persistent (as long as for 1 year) and the high arsenic concentrations that are attained in water may be hazardous to humans and livestock (Hill 1960). Acrolein is extremely effective in killing submerged weeds that are difficult to control with other herbicides (Hill 1960). Acrolein has also been used as an herbicide in ponds, drains, and other bodies of water (Donohue et al. 1966). In Australia, the concentration of acrolein in irrigation canals to control various species of *Elodea, Potamogeton,* and *Vallisneria* is usually less than 15,000 µg/L (Bowmer and Higgins 1976). In general, acrolein has a low order of toxicity to terrestrial plants (Donohue et al. 1966). Most field and garden crops can tolerate water with as much as 15,000 µg acrolein/L without serious adverse effects (Bartley and Hattrup 1975). Acrolein, as discussed later, has comparatively low persistence and low accumulation in aquatic ecosystems. One disadvantage to its use as an herbicide is its pungent, irritating odor (Hill 1960). At recommended treatment concentrations, however, acrolein kills fish and other aquatic organisms; therefore, acrolein should be used only in aquatic systems where these resources are considered expendable (Reinert and Rodgers 1987).

Acrolein has been used to control bacteria, fungi, algae, and molluscs in cooling-water systems: 1,500 µg/L killed as much as 95% of the target species in a once-through treatment (Donohue et al. 1966). Acrolein has been applied directly to the marine environment to control the growth and settlement of mussels (*Mytilus edulis*) and other fouling organisms in cooling-water systems of coastal steam-electric-station power plants (EPA 1980; Rijstenbil and van Galen 1981). Mussels in marine cooling-water systems are controlled with 600 µg acrolein/L for 8 h daily for 3 days or with 700 µg/L for 3 h daily for 2 weeks (Rijstenbil and van Galen 1981). Acrolein prevents the growth of microorganisms in liquid fuels such as jet fuels, in feed lines of subsurface wastewater injectors, and in water conduits of paper manufacturing plants (EPA 1980; Beauchamp et al. 1985).

Environmental Chemistry

General

Acrolein, the simplest member of the class of unsaturated aldehydes, has a pungent, irritating odor. It is volatile, flammable, and explosive and requires elaborate and specific conditions for storage and use. The half-time persistence of acrolein in freshwater is usually less than 50 h; in seawater it is less than 20 h and in the atmosphere less than 3 h. Biochemical and toxic effects of acrolein are caused by its rapid and essentially irreversible reaction with sulfhydryl compounds to form a stable thiol ether; however, many compounds can mitigate or block its toxicity. Acrolein is eventually metabolized to acrylic acid and glyceraldehyde; glycidaldehyde--an intermediate metabolite with mutagenic and carcinogenic properties--has been produced in vitro but not in vivo.

Chemical Properties

Acrolein is soluble in water and in many organic solvents including ethanol, acetone, and ether (Table 1; Beauchamp et al. 1985). Acrolein is a highly reactive molecule with two reactive centers: one at the carbon-carbon double bond and the other at the aldehydic group. Typical reactions involving acrolein are shown in detailed figures in Beauchamp et al. (1985). Acrolein is extremely volatile, flammable, and explosive (Table 1; Reinert and Rodgers 1987), especially in sunlight or in the presence of alkali or strong acid (Albin 1962; EPA 1980). A potential hazard in handling acrolein is its rapid exothermic polymerization caused by the use of insufficient hydroquinone inhibitor or lack of strict control of pH (Beauchamp et al. 1985). Commercial acrolein should be maintained at pH 6.0 and contain less than 3% water and 0.1-0.25% hydroquinone as a polymerization inhibitor. Atypical commercial sample contains about 97% acrolein, 0.5% other carbonyls, and 2.5% water. The addition of hydroquinone (0.1-0.25%) prevents the vinyl polymerization of acrolein, and controlling the pH between 5 and 6 by acetic acid increases stability of commercial acrolein by preventing aldol condensation. Elaborate and specific conditions are now prescribed for the storage of acrolein and include vents and safety valves, construction materials, fire control, spills, and waste disposal (Beauchamp et al. 1985). Commercial acrolein is stored and shipped under a blanket of oxygen-free inert gas (Albin 1962).

Table 1. Chemical and other properties of acrolein.[a]

Variable	Data
Chemical name	2-Propenal
Alternate names	Acraaldehyde, acraldehyde, acrolein, acryladehyde, acrylaldehyde, acrylic aldehyde, allyl aldehyde, aqualin, aquilin, Magnacide H, propenal
CAS Number	107-02-8
Structural formula	CH_2=CHCHO
Molecular weight	56.06
Specific gravity	0.8427-0.8442
Physical state	Colorless or yellow liquid at 25° C
Odor	Pungent, irritating
Boiling point	52.5-53.5° C
Melting point	-86.95° C
Solubility	
Water	206-208 g/L
Organic solvents	Miscible
Log K_{ow}	0.01
Vapor pressure	215-220 mm Hg at 20° C
Explosive limits of vapor and air	
Upper limit	31% acrolein
Lower limit	2.8% acrolein

[a] Hill (1960), Anderson and Hood (1962), Folmar (1977), EPA (1980), Hudson et al. (1984), Beauchamp et al. (1985), Mayer (1987), Reinert and Rodgers (1987), Ballantyne et al. (1989), Sine (1991), Agency for Toxic Substances and Disease Registry [ATSDR] (1990), National Institute for Safety and Health [NIOSH] (1990).

Spectrophotometric determination with 4-hexylresorcinol and a fluorometric method with m-aminophenol are the most commonly used procedures for the determination of acrolein; however, gas chromatography and high performance liquid chromatography procedures are also used (EPA 1980; Kissel et al. 1981; Nishikawa and Hayakawa 1986). Acrolein concentrations in rainwater between 4 and 200 µg/L can be measured rapidly (in less than 80 min) without interference from related compounds; the method involves acrolein bromination and analysis by gas chromatography with electron capture detection (Nishikawa and Hayakawa 1986). Kissel et al. (1981) emphasize that water samples from potential acrolein treatment systems require the use of water from that system in preparing blanks, controls, and standards and that acrolein measurements should be made at the anticipated use concentrations.

Persistence

Degradation and evaporation seem to be the major pathways for acrolein loss in water; smaller amounts are lost through absorption and uptake by aquatic organisms and sediments (EPA 1980; Reinert and Rodgers 1987). The half-time persistence of acrolein in freshwater is 38 h at pH 8.6 and 50 h at pH 6.6; degradation is more rapid when initial acrolein concentrations are less than 3,000 µg/L (Bowmer and Higgins 1976). At pH 5, acrolein reacts by reversible hydrolysis to produce an equilibrium mixture with 92% beta-hydroxypropionaldehyde and 8% acrolein; in alkali, the primary reaction is consistent with a polycondensation reaction (EPA 1980). In natural waters, acrolein degradation proceeds to carboxylic acid via a microbial pathway (EPA 1980); beta-hydropropionaldehyde is readily biotransformed in about 17.4 days (Reinert and Rodgers 1987).

Acrolein is applied to irrigation canals to control submerged aquatic weeds at greatly different time-concentration treatments. Regardless of time-concentration regimens--which vary from 100 µg/L for 48 h in the United States to 15,000 µg/L for several hours in Australia--the daily decay rate constants are remarkably

similar, ranging from 0.14 to 0.21, and are probably affected by variations in weed density (O'Loughlin and Bowmer 1975; Parent et al. 1992). In one case, acrolein applied to the Columbia River at an average initial concentration of 125 µg/L degraded to 25 µg/L after 48 h in samples greater than 65 km from the application point--a loss of 80% (EPA 1980). High initial concentrations (50,000 - 160,000 µg/L) of acrolein in natural waters degraded 57 to 80% in 192 h, suggesting that high concentrations can alter the rate of hydrolysis (Kissel et al. 1981). In seawater, the half-time persistence of acrolein was less than 20 h (Rijstenbil and van Galen 1981). In photochemical smog, acrolein is comparatively unstable and not likely to persist; the dominant removal mechanism involves hydroxide attack on acrolein, and the atmospheric half-life persistence is 2-3 h under these conditions (Beauchamp et al. 1985).

Metabolism

Biochemical and toxic effects of acrolein are probably caused by its reaction with critical protein and nonprotein sulfhydryl groups (EPA 1980; Beauchamp et al. 1985; Heck et al. 1986). The reaction of acrolein with sulfhydryl compounds is rapid and essentially irreversible, resulting in the formation of a stable thiol ether (Beauchamp et al. 1985; Heck et al. 1986). Metabolism of acrolein is believed to result in the formation of acrylic acid and glyceraldehyde (Figure). The postulated metabolites of acrolein can be oxidized to carbon dioxide (Beauchamp et al. 1985). Acrylic acid does not seem to represent a significant toxic hazard when compared with the parent acrolein because at low airborne concentrations of less than 1,000 acrolein/L, the quantity of acrylic acid produced by metabolism is negligible. Thus, metabolism to acrylic acid after inhalation should be regarded as a detoxification pathway. Conjugation of acrylic acid with glutathione represents another elimination and detoxification pathway (Beauchamp et al. 1985). In-vitro studies of acrolein metabolism in mammals suggested that acrolein exposures may result in exposure to glycidaldehyde, an intermediate in acrolein metabolism (Figure). The major toxic effects of acrolein exposure--including irritation, ciliastasis, and hypersensitivity--are probably due either to the parent acrolein or to the reaction of glycidaldehyde with cell proteins. Glycidaldehyde is a potent mutagen and carcinogen; however, no evidence is available showing that acrolein can produce glycidaldehyde in vivo (Beauchamp et al. 1985). Acrolein is more toxic when inhaled than when taken orally (EPA 1980). Inhalation of acrolein decreased the concentrations of protein and nonprotein sulfhydryl groups in nasal mucosal tissue (Heck et al. 1986). Acrolein is highly reactive towards thiol groups and rapidly conjugates with glutathione and cysteine (EPA 1980). When glutathione is depleted, acrolein potentiates the nasal toxicity of formaldehyde to rats (Heck et al. 1986).

Acrolein is a metabolite of allyl alcohol and cyclophosphamide, and these compounds should be considered in acrolein metabolism schemes (Beauchamp et al. 1985; Cohen et al. 1992). Allyl alcohol in the presence of NADPH and liver or lung microsomes degrades to acrolein, acrylic acid, and glycidol (Figure).

When added to water as an aquatic herbicide, acrolein undergoes rapid decomposition, especially in the sunlight. At the same time, it reacts rapidly with amines, alcohols, and mercaptans of aquatic plants, destroying cell structure and killing the plants (Parent et al. 1992). Mammals drinking acrolein-contaminated water rapidly convert acrolein to saturated alcohol compounds because of the low pH in the upper portion of their GI tracts; the primary breakdown product is beta-propionaldehyde (EPA 1980).

Many compounds including glutathione, 2-mercaptoethanol, beta-dimethylcysteamine, penicillamide, gamma-mercaptopropionylglycine, and N-acetylcysteine mitigate or block the toxic effects of acrolein (EPA 1980; Beauchamp et al. 1985; Heck et al. 1986). In frogs (*Rana japonica*), sulfhydryl compounds reduce the effects of acrolein on excitation-contraction uncoupling in skeletal muscle (Fujino et al. 1985). In mice, cysteine reduced the cytotoxic effects of acrolein on tumor cells; in rabbits, cysteine mitigated acrolein-induced alveolar macrophage calcium-dependent ATP-ase, phagocytosis, and adhesiveness (EPA 1980). In male rats, cysteine and ascorbic acid antagonized the acute lethal effects of orally-administered acrolein, and 2-mercaptoethanol antagonized the inhibitory effect of acrolein on liver DNA-polymerase (EPA 1980).

Lethal and Sublethal Effects

General

Acrolein degrades quickly in soils and in plant tissues regardless of mode of administration. Most terrestrial crop plants easily tolerate 25,000 µg of acrolein/L of irrigation water and some can tolerate 70,000-80,000 µg/L without adverse effects. Terrestrial plants were adversely affected at atmospheric concentrations of 500 µg

acrolein/L air, but this concentration exceeds the recommended value of 110 µg/L (0.25 mg/m^3) air for protection of human health in occupational settings.

Adult fruitflies (*Drosophila melanogaster*) were comparatively resistant to acrolein and had lowered survival when reared in culture media with greater than 3,700,000 µg acrolein/L. At recommended concentrations for the control of nuisance submerged aquatic weeds (frequently 100-1,000 µg/L, often greater than 9,600 µg/L), acrolein was lethal or harmful to almost all aquatic vertebrates and invertebrates tested in short-term exposures. The most sensitive groups of tested aquatic organisms in short-term assays were frog tadpoles (dead at 7 µg/L) and representative species of fish (reduced survival at 14-62 µg/L) and crustaceans (death or immobilization at 34-80 µg/L). Adverse effects of acrolein on birds were observed at acute oral doses of 9,100 µg/kg BW (reduced survival), at concentrations greater than 51 µg/kg egg for egg injection (abnormal development and reduced survival), and at greater than 50,000 µg/L air (respiratory tract histopathology): In mammals, acrolein is a strong cytotoxic and ciliostatic agent that is irritating to mucous membranes of dermal, ocular, gastrointestinal, and respiratory systems and is systemically toxic by all routes of exposure. Adverse effects of acrolein are documented in sensitive species of mammals under the following regimens: 50 µg/L air for 1 min (increased blood pressure and heart rate); 300 µg/L air for 10 min (ocular and nasal irritation); 500 to 1,000 µg/L air (repelled by odor); 660 µg/L air for 24 days (reduced survival); 8,000 to 11,000 µg/L air for 4-6 h or 875,000 µg/L air for 1 min (death); dietary concentrations equivalent to 500 µg/kg BW for 102 weeks (decreased survival); 850-6,000 µg/kg BW by intravenous injection (liver necrosis, embryo resorption); and single oral doses between 4,000 and 28,000 µg/kg BW (death).

Acrolein was mutagenic to certain microorganisms and to the fruitfly; mutagenicity may be due, in part, to glycidaldehyde, an acrolein metabolite. Injected into the amniotic fluid, acrolein is teratogenic to rats; teratogenicity may be due to acrylic acid, an acrolein metabolite. There is limited evidence that acrolein acts as a weak carcinogen and tumor promoter. Acrolein interacts with other chemicals, sometimes synergistically, additively, or antagonistically. Also, some chemicals normally contain acrolein as an impurity or yield acrolein as a metabolite.

Terrestrial Plants and Invertebrates

Most crop plants easily tolerate irrigation water with 25,000 µg of acrolein/L and many tolerate 70,000 to 80,000 µg/L without adverse effects--including corn (*Zea mays*), cotton (*Gossypium hirsutum*), milo (*Sorghum spp*.), squash *(Cucurbita* spp.), castor bean (*Ricinus communis*), tomato (*Lycopersicon esculentum*), alfalfa (*Medicago sativa*), and sugarcane (*Saccharum officinarum*; Ferguson et al. 1961). Acrolein degrades quickly in soils and plant tissues regardless of mode of administration (Ferguson et al. 1961). Atmospheric concentrations of 500 µg acrolein/L and higher were harmful to certain plants (Beauchamp et al. 1985). Leaves of the pinto bean (*Phaseolus* spp.) and the morning glory (*Ipomoea* spp.) developed brown foliar lesions after exposure to 500 µg/L air for 4-7 h; damage was more severe if the plants were moist during exposure. Leaves of the radish (*Raphanus* spp.) developed lesions after exposure to 1,500 µg acrolein/L air for 6-7 h; however, leaves of the geranium (*Geranium* spp.) and the tomato showed no adverse effects after exposure to 1,500 µg/L air for 7 h (Beauchamp et al. 1985).

Acrolein inhibits DNA, RNA, and protein synthesis in the bacterium *Escherichia coli*, and this inhibition probably accounts for its cytotoxic and inhibitory effects on *E. coli* cell division (EPA 1980; Beauchamp et al. 1985). Acrolein is demonstrably mutagenic to microorganisms and to larvae of the fruitfly (*Drosophila melanogaster*). Acrolein-induced mutagenicity--including point mutations, sister chromatid exchanges, and chromosome breakages--has been observed in selected strains of bacteria (*E. coli, Salmonella typhimurium*), yeast (*Saccharomyces cerevisiae*), fruitfly larvae, and cultured Chinese hamster ovary cells (EPA 1980; Beauchamp et al. 1985; Sierra et al. 1991; Cohen et al. 1992). Acrolein's mutagenicity may be due to the metabolite glycidaldehyde; glycidaldehyde was mutagenic to bacteria and yeast under controlled conditions (Beauchamp et al. 1985; Sierra et al. 1991). Studies with *D. melanogaster* show that acrolein is mutagenic in the sex-linked recessive lethal test when injected but not when fed (Sierra et al. 1991). Acrolein caused 2.2% sexlinked mutations in *D. melanogaster*--the highest percentage recorded among several tested aldehydes (EPA 1980). In studies by Comendador (1984), early embryonic stages of fruitflies were most sensitive to the mutagenic properties of acrolein and sensitivity decreased with increasing development to the point that adults showed negligible mutagenic responses. Adults of the fruitfly were generally resistant to acrolein; mortality was

25% when the culture medium contained 3,700,000 µg of acrolein/L, 50% at 8,600,000 µg/L, and 75% at 22,100,000 µg/L (Comendador 1984).

Aquatic Organisms

Adverse effects of acrolein on sensitive groups of aquatic organisms are documented (Table 2) at concentrations--in µg acrolein/L medium--as low as 7 for frog tadpoles (death), 14-62 for fish (death), 34-80 for crustaceans (death, immobilization), 50 for oysters (reduction in shell growth rate), 100-200 for freshwater algae (DNA and RNA reduction, photosynthesis inhibition), 151 for gastropods (death), >151 for insects (death), 500-2,000 for macrophytes (leaf cell deterioration, death), 1,250 for trematodes (death of miracidia in 20 min), and 62,000 for bacteria (growth reduction). Aquatic vertebrates were more sensitive than invertebrates (Holcombe et al. 1987), and younger fish were more sensitive than older fish (Burdick et al. 1964). Aquatic insects do not avoid acrolein at concentrations that repel fish (Folmar 1978).

As an herbicide, acrolein is most effective in controlling dense accumulations of submerged weeds in habitats where waterflow is rapid and uniform, such as irrigation canals and rapidly-flowing streams (Ferguson et al. 1961). Acrolein is lethal to various genera of submerged plants (*Hydrodictyon, Spirogyra, Potamogeton, Zannichellia, Cladophora, Ceratophyllum, Elodea, Chara, Najas*) at 1,500 to 7,500 µg/L (Ferguson et al. 1961; Beauchamp et al. 1985). But some floating plants (*Pistia, Eichhornia, Jussiaea*) are more resistant to acrolein than submerged plants and require concentrations that are at least double those necessary for submerged forms (Ferguson et al. 1961). Acrolein has little effect on emergent aquatic macrophytes and should not be used to control emergents (Ferguson et al. 1961). In Australia, acrolein is the only herbicide now used for control of submerged aquatic weeds in larger irrigation canals (Bowmer et al. 1979); effective plant control was obtained at 9.6-28.8 mg/L for 3 h (Bowmer and Smith 1984). In the United States, the U.S. Bureau of Reclamation controls aquatic algae and weeds at lower concentrations (0.1 mg/L) and longer exposures (48 h; Folmar 1980). In the Columbia River basin in the state of Washington, acrolein is used to control submerged aquatic macrophytes at concentrations of 0.1 mg/L for 48 h or 1.0 mg/L for 4 to 8 h with applications every 3 to 5 weeks (Bartley and Hattrup 1975). Vegetation destruction by acrolein is maximal 1 week after application, and green filamentous algae are usually the first plants to return after 1 month (Ferguson et al. 1961). Biomass and species diversity were altered in acrolein-treated phytoplankton populations in Egyptian irrigation canals 1 year after treatment (Kobbia 1982). Although acrolein is a powerful cytotoxic agent, its inhibitory effects at sublethal concentrations on plant mitosis, nucleic acid synthesis, and protein synthesis are considered completely reversible (Marano and Puiseux-Dao 1982).

Table 2. Acrolein effects on representative aquatic organisms.

Taxonomic group, organism, concentration, and other variables	Effect	Reference[a]
Bacteria, Algae, and Macrophytes		
Fresh water algae, *Anabaena* sp.; 690 µg/L; 24-h exposure	50% reduction in photosynthesis at 25° C	1
Aquatic bacteria, 3 species		
62,000 µg/L; 48-h exposure	Some growth reduction, but recovery by 120 h	2
125,000 µg/L; 120-h exposure	LC100	2
500,000 µg/L; 2-h exposure	LC100	2
Freshwater alga, *Cladophora glomerata*		
100 µg/L	Onset of photosynthesis inhibition at 30° C	1
760 µg/L; 24-h exposure	50% reduction in photosynthesis at 30° C	1

1,000 µg/L;24-h exposure	50% reduction in photosynthesis at 25° C	1
Alga, *Dunaliella bioculata*		
100 µg/L; 48-h exposure	DNA concentration reduced 28%	3
200 µg/L; 48-h exposure	DAN concentration reduced 36% and RNA 28%	3
400 µg/L; 48-h exposure	DNA reduced 93%, RNA 68%, and proteins 74%	3
1,000 µg/L; 48-h exposure	No development in 48 h	3
8,000 µg/L; 3-h exposure	Ultrastructural anomalies, and cytoplasmic inclusions	4
Elodea, *Elodea canadensis*		
Sublethal (actual exposure concentration and duration unknown)	Growth stimulation (from reduced competition by aufwuchs, bacteria, and epiphytic algae)	5
500 µg/L; 24-h exposure	Leaf cell deterioration	6,7
2,800 µg/L; 3-h exposure in irrigation canal	80% reduction in density; recovery began in 17 days	5
15,000 µg/L; 2-6 h exposure in Australian canals	Effective control for up to 21 km in flowing-water irrigation canals	8
18,000 µg/l; 2 to 12 h exposure in smaller channels and up to 72 h in major canals; New South Wales	Effective control	5
22,000 µg/L; 3-h exposure in irrigation canal	94% reduction in biomass after 14 days	5
Filamentous algae, unidentified		
500 µg/L; 5-months exposure; petroleum-refinery recirculating cooling-water system	Effective control	9
1,000 µg/L; 20-h exposure in Arizona irrigation canal	Effective control for 2 weeks	10
3,500 µg/L; 2-weeks exposure in petroleum refinery cooling water	Lethal	9
5,000 µg/L; 1-week exposure in petroleum refinery cooling water	Lethal	9
Freshwater alga, *Enteromorpha intestinalis*		
1,800 µg/L; 24-h exposure	50% reduction in photosynthesis at 25° C	1
2,500 µg/L for 24 h	50% reduction in photosynthesis at 20° C	1
>5,000 µg/L for 24 h	50% reduction in photosynthesis at 15° C	1
Freshwater plants; 6 species of submerged plants, 2 species of floating plants, 4 groups of phytoplankton; irrigation drains, Egypt; 15,000-25,000 µg/L for 45 min, repeated 4 times;	Effective control of all plants within 2-7 days, Phytoplankton recovery over 1-year period was most rapid for the Cyanophyceae, followed by the Bacilliarophyceae, Chlorophycae, and Euglenophyceae, and resulting in altered biodiversity when compared with a control canal	11

Submerged macrophytes, 3 species (*Najas* sp., *Ceratophyllum* sp., and *Ipomoea* sp.); 25,000 µg/L	All dead 1 week after application	6
Floating pondweed, *Potamogeton carinatus*		
2,000 µg/L for 12 h	LC50	12
10,000-15,000 µg/L for >1 h (actual exposure time unknown)	LC50	12
15,000 µg/L for 1.7 h	LC50	12
22,000-26,000 µg/L for >1 h (actual exposure time unknown)	LC80	12
Pondweed, *Potamogeton crispus;* 20,000 µg/L for 5 h	All dead in 8 days	6
Pondweed, *Potamogeton tricarinatus;* 4,000 µg/L; 1-h exposure in irrigation canal	Minimum effective concentration	5
Submerged macrophyte, *Vallisneria gigantea*; 26,000 µg/L for 1 h in irrigation canal	Minimum effective concentration	5
Ribbonweed, *Vallisneria spiralis*		
1,600 (95% confidence interval [CI] of 1,300-2,000) µg/L	50% reduction in biomass	12
3,700 (95% CI of 3,200-4,600) µg/L for 1 h	80% reduction in biomass	12
Invertebrates		
Snail, *Aplexa hypnorum*; 151 µg/L for 96 h	Less than 50% mortality	13
Snail, *Australorbis glabratus*		
1,250 µg/L for 24 h	All adults and 90% of embryos survived	7
2,500 µg/L for 24 h	35% of adults and 40% of embryos died	7
10,000 µg/L for 24 h	90% of adults and 100% of embryos died	6,7
Barnacle, *Balanus ebarneus*; 1,600-2,100 µg/L for 48 h	LC50	6
American oyster, *Crassostrea virginica*; 50-55 µg/L for 96 h	50% reduction in shell growth rate	6,14,15
Daphnid, *Daphnia magna*		
17-34 µg/L	MATC[b]	6,16
51 (95% CI of 43 to 62) µg/L for 48 h	50% immobilized	13
57-80 µg/L for 48 h	LC50	6
Mayfly, *Ephemerella walkeri*; 100 µg/L for 1 h	No avoidance of acrolein by nymphs	17
Freshwater snails, 3 species	All dead	14

(*Physa, Biomphalaria*, *Bulinus*); 25,000 µg/L for 3.5-4 h		
Common mussel, *Mytilus edulis*		
200-1,000 µg/L; exposed for as much as 8 h daily for 3 days	Valves closed immediately after start of exposure to acrolein regardless of concentration or duration; effect in 45% of mussels at 200 µg/L, 80% at 400 µg/L, and 90% at 600 µg/L	8
600 µg/L; single 8-h exposure followed by 48-h of uncontaminated seawater	70% of the mussels (1-2.5 mm shell length) in the cooling water systems of power plants became detached in 3 days vs. 13% of controls	18
600 µg/L; 8-h exposure daily for 3 days	97% of mussels became detached	18
600 µg/L; 29-h continuous exposure	100% detachment	18
Brown shrimp, *Penaeus aztecus*		
100 µg/L for 48 h	LC50	14
100 µg/L for 48 h	50% loss in equilibrium	6,15
Trematode, *Schistosoma mansoni*		
1,250 µg/L for 20 min	Killed all miracidia	7
2,500 µg/L	Killed all miracidia in 10 min, and all cercariae in 18 min	7
Midge, *Tanytarsus dissimilis*; 151 µg/L for 48 h	Less than 50% mortality	13
Vertebrates		
Bowfin, *Amia calva*; 62 µg/L for 24 h	LC50, fry	14
Goldfish, *Carassius auratus*		
80 µg/L for 24 h	LC50	6
1,000-2,000 µg/L for 3 h	Fatal	14
White sucker, *Catostomus commersoni*; 14 (95% CI of 8-25) µg/L for 96 h	LC50	13
Longnose killifish, *Fundulus similis*; 240 µg/L for 48 h	LC50	6,15
Western mosquitofish, *Gambusia affinis*		
61 µg/L for 48 h	LC50	6,14
149 µg/L for 24 h	LC50	14
Bluegill, *Lepomis macrochirus*		
13 µg/L for 28 days	Whole fish, bioconcentration factor of 344	6
33 (95% CI of 27-40) µg/L for 96 h	LC5	13
79 µg/L for 24 h	LC50	6,19
90-100 µg/L for 96 h	LC50	6,14

Largemouth bass, *Micropterus salmoides*		
160 µg/L for 96 h	LC50	6,14
183 µg/L for 24 h	LC50	14
Rainbow trout, *Oncorhynchus mykiss*		
8 µg/L for 48 h	None dead	20
16 (95% CI of 14-19) µg/L for 96 h	LC50	13
20, 50, or 100 µg/L; exposure for 4 h; trout collected 1, 4 and 7 days postexposure; cooked fillets evaluated for odor and taste by human panel	Unacceptable organoleptic qualities were recorded for fillets 1 and 4 days (P = 0.05) after treatment with 100 µg/L; some unacceptable qualities were detected 1 and 4 days after treatment with 50 µg/L, and at 7 days after treatment with 100 µg/L	17
29 (95% CI of 22-37) µg/L for 96 h	LC50	21
48 µg/L for 48 h	LC32	6, 20
65 µg/L for 24 h	LC50, fingerlings	6
77 µg/L for 20.5 h	LC50	21
90 µg/L for 4.8 h	No deaths	20
96 µg/L for 48 h	All dead	20
100 µg/L for 1 h	Avoidance by fry	6, 14, 23
150 µg/L	Lethal	22
240 µg/L for 4.8 h	LC10	20
410 µg/L for 4.8 h	LC70	20
>500 µg/L for 4.8 h	All dead	20
Chinook salmon, *Oncorhynchus tshawytscha*; 80 µg/L for 24 h	LC50	6, 19
Fathead minnow, *Pimephales promelas*		
11.4-41.7 µg/L	MATC[b]	6, 16
14 (95% CI of 8-25) µg/L for 96 h	LC50	13
84 µg/L for 6 days	LC50	6
115 µg/L for 48 h	LC50	6, 14
150 µg/L for 24 h	LC50	14
Harlequin fish, *Rasbora heteromorpha*; 130 µg/L for 48 h	LC50	14
Brown trout, *Salmo trutta*		
46 µg/L for 24 h	LC50	6, 14, 19
1,500 µg/L for 76-138 min	All dead	19
6,000 µg/L for 28-61 min	All dead	19
16,000 µg/L for 15-39 min	All dead	19
Frog, *Xenopus laevis*, tadpoles; 7 (95% CI of 6-8) µg/L for 96 h	LC50	13

[a] 1, Fritz-Sheridan 1982; 2, Starzecka 1975; 3, Marano and Puiseux-Dao 1982; 4, Baron-Marano and Izard 1968; 5, Bowmer and Smith 1984; 6, EPA 1980; 7, Ferguson et al. 1961; 8, Bowmer et al. 1979; 9, Donohue et al. 1966; 10, Corbus 1982; 11, Kobbia 1982; 12, Bowmer and Sainty 1977; 13, Holcombe et al. 1987; 14, Folmar 1977; 15, Mayer 1987; 16, Beauchamp et al. 1985; 17, Folmar 1978; 18; Rijstenbil and van Galen 1981; 19, Burdick et al. 1964; 20, Bartley and Hattrup 1975; 21; McKim et al. 1987; 22, Kissel et al. 1981; 23, Folmar 1976.

[b] Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Acrolein in concentrations sufficient to control nuisance submerged aquatic weeds may also kill snails, crayfish, shrimp, fish, and toads (Ferguson et al. 1961). In one case, acrolein was used to control *Potamogeton* and *Chara* in an Ohio farm pond during June 1960 (Hill 1960). Acrolein was applied at 16,100 µg/L to a 0.1 ha portion of the 0.7 ha pond. Within 1 h of application, many dead amphibian tadpoles and small bluegills (*Lepomis macrochirus*) were recovered. In 24 h, *Chara* had turned white and *Potamogeton* brown; both plant species seemed dead; fish were swimming in the treated area. In 72-96 h, several large dead walleyes (*Stizostedion vitreum vitreum*) were found. One week posttreatment, all algae and weeds in the treated area were dead; weeds were present in the untreated areas. The treated section remained weed-free for 4-6 weeks; after 8 weeks, the treated area was heavily infested with *Chara*. Hill (1960) concluded that tadpoles, walleyes, and small bluegills were more susceptible to acrolein toxicity than larger bluegills and bass (*Micropterus* spp.) in the pond. Acrolein is also effective in controlling trematodes that cause schistosomiasis wherein snails are the intermediate host, especially in irrigation systems. For example, native species of snails (*Lymnaea, Helisoma*), along with *Potamogeton* weeds, were destroyed within 12 km in the main irrigation canal of Kern County, California, after a single application of acrolein (Ferguson et al. 1961).

Acrolein was the most toxic of 15 herbicides tested for toxicity to fish (EPA 1980). Responses by rainbow trout (*Oncorhynchus mykiss*) surviving 77 µg acrolein/L, a concentration that killed 50% in about 21 h, were characteristic of respiratory irritants (McKim et al. 1987). These responses included a steady increase in cough rate; decreases in ventilation rate, oxygen utilization, and heart rate; increases in hematocrit; and decreases in total arterial oxygen, carbon dioxide, and pH (McKim et al. 1987). In studies by Bartley and Hattrup (1975), no-observable-effect concentrations of acrolein for rainbow trout were 240 µg/L for exposures of 4.8 h and 48 µg/L for exposures of 48 h; these values are below the concentrations that control aquatic weeds. In the same study, rainbow trout that survived exposure to high sublethal concentrations for 48 h were unable to recover completely after acrolein treatments were ended. Trout and other teleosts are poorly adapted to detoxify acrolein and other xenobiotic aldehydes (Parker et al. 1990). The low metabolic capacity of fish liver aldehyde dehydrogenase for aldehydes, in general, suggests that these compounds may be hazardous to fish populations (Parker et al. 1990). Applications of acrolein to waters where fish may be taken for human consumption should be made with caution; rainbow trout surviving exposure to acrolein in reservoirs or connecting canals frequently presented odor and taste problems to human consumers (Folmar 1980).

Acrolein is used also to control fouling organisms in cooling water systems. Effective control was established in a once-through cooling system of a steel mill with continuous application of 200 µg acrolein/L (Donohue et al. 1966). Acrolein controlled bacteria in condenser pipes of a powerplant cooling system but only at extremely high concentrations of 125,000 µg/L for 120 h or 500,000 µg/L for 2 h (Starzecka 1975). Acrolein reduced settlement of young mussels (*Mytilus* sp.) in cooling seawater systems of power plants (Rijstenbil and van Galen 1981). In recirculating cooling water systems, algae and bacteria can be controlled at 500 µg/L for 5 months or at 5,000 µg/L for 1 week (Table 2).

Birds

Acrolein was lethal to birds at single oral doses of 9,100 µg/kg BW (Table 3). Observed signs of acrolein poisoning in subadult mallards (*Anas platyrhynchos*) after oral administration included regurgitation, a reluctance to leave the swimming area, slow responses, muscular incoordination, heavy-footed walking, phonation, wing tremors, running and falling, weakness, and withdrawal (Hudson et al. 1984). Treatment concentrations as low as 3,300 µg/kg BW have produced signs of acrolein poisoning. These signs appeared as soon as 10 min after administration and persisted for as long as 36 days. At lethal oral concentrations, deaths occurred as soon as 32 min posttreatment and continued for several days (Hudson et al. 1984). Acrolein was lethal to developing avian embryos when whole eggs were injected with 51 to 182 µg/kg FW; in descending order, embryos were most sensitive when acrolein was administered by way of the yolk sac (51 µg/kg), by the inner shell (82 µg/kg), and by the air sac (182 µg/kg; Table 3). Acrolein is 50 times more toxic to embryos of the domestic chicken (*Gallus* sp.) than acrylonitrile and 100 times more toxic than acrylamide (Kankaanpaa et al. 1979). Acrolein inhibits mucus transport in the trachea of the domestic chicken (Denine et al. 1971), probably

through ciliostatic action (EPA 1980). Adverse effects of acrolein were observed on chicken respiratory tract physiology and pathology at greater than 50,000 µg/L air (Table 3).

Table 3. Acrolein effects on birds.

Organism, route of administration, dose, and other variables	Effect	Reference[a]
Mallard, *Anas platyrhynchos*; oral route; 9,100 µg/kg body weight (BW), 95% confidence interval [CI] of 6,300-13,100 µg/kg BW	LD50, age 3-5 months	1
Domestic chicken, *Gallus sp.*		
Inhalation route		
Adults subjected to 50,000 or 200,000 µg acrolein/L (113 or 454 mg/m^3) air via an endotracheal cannula for up to 27 days	Decreases in trachea complement of ciliated and goblet cells; inhibited mucus transport activity in trachea; lymphocytic inflammatory lesions in the tracheal mucosa. Changes were more pronounced at the higher dose and with increasing exposure	2
Air sac injection route. Embryos, 2-3 days old; examined at day 13		
>127 µg/kg fresh weight (FW) whole egg	Dose-dependent decrease in survival	3
182 µg/kg FW whole egg	LD50	3
1,818 µg/kg FW whole eff	LD80	3
Air sac injection route. Embryos, 3-days old		
1 µg/kg FW whole egg	20% developmental abnormalities vs. 5% in controls	4
10 µg/kg FW whole egg	No malformations	4
1,000 µg/kg FW whole egg	Lethal	
Inner shell injection of membrane on heart route. Embryos, 72-76 h old; examined on day 14 of incubation		
25 µg/kg FW whole egg	No deaths or malformations	5
51 µg/kg FW whole egg	50% dead or malformed	5
82 µg/kg FW whole egg	LD50	5
102 µg/kg FW whole egg	71% dead, 6% malformed	5
203 µg/kg FW whole egg	97% dead, 3% malformed	5
Yolk-sac injection route. Embryos 3-days old, examined at day 14		
51 µg/kg FW whole egg	LD50	6
1,018 µg/kg FW whole egg	LD90; no evidence of increased teratogenicity over controls	6

[a] 1, Hudson et al. 1984; 2, Denine et al. 1971; 3, Chhibber and Gilani 1986; 4, Beauchamp et al. 1985; 5, Korhonen et al. 1983; 6, Kankaanpaa et al. 1979.

Malformations of the eye, coelom, neck, back, wings, and legs were observed in surviving acrolein-treated chicken embryos (Korhonen et al. 1983) after whole eggs were injected with greater than 51 µg acrolein/kg FW (Table 3). In other studies, acrolein showed no clear evidence of teratogenicity in chicken embryos, although there is a dose-dependent embryotoxic effect (Beauchamp et al. 1985; Chhibber and Gilani 1986). Acrolein-treated chicken embryos had a higher frequency of abnormal limbs, abnormal neck, and everted viscera than the controls, but the frequency was not dose-related. The overall incidence of abnormal embryos when treated at age 48 h was 24% but only 4% in controls; in embryos given acrolein at age 72 h, these values were 26% and 12% in controls (Chhibber and Gilani 1986).

Mammals

Acrolein is a strong cytotoxic and ciliostatic agent; its irritating effects on mucous membranes and its acute inhalation toxicity in mammals are well documented (Feron and Kruysse 1977; Feron et al. 1978; EPA 1980; Astry and Jakab 1983; Beauchamp et al. 1985; Leach et al. 1987; Leikauf et al. 1989). A characteristic of acrolein is its pungent, offensive, and acrid smell that is highly irritating to ocular and upper respiratory-tract mucosae (Beauchamp et al. 1985). Acrolein is toxic by all routes of exposure, and many of its toxic and biochemical effects are produced by interfering with critical sulfhydryl groups (Srivastava et al. 1992). In isolated rat-liver fractions, acrolein is a potent inhibitor of the high-affinity aldehyde dehydrogenase isozymes in mitochondrial and cytosolic fractions (Mitchell and Petersen 1988). Acrolein impairs DNA replication in vitro and inhibits certain mitochondrial functions (Feron et al. 1978). Studies with isolated rat livermembrane proteins revealed that acrolein inhibits plasma membrane enzymes and alters the membrane protein profile; this may be due to acrolein-induced polymerization of plasma-membrane proteins (Srivastava et al. 1992).

Measurable adverse effects of acrolein have been documented in representative species of mammals, but the severity of the effects are contingent on the mode of administration, concentration, dose, and duration of exposure (Table 4). Single oral doses of 4,000 µg/kg BW were lethal to guinea pigs and 28,000 µg/kg BW to mice; diets containing the equivalent of 500 µg/kg BW and more decreased survival in rats after 102 weeks (Table 4). Concentrations of 60,000 µg acrolein/L in drinking water had no measurable adverse effects on cows (*Bos* sp.) after 24 h; rats initially rejected drinking water containing 200,000 µg/L but eventually tolerated this concentration (Table 4). Dermal toxicity seems low; rabbits that were immersed up to their necks in water containing 20,000 µg acrolein/L for 60 min showed no adverse effects (Table 4). No dermal sensitization occurred in healthy female guinea pigs (*Cavia* spp.) after repeated skin exposures to acrolein (Susten and Breitenstein 1990). In undiluted liquid or pungent vapor form, however, acrolein produces intense irritation of the eye and mucous membranes of the respiratory tract, and direct contact with the liquid can produce skin or eye necrosis (Beauchamp et al. 1985). A single intravenous injection of 850 µg acrolein/kg BW produced liver necrosis in rats; 6,000 µg/kg BW caused increased embryo resorption in mice (Table 4). Rats receiving near-lethal doses of acrolein by subcutaneous injection had liver and kidney damage and lung pathology (EPA 1980). Although subcutaneous injections revealed LD50 values between 164,000 and 1,022,000 µg/kg BW in rabbits, these results are questionable because acrolein may be sequestered at the injection site and delay delivery to the systemic circulation (Beauchamp et al. 1985). A single intraperitoneal injection of 1,000 µg/kg BW caused peritonitis in rats, and 7,000 µg/kg BW was lethal to mice; daily injections of 1,000 µg/kg BW were eventually lethal to rats (Table 4). Sublethal intraperitoneal injections of acrolein induced ascites, increased hematocrit, and prolonged sleeping times (Beauchamp et al. 1985). Acquired tolerance to acrolein in mice given repeated intraperitoneal injections suggests that an increased metabolism can partially explain the acquired tolerance (Warholm et al. 1984).

The largest number of studies of the toxicity of acrolein in animals was conducted by way of inhalation, probably because acrolein has an appreciable vapor pressure under ambient conditions and inhalation is the principal exposure for humans (Beauchamp et al. 1985). Because of their intolerance to sharp and offensive odor and to intense irritation of conjunctiva and the upper respiratory tract, humans have not suffered serious intoxication from acrolein. The strong lacrimatory effect of acrolein usually is a warning to occupational workers. Physiological perception of acrolein by humans begins at about 500 to 1,000 µg/L air with eye and nasal irritation; the irritating effects compel afflicted individuals to immediately leave the polluted area (Beauchamp et

al. 1985). Laboratory animals died from inhalation of 8,000-11,000 µg/L after 4-6 h, mice from 875,000 µg/L after 1 min and rats from 660 µg/L after 24 days (Table 4). Animals dying from acute and subacute exposure to acrolein vapor had lung injury with hemorrhagic areas and edema (Albin 1962). Repeated exposures of hamsters, rats, and rabbits to high sublethal concentrations of acrolein caused ocular and nasal irritation, growth depression, and respiratory tract histopathology in all species (Feron and Kruysse 1977; Table 4). However, repeated exposures to low, tolerated concentrations of acrolein did not produce toxicological effects (Albin 1962), suggesting that acrolein effects are not cumulative and that minimal damage is quickly repaired.

Table 4. Acrolein effects on selected mammals

Organism, route of administration, dose, and other variables	Effect	References[a]
Cow, *Bos* sp.; drinking water route; lactating dairy cows given 60,000 µg acrolein/L for 24 h	No change in feed or water intake or milk production; acrolein residues in milk <500 µg/L	1
Dog, *Canis familiaris*; inhalation route		
220, 1,000 or 1,800 µg/L air (0.5, 2.3, or 4.1 mg/m^3); continuous exposure for 90 days	Low concentration group appeared normal and gained weight. At 1,000 µg/L, ocular and nasal discharges. At the high concentration, severe irritation evident plus nonspecific inflammation of brain, heart, lung, liver, and kidney; no deaths	2
400-600 µg/L air for 1-3 min	81-84% of acrolein retained; accumulations greater in upper respiratory tract than lower respiratory tract	3,4
700 or 3,700 µg/L air (1.6 or 8.4 mg/m^3); exposure for 8 h daily, 5 days	Low concentration group appeared normal and gained weight. High concentration group visibly affected with weight loss, excessive salivation, ocular discharges, labored breathing, and histopathology of lung, liver, and kidney; blood and serum chemistry normal	2
150,000 µg/L air (340 mg/m^3) for 30 min	LC50	3, 5, 6
Guinea pig, *Cavia* spp.; inhalation route		
200, 1,000 or 1,800 µg/L continuously for 90 days	The low concentration group appeared normal. At 1,000 µg/L, pulmonary inflammation and liver necrosis. At high concentration, all had nonspecific inflammation of brain, heart, lung, liver, and kidney	2
400-1,000 µg/L for 2 h	Decreased respiratory rate; effects reversed after exposure stopped	6,7

400-1,000 µg/L for as long as 12 h	Concentration-related increases in respiratory resistance together with prolonged and deepened respiratory cycles	3
700 or 3,700 µg/L; 8 h daily, 5 days weekly for 6 weeks	Low concentration group seemed normal. At high concentration, histopathology of lung, liver, and kidney	2
10,500 µg/L for 6 h	LC50	6
20,000 µg/L for 10 min	Bronchioconstriction	6
Cat, *Felis domesticus*; inhalation route		
650,000 µg/L air for 2.25 h	Died within 18 h	6
870,000 µg/L air for 2.5 h	Died during exposure	6
Human, *Homo sapiens*; inhalation route		
20 µg/L air	Threshold for affecting electrocortical activity	6
30-40 µg/L air	Odor threshold for the most acrolein-sensitive people	6
90-300 µg/L air	Increasing concentration and increasing exposure caused increasing eye blinking, irritation, and decreasing respiratory frequency	8
140-150 µg/L air for 2 min	Eye irritation in 30% of subjects	6
250 µg/L air for 5 min	Moderate irritation of sensory organs	3, 5
300 µg/L air for 10 min	Considerable acute irritation	8
300-500 µg/L air	Odor threshold for most people	3, 6
1,000 µg/L air for 1 min	Slight nasal irritation	3, 5
1,000 µg/L for 5 min	Moderate nasal irritation; intolerable eye irritation	3,5
1,800 µg/L air for 1 min	Slight eye irritation	3
5,500 µg/L air for 20 sec	Painful eye and nasal irritation	3, 5
21,800 µg/L air for 1 sec	Intolerable	3, 5
Syrian golden hamster, *Mesocricetus auratus*		
Gavage route; 1,000 µg/animal, equivalent to about 4,000 µg/kg BW	Fatal within a few hours	11, 12
Inhalation route		
400 or 1,400 µg/L air, exposure for 6 h daily, 5 days weekly for 13 weeks	No adverse effects at low concentrations nasal histopathology at high concentration	9
4,000 µg/L air (9.2 mg/m^3); 7 h daily, 5 days weekly for 52 weeks	No effect on survival; no indication of cancer. Abnormal behavior, growth retardation, increased lung weight, decreased liver weight, nasal histopathology	10
6,000 µg/L air (13.8 mg/m^3) for 4 h	Cytotoxic to airway cells	3
25,400 µg/L air for 4 h	LC50	6, 10
Mouse, *Mus* sp.		
Drinking water route; 24,000 µg/L for 18 months	Death	29

Inhalation route		
10 µg/L air continuously for 5 weeks	Some reduction in pulmonary compliance	4
1,000-2,000 µg/L (2.3-4.6 mg/m^3) air for 24 h	Decreased pulmonary ability to kill bacteria *Staphylococcus aureus* and *Proteus mirabilis*	3
1,700 µg/L air for 10 min	50% reduction in respiratory rate	6, 14
3,000 or 6,000 µg/L air for 8 h	Concentration-dependent impairment of pulmonary antibacterial responses	15
6,000-15,000 µg/L air; 6 h daily, 5 days weekly for 6 weeks	Decreased body weight (6%) in all test groups, but not concentration-related	3
66,000 µg/L for 6 h	LC50, 24 h post-exposure	6
175,000 µg/L air for 10 min	LC50	3, 5, 6
875,000 µg/L air for 1 min	LC50	3, 5, 6
Intraperitoneal injection route		
4,000 µg/kg BW; single injection	Plasma total lactic dehydrogenase activity (LDH) increased 5 times, with peak after 10 h	16
4,000 µg/kg BW; multiple daily or weekly injections	Progressively less pronounced effect on LDH activity	16
7,000 µg/kg BW; single injection	LD50	16
12,000 µg/kg BW; preceded by daily injections of 4,000 µg/kg BW for 5 days	50% mortality	16
Oral route; 28,000 µg/kg BW	Acute oral LD50	3, 4, 5, 6
Rabbit, *Oryctolagus* sp.		
Dermal route; immersed up to necks for 60 min in water with 20,000 µg/L	No adverse effects	1
Drinking water route		
9,000 µg/L for 13 days	Miscarriages	29
36,000 µg/L for 13 days	Stomach ulcers	29
Inhalation route		
400 or 1,400 µg/L; 6 h daily, 5 days weekly for 13 weeks	No adverse effects at low concentration; some signs of distress at 1,400 µg/L	9
600 µg/L; 4 h daily for 30 days	No ocular effects	2
1,700-2,400 µg/L for 10 min; with or without 1,000 µg ozone/L	Acrolein alone had no effect on respiratory rate. Ozone-acrolein mixtures produced a marked decrease in respiratory rate	6
4,900 µg/L air, 6 h daily, 5 days weekly for 13 weeks	Ocular and nasal irritation, growth depression, respiratory tract histopathology	10
6,500-10,500 µg/L; exposure duration unknown	Emphysema, tracheobronchitis, some deaths	2
10,500 µg/L air for 6 h	LC50	6
Intravenous injection route; 3,000, 4,500 or 6,000 ug acrolein/kg BW on day 9 of	Embryo resorption was significantly higher in 6,000 µg/kg group vs. controls, but was the same as	6

gestation; killed on day 28 of gestation	controls in lower concentration groups	
Percutaneous injection route		
164,000 µg/kg BW	LD50 for 20% acrolein in mineral spirits	3, 5
238,000 µg/kg BW	LD50 for 10% acrolein in mineral spirits	3, 5
335,000 µg/kg BW	LD50 for 20% acrolein in water	3, 5
562,000 µg/kg BW	LD50 for undiluted acrolein	3, 5
1,022,000 µg/kg BW	LD50 for 10% acrolein in water	3, 5
Domestic sheep, *Ovis aries*; inhalation route via cervical trachea; ewes, 3-4 years old; exposed to smoke containing high (but unknown) concentrations of acrolein for 20 min; killed 1-22 days after exposure	Within 24 h of exposure there was sloughing of total cervical tracheal epithelium and a 35% reduction in tracheal basal cells; trachea was normal 18-22 days after exposure	13
Baboon, *Papio anubis*; inhalation route. Juveniles exposed to air concentrations of 12,000-2,780,000 µg acrolein/L (272-63,100 mg/m^3) for 5 min, then tested for learned avoidance/escape response	Avoidance/escape response enhanced in all animals at all concentration tested. The group exposed to 1,025,000 µg/L air died with respiratory complications within 24 h post-exposure. The group exposed to the highest concentration of 2,780,000 µg/L for 5 min died within 90 min postexposure with severe respiratory complications	17
Laboratory white rat, *Rattus* sp.		
Dermal route; exposure duration and dose unknown	Skin burns; severe ocular effects	18
Drinking water route		
5,000, 13,000, 32,000, 80,000 or 200,000 µg/L for 12 weeks	Water consumption in the 200,000 µg/L group was reduced by about 33% for the first 3 weeks; by week 12, all groups appeared normal and had apparently adapted to the odor and taste of acrolein	4
80,000 µg/L for 3 days	Some deaths	29
100,000 or 250,000 µg/L for 124 weeks	No increase in tumors over controls; no decrease in survival	11
100,000, 250,000 or 625,000 µg/L for 120 weeks	No significant decrease in survival when compared to controls. The 100,000 µg/L group had a 30% frequency of liver neoplasms and a 5% frequency of adrenal cortex neoplasms; however, no neoplasms were found in the 250,000 µg/L group. The 625,000 µg/L group had a 10% frequency of liver neoplasms vs. 25% in controls	12
200,000 µg/L for 90 days	No adverse effects	1
600,000, 1,200,000 or 1,800,000 µg/L for 60 days	Rats in the two high-concentration groups refused to drink and all died, apparently from dehydration. In the low-concentration group 20% died, but survivors were not dehydrated and had no tissue pathology	4
625,000 µg/L for 100 weeks	No decrease in survival; 20% of females developed adrenal cortical ademonas and 10% had neoplastic	6

	nodules in the adrenal cortex vs. 0% in controls	
625,000 µg/L for 104 weeks	No decrease in survival. Increased frequency of adrenal cortex adenomas in females; 25% vs. 1.3% in controls	11
Inhalation route		
10 or 50 µg/L air for 1 min	Increased blood pressure and heart beat rate	19
10,500, 1,000, or 2,400 µg/L air for 3 h	At 500 µg/L and higher, effects on respiratory mucosa included depletion of nonprotein sulfhydryl (NPSH) concentration and slight decrease in protein sulfhydryl (PSH) concentration. Effects on olfactory mucosa showed no changes in PSH at all test concentrations, but significant depletion of NPSH in the two high-concentration groups	20
100, 1,000, or 3,000 µg/L air, exposed 6 h daily, 5 days weekly for 3 weeks	No adverse effects in the two low-concentration groups. The high concentration group had depressed spleen weight and body weight and extensive nasal histopathology	14
150, 510, or 1,520 µg/L air; continuous exposure for 61 days	At low concentration, no respiratory tract lesions or deaths. At 510 µg/L, bronchial epithelium abnormalities but all survived. At high concentration, reduced survival; bronchopneumonia and bronchial abnormalities in survivors	6
220 or 660 µg/L air; exposed continuously for 60 days	No deaths at 220 µg/L; 70% died within 24 days at 660 µg/L	2
220, 1,000 or 1,800 µg/L air; exposed continuously for 90 days	The low concentration group appeared normal and gained weight. At 1,000 µg/L, liver necrosis and pulmonary hemorrhage. At 1,800 µg/L, all had nonspecific inflammation of brain, heart, lung, liver, and kidney	2
400 µg/L air; exposed 6 h daily, 5 days weekly for 13 weeks	Nasal histopathology	9
400, 1,400, or 4,000 µg/L air; exposed 6 h daily, 5 days weekly for 62 days	Some bronchial histopathology at 1,400 µg/L; some deaths among males at 4,000 µg/L	6
520 µg/L (1.2 mg/m^3); continuous exposure for 30 days	Decreased growth, altered liver enzyme activity	3
550 ug/L air; continuous exposure for up to 77 days	Upper respiratory irritation, reduced resistance to infection by *Salmonella*, and increased pulmonary macrophages; all effects disappeared by day 63	6
700 or 3,700 µg/L air; exposed 8 h daily, 5 days weekly for 6 weeks	No adverse effects noted at low concentration. At 3,700 µg/L histopathology of lung, liver,	2

	and kidney	
2,000 µg/L air for 40 h	Increased hepatic alkaline phosphatase activity; increased liver and adrenal weight	3
2,500-5,000 µg/L air for 1 min	Cardioinhibitory effect that was reversed within 10 sec after inhalation of acrolein ceased	19
4,900 µg/L air; exposed 6 h daily, 5 days weekly for 13 weeks	50% mortality during first 4 weeks with no deaths thereafter. Survivors had depressed growth and respiratory tract histopathology	9
6,000-8,888 µg/L air; exposed 6 h daily, 5 days weekly for 3 weeks	Most died within 5 exposure days	14
8,000-8,300 µg/L air for 4 h	LC50 within 14 days; death due to lung injury	5, 6, 21
26,000 µg/L air for 1 h	LC50	21
43,500-304,000 µg/L air for 30 min	Respiratory distress; nasal and ocular irritation; some deaths in 4-5 days; pulmonary edema; bronchial degeneration; excess blood in heart, liver, and kidney	2, 6
131,000 µg/L air for 30 min	50% dead; tracheobronchial pathology	6
283,000 µg/L air; daily 10-min exposures for 6 months	No deaths; some bronchial pathology	6
326,000 µg/L air; daily 10-min exposures for 6 months	50% dead; tracheobronchial pathology	6
435,000 µg/L air; daily 10-min exposures for 6 months	All dead; severe histopathology of respiratory tract	6
5,00,000-10,000,000 µg/L air for 5 min	Rats on a motor-driven exercise wheel were incapacitated within 5-7 min and died shortly thereafter	17
Intraamniotic injection route		
Embryos given 0.1, 1, 10, or 100 µg of acrolein on day 13 of gestation; examined on day 20 of gestation	98-100% dead at 10 and 100 µg; 85% of live fetuses receiving 1 µg were malformed (edema, hydrocephaly, cleft palate, defects of limbs and tail); no teratogenic effects at 0.1 µg	6
Intraperitoneal injection route		
1,000 µg/kg BW, single injection	Peritonitis	22
1,000 µg/kg BW daily for at least 5 days	Lethal	22
2,000 µg/kg BW twice a week for 6 weeks followed by uracil as 3% of the diet for 20 weeks, then control diet for 6 weeks	Acrolein followed by uracil produced a 60% incidence of papilloma in urinary bladder in treated group (acrolein plus uracil) vs. 27% in water control (uracil only). No tumors in either group	22
2,500 µg/kg BW daily	All dead after second dose	3
3,360 µg/kg BW; single injections; tissues analyzed after 24 h	Most (89%) of the acrolein recovered was in the acid-soluble fraction of	3

	the liver, 3% in the liver lipids, and minor amounts (0.4-1.7%) in liver proteins RNA and DNA fractions	
Intravenous injection route		
50-500 µg/kg BW to spontaneously hypersensitive rats	At 50-200 µg/kg BW, blood pressure increased; at 300-500 µg/kg BW, blood pressure decreased	23
250-1,000 µg/kg BW	Increased blood pressure within 5 sec which peaked at 20-30 sec and lasted about 1 min	19
850 or 1,700 µg/kg BW	Liver necrosis	3
10,000 µg/kg BW	Cardioinhibitory effects	19
In vitro studies		
Cultured embryos		
4,500 µg/L serum medium	Growth retardation; 50% malformation frequency among survivors	24, 25
6,700 µg/L serum medium	Mortality of 64%; all surviving embryos malformed	24, 25
7,800-9,000 µg/L serum medium	All dead	24, 25
160 µg/L serum-free medium	50% frequency of malformations in brain, facial area, and heart	25
300-1,100 µg/L serum-free medium	50%-100% lethal	25
Cultured myocytes and fibroblasts from neonatal heart		
600 µg/L culture medium for 4 h	Myocyte ATP levels reduced	26
2,800 µg/L culture medium for 4 h	Irreversible cell lysis and ciliostasis	26
Isolated liver fractions		
1,700 µg/L medium	Mitochondrial aldehyde dehydrogenase (ALDH) activity inhibited 91%; cytosolic ALDH activity inhibited 33%	27
2,700 µg/L medium; 5 sec preincubation in aldehyde substrate	Inhibition of mitochondrial and cytosolic ALDH	27
Oral route		
Daily gavage of 50, 500, or 2,500 µg/kg BW for 102 weeks	Dose-related mortality in males during first year and in females during entire study; significant lethality in the 500 and 2,500 µg/kg groups. No increased incidence of microscopic neoplastic or nonneoplastic lesions in treated rats; decreased creatinine phosphokinase levels in treated rats	28
Two treatments of 4,000-10,000 µg/kg BW (estimated), 2-3 days apart; total dose of 8,000-20,000 µg/kg BW	All died shortly after the second dose	12

5,000 µg/kg BW daily for 9 days via stomach intubation	No deaths	3
10,000 µg/kg BW, single stomach intubation	Fatal	3
25,000 µg/kg BW, single gastric dose	LD50 within 48 h	22
42,000-46,000 µg/kg BW, single dose	LD50 within 14 days	3, 4, 5, 6, 18,22
Squirrel monkey, *Saimiri sciurea*; Inhalation route		
220, 1,000, or 1,800 µg/L air; continuous exposure for 90 days	Low concentration group appeared normal and gained weight; 1,000 µg/L monkeys were visibly affected with ocular and nasal discharges. No deaths at 1,800 µg/L, but excessive salivation, ocular discharges, and hyperplasia of trachea	2
700 or 3,700 µg/L air; 8 h daily, 5 days weekly for 6 weeks	Low concentration group appeared normal. High dose group had weight loss; histopathology of lung, liver, and kidney; 22% mortality (2 of 9 died on days 6 and 9 of exposure) excessive salivation, and frequent blinking	2

[a] 1, Ferguson et al. 1961; 2, Lyon et al. 1970; 3, EPA 1980; 4, NRC 1977; 5, Albin 1962; 6, Beauchamp et al. 1985; 7, Leikauf et al. 1989; 8, Weber-Tschopp et al. 1977; 9, Feron et al. 1978; 10, Feron and Kruysse 1977; 11, Lijinsky and Reuber 1987; 12, Lijinsky 1988; 13, Barrow et al. 1992; 14, Leach et al. 1987; 15 Astry and Jakab 1983; 16, Warholm et al. 1984; 17, Kaplan 1987; 18, Sine 1991; 19, Egle and Hudgins 1974; 20, Heck et al. 1986; 21, Ballantyne et al. 1989; 22, Cohen et al. 1992; 23, Green and Egle 1983; 24, Slott and Hales 1987; 25, Slott and Hales 1986; 26, Toraason et al. 1989; 27, Mitchell and Petersen 1988; 28, Parent et al. 1992; 29, ATSDR 1990.

Inhaled acrolein--in µg acrolein/L air--had sublethal effects at 10-50 for 1 min on rats (increased blood pressure and heart rate); at 10 for 5 weeks on mice (reduction in pulmonary compliance); at 140-150 for 2 min on humans (eye irritation in 30%); at 300-500 on humans (odor threshold); at 300 for 10 min on humans (acute irritation); at 400 for 13 weeks on rats (nasal histopathology); at 400-600 for 1-3 min on dogs (accumulations in upper respiratory tract); and at 1,000 for 90 days on dogs, monkeys, and guinea pigs (ocular and nasal discharges; Table 4). Sublethal effects of inhaled acrolein in representative small laboratory mammals were greatest on the upper respiratory tract and bronchial airways and included edema, ciliastasis, inflammation, degenerative loss of epithelia, altered ventilatory function, and bronchoconstriction (Feron and Kruysse 1977; Feron et al. 1978; EPA 1980; Astry and Jakab 1983; Beauchamp et al. 1985; Barkin et al. 1986; Leach et al. 1987; Leikauf et al. 1989; Table 4). Typical signs of toxicity from inhaled acrolein in small mammals include ocular and nasal irritation; growth depression; shortness of breath; lesions in the urinary tract, respiratory tract, trachea, and nasal passages; laryngeal edema; reduced resistance to bacterial infection; enlarged liver and heart; elevated blood pressure and heart rate; altered enzyme activities; and protein synthesis inhibition (EPA 1980; Beauchamp et al. 1985; Leach et al. 1987; Table 4). Signs of inhaled acrolein toxicity varied significantly with dose and species. For example, acrolein toxicity in rats at environmental concentrations was confined to local pathologic nasal changes, including metaplastic, hyperplastic, and dysplastic changes in the mucous, respiratory, and olfactory epithelium of the nasal cavity (Leach et al. 1987). Some inhaled toxicants, including acrolein, can prolong bacterial viability in the lung and thus enhance severeness of the disease. Mice convalescing from viral pneumonia became severely deficient in antibacterial defenses when exposed to acrolein (Astry and Jakab 1983). But acrolein-treated mice subjected to 100 µg/L air (5 consecutive daily 3-h

exposures) were not significantly sensitive to pulmonary bacteria *Klebsiella pneumoniae* or *Streptococcus zooepidemicus* (Aranyi et al. 1986).

Acrolein may be a carcinogen, cocarcinogen, or tumor initiator. As an aldehyde with strong affinity to sulfhydryl groups, acrolein is theoretically expected to remove free tissue thiols--compounds that protect bronchial epithelia against attack by carcinogens (Feron and Kruysse 1977; Feron et al. 1978). Carcinogenicity from inhalation of acrolein has not been reported (Lijinsky and Reuber 1987), and acrolein was not an evident cofactor in studies of respiratory-tract carcinogenesis with hamsters (*Cricetus* spp.) exposed to benzo(a)pyrene or diethylnitrosamine (Feron and Kruysse 1977). Moreover, long-term studies with rodents given acrolein by gavage did not increase incidences of neoplastic or nonneoplastic lesions (Parent et al. 1992). Other studies, however, suggest that acrolein is carcinogenic. Compounds closely related to acrolein are carcinogenic to rodents and humans and include acrylonitrile (vinyl cyanide) and vinyl acetate (Lijinsky 1988). Glycidaldehyde--an acrolein intermediate metabolite--is classified as an animal carcinogen by The International Agency for Research on Cancer; however, no convincing data are available on the carcinogenic potential of acrylic acid and other acrolein metabolites (Beauchamp et al. 1985). Acrolein at least partially can account for the initiating activity of cyclophosphamide carcinogenesis (Cohen et al. 1992). Cyclophosphamide and its analogs are a group of chemotherapeutic and immunosuppressive drugs; toxic side effects of this drug group are attributed to its metabolites, especially acrolein (Cohen et al. 1992). Acrolein is a suspected carcinogen because of its 2,3-epoxy metabolite and its weak mutagenic activity in the *Salmonella* screen (Leach et al. 1987). Acrolein may be a weak carcinogen, as judged by the increased frequency of adrenal adenomas in female rats after exposure for 2 years to drinking water with 625,000 µg acrolein/L (Lijinsky and Reuber 1987). Acrolein has cancer-initiating activity in the rat urinary bladder, but studies with N-[4-(5-nitro-2-furyl)-2 thiazoyl] formamide precluded evaluation of acrolein as promoting a complete carcinogenic activity from low rodent survival (Cohen et al. 1992). Additional studies seem needed to evaluate the carcinogenic potential of acrolein.

After intraamniotic injection, acrolein is teratogenic to rats in vivo but not in vitro. When administered intraamniotically to the whole embryo culture system of the rat on day 13 of gestation, acrolein caused edema, hydrocephaly, open eyes, cleft palate, abnormal umbilical cord, and defects of the limbs and face (Slott and Hales 1986). Beauchamp et al. (1985) suggest that acrolein-associated teratogenicity is caused by acrylic acid, an acrolein metabolite. Acrylic acid injected into amniotic fluid of rats on day 13 of gestation produced a dose-dependent increase in the percentage of fetuses with skeletal and other abnormalities (Beauchamp et al. 1985).

Acrolein can react synergistically, additively, or antagonistically with other chemicals (Beauchamp et al. 1985). Rat embryos were protected by glutathione against acrolein-induced mortality, growth retardation, and developmental abnormalities-provided that glutathione was concurrently present with acrolein. When rat embryos were cultured in the presence of acrolein for 2 h prior to glutathione exposure, there was no protection against acrolein-induced embryolethality, teratogenicity, and growth retardation (Slott and Hales 1987). Acrolein effects--including altered liver enzyme activity in rats--were reduced by pretreatment of animals with chemicals that inhibited protein synthesis (NRC 1977). Exposure to acrolein is sometimes accompanied by exposure to formaldehyde and other short-chain saturated aliphatic aldehydes, which in combination cause allergic contact dermatitis (Susten and Breitenstein 1990). A 40-mL puff of cigarette smoke contains 8.2 µg of acrolein and 4.1 µg of formaldehyde; irritation, ciliastasis, and pathologic changes of the respiratory tract from both compounds have been widely studied (Egle and Hudgins 1974). The toxicities of acrolein and formaldehyde seem similar; both exert their principal effects in the nasal passages (Leach et al. 1987). Acrolein in combination with formaldehyde was synergistic in reducing respiratory rates in mice; however, mixtures of sulfur dioxide and acrolein were antagonistic (Beauchamp et al. 1985). Formaldehyde pretreatment (15,000 µg/L, 6 h daily for 9 days) of rats protects against respiratory-rate depression by acrolein. Rats pretreated with formaldehyde had a 50% respiratory-rate depression at 29,600 µg acrolein/L versus 6,000 µg/L from acrolein alone (Babiuk et al. 1985), suggesting cross tolerance. Effects of interaction of acrolein with other toxicants are not comparable between rodents and humans. In rodents, the presence of irritant gases in smoke--such as acrolein--may delay the effects of other toxicants. In humans, however, the inhalation of acrolein and other irritant gases may cause a hypoxemic effect that can enhance the effects of hypoxia-producing gases (Kaplan 1987).

Some chemicals normally contain acrolein as a metabolite or impurity. For example, allylamine toxicity to the rat cardiovascular system is believed to involve metabolism of allylamine to the highly reactive acrolein (Toraason et al. 1989). Certain mercapturic acids can be used as biological markers of exposure for chemicals that are metabolized to acrolein and excreted as mercapturic acid in the urine (Sanduja et al. 1989). In one

case, rats given 13,000 µg acrolein/kg BW by gavage excreted 79% of the acrolein and 3-hydroxypropylmercapturic acid (3-OHPrMCA) in urine within 24 h. These data suggest that 3OHPrMCA can be used as a marker of exposure to allylic and other compounds that lead to the formation of acrolein (Sanduja et al. 1989). The common industrial chemical MDP (2-methoxy-3,4-dihydro-2PH-pyran) is frequently contaminated with acrolein during its synthesis; MDP causes severe irritancy and death of rats from accumulation of acrolein vapor (Ballantyne et al. 1989). Sparging acrolein-contaminated MDP with nitrogen gas before atmospheric release significantly reduced or abolished lethal toxicity to rats (Ballantyne et al. 1989).

Recommendations

Agricultural crops can usually tolerate as much as 15,000 µg of acrolein/L of irrigation water; however, aquatic invertebrates and fish die in acute exposures to 55-68 µg/L or in chronic exposures to greater than 21 µg/L (Table 5). Those who use acrolein to control submerged aquatic macrophytes are strongly advised that acrolein treatment at recommended application concentrations also eliminates nontarget fish and aquatic invertebrates. No acrolein criteria are now available or promulgated by regulatory agencies for the protection of avian and terrestrial wildlife; this seems to be a high-priority research need. Beauchamp et al. (1985) recommend additional research in several areas: long-term effects of acrolein inhalation on carcinogenicity and respiratory histology with rodent models; biochemical mechanisms of acrolein toxicity; genotoxic potential with chromosome breakage and exchange systems; acute and chronic toxicity from interaction effects of acrolein with other gases; and fate of accumulated acrolein in animals.

Table 5. Proposed acrolein criteria for the protection of living resources and human health.

Resource, criterion, and other variables	Concentration	Reference[a]
Agricultural Crops		
Irrigation water, tolerated level	<15,000 µg/L	1
Aquatic life		
Freshwater organisms		
Sensitive species, tolerated level		
Acute exposures	<68 µg/L	2
Chronic exposures	<21 µg/L	2
Rainbow trout, safe level	20 µg/L for <48 h or 200 µg/L for <4.8 h	3
Marine organisms; acute exposures, tolerated level	<55 µg/L	2
Laboratory white rat		
Air		
Maximum daily average	<13 µg/L (<0.03 mg/m^3)	7
Maximum daily	<44 µg/L (<0.1 mg/m^3)	7
Human health		
Air		
Maximum allowable emission concentration in populated areas of former Soviet Union	132 µg/L (0.3 mg/m^3)	4
No observable effect level	<22 µg/L (<0.05 mg/m^3)	4
90-day confined space (i.e., submarines) guideline	22 µg/L (0.05 mg/m^3)	5
Odor threshold	<44 µg/L (<0.1 mg/m^3)	4
Maximum acceptable concentration in room air of former Soviet Union	44 µg/L (0.1 mg/m^3)	2,4

Irritation threshold mg/m^3)	44-88 µg/L (0.1-0.2 mg/m^3)	4
Occupational exposure standard (8 h daily, 40 h work week) in United States; not to exceed in most European countries, Australia, and Japan	100-110 µg/L (0.25 mg/m^3)	2, 4, 5, 6, 8
Occupational exposure standard in Hungary and former Soviet Union	308 µg/L (0.7 mg/m^3)	4
Maximum 15-min exposure limit in USA workplace	300-352 µg/L (0.8 mg/m^3)	4, 8
Ceiling standard for occupational exposure in the former Czechoslovakia	440 µg/L (1.0 mg/m^3)	4
Acceptable ambient air concentrations		
New York	0.83 µg/m^3 for 1 year	9
Florida	2.5 µg/m^3 for 8 hr	9
North Dakota	8.0 µg/m^3 for 1 hr	9
North Carolina	80 µg/m^3 for 15 min	9
Diet		
Water plus consumption of contaminated aquatic organisms from that water body	<320 µg/L medium	2
Consumption of contaminated aquatic organisms alone	<780 µg/L medium	2
Food packaging materials; food starch	<0.6%	2
Total daily intake	<47.8 µg = <0.68 µg/kg body weight daily for a 70-kg person	2

[a] 1, Ferguson et al. 1961; 2, EPA 1980; 3, Bartley and Hattrup 1975; 4, Beauchamp et al. 1985; 5, Lyon et al. 1970; 6, Leach et al. 1987; 7, NRC 1977; 8, NIOSH 1990; 9, ATSDR 1990.

The human threshold concentration of acrolein in the United States for an 8-h workday and 40-h workweek is 110 µg/L (0.25 mg/m^3) air; the shortterm exposure limit is 350 µg/L (0.8 mg/m^3) air and is predicated on continuous exposure of workers for short intervals (Table 5; Beauchamp et al. 1985). Humans can tolerate a total daily intake of 47.8 µg of acrolein, equivalent to 0.68 µg/kg BW by a 70-kg individual (Table 5).

For handling acrolein, gloves, vapor-proof goggles or a full-face mask, and other protective clothing are mandatory (Albin 1962; Beauchamp et al. 1985; NIOSH 1990). Acrolein spills should be neutralized with 10% sodium bisulfite solutions (Albin 1962). Air packs or fresh-air breathing masks, safety showers, and eye baths should be available wherever acrolein is handled (Beauchamp et al. 1985). Purging confined areas with nitrogen is recommended prior to entering a suspected acrolein-contaminated enclosure. The eyes are particularly susceptible to liquid acrolein and, if exposed, should receive prompt treatment, although severe residual injury is probable regardless of treatment; dilute solutions of acrolein may also cause residual eye injury. Acrolein represents a serious fire hazard because of its high flammability and potential for vapors to form explosive mixtures with air. Flame-proof electrical equipment and proper grounding is required to prevent acrolein ignition. Individuals exposed to acrolein by inhalation should be removed from the area and given oxygen; subsequent

treatment by physicians of pulmonary inflammation with corticosteroids and hydroxocobalamin is recommended even if there are no symptoms (Beauchamp et al. 1985) because adverse effects from acrolein exposure may not become apparent until 4-24 h after exposure (Albin 1962). Oxygen therapy should be continued and analgesics given for relief of other symptoms as necessary (Beauchamp et al. 1985). There are many synthetic and natural sources of acrolein; however, special precautions are recommended when acrolein occurs as a contaminant in the synthesis of widely used chemicals such as 2-methyoxy-3,4-dihydro-2H pyran (Ballantyne et al. 1989).

Acknowledgments

I thank L. Garrett and W. Manning for library services; M. Holmes for secretarial assistance; and S. J. Hamilton, P. F. P. Henry, O. H. Pattee, and several anonymous reviewers for scientific and technical reviews of the manuscript.

Cited Literature

Albin, T. B. 1962. Handling and toxicology. Pages 234-239 *in* C. W. Smith, editor. Acrolein. John Wiley, New York.

Anderson, E. A., and G. C. Hood 1962. Physical properties. Pages 7-50 *in* C. W. Smith, editor. Acrolein. John Wiley, New York.

Agency for Toxic Substances and Disease Registry (ATSDR). 1990. Toxicological profile for acrolein. U.S. Public Health Service, TP-90-01. 145 pp.

Aranyi, C., W. J. O'Shea, J. A. Graham, and F. J. Miller. 1986. The effects of inhalation of organic chemical air contaminants on murine lung host defenses. Fundamental and Applied Toxicology 6:713-720.

Astry, C. L., and G. J. Jakab. 1983. The effects of acrolein exposure on pulmonary antibacterial defenses. Toxicology and Applied Pharmacology 67:49-54.

Babiuk, C., W. H. Steinhagen, and C. S. Barrow. 1985. Sensory irritation response to inhaled aldehydes after formaldehyde pretreatment. Toxicology and Applied Pharmacology 79:143-149.

Ballantyne, B., D. E. Dodd, I. M. Pritts, D. J. Nachreiner, and E. H. Fowler. 1989. Acute vapour inhalation toxicity of acrolein and its influence as a trace contaminant in 2-methyoxy-3, 4-dihydro-2H-pyran. Human Toxicology 8:229-235.

Barkin, P., W. Jung, P. Pappagianopoulos, C. Balkas, D. Lamborghini, J. Burke, and C. Hales. 1986. The role of the bronchial circulation in production of pulmonary edema in dogs exposed to acrolein in smoke. The American Review of Respiratory Disease 133:A270.

Beauchamp, R. O., Jr., D. A. Andjelkovich, A. D. Kligerman, K. T. Morgan, and H. d'A. Heck. 1985. A critical review of the literature on acrolein toxicity. CRC Critical Reviews in Toxicology 14:309-380.

Baron-Marano, F. L., and M. C. Izard. 1968. Observation d'anomalies ultrastructurales dans la descendance d'algues traitées par l'acroléine. Comptes Rendues Hebdomadaires des Séances de l'Académie des Sciences. D, Sciences Naturelies 267:2137-2139.

Barrow, R. E., C-Z. Wang, R. A. Cox, and M. J. Evans. 1992. Cellular sequence of tracheal repair in sheep after smoke inhalation injury. Lung 170:331-338.

Bartley, T. R. and A. R. Hattrup. 1975. Acrolein residues in irrigation water and effects on rainbow trout. U.S. Department of the Interior, Denver Engineering and Research Center, Bureau of Reclamation Report REC-ECR-75-8.11 pp.

Bowmer, K. H. and M. L. Higgins. 1976. Some aspects of the persistence and fate of acrolein herbicide in water. Archives of Environmental Contamination and Toxicology 5:87-96.

Bowmer, K. H. and G. R. Sainty. 1977. Management of aquatic plants with acrolein. Journal of Aquatic Plant Management 15:40-46.

Bowmer, K. H. G. R. Sainty, G. Smith, and K. Shaw. 1979. Management of *Elodea* in Australian irrigation systems. Journal of Aquatic Plant Management 17:4-12.

Bowmer, K. H., and G. H. Smith. 1984. Herbicides for injection into flowing water: acrolein and endothalamine. Weed Research 24:201-211.

Burdick, G. E., H. J. Dean, and E. J. Harris. 1964. Toxicity of aqualin to fingerling brown trout and bluegills. New York Fish and Game Journal 11:106-114.

Chhibber, G., and S. H. Gilani. 1986. Acrolein and embryogenesis: an experimental study. Environmental Research 39:44-49.

Cohen, S. M., E. M. Garland, M. St. John, T. Okamura, and R. A. Smith. 1992. Acrolein initiates rat urinary bladder carcinogenesis. Cancer Research 52:3577-3581.

Comendador, M. A. 1984. Variation of sensitivity to acrolein during the development of *Drosophila melanogaster*. Brazilian Journal of Genetics 7:411-417.

Corbus, F. G. 1982. Aquatic weed control with endothall in a Salt River project canal. Journal of Aquatic Plant Management 20:1-3.

Denine, E. P., S. L. Ribbins, and C. J. Kensler. 1971. The effects of acrolein inhalation on the tracheal mucosa of the chicken. Toxicology and Applied Pharmacology 19:416.

Donohue, J. M., A. J. Piluso, and J. R. Schreiber. 1966. Acrolein--a biocide for slime control in cooling water systems. Materials Protection 5:22-24.

Egle, J. L., Jr., and P.M. Hudgins. 1974. Dose-dependent sympathomimetic and cardioinhibitory effects of acrolein and formaldehyde in the anesthetized rat. Toxicology and Applied Pharmacology 28:358-366.

Ferguson, F. F., C. S. Richards, and J. R. Palmer. 1961. Control of *Australorbis glabratus* by acrolein in Puerto Rico. U.S. Department of Health Education and Welfare, Public Health Reports 76:461-468.

Feron, V. J., and A. Kruysse. 1977. Effects of exposure to acrolein vapor in hamsters simultaneously treated with benzo[a]pyrene or diethylnitrosamine. Journal of Toxicology and Environmental Health 3:379-394.

Feron, V. J., A. Kruysse, H. P. Til, and H. R. Immel. 1978. Repeated exposure to acrolein vapour: subacute studies in hamsters, rats and rabbits. Toxicology 9:47-57.

Fischer, R. F. 1962. Polymers from acrolein. Pages 225-233 *in* C. W. Smith, editor. Acrolein. John Wiley, New York.

Folmar, L. C. 1976. Overt avoidance reaction of rainbow trout fry to nine herbicides. Bulletin of Environmental Contamination and Toxicology 15:509-514.

Folmar, L. C. 1977. Acrolein, dalapon, dichlobenil, diquat, and endothal: bibliography of toxicity to aquatic organisms. U.S. Fish and Wildlife Service Technical Paper 88. 16 pp.

Folmar, L. C. 1978. Avoidance chamber responses of mayfly nymphs exposed to eight herbicides. Bulletin of Environmental Contamination and Toxicology 19:312-318.

Folmar, L. C. 1980. Effects of short-term field applications of acrolein and 2,4-D (DMA) on flavor of the flesh of rainbow trout. Bulletin of Environmental Contamination and Toxicology 24:217-224.

Fritz-Sheridan, R. P 1982. Impact of the herbicide Magnacide-H (2-propenal) on algae. Bulletin of Environmental Contamination and Toxicology 28:245-249.

Fujino, M., T. Arima, Y. Sato, and H. Tako. 1985. Suppression of action of some excitation-contraction (E-C) uncoupling agents and mechanism in E-C coupling in single skeletal muscle fibers of frog, *R. japonica*. Journal of the Physiological Society of Japan 47:519.

Green, M. A., and J. L. Egle, Jr. 1983. The effects of acetaldehyde and acrolein on blood pressure in guanethidine-pretreated hypertensive rats. Toxicology and Applied Pharmacology 69:29-36.

Heck, H. d'A., M. Casanova, M. J. McNulty, and C. W. Lam. 1986. Mechanisms of nasal toxicity induced by formaldehyde and acrolein. Pages 235-247 *in* C. S. Barrow, editor. Toxicology of the nasal passages. Hemisphere Publishing Company, New York.

Hill, R. D. 1960. The use of acrolein; acryladehyde; 2-propenal in the treatment of submerged weeds in farm ponds. Ohio Agricultural Experiment Station, Mimeographed 3 pp.

Holcombe, G. W., G. L. Phipps, A. H. Sulaiman, and A. D. Hoffman. 1987. Simultaneous multiple species testing: acute toxicity of 13 chemicals to 12 diverse freshwater amphibian, fish, and invertebrate families. Archives of Environmental Contamination and Toxicology 16:697-710.

Hudson, R. H, R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish and Wildlife Service Resource Publication 153. 90 pp.

Kankaanpaa, J., E. Elovaara, K. Hemminki, and H. Vainio. 1979. Embryotoxicity of acrolein, acrylonitrile, and acrylamide in developing chick embryos. Toxicology Letters 4:93-96.

Kaplan, H. L. 1987. Effects of irritant gases on avoidance/escape performance and respiratory response of the baboon. Toxicology 47:165-179.

Kissel, C. L., J. L. Brady, A. M. Guerra, M. J. Meshishnek, B. A. Rockie, and F. F. Caserio, Jr. 1981. Monitoring acrolein in naturally occurring systems. Pages 102-116 *in* J. L. Johnson, J. R. Stanford, C. C. Wright, and A. G. Ostroff, editors. Water for subsurface injection: proceedings of the second symposium. ASTM STP 735, American Society for Testing and Materials, Philadelphia, Pennsylvania.

Kobbia, I. A. 1982. Response of phytoplankton populations in some Egyptian irrigation drains to the aquatic weed herbicide "acrolein". Egyptian Journal of Botany 25:41-67.

Korhonen, A., K. Hemminki, and H. Vainio. 1983. Embryotoxic effects of acrolein, methacrylates, guanidines and resorcinol on three day chicken embryos. Acta Pharmacologica et Toxicologica 52:95-99.

Leach, C. L., N. S. Hatoum, H. V. Ratajczak, and J. M. Gerhart. 1987. The pathologic and immunologic effects of inhaled acrolein in rats. Toxicology Letters 39:189-198.

Leikauf, G. D., L. M. Leming, J. R. O'Donnell, and C. A. Doupnik. 1989. Bronchial responsiveness and inflammation in guinea pigs exposed to acrolein. Journal of Applied Physiology 66:171-178.

Lijinsky, W. 1988. Chronic studies in rodents of vinyl acetate and compounds related to acrolein. Annals of the New York Academy of Sciences 534:246-254.

Lijinsky, W., and M.D. Reuber. 1987. Chronic carcinogenesis studies of acrolein and related compounds. Toxicology and Industrial Health 3:337-345.

Lyon, J. P., L. J. Jenkins, Jr., R. A. Jones, R. A. Coon, and J. Siegel. 1970. Repeated and continuous exposure of laboratory animals to acrolein. Toxicology and Applied Pharmacology 17:726-732.

Macko, V., J. A. A. Renwick, and J. F. Rissler. 1978. Acrolein induces differentiation of infection structures in the wheat stem rust fungus. Science 199:442-443.

Marano, F., and S. Puiseux-Dao. 1982. Acrolein and cell cycle. Toxicology Letters 14: 143-149.

Mayer, F. L. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U.S. Environmental Protection Agency, Report EPA/600/8-87/017. 274 pp.

McKim, J. M., P. K. Schmeider, G. J. Niemi, R. W. Carlson, and T. R. Henry. 1987. Use of respiratory cardiovascular responses of rainbow trout (*Salmo gairdneri*) in identifying acute toxicity syndromes in fish: part 2. Malathion, carbaryl, acrolein and benzaldehyde. Environmental Toxicology and Chemistry 6:313-328.

Mitchell, D. Y., and D. R. Petersen. 1988. Inhibition of rat liver aldehyde dehydrogenases by acrolein. Drug Metabolism and Disposition 16:37-42.

National Institute for Occupational Safety and Health (NIOSH). 1990. NIOSH pocket guide to chemical hazards. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control:32-33.

National Research Council (NRC) 1977. Acrolein. Pages 553-556 *in* Drinking water and health. National Academy of Sciences, Washington, D.C.

Nishikawa, I., and T. Hayakawa. 1986. Bromination and gas chromatographic determination of micro amounts of acrolein in rain water. Journal of Chromatography 551:566-570.

O'Loughlin, E. M., and K. H. Bowmer. 1975. Dilution and decay of aquatic herbicides in flowing channels. Journal of Hydrology 26:2 17-235.

Parent, R. A., H. E. Caravello, and J. E. Long. 1992. Two-year toxicity and carcinogenicity study of acrolein in rats. Journal of Applied Toxicology 12:131-139.

Parker, L. M., D. J. Lauren, J. B. Cooke, and D. E. Hinton. 1990. Metabolism of endogenous and xenobiotic aldehydes by rainbow trout (*Oncorhynchus mykiss*) liver fractions. Aquatic Toxicology 18:1-12.

Reinert, K. H., and J. H. Rodgers. 1987. Fate and persistence of aquatic herbicides. Reviews of Environmental Contamination and Toxicology 98:61-98.

Rijstenbil, J. W., and G. C. van Galen. 1981. Chemical control of mussel settlement in a cooling water system using acrolein. Environmental Pollution 25A:187-195.

Sanduja, R., G. A. Ansari, and P. J. Boor. 1989. 3-hydroxypropylmercapturic acid: a biologic marker of exposure to allylic and related compounds. Journal of Applied Toxicology 9:235-238.

Sierra, L. M., A. R. Barros, M. Garcia, J. A. Ferreiro, and M. A. Comendador. 1991. Acrolein genotoxicity in *Drosophila melanogaster*. I. Somatic and germinal mutagenesis under proficient repair conditions. Mutation Research 260:247-256.

Sine, C., editor. 1991. Farm chemicals handbook '91. Meister Publishing Company, Willoughby, Ohio.

Slott, V. L., and B. F. Hales. 1986. The embryolethality and teratogenicity of acrolein in cultured rat embryos. Teratology 34:155-163.

Slott, V. L., and B. F. Hales. 1987. Protection of rat embryos in culture against the embryotoxicity of acrolein using exogenous glutathione. Biochemical Pharmacology 36:2187-2194.

Smith, C. W., editor. 1962. Acrolein. John Wiley, New York. 273 pp.

Srivastava, S.C., R. K. Upreti, and A. M. Kidwai. 1992. Action of acrolein on rat liver membrane proteins and enzymes. Bulletin of Environmental Contamination and Toxicology 49:98-104.

Starzecka, A. 1975. The influence of acrolein and hydrocryle on the development dynamics of aquatic bacteria. Acta Hydrobiologia 17:391-403.

Susten, A. S., and M. J. Breitenstein. 1990. Failure of acrolein to produce sensitization in the guinea pig maximization test. Contact Dermatitis 22:299-300.

Toraason, M., M. E. Luken, M. Brietenstein, J. A. Krueger, and R. E. Biagini. 1989. Comparative toxicity of allylamine and acrolein in cultured myocytes and fibroblasts from neonatal rat heart. Toxicology 56:107-117.

U.S. Environmental Protection Agency (EPA). 1980. Ambient water quality criteria for acrolein. Report EPA 440/5-80-016. 94 pp.

Warholm, M., B. Holmberg, J. Hogberg, T. Kronevi, and A. Gotharson. 1984. The acute effects of single and repeated injections of acrolein and other aldehydes. International Journal on Tissue Reactions 6:61-70.

Weber-Tschopp, A., T. Fischer, R. Gierer, and E. Grandjean. 1977. Experimentelle reizwirkungen von akrolein auf den menschen. International Archives of Occupational and Environmental Health 40:117-130.

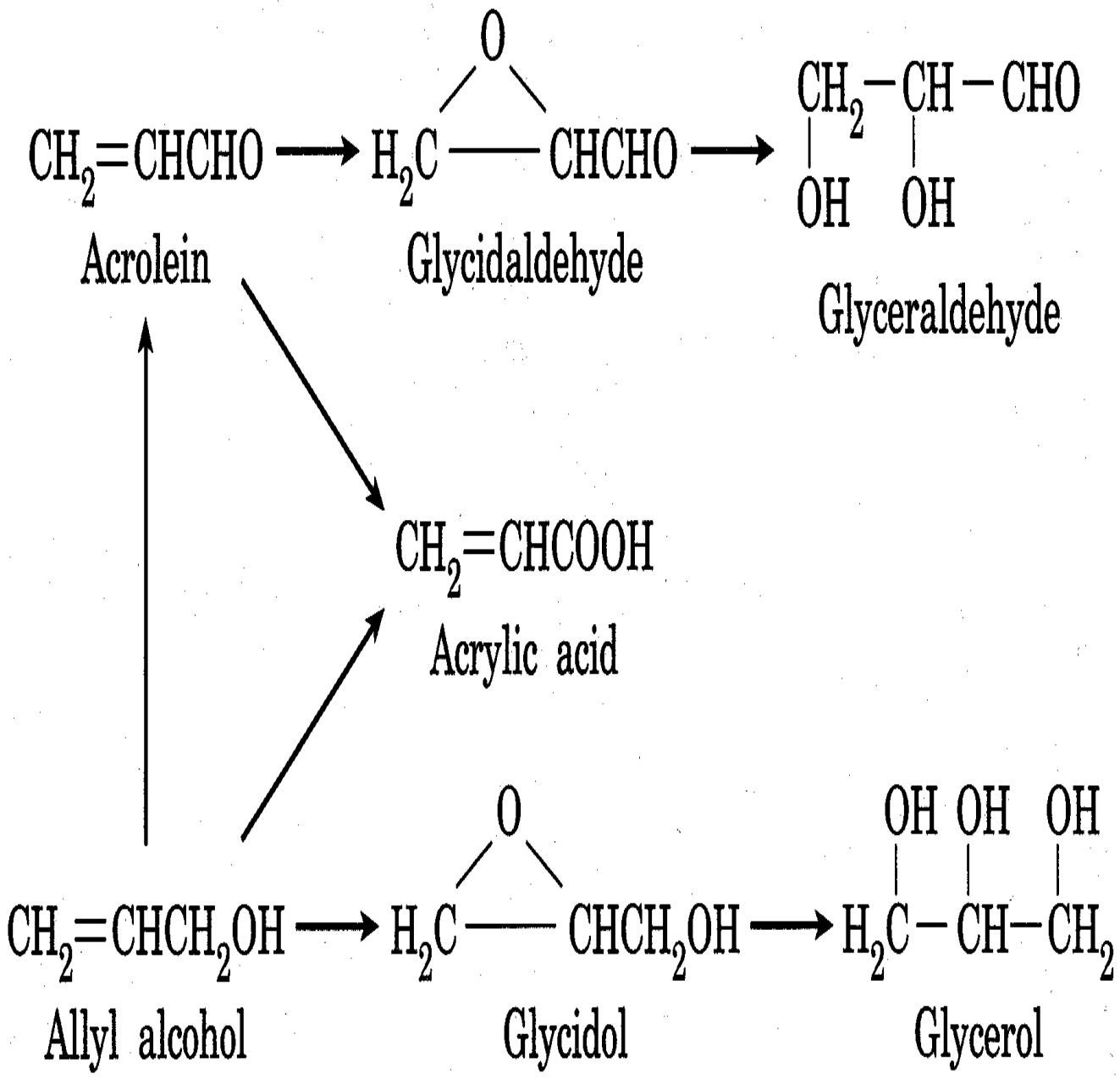


Figure. Proposed scheme for in vitro mammalian metabolism of acrolein and allyl alcohol, a precursor of acrolein (Beauchamp et al. 1985; ATSDR 1990).

Biological Report 26
December 1994

Contaminant Hazard Reviews
Report No. 29

RADIATION HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Environmental Science Center
U.S. National Biological Service
Laurel, MD 20708

TABLES

FIGURES

RADIATION HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Environmental Science Center
U.S. National Biological Service
Laurel, MD 20708

Abstract

This account is a selective review and synthesis of the voluminous technical literature on radiation and radionuclides in the environment and their effects on notably fishes, wildlife, invertebrates, and other natural resources. The subtopics include the physical and biological properties of the electromagnetic spectrum and of charged particles; radiation sources and uses; concentrations of radionuclides in field collections of abiotic materials and living organisms; lethal and sublethal effects, including effects on survival, growth, reproduction, behavior, metabolism, carcinogenicity, and mutagenicity; a synopsis of two case histories of massive releases of radionuclides into the biosphere (military weapons tests at the Pacific Proving Grounds and the Chernobyl nuclear reactor accident); currently proposed radiological criteria for the protection of human health and natural resources; and recommendations for additional research. A glossary is included.

Key words: Radioactivity, radionuclides, radioecology, Chernobyl, Pacific Proving Grounds, wildlife, aquatic organisms, invertebrates, flora, radiological protection criteria.

Life on earth has evolved under the ubiquitous presence of environmental solar, X-ray, gamma, and charged-particle radiation. On a global basis, radiation from natural sources is a far more important contributor to radiation dose to living organisms than radiation from anthropogenic sources (Aarkrog 1990). However, ionizing radiation can harm biological systems (Aarkrog 1990; Nozaki 1991; Severa. and Bar 1991), and this harm can be expressed (1) in a range of syndromes from prompt lethality to reduced vigor, shortened life span, and diminished reproductive rate by the irradiated organism and (2) by the genetic transmission of radiation-altered genes that are most commonly recessive and almost always disadvantageous to their carriers (Bowen et al. 1971). Direct effects of radiation were documented in lampreys in 1896-soon after H. Becquerel discovered radioactivity-and in brine shrimp (*Artemia sp*.) in 1923 (Whicker and Schultz 1982a). Genetic effects of ionizing radiation and thus X-rays as a mutagenic agent were first documented in 1927 in fruit flies, *Drosophila melanogaster* (Evans 1990). The discovery of radioactivity of nuclear particles and the discovery of uranium fission resulted in a great upsurge of nuclear research. During and shortly after World War II, nuclear reactors, nuclear weapons, and radionuclides as tracers in almost all scientific and technical fields were developed rapidly (Severa and Bar 1991). In the early 1940's when fission of uranium and transuranic nuclei became possible in reactors and in explosions of nuclear weapons, environmental radiation from anthropogenic sources began to cause serious concerns (Aarkrog 1990). The first nuclear explosion resulted from a 19-kiloton (TNT-equivalent) source in New Mexico in July 1945 (Whicker and Schultz 1982a). On 6 August 1945, about 75,000 people were killed when the United States Army Air Corps dropped a uranium nuclear bomb on Hiroshima, Japan; on 9 August 1945, about 78,000 Japanese were killed and more than 100,000 injured when a plutonium nuclear bomb was detonated at Nagasaki (Kudo et al. 1991). The former Soviet Union detonated its first nuclear device in August 1949, and in 1952 the United Kingdom exploded a device in Australia (Whicker and Schultz 1982a). Since 1960, nuclear devices have also been detonated by France, India, and The People's Republic of China. Nuclear devices have been developed that can release energy in the megaton range. The first such device was detonated by the United States in 1954 at Bikini Atoll and accidentally contaminated Japanese fishermen and Marshall Island natives. Between 1945 and 1973, an estimated 963 nuclear tests were conducted by The People's Republic of China, France, the former Soviet Union, the United Kingdom, and the United States; 47% of them were atmospheric, and 53% subterraneous (Whicker and Schultz 1982a). Today, the most important environmentally damaging anthropogenic radiation comes from atmospheric testing of nuclear weapons that was conducted 20 to 30 years ago, authorized discharges to the sea from nuclear reprocessing plants, and the Chernobyl accident in 1986 (Aarkrog 1990). By the year 2000, the United States will have an estimated 40,000 tons of spent nuclear fuel that will be stored at some 70 sites and await disposal; by 2035, after all existing nuclear plants have completed 40 years of operation, about 85,000 metric tons will be awaiting disposal (Slovic et al. 1991).

This report was initiated in response to a request for information on radiation from environmental contaminant specialists of the U.S. Fish and Wildlife Service. Specifically, general information was requested on radiation nomenclature, sources and uses, fate, effects, concentrations in field collections, and protection criteria. More detailed information was requested on radiation hazards to living organisms, especially fishes and wildlife. The report is an introduction to the broader fields of radioecology and radiation risk assessment and is intended primarily for use by service personnel, I emphasize that the published literature in these subject areas is particularly voluminous and that I selected for synthesis a comparatively small and highly selective portion of the available information. For more detailed information on various aspects of radiation in the environment, readers are strongly advised to consult at least several of the many reviews [1] that I found particularly useful.

[1] National Academy of Sciences (NAS) 1957, 1971; Glasstone 1958; Schultz and Klement 1963; Nelson and Evans 1969; Nelson 1971; Polikarpov 1973; Cushing 1976; Nelson 1976; International Atomic Energy Agency (IAEA) 1976, 1992; International Commission on Radiological Protection (ICRP) 1977,1991a 1991b; Luckey 1980; Whicker and Schultz 1982a, 1982b; League of Women Voters (LWV) 1985; Hobbs and McClellan 1986; United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1988; Becker 1990; Kiefer 1990; Majumdar et al. 1990; Brisbin 1991; Kershaw and Woodhead 1991; Sankaranarayanan 1991a, 1991b, 1991c; National Council on Radiation Protection and Measurements (NCRP) 1991; Severa and Bar 1991.

Physical Properties of Radiation

General

Radiation is usually defined as the emission and propagation of energy through space in the form of waves and subatomic particles (Weast 1985; Kiefer 1990). For regulatory purposes in the United States, radiation is narrowly defined as α, β, , or X-rays; neutrons; and high-energy electrons, protons, or other atomic particles; but not radio-waves or visible, infrared, or ultraviolet light (U.S. Code of Federal Regulations [CFR] 1990). Readers may wish to consult the glossary at this time.

In current atomic theory, all elementary forms of matter consist of small units called *atoms*. All atoms of the same element have the same size and weight; atoms of different elements differ in size and weight. Atoms of the same element or of different elements may unite to form compound substances called *molecules*. Each atom consists of a central nucleus and several negatively charged electrons in a cloud around the nucleus. The nucleus is composed of positively charged particles called *protons*, and particles without charge are called *neutrons*. Electrons are arranged in successive energy levels around the nucleus, and the extranuclear electronic structure of the atom is characteristic of the element. Electrons in the inner shells are tightly bound to the nucleus but can be altered by high energy waves and particles (Weast 1985). Based on the number of protons in their nucleus (= the atomic number), atoms are classified chemically into 92 naturally occurring elements and another dozen or so artificial elements (Rose et al. 1990; Severa and Bar 1991). Atoms of the same element may occur as isotopes that differ in the number of neutrons that accompany the protons in the nucleus. The sum of the number of protons and neutrons in the nucleus is called the *mass number* (see Glossary) and is indicated by a superscript that precedes the chemical symbol of the element. For example, three isotopes of hydrogen (one proton) are denoted as ^{1}H (no neutrons), ^{2}H (1 neutron, also known as deuterium), and ^{3}H (2 neutrons, also known as tritium). A nuclide is an elemental form that is distinguished from others by its atomic and mass numbers. Some nuclides, such as ^{238}U and ^{137}Cs, are radioactive and spontaneously decay to a different nuclide with the emission of characteristic energy particles or electromagnetic waves; isomers of a given nuclide that differ in energy content are metastable (i.e., ^{115m}Cd) and characterized in part by the half-life of the isomer (Rose et al. 1990; Severa and Bar 1991).

Chemical forms with at least one radioactive atomic nucleus are radioactive substances. The capability of atomic nuclei to undergo spontaneous nuclear transformation is called *radioactivity*. Nuclear transformations are accompanied by emissions of nuclear radiation (Severa and Bar 1991). The average number of nuclei that disintegrates per unit time (= activity) is directly proportional to the total number of radioactive nuclei; the time for 50% of the original nuclei to disintegrate (= half-life or Tb ½) is equal to ln 2/decay constant for that element (Kiefer 1990). Radiations with sufficient energy to interact with matter to produce charged particles are called *ionizing radiations* (Hobbs and McClellan 1986; UNSCEAR 1988). Radiation injury is related to the production of ions inside the cell. Ionizing radiations include electromagnetic radiation such as gamma ( ) and X-rays and particulate or corpuscular radiation such as alpha (α) particles, beta (β) particles, electrons, positrons, and neutrons. Ionizing radiation may be produced from manufactured devices such as X-ray tubes or from the disintegration of radioactive nuclides. Some nuclides occur naturally, but others may be produced artificially, for example, in nuclear reactors. The basic reaction of ionizing radiation with molecules is either ionization or excitation. In ionization, an orbital electron is ejected from the molecule and forms an ion pair. Directly ionizing particles are charged and possess the energy to produce ionizations along their paths from impulses imparted to orbital electrons by electrical forces between the charged particles and electrons. In excitation, an electron is raised to a higher energy level. Indirectly ionizing radiations are not charged and penetrate a medium until they collide with elements of the atom and liberate energetically charged ionizing particles.

Electromagnetic Spectrum

The electromagnetic spectrum is defined as the ordered array of known electromagnetic radiations including cosmic rays; gamma rays; X-rays; ultraviolet, visible, and infrared radiations; and radiowaves (Weast 1985). The energy transfer by electromagnetic waves can be described by discrete processes with elementary units called *photons* (Kiefer 1990). Their energy, E, is given by E = hv, where h is Planck's constant and v is the frequency. Because velocity C, wavelength , and frequency v are related (C = v), E = hc/ (Kiefer 1990). The relations between E, v, and for parts of the total spectrum of the electromagnetic waves are shown in Figure 1. The high energy radiation that enters the earth's atmosphere from outer space is known as primary cosmic rays. On

interaction with the nuclei of atoms in the air, secondary cosmic rays and a variety of reaction products (cosmogenic nuclides) such as ^{3}H, ^{7}Be, ^{10}Be, ^{14}C, ^{22}Na, and ^{24}Na are produced (UNSCEAR 1988).

Radionuclides

Radioactive nuclides contain atoms that disintegrate by emission of subatomic particles and gamma or X-ray photons (Weast 1985; Hobbs and McClellan 1986; Kiefer 1990; Rose et al. 1990). In alpha decay, a helium nucleus of 2 protons and 2 neutrons is emitted and reduces the mass number by 4 and the atomic number by 2. In beta decay, an electron--produced by the disintegration of a neutron into a proton, an electron, and an antineutrino--is emitted from the nucleus and increases the atomic number by 1 without changing the mass number. Sometimes a positron together with a neutrino is emitted. And sometimes an electron may be captured from the K (outermost) shell of the atom; the resultant electron hole in the K shell is filled by electrons from outer orbits and causes the emission of X-rays. Alpha and beta decay generally leave the resultant daughter nuclei in an excited state that is deactivated by emission of photons. Although emission accompanies most decays, it is not always detected, especially not with light β emitters such as ^{3}H, ^{14}C, ^{32}P, and ^{35}S. The half-life of individual radionuclides can be measured (i.e., the time during which half the atoms of the radionuclide spontaneously decay to a daughter nuclide). Another form of nuclear breakdown is fission in which the nucleus breaks into two nuclides of approximately half the parent's size (Rose et al. 1990). The symbol, mass number, atomic number, half-life, and decay mode of all radionuclides mentioned herein are listed in Table 1.

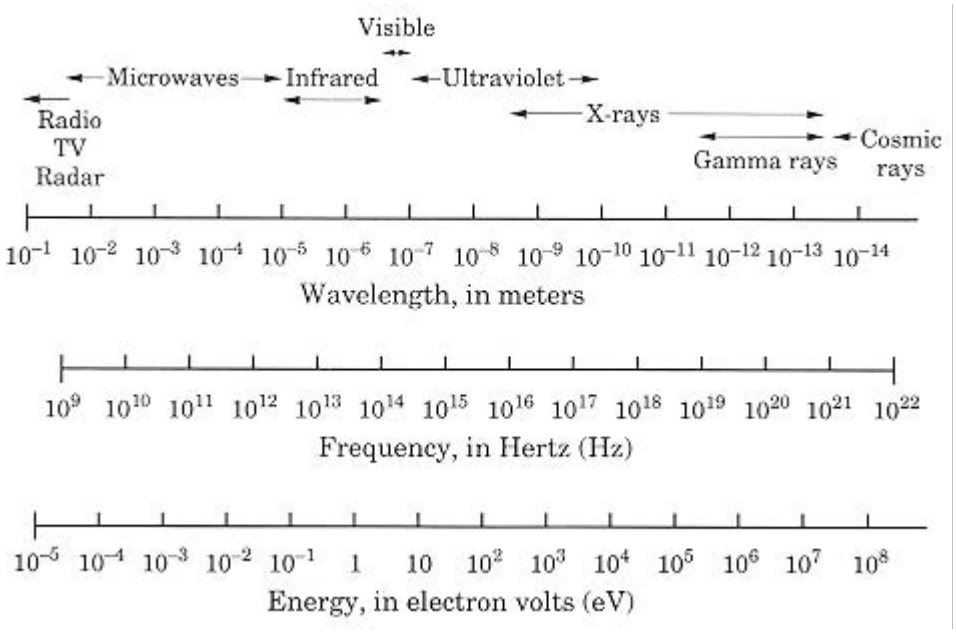


Fig. 1. The spectrum of electromagnetic waves, showing relation between wavelength, frequency, and energy (modified from Kiefer 1990).

Four general groups of radionuclides are distinguished: (1) a long half-life group (i.e., Tb ½ >10^{9} years) of elements including ^{238}U, ^{235}U, ^{232}Th, ^{40}K, ^{87}Rb, and ^{143}Sm that were formed about 4.5 billion years ago; (2) shorter-lived daughters of U and Th such as Ra and Rn that form as a result of the decay of their long-lived parents; (3) nuclides (i.e., ^{14}C and ^{3}H) formed by continuing natural nuclear transformations that are driven by cosmic rays, natural sources of neutrons, or energetic particles that are formed in the upper atmosphere by cosmic rays; and (4) nuclides that are formed as a result of nuclear weapons tests, nuclear reactor operations, and other human activities. Important members of this group include ^{90}Sr, ^{137}Cs, ^{14}C, and ^{3}H; note that many members of the third group such as ^{14}C and ^{3}H are also formed in this fourth fashion (Rose et al. 1990).

Radioactive decay usually does not immediately lead to a stable end product but to other unstable nuclei that form a decay series (Kiefer 1990). The most important examples of unstable nuclei are started by heavy, naturally occurring nuclei. Because the mass number changes only with α-decay, all members of a series may be classified according to their mass numbers (see the uranium-238 decay series in Figure 2). A total of three natural decay series--formed at the birth of our planet--are named after their parent isotope: ^{232}Th, ^{235}U, and ^{238}U (Fig. 3). Several shorter decay series also exist. For example, ^{90}Sr decays with a Tb ½ of 28 years by β emission to ^{90}Y, which in turn disintegrates (β emission) with a Tb ½ of 64 h to the stable ^{90}Zr (Kiefer 1990). Other examples of known radionuclides since the earth's origin include ^{40}K and ^{87}Rb. In hazard assessments, all members of a decay series must be considered.

Linear Energy Transfer

The deposition of energy in an exposed body is mediated almost exclusively by charged particles. These particles cause ionizations but lose energy with each ionization until they reach the end of their ranges. Depending on the type of particle, the ionizations are more or less closely spaced and described by the energy loss of a traversing particle. The linear energy transfer (LET) is defined as the amount of locally absorbed energy per unit length, that is, only the energy fraction that leads to ionizations or excitations in the considered site is counted (Kiefer 1990; ICRP 1991a). Because radiation effects are dependent on the nature of the radiation, a weighting factor is used to modify the absorbed dose and to define the dose equivalent; this factor--now called the Radiation Weighting Factor--is a function of LET. Approximate weighting values range from 1 (X-rays, electrons, gamma rays) to 10 (neutrons, protons, singly charged particles of rest mass greater than one atomic mass of unknown energy) and to 20 (alpha particles and multiply-charged particles of unknown energy; ICRP 1977; Whicker and Schultz 1982a; Hobbs and McClellan 1986; Severa and Bar 1991). The relation between radiation type and energy to weighting factors is shown in Table 2.

Table 1. Selected radionuclides: symbol, mass number, atomic number, half-life, and decay mode (modified from Whicker and Schultz 1982a, 1982b; Weast 1985; Kiefer 1990; Severa and Bar 1991).

Table 1. Nuclide	Symbol	Mass number	Atomic number	Half-life	Major decay mode [a]
Hydrogen-3	^{3}H	3	1	12.26 years	β^-
Beryllium-7	^{7}Be	7	4	53.3 days	EC
Beryllium-10	^{10}Be	10	4	1,600,000 years	β^-
Carbon-14	^{14}C	14	6	5,730 years	β^-
Sodium-22	^{22}Na	22	11	2.6 years	β^+, EC
Sodium-24	^{24}Na	24	11	15 h	β^-
Phosphorus-32	^{32}P	32	15	14.3 days	β^-
Sulphur-35	^{35}S	35	16	87 days	β^-
Argon-39	^{39}Ar	39	18	261 years	β^-
Potassium-40	^{40}K	40	19	1,250,000,000 years	β^- β^+, EC
Potassium-42	^{42}K	42	19	12.4 h	β^-
Calcium-45	^{45}Ca	45	20	164 days	β^-
Chromium-51	^{51}Cr	51	24	28 days	EC
Manganese-54	^{54}Mn	54	25	312 days	EC
Manganese-56	^{56}Mn	56	25	2.6 h	β^-
Iron-55	^{55}Fe	55	26	2.7 years	EC

Table 1. Nuclide	Symbol	Mass number	Atomic number	Half-life	Major decay mode [a]
Iron-59	^{59}Fe	59	26	45 days	β^-
Cobalt-57	^{57}Co	57	27	271 days	EC
Cobalt-58	^{58}Co	58	27	71 days	β^+, EC
Cobalt-60	^{60}Co	60	27	5.3 years	β^-
Nickel-63	^{63}Ni	63	28	100 years	β^-
Nickel-65	^{65}Ni	65	28	2.5 h	β^-
Copper-64	^{64}Cu	64	29	12.7 h	β^- β^+, EC
Zinc-65	^{65}Zn	65	30	244 days	β^+, EC
Selenium-75	^{75}Se	75	34	118 days	EC
Krypton-85	^{85}Kr	85	36	10.72 years	β^-
Rubidium-86	^{86}Rb	86	37	18.6 days	β^-
Rubidium-87	^{87}Rb	87	37	49,000,000,000 years	β^-
Strontium-85	^{85}Sr	85	38	64.8 days	EC
Strontium-89	^{89}Sr	89	38	50.5 days	β^-
Strontium-90	^{90}Sr	90	38	29 years	β^-
Yttrium-90	^{90}Y	90	39	64 h	β^-
Yttrium-91	^{91}Y	91	39	59 days	β^-
Zirconium-95	^{95}Zr	95	40	65 days	β^-
Niobium-95	^{95}Nb	95	41	35 days	β^-
Molybdenum-99	^{99}Mo	99	42	66 h	β^-
Technetium-99	^{99}Tc	99	43	213,000 years	β^-
Technetium-99m	^{99m}Tc	99	43	6 h	IT
Ruthenium-103	^{103}Ru	103	44	40 days	β^-
Ruthenium-106	^{106}Ru	106	44	373 days	β^-
Rhodium-106	^{106}Rh	106	45	29.8 s	β^-
Palladium-109	^{109}Pd	109	46	14 h	β^-
Silver-108m	^{108m}Ag	108	47	130 years	EC, IT
Silver-110m	^{110m}Ag	110	47	250 days	β^-, IT
Silver-110	^{110m}Ag	110	47	24.6 s	β^-, IT
Silver-111	^{111}Ag	111	47	7.5 days	β^-
Silver-113	^{113}Ag	113	47	5.3 h	β^-
Cadmium-109	^{109}Cd	109	48	462 days	EC
Cadmium-113m	^{113m}Cd	113	48	13.7 years	β^-
Cadmium-115m	^{115m}Cd	115	48	44.6 days	β^-
Cadmium-115	^{115}Cd	115	48	54 h	β^-
Tin-123	^{123}Sn	123	50	129 days	β^-
Tin-126	^{126}Sn	126	50	100,000 years	β^-

Table 1. Nuclide	Symbol	Mass number	Atomic number	Half-life	Major decay mode [a]
Antimony-124	^{124}Sb	124	51	60 days	β^-
Antimony-125	^{125}Sb	125	51	2.7 years	β^-
Antimony-127	^{127}Sb	127	51	3.8 days	β^-
Tellurium-127m	^{127m}Te	127	52	109 days	IT, β^-
Tellurium-129m	^{129m}Te	129	52	33 days	IT, β^-
Tellurium-129	^{129}Te	129	52	69.5 min	β^-
Tellurium-132	^{132}Te	132	52	78.2 h	β^-
Iodine-125	^{125}I	125	53	60 days	β^-, EC
Iodine-129	^{129}I	129	53	16,000,000 years	β^-
Iodine-130	$^{130}1$	130	53	12.4 h	β^-
Iodine-131	^{131}I	131	53	8 days	β^-
Xenon-131	^{131}Xe	131	54	11.9 days	IT
Xenon-133	^{133}Xe	133	54	5.3 days	β^-
Xenon-135	^{135}Xe	135	54	9.1 h	β^-
Cesium-134	^{134}Cs	134	55	2.06 years	β^-
Cesium-135	^{135}Cs	135	55	3,000,000 years	β^-
Cesium-137	^{137}Cs	137	55	30.2 years	β^-
Barium-140	^{140}Ba	140	56	12.8 days	β^-
Lanthanum-140	^{140}La	140	57	40 h	β^-
Cerium-141	^{141}Ce	141	58	33 days	β^-
Cerium-143	^{143}Ce	143	58	33 h	β^-
Cerium-144	^{144}Ce	144	58	284 days	β^-
Praseodymium-143	^{143}Pr	143	59	13.6 days	β^-
Praseodymium-144	^{144}Pr	144	59	7.2 min	IT
Praseodymium-147	^{147}Pr	147	59	13.4 min	β^-
Neodymium-147	^{147}Nd	147	60	11 days	β^-
Promethium-147	^{147}Pm	147	61	2.6 years	β^-
Samarium-143	^{143}Sm	143	62	8.8 min	β^-, EC
Samarium-151	^{151}Sm	151	62	90 years	β^-
Europium-152	^{152}Eu	152	63	13.4 years	EC, β^-
Europium-155	^{155}Eu	155	63	15.2 days	β^-
Tungsten-181	^{181}W	181	74	121 days	EC
Tungsten-185	^{185}W	185	74	75 days	β^-
Tungsten-187	^{187}W	187	74	24 h	β^-
Gold-198	^{198}Au	198	79	2.7 days	β^-
Mercury-203	^{203}Hg	203	80	47 days	β^-
Mercury-206	^{206}Hg	206	80	8.1 min	β^-

Table 1. Nuclide	Symbol	Mass number	Atomic number	Half-life	Major decay mode [a]
Thallium-206	$^{106}_{Tl}$	206	81	4.3 min	β^-
Thallium-207	$^{207}_{Tl}$	207	81	4.8 min	β^-
Thallium-208	$^{208}_{Tl}$	208	81	3 min	β^-
Thallium-210	$^{210}_{Tl}$	210	81	1.3 min	β^-
Lead-210	$^{210}_{Pb}$	210	82	22.3 years	β^-
Lead-211	$^{211}_{Pb}$	211	82	36.1 min	β^-
Lead-212	$^{212}_{Pb}$	212	82	10.6 h	β^-
Lead-214	$^{214}_{Pb}$	214	82	26.8 min	β^-
Bismuth-210	$^{210}_{Bi}$	210	83	5.0 days	β^-
Bismuth-211	$^{211}_{Bi}$	211	83	2.2 min	β^-
Bismuth-212	$^{212}_{Bi}$	212	83	1.0 h	β^-, α
Bismuth-214	$^{214}_{Bi}$	214	83	19.9 min	β^-
Bismuth-215	$^{215}_{Bi}$	215	83	7.4 min	β^-
Polonium-210	$^{210}_{Po}$	210	84	138.4 days	α
Polonium-211	$^{211}_{Po}$	211	84	0.52 s	α
Polonium-212	$^{212}_{Po}$	212	84	0.0000003 s	α
Polonium-214	$^{214}_{Po}$	214	84	0.000163 s	α
Polonium-215	$^{215}_{Po}$	215	84	0.00178 s	α
Polonium-216	$^{216}_{Po}$	216	84	0.15 s	α
Polonium-218	$^{218}_{Po}$	218	84	3.1 min	α
Astatine-215	$^{215}_{At}$	215	85	0.0001 s	α
Astatine-218	$^{218}_{At}$	218	85	1.6 s	α
Astatine-219	$^{219}_{At}$	219	85	0.9 min	α
Radon-218	$^{218}_{Rn}$	218	86	0.0356 s	α
Radon-219	$^{219}_{Rn}$	219	86	3.96 s	α
Radon-220	$^{220}_{Rn}$	220	86	56 s	α
Radon-222	$^{222}_{Rn}$	222	86	3.8 days	α
Francium-223	$^{223}_{Fr}$	223	87	21.8 min	β^-
Radium-223	$^{223}_{Ra}$	223	88	11.4 days	α
Radium-224	$^{224}_{Ra}$	224	88	3.7 days	α
Radium-226	$^{226}_{Ra}$	226	88	1,620 years	α
Radium-228	$^{228}_{Ra}$	228	88	5.75 years	β^-
Actinium-227	$^{227}_{Ac}$	227	89	21.8 years	β^-
Actinium-228	$^{228}_{Ac}$	228	89	6.13 h	β^-
Thorium-227	$^{227}_{Th}$	227	90	18.8 days	α
Thorium-228	$^{228}_{Th}$	228	90	1.91 years	α
Thorium-230	$^{230}_{Th}$	230	90	75,400 years	α

Table 1. Nuclide	Symbol	Mass number	Atomic number	Half-life	Major decay mode [a]
Thorium-231	^{231}Th	231	90	25.6 h	β^-
Thorium-232	^{232}Th	232	90	14,000,000,000 years	α
Thorium-234	^{234}Th	234	90	24 days	β^-
Protactinium-231	^{231}Pa	231	91	32,700 years	α
Protactinium-234	^{234}Pa	234	91	6.7 h	β^-
Protactinium-234m	^{234m}Pa	234	91	1.17 min	β^-, IT
Uranium-233	^{233}U	233	92	160,000 years	α
Uranium-234	^{234}U	234	92	245,000 years	α
Uranium-235	^{235}U	235	92	710,000,000 years	α
Uranium-236	^{236}U	236	92	23,400,000 years	α
Uranium-238	^{238}U	238	92	4,470,000,000 years	α
Neptunium-235	^{235}Np	235	93	1.08 years	EC
Neptunium-237	^{237}Np	237	93	2,140,000 years	α
Neptunium-239	^{239}Np	239	93	2.35 days	β^-
Neptunium-241	^{241}Np	241	93	13.9 min	β^-
Plutonium-238	^{238}Pu	238	94	87.7 years	α
Plutonium-239	^{239}Pu	239	94	24,110 years	α
Plutonium-240	^{240}Pu	240	94	6,537 years	α
Plutonium-241	^{241}Pu	241	94	14.4 years	β^-
Plutonium-242	^{242}Pu	242	94	376,000 years	α
Plutonium-244	^{244}Pu	244	94	82,000,000 years	α
Americium-241	^{241}Am	241	95	458 years	α
Americium-243	^{243}Am	243	95	7,370 years	α
Curium-241	^{241}Cm	241	96	33 days	EC
Curium-242	^{242}Cm	242	96	463 days	α
Curium-243	^{243}Cm	243	96	28.5 years	α
Curium-244	^{244}Cm	244	96	18.1 years	α
Curium-247	^{247}Cm	247	96	15,600,000 years	α
Curium-248	^{248}Cm	248	96	340,000 years	α
Curium-250	^{250}Cm	250	96	7,400 years	SF
Californium-252	^{252}Cf	252	98	2.6 years	α, SF

[a] Observed modes of decay for all radioactive species: α = particle emission; β = beta emission, β^+ = positron emission; EC = electron capture resulting in X-ray emission; IT = isomeric transition from higher to lower energy state; SF = spontaneous fission.

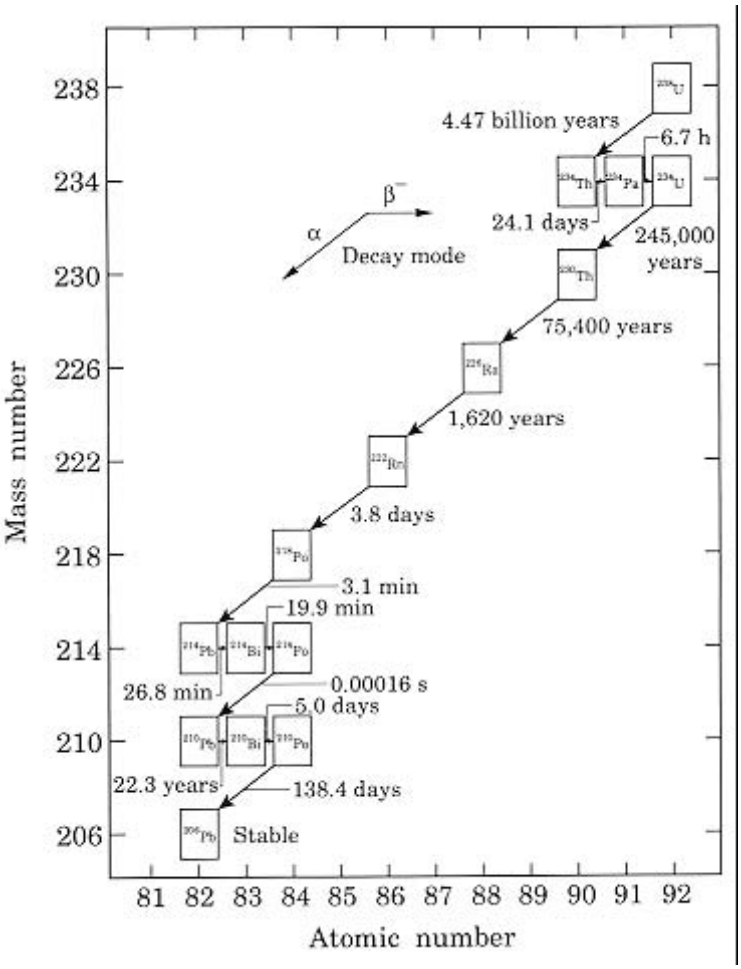


Fig. 2. The principal uranium-238 decay series, indicating major decay mode and physical half-time of persistence (modified from Cecil and Gessell 1992).

New Units of Measurement

A variety of units have been used for the assessment of exposures to ionizing radiation. The current international standard terminology is shown in Table 3. In this report, I use only the new terminology; this frequently necessitated data transformation of units from early published accounts into the currently accepted international terminology.

Table 2. Radiation weighting factors for various types of ionizing radiations (International Commission on Radiological Protection 1991a).

Radiation type and energy range	Radiation weighting factor
X-rays, gamma rays, beta particles, electrons, muons; all energies	1
Neutrons	
10 keV	5
10 keV-100 keV	10
>100 keV-2 MeV	20
>2 MeV-20 MeV	10
>20 MeV	5
Protons	5
Alpha particles, fission fragments, heavy nuclei	20

Table 3. New units[a] for use with radiation and radioactivity (International Commission on Radiological Protection 1977, 1991a; Hobbs and McClellan 1986; United Nations Scientific Committee on the Effects of Atomic Radiation 1988).

Variable	Old unit	New unit	Old unit in terms of new unit
Activity	Curie (Ci) = 3.7 x 10^{10} disintegrations /s (dps)	Becquerel (Bq) = 1 dps	1 Ci = 3.7 x 10^{10} Bq
Exposure	Roentgen (R) = 2.58 x 10^{-4} Coulombs/kg	Coulomb/kg (C/kg)	1 R = 2.58 x 10^{-4} C/kg
Absorbeddose	Rad 100 erg/g	Gray (GY) = 1 J/kg	1 Rad = 0.01 Gy
Dose equivalent	Rem = damage effects of 1 R	Sievert (Sv) = 1 J/kg	1 Rem = 0.01 Sv

[a] See Glossary.

Sources and Uses

General

Most external exposure of living organisms to radiation is from naturally occurring electromagnetic waves, and most internal exposure is from naturally occurring radionuclides such as potassium-40. Natural radiation doses vary significantly with altitude, radionuclide concentrations in the biogeophysical environment, and uptake kinetics. The major source of global anthropogenic radioactivity is fallout from military atmospheric-weapons testing; locally, radiation levels tend to be elevated near nuclear power-production facilities, nuclear-fuel reprocessing plants, and nuclear-waste disposal sites. Dispersion of radioactive materials is governed by a variety of physical chemical, and biological vectors, including winds, water currents, plankton, and avian and terrestrial wildlife.

Natural Radioactivity

Exposure to natural sources of radiation is unavoidable. Externally, individuals receive cosmic rays, terrestrial X-rays, and gamma radiation. Internally, naturally occurring radionuclides of Pb, Po, Bi, Ra, Rn, K, C, H, U, and Th contribute to the natural radiation dose from inhalation and ingestion. Potassium-40 is the most abundant radionuclide in foods and in all tissues. The mean effective human dose equivalent from natural radiations is 2.4 milliSieverts (mSv); this value includes the lung dose from radon-daughter products and is about 20% higher than a 1982 estimate that did not take lung dose into account (Table 4).

Table 4. Annual effective dose equivalent to humans from natural sources of ionizing radiation (Whicker and Schultz 1982a; Hobbs and McClellan 1986; United Nations Scientific Committee on the Effects of Atomic Radiation 1988; Aarkrog 1990).

Source of radiation	Dose equivalents (mSv)
Cosmic rays	
Ionizing component	0.30
Neutron component	0.06
Cosmogenic radionuclides (mainly ^{3}H and ^{14}C)	0.02
Primordial radionuclides	
Potassium-40	0.33
Rubidium-87	0.01
Uranium-238 series	1.34
Thorium-232 series	0.34
Total	2.4

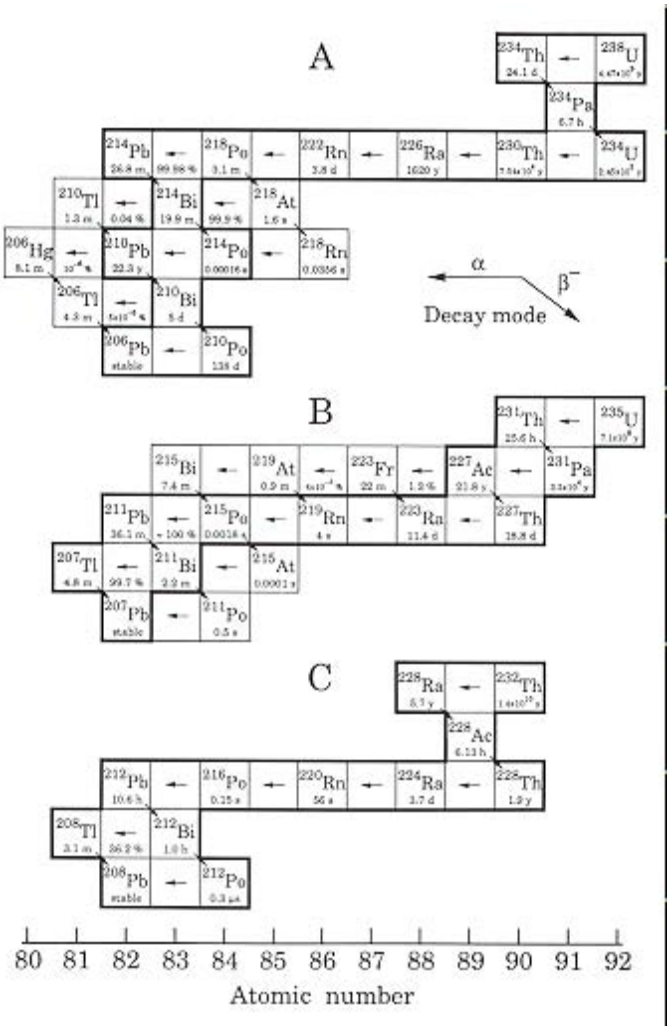


Fig. 3. The three, still-existing natural decay series. A. Uranium-238; B. Uranium-235; and C. Thorium-232 (modified from Holtzman 1969; LWV 1985; UNSCEAR 1988; Kiefer 1990; Rose et al. 1990). Principal decay products occur inside the heavy borders.

Table 5. Annual whole-body radiation doses to humans from various sources (Gray et al. 1989).

Source of radiation	Dose (mSv)
Natural external background	
Denver, Colorado	1.65
Washington State, mean	0.88
United States, average	0.84
Hanford, Washington	0.59
Average medical dose per capita, United States	0.36
Average internal dose from natural radioactivity, United States	0.25
Global weapons fallout	0.05
Consumer product radiation (TV, smoke detector, and other sources)	0.02
Total	1.27-2.33

The dose of natural radiation that an organism receives depends on height above sea level, amount and type of radionuclides in the soil of its neighborhood, and the amount taken up from air, water, and food (ICRP 1977; Whicker and Schultz 1982a; Hobbs and McClellan 1986; UNSCEAR 1988; Aarkrog 1990; Kiefer 1990; Nozaki 1991). Natural radiations in various ecosystems result in radiation dose equivalents that usually are between <0.005 and 2.07 mSv annually (Fig. 4). Radiation doses are substantially higher at atypically elevated local sites (Table 5), such as Denver, and sometimes exceed 17 mSv annually in mountainous regions of Brazil and the former Soviet Union (Whicker and Schultz 1982a).

Anthropogenic Radioactivity

Nuclear explosions and nuclear power production are the major sources of anthropogenic activity in the environment. But radionuclide use in medicine, industry, agriculture, education, production and transport, and disposal from these activities present opportunities for wastes to enter the environment (Whicker and Schultz 1982a; Table 6). Radiation was used as early as 1902 in the treatment of diseases such as an enlarged thymus, tinea capitis, acne, and cancers of childhood and adolescence (Bowden et al. 1990). The use of X-rays by physicians and dentists represents the largest source of annual dose equivalent of the U.S. population to artificial radiation: 0.78-1.01 mSv to bone marrow and 0.016 mSv to the upper GI tract; radiopharmaceuticals contribute an additional 0. 14 mSv or a yearly total mean dose of 0.94-1.17 mSv to bone marrow (Hobbs and McClellan 1986).

Table 6. Sources and applications of atomic energy (Joseph et al. 1971).

Source and output	Application
Nuclear reactor	Electric power (stationary or portable plants), desalination,
Steam, electricity	propulsion of submarines and surface ships
Heat, electricity, neutrons	Spacecraft and satellite power, spacecraft propulsion, research and special materials production
Nuclear explosives, kinetic energy	Military and civilian applications: large-scale earth moving, subsurface excavation, mineral extraction from underground
Encapsulated radioisotopes	Marine navigation aids, unmanned weather stations,
Electricity	spacecraft project power, artificial human organs
Beta and gamma radiation	Food preservation, polymerization, sterilization of medical supplies, thickness gauges
Radionuclides, beta and gamma radiation	Medical uses, tracers in scientific research, measures of manufacturing processes

Atmospheric testing of nuclear weapons is an important human source of environmental radiation (Hobbs and McClellan 1986; UNSCEAR 1988; Aarkrog 1990; Table 7). The first test explosion of a nuclear weapon took place in 1945. Atmospheric tests by the United States, the former Soviet Union, and the United Kingdom continued until they were banned in 1963. France and the People's Republic of China continued to conduct limited atmospheric tests, although no atmospheric nuclear explosions have taken place since 1980. Large nuclear explosions in the atmosphere carry most of the radioactive material into the stratosphere where it remains for 1 to 5 years, depending on the altitude and the latitude; fallout can occur years after an explosion injected material into the atmosphere. Smaller explosions carry the radioactive material only into the troposphere, and fallout occurs within days or weeks. Fallout was highest in the temperate regions and in the northern hemisphere where most of the testing was done. The most abundant radionuclides from atmospheric tests to date are $^{14}C > {}^{137}Cs > {}^{95}Zr > {}^{90}Sr > {}^{106}Ru > {}^{144}Ce > {}^{3}H$. Of the many radionuclides produced in nuclear and thermonuclear explosions, the primary contributors to human radiation exposure include ^{14}C, $^{89+90}Sr$, ^{95}Zr, ^{106}Ru, ^{131}I, ^{137}Cs, ^{141}Ce, and ^{144}Ce; isotopes of plutonium and americium--although present in quantity--are not significant contributors because of their low solubility. The primary dose from fallout radiation is through external gamma radiation, assimilation through the food chain, or beta radiation of the skin.

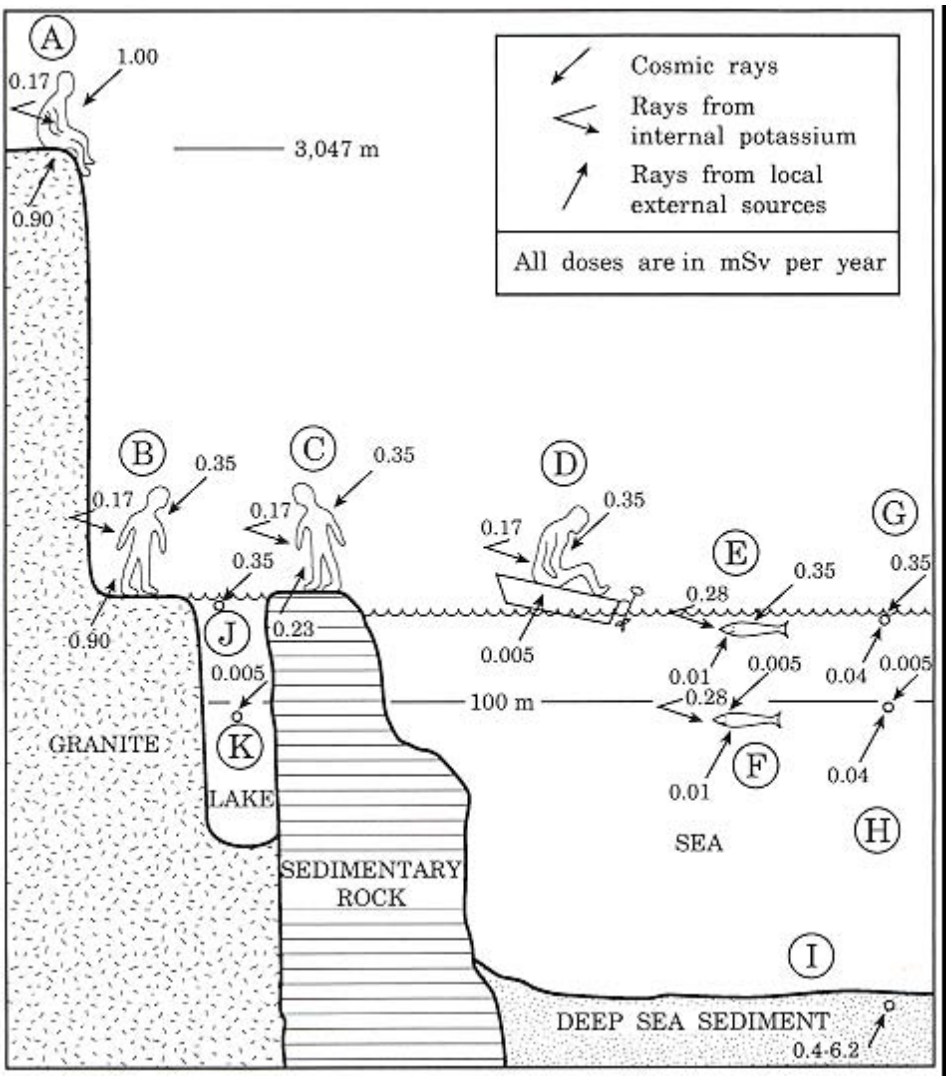


Fig. 4. Natural radiations in selected radiological domains (modified from Folsom and Harley 1957). A. Human over granite at 3,047 m (10,000 feet) elevation above sea level; total annual dose equivalent of 2.07 mSv (cosmic rays 1.00, granite 0.90, internal emitters 0.17); B. Human over granite at sea surface; total annual dose of 1.42 mSv; C. Human over sedimentary rock at sea level; total annual dose of 0.75 mSv; D. Human over sea; total annual dose of 0.525 mSv; E. Large fish in sea near surface; total annual dose of 0.64 mSv; F. Large fish in sea at depth of 100 m; total annual dose of 0.295 mSv; G. Microorganism in water near sea surface; total annual dose of 0.39 mSv, H. Microorganism in water >100 m deep in sea; total annual dose of 0.045 mSv; I. Microorganism buried in deep sea sediments; total annual dose between 0.4 and 6.2 mSv, J. Microorganism near freshwater surface; total annual dose of 0.35 mSv; K. Microorganism 100 m deep in a fresh-water lake; total annual dose of 0.005 mSv.

Radioisotope thermoelectric generators (RTG) are sometimes used as power sources for space systems. In April 1964, a United States RTG navigational satellite, SNAP 9A, reentered the atmosphere and burned up at high altitude over the Mozambique Channel, releasing 629 trillion becquerels (TBq), equivalent to 17,000 Ci of ^{238}Pu and 0.48 TBq of ^{239}Pu (Whicker and Schultz 1982a; Richmond 1989). In January 1978, a Soviet RTG satellite, Kosmos 954, reentered the atmosphere over Canada and spread radiouranium across parts of that country (Richmond 1989). The amount of radioactive materials in space applications is expected to increase (Richmond 1989).

Significant amounts of radioactivity are present in the Great Lakes basin, which has numerous nuclear reactors and uranium-mine waste areas (Joshi 1991). The prevailing low levels of artificially produced radionuclides, arising largely from previous fallout (Table 8), provide small doses of radiation to residents who consume lake water. Radionuclides enter the Great Lakes ecosystem from natural and anthropogenic processes. The main natural processes that introduce radioactivity are the weathering of rocks, which contain uranium-and thorium-series radionuclides, and fallout of cosmic ray-produced radionuclides such as ^{3}H, ^{7}Be, and ^{14}C. Anthropogenic radioactivity is created, for example, by uranium mining, milling, and fuel fabrication; releases of artificially produced radionuclides by nuclear power reactors and nuclear fuel processing plants; medical uses of radioisotopes; and coal-fired electrical generating plants (Joshi 1991).

Table 7. Annual effective dose equivalent from nuclear-weapons testing to humans in the north temperate zone (Aarkrog 1990).

Nuclide	Dose (mSv[a])
^{3}H	0.05
^{14}C	2.6
^{90}Sr	0.18
^{95}Zr	0.29
^{106}Ru	0.14
^{131}I	0.05
^{137}Cs	0.88
^{144}Ce	0.09
Pu and Am nuclides	0.09
Other nuclides	0.08
Total	4.45[b]

[a] External, 24%; inhalation, 5%; ingestion, 71%.

[b] Equivalent to 1.85 times the natural background dose.

Production of power from nuclear reactors involves uranium mining, fuel fabrication, the reactor operations, and storage of wastes. All of these processes may expose humans and the environment to radiation (Hobbs and McClellan 1986). Uranium production in the United States was 12,300 tons of U_3O_8 in 1977, primarily from western states, Texas, and Florida (Whicker and Schultz 1982a). Mining from deep shafts or open pits is the preferred method of uranium extraction, although in Florida it is produced as a byproduct of phosphate mining. Mines disperse radionuclides of uranium, thorium, and radium, which are associated with dust particles, and radon, which emanates from ore as a gas and decays to create a series of radioactive daughters. Groundwater also contains radionuclides of the uranium series. As many as 18 operating uranium mills were close to major mining centers in the western states. Collectively, these mills process or processed about 30,000 tons of ore daily and use acid or alkali leach methods to extract 90% to 95% of the uranium from ore. Uranium is barreled at the mill for shipment as uranium oxide or as salt concentrates (yellowcake) that contain 70-90% U_3O_8 by weight. Residues of the uranium extraction process are usually pumped as a slurry to liquid-retention impoundments; about 0.55 TBq of ^{230}Th and ^{226}Ra enter tailings each day from milling operations. Radium-226 produces gaseous ^{222} Rn; daughters of ^{222} Rn, such as ^{210}Pb, expose the surrounding biota to measurable radiation. Purification of yellowcake to UF_6 (uranium hexafluoride) and its enrichment to ^{235}U causes a loss of about 0.55 TBq annually. Nuclear reactor fuel contains about 3% ^{235}U. A nuclear explosion in a nuclear reactor is highly unlikely because the nuclear fuel that is suitable for weapons must contain more than

90% ^{235}U. Following enrichment, UF_6 is hydrolyzed to uranyl fluoride, converted to ammonium diuranate, and calcined to the dioxide UO_2. Uranium dioxide pellets at one time were prepared by as many as 10 commercial fuel fabrication plants and subsequently transported to nuclear reactors (Whicker and Schultz 1982a). In the current light-water cooled reactors the most abundant radionuclides in the reactor effluents under normal conditions are ^{3}H, ^{58}Co, ^{60}Co, ^{85}Kr, ^{85}Sr, ^{90}Sr, ^{130}I, ^{131}I, ^{131}Xe, ^{133}Xe, ^{134}Cs, ^{137}Cs, and ^{140}Ba (Hobbs and McClellan 1986). Gaseous and volatile radionuclides such as ^{85}Kr, ^{131}Xe, and ^{133}Xe contribute to the external gamma dose, whereas the others contribute to the dose externally by surface deposition and internally by way of the food chain. The mean dose from environmental releases of all radionuclides from nuclear reactors in the United States is less than 0.01 mSv/year (Hobbs and McClellan 1986). Nuclear fission follows the capture of a neutron by an atom of fissionable material such as ^{235}U or ^{239}Pu. The fission releases 1 to 3 neutrons and, if additional fissionable material is present in sufficient quantity and in the right configuration, a chain reaction occurs (Hobbs and McClellan 1986). Radionuclides formed per megaton of fission include fission products (^{89}Sr, ^{90}Sr, ^{95}Zr, ^{103}Ru, ^{106}Ru, ^{131}I, ^{137}Cs, ^{144}Ce), and activation products in air (^{3}H, ^{14}C, ^{39}Ar) and soil (^{24}Na, ^{32}P, ^{42}K ^{45}Ca, ^{55}Fe, ^{59}Fe; Whicker and Schultz 1982a). Fission-product radionuclides of potential biological importance include ^{90}Sr, ^{137}Cs, ^{131}I, ^{129}I, ^{144}Ce, ^{103}Ru, ^{106}Ru, ^{95}Zr, ^{140}Ba, ^{91}Y, ^{143}Ce, ^{147}Nd (Kahn 1971; Whicker and Schultz 1982a), and others (Table 9).

Table 8. Estimated fallout of ^{90}Sr and ^{137}Cs over the Great Lakes, 1954-83, in cumulative millions of Bq/km^2 (Joshi 1991).

Great Lake	Cesium-137	Strontium-90	**Total**
Superior	2,429	1,491	3,920
Michigan	2,738	1,680	4,418
Huron	2,670	1,638	4,308
Erie	2,859	1,754	4,613
Ontario	2,773	1,701	4,474
Total	13,469	8,264	21,733

Table 9. Fission products per kg ^{235}U reactor charge at 100 days cooling (modified from Renn 1957).

		Trillions of becquerels/kg^{235}U	
Product	Grams	Beta	Gamma
Short-lived[a]	15.93	7,217	6,002
Long-lived[b]	16.61	698	755
Inactive fission products	230.00	—	—
Total	262.54	8,045	6,757

a ^{90}Y, ^{106}Rh, ^{144}Ce, ^{95}Zr, ^{95}Nb, ^{91}Y, ^{89}Sr, ^{103}Ru, ^{141}Ce, ^{137}Ba, ^{106}Ru, ^{143}Pr, ^{140}Ba, ^{140}La, ^{131}I.

b ^{137}Cs, ^{90}Sr, ^{144}Pr, ^{129}Te.

Most of the world's supply of uranium consists of about 0.7% ^{235}U and 99% ^{238}U. In theory, about 2.27 kg of ^{235}U can release energy equivalent to 20,000 tons of TNT (Hobbs and McClellan 1986). Uranium-238 and ^{232}Th can be converted into fissionable material after neutron capture. Radionuclides of biological significance that are produced by neutron activation in nuclear reactors include ^{3}H, ^{14}C, ^{24}Na, ^{32}P, ^{35}S, ^{45}Ca, ^{54}Mn, ^{55}Fe, $^{57+58+60}Co$, ^{65}Zn, ^{239}Pu, ^{239}Np, ^{241}Am, and ^{242}Cm (Whicker and Schultz 1982a). Nuclear energy can also be released by fusion of smaller nuclei into larger nuclei that is accompanied by a decrease in mass

(Hobbs and McClellan 1986). Fusion reactors—which do not yet exist—require very high temperatures of several million degrees; no fission products are produced in the fusion process (Whicker and Schultz 1982a).

Table 10. Radioactive waste disposal at sea.

Disposer, and other variables	Quantity, in trillions of becquerels (TBq)	Reference[a]
United States		
Atlantic Ocean, 1951-60 vs. 1961-67	2,939 vs. 2	1
Pacific Ocean, 1951-60 vs. 1961-67	527 vs. 16	1
United Kingdom		
1951-67, alpha vs. beta	123 vs. 1,631	1
Sellafield, alpha (primarily Pu and Am)		
1968-70	50-61	2
1971 vs. 1972	99 vs. 143	2
1973 vs. 1974	181 vs. 17	2
Sellafield reprocessing plant[b]		
1980 vs. 1981	5,145 vs. 4,451	3
1982 vs. 1983	4,005 vs. 3,112	3
1984 vs. 1985	1,835 vs. 646	3
Europe		
Germany, Netherlands, Belgium, France; 1961; alpha vs. beta plus gamma	6 vs. 220	1
France, Cap de la Hague reprocessing plant[c]		
1980 vs. 1981	503 vs. 455	3
1982 vs. 1983	694 vs. 683	3
1984 vs. 1985	670 vs. 674	3

[a] 1, Joseph et al. 1971; 2, Hetherington et al. 1976; 3, UNSCEAR 1988.

[b] Effluent composition primarily ^{137}Cs and ^{241}Pu.

[c] Effluent composition primarily ^{106}Ru and ^{125}Sb.

Radioactive wastes are currently stored in underground tanks or in temporary storage at reactor sites for recycling or disposal (Whicker and Schultz 1982a). For low level wastes, containment and isolation are the preferred disposal options, including burial, hydraulic injection into deep geological strata, and ocean disposal (Table 10). Options for the disposal of high-level wastes include retrievable surface storage and entombment in deep geological strata; many risks are associated with these options, and more suitable alternative disposals are needed. Spent nuclear fuel elements are usually stored for about 3 months to allow the decay of shorter-lived radionuclides before reprocessing or disposal. Reprocessing involves extractions to separate uranium and plutonium from the fission products into UF_6 and plutonium dioxide. Longer-lived fission products such as ^{90}Sr and ^{137}Cs are sometimes chemically separated and encapsulated for storage or disposal. Fuel reprocessing tends to release measurable quantities of various radionuclides that are detected in fishes, wildlife, and food for humans (Whicker and Schultz 1982a). Liquid discharges from the Sellafield reprocessing plant (Table 10) have been reduced by a factor of more than 100 since the mid-1970's (Aarkrog 1990). Human populations that consume higher than average quantities of marine fish and shellfish from the Sellafield area theoretically receive about 3.5 mSv annually from radioactivity associated with nuclear power production. Human populations in the vicinity of nuclear-power production with discharges directly into the marine environment--except Sellafield--generally receive less than 0.05 mSv annually from this source (Aarkrog 1990).

Radioactive transuranic elements with atomic numbers that are greater than 92 have been introduced into the environment since the 1940's from atmospheric testing of nuclear weapons, discharges of nuclear wastes, and nuclear fuel reprocessing (Noshkin et al. 1971; Hetherington et al. 1976; Sibley and Stohr 1990; Morse and Choppin 1991). Transuranic isotopes with half-lives of more than 10,000 years (i.e., ^{247}Cm, ^{248}Cm, ^{239}Pu, ^{242}Pu, ^{244}Pu, ^{237}Np) will persist over geologically significant time periods. Transuranics at detectable but considered nonhazardous levels to biota are now widely dispersed throughout the environment in most waters, soils, sediments, and living organisms including humans. Of current primary concern are ^{244}Cm, ^{241}Am, $^{238+239+240+241}Pu$, and ^{237}Np—especially americium-241, which is increasing globally as a result of ^{242}Pu decay (Sibley and Stohr 1990; Morse and Choppin 1991). However, the estimated peak dose received from Pu and Am radioisotopes seems to be decreasing in the vicinity of the Sellafield nuclear-fuel reprocessor (Table 11). Miscellaneous exposures include radiations from television sets, luminous dial watches, smoke detectors, electron microscopes, building materials, and air travel (Hobbs and McClellan 1986). Most of the exposure in building materials is due to naturally occurring radionuclides; similarly, air travel increases radiation exposure of travellers from increased exposure to cosmic radiations. Dose equivalent rates can be as much as 3 times higher for cigarette smokers than for nonsmokers because of inhalation of ^{210}Po and ^{210}Pb from the cigarette. Some of the lung dose is also received from radionuclides that are released during combustion of fossil fuels, which contain small quantities of naturally occurring radionuclides (Hobbs and McClellan 1986).

Dispersion

Radioactive materials are cycled throughout the environment by a variety of physical, chemical, and biological vectors. Dispersion through the atmosphere is governed by the magnitude, frequency, and direction of the wind; in the hydrosphere, transport is modified by water depth, motion, temperature, winds, tides, and groundwater (Whicker and Schultz 1982b). Deposition from the atmosphere is a function of particle size, precipitation, and dry deposition. Small radioactive particles may be elevated into the airstream from the ground surface; resuspension is a function of disturbances by wind at the soil surface, atmospheric variables (i.e., velocity, turbulence, density, viscosity), and soil-ground variables such as texture, cohesiveness, moisture content, density, vegetation cover, ground surface roughness, and topography (Whicker and Schultz 1982b). Only 1 kg of the original 15 kg of Pu was fissioned from the dropping of the plutonium nuclear bomb on Nagasaki, Japan, on 9 August 1945 (Kudo et al. 1991). The remaining 14 kg of Pu escaped into the environment. Local fallout accounted for about 37 g or 0.26% of the total global fallout; the highest measured $^{239+240}Pu$ concentration was 64 Bq/kg soil about 2.8 km from ground zero (Kudo et al. 1991).

Table 11. Theoretical peak dose, in microsieverts per year, received from plutonium and americium by three human populations (McKay and Pattenden 1990).

	Year		
Population	1973	1987	2000
Average person near Sellafield nuclear fuel reprocessor	24	4	2
Critical group, mainly agricultural workers	35	20	16
Heavy consumers of Irish Sea fish and shellfish in local fishing communities	—	250	55-90

Biological agents can also transport radioactive wastes. Birds, especially waterfowl, disperse accumulated radiocesium and other radionuclides along their migratory flyways (Brisbin 1991). Native mammalian herbivores and their predators that have come in contact with radioactivity in food or soils disperse the material in their feces, urine, or regurgitated pellets (O'Farrell and Gilbert 1975). For example, the black-tailed jackrabbit (*Lepus californicus*) in the vicinity of radioactive waste-disposal trenches dispersed radioactive fecal pellets over an area of 15 km^2; elevated radioactivity readings were recorded in jackrabbits and in their predators, including feces of coyotes (*Canis latrans*) and bones of hawks (O'Farrell and Gilbert 1975).

Biological transport of trace elements and radionuclides in the sea is provided mainly by phytoplankton and zooplankton because of their (1) ability to accumulate these elements to high levels, (2) diurnal vertical migration, and (3) production of detritus in the form of fecal pellets, molts, and carcasses (Lowman et al. 1971). Considerations related to biomass, feeding rates, conversion efficiencies, migratory habits of zooplankton, and the chemical properties of trace elements suggest that the major downward transport of these elements and radionuclides is through gravitational action on fecal pellets, molts, and carcasses; direct biological transport accounts for less than 10% of the total downward movement. In estuarine and near-shore regions, the bottom sediments and their associated epiphyton often significantly influence the distribution of added radionuclides. Large populations of sessile filter feeders may drastically increase the rate of sedimentation of added trace elements and radionuclides (Table 12).

In some coastal areas, some of the radionuclides that are discharged into coastal waters from industrial establishments are recycled by the air-sea interface back onto land (McKay and Pattenden 1990). At the sea surface, aerosol is generated by bubble bursting and wave shearing. The aerosol is advected to land by onshore winds and deposited in coastal regions. Sea-to-land transfer has been documented from the vicinity of nuclear-fuel reprocessing facilities in England, Scotland, and France; however, the sea-to-land transfer pathway was only about 8% of that from the seafood pathway (McKay and Pattenden 1990). The solubility of different radionuclides at the sediment-seawater interface is variable. Plutonium solubility, for example, depends on pH, Eh, ionic strength, complexing ions, organic chelators, living accumulator organisms, and oxidation state (Mo and Lowman 1976). The oceanic distributions of many nuclides are strongly controlled by interactions with particulate matter (Nozaki 1991). Thorium is an extreme case; the high reactivity of this element accounts for its residence of only a few decades in the ocean from where it is removed largely by vertical transport in association with settling particulate matter. Lead-210 and ^{231}Pa are also particle-reactive but to a lesser extent than Th. Their oceanic mean residence time is about 100 years. The mean oceanic residence time of ^{227}Ac and Ra isotopes is about 1,000 years because of particulate scavenging; these nuclides are supplied by insoluble parents in underlying sediments and are released to overlying waters by porewater diffusion. Radium-228 can serve as a novel tracer in ocean circulation for about 30 years; ^{227}Ac can be used for about 100 years. The distribution of ^{226}Ra is largely governed by biogeochemical cycling, much like dissolved silica (Nozaki 1991).

Table 12. Time required to transport selected radionuclides added into marine waters at surface from the upper mixed layer by biological transport. Processes include diurnal vertical migration, fecal pellets, and sinking of dead matter (Lowman et al. 1971).

	Time required to transport radionuclides (in years)		
Radionuclide	Eastern North Pacific	Coastal areas	Upwelling areas
^{54}Mn	74	7	3
$^{55+59}Fe$	7.2	0.7	0.3
$^{57+58+60}Co$	220	20	8.8
^{65}Zn	12	1.1	0.5
^{95}Zr	5.4	0.5	0.2
^{210}Pb	7.3	0.7	0.3

Radionuclide Concentrations in Field Collections

General

The wide dispersion of anthropogenic radiocontaminants has significantly altered natural background levels of radioactivity in many parts of the globe. Radionuclide concentrations in selected abiotic materials and living organisms were usually elevated in samples from the vicinity of human nuclear activities, especially atmospheric military tests. Radionuclide concentrations in organisms were significantly modified by age, sex, diet, metabolism, trophic level, proximity to point source, and many other biological, chemical, and physical variables,

as discussed later. Additional and more detailed data on environmental radionuclide concentrations and isotopic composition and levels of radioactive wastes discharged into the biosphere from nuclear plants and other anthropogenic activities are given in Schultz and Klement (1963), Nelson and Evans (1969), Nelson (1971), IAEA (1976), Whicker and Schultz (1982a, 1982b), and UNSCEAR (1988).

Abiotic Materials

Radionuclide concentrations in selected nonliving materials (Table 13) show that concentrations are elevated in samples from the site of repeated nuclear detonations, near nuclear-fuel reprocessing and waste facilities, and from locations that receive radioactive fallout from atmospheric military tests. Rocks, especially granite, had high levels of naturally occurring radionuclides such as ^{40}K. Concentrations were usually low or negligible in drinking water and in cow's milk for human consumption. Nuclear-weapons testing has released large amounts of radionuclides into the environment. Between 1961 and 1966, for example, the Republic of Korea received fallout from nuclear tests by the former Soviet Union in 1961 and by the United States in 1962 and from 3 explosions by the People's Republic of China (Bai 1969). The highest levels of total combined β and activity in various Korean samples during 1962-64, in Bq/L or Bq/kg, were 0.0002 in air, 133 in water, 1,572 in milk, 2,023 in rain, 16,428 in plants, and 99,345 in soils (Bai 1969).

Table 13. Radionuclide concentrations in field collections of selected materials. Concentrations are in becquerels per kilogram fresh weight (FW) or dry weight (DW).

Table 13 Material, radionuclide, and other variables	Concentration (in Bq/kg or Bq/L)	Reference [a]
Common rock types		
Shale, limestone, sandstone, basalt		
^{40}K	63-518 DW	2
^{232}Th	4-48 DW	2
^{238}U	6-44 DW	2
Granite vs. beach sands		
^{40}K	1,184 DW vs. 100 DW	2
^{232}Th	74 DW vs. 25 DW	2
^{238}U	62 DW vs. 37 DW	2
Drinking water		
Mol, Belgium, 1983, near former nuclear fuel reprocessing plant closed in 1974, ^{129}I	Max. 0.000082 FW	3
United States, nationwide		
1977 vs. 1981		
^{238}Pu	Max. 0.00004 FW vs. max. 0.0004 FW	1,4
^{239}Pu	Max. 0.0004 FW vs. max. 0.0003 FW	1,4
^{234}U	Max. 0.093 FW vs. max. 2.19 FW	1,4
^{235}U	Max. 0.0026 FW vs. max. 0.027 FW	1,4
^{238}U	Max. 0.067 FW vs. max. 0.562 FW	1,4
1988		
^{131}I	Max. 0.011 FW	5
^{238}Pu	Max. 0.002 FW	6

Table 13 Material, radionuclide, and other variables	Concentration (in Bq/kg or Bq/L)	Reference [a]
$^{239+240}Pu$	Max. 0.0003 FW	6
^{226}Ra	Usually <0.007 FW; max. 0.24 FW	6
^{90}Sr	Max. 0.018 FW	6
^{234}U	Max. 0.090 FW	6
^{235}U	Max. 0.007 FW	6
^{238}U	Max. 0.183 FW	6
1989, ^{131}I	Max. 0.022 FW	7
1990, ^{131}I	Max. 0.022 FW	8
Freshwater		
Vicinity of nuclear weapons tests and operation of nuclear reactors, maximum values		
^{141}Ce	0.08 FW	2
^{144}Ce	0.41 FW	2
^{137}Cs	0. 18 FW	2
^{131}I	5.2 FW	2
^{54}Mn	0.05 FW	2
^{103}Ru	0.25 FW	2
^{106}Ru	1.1 FW	2
^{89}Sr	1.9 FW	2
^{90}Sr	0.66 FW	2
$^{95}Zr/^{95}Nb$	2.4 FW	2
Typical maximum concentrations		
^{3}H	0.6 FW	2
^{40}K	0.2 FW	2
^{210}Pb	0.01 FW	2
^{210}Po	0.008 FW	2
^{226}Ra	0.11 FW	2
^{87}Rb	0.00007 FW	2
^{222}Rn	6.7 FW	2
^{232}Th	0.0002 FW	2
^{234}U	0. 12 FW	2
^{235}U	0.002 FW	2
^{238}U	0.06 FW	2
Groundwater		
United States, nationwide, ^{222}Rn, 1981 vs. 1982	Usually <10 FW, max. 388 FW vs. max. 90 FW	1,9
Lakewater		
Canada 1984-87, ^{226}Ra		
Near uranium tailings area, dissolved vs. total	0. 12 FW vs. 0.56 FW	10
Control site, dissolved vs. total	0.012 FW vs. 0.009 FW	10

Table 13 Material, radionuclide, and other variables	Concentration (in Bq/kg or Bq/L)	Reference [a]
Great Lakes, 1973 vs. 1981		
^{137}Cs	0.003 FW vs. 0.0006-0.002 FW	11
^{3}H	12.6 FW vs. 6.7-13.5 FW	11
^{90}Sr	0.019-0.047 FW vs. 0.016-0.024 FW	11
Milk, (cow) pasteurized		
Mol, Belgium, 1983, near former nuclear fuel reprocessing plant, ^{129}I	Max. 0.0005 FW	3
United States, nationwide		
1975 vs. 1977		
^{14}C	17.7-18.8 FW vs.—[b]	12
^{137}Cs	Max. 1.07 FW vs. max. 1.04 FW	4,12
^{129}I	— vs. ND[c]	4
^{131}I	ND vs. max. 0.59 FW	4,12
^{89}Sr	ND vs. max. 0.22 FW	4,12
^{90}Sr	Max. 0.17 FW vs. max. 0.27 FW	4,12
1978 vs. 1981		
^{137}Cs	Max. 0.92 FW vs. max. 0.66 FW	9,13
^{131}I	Max. 0.29 FW vs. max. 0.48 FW	9,13
^{89}Sr	Max. 0.15 FW vs. max. 0.07 FW	9,13
^{90}Sr	Max. 0.32 FW vs. max. 0.14 FW	9,13
1982 vs. 1988		
^{137}Cs	Max. 0.67 FW vs. max. 0.70 FW	1,15,16
^{131}I	Max. 0.25 FW vs. max. 0.48 FW	1,15,16
^{89}Sr	Max. 0.07 FW vs. 0.007-0.09 FW	1,16
^{90}Sr	Max. 0.13 FW vs. max. 0.07 FW	1,16
1983, ^{14}C	16.1-17.5 FW	14
1989 vs. 1990		
^{137}Cs	Max. 0.78 FW vs. max. 0.67 FW	5,7,8, 14,17,18, 19
^{131}I	Max. 0.66 FW vs. max. 0.48 FW	5,7,8, 14,17,18,
^{89}Sr	Max. 0.11 FW vs. —	5,14,17, 18
^{90}Sr	Max. 0.18 FW vs. —	5,14,17, 18
Precipitation		
United States, nationwide		
1978		
^{238}Pu	Max. 0.0004 FW	13
^{239}Pu	Max. 0.0006 FW	13

Table 13 Material, radionuclide, and other variables	Concentration (in Bq/kg or Bq/L)	Reference [a]
^{234}U	Max. 0.004 FW	13
^{235}U	Max. 0.0001 FW	13
^{238}U	Max. 0.003 FW	13
1987 vs. 1988		
^{238}Pu	Max. 0.0007 vs. max. 0.001FW	5,15
$^{239+240}Pu$	Max. 0.0003 FW vs. max. 0.0005 FW	5,15
^{234}U	Max. 0.013 FW vs. max. 0.002 FW	5,15
^{235}U	Max. 0.0004 1FW vs. max. 0.0003 FW	5,15
^{238}U	Max. 0.0026 FW vs. max. 0.002 FW	5,15
Seawater		
Major fallout radionuclides in surface seawater, typical concentrations		
^{14}C	0.0004-0.001 FW	2
^{137}Cs	0.005-0.04 FW	2
^{3}H	0.3-1.8 FW	2
^{90}Sr	0.003-0.026 FW	2
^{239}Pu	0.000004-0.00005 FW	2
Natural radionuclides in surface seawater, typical concentrations		
^{3}H	0.022-0.111 FW	2
^{14}C	0.007 FW	2
^{40}K	11.8 FW	2
^{210}Pb	<0.0003 FW	2
^{210}Po	0.0002-0.001 FW	2
^{226}Ra	0.0016 FW	
^{228}Ra	0.00004-0.004 FW	2
^{87}Rb	0.107 FW	
^{228}Th	0.00007-0.0001 FW	2
^{230}Th	<0.00005 FW	2
^{232}Th	<0.00003 FW	2
^{234}U	0.048 FW	2
^{235}U	<0.002 FW	2
^{238}U	0.044 FW	2
Sediments		
Deep Ocean		
^{232}Th	1-74 DW	2
^{238}U	5-37 DW	2
Hanford, Washington, 1973, plutonium processing waste pond		
^{241}Am	2,627 DW	20
^{238}Pu	4,144 DW	20
$^{239+240}Pu$	4,477 DW	20

Table 13 Material, radionuclide, and other variables	Concentration (in Bq/kg or Bq/L)	Reference [a]
Hudson River estuary, 1970, ^{137}Cs, bottom sediments vs. suspended sediments	75 DW vs. 152 DW	21
Soils		
Belgium, Mol, near former nuclear fuel reprocessing plant, 1983, ^{129}I	Max. 0.2 DW	3
Tennessee, 1974, ^{137}Cs; 12-22 cm depth; accidentally contaminated in 1944 vs. control site	Usually near 185,00 DW, max. 740,000 DW vs. <222 DW	22
Water, various locations		
Hanford, Washington; plutonium processing waste ponds		
^{241}Am	0.04 FW	20
^{238}Pu	0.0003 FW	20
$^{239+240}Pu$	0.00007 FW	20
Hudson River estuary, 1970, ^{137}Cs, dissolved vs. suspended	0.01 FW vs. 0.005 FW	21
Italy, 1971, nuclear power station		
^{60}Co	Max. 0.06 FW	23
^{137}Cs	Max. 0.33 FW	23

[a] 1, U.S. Environmental Protection Agency (EPA) 1982b; 2, International Atomic Energy Agency (IAEA) 1976; 3, Handl et al. 1990; 4, EPA 1977; 5, EPA 1989c; 6, EPA 1990a; 7, EPA 1990c; 8, EPA 1991; 9, EPA 1982a; 10, Clulow et al. 1991; 11, Joshi 1991; 12, EPA 1975; 13, EPA 1979; 14, EPA 1990a; 15, EPA 1989a; 16, EPA 1989b; 17, EPA 1989d; 18, EPA 1990b; 19, EPA 1990d; 20, Emery et al. 1976; 21, Wrenn et al. 1971; 22, Dahlman and Voris 1976; 23, Smedile and Queirazza 1976.

[b] — = no data.

[c] ND = not detectable.

Water in the Great Lakes in 1981 contained measurable concentrations of ^{137}Cs, ^{3}H, and ^{90}Sr and detectable but extremely low concentrations of ^{241}Am, ^{113m}Cd, ^{144}Ce, ^{210}Pb, $^{239+240}Pu$, ^{226}Ra, ^{125}Sb, and ^{228}Th (Joshi 1991). Radiocesium-137 in water from the Hudson River estuary, New York, decreased tenfold between 1964 and 1970, but the ^{137}Cs content in fishes and in sediments remained relatively constant (Wrenn et al. 1971). The effluent from the United Kingdom's Atomic Energy Agency Sellafield facility on the Cumberland Coast of the Irish Sea contained ^{90}Sr and ^{137}Cs, which are soluble in seawater and tend to remain in solution, and ^{106}Ru, ^{144}Ce, and $^{95}Zr/^{95}Nb$, which are relatively insoluble in seawater and coprecipitate or adsorb on free inorganic and organic surfaces (Pentreath et al. 1971).

Soils in the vicinity of an English nuclear-fuel reprocessing facility in 1979-85 contained as much as 42 times more ^{241}Am, 12 times more ^{137}Cs, 13 times more ^{90}Sr, and 87 times more $^{239+240}Pu$ than soils from a reference site (Curtis et al. 1991). In the United States, radiological trends in abiotic materials were difficult to interpret. For example, one nationwide monitoring program for radionuclide concentrations in air, drinking water, milk, groundwater, and precipitation (Table 13) was not consistent in the selection of measured radionuclides, frequency of sampling, and types of analyzed samples.

Aquatic Ecosystems

Field studies indicated that effects of radiation on marine ecosystems cannot be demonstrated at prevailing dose rates (Templeton et al. 1971).Two major periods of worldwide fallout occurred in Arctic ecosystems. The first and most sustained occurred during 1953-59 and the second during 1961-64, reflecting the atmospheric nuclear-weapons test regimes of Great Britain, the former Soviet Union, and the United States (Hanson 1976). Military accidents created localized radiocontamination of the Arctic environment. In one case, a B-52 aircraft from the U.S. Air Force crashed on the ice in northwestern Greenland in January 1968. Plutonium from the nuclear weapons on board contaminated the benthos (Fig. 5). The $^{239+240}Pu$ concentrations in various environmental samples declined at a much faster rate than the physical half-life of ^{239}Pu (24,000 years), suggesting that Pu becomes increasingly unavailable to the benthos over time as a result of dispersion from the epicenter and a dilution effect (Aarkrog 1990).

In marine environments, the major portion of the background dose rate in plankton and fishes arises from the incorporated activity of natural alpha emitters, such as ^{210}Po , and from ^{40}K; in molluscs, crustaceans, and benthos, the gamma radiation from the seabed provides the major background dose (IAEA 1976). The situation is similar in freshwater environments, although water that contains appreciable levels of ^{222}Rn and its daughter radionuclides may exert an additional burden, especially to phytoplankton. Artificial radionucludes that contribute significantly to background concentrations of marine organisms include ^{239}Pu and ^{90}Sr; of freshwater organisms, ^{137}Cs and ^{90}Sr (IAEA 1976). The total natural radiation received by a marine flounder (*Pleuronectes platessa*) in the Irish Sea consisted of 63% from radiations from seabed sediments, 16% from ^{40}K in seawater, 15% from internal ^{40}K and 6% from cosmic radiation (Templeton et al. 1971). The estimated dose rates in aquatic environments from natural background are as high as 3.5 mGy annually and of the same order as those in most terrestrial environments. By 1976, the estimated dose rates from global fallout had declined to the same range as natural dose rates, although environments that receive radioactive wastes had variable responses (IAEA 1976).

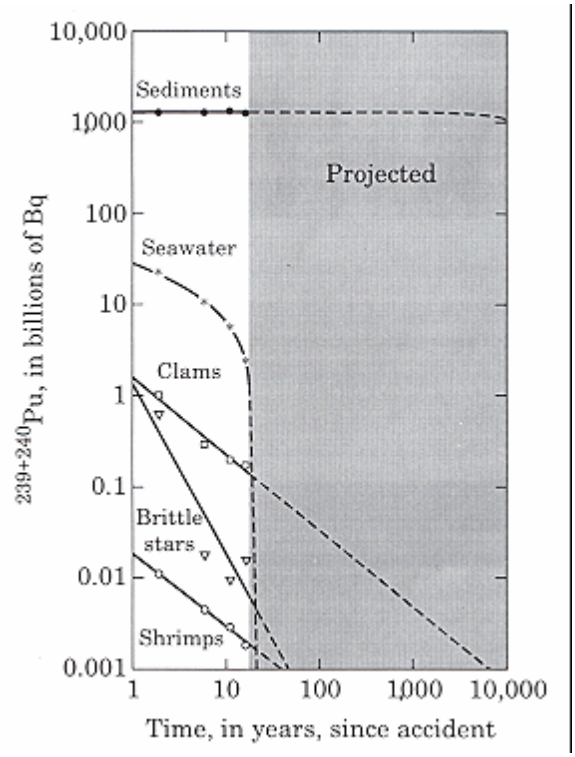


Fig. 5. Plutonium-239 + 240 in environmental samples at Thule, Greenland, between 1970 and 1984, after a military accident in 1968 (modified from Aarkrog 1990). In the contaminated area of 3.2 x 10^9 m^2, the fresh

weight biomass of shrimps was 0.11 x 10^9 kg, of brittle star echinoderms 0.06 x 10^9 kg, and of clam (*Macoma balthica*) soft parts 0.32 x 10^9 kg. The seawater mass was 3 x 10^{14} kg, and the dry weight of the upper 15 cm sediment layer was 3 x 10^{11} kg.

Increasing levels of ^{137}Cs in fish muscles in Minnesota between 1954 and 1966 reflect fallout from atmospheric nuclear testing. The effective half-life of ^{137}Cs in these lakes, as judged from small fishes, is about 30 months (Gustafson 1969). In game fish from Colorado, ^{137}Cs in muscle was as much as 7 times higher in 1968 than in 1965; higher in fishes in mountain lakes than in fishes from reservoirs in the plains, foothills, lakes, and rivers; and highest in trout from alpine lakes and reservoirs (Nelson and Whicker 1969). In 1966, ^{137}Cs levels in trout from Colorado alpine lakes were 8 to 18 times higher than mean levels in muscle of deer from Colorado during the same period and 20 to 300 times higher than in domestic meat products (Nelson and Whicker 1969). Radionuclides in livers of tunas from southern California during 1964-70 originated mainly from weapons tests in 1961-62, although ^{65}Zn may have reached southern California waters from nuclear reactors in Hanford (Washington) and from French or Chinese nuclear tests (Folsom et al. 1971).

Many variables modify radionuclide concentrations in biota. In general, lower trophic levels of aquatic organisms usually have greater concentrations of radionuclides than higher trophic levels (Bowen et al. 1971). However, radionuclide concentrations in biota are modified significantly by the organism's age, size, sex, tissue, season of collection, and other variables--and these have to be acknowledged when integrating radiological analyses. For example, older *Fucus vesiculosus* had higher radioactivity concentrations than younger algae; concentrations of ^{60}Co and ^{54}Mn were highest in older parts of plants during spring and summer; and ^{137}Cs and ^{40}K were highest in receptacles and new vegetative fronds (Carlson and Erlandsson 1991). Changes in concentrations of ^{60}Co and ^{137}Cs in freshwater plankton from the discharge canal of an Italian nuclear power station seem to reflect changes in water concentrations of these isotopes; changes were lowest in winter and highest in summer (Smedile and Queirazza 1976). Marine bivalve molluscs and algae from Connecticut in 1960 and 1961 had the highest levels of gross beta radioactivity in spring and summer and the lowest in winter (Table 14; Hatfield et al. 1963); natural ^{40}K probably accounted for most of the beta radioactivity. Similar seasonal variations in gross beta radioactivity in other species of marine algae and molluscs were documented, suggesting a correspondence with periods of dormancy and activity (Hatfield et al. 1963). Although fat in the livers of crabs accounted for 47% of the fresh weight (74% on a dry weight basis), the gross beta activity of the fat fraction amounted to less than 0.5% of the total radioactivity, suggesting that radiological liver analyses be conducted on the basis of nonfat solids (Chakravarti and Eisler 1961). In some locations of a ^{137}Cs-contaminated reservoir, males of the mosquitofish (*Gambusia holbrooki*) contained higher ^{137}Cs concentrations than females and smaller females contained more ^{137}Cs than larger females (Newman and Brisbin 1990). Strontium-90 concentrations in the carapace bone of turtles from 5 southwestern states in 1970 were used as indicators of ^{90}Sr fallout. However, older turtles tended to have lower concentrations of ^{90}Sr, and concentrations differed geographically; concentrations were highest in Georgia and increasingly lower in Tennessee, Mississippi, Arkansas, and Florida (Table 14; Holcomb et al. 1971).

Table 14. Radionuclide concentrations in field collections of selected living organisms. Concentrations are in becquerels per kilogram fresh weight (FW), dry weight (DW), or ash weight (AW).

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Terrestrial plants		
Sweet potato, *Ipomoea batatas*, Nagasaki, Japan, 1945, postatomic detonation		
^{137}Cs	0.09 DW	1
$^{239+240}Pu$	0.01 DW	1
Lichens, various species, Alaska and Greenland		
^{238}Pu		
1971 vs. 1972	0.4 DW vs. 0.9 DW	2
1973	0.4 DW	2
$^{239+240}Pu$		
1971 vs. 1972	7.4 DW vs. 10.3 DW	2
1973 vs. 1974	5.4 DW vs. 9.6 DW	2
Reed canarygrass, *Phalaris arundinacea*, Columbia River Washington, 1985-87, near reactor, ^{90}Sr	Max. 1,480-1,850 DW	3
Largetooth aspen, *Populus grandidentata*, ^{226}Ra		
Near uranium tailing plant vs. control site		
Leaves	53 DW vs. 4 DW	4
Stems	99 DW vs. 5 DW	4
Elliot Lake, Canada, 1984-87 vs. control site		
Leaves	252 DW vs. 46 DW	5
Stems	223 DW vs. 4 DW	5
Trembling aspen, *Populus tremuloides*, ^{226}Ra		
Near uranium tailings plant vs. control site		
Leaves	42 DW vs. 11-15 DW	4
Stems	69 DW vs. 3-11 DW	4
Vegetation		
Belgium, near former nuclear fuel reprocessing plant, 1983, ^{129}I	Max. 0.09 FW	6
California, deer forage plants, three spp., 1968-69, ^{137}Cs	414-514 DW	7
Colorado, mule deer diet, all plants, ^{90}Sr		
1962-63 vs. 1963-64	2,242 AW vs. 4,499 AW	8
1964-65 vs. 1965-66	3,492 AW vs. 2,257 AW	8

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Colorado, mule deer diet, eight species of forage plants, ^{90}Sr, 1963-64 vs. 1964-65	1,258-17,412 AW vs. 828-16,620 AW	8
Finland, reindeer forage plants, 1961, Lapland		
Lichen, *Cladonia alpestris*		
^{137}Cs	466,200 AW	11
^{90}Sr	53,428 AW	11
Lichen mixture		
^{137}Cs	133,200 AW	11
^{90}Sr	19,980 AW	11
Other forage plants		
^{137}Cs	962-8,800 AW	11
^{90}Sr	266-1,924 AW	11
Florida, April 1969, ^{137}Cs	Max. 0.65 DW	12
Georgia, deer browse, 29 species, 1965-66		
^{144}Ce	Max. 373 DW	13
^{60}Co	Max. 15 DW	13
^{137}Cs	Max. 104 DW	13
^{54}Mn	Max. 118 DW	13
^{106}Ru	Max. 226 DW	13
^{125}Sb	Max. 56 DW	13
^{90}Sr	Max. 377 DW; max. 2,005 AW	13
^{95}Zr	Max. 63 DW	13
^{65}Zn	Max. 22 DW	13
Tennessee, 1974, ^{137}Cs, from soil accidentally contaminated in 1944		
Roots	Usually 3,700 DW; max. 111,000 DW	14
Trees	74-5,920 DW	14
Ground vegetation	592-3,996 DW	14
Ginger, *Zingiber officinale*, root, Nagasaki, Japan, 1945, postatomic detonation		
^{137}Cs	0.07 DW	1
$^{239+240}Pu$	0.04 DW	1
Aquatic plants		
Algae, decomposing; Hanford, Washington, 1973; plutonium processing pond		
^{241}Am	9,472 DW	15
^{238}Pu	36,482 DW	15
$^{239+240}Pu$	22,755 DW	15

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Algae and macrophytes, ^{137}Cs, Hudson River, 1970	1.5-5.6 FW	16
Algae, South Carolina, 1971-72, reactor discharge, ^{137}Cs	12,284 DW	17
Brown algae, *Fucus vesiculosus*	3.2 DW vs. 0.09 DW	18
Ireland, 1985-86, $^{239+240}Pu$, northeast coast vs. western seaboard		
Sweden, 1984, vicinity of nuclear plant		
^{58}Co	20-23 DW	19
^{61}Co	1,700-2,003 DW	19
^{137}Cs	7-16 DW	19
^{40}K	735-966 DW	19
^{54}Mn	36-60 DW	19
^{65}Zn	90-144 DW	19
Seaweed, *Porphyra* sp., 1974, Cumbrian coast UK, <2 km from beach		
^{241}Am	458 FW	20
^{242}Cm	18 FW	20
^{238}Pu	37 FW	20
$^{239+240}Pu$	162 FW	20
Sea lettuce, *Ulva lactuca*, whole, Connecticut, 1960, gross beta activity		
May	5,402-6,253 AW	21
August	5,291-8,066 AW	21
December	2,183-3,700 AW	21
Aquatic invertebrates		
Clams, 15 species, freshwater, 1960, Tennessee River, near Oak Ridge, ^{90}Sr, shell	15-921 AW	23
Connecticut, 1960, gross beta activity		
American oyster, *Crassostrea virginica*, soft parts		
May	2,553-3,589 AW	21
August	2,775-4,551 AW	21
December	851-1,850 AW	21
Mussel, *Mytilus edulis*, soft parts, August vs. December	3,256-4,551 AW vs. 3,034-3,108 AW	21
Crabs, Hudson River, 1970, ^{137}Cs	0.6 FW	16
Crustaceans, marine; fallout radionuclides, typical values		

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{110m}Ag	37.0 FW	24
^{60}Co	24.1 FW	24
^{54}Mn	2.2 FW	24
^{65}Zn	2.6 FW	24
Crustaceans, marine; natural radionuclides, typical values		
^{14}C	22.2 FW	24
^{3}H	0.1 FW	24
^{40}K	92.5 FW	24
^{210}Pb	2.2 FW	24
^{210}Po	37.0 FW	24
^{87}Rb	1.5 FW	24
Molluscs, bivalves, Hudson River, 1970, ^{137}Cs, soft parts	3 FW	16
Molluscs, freshwater; fallout radionuclides, typical values		
^{14}C	4-11 FW	24
^{3}H	0.1-159 FW	24
^{54}Mn	4-518 FW	24
Molluscs, marine; fallout radionuclides, typical values		
$^{141+144}Ce$	5-1,813 FW	24
^{57}Co	2-16 FW	24
^{60}Co	1-26 FW	24
^{137}Cs	5-25 FW	24
^{55}Fe	14-5,180 FW	24
^{54}Mn	2-222 FW	24
^{63}Ni	1-555 FW	24
^{239}Pu	Max. 0.02 FW	24
$^{103+106}Ru$	1-518 FW	24
^{110m}Ag	0.1-155 FW	24
^{65}Zn	0.7-425 FW	24
$^{95}Zr/^{95}Nb$	3-925 FW	24
Molluscs, marine; natural radionuclides		
^{14}C	18 FW	24
^{3}H	0.1 FW	24
^{40}K	107 FW	24
^{210}Pb	0.3 FW	24
^{210}Po	25 FW	24
^{87}Rb	2 FW	24
Mussel, *Mytilus edulis*, soft parts		

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Irish coastal waters, August 1988		
^{134}Cs	<0.7 DW	18
^{137}Cs	Usually <3 DW; max. 9 DW	18
^{40}K	182-355 DW	18
^{238}Pu	Usually <0.003 DW; max. 0.21 DW	18
$^{239+240}Pu$	Usually <0.035 DW; max. 1 DW	18
England, 1986-87, near nuclear plant		
^{110m}Ag	13 FW	25
^{241}Am	9-15 FW	25
^{144}Ce	6 FW	25
^{60}Co	3-7 FW	25
^{134}Cs	11 FW	25
^{137}Cs	5-31 FW	25
^{40}K	25-188 FW	25
^{95}Nb	3-106 FW	25
^{103}Ru	4-169 FW	25
^{106}Ru	64-151 FW	25
^{95}Zr	3-36 FW	25
Plankton, ^{137}Cs, Hudson River, 1970	2 FW	16
Plankton, Italy, 1971, near nuclear power station		
^{60}Co	Max. 203 FW	26
^{137}Cs	Max. 1,113 FW	26
Plankton, marine; fallout radionuclides, typical values		
$^{141+144}Ce$	14-17,760 FW	24
^{57}Co	85 FW	24
^{60}Co	11-592 FW	24
^{137}Cs	18-1,332 FW	24
^{155}Eu	14 FW	24
^{54}Mn	196 FW	24
^{63}Ni	4-14 FW	24
^{147}Pm	122 FW	24
$^{103+106}Ru$	11-1,110 FW	24
^{125}Sb	33 FW	24
^{90}Sr	0.7-12 FW	24
$^{95}Zr/^{95}Nb$	74-29,600 FW	24
Plankton, marine; natural radionuclides, typical values		
^{14}C	11 FW	24
^{3}H	0.1 FW	24

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{40}K	92 FW	24
^{210}Pb	9-25 FW	24
^{210}Po	22-62 FW	24
^{226}Ra	0.7 FW	24
^{228}Th	0.4-2 FW	24
^{234}U	0.7-2 FW	24
^{235}U	0.02-0.07 FW	24
^{238}U	0.7-2 FW	24
Polychaete annelid worms, marine; England, 1984-86; near nuclear plant vs. control location		
Arenicola marina		
^{137}Cs	132-321 FW vs. 3 FW	25
^{40}K	162-307 FW vs. 90 FW	25
^{238}Pu	14-16 FW vs. <0.05 FW	25
$^{239+240}Pu$	60-72 FW vs. 0.01 FW	25
Nereis diversicolor		
^{137}Cs	41-358 FW vs. 6 FW	25
^{40}K	23-148 FW vs. 134 FW	25
^{238}Pu	6-11 FW vs. <0.02 FW	25
$^{239+240}Pu$	25-48 FW vs. 0.03 FW	25
Clam, *Rangia cuneata*, Neuse River, North Carolina, 1965-67, soft parts; before Chinese nuclear tests in May and December 1966 vs. posttest		
^{144}Ce	5.3 FW vs. 7.2 FW	27,28
^{137}Cs	1.0 FW vs. 1.6 FW	27,28
^{55}Fe	0.12 FW vs. 0.75 FW	27,28
^{54}Mn	2.5 FW vs. 2.7 FW	27,28
^{106}Ru	2.1 FW vs. 2.7 FW	27,28
^{65}Zn	0.4 FW vs. 0.8 FW	27,28
Sea urchin, *Strongylocentrotus purpuratus*, 1966		
^{210}Pb	Max. 2 AW	29
^{210}Po	Max. 7 AW	29
Fishes		
Goldfish, *Carassius auratus* from plutonium processing waste pond, Hanford, Washington, 1973		
^{241}Am, whole vs. muscle	399 DW vs. 14 DW	15
$^{238+239+240}Pu$, whole vs. muscle	351 DW vs. 10 DW	15

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Colorado, 1965-66, ^{137}Cs, muscle, maximum values		
Cutthroat trout, *Oncorhynchus clarki*	59 FW	30
Rainbow trout, *Oncorhynchus mykiss*	117 FW	30
Sockeye (kokanee) salmon, *Oncorhynchus nerka*	8 FW	30
Brook trout, *Salvelinus fontinalis*	215 FW	30
Lake trout, *Salvelinus namaycusch*	25 FW	30
Brown trout, *Salmo trutta*	121 FW	30
Columbia River, Washington; near nuclear facility, 1961, ^{239}Np, muscle		
Chiselmouth, *Acrocheilus alutaceus*	Max. 14,900 FW	31
Bridgelip sucker, *Catostomus columbianus*	Max. 5,600 FW	31
Largescale sucker, *Catostomus macrocheilus*	Max. 3,600 FW	31
Mountain whitefish, *Prosopium williamsoni*	Max. 18,800 FW	31
Freshwater fish, whole body; fallout radionuclides, typical values		
^{14}C	4-7 FW	24
^{137}Cs	1-973 FW	24
^{55}Fe	1-3 FW	24
^{3}H	0.1-159 FW	24
^{54}Mn	11 FW	24
^{85}Sr	0.04-0.4 FW	24
^{89}Sr	0.2-40 FW	24
^{90}Sr	0.04-177 FW	24
$^{95}Zr/^{95}Nb$	2.2-2.6 FW	24
Freshwater fishes, 1963-64, ^{210}Pb, bone vs. soft tissues	2.5 AW vs. 0.2 AW	29
Freshwater fishes, whole body, ^{137}Cs; Red Lakes, Minnesota		
1954-57	0.7-2.4 FW	32
1959-62	3-12 FW	32
1963-66	8-22 FW	32
Freshwater fishes, typical maximum concentrations, whole body		
^{3}H	0.5 FW	24
^{40}K	130 FW	24

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{87}Rb	8 FW	24
^{238}U	0.1 FW	24
^{234}U	0.2 FW	24
^{226}Ra	129 FW	24
^{210}Pb (bone)	3 FW	24
^{210}Po (liver)	18 FW	24
^{232}Th	0.05 FW	24
^{235}U	0.004 FW	24
Mosquitofish, *Gambusia holbrooki*, ^{137}Cs, April 1987; from South Carolina reservoir contaminated with ^{137}Cs between 1961 and 1964, whole body	Max. 2,230 FW	33
Hudson River, 1970, ^{137}Cs		
Atlantic sturgeon, *Acipenser oxyrhynchus* muscle	0.6 FW	16
American eel, *Anguilla rostrata*, muscle	1.3 FW	16
Mummichog, *Fundulus heteroclitus*, whole	2.0 FW	16
Catfish, *Ictalurus* sp., muscle	1.9 FW	16
White perch, *Morone americana*, muscle vs. whole body	0.8 FW vs. 0.8 FW	16
Striped bass, *Morone saxatilis*, muscle	0.9 FW	16
Yellow perch, *Perca flavescens*, muscle	1.5 FW	16
Italy, 1971, near nuclear power station, whole fish, various species		
^{60}Co	Max. 9 DW	26
^{137}Cs	Max. 104 DW	26
Lake Ontario, ^{137}Cs, 1981		
Common carp, *Cyprinus carpio*, bone vs. other tissues	5 FW vs. <5 FW	34
Northern pike, *Esox lucius*		
Bone, liver	5 FW	34
Roe	15 FW	34
Other tissues	<5 FW	34
Coho salmon, *Oncorhynchus kisutch*		
GI tract	5 FW	34
Liver	13 FW	34
Other tissues	<5 FW	34
Largemouth bass, *Micropterus*	3,677 DW	17

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
salmoides, South Carolina, reactor discharge, 1971-72, ^{137}Cs, whole		
Marine fishes, whole body, fallout radionuclides, typical values		
^{110m}Ag	2-3 FW	24
$^{141+144}Ce$	2-1,036 FW	24
^{60}Co	1-13 FW	24
^{137}Cs	2-3 FW	24
^{55}Fe		
Gonad	8,140-10,360 FW	24
Liver	59,940-68,820 FW	24
Muscle	37-3,922 FW	24
^{54}Mn	0.07-2 FW	24
^{239}Pu	Max. 0.005 FW	24
$^{103+106}Ru$	2-244 FW	24
$^{95}Zr/^{95}Nb$	1-277 FW	24
^{65}Zn	2-7 FW	24
Marine fishes, whole body, natural radionuclides, typical values		
^{14}C	15 FW	24
^{3}H	0.1 FW	24
^{40}K	92 FW	24
^{210}Pb	5 FW	24
^{210}Po	33 FW	24
^{226}Ra	0.2 FW	24
^{87}Rb	1 FW	24
^{234}U	1 FW	24
^{235}U	0.05 FW	24
^{238}U	1 FW	24
Golden shiner, *Notemigonus crysoleucas*, whole, ^{137}Cs, Hudson River estuary		
1966 vs. 1968	0.9 FW vs. 0.8 FW	16
1969 vs. 1970	0.7 FW vs. 0.5 FW	16
Oceanic fishes, 1962-64, bone vs. soft parts		
^{210}Pb	10 AW vs. 0.06 AW	29
^{210}Po	12 AW vs. 0.1 AW	29
^{226}Ra	2 AW vs. 0.06 AW	29
Plaice, *Pleuronectes platessa*, near nuclear facility, England		
1968 vs. 1969, ^{137}Cs		

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Gut contents	44-181 FW vs. 126-266 FW	35
Muscle	26-70 FW vs. 89-152 FW	35
1968, gut contents		
^{144}Ce	880-1,150 FW	35
^{106}Ru	1,343-5,143 FW	35
$^{95}Zr/^{95}Nb$	3,122-5,794 FW	35
Albacore, *Thunnus alalunga* southern California near San Diego, liver		
Summer 1964 vs. summer 1965		
^{110m}Ag	3 FW vs. 4 FW	36
^{60}Co	7 FW vs. 7 FW	36
^{40}K	71 FW vs. 72 FW	36
^{54}Mn	39 FW vs. 22 FW	36
^{65}Zn	46 FW vs. 14 FW	36
Summer 1968 vs. summer 1970		
^{60}Co	2 FW vs. 2 FW	36
^{40}K	81 FW vs. 78 FW	36
^{54}Mn	2 FW vs. 0.6 FW	36
^{65}Zn	25 FW vs. 9 FW	36
Yellowfin tuna, *Thunnus albacares*, 1968, near San Diego, liver		
^{60}Co	1 FW	36
^{40}K	93 FW	36
^{54}Mn	1 FW	36
^{65}Zn	3 FW	36
Tunas, 1970-71, Hawaii, liver		
^{108m}Ag	0.03-2 FW	36
^{110m}Ag	0.01-7 FW	36
^{60}Co	0.9-3 FW	36
^{40}K	68-83 FW	36
^{65}Zn	5-27 FW	36
Reptiles		
Snakes, two species (*Elaphe obsoleta*, *Nerodia taxispilota*), Aiken, South Carolina; whole animal, ^{137}Cs		
Site contaminated with ^{137}Cs between 1961 and 1970, *Elaphe vs*. *Nerodia*		
1972	6,037 FW vs. 7,629 FW	58
1976	592 FW vs. 1,333 FW	58
1980	296 FW vs. 1,037 FW	58
Uncontaminated site, both species, 1972-80	<37 FW	58
Snakes, 19 species, whole,		

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
vicinity of Aiken, South Carolina, March 1971-November 1972, $^{134+137}Cs$		
Near reactor effluent stream	4,870 FW, max. 38,200 FW	9
Near reactor cooling reservoir	1,025 FW, max. 5,159 FW	9
Uncontaminated habitats	92 FW	9
Slider turtle, *Trachemys scripta*, from radioactive reservoirs, Aiken, South Carolina, whole body		
High-level waste pond vs. low-level waste pond		
^{137}Cs	3,020 FW vs. 1,002 FW	37
^{90}Sr	94,030 FW vs. 2,236 FW	37
Control sites		
^{137}Cs	0.001 FW	37
^{90}Sr	0.2 FW	37
Turtles, southeastern USA, 1970, ^{90}Sr, exoskeleton		
Snapping turtle, *Chelydra serpentina*	784 (284-1,283) AW	38
Gopher tortoise, *Gopherus polyphemus*	4,765 AW	38
Common mud turtle, *Kinosternon sabrubrum*	1,309 (569-2,904) AW	38
Missouri slider, *Pseudemys floridana hoyi*	1,761 AW	38
Peninsula cooter, *Pseudemys floridana peninsularis*	33 (ND-48) AW	38
Pond slider, *Pseudemys scripta*	777 (188-2,190) AW	38
Loggerhead musk turtle, *Sternotherus minor minor*	24 (ND-48) AW	38
Common musk turtle, *Sternotherus odoratus*	525 (52-999) AW	38
Common box turtle, *Terrapene carolina*	1,087 (48-2,856) AW	38
Birds		
Ruffed grouse, *Bonasa umbellus*; near uranium tailings discharge, Canada, Elliot Lake, 1987-88, ^{226}Ra		
Bone vs. gut contents	10-28 DW vs. 7-22 DW	4
Liver vs. muscle	5-12 DW vs. 1.5-1.9 DW	4
Canada goose, *Branta canadensis moffitti*; Columbia River, Washington, 1985-87, near reactor; eggshell, ^{90}Sr	18-60 DW	39
American coot, *Fulica americana*; Hanford, Washington, June 1974-January 1977		

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{137}Cs (Hanford vs. control ponds)		
Bone	7,400 vs. 37 DW	40
Gut contents	125,800 vs. 29 DW	40
Liver	16,280 vs. 26 DW	40
Muscle	21,090 vs. 0.7 DW	40
^{90}Sr (Hanford only)		
Bone	96 DW	40
Gut contents	159 DW	40
Liver	18 DW	40
Muscle	10 DW	40
Barn swallow, *Hirundo rustica*; Idaho, 1976-77, nesting near radioactive leaching ponds		
Whole adults		
^{140}Ba	800 FW	41
^{134}Cs	1,300 FW	41
^{137}Cs	6,400 FW	41
^{51}Cr	16,100 FW	41
^{60}Co	1,480 FW	41
^{131}I, whole vs. thyroid	5,500 FW vs. 3,330,000 FW	41
^{24}Na	8,600 FW	41
^{75}Se	5,000 FW	41
^{65}Zn	5,900 FW	41
Nests		
^{140}Ba	1,200 DW	41
^{134}Cs	13,800 DW	41
^{137}Cs	92,000 DW	41
^{141}Ce	1,200 DW	41
^{144}Ce	4,000 DW	41
^{51}Cr	230,000 DW	41
^{131}I	800 DW	41
^{65}Zn	1,800 DW	41
Massachusetts, 1973-75, 15 passerine species, trapped near nuclear power station, whole body		
Northern bobwhite, *Colinus virginianus*		
^{137}Cs	Max. 73 FW	42
^{131}I	Max. 6 FW	42
^{40}K	Max. 131 FW	42
$^{95}Zr/^{95}Nb$	Max. 4 FW	42
Blue jay, *Cyanocitta cristata*		
^{137}Cs	28 FW; max. 65 FW	42
^{131}I	1 FW; max. 9 FW	42

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{40}K	96 FW; max. 181 FW	42
$^{95}Zr/^{95}Nb$	2 FW; max. 6 FW	42
13 species		
^{137}Cs	Max. 82 FW	42
^{131}I	Max. 18 FW	42
^{40}K	Max. 268 FW	42
$^{95}Zr/^{95}Nb$	Max. 40 FW	42
United Kingdom, Ravenglass estuary, 1980-84, near nuclear plant		
Mallard, *Anas platyrhynchos*		
^{134}Cs, muscle	87 FW	25
^{137}Cs, muscle vs. liver	167 FW vs. 126 FW	25
$^{239+240}Pu$, liver	3.4 FW	25
^{238}Pu, liver	1.1 FW	25
Greylag goose, *Anser anser*		
^{137}Cs, muscle vs. liver	58 FW vs. 28 FW	25
^{238}Pu, muscle vs. liver	0.03 FW vs. 3 FW	25
$^{239+240}Pu$, muscle vs. liver	0.1 FW vs. 13 FW	25
Carrion crow, *Corvus corone*		
^{137}Cs, Ravenglass vs. control location		
Muscle	162 FW vs. 17 FW	25
Liver	131 FW vs. 8 FW	25
Lesser black-backed gull, *Larus marinus*		
^{137}Cs, muscle vs. liver	158 FW vs. 163 FW	25
$^{239+240}Pu$, muscle vs. liver	0.1 FW vs. 5 FW	25
Common black-headed gull, *Larus ridibundus*, whole chick		
^{134}Cs	0.8 FW	25
^{137}Cs	25 FW	25
^{238}Pu	0.1 FW	25
$^{239+240}Pu$	0.5 FW	25
Eurasian oystercatcher, *Haematopus ostralegus*, Ravenglass vs. control location		
^{137}Cs		
Muscle	613 FW vs. 22 FW	25
Liver	463 FW vs. 20 FW	25
^{238}Pu		
Muscle	0.2 FW vs. <0.01 FW	25
Liver	1.8 FW vs. 0.04 FW	25
$^{239+240}Pu$		
Muscle	0.5 FW vs. 0.04 FW	25
Liver	4.1 FW vs. 0.09 FW	25
Bar-tailed godwit, *Limosa lapponica lapponica*		

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{137}Cs, muscle vs. liver	478 FW vs. 510 FW	25
^{238}Pu, muscle vs. liver	<0.02 FW vs 0.2 FW	25
$^{239+240}Pu$, muscle vs. liver	0.03 FW vs. 0.9 FW	25
Red-breasted merganser, *Mergus serrator*		
^{134}Cs, muscle vs. liver	8 FW vs. 13 FW	25
^{137}Cs, muscle vs. liver	144 FW vs. 251 FW	25
^{238}Pu, muscle vs. liver	<0.01 FW vs. <0.04 FW	25
$^{239+240}Pu$, muscle vs. liver	0.02 FW vs <0.04 FW	25
Eurasian curlew, *Numenius arquata*		
^{137}Cs, Ravenglass vs. control location		
Muscle	140 FW vs. 49 FW	25
Liver	104 FW vs. 99 FW	25
^{238}Pu, Ravenglass vs. control location		
Muscle	0.09 FW vs. <0.02 FW	25
Liver	0.14 FW vs. <0.05 FW	25
$^{239+240}Pu$, Ravenglass vs. control location		
Muscle	0.09 FW vs. <0.02 FW	25
Liver	0.14 FW vs. <0.05 FW	25
Marine mammals		
Bearded seal, *Erignathus barbatus*; Alaska, 1963		
Bone		
^{210}Pb	Max. 2.7 AW	29
^{226}Ra	2.4 AW	29
Soft tissues, ^{210}Pb	Max. 0.2 AW	29
Gray seal, *Halichoerus grypus*, North Sea and northeast Atlantic Ocean, 1987		
Females, milk vs. muscle		
^{241}Am	<0.0002 FW vs. <0.0005 FW	43
^{134}Cs	0.6 (0.4-0.7) FW vs. <0.002 FW	43
^{137}Cs	2.9 (1.1-4.8) FW vs. 14.3 FW	43
^{40}K	107 (67-215) FW vs. 0.2 FW	43
^{238}Pu	<0.0002 FW vs. <0.0005 FW	43
$^{239+240}Pu$	<0.0002 FW vs. <0.0005 FW	43
Pup, muscle vs. liver		
^{241}Am	<0.0003 FW vs. <0.0003 FW	43
^{134}Cs	Max. 0.003 FW vs. max. 0.00 1 FW	43
^{137}Cs	Max. 0.03 FW vs. max. 0.02 FW	43
^{40}K	Max. 0.2 FW vs. max. 0.2 FW	43
^{238}Pu	Max. 0.0005 FW vs. max. 0.001 FW	43
$^{239+240}Pu$	Max. 0.002 FW vs. max. 0.004 FW	43
Spotted seal, *Phoca largha*; Alaska, 1963, bone vs. soft tissues		
^{210}Pb	2 AW vs. 0.1 AW	29

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{226}Ra	3 AW vs. no data	29
Sperm whale, *Physeter catodon*; Alaska, 1965, bone vs. soft tissue		
^{210}Pb	135 AW vs. 0.37 AW	29
^{210}Po	114 AW vs. 23 AW	29
Terrestrial mammals		
Cattle, *Bos* sp.		
Nevada, 1973, grazing for 3 years in area contaminated in 1957 with transuranic radionuclides		
^{241}Am		
Bone vs. liver	Max. 1 FW vs. max. 0.6 FW	44
Lymph nodes vs. lungs	Max. 24 FW vs. max. 2 FW	44
Other tissues	<0.6 FW	44
^{238}Pu		
Lungs, lymph nodes	Max. 3 FW	44
Testes	Max. 0.8 FW	44
Other tissues	<0.6 FW	44
$^{239+240}Pu$		
Bone vs. liver	Max. 3 FW vs. max. 34 FW	44
Lungs vs. lymph nodes	Max. 34 FW vs. max. 85 FW	44
Muscle vs. other tissues	Max. 7 FW vs. <1.2 FW	44
Europe, ^{129}I, thyroids		
1978		
Belgium vs. Germany	0.017-3.7 FW vs. max. 0.03 FW	6
Italy vs. Netherlands	Max. 0.05 FW vs. max. 0.03 FW	6
1979, Netherlands	Max. 0.07 FW	6
1980, Netherlands	0.07-0.6 FW	6
1981, Germany	Max. 0.02 FW	6
Beaver, *Castor canadensis*; Canada, 1984-87, adults, ^{226}Ra; from watershed containing uranium tailings vs. control site		
Bone	115 DW vs. 20 DW	5
Gut contents	62 DW vs. 9 DW	5
Kidney	9 DW vs. 2DW	5
Liver	2.7 DW vs. 1.4 DW	5
Muscle	2.9 DW vs. 1.0 DW	5
Georgia and South Carolina, 1964-66, ^{137}Cs, whole organism		
Domestic dog, *Canis familiaris*	23 FW	45
Coyote, *Canis latrans*	26 FW	45
Bobcat, *Lynx rufus*	117-561 FW	45
Cotton rat, *Sigmodon hispidus*	16-29 FW	45
Eastern cottontail, *Sylvilagus floridanus*	19-35 FW	45
Gray fox, *Urocyon*	34-169 FW	45

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
cinereoargentatus		
Red fox, *Vulpes fulva*	23-60 FW	45
Humans, *Homo sapiens*;		
Denmark, ^{137}Cs, annual dietary loading		
1964	71.9 FW	46
1985	1.4 FW	46
1986-87	12.6 FW	46
Black-tailed jack rabbit, *Lepus californicus*; Nevada test site, bone, ^{90}Sr		
1952-66	74-476 AW	47
1958 (1-year post detonation), ground zero vs. 32-700 km distant	373 AW vs. 88-198 AW	48
1959, ground zero	329 AW	48
1959, 32 km vs. 120-700 km	466 AW vs. 95-222 AW	48
1961, within 160 km of ground zero	143 AW	48
Mule deer, *Odocoileus hemionus*; 1961-65, Colorado, femur, ^{90}Sr		
1961-62 vs. 1962-63	Max. 215 AW vs. max. 528 AW	8
1963-64 vs. 1964-65	Max. 777 AW vs. max. 637 AW	8
Black-tailed deer, *Odocoileus hemionus columbianus*; California		
Muscle vs. rumen contents, 1968-69, ^{137}Cs		
Summer	37 DW vs. 48 DW	7
Fall	33 DW vs. 37 DW	7
Winter	48 DW vs. 67 DW	7
Mendocino County, California, mandible, yearlings, ^{90}Sr		
1952-53 vs. 1954	3-11 AW vs. 26-34 AW	49
1955 vs. 1956	29-124 AW vs. 112 AW	49
1957 vs. 1958	87-239 AW vs. 134-228 AW	49
1959 vs. 1960	243-533 AW vs. 204-332 AW	49
White-tailed deer, *Odocoileus virginianus* Georgia, 1965-66		
^{137}Cs		
Heart vs. kidney	127 FW vs. 149 FW	13
Liver vs. lung	70 FW vs. 73 FW	13
Muscle vs. spleen	126 FW vs. 126 FW	13
Tongue	172 FW	13
^{90}Sr, mandible		
Age 1.5 years	940 AW	13
Age 2.5 years	828 AW	13
Age 3.5 years	799 AW	13

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Southeastern United States		
^{137}Cs, Muscle, 1967-71		
Alluvial region (LA, MS, FL, SC, NC)	85 (9-650) FW	50
Lower Coastal Plain (SC, GA, FL, VA, NC)	1,036 (9-5,658) FW	50
Mountain region (WV, KY, MD, NC, TN, GA)	78 (9-401) FW	50
Piedmont region (GA, SC, AL)	105 (9-383) FW	50
Upper Coastal Plain region (MD, NC, GA, VA, MS, LA, AK)	154 (9-1,752) FW	50
^{90}Sr, bone, 1969		
Lower Coastal Plain	1,172 (376-1,766) FW	50
Mountain region	499 (148-888) FW	50
Piedmont region	471 (263-683) FW	50
Muskrat, *Ondatra zibethicus*; August 1960, Oak Ridge, Tennessee, from settling basin for radioactive wastes, single most radioactive animal		
Brain vs. eyes		
^{60}Co	10,545 DW vs. 39,960 DW	51
^{137}Cs	392,200 DW vs. 640,100 DW	51
^{65}Zn	21,016 DW vs. 36,593 DW	51
Femur		
^{60}Co	5,920 DW	51
^{137}Cs	121,360 DW	51
^{90}Sr	7,030,000 DW	51
^{65}Zn	28,601 DW	51
Kidney vs. spleen		
^{60}Co	279,720 DW vs.47,730 DW	51
^{137}Cs	954,600 DW vs. 799,200 DW	51
Liver		
^{60}Co	156,880 DW	51
^{137}Cs	629,000 DW	51
^{65}Zn	78,440 DW	51
Muscle		
^{60}Co	8,103 DW	51
^{134}Cs	13,949 DW	51
^{137}Cs	1,265,400 DW	51
^{65}Zn	19,610 DW	51
Teeth		
^{137}Cs	64,010 DW	51
^{90}Sr	9,916,000 DW	51
^{65}Zn	25,789 DW	51

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Pelt		
^{60}Co	15,022 DW	51
^{137}Cs	204,980 DW	51
^{90}Sr	37,000 DW	51
^{65}Zn	26,196 DW	51
Domestic sheep, *Ovis aries*		
Near nuclear fuel reprocessing facility vs. control site, England, 1983		
Bone		
^{241}Am	1 FW vs. 0.003 FW	52
$^{239+240}Pu$	0.6 FW vs. 0.002 FW	52
Liver		
^{241}Am	1 FW vs. 0.002 FW	52
^{137}Cs	8 FW vs. 0.2 FW	52
$^{239+240}Pu$	2 FW vs. 0.008 FW	52
Lung		
^{241}Am	0.3 FW vs. 0.003 FW	52
$^{239+240}Pu$	0.4 FW vs. 0.002 FW	52
Muscle		
^{241}Am	0.03 FW vs. 0.0005 FW	52
^{137}Cs	49 FW vs. 0.2 FW	52
$^{239+240}Pu$	0.007 FW vs. 0.0008 FW	52
Near nuclear fuel reprocessing plant, England, winter 1986-87		
^{241}Am		
Bone vs. liver	0.03-0.7 FW vs. 0.03-0.8 FW	53
Lung vs. muscle	0.009-0.1 FW vs. 0.002-0.03 FW	53
Whole sheep	0.27-4 FW	53
^{137}Cs		
Bone vs. liver	1.3-14 FW vs. 1.8-30 FW	53
Lung vs. muscle	1.5-16 FW vs. 4.6-42 FW	53
Whole sheep	159-748 FW	53
$^{239+240}Pu$		
Bone vs. liver	0.024-0.2 FW vs. 0.07-0.9 FW	53
Lung vs. muscle	0.005-0.02 FW vs. 0.0005-0.005 FW	53
Whole sheep	0.02-2 FW	53
Serbia, 1988, wildlife		
Roe deer, *Capreolus sp*.; bone vs. muscle		
^{137}Cs	ND vs. 0.2 AW	54
^{40}K	23 AW vs. 39 AW	54
^{90}Sr	6 AW vs. 0.6 AW	54
Fallow deer, *Dama sp*.; bone vs. muscle		

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{137}Cs	ND vs. 0.1 AW	54
^{40}K	8 AW vs. 45 AW	54
^{90}Sr	10 AW vs. 0.3 AW	54
Wild hare, *Lepus* sp.; bone vs. muscle		
^{137}Cs	ND vs. 0.1 AW	54
^{40}K	26 AW vs. 52 AW	54
^{90}Sr	18 AW vs. ND	54
Wild boar, *Sus scrofa*; bone vs. muscle		
^{137}Cs	ND vs. 0.4 AW	54
^{40}K	21 AW vs. 56 AW	54
^{90}Sr	34 AW vs. 2 AW	54
Common shrew, *Sorex araneus*; 1988, England, muscle; shrews from mineral soils vs. peaty soils		
^{134}Cs	7 FW vs. 16 FW	55
^{137}Cs	58 FW vs. 161 FW	55
Integrated studies		
Brazil, site of radiological accident in September 1987 at Goiania wherein ^{137}Cs was deposited on soil for 3 weeks before remedial action. Rainwater runoff contaminated the waterways 3 weeks postaccident, up to 12 km from accident area, ^{137}Cs		
Fish muscle	Max. 200 FW	56
Sediments	Max. 1,300 DW	56
Surface waters and suspended particulates	<1 FW	56
10 months postaccident, up to 80 km downstream, ^{137}Cs		
Fish muscle		
Pike, *Hoplias* sp.	14 FW	56
Piranha, *Seerasalmus sp*.	10 FW	56
Sediments	100 DW	56
Water hyacinth, *Eichornia* sp.	Max. 0.4 FW	56
Great Lakes, ^{137}Cs, 1981		
Aquatic plants vs. clams	1.4 FW vs. 0.3 FW	34
Fish vs. plankton	1.5 FW vs. 0.1 FW	34
Sediments vs. water	24 FW vs. 0.0007 FW	34
Irish Sea and North Sea, 1983, invertebrates vs. fish		
^{241}Am	Max. 75 FW vs. max. 0.05 FW	57

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
^{242}Cm	Max. 2 FW vs. max. 0.0003 FW	57
$^{243+244}Cm$	Max. 0.5 FW vs. 0.0003 FW	57
^{238}Pu	14 FW vs. 0.01 FW	57
$^{239+240}Pu$	54 FW vs. 0.04 FW	57
^{241}Pu, invertebrates only	Max. 1,000 FW	57
Japan, Nagasaki, 1945 post-atomic detonation		
Fish vs. snail		
^{137}Cs	0.01 DW vs. 0.02 DW	1
$^{239+240}Pu$	0.03 DW vs. 0.03 DW	1
South Carolina, watershed of a former reactor effluent stream, ^{137}Cs, 1971 vs. 1981		
Plants	14,000-19,000 DW vs. 2,600-9,600 DW	10
Arthropods	9,600-16,000 DW vs. 700-3,300 DW	10
South Carolina; reactor cooling impoundment accidentally contaminated in 1961-64 with ^{137}Cs, ^{90}Sr, and various transuranics; samples collected September 1983-February 1984		
^{137}Cs		
Water vs. sediments	0.76 FW vs. max. near 40,000 DW	22
Aquatic macrophytes vs. benthic invertebrates	Max. near 30,000 DW vs. 930-14,000 DW	22
Fish muscle	2,100-8,000 FW; 21,000 DW	22
Turtle muscle	2,100 FW	22
Waterfowl muscle	3,100 FW; 15,000 DW	22
^{90}Sr		
Water vs. sediments	0.14 FW vs. max. near 400 DW	22
Aquatic macrophytes vs. benthic invertebrates	Max. 2,600 DW vs. 42-7,900 DW	22
Fish bone ash vs. fish muscle	12,000-23,000 DW vs. 86-470 DW	22
Turtle shell and bone ash	12,000 DW	22
Waterfowl muscle vs. waterfowl bone ash	14 DW vs. 420 DW	22
^{238}Pu		
Water vs. sediments	0.0000034 FW vs. max. 10 DW	22
Aquatic macrophytes vs. fish muscle	Max. 0.5 DW vs. 0.004 DW	22
Turtle shell ash vs. waterfowl bone ash	0.1 DW vs. 100 DW	22
Waterfowl muscle	0.013 DW	22
$^{239+240}Pu$		
Water	0.0000088 FW	22

Table 14. Ecosystem, organism, radionuclide, and other variables	Concentration (in Bq/kg[a])	Reference[b]
Sediments	Max. near 85 DW	22
Aquatic macrophytes	Max. near 1.2 DW	22
Turtle shell ash	ND	22
Waterfowl muscle	0.008 DW	22
^{241}Am		
Water vs. sediments	0.000023 FW vs. max. 40 DW	22
Turtle shell ash vs. waterfowl muscle	ND vs. 0.015 DW	22
^{244}Cm		
Water vs. sediments	0.00064 FW vs. max. 18 DW	22
Fish liver vs. turtle shell ash	11 DW vs. 0.2 DW	22
Waterfowl muscle	0.071 DW	22

[a]Values originally expressed in strontium units (1 nCi ^{90}Sr/g calcium AW) were transformed to Bq/kg AW by a multiplication factor of 98.4.

[b]1, Kudo, et al. 1991; 2, Hanson 1976; 3, Rickard and Price 1990; 4, Clulow et al. 1992; 5, Clulow et al. 1991; 6, Handl et al. 1990; 7, Book 1969; 8, Farris et al. 1969; 9, Brisbin et al. 1974; 10, Brisbin et al. 1989; 11, Miettinen 1969; 12, Cummings et al. 1971; 13, Plummer et al. 1969; 14, Dahlman and Voris 1976; 15, Emery et al. 1976; 16, Wrenn et al. 1971; 17, Shure and Gottschalk 1976; 18, Crowley et al. 1990; 19, Carlson and Erlandsson 1991; 20, Hetherington et al. 1976; 21, Hatfield et al. 1963; 22, Whicker et al. 1990; 23, Nelson 1963; 24, IAEA 1976; 25, Lowe 1991; 26, Smedile and Queirazza 1976; 27, Wolfe and Schelske 1969; 28, Wolfe and Jennings 1971; 29, Holtzman 1969; 30, Nelson and Whicker 1969; 31, Poston et al. 1990; 32, Gustafson 1969; 33, Newman and Brisbin 1990; 34, Joshi 1991; 35, Pentreath et al. 1971; 36, Folsom et al. 1971; 37, Lamb et al. 1991; 38, Holcomb et al. 1971; 39, Rickard and Price 1990; 40, Cadwell et al. 1979; 41, Millard and Whicker 1990; 42, Levy et al. 1976; 43, S. S. Anderson et al. 1990; 44, Gilbert et al. 1989; 45, Jenkins et al. 1969; 46, Aarkrog 1990; 47, Romney et al. 1971; 48, Neel and Larson 1963; 49, Schultz and Longhurst 1963; 50, Jenkins and Fendley 1971; 51, Kaye and Dunaway 1963; 52, Curtis et al. 1991; 53, Ham et al. 1989; 54, Veskovic and Djuric 1990; 55, Lowe and Horrill 1991; 56, Godoy et al. 1991; 57, United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1988; 58, Bagshaw and Brisbin 1984.

[c]ND = non detectable.

Consumption of shellfish represents a negligible radiological risk to humans (Crowley et al. 1990), although bivalve molluscs seem to be effective accumulators of radioisotopes. After the Chinese nuclear tests in May and December 1966, concentrations of ^{144}Ce, ^{103}Ru, ^{95}Zr, ^{95}Nb, ^{140}Ba, and ^{140}La in three species of bivalves in the Neuse River, North Carolina, increased suddenly (Wolfe and Schelske 1969). In 1973, Pacific oysters (*Crassostrea gigas*) from the discharge canal of a nuclear power plant in Humboldt Bay, California, rapidly accumulated ^{54}Mn, ^{60}Co, ^{65}Zn, and ^{137}Cs within 30 min of release. Isotope uptake correlated positively with particulates in the water, including living microorganisms, organic detritus, inorganic materials, and especially resuspended bottom sediments (Harrison et al. 1976). Although concentrations of cesium and plutonium in mussels (*Mytilus edulis*) from most Irish estuaries are essentially the same as global fallout levels, concentrations were elevated in mussels from the northeast coast (Crowley et al. 1990).

Birds

Television and newspaper reporters attributed radionuclides to a decline in bird numbers at the Ravenglass estuary, England, particularly of the common black-headed gull (*Larus ridibundus*), although the concentrations of radionuclides in the avian diet, body tissues, and general environment were at least 1,000 times too low to have had any effect (Table 14; Lowe 1991). Although Eurasian oystercatchers (*Haematopus ostralegus*) and shelducks (*Tadorna tadorna*) had the highest concentrations of ^{137}Cs in their tissues, the breeding success and population sizes of these birds were not affected. Black-headed gulls had less radiocontamination than other

birds at Ravenglass, but their population continued to decline. The most probable cause was a combination of an uncontrolled fox population, a severe outbreak of myomatosis in rabbits (normal fox prey), and a drought--all in the same year (Lowe 1991). Nesting success of birds was unaffected in the vicinity of nuclear power plants. For example, nesting barn swallows (*Hirundo rustica*) near radioactive leaching ponds had normal nesting success despite their consumption of arthropods from the pond and use of contaminated mud for nest construction (Millard and Whicker 1990; Table 14). Adult swallows received a total internal dose rate of 219 uGy/day, mostly (72%) from ^{24}Na; daily dose rates to eggs and nestlings during the nesting season were 840 uGy and 2,200 uGy. The total dose to eggs and nestlings (54 mGy) and adults (450 mGy) had no measurable effect on survival and was below accumulated doses reported to cause death of passerines (Millard and Whicker 1990).

Strontium-90 behaves much like calcium in the biological environment. In birds, ^{90}Sr is expected to occur in bone and in the calcium-rich eggshell. In one case, a positive relation was demonstrated between reactor releases of ^{90}Sr to the Columbia River and ^{90}Sr concentrations in reed canary grass (*Phalaris arundinacea*) and eggshells of the Canada goose (*Branta canadensis moffitti*; Rickard and Price 1990).

No human health problem is anticipated from consumption of ruffed grouse (*Bonasa umbellus*) that are contaminated with ^{226}Ra in Canada or of American coots (*Fulica americana*) contaminated with ^{137}Cs in Washington state. Tissues of ruffed grouse that were collected near discharged uranium tailings in Canada in 1987-88 did not contain grossly elevated levels of ^{226}Ra over controls; consumption of grouse by humans did not present a radiological health problem (Clulow et al. 1992). Based on ^{137}Cs alone, humans who consume a single contaminated American coot captured at Hanford, Washington, would receive about 1.1% of the annual radiation protection dose of 1.70 mSv by individuals and populations in uncontrolled areas (Cadwell et al. 1979).

Mammals

Diets in Denmark contained elevated loadings of ^{137}Cs in 1964 because of the intensive atmospheric nuclear-test series by the United States and the former Soviet Union in 1961 and 1962. Total ^{137}Cs intake declined in the Danish population from 72 Bq/kg BW in 1964 to less than 2 in 1985 but rose to about 13 in 1986 from the effects of debris from Chernobyl on dietary ^{137}Cs during the first year after the accident (Aarkrog 1990). The estimated dose equivalent from ^{137}Cs to human consumers of fish from the Great Lakes is about 0.01 uSv/kg fresh weight (FW) muscle of fish from Lakes Erie and Ontario and 0.06-0.07 uSv/kg from fish in Lakes Superior and Huron (Joshi 1991). The guide for the protection of the general public from radiation is less than 5 mSv annually, and consumption of fish that contains a dose equivalent greater than 0.02 uSv/kg fish flesh is not recommended (Joshi 1991). Some Scandinavians now receive a dose equivalent of about 5 mSv/year from intake of radiocesium in the diet (Johanson 1990). In Finland, uptake of radionuclides by humans in Finnish Lapland and in other areas with an arctic climate is attributed to ecological factors and to a high amount of local fallout. For example, reindeer-herding Finnish Lapps contained about 50 times more ^{137}Cs and 10 times more ^{55}Fe than other Finns during 1961-67. For ^{137}Cs, this disparity is attributed mainly to the reliance by Finns on reindeer meat--which contains high levels of ^{137}Cs as a result of reindeer feeding on lichens--and secondarily, on freshwater fish and cow's milk (Miettinen 1969).

In the United States, the estimated annual whole body human radiation dose equivalent is 1.61 mSv, mostly from natural sources (0.85 mSv) and medical sources (0.70 mSv) but also from fallout (0.03 mSv), miscellaneous sources (0.02 mSv), occupational hazards (0.008 mSv), and nuclear power (0.0001 mSv; League of Women Voters [LWV] 1985). Radiation doses to people who live near the Hanford nuclear industrial and research site in the state of Washington are well below existing regulatory standards. Only trace amounts of radionuclides from Hanford have been detected in the offsite environment (Gray et al. 1989). In December 1984, radon levels as much as 130 times greater than considered safe under the current guideline for underground uranium miners were discovered in human residences in eastern Pennsylvania, New Jersey, and New York. About 25% of all residences in 10 states exceeded the action level for radon of 0.185 Bq/L air (Cross 1990; Oge and Dickson 1990). The significance of this observation to avian and terrestrial wildlife merits investigation.

As a result of nuclear weapons testing, mandibles of Columbian black-tailed deer (*Odocoileus hemionus columbianus*) from California increased from less than 9 Bq ^{90}Sr/kg ash weight (AW) to more than 204 Bq/kg AW between 1952 and 1960 (Table 14; Schultz and Longhurst 1963). Age and season affected strontium kinetics in male mule deer (*Odocoileus hemionus hemionus*) during the period of antler growth; these variables did not affect strontium kinetics in females (Schreckhise and Whicker 1976). The concentrations of ^{90}Sr in forage of mule deer were higher in summer than in winter and the differences were of sufficient magnitude to account for the ^{90}Sr variations in mule deer antlers (Farris et al. 1969); ^{137}Cs concentrations were similar in the forage and flesh of the white-tailed deer (*Odocoileus virginicanus*; Cummings et al. 1971). Levels of iodine-129 in thyroids of mule deer and pronghorns (*Antilocapra americana*) increased with proximity to nuclear-fuel reprocessing plants in Colorado, Idaho, New Mexico, and Wyoming during 1972-76, although levels were considered of no consequence to the health of the animals (Markham et al. 1983).

Radium-226, a bone-seeking α-emitter with a half-life of 1,600 years, may cause tissue damage and possibly subsequent osteosarcoma. Elevated ^{226}Ra concentrations have been reported in tissues of the beaver (*Castor canadensis*) from the Serpent River watershed, Canada, the recipient of uranium tailings during 1984-87 (Table 14). Measurable levels of ^{226}Ra were also found in feces of snowshoe hares (*Lepus americanus*) from this area and in black cutworms (*Agrotis ipsilon*) eaten by herring gulls (*Larus argentatus*) on the tailings (Clulow et al. 1991). Maximum levels in tissues of beavers from this watershed were less than 5 Bq ^{232}Th/kg dry weight (DW) in all tissues, 15 Bq ^{228}Th/kg DW bone, less than 5 Bq ^{228}Th/kg DW muscle and liver, 70-160 Bq ^{210}Po/kg DW bone, 11-75 Bq ^{210}Po/kg DW muscle, and 35-65 Bq ^{210}Po/kg DW liver. Consumption of these beavers would not be hazardous to human health. In the worst case, humans who consume substantial (71 kg) amounts of flesh of beavers from the Serpent River drainage system would receive less than 10% of the annual limits set by Canadian regulatory authorities (Clulow et al. 1991).

Cesium-137 levels in gray seals (*Halichoerus grypus*) in 1987 seem to reflect ^{137}Cs levels in their fish diet, but there is no biomagnification of ^{137}Cs and other radionuclides. An estimated 29% of the ^{137}Cs in the diets of gray seals is from the Chernobyl accident and 71% from the nuclear facility at Sellafield, United Kingdom. The dose to gray seals from their diet is about 36 mSv annually and higher than the permissible dose limit of 5 mSv/year allowed the general public but below the current limit for radiation workers of 50 mSv/year (S.S. Anderson et al. 1990).

The weekly dose rates from internal radionuclides were markedly different in muskrats (*Ondatra zibethicus*) and cotton rats (*Sigmodon hispidus*) collected at Oak Ridge, Tennessee, in August 1960 (20-1,112 mSv in muskrats vs. 3 mSv in cotton rats); the difference is probably due to differences in diets and habitats (Kaye and Dunaway 1963). Foxes and wildcats contain 2 to 16 times more ^{137}Cs than their prey organisms such as rats and rabbits (Jenkins et al. 1969), suggesting food-chain magnification. The biological half-life of ^{137}Cs is about 30 days in foxes, dogs, and pigs but about 60 days in humans (Jenkins et al. 1969). Black-tailed jackrabbits (*Lepus californicus*) in 1958, 1 year after contamination at the Nevada test site, averaged 1,908 Bq ^{90}Sr/kg AW bone within a 160-km radius from ground zero; in 1961, the average in the same population was only 984 Bq ^{90}Sr/kg AW bone, and the few higher values were restricted to older animals (Neel and Larson 1963). The authors concluded that ^{90}Sr from fallout in jackrabbits is at its maximum at an early time after contamination and that biological availability is later reduced by natural (unspecified) mechanisms. Jackrabbits at the Nevada test site also contained certain neutron activation products, including isotopes of Co, Mn, and W (Romney et al. 1971).

Radionuclide concentrations in sheep and cattle that grazed near a nuclear-fuel reprocessing facility amounted to a small fraction of the recommended limits. Americium-241, ^{137}Cs, and $^{239+240}$Pu in bone, liver, lung, and muscle of beef cattle from the vicinity of a nuclear-fuel reprocessing facility in England were quite low between September and December 1986 and practically indistinguishable from control samples. Maximum concentrations, in Bq/kg FW, were 0.0015 $^{239+240}$Pu in lung, 0.019 ^{241}Am in liver, and 3.1 ^{137}Cs in muscle (Curtis et al. 1991). Levels of ^{129}I were elevated in thyroids of cows near Mol, Belgium, in 1978 in the vicinity of a nuclear reprocessing plant closed in 1974 (Table 14; Handl et al. 1990).

Case Histories

Military weapons tests on the Pacific Proving Grounds in the 1940's and 1950's greatly elevated local concentrations of radionuclides, and an accident at the Chernobyl nuclear power plant in the former Soviet Union in 1986 dispersed comparatively low concentrations of radionuclides over a wide geographical area. Both cases are briefly reviewed.

Pacific Proving Grounds

The first artificial, large-scale introduction of radionuclides into a marine environment was at Bikini Atoll in 1946. In succeeding years through 1958, Bikini and Eniwetok became the Pacific Proving Grounds where 59 nuclear and thermonuclear devices were detonated between 1946 and 1958 (Welander 1969; Templeton et al. 1971; Bair et al. 1979; Table 15). Gross radiation injury to marine organisms has not been documented, possibly because seriously injured individuals do not survive and the more subtle injuries are difficult to detect. On land, the roof rat (*Rattus rattus*) survived heavy initial radiation by remaining in deep burrows. Terrestrial vegetation was heavily damaged by heat and blast but generated regrowth in 6 months. The land-dwelling hermit crab (*Coenobita* sp.) and coconut crab (*Birgus latro*) were subjected to higher levels of chronic radiation from internally deposited radionuclides than any other studied Atoll organism; levels remained constant in *Coenobita* at 166,000 Bq of ^{90}Sr/kg skeleton and 16,835 Bq ^{137}Cs/kg muscle for 2 years; *Birgus* contained 25,900 Bq ^{90}Sr/kg skeleton and 3,700 Bq ^{137}Cs/kg muscle for 10 years (Templeton et al. 1971). A survey in August 1964 at Eniwetok and Bikini Atolls (Welander 1969; Table 15) showed that general levels of radioactivity were comparatively elevated and highest in soils and increasingly lower in aquatic invertebrates, groundwater, shorebirds, plants, rats, zooplankton, algae, fishes, sediments, seawater, and seabirds. Cobalt-60 was in all samples of animals, plants, water, sediments, and soils and was the major radionuclide in the marine environment; on land, cesium-137 and ^{90}Sr predominated. All samples contained traces of ^{54}Mn; ^{106}Ru and ^{125}Sb were in groundwater, and soil and trace concentrations were in animals and plants. Trace amounts of ^{207}Bi and ^{144}Ce were usually detected in algae, soils, and land plants. Iron-55 was comparatively high in vertebrates, and ^{239}Pu was found in the soil and in the skin of rats and birds (Welander 1969).

Table 15. Radionuclide concentrations in selected samples from the Pacific Proving Ground. Concentrations are in becquerels/kg fresh weight (FW) or dry weight (DW).

Table 15 Location, sample, radionuclide, and other variables	Concentration, in Bq/kg or Bq/L	Reference[a]
Bikini Atoll		
Samples with highest concentrations, August 1964		
^{207}Bi, sediments	Max. 6,660 DW	1
^{144}Ce, marine algae	Max. 1,739 DW	1
^{137}Cs, land invertebrates	Max. 14,060 DW	1
^{57}Co, sediments	Max. 3,400 DW	1
^{60}Co, marine invertebrates	Max. 35,150 DW	1
^{54}Mn, sediments	Max. 962 DW	1
^{106}Ru, sediments	Max. 10,360 DW	1
^{125}Sb, groundwater	Max. 12,950 DW	1
Seawater, 1972, ^{55}Fe	Max. 0.025 FW	2
Sediments		
1958 vs. 1972, ^{55}Fe	Max. 777,000 DW vs. 11,100 DW	2
August 1964, ground zero		
^{207}Bi	6,660 DW	1
^{57}Co	3,404 DW	1

Table 15 Location, sample, radionuclide, and other variables	Concentration, in Bq/kg or Bq/L	Reference[a]
^{60}Co	9,620 DW	1
^{54}Mn	962 DW	1
^{106}Ru	10,360 DW	1
^{125}Sb	3,663 DW	1
Eniwetok Atoll, August 1964		
Whole marine algae vs. whole marine fishes		
^{207}Bi	181 DW vs. 74 DW	1
^{144}Ce	814 DW vs. nondetectable (ND)	1
^{137}Cs	52 DW vs. 21 DW	1
^{60}Co	355 DW vs. 888 DW	1
^{54}Mn	48 DW vs. 70 DW	1
^{106}Ru	96 DW vs. ND	1
^{125}Sb	34 DW vs. ND	1
Terrestrial invertebrates vs. terrestrial vegetation		
^{207}Bi	6 DW vs. 10 DW	1
^{144}Ce	5 DW vs. 888 DW	1
^{137}Cs	No data vs. 12,580 DW	1
^{60}Co	888 DW vs. 141 DW	1
^{54}Mn	281 DW vs. 296 DW	1
^{106}Ru	15 DW vs. 19 DW	1
^{125}Sb	ND vs. 8 DW	1
Seabirds (whole) vs. shorebirds (whole)		
^{207}Bi	ND vs. ND	1
^{57}Co	12 DW vs. ND	1
^{60}Co	340 DW vs. 4,810 DW	1
^{137}Cs	ND vs. 4,440 DW	1
^{64}Mn	81 DW vs. ND	1
^{106}Ru, ^{125}Sb	ND vs. ND	1
Roof rat, *Rattus rattus*; whole		
^{207}Bi	5 DW	1
^{144}Ce	362 DW	1
^{60}Co	888 DW	
^{137}Cs	19,980 DW	1
^{54}Mn	1 DW	1
^{106}Ru, ^{125}Sb	ND	1
Samples with highest concentrations		
^{207}Bi, marine plankton	Max. 333 DW	1
^{144}Ce, soils	Max. 2,109 DW	1
^{137}Cs, rats	Max. 19,980 DW	1

Table 15 Location, sample, radionuclide, and other variables	Concentration, in Bq/kg or Bq/L	Reference[a]
^{57}Co, sediments	Max. 740 DW	1
^{61}Co, marine invertebrates	Max. 6,290 DW	1
^{14}Mn, land plants	Max. 296 DW	1
^{106}Ru, soils	Max. 4,440 DW	1
^{125}Sb, soils	Max. 703 DW	1
Soils vs. sediments		
^{207}Bi	20 DW vs. 218 DW	1
^{144}Ce	2,109 DW vs. no data	1
^{137}Cs	2,072 DW vs. 814 DW	1
^{57}Co	No data vs. 740 DW	1
^{60}Co	2,849 DW vs. 1,073 DW	1
^{54}Mn	44 DW vs. 148 DW	1
^{106}Ru	4,440 DW vs. 3,700 DW	1
^{125}Sb	703 DW vs. 407 DW	1
Eniwetok Atoll,		
Runit Island		
(8 nuclear detonations between 1948 and 1958)		
Roof rat, whole		
Immediate vicinity of detonations;		
1967 vs. 1973, ^{137}Cs		
Bone	21,978 DW vs. 81,363 DW	3
Intestine	137,344 DW vs. no data	3
Kidney	189,958 DW vs. 126,799 DW	3
Liver	83,657 DW vs. 83,583 DW	3
Muscle	137,122 DW vs. 156,880 DW	3
Skin	13,209 DW vs. 77,256 DW	3
200 m vs. 2,460 m; 1967, ^{60}Co		
Bone	185 DW vs. ND	3
Intestine	8,251 DW vs. no data	3
Kidney	110,223 DW vs. 333 DW	3
Muscle	499 DW vs. 266 DW	3
Skin	259 DW vs. ND	3
Soils		
^{137}Cs, 1967		
Ground zero vs. 200 m	1,258 DW vs. 399 DW	3
1,030 m vs. 2,460 m	88 DW vs. 18 DW	3
^{137}Cs, 1971		
Ground zero vs. 200 m	4,736 DW vs. 403 DW	3
1,030 m	44 DW	3
^{60}Co, 1967		
Ground zero vs. 200 m	1,221 DW vs 66 DW	3
1,030 m	25 DW	3
^{60}Co, 1971		
Ground zero vs. 200 m	1,110 DW vs. 133 DW	3
1,030 m vs. 2460 m	40 DW vs. 4 DW	3
1973, 2,460 m		

Table 15 Location, sample, radionuclide, and other variables	Concentration, in Bq/kg or Bq/L	Reference[a]
^{137}Cs	11 DW	3
^{60}Co	52 DW	3
Terrestrial vegetation		
Ground zero, 1967 vs. 1971		
^{137}Cs	16,199-93,380 DW vs. 34,780-94,239 DW	3
^{60}Co	Max. 1,221 DW vs. max. 2,775 DW	3
1,030 m, 1967 vs. 1971		
^{137}Cs	296-2,035 DW vs. 333-1,961 DW	3
^{60}Co	Max. 14 DW vs. max. 48 DW	3

[a]1, Welander 1969; 2, Schell 1976; 3, Bastian and Jackson 1976.

Chernobyl

General

Several accidents in nuclear facilities have been extensively analyzed and reported. The three most widely publicized accidents were at Windscale (now known as Sellafield), United Kingdom, in 1957; Three Mile Island, Pennsylvania, in 1979; and Chernobyl, Ukraine, in 1986 (UNSCEAR 1988; Severa and Bar 1991). The accident at Windscale released about 750 trillion (T)Bq of ^{131}I, 22 TBq of ^{137}Cs, 3 TBq of ^{89}Sr, 0.33 TBq of ^{90}Sr, and twice the amount of noble gases that were released at Chernobyl but 2,000 times less ^{131}I and ^{137}Cs. The Three Mile Island accident released about 2% as much noble gases and 50,000 times less ^{131}I than the Chernobyl accident. The most abundant released radionuclides at Three Mile Island were ^{133}Xe, ^{135}Xe, and ^{131}I, but the collective dose equivalent to the population during the first post-accident days was less than 1% of the dose accumulated from natural background radiation in 1 year.

The most serious accident of a nuclear reactor occurred on 26 April 1986 at one of the four units at Chernobyl when at least 3,000,000 TBq were released from the fuel during the accident (Table 16). The accident happened while a test was conducted during a normal scheduled shutdown and is attributed mainly to human error: "...the operators deliberately and in violation of rules, withdrew most control rods from the core and switched off some important safety systems..." (UNSCEAR 1988). The first power peak reached 100 times the nominal power within 4 s. Energy released in the fuel by the power excursion suddenly ruptured part of the fuel into minute pieces. Small, hot fuel particles caused a steam explosion. After 2 or 3 s, another explosion occurred, and hot pieces of the reactor were ejected. The damage to the reactor allowed air to enter, causing combustion of the graphite. About 25% of the released radioactive materials escaped during the first day of the accident; the rest, during the next 9 days (UNSCEAR 1988). The initial explosions and heat from the fire carried some of the radioactive materials to an altitude of 1,500 m where they were transported by prevailing winds (Fig. 6) and caused widespread radioactive contamination of Europe and the former Soviet Union, initially with ^{131}I, ^{134}Cs, and ^{137}Cs (Smith and Clark 1986; Anspaugh et al. 1988; Clark and Smith 1988; UNSCEAR 1988; Aarkrog 1990; Johanson 1990; Brittain et al. 1991; Palo et al. 1991). Long-range atmospheric transport spread the radioactive materials through the northern hemisphere where it was first detected in Japan on 2 May, in China on 4 May, in India on 5 May, and in Canada and the United States on 5-6 May 1986 (UNSCEAR 1988). Airborne activity was also detected in Turkey, Kuwait, Monaco, and Israel in early May. No airborne activity from Chernobyl has been reported south of the equator (UNSCEAR 1988). Among the reactors now operating in the former Soviet Union, 13 are identical to the one in Chernobyl, Ukraine, including units in Chernobyl, Leningrad, Kursk, and Smolensk (Mufson 1992).

Table 16. Selected fission products in the Chernobyl reactor core and their estimated escape into the environment (Severa and Bar 1991).

	Trillions of becquerels (TBq)	
Radionuclide	In core	Escaped[a]
^{85}Kr	33,000	33,000
^{133}Xe	1,700,000	1,700,000
^{131}I	1,300,000	260,000
^{132}Te	320,000	48,000
^{134}Cs	190,000	19,000
^{137}Cs	290,000	37,700
^{99}Mo	4,800,000	110,400
^{95}Zr	4,400,000	140,800
^{103}Ru	4,100,000	118,900
^{106}Ru	2,000,000	58,000
^{140}Ba	2,900,000	162,400
^{141}Ce	4,400,000	101,200
^{144}Ce	3,200,000	89,600
^{89}Sr	2,000,000	80,000
^{90}Sr	200,000	8,000
^{239}Np	140,000	4,200
^{238}Pu	1,000	30
^{239}Pu	850	25
^{240}Pu	1,200	36
^{241}Pu	170,000	5,100
^{242}Cm	26,000	780

[a] Aarkrog (1990) estimates escapement of 100,000 TBq of ^{137}Cs; 50,000 TBq of ^{134}Cs; and 35,000 TBq of ^{106}Ru. Aarkrog (1990) also includes the following radionuclides in the Chernobyl escapement: 1,500 TBq of ^{110}Ag, 3,000 TBq of ^{125}Sb, 6 TBq of ^{241}Am, and 6 TBq of $^{243+244}Cm$.

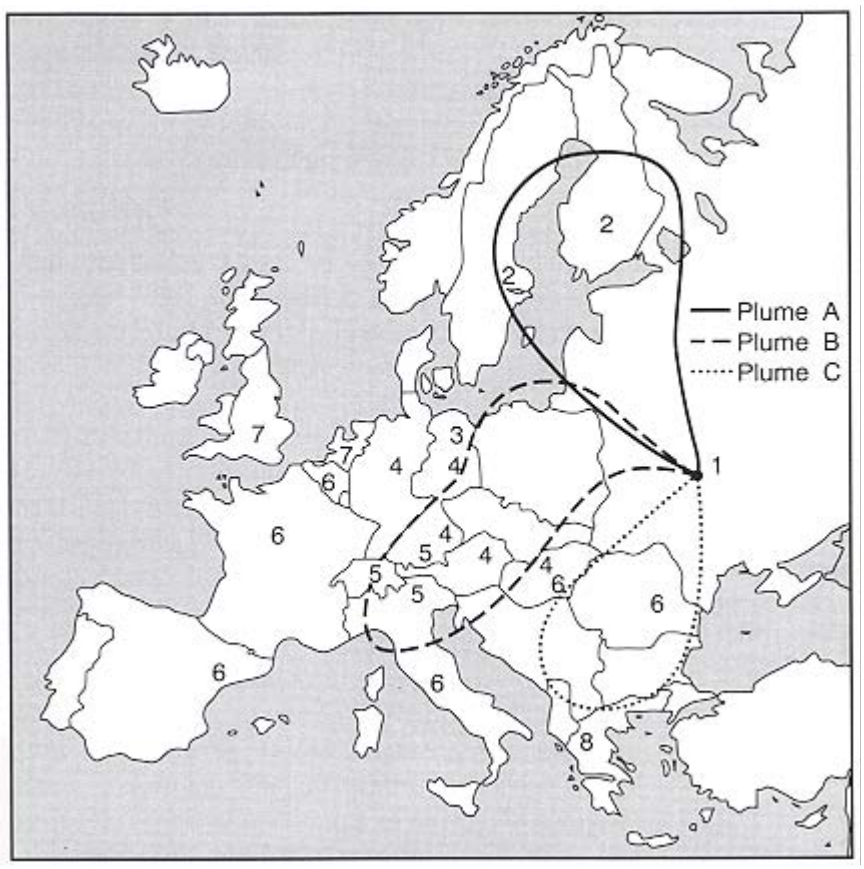


Fig. 6. Chernobyl air plume behavior and reported initial arrival times of detectable radioactivity. Plume A originated from Chernobyl on 26 April 1986, Plume B on 27-28 April, and Plume C on 29-30 April. The *numbers* indicate initial arrival times: 1, 26 April; 2, 27 April; 3, 28 April; 4, 29 April; 5, 30 April; 6, 1 May; 7, 2 May; and 8,3 May (UNSCEAR 1988; country boundaries in 1986).

Effective dose equivalents from the Chernobyl accident in various regions of the world were highest in southeastern Europe (1.2 mSv), northern Europe (0.97 mSv), and Central Europe (0.93 mSv; Table 17). In the first year after the accident, whole-body effective dose equivalents were highest in Bulgaria, Austria, Greece, and Romania (0.5-0.8 mSv); Finland, Yugoslavia, Czechoslovakia, Italy (0.3-0.5 mSv); Switzerland, Poland, USSR, Hungary, Norway, Germany, and Turkey (0.2-0.3 mSv); and elsewhere (<0.2 mSv; UNSCEAR 1988). Thyroid dose equivalents were significantly higher than whole-body effective dose equivalents because of significant amounts of ^{131}I in the released materials. Thyroid dose equivalents were as high as 25 mSv to infants in Bulgaria, 20 mSv in Greece, and 20 mSv in Romania; the adult thyroid dose equivalents were usually 80% lower than the infant dose equivalents (UNSCEAR 1988).

Table 17. Regional total effective human dose-equivalent commitment from the Chernobyl accident (UNSCEAR 1988; Aarkrog 1990).

Region	Effective dose equivalent (mSv)
Southeastern Europe	1.2
Northern Europe	0.97
Central Europe	0.93
Former Soviet Union	0.81
Southwest Asia, West Europe	>0.1-<0.2
North Africa, Greenland, East Africa, Central Africa, South Asia, West Africa	>0.01-<0.l
East Asia, Southwest Europe, Southeast Asia, North America, Caribbean, South America, Central America	<0.01

Local Effects

At Chernobyl, at least 115 humans received acute bone-marrow doses of greater than 1 Gy, as judged by lymphocyte aberrations (UNSCEAR 1988). The death toll within 3 months of the accident was at least 30 individuals, usually from groups that received more than 4 Gy, including the reactor's operating staff and the fire-fighting crew. Local residents were evacuated from a 30-km exclusion zone around the reactor because of increasing radiation levels; more than 115,000 people, including 27,000 children, were evacuated from the Kiev region, Byelorussia, and the Ukraine. Tens of thousands of cattle were also removed from the contaminated area, and consumption of locally produced milk and other foods was banned. Agricultural activities were halted and a large-scale decontamination effort was made (UNSCEAR 1988). The radiological effect of the accident to individual risk was insignificant outside a limited local region, either because contamination levels were generally low or because remedial actions to ban the consumption of highly contaminated foodstuffs prevented high exposures (UNSCEAR 1988).

Biological effects of the Chernobyl accident on local natural resources were documented by Sokolov et al. (1990). They concluded that the most sensitive affected ecosystems at Chernobyl were the soil fauna and pine forest communities and that the bulk of the terrestrial vertebrate community was not adversely affected by released ionizing radiation. Pine forests seemed to be the most sensitive ecosystem. One stand of 400 ha of *Pinus silvestris* died and probably received a dose of 80-100 Gy; other stands experienced heavy mortality of 10-12 year old trees and as much as 95% necrotization of young shoots; these pines received an estimated dose of 8-10 Gy. Abnormal top shoots developed in some *Pinus*, and these probably received 3-4 Gy. In contrast, leafed trees such as birch (*Betula* sp.), oak (*Quercus sp.*), and aspen (*Populus* sp.) in the Chernobyl Atomic Power Station zone survived undamaged, probably because they are about 10 times more radioresistant than pines. There was no increase in the mutation rate of the spiderwort *Arabidopsis thaliana*, a radiosensitive plant, suggesting that the dose rate was less than 0.05 Gy/h in the Chernobyl locale. Populations of soil mites were reduced in the Chernobyl area, but no population showed a catastrophic drop in numbers. By 1987, soil microfauna--even in the most heavily contaminated plots--was comparable to controls. Flies (*Drosophila* spp.) from various distances from the accident site and bred in the laboratory had higher incidences of dominant lethal mutations (14.7%, estimated dose of 0.8 m Gy/h) at sites nearest the accident than controls (4.3%). Fish populations seemed unaffected in July-August 1987, and no grossly-deformed individuals were found; however, $^{134+137}$Cs levels were elevated in young fishes. The most heavily contaminated teleost in May 1987 was the carp (*Carassius carassius*). But carp showed no evidence of mutagenesis, as judged by chromosomal aberrations in cells from the corneal epithelium of some carp as far as 60 km from Chernobyl (Sokolov et al. 1990).

Several rodent species compose the most widely distributed and numerous mammals in the Chernobyl vicinity. It was estimated that about 90% of rodents died in an area that received 60 Gy and 50% in areas that received 6-60 Gy. Rodent populations seemed normal in spring 1987, and this was attributed to migration from adjacent nonpolluted areas. The most sensitive small mammal was the bank vole (*Clethrionomys glareolus*),

which experienced embryonic mortality of 34%. The house mouse (*Mus musculus*) was one of the more radioresistant species. *Mus* from plots receiving 0.6-1 mG/h did not show signs of radiation sickness, were fertile with normal sperm, bred, and produced normal young. Some chromosomal aberrations were evident, namely, an increased frequency of reciprocal translocations (Sokolov et al. 1990). During the early period after the accident, there was no evidence of increasing mortality, decline in fecundity, or migration of vertebrates as a result of the direct action of ionizing radiation. The numbers and distributions of wildlife species were somewhat affected by the death of the pine stand, the evacuation of people, the termination of cultivation of soils (the crop of 1986 remained standing), and the evacuation of domestic livestock. No changes in survival or species composition of game animals and birds were recorded. In fact, because humans had evacuated and hunting pressure was negligible, many game species, including foxes, hares, deer, moose, wolves, and waterfowl moved into the zone in fall 1986-winter 1987 from the adjacent areas in a 50-60 km radius (Sokolov et al. 1990).

Nonlocal Effects

The partial meltdown of the 1,000-megawatt reactor at Chernobyl on 26 April 1986 released large amounts of radionuclides into the environment--especially ^{131}I, ^{137}Cs, and ^{134}Cs--and widely dispersed and deposited radioactive material in Europe and throughout the northern hemisphere (UNSCEAR 1988; Palo et al. 1991; Table 18). Transuranics and to some extent ^{90}Sr were deposited closer to the accident site than more volatile radionuclides such as radiocesium; accordingly, radiological problems changed quantitatively and qualitatively with increasing distance from the accident site (Aarkrog 1990).

Table 18. Radionuclide concentrations in biotic and abiotic materials from various geographic locales before or after the Chernobyl nuclear accident on 26 April 1986. All concentrations are in Bq/kg fresh weight (FW) or dry weight (DW), unless noted otherwise.

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
Alaska and Yukon Territories		
Barren-ground caribou (*Rangifer tarandus granti*); porcupine herd; March-November 1987; ^{137}Cs		
Feces	Max. 802 DW	1
Muscle	133 (26-232) FW	1
Rumen contents	Max. 538 DW	1
Albania		
^{137}Cs; 2 May-19 May 1986		
Air	Max. 1.8 Bq/m^3	2
Milk vs. wheat flour	Max. 380 FW vs. max. 236 FW	2
^{131}I; cow's milk; 2 May-19 May 1986	Max. 3,500 FW	2
Canada		
Caribou, *Rangifer tarandus*; northern Quebec; 1986 (post-Chernobyl)-1987; muscle; ^{137}Cs	166-1,129 FW	3
Czechoslovakia [in 1986]		
$^{134+137}Cs$; 1986 (post-Chernobyl)		
Barley, *Hordeum vulgare*	7 DW	4
Cow, *Bos* sp., milk		
May	42 FW	4

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
July	10 FW	4
December	7 DW	4
Wheat, *Triticum* sp.	16 DW	4
$^{134+137}Cs$; domestic pig, *Sus* sp.; muscle; July 1986 vs. July 1987	15-22 FW vs. 22 FW	4
Danube River, Hungary-Yugoslavia [in 1986]		
Water; 1986; post-Chernobyl		
^{134}Cs	0.015 FW	5
^{137}Cs	0.096 FW	5
^{103}Ru	0.070 FW	5
Fish, various species; 1986 (post-Chernobyl) vs. 1987		
^{134}Cs	8 FW vs. 4 FW	5
^{137}Cs	13 FW vs. 12 FW	5
^{103}Ru	1 FW vs. <1 FW	5
^{106}Ru	4 FW vs. 3 FW	5
Sediments; 1986 (post-Chernobyl) vs. 1988		
^{134}Cs	500 DW vs. 80 DW	5
^{137}Cs	750 DW vs. 200 DW	5
Algae; 1986 (post-Chernobyl) vs. 1988		
^{134}Cs	275 FW vs. 25 FW	5
^{137}Cs	625 FW vs. 100 FW	5
Finland		
Finish Lapland; ^{137}Cs; 1979-84 vs. 1986 (post-Chernobyl)		
Arboreal lichens	120 DW vs. 590 DW	7
Ground lichens	230 DW vs. 900 DW	7
Birch, *Betula* sp.	68 DW vs. 51 DW	7
Horsetails, *Equisetum* sp.	203 DW vs. 280 DW	7
Bilberry, *Vaccinium* sp.	120 DW vs. 590 DW	7
Lichens; ^{137}Cs		
From reindeer herding areas; 1986 (post-Chernobyl) vs. 1987	900 DW vs. 800 DW	8
Isolated areas; 1986 (post-Chernobyl)-1987	3,000-10,000 DW	8
Lake Paijanne (estimated ^{137}Cs Chernobyl loading of 20,000 Bq/m^2); ^{137}Cs; whole fish; three species (northern pike, *Esox lucius*; yellow perch, *Perca flavescens*;		

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
roach, *Rutilus rutilus*)		
1986; pre-Chernobyl vs. post-Chernobyl	580 FW vs. 1,250 FW	6
1987	1,000-2,000 FW	6
1988	160-2,000 FW	6
Reindeer, *Rangifer tarandus*; muscle; ^{137}Cs		
1964-65 (following nuclear tests) vs. 1985-86 (pre-Chernobyl)	Max. 2,500-2,600 FW vs. 300 FW	7,8
1986-87 vs. 1987-88	720 FW, max. 16,000 FW vs. 640 FW, max. 9,000 FW	8
France		
Cows, fed hay (harvested post-Chernobyl) diet containing 5,500 $^{134+137}Cs$/kg for mean daily intake of 15,900 Bq	A plateau was observed in milk after 15 days and in meat after 50-60 days; radiocesium transfer coefficients from diet were 1.1% for milk and 2.0-2.7% for meat	9
Calves fed $^{l34+137}Cs$-contaminated milk from birth to age 80 days	Transfer coefficient from milk to meat was 16%	9
Germany [in 1986]		
Soils; 24 June 1986		
^{134}Cs	Max. 602 Bq/m^2 DW	10
^{137}Cs	Max. 1,545 Bq/m^2 DW	10
^{103}Ru	Max. 808 Bq/m^2 DW	10
Pasture vegetation; May 1986		
^{134}Cs	20 FW	10
^{137}Cs	40 FW	10
^{131}I	75 FW	10
Cow; milk; May 1986		
^{134}Cs	140 FW	10
^{137}Cs	250 FW	10
^{131}I	250 FW	10
^{103}Ru	250 FW	10
Human, *Homo sapiens*		
Intake per person		
^{134}Cs; 1986 vs. 1987	354 Bq vs. 8 Bq	10
^{137}Cs; 1986 vs. 1987	728 Bq vs. 37 Bq	10
Whole body dose (Bonn and vicinity); 1986 vs. 1987	0.0147 mSv (0.008 from ^{137}Cs, 0.0067 from ^{134}Cs) vs. 0.00056 mSv (0.0004 from ^{137}Cs, 0.00016 from ^{134}Cs)	10
Thyroid, ^{129}I	Negligible	11

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
Greece		
Alfalfa, *Medicago sativa*; June 1986		
^{134}Cs	2,303 DW	12
^{137}Cs	4,551 DW	12
^{103}Ru	358 DW	12
^{106}Ru	1,075 DW	12
Lichen, *Ramalina fraxinea* vs. moss, *Homalothecium sericium*; 1986 (post-Chernobyl); after decay of short-lived radionuclides		
^{134}Cs	426 FW vs. 1,121 FW	13
^{137}Cs	951 FW vs. 2,612 FW	13
^{40}K	222 FW vs. 278 FW	13
^{103}Ru	63 FW vs. 115 FW	13
^{106}Ru	436 FW vs. 1,365 FW	13
Rye grass, *Lolium perenne*; June 1986		
^{134}Cs	3,518 DW	12
^{137}Cs	7,090 DW	12
^{103}Ru	708 DW	12
^{106}Ru	1,747 DW	12
Plants, various; measured about 4 months post-Chernobyl; ^{137}Cs; values represent about 9% of initial Chernobyl radioactivity		
Aromatic plants; 11 species	22-11,344 FW; 26-22,000 DW	13
Cereals; four species	11-2,257 FW; 11-2,775 DW	13
Fruit bearing trees; seven species	85-1,572 FW; 122-2,116 DW	13
Fungi; four species	103-5,553 FW; 214-11,418 DW	13
Marine algae; four species	85-139 FW; 529-917 DW	13
Mosses and lichens; six species	1,184-9,413 FW; 1,110-18,847 DW	13
Vegetables; 18 species	18-244 FW; 18-299 DW	13
Northern Greece; May 1986; ^{131}I		
Grasses	Max. 1,500 FW	14
Milk; cow vs. domestic sheep, *Ovis aries*	Max. 300 FW vs. max. 800 FW	14
Domestic sheep; thyroid; ^{131}I; maximum values; 1986		
27 June vs. 2 July	4,000 FW vs. 15,600 FW	15

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
3 July vs. 5 July	618,000 FW vs. 9,000 FW	15
29 July vs. 20 August	8,500 FW vs. 600 FW	15
Italy		
Honey bee, *Apis* spp.; honey; 10 May 1986		
^{134}Cs	Max. 171 FW	16
^{137}Cs	Max. 363 FW	16
^{131}I	Max. 1,051 FW	16
^{103}Ru	Max. 575 FW	16
Cow		
Fed diets contaminated with Chernobyl ^{137}Cs for 8 months before slaughter		
Female vs. fetus		
Amniotic fluid	Max. 82 FW vs. —[b]	17
Blood	Max. 13 FW vs. max. 44 FW	17
Muscle	Max. 179 FW vs. max. 126 FW	17
Kidney	Max. 232 FW vs. max. 139 FW	17
Liver	Max. 163 FW vs. max. 115 FW	17
Placenta	Max. 93 FW vs. —	17
Rodent, *Mus musculus domesticus*; carcass less internal organs; ^{137}Cs		
October-November 1981 vs. May 1986	5 DW vs. 43 DW	18
October-November 1986 vs. May 1987	20 DW vs. 18 DW	18
Northwest Saluggia, May 1986		
^{137}Cs, pasture grass vs. cow's milk	8,000 DW vs. 180 FW	19
^{131}I, pasture grass vs. cow's milk	12,000 DW vs. 870 FW	19
Rabbit, *Oryctolagus* sp.; fed Chernobyl-contaminated alfalfa meal diet containing, in Bq/kg FW, 856 ^{137}Cs, 369 ^{134}Cs, and 540 ^{40}K; or normal diet (112 ^{137}Cs, 41 ^{134}Cs, 503 ^{40}K) for various intervals		
Control diet		
Whole animal	16 ^{137}Cs FW, 7 ^{134}Cs FW, 87 ^{40}K FW	20
Muscle	22 ^{137}Cs FW, 8 ^{134}Cs	20

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
	FW, 117 ^{40}K FW	
21 days on contaminated diet followed by 21 days on control diet		
Whole animal	20 ^{137}Cs FW, 9 ^{134}Cs FW, 79 ^{40}K FW	20
Muscle	31 ^{137}Cs FW,128 ^{134}Cs FW, 117 ^{40}K FW	20
42 days on contaminated diet		
Whole animal	81 ^{137}Cs FW, 32 ^{134}Cs FW, 85 ^{40}K FW	20
Muscle	112 ^{137}Cs FW, 44 ^{134}Cs FW, 124 ^{40}K FW	20
Japan		
^{137}Cs		
Milk; cow; May 1986	Max. 0.6 FW	21
Soil; estimated deposition from Chernobyl	180 Bq/m^2 DW	21
$^{134+137}$Cs; humans, children; estimated internal dose through milk consumption		
1986	0.0006 mSv	21
1987	0.0003 mSv	21
1988	0.0001 mSv	21
^{131}I, grass vs. cow's milk		
10-11 May 1986	65 FW vs. 4.3 FW	22
30 May 1986	14 FW vs. ND[c]	22
Monaco		
Air, Bq/m^3, 26 April 1986; Monaco vs. Chernobyl (Former Soviet Union)		
^{134}Cs	8.2 vs. 53	50
^{137}Cs	1.6 vs. 120	50
^{103}Ru	3.5 vs. 280	50
^{131}I	4.6 vs. 750	50
^{106}Ru	3.0 vs. 110	50
^{140}Ba	9.8 vs. 420	50
^{99}Mo	3.8 vs. 490	50
^{141}Ce	3.7 vs. 190	50
^{144}Ce	2.5 vs. 110	50
^{95}Zr	1.2 vs. 590	50
Marine copepods, 3		

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
species; 6 May 1986; whole organism vs. fecal pellets		
^{103}Ru	280 DW vs. 16,000 DW	49
^{106}Ru	70 DW vs. 5,800 DW	49
^{134}Cs	22 DW vs. 3,400 DW	49
^{137}Cs	34 DW vs. 6,300 DW	49
^{141}Ce	20 DW vs. 900 DW	49
^{144}Ce	100 DW vs. 2,500 DW	49
Mussel, *Mytilus galloprovincialis*; soft parts; 6 May vs. 14 August 1986		
^{103}Ru	480 FW vs. 9.6 FW	51
^{106}Ru	121 FW vs. 11.2 FW	51
^{131}I	84 FW vs. <2 FW	51
^{134}Cs	6 FW vs. 0.1 FW	51
^{137}Cs	5.2 FW vs. 0.3 FW	51
Netherlands		
^{134}Cs; grass silage; 1986 (post-Chernobyl) vs. 1987	Max. 50 DW vs. 2 DW	23
^{137}Cs; grass silage; 1986 (post-Chernobyl) vs. 1987	Max. 172 DW vs. 9 DW	23
^{137}Cs-contaminated roughage fed to lactating cows		
10.3 Bq ^{137}Cs/kg FW; grass	1.0-1.6 FW milk	24
173-180 Bq ^{137}Cs/kg FW; grass silage	12-28 FW milk	24
260-271 Bq ^{137}Cs/kg DW; grass	5.4-6.2 FW milk	24
^{40}K; grass silage; 1986 vs. 1987	910 DW vs. 1,028 DW	23
Norway		
Alpine lake and vicinity; $^{134+137}Cs$		
Dwarf birch, *Betula nana*; leaves; August 1986	4,000 FW	25
Lichens; August 1986	60,000 FW	25
Willow, *Salix spp*.; leaves; September 1980 vs. August 1986	<50 PW vs. 600 FW	25
Lake sediment; upper 10 cm; July-August 1986	1,050 FW	25
Aquatic organisms; July-August 1986		
Cladoceran, *Bosmina longispina*, whole	5,300 FW	25

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
Amphipod, *Gammarus lacustris*, whole	6,700 FW	25
Mayfly, *Siphlonurus lacustris*, whole	2,800 FW	25
Stonefly, 2 spp., whole	1,300-4,120 FW	25
Minnow, *Phoxinus phoxinus*, whole	8,800 FW	25
Brown trout, *Salmo trutta*		
Muscle		
1985 (pre-Chernobyl) vs. June 1986	<100 FW vs. 300 FW	25
August 1986 vs. June 1988	7,000 FW vs. 4,000 FW	25
Eggs vs. milt; July-August 1986	1,740-3,600 FW vs. 1,300 FW	25
Dovrefjell, May 1986 vs. August 1990; ^{137}Cs		
Earthworms (*Lumbricus rubellus*, *Allobophora caliginosa*), whole	121 FW vs. 74 FW	52
Eurasian woodcock, *Scolopax rusticola*, breast muscle	737 FW vs. 53 FW	52
Litter	14,400 DW vs. 2,900 DW	52
Mushroom, *Lactarius* spp.; post-Chernobyl; $^{134+137}Cs$	Max. 445,000 FW	26
Reindeer; muscle; $^{134+137}Cs$		
1986; post-Chernobyl	10,000-50,000 FW	27
January 1987 vs. September 1988	Max. 56,000 FW vs. max. 13,900 FW	28
Reindeer; two groups of adult females were fed lichen diets containing 45,000 Bq $^{134+137}Cs$/kg ration for 35 days; one group received daily oral administration of 250 mg ammonium-ferrohexacyanoferrate (Giese salt)	Both groups accumulated 400 Bq/kg FW daily in muscle. Retention time of Cs isotopes was 25 days without Giese salt and only 7-10 days when treated with Giese salt	29
Poland		
Freshwater fish; four species; muscle; January 1987; $^{134+137}Cs$	4.5-6.1 FW	30
Southern Baltic Sea, $^{134+137}Cs$; pre-Chernobyl (1982-February 1986) vs. post-Chernobyl (June 1986-July 1987)		
Water	(13.8-19.8) Bq/m^3 vs. (59-100) Bq/m^3	30

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
Atlantic cod, *Gadus morhua*; muscle	(1.4-2.3) FW vs. (5.0-7.4) FW	30
Flounder, *Pleuronectes flesus*; muscle	(1.1-4.5) FW vs. (3.4-6.7) FW	30
Spain		
Song thrush, *Turdus philomelos*; edible tissues; November 1986 vs. November 1987		
^{134}Cs	Max. 90 DW for adults and young vs. max. 7 DW for adults and 5 DW for young	31
^{137}Cs	Max. 208 DW vs. max. 27 DW for adults and 22 for young	31
^{90}Sr	Max. 23 DW vs. max. 7 DW	31
Sweden		
Moose, *Alces alces*; central Sweden; muscle; ^{137}Cs		
September 1986; adults vs. calves	300 FW vs. 500 FW	32
1986; all age groups	20-3,000 FW	33
September 1987; adults vs. calves	201 FW vs. 401 FW	32
1987, all age groups	Max. 1,600 FW	34
September 1988, adults vs. calves	640 FW vs. 1,300 FW	32
1988, all age groups	Max. 2,500 FW	34
Moose dietary plants; 1986 (post-Chernobyl)-1988; ^{137}Cs		
Birches, *Betula* spp.; leaves	1,200 DW	34
Heather, *Calluna vulgaris*; whole	13,000-32,000 DW	34,35
Sedges, *Carex* spp.; whole	12,000 DW	35
Hair grass, *Deschampia flexuosa*; whole	1,900 DW	34
Fireweed, *Epilobium angustifolium*; whole	400 DW	34
Grasses, various species; blades	2,500 DW	34
Buckbean, *Menyanthes trifoliata*; whole	3,800 DW	34
Pine, *Pinus sylvestris*; shoots	2,500 DW	34
Aspen, *Populus tremula*; leaves	700 DW	34
Willows, *Salix* spp.; leaves	300 DW	34
Mountain ash, *Sorbus aucuparia*; leaves	1,300 DW	34
Bilberry, *Vaccinium myrtillus*; leaves		
July 1986	2,000 FW; 4,000 DW	32,34

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
July 1987 vs. July 1988	1,138 FW vs. 600 FW	32
Bog whortleberry, *Vaccinium uliginosum*; foliage	5,900 DW	34
Cowberry, *Vaccinium vitis-idaea*; foliage	7,500 DW	34
Cow's milk; ^{137}Cs; July 1986 vs. 1987	Usually <250 FW, max. 375 FW vs. usually <70 FW, max. 120 FW	36
Lichen, *Bryoria fuscescens*; ^{137}Cs; 4 June 1986	34,000-120,000 DW	35
Roe deer, *Capreolus* sp.; muscle; ^{137}Cs; 1986 (post-Chernobyl)	20-12,000 FW	33
Lichens, *Cladina* spp.; ^{137}Cs; 1986 (post-Chernobyl)	Max. 40,000 DW	35
Bank vole, *Clethrionomys glareolus*; collected from soil containing various concentrations of $^{134+137}Cs$; voles analyzed less skull and digestive organs		
1,800 Bq/m^2 soil (control)	Voles had 9 Bq ^{134}Cs/kg FW and 39 of ^{137}Cs; mutation frequency of 1.3; total irradiation of 0.0042 mGy daily	37
22,000 Bq/m^2 soil	In Bq/kg FW, voles had 279 ^{134}Cs and 1,031 ^{137}Cs; mutation frequency was 1.5; daily dose rate of 0.0088 mGy	37
90,000 Bq/m^2 soil	Voles had 1,356 Bq ^{134}Cs/kg FW and 5,119 of ^{137}Cs; mutation frequency 1.9; daily dose 0.0268 mGy	37
145,000 Bq/m^2 soil	Voles had 2,151 Bq ^{134}Cs/kg FW and 7,784 ^{137}Cs; mutation frequency 2.6; daily dose of 0.0394 mGy	37
Buckbean, *Menyanthes trifoliata*; foliage; ^{137}Cs; 1985 vs. 1987	1,800 DW vs. 3,880 DW	35
Reindeer dietary	Usually 40,000-60,000 DW;	38

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
lichens; ^{137}Cs; April 1986	max. 120,000 DW	
Reindeer		
Moved in November 1986	^{137}Cs content in muscle	39
from a highly contaminated area (>20,000 Bq $^{137}Cs/m^2$) to a less-contaminated area (<3,000 Bq/m^2) Of natural pasture	declined from 12,000 FW in November to about 3,000 FW in April	
Muscle; ^{137}Cs; 1986 (post-Chernobyl)	100-40,000 FW	33
Rodents and insectivores;		
July-August 1986; ^{137}Cs		
Control site, soil	1,800 Bq/m^2	40
Bank vole; whole less skull, stomach, viscera	39 FW	40
Common shrew, *Sorex araneus*; whole less skull, stomach, viscera	48 FW	40
Site 2, soil	22,000 Bq/m^2	40
Bank vole vs. common shrew	676 FW vs. 751 FW	40
Site 3, soil	90,000 Bq/m^2	40
Bank vole vs. common shrew	5,119 FW vs. 3,233 FW	40
Site 4, soil	145,000 Bq/m^2	40
Bank vole vs. common shrew	7,993 FW vs. 6,289 FW	40
Syria		
^{137}Cs; Air; 7-10 May 1986	0.12 Bq/m^3	41
^{131}I; 7-10 May 1986; air vs. goat's milk	4 Bq/m^3 vs. 55 FW	41
United Kingdom		
Upland pastures		
Sphagnum moss, *Sphagnum* sp,; September 1986		
^{110m}Ag	202 DW	42
^{144}Ce	202 DW	42
^{134}Cs	8,226 DW	42
^{137}Cs	17,315 DW	42
^{106}Ru	1,893 DW	42
^{125}Sb	294 DW	42
Vegetation; $^{134+137}Cs$; June 1986 vs. January 1989	about 6,000 DW vs. 1,000 DW	43
Marine molluscs; 7 species; near nuclear plant; 1984 (pre-Chernobyl) vs. 1986 (post-Chernobyl)		

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
^{110m}Ag	<77 FW vs. 13-77 FW	44
^{60}Co	<29 FW vs. 16-32 FW	44
^{134}Cs	<14 FW vs. 37-388 FW	44
^{137}Cs	<139 FW vs. 31-836 FW	44
^{40}K	<59 FW vs. 57-61 FW	44
^{238}Pu	<27 FW vs. 11-22 FW	44
$^{239+240}Pu$	<107 FW vs. 19-89 FW	44
^{106}Ru	<632 FW vs. 124-1,648 FW	44
^{125}Sb	ND vs. 29 FW	44
Eurasian oystereatcher, *Haematopus ostralegas*; near nuclear reactor; June 1986; egg contents vs. egg shells		
^{134}Cs	4 FW vs. — [b]	44
^{137}Cs	18 FW vs. 6 FW	44
^{238}Pu	0.2 FW vs. 1.1 FW	44
$^{239+240}Pu$	0.05 FW vs. 4.6 FW	44
Red grouse, *Lagopus lagopus*; muscle; November 1986-February 1987		
^{134}Cs; cock vs. hen	325 FW vs. 602 FW	45
^{137}Cs; cock vs. hen	962 FW vs. 1,684 FW	45
Common black-headed gull, *Larus ridibundus ridibundus*; near nuclear reactor; 1980 vs. June 1986		
Egg contents		
^{134}Cs	ND vs. 22 FW	44
^{137}Cs	10 FW vs. 43 FW	44
^{238}Pu	0.02 FW vs. 0.01 FW	44
$^{239+240}Pu$	0.05 FW vs. 0.04 FW	44
Egg shells		
^{134}Cs	— vs. 7 FW	44
^{137}Cs	— vs. 16 FW	44
^{238}Pu	<0. 17 FW vs. 0.4 FW	44
$^{239+240}Pu$	0.6 FW vs. 1.6 FW	44
Eurasian woodcock, *Scolopax rusticola*; muscle; November 1986-February 1987		
^{134}Cs	13 FW	45
^{137}Cs	42 FW	45
Black grouse, *Tetrao tetrix*; ^{137}Cs , November 1986-February 1987; diet vs. muscle	167 FW vs. 270 FW	45
Cow's milk; 5-8 May 1986		

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
^{137}Cs	Max. 150 FW	46
^{131}I	Max. 127 FW	46
Roe deer, *Capreolus capreolus*; ^{137}Cs; muscle; November 1986-February 1987		
Calves	711 FW	45
Hinds	375-586 FW	45
Stags	1,564 FW	45
Red deer, *Cervus elephus*; muscle; November 1986-February 1987		
^{134}Cs; calf vs. hind	186 FW vs. 112 FW	45
^{137}Cs; calf vs. hind	535 FW vs. 311 FW	45
Brown hare, *Lepus capensis*; ^{137}Cs; female; November 1986-February 1987; diet vs. muscle	198 FW vs. 656 FW	45
Blue hare, *Lepus timidus*; ^{137}Cs; November 1986-February 1987		
Males; diet vs. muscle	808 FW vs. 1,677 FW	45
Females; diet vs. muscle	577 FW vs. 1,440 FW	45
Rabbit, *Oryctolagus* sp.; muscle; male; November 1986-February 1987		
^{134}Cs	6 FW	45
^{137}Cs	15 FW	45
Domestic sheep		
Muscle; ^{137}Cs; September 1986 vs. July 1987	1,500 FW vs. 1,170 FW	42
Liver; ^{110m}Ag; ewes vs. lambs		
September 1986	34 FW vs. 17 FW	47
July 1987 55	FW vs. <8 FW	47
Diet (rye grass and vegetation); ^{110m}Ag; 1986 vs. 1987	32 DW vs. 10-30 DW	47
Lambs fed a milk replacement diet containing 950 Bq ^{137}Cs/kg ration for 21 days. After weaning, lambs were fed silage contaminated with fallout radiocesium plus ionic $^{134}CsCl$	Absorption during the first 21 days was about 90%, equivalent to 975 Bq ^{137}Cs/kg BW. During the silage feeding period, uptake of ionic ^{134}Cs was about twice that of fallout ^{134}Cs	48

Table 18 Locale, radionuclide, sample, and other variables	Concentration	Reference[a]
for 3 weeks	present in silage	
Red fox, *Vulpes vulpes*; muscle; November 1986-February 1987; vixen		
^{134}Cs	176 FW	45
^{137}Cs	461-643 FW	45

[a]1, Allaye-Chan et al. 1990; 2, Kedhi 1990; 3, Crete et al. 1990; 4, Kliment 1991; 5, Conkic et al. 1990; 6, Korhonen 1990; 7, Rissanen and Rahola 1989; 8, Rissanen and Rahola 1990; 9, Daburon et al. 1989; 10, Clooth and Aumann 1990; 11, Handl et al. 1990; 12, Douka and Xenoulis 1991; 13, Sawidis 1988; 14, Assimakopoulos et al. 1989; 15, Ionannides and Pakou 1991; 16, Tonelli et al. 1990; 17, Calamosca et al. 1990; 18, Cristaldi et al. 1990; 19, Spezzano and Giacomelli 1991; 20, Battiston et al. 1991; 21, Imanaka and Koide 1990; 22, Aii et al. 1990; 23, Voors and Van Weers 1991; 24, Vreman et al. 1989; 25, Brittain et al. 1991; 26, Hove et al. 1990a; 27, Skogland and Espelien 1990; 28, Eikelmann et al. 1990; 29, Mathiesen et al. 1990; 30, Grzybowska 1989; 31, Baeza et al. 1991; 32, Palo et al. 1991; 33, Johanson 1990; 34, Bothmer et al. 1990; 35, Eriksson 1990; 36, Johanson et al. 1989; 37, Cristaldi et al. 1991; 38, Jones 1990; 39, Jones et al. 1989; 40, Mascanzoni et al. 1990; 41, Othman 1990; 42, Coughtrey et al. 1989; 43, Crout et al. 1991; 44, Lowe 1991; 45, Lowe and Horrill 1991; 46, Clark and Smith 1988; 47, Beresford 1989; 48, Moss et al. 1989; 49, Fowler et al. 1987; 50, Whitehead et al. 1988b; 51, Whitehead et al. 1988a; 52, Kalas et al. 1994.

[b] — = no data.

[c] ND = not detectable.

Soil and Vegetation. The radiocesium fallout in Sweden was among the highest in western Europe--exceeding 60,000 Bq/m^2 on Sweden's Baltic coast--and involved mainly upland pastures and forests (Johanson 1990; Brittain et al. 1991; Palo et al. 1991). In Norway, radiocesium deposition from the Chernobyl accident ranged from less than 5,000 to more than 200,000 Bq/m^2 and greatly exceeded the deposition from prior nuclear weapons tests (Hove et al. 1990a). In Italy, heavy rainfall coincident with the passage of the Chernobyl radioactive cloud caused high local deposition of radionuclides in soil, grass, and plants (Battiston et al. 1991). The Chernobyl plume reached Greece on 1 May 1986. A total of 14 gamma emitters were identified in the soil and vegetation in May 1986, and three (^{134}Cs, ^{137}Cs, ^{131}I) were also detected in the milk of free-grazing animals in the area (Assimakopoulos et al. 1989). Radiocesium-134 and ^{137}Cs intake by humans in Germany during 1986-87 was mainly from rye, wheat, milk, and beef (Clooth and Aumann 1990). In the United Kingdom, elevated concentrations of radionuclides of iodine, cesium, ruthenium, and others were measured in the air and in rainwater during 2-5 May 1986 (Smith and Clark 1986). The background-activity concentrations were about three times normal levels in early May, and those of ^{131}I approached the derived emergency reference level (DERL) of drinking water of 5 mSv ^{131}I (equivalent to a thyroid dose of 50 mSv); however, ^{131}I levels were not elevated in foodstuffs or cow's milk (Smith and Clark 1986). Syria--1,800 km from Chernobyl--had measurable atmospheric concentrations of ^{137}Cs and ^{131}I and near-detection limit concentrations of ^{144}Ce, ^{134}Cs, ^{140}La, and ^{106}Ru (Othman 1990). The maximum ^{131}I thyroid dose equivalent received by Syrians was 116 uSv in adults and ^{210} uSv in children; 1 year later, these values were 25 uSv in adults and 70 uSv in a 10-year-old.

The amount of fallout radioactivity deposited on plant surfaces depends on the exposed surface area, the developmental season of the plants, and the external morphology. Mosses, which have a relatively large surface area, showed the highest concentrations of radiocesium. (Table 18). In northern Sweden, most of the radiocesium fallout was deposited on plant surfaces in the forest ecosystem and was readily incorporated into living systems because of browsing by herbivores and cesium's chemical similarity to potassium (Palo et al. 1991). Forest plants seemed to show less decrease than agricultural crops in ^{137}Cs activity over time (Bothmer et al. 1990). For example, the effective retention half-life of ^{137}Cs from Chernobyl was 10-20 days in

herbaceous plants and 180 days in chestnuts, *Castanea* spp. (Tonelli et al. 1990). The radioactive fallout from the Chernobyl accident also resulted in high ^{137}Cs levels in Swedish pasture grass and other forage, although levels in grain were relatively low (Andersson et al. 1990). Radiocesium isotopes were still easily measurable in grass silage that was harvested in June 1986 and used as fodder for dairy cows in 1988 (Voors and Van Weers 1991). The rejection of the first harvests of radiocesium-contaminated perennial pasture and in particular of rye grass (*Lolium perenne*) does not constitute a safe practice because later harvests--even 1 year after the contamination of the field--may contain very high values as in Greece (Douka and Xenoulis 1991).

Aquatic Life. After Chernobyl, the consumption of freshwater fishes by Europeans declined, fish-license sales dropped by 25%, and the sale of fish from radiocesium-contaminated lakes was prohibited (Brittain et al. 1991). Many remedial measures have been attempted to reduce radiocesium loadings in fishes, but none has been effective to date (Hakanson and Andersson 1992). Radiocesium concentrations in muscle of fishes from the southern Baltic Sea increased 3 to 4 times after Chernobyl (Grzybowska 1989), and $^{134+137}Cs$ and ^{106}Ru in fishes from the Danube River increased by a factor of 5; however, these levels posed negligible risk to human consumers (Conkic et al. 1990). Chernobyl radioactivity, in particular ^{141}Ce and ^{144}Ce, that entered the Mediterranean as a single pulse, was rapidly removed from surface waters and transported to 200 m in a few days primarily in fecal pellets of grazing zooplankton (Fowler et al. 1987). Bioconcentration factors (BCF) of ^{137}Cs in fishes from Lake Paijanne, Finland--a comparatively contaminated area--ranged from 1,250 to 3,800; the highest BCF values were measured in the predatory northern pike (*Esox lucius*) 3 years after the Chernobyl accident; consumption of these fishes was prohibited (Korhonen 1990).

After the Chernobyl accident, radiocesium. isotopes were also elevated in trees and lichens that bordered an alpine lake in Scandinavia and in lake sediments, invertebrates, and fishes (Table 18). Radiocesium levels in muscle of resident brown trout (*Salmo trutta*) remained elevated for at least 2 years (Brittain et al. 1991). People who consumed food near this alpine lake derived about 90% of their effective dose equivalent from the consumption of freshwater fish, reindeer meat, and milk. The average effective dose equivalent of this group during the next 50 years is estimated at 6-9 mSv with a changed diet and 8-12 mSv without dietary changes (Brittain et al. 1991).

Wildlife. Reindeer (*Rangifer tarandus*)--*also* known as caribou in North America--are recognized as a key species in the transfer of radioactivity from the environment to humans because (1) the transfer factor of radioactivity from reindeer feed to reindeer muscle is high, (2) lichens--which constitute a substantial portion of the reindeer diet--are efficient accumulators of Sr, Cs, and actinide radioisotopes and, (3) reindeer feed is not significantly supplemented with grain or other feeds of low contamination (Jones et al. 1989; Rissanen and Rahola 1989; 1990; Eikelman et al. 1990; Skogland and Espelien 1990). During 1986-87, about 75% of all reindeer meat from Sweden was unfit for human consumption because ^{137}Cs exceeded 300 Bq/kg FW. In May 1987, the maximum permissible level of ^{137}Cs in Swedish reindeer, game, and freshwater fish was raised to 1,500 Bq/kg FW; however, about 25% of slaughtered reindeer in 1987-89 still exceeded this limit (Ahman et al. 1990b). Concentrations in excess of 100,000 Bq $^{134+137}Cs$/kg FW lichens have been recorded in the most contaminated areas and in the 1986-87 season was reflected in reindeer muscle concentrations of greater than 50,000 Bq/kg FW from the most contaminated areas of central Norway (Roed et al. 1991). Norwegian reindeer with 60,000-70,000 Bq ^{137}Cs/kg FW in muscle receive an estimated yearly dose of 500 mSv (Jones 1990). The maximum radiation dose to reindeer in Sweden after the Chernobyl accident was about 200 mSv/year with a daily dose rate of about 1 mSv during the winter period of maximum tissue concentrations (Jones et al. 1989). In general, reindeer calves had higher ^{131}Cs levels in muscle than adult females (4,700 vs. 2,700 Bq/kg FW) during September 1988, suggesting translocation to the fetus (Eikelmann et al. 1990). Two reindeer herds in Norway that were heavily contaminated with radiocesium had a 25% decline in survival of calves; survival was normal in a herd with low exposure (Skogland and Espelien 1990). Several compounds inhibit uptake and reduce retention of ^{137}Cs in reindeer muscle from contaminated diets, but the mechanisms of the action are largely unknown. These compounds include zeolite--a group of tectosilicate minerals--when fed at 25-50 g daily (Ahman et al. 1990a); ammonium hexacyanoferrate--also known as Prussian Blue or Giese salt--at 0.3-1.5 g daily (Hove et al. 1990b; Mathiesen et al. 1990; Staaland et al. 1990); bentonite--a montmorillonite clay--when fed at 2% of diet (Ahman et al. 1990a); and high intakes of potassium (Ahman et al. 1990a). Much additional work seems needed on chemical and other processes that hasten excretion and prevent uptake and

accumulation of radionuclides in livestock and wildlife. Reindeer herding is the most important occupation in Finnish Lapland and in portions of Sweden (Rissanen and Rahola 1989). Swedish Lapland reindeer herders have experienced a variety of sociocultural problems as a result of the Chernobyl accident. The variability of contamination has been compounded by the variability of expert statements about risk, the change in national limits of Bq concentrations set for meat marketability, and the variability of the compensation policy for slaughtered reindeer. These concerns may result in fewer Lapps becoming herders and a general decline in reindeer husbandry (Beach 1990).

Caribou in northern Quebec contained as much as 1,129 Bq ^{137}Cs/kg muscle FW in 1986-87, but only 10-15% of this amount originated from Chernobyl; the remainder is attributed to fallout from earlier atmospheric nuclear tests (Crete et al. 1990). The maximum concentration of ^{137}Cs in meat of caribou (*Rangifer tarandus granti*) from the Alaskan Porcupine herd after the Chernobyl accident did not exceed 232 Bq/kg FW, and this is substantially below the recommended level of 2,260 Bq ^{137}Cs/kg FW (Allaye-Chan et al. 1990). Radiocesium transfer in an Alaskan lichen-reindeer-wolf (*Canis 1upus*) food chain has been estimated. If reindeer forage contained 100 Bq/kg DW in lichens and 5 Bq/kg DW in vascular plants, the maximum winter concentrations--at an effective half-life of 8.2 years in lichens and 2.0 years in vascular plants--was an estimated 20 Bq/kg FW in reindeer-caribou skeletal muscle and 24 Bq/kg FW in wolf muscle (Holleman et al. 1990).

The radioactive body burden of exposed reindeer and the character of chromosomal aberrations--which was different in exposed and nonexposed reindeer--indicated a genetic effect of radiation from the Chernobyl accident (Roed et al. 1991). Chromosomal aberrations in Norwegian female reindeer positively correlated with increasing radiocesium concentrations in flesh (Skogland and Espelien 1990). The frequency of chromosomal aberrations in reindeer calves from central Norway were greatest in those born in 1987 when tissue loadings were equivalent to fetal doses of 70-80 mSv and lower in 1988 (50-60 mSv) and 1989 (40-50 mSv), strongly suggesting a dose-dependent induction (Roed et al. 1991). Mutagenicity tests with feral rodents have also been used successfully to evaluate the biological effects of the radiation exposure from the Chernobyl accident. Increased mutagenicity in mice (*Mus musculus domesticus*) was evident as judged by tests of the bone-marrow micronucleus at 6 months and 1 year after the accident. Rodents with increased chromosomal aberrations also had ^{137}Cs burdens that were 70% higher 6 months after the accident and 55% higher after 1 year, but elevated radiocesium body burdens alone were not sufficient to account for the increase in mutagenicity (Cristaldi et al. 1990). In bank voles, however, mutagenicity (micronucleated polychromatic erythrocytes) correlated well with the ^{137}Cs content in muscle and in the soil of the collection locale (Cristaldi et al. 1991). The estimated daily absorbed doses (4.2-39.4 uGy) were far lower than those required to produce the same effect in the laboratory (Cristaldi et al. 1991).

For many households in Sweden, moose (*Alces alces*) are an important source of meat (Palo et al. 1991). Radiocesium concentrations in the foreleg muscle of moose in Sweden during 1987-88 were highest in fall when the daily dietary intake of the animals was about 25,000 Bq ^{137}Cs and lowest during the rest of the year when the mean daily intake was about 800 Bq (Bothmer et al. 1990). Cesium-137 levels in moose flesh did not decrease significantly for about 2 years after the Chernobyl accident (Johanson 1990). The selection of food by moose is paramount to the uptake of environmental contaminants and the changes in tissue levels over time. Increased foraging on highly contaminated plant species, such as bilberry (*Vaccinium myrtillus*), aquatic plants, and mushrooms, may account for the increased ^{137}Cs radioactivity in moose (Palo et al. 1991). For reasons that are not yet clear, transfer coefficients of ^{137}Cs from diet to muscle were about the same in moose (0.03) and beef cattle (0.02) but were significantly higher in sheep (0.24) (Bothmer et al. 1990).

The song thrush (*Turdus philomelas*) collected in Spain in November 1986 had elevated concentrations of ^{134}Cs, ^{137}Cs , and ^{90}Sr; the contamination probably occurred in central and northern Europe before the bird's migration to Spain (Baeza et al. 1991). Spaniards who ate songthrushes that were contaminated with radiocesium isotopes usually received about 58 uSv/year, which is well below the current international guidelines (Baeza et al. 1991). Consumption of game or wildlife in Great Britain after the Chernobyl accident probably also do not exceed the annual limits of intake (ALI) based on $^{134+137}$Cs concentrations in game and the numbers of animals that can be eaten in 1 year before ALI is exceeded (Lowe and Horrill 1991). For example, a person that eats hares with 3,114 Bq $^{134+137}$Cs/kg FW in muscle would have to consume 99 hares

before exceeding the ALI; for the consumption of red grouse (3,022 Bq/kg), this number is 441 grouse; and for the consumption of woodcock (55 Bq/kg), it is 45,455 woodcocks (Lowe and Horrill 1991). Rabbits (*Oryctolagus* sp.) from northeastern Italy that were fed Chernobyl-contaminated alfalfa meal (1,215 Bq $^{134+137}$Cs/kg diet) had a maximum of 156 Bq/kg muscle FW of $^{134+137}$Cs, a value much lower than the current Italian guideline of 370 Bq/kg FW for milk and children's food and 600 Bq/kg FW for other food (Battiston et al. 1991). More than 85% of the ingested radiocesium was excreted by rabbits in feces and urine; about 3% was retained (Battiston et al. 1991).

Cesium radioactivity in tissues and organs of the wolverine (*Gulo gulo*), lynx (*Felis lynx*), and Arctic fox (*Alopex logopus*) in central Norway after the Chernobyl accident was highly variable. In general, cesium-137 levels were substantially lower in these carnivores than in lower trophic levels (Ekker et al. 1990), suggesting little or no food-chain biomagnification, and at variance with results of studies of the omnivore and herbivore food chain.

Domestic Animals. Radiocesium isotopes from the Chernobyl accident transferred easily to grazing farm animals (Hove et al. 1990a). Both ^{134}Cs and ^{137}Cs were rapidly distributed throughout the soft tissues after dietary ingestion and were most highly concentrated in muscle (Book 1969; Van Den Hoek 1989). Radiocesium activity in milk and flesh of Norwegian sheep and goats increased 3 to 5 fold 2 years after the accident and coincided with an abundant growth and availability of fungal fruit bodies in which $^{134+137}$Cs levels were as much as 100 times greater than green vegetation (Hove et al. 1990a). In cattle, coefficients of radiocesium transfer from diet to muscle were about 2.5% in adults and 16% in calves; the higher value in calves was probably due to a high availability of cesium from the gastrointestinal tract and to daily uptake of potassium in growing animal muscle (Daburon et al. 1989). There was no correlation between the retention of ^{137}Cs and the pregnancy stage in cattle (Calamosca et al. 1990). Radiocesium concentrations in pork in Czechoslovakia did not decline between 1986 and 1987 because the feed of pigs during this period contained milk byproducts contaminated with $^{134+137}$Cs (Kliment 1991).

Sheep farming is the main form of husbandry in the uplands of western Cumbria and northern Wales, a region that received high levels of radiocesium fallout during the Chernobyl accident. Afterwards, typical vegetation activity concentrations were about 6,000 Bq/kg (down to about 1,000 Bq/kg in January 1989). But concentrations in sheep muscle exceeded 1,000 Bq ^{137}Cs/kg FW, which is the United Kingdom's dietary limit for human-health protection (Crout et al. 1991). Contaminated lambs--which usually had higher concentrations of ^{137}Cs than ewes--that were removed to lowland pastures (<50 Bq/kg vegetation) rapidly excreted radiocesium in feces and urine, and cesium body burdens had an effective half-life of 11 days. This practice should not significantly increase radiocesium levels in the soil and vegetation of lowland pastures (Crout et al. 1991). The absorption and retention of radiocesium by suckling lambs is highly efficient, about 66%. Fecal excretion was an important pathway after the termination of ^{137}Cs ingestion. In weaned animals, the absorption of added ionic cesium was about twice that of cesium fallout after the accident at Chernobyl (Moss et al. 1989). Silver-110m was also detected in the brains and livers of ewes and lambs in the United Kingdom. The transfer of ^{110m}Ag was associated with perennial rye grass that was harvested soon after deposition in 1986. Silver-110m was taken up to a greater extent than ^{137}Cs in liver, but unlike ^{137}Cs, ^{110m}Ag was not readily translocated to other tissues. Other than cesium isotopes and ^{131}I, ^{110m}Ag was the only detected nuclide in sheep tissues (Beresford 1989).

Atmospheric deposition of ^{137}Cs from Chernobyl to vegetation and eventually to the milk of sheep, cows, and goats on contaminated silage was reported in Italy, the Netherlands, Japan, and the United Kingdom (Book 1969; Belli et al. 1989; Pearce et al. 1989; Voors and Van Weers 1989; Aii et al. 1990; Monte 1990). The effective half-life of ^{137}Cs was 6.7 days in pasture grass and 13.6 days in milk (Spezzano and Giacomelli 1991). The average transfer coefficient of $^{134+137}$Cs from Chernobyl from a 70% grass-silage diet to milk of Dutch dairy cows was about 0.250%/liter/day (Voors and Van Weers 1991). In goats (*Capra* sp.), about 12% of orally administered ^{137}Cs was collected in milk within 7 days after dosing (Book 1969).

Iodine-131 was one of the most hazardous radionuclides released in the Chernobyl accident because it is easily transferred through the pasture-animal-milk pathway and rapidly concentrated in the thyroid gland to an extent unparalleled in any other organ. Because of its high specific activity, ^{131}I can transmit a high dose of radiation to the thyroid (Ionannides and Pakou 1991). Iodine-131 levels of 618,000 Bq/kg FW in sheep thyroids from northwestern Greece on 3 July 1986 are similar to maximal ^{131}I concentrations in sheep thyroids in Tennessee in 1957 after global atmospheric fallout from military weapons tests and in London after the Windscale accident (Ionannides and Pakou 1991). Iodine-131 has an effective whole-body half-life of about 24 h and is rapidly excreted from sheep and cows (Assimakopoulos et al. 1989). The effective half-life of ^{131}I was 3.9 days in pasture grass and 5 days in cow's milk (Spezzano and Giacomelli 1991). The transfer coefficients of ^{131}I from vegetation to cow's milk was 0.007% day/L milk; this value was 57 times higher (0.4) in sheep (Monte 1990), but the mechanism to account for this large interspecies difference is not clear.

Effects: Nonionizing Radiations

Living organisms are constantly exposed to nonionizing electromagnetic radiations, including ultraviolet, visible, infrared, radio, and other low energy radiations that form an integral part of the biosphere. Emissions from anthropogenic sources such as radios, microwave ovens, television communications, and radar significantly altered the character of our natural electromagnetic field (Garaj-Vrhovac et al. 1990). Although the primary focus of my review is on ionizing radiations, an assumption that low energy electromagnetic waves cannot elicit significant biological responses would be misleading. For example, behavioral and biochemical changes are reported in rats, monkeys, rabbits, and other laboratory animals after exposure to nonionizing electromagnetic radiations; the severity of the effect is associated with the type and duration of the radiation and with various physicochemical variables (Ghandi 1990). Selected examples follow.

Ultraviolet radiation in mammals causes the aging of skin, making it wrinkled and leathery (Kligman and Kligman 1990). Dermatologists of the late nineteenth century described the devastating effects of sunlight on the skin of farmers and sailors when compared with indoor workers. Photoaged skin has a variety of neoplasms, deep furrows, extensive sagging, and profound structural alterations that are quite different from those in protected, intrinsically aged skin (Kligman and Kligman 1990). Similar results were documented of skin of guinea pigs (Davidson et al. 1991) and rodents (Ananthaswamy and Pierceall 1990; Ronai et al. 1990) after exposure to ultraviolet radiation. Ultraviolet radiation causes eye cancer in cattle (Anderson and Badzioch 1991), interferes with wound healing in guinea pig skin (Davidson et al. 1991), is a potent damaging agent of DNA and a known inducer of skin cancer in experimental animals (Ronai et al. 1990), and interferes with an immune defense mechanism that normally protects against skin cancer (Ananthaswamy and Pierceall 1990). Aquatic organisms exposed to ultraviolet radiation show disrupted orientation, decreased motility, and reduced pigmentation in *Peridinium gatunense*, a freshwater alga (Hader et al. 1990); effects were similar in several species of marine algae (Lesser and Shick 1990; Hader and Hader 1991; Shick et al. 1991). Increased lipid peroxidation rates and a shortening of the life span after ultraviolet exposure were reported in the rotifer *Asplanchna brightwelli* (Sawada et al. 1990). Cells of the goldfish (*Carassius auratus*) were damaged, presumably by DNA impairment, from UV exposure (Yasuhira et al. 1991).

Visible radiation adversely affected survival and growth of embryos of the chinook salmon (*Oncorhynchus tshawytscha*; Eisler 1961), chloroplast structure in the symbiotic marine dinoflagellate *Symiodinium sp*. (Lesser and Shick 1990), and in-vitro growth of cultured mammalian cells (Karu 1990). Infrared radiation contributes significantly to skin photoaging, producing severe elastosis; the epidermis and the dermis were capable of self-restoration when the exogenous injury ceased (Kligman and Kligman 1990).

Investigations of the cellular effects of radiofrequency radiation provide evidence of damage to various types of avian and mammalian cells. These effects involve radiofrequency interactions with cell membranes, especially the plasma membrane. Effects include alterations in membrane cation transport, Na^+/K^+-ATPase activity, protein kinase activity, neutrophil precursor membrane receptors, firing rates and resting potentials of neurons, brain cell metabolism, DNA and RNA syntheses in glioma cells, and mitogenic effects on human lymphocytes (Cleary 1990). Microwaves inhibit thymidine incorporation by DNA blockage in cultured cells of the Chinese hamster; irradiated cells had a higher frequency of chromosome lesions (Garaj-Vrhovac et al. 1990). Microwaves induce teratogenic effects in mice when the intensity of exposure places a thermal burden on the dams and fetuses, reducing fetal body mass and increasing number of resorptions (O'Connor 1990).

Extremely low frequency (ELF) electromagnetic fields--similar to fields that emanate from electrical appliances and the electrical power distribution network, usually less than 300 Hz--are used therapeutically in the healing of human nonunion bone fractures, in the promotion of nerve regeneration, and in acceleration of wound healing (Anderson 1990). ELF electric and magnetic fields produce biological effects, usually subtle, and of low hazard in short-term exposure. These effects include altered neuronal excitability, neurochemical changes, altered hormone levels, and changes in behavioral responses. For example, electric-field perception has been reported in humans, mice, pigs, monkeys, pigeons, chickens, and insects; altered cardiovascular responses in dogs and chickens; and altered growth rate of chicks. No deleterious effects of ELF fields on mammalian reproduction and development or on carcinogenesis and mutagenesis have been documented (Anderson 1990). ELF fields had no effect on the growth of bone in chicks (Coulton and Barker 1991). However, adult eastern newts (*Notophthalmus viridescens*), regenerating amputated forelimbs, had grossly abnormal forelimbs 12% of the time when exposed for 30 days to ELF fields of the type reported to facilitate healing of human bone fractures (Landesman and Douglas 1990). Additional studies are recommended on the biological effects of nonionizing radiations on fishes and wildlife, especially ELF radiations.

Effects: Ionizing Radiations

General

High acute doses of ionizing radiation produce adverse biological effects at every organizational level: molecule, cell, tissue-organ, whole animal, population, community, and ecosystem (ICRP 1977; Whicker and Schultz 1982b; LWV 1985; Hobbs and McClellan 1986; UNSCEAR 1988; Kiefer 1990; Severa and Bar 1991). Typical adverse effects of ionizing radiation include cell death (McLean 1973; LWV 1985; Kiefer 1990), decreased life expectancy (Lorenz et al. 1954; Brown 1966; Hobbs and McClellan 1986; Kiefer 1990; Rose 1992), increased frequency of malignant tumors (Lorenz et al. 1954; ICRP 1977; Hobbs and McClellan 1986; UNSCEAR 1988; Hopewell 1990; Kim et al. 1990; Little 1990; Nagasawa et al. 1990; Raabe et al. 1990; Fry 1991), inhibited reproduction (ICRP 1977; Barendson 1990; Kiefer 1990; Rose 1992), increased frequency of gene mutations ICRP 1977; Whicker and Schultz 1982b; Hobbs and McClellan 1986; Abrahamson 1990; Evans 1990; Kiefer 1990; Thacker 1990; Sankaranarayanan 1991a; 1991b; Rose 1992), leukemia (ICRP 1977; Kiefer 1990), altered blood-brain barrier function (Trnovec et al. 1990), and reduced growth and altered behavior (Rose 1992). Species in kingdoms have a wide variation in sensitivity, and sometimes at low radiation exposures the response is considered beneficial (Luckey 1980; Rose 1992). Overall, the lowest dose rate at which harmful effects of chronic irradiation have been reliably observed in sensitive species is about 1 Gy/year; this value for acute radiation exposures is about 0.01 Gy (Rose 1992).

In general, the primitive organisms are the most radioresistant taxonomic groups and the more advanced complex organisms--such as mammals--are the most radiosensitive (Fig. 7). The early effects of exposure to ionizing radiation result primarily from cell death; cells that frequently undergo mitosis are the most radiosensitive, and cells that do not divide are the most radioresistant. Thus, embryos and fetuses are particularly susceptible to ionizing radiation, and very young animals are consistently more radiosensitive than adults (McLean 1973; Hobbs and McClellan 1986). In addition to the evolutionary position and cell mitotic index, many extrinsic and intrinsic factors modify the response of a living organism to a given dose of radiation. Abiotic variables include the type and energy of radiation, exposure rate, length of exposure, total exposure and absorbed dose, dose rate, spatial distribution of dose, season, temperature, day length, and environmental chemicals; biotic variables include the species, type of cell or tissue, metabolism, sex, nutritional status, sensitizing or protective substances, competition, parasitism, and predation (Whicker and Schultz 1982b; Hobbs and McClellan 1986; UNSCEAR 1988; Kiefer 1990).

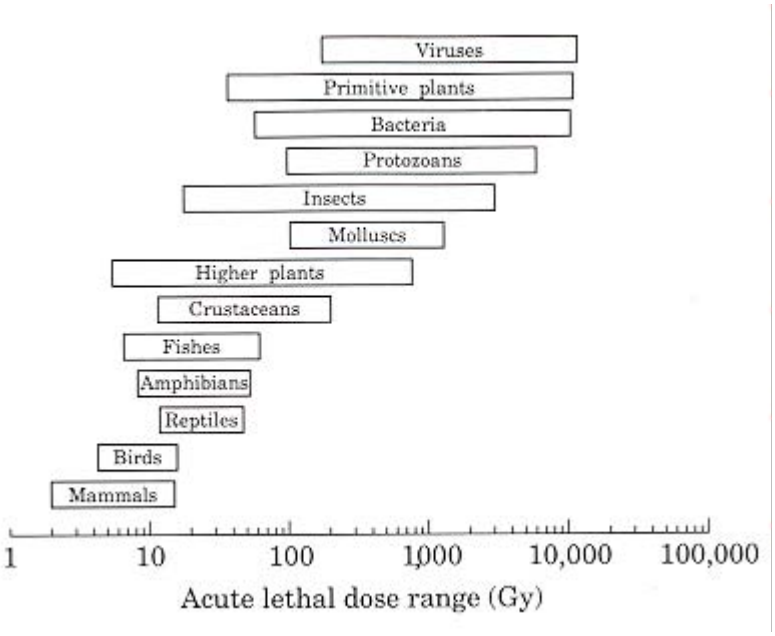


Fig. 7. Acute radiation dose range fatal to 50% (30 days postexposure) of various taxonomic groups (modified from Whicker and Schultz 1982b; Hinton and Scott 1990).

Radiosensitivity of cells is related directly to their reproductive capacity and indirectly to their degree of differentiation (Hobbs and McClellan 1986). Early adverse effects of exposure to ionizing radiation are due mainly to the killing of cells. Cell death may result from the loss of reproductive integrity, that is, when after irradiation a cell fails to pass through more than one or two mitoses. Reproductive death is important in rapidly dividing tissues such as bone marrow, skin, gut lining, and germinal epithelium. When the whole animal is exposed to a large dose of ionizing radiation, some tissues are more prone to damage than others. Death rates of mammalian reproductive cells from ionizing radiations is modified by variations in the linear energy transfer of the radiation, the stage in the cell cycle, cell culture conditions, and sensitizing and protecting compounds (Barendsen 1990). The chemical form of the main stage of the acute radiation syndrome depends on the size and distribution of the absorbed dose. It is determined mainly by damage to blood platelets and other blood-forming organs at 4-5 Gy, to epithelial cells lining the small intestine at 5-30 Gy, and to brain damage at more than 30 Gy; death usually occurs within 48 h at more than 30 Gy (McLean 1973).

Cellular DNA is extremely sensitive to ionizing radiation, although other cell constituents may approach DNA in sensitivity (IAEA 1976; Billen 1990; Kiefer 1990; Lett 1990; Lucke-Huhle et al. 1990; Woloschak et al. 1990a; Shadley et al. 1991). Radiation-induced mutations are explainable on the basis of chromatin and DNA organization in cells and the biophysical properties of ionizing radiation (Sankaranarayanan 1991b). Based on studies of spontaneous and radiation-induced mutations in the mouse (Sankaranarayanan 1991a), more than 67% of the ionizing radiation-induced mutations are lethal and almost all mutations, including enzyme activity variants, dominant visibles, and dominant skeletal mutations, are lethal. These findings are consistent with the view that most radiation-induced mutations in germ cells of mice are due to DNA deletions (Sankaranarayanan 1991a).

Experimental animal data clearly demonstrate that ionizing radiation at relatively high doses and delivered at high dose rates is mutagenic (Hobbs and McClellan 1986). However, radiation-induced genetic damage in the offspring of exposed parents has not been credibly established in any study with humans (Abrahamson 1990). In one human population--the ethnically isolated Swedish reindeer breeding Lapps--elevated concentrations of fallout products have been ingested via the lichen-reindeer-human food chain since the 1950's. However, during 1961-84, incidences of genetic damage did not increase in Lapps (Wiklund et al. 1990).

Radiation is carcinogenic. The frequency of death from cancer of the thyroid, breast, lung, esophagus, stomach, and bladder was higher in Japanese survivors of the atomic bomb than in nonexposed individuals, and carcinogenesis seems to be the primary latent effect of ionizing radiation. The minimal latent period of most

cancers was less than 15 years and depended on an individual's age at exposure and site of cancer. The relation of radiation-induced cancers to low doses and the shape of the dose-response curve (linear or non-linear), the existence of a threshold, and the influence of dose rate and exposure period must be determined (Hobbs and McClellan 1986).

Radioactive materials that gain entry to the body, typically through ingestion or inhalation, exert effects that are governed by their physical and chemical characteristics which, in turn, influence their distributions and retention inside the body. The effective half-life includes physical and biologic half-times. In addition, the type of radiation (i.e., αβ) and its retention and distribution kinetics govern the radiation-dose pattern. In general, the radiation dose from internal emitters is a function of the effective half-life, energy released in the tissue, initial amount of introduced radioactivity, and mass of the organ (Hobbs and McClellan 1986). Retention of radionuclides by living organisms is quite variable and modified by numerous biologic and abiotic variables. For example, ^{137}Cs retention in selected animals varies significantly with the body weight, diet, and metabolism of an organism (Fig. 8). The time for 50% persistence of ^{137}Cs is between 30 and 430 days in ectotherms and was longer at lower temperatures and shortest in summer and under conditions of inadequate nutrition (Hinton and Scott 1990). In mammals, the ^{137}Cs biological half-life was between 6 and 43 days in rodents, dogs, mule deer, reindeer, and monkeys; in humans, this value ranged from 60 to 160 days. The biological half-life of ^{90}Sr ranges from 122 to 6,000 days in ectotherms and is longer at colder temperatures and under laboratory conditions. In mammals and under conditions of chronic intake, the ^{90}Sr biological half-life was 533 days in rats, 750 days in humans, and at least 848 days in beagles (Hinton and Scott 1990).

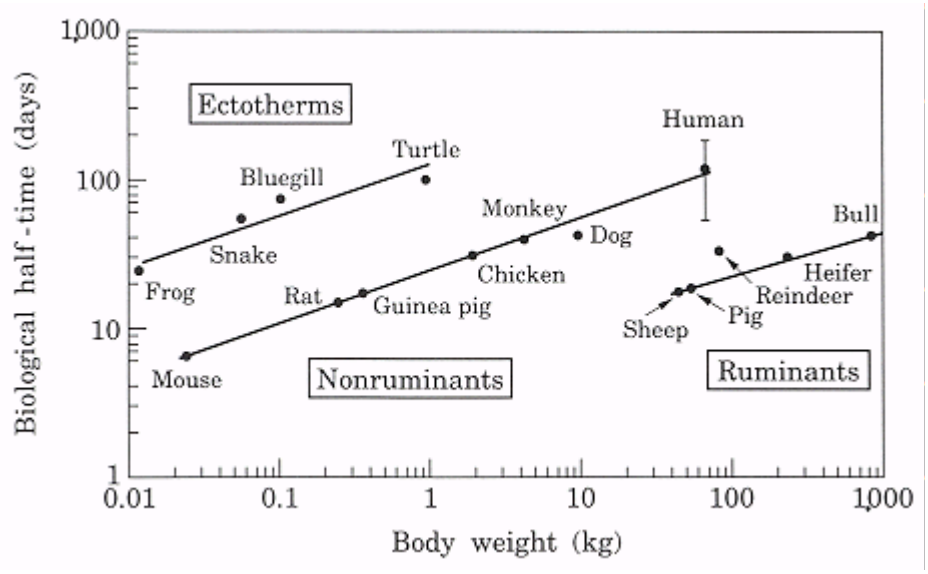


Fig. 8. Relation between diet, metabolism, and body weight with half-life retention of longest-lived component of cesium-137. Data are from selected ruminant and nonruminant mammals (Richmond 1989) and ectotherms (Hinton and Scott 1990).

Terrestrial Plants and Invertebrates

Radiosensitive terrestrial plants exposed to single doses of ionizing radiation had reduced growth at 0.5-1.0 Gy and reduced survival at 3.0-4.1 Gy (Table 19); chronic exposures of 0.2-0.65 Gy/day adversely affected sensitive forest ecosystems (Table 19). Chronic gamma irradiation of 131 Gy/year and higher of mixed forest ecosystems caused the disappearance of trees and shrubs and subsequent erosion of the soil (Poinsot-Balaguer et al. 1991). The radiation sensitivity of five plant communities suggested that pine (*Pinus* spp.) forests were the most sensitive and that deciduous evergreen forests, tropical rain forests, herbaceous rock-outcrop communities, and abandoned cropland were increasingly less sensitive (McCormick 1969). Neutrons were 3 to 4 times more effective than gamma rays in root growth inhibition (Witherspoon 1969). Altitude affects the response of vegetation to ionizing radiation. Peas (*Pisum sativum*) in gardens at 2,225-3,750 m above mean

sea level and exposed to 0, 5, 10, or 50 Gy had reduced growth from all treatments at increasing altitudes; however, a dose-response growth curve was evident only at less than 3,049-m altitude (Osburn 1963). Seeds of tobacco (*Nicotiana tabacum*) exposed to cosmic rays aboard a spacecraft had a higher mutation rate than controls; effects occurred at total doses as low as 0.1-0.2 Gy (Gaubin et al. 1990), but this needs verification.

Table 19. Radiation effects on selected terrestrial plants.

Table 19. Species, dose, and other variables	Effect	Reference[a]
Tropical rainforest tree, *Dacryodes excelsa*, 4 to 280 Gy/year	Growth stimulation	1
Deciduous evergreen forest		
40 Gy yearly	Minor effects	2
100 Gy yearly	Severe sublethal effects	2
350 Gy yearly	Lethal	2
Deciduous plants, 13 species		
4 to 15 Gy, single fast neutron doses	Shoot growth inhibited by >85%	3
60 to 85 Gy, single gamma radiation dose	Shoot growth inhibited by >85%	3
Forest ecosystem, northern Wisconsin, experimentally exposed to a ^{137}Cs point source for 5 months during a growing season. Distance from source (meters) and daily exposure (Gy)		
5 m, 15 Gy	No vegetation	4
5-10 m, 5-15 Gy	Lower plants present	4
10-15 m, 1.5 Gy	Resistant trees and shrubs present	4
10-15 m, 2.5-5.0 Gy	Some growth	4
20-30 m, 0.65-1.5 Gy	Resistant angiosperm trees	4
30-50 m, 0.2-0.65 Gy	Angiosperm trees present	4
50 m, 0.2 Gy	Original northern forest	4
Herbaceous rock outcrop community		
90 Gy yearly	Minor effects	2
400 Gy yearly	Severe sublethal effects	2
1,000 Gy yearly	Lethal	2
Mango, Queensland *Mangifera indica,* fruit irradiated postharvest, single dose, 250 or 750 Gy	At 250 Gy, skin and pulp color inhibited 50% due to irradiation-induced suppression of chlorphyll breakdown and reduction in carotenoid production. At 750 Gy, fruit respiration increased for 3-5 days, but no effect on fruit firmness	5
Mixed oak forest, southern France, experimentally irradiated for 18 years by a ^{137}Cs source at dose rates between 0.3 and 116 mGy/h, equivalent to a yearly rate between 2.6 and 1,016 Gy	At 60-100 mGy/h (525-876 Gy yearly), all trees, shrubs, and litter were absent; low overall insect density; soil deficient in carbon, nitrogen, and water. At 15 mGy/h (131 Gy yearly), woody	6

Table 19. Species, dose, and other variables	Effect	Reference[a]
	plants were present, but visibly abnormal	
Tobacco, *Nicotiana tabacum,* 55 Gy/year	Growth stimulation	1
Pine forest		
1-10 Gy yearly	Minor effects	2
20 Gy yearly	Severe sublethal effects	2
30 Gy yearly	Lethal	2
Slash pine, *Pinus elliottii,* acute single exposure of 3 Gy	50% dead 1-4 months after exposure; no other deaths in 2 years	2
Sugar pine, *Pinus lambertiana,* acute single exposure of 4.1 Gy	LD50 (30 days postexposure)	1
Longleaf pine, *Pinus palustris*		
0.5 Gy, single dose	Growth inhibition	1
8 Gy, acute single exposure	50% of trees <5 years old died in 1-4 months; others survived for at least 2 years	2
>28 Gy, acute single exposure	Fatal to 50% of trees >5 years old in 1-4 months; no other deaths in 2 years	2
Winter wheat, *Triticum aestivum,* acute single exposure of 1.0 Gy	Growth inhibition	1
Tropical rainforest		
70 Gy yearly	Minor effects	2
350 Gy yearly	Severe sublethal effects	2
400 Gy yearly	Lethal	2
Vegetation, abandoned crop land		
50 Gy yearly	Minor effects	2
450 Gy yearly	Severe sublethal effects	2
1,500 Gy yearly	Lethal	2
Bean, *Vicia faba,* 58-100 Gy/year	Growth stimulation	1

[a]1, Rose 1992; 2, McCormick 1969; 3, Witherspoon 1969; 4, Zavitokovski and Rudolph 1971; 5, Boag et al. 1990; 6, Poinsat-Balaguer et al. 1991.

Sometimes, irradiation prevents the usual colonizing vegetation from becoming established (Poinsot-Balaguer et al. 1991). Germination and survival of shrub seedlings have been much slower in nuclear test sites than in undisturbed sites (Romney et al. 1971). The return to its original state of the perennial shrub vegetation takes decades on a radiation-disturbed site, although native annual species and grasses have grown abundantly within 12 months. Transplanting of shrubs into radiation-disturbed areas has been largely unsuccessful because of intense browsing by rabbits and other small mammals (Romney et al. 1971). A nuclear detonation damages terrestrial vegetation by heat, blast, or radiation. Plant injury from thermal or ionizing radiation at an above-ground detonation site varied with stem rigidity and stability of the substratum, although radiation effects are ordinarily masked by damage from blasts. A typical nuclear detonation at the Nevada test site--an airburst of a 20- to 40-kiloton yield--denuded a zone of desert within a 0.8-km radius of shrub vegetation. Recovery at the Nevada site seemed complete within 4 years, suggesting little relation between fatal

injury, morphological aberration in vegetation, and ionizing radiation from nuclear detonations (Shields and Wells 1963). A northern Wisconsin forest experimentally subjected to a ^{137}Cs radiation source for 5 months showed several trends: (1) herbaceous and shrub species with a spreading form of growth are more radioresistant than upright forms; (2) larger pines and oaks are more radioresistant than smaller trees; (3) perennial plants with shielded buds and vigorous asexual reproduction are relatively radioresistant; (4) plants that are adapted to extreme habitats such as old fields and granite rock outcrops and plants that are typical of early successional stages are relatively radioresistant; (5) all plants are more radiosensitive during the growing season than during the dormant season; and (6) reproductive stages are always more radiosensitive than vegetative stages (Zavitokovski and Rudolph 1971). The recovery of vegetation in a tropical rain forest in Puerto Rico--after plants were deliberately subjected to lethal doses of gamma radiation--closely resembled secondary succession after other types of disturbances such as mechanical stripping and treatment with the Picloran herbicide (Jordan 1969).

Hormesis--the beneficial physiological stimulation by low doses of a potentially harmful agent--is documented of ionizing radiation and many species of terrestrial plants and invertebrates (Luckey 1980). Radiation hormesis in plants includes increased germination, growth, survival, and yield. Some species of terrestrial invertebrates had increased fecundity, growth, survival, disease resistance, and longevity after exposure to low sublethal doses of ionizing radiation (Luckey 1980).The growth and development of some terrestrial invertebrates are stimulated at comparatively high sublethal acute doses (i.e., 2 Gy in silkworm [*Bombyx mori*]), but survival is reduced at 10 Gy; in all cases, younger stages were the most sensitive (Table 20). Cockroaches (*Blaberus giganteus*) adapted to the dark reportedly can visually detect radiation sources as low as 0.001 mGy (Rose 1992), however, the mechanisms are not understood.

Table 20. Radiation effects on selected terrestrial invertebrates.

Species, dose, and other variables	Effect	Reference[a]
Caribbean fruit fly, *Anastrepha suspensa*; larvae, heavily parasitized by the hymenopteron *Diachasmimorpha longicaudata*, exposed to single acute exposures of 10 to 70 Gy	50% of control flies developed into adults vs. 25% at 10 Gy, and <1% at 30 Gy. At 40 Gy and higher, no adults were recovered but parasite development was the same at all doses	1
Silkworm, *Bombyx mori*; eggs, acute single exposure of 2, 5, or 10 Gy	At 2 Gy, an average increase of 23% in larval mass, cocoon shell weight, and silk production; no stimulatory effect at 5 Gy; at 10 Gy, larval development inhibited	2
Mediterranean fruit fly, *Ceratitis capitata*; females, acute single exposure of 150-155 Gy	Inhibited oviposition	3
Moth, *Ectomyelois ceratoniae*; male pupae, age 3 or 5 days, acute single exposure of 50 to 500 Gy	Younger pupae were more sensitive than older pupae. Only 3% of pupae developed into adults at 500 Gy. At >250 Gy, progeny development reduced 50%. Normal fecundity at 100-250 Gy when mated with control females	4
Leafmining fly, *Liriomyza trifolii*; immature stages, on artificially infested bean	All dead at >750 Gy; 80% dead at 250 Gy; eggs and prepupae were the most sensitive	5

Species, dose, and other variables	Effect	Reference[a]
seedlings; acute single exposure of 25 to 2,000 Gy	stage; no phytotoxic effects	

[a] 1, Sivinski and Smittle 1990; 2, Yusifov et al. 1990; 3, McInnes and Wong 1990; 4, Al-Izzi et al. 1990; 5, Yathom et al. 1990.

Following the successful application of radiation to sterilize male screw-worm flies (*Cochliomyia hominivorax*), various insect pests became the target of similar techniques throughout the world (Al-Izzi et al. 1990). The technique has suppressed populations of the Mediterranean fruit fly (*Ceratitis capitata*), a major pest of fruits, although results have not been as spectacular as with the screw-worm fly (McInnes and Wong 1990). The pestiferous Caribbean fruit fly (*Anastrepha suspensa*), heavily parasitized by a beetle, became sterile after acute exposures to ionizing radiation, although beetles remained fecund. Mass rearing and inundative release of the radioresistant beetle parasite is now considered an option for control of the Caribbean fruit fly (Table 20).

Aquatic Organisms

Among aquatic organisms, it is generally acknowledged that primitive forms are more radioresistant than complex vertebrates and that older organisms are more resistant than the young (Donaldson and Foster 1957; Bonham and Welander 1963; Templeton et al. 1971; Table 21). Developing eggs and young of some species of freshwater fishes are among the most sensitive tested aquatic organisms; death was observed at acute doses of 0.3-0.6 Gy, and minor effects on physiology or metabolism were observed at chronic daily dose rates of 0.01 Gy (Bonham and Welander 1963; Templeton et al. 1971; IAEA 1976; Table 21). Radiosensitivity correlated positively with the metabolic rate of the dividing cell, which accounts for the radioresistance of dormant eggs of aquatic invertebrates and the general sensitivity of early embryonic stages of all aquatic species (Donaldson and Foster 1957; Table 21).

Table 21. Radiation effects on selected aquatic organisms.

Table 21. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
Algae		
Diatom, *Nitzchia closterium*; acute single exposure of 100 Gy	Lethal	1
Euglena, *Euglena gracilis*; acute single exposure of 550 Gy	Tolerated	1
Freshwater algae, seven species, held in water containing 1,110 Bq ^{226}Ra/L for as long as 14 days	After 24 h, four species (*Ankistrodesmus falcatus*, *Chlorella vulgaris*, *Coelastrium cambricum*, *Scenedesmus obliquus*) had decreased oxygen production by 22-37%; after 14 days, no effect on growth or protein content	2
Various species, single acute exposure		
80-1,000 Gy	LD50, 45 days, postexposure	3
250-6,000 Gy	LD100, 45 days after single exposure	3
Protozoans, various species, acute single exposure		

Table 21. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
100-300 Gy	LD50, up to 40 days postexposure	3
180-12,500 Gy	LD100, up to 40 days postexposure	3
Coelenterates		
Sea anemone, *Anthopleura xanthogrammica*; 0.2 Gy, acute single exposure	Tentacles withdrawn	1
Jellyfish, *Aurelia aurita*; acute single exposure		
50-150 Gy	No deaths in 60 days	4
50-400 Gy	Dose-dependent increase in developmental abnormalities and abnormal budding rates and patterns	4
100 Gy	Metamorphosis and budding inhibited; reduction in pulsation rate	4
150 Gy	Inhibited reproduction	4
200 Gy	60% died in 60 days	4
400 Gy	90% died in 30 days	4
Molluscs		
Water snail, *Physa heterostropha*; exposure of 2.4-5.5 Gy daily for 1 year	Increased growth rate	1
Various species, acute single exposure		
50-200 Gy	LD50, up to 2 years postexposure	3
100-500 Gy	LD100, up to 2 years postexposure	3
Crustaceans		
Brine Shrimp, *Artemia salina*; acute single exposure		
0.004 Gy	No adverse effects on development of cysts	5
0. 1-9 Gy	Decreased development when exposed as cysts	5
4.5-9 Gy	LD50, nauplii, 20-25 days postexposure	6
130 Gy	LD50, adults, 25 days after exposure	6
486-2,084 Gy	Dose-dependent delay in development of eggs	7
3,000 Gy	LD50, cysts	5
Blue crab, *Callinectes sapidus*; continuous exposure to 0.76 Gy daily for 1 year	Increased growth rate	1
Shore crab, *Carcinus maenus*		
Americium-241, dose unknown	After 8 days, bioconcentration factors (BCF) were 145 in whole crab, 960 in gills, and 240 in exoskeleton; 50% elimination in 45 days	8
Plutonium-237, dose unknown	After 8 days, BCF values were	8

Table 21. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
	75 in whole crab, 340 in gills, and 70 in exoskeleton; 50% elimination in 55 days	
Daphnid, *Daphnia pulex*; daily exposure to 8.2-17.8 Gy for 1 year	Increased growth rate	1
Various species, single acute exposure		
5-900 Gy	LD50, up to 80 days postexposure	3
50-800 Gy	LD100, up to 80 days postexposure	3
Annelids		
Polychaete, *Neanthes arenaceodentata*; acute single exposure		
1-4 Gy	Adverse effects on reproduction	9
2-100 Gy	Significant increase in frequency of chromosomal aberrations	9
>100 Gy	Decreased life span	9
>500 Gy	Death	9
Fishes		
Common carp, *Cyprinus carpio*		
Adults, 3 Gy, acute single exposure	No effect on growth	1
Fertilized eggs, exposed through hatch		
144 million Bq ^{238}Pu/L	Increased abnormalities	10
277 million Bq ^{238}Pu/L	Decreased hatch	10
44 million Bq ^{232}U/L	Increased abnormalities	10
815 million Bq ^{232}U/L	Decreased hatch	10
Anchovy, *Engraulis* sp.; fertilized eggs, ^{90}Sr-^{90}Y, continuous exposure		
7.4 Bq/L	Increased developmental abnormalities	10
740 Bq/L	Decreased hatch, retarded growth rate	10
Fishes, various species, acute single exposure		
6-30 Gy	LD50, up to 460 days postexposure	3
3.7-200 Gy	LD100, up to 460 days postexposure	3
Pinfish, *Lagodon rhomboides*; exposure to 0.197 Gy daily for 1 year	Increased growth rate	1
Bluegill, *Lepomis macrochirus*; acute single exposure of 10, 20, or 30 Gy	At 20 and 30 Gy, serum proteins were reduced more than 50% within 24 h; damage to the GI capillary system and injury to the gastroepithelium accounted for the excessive protein loss	12
Marine teleosts, 6 species,	LD50	11

Table 21. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
10-55 Gy, acute single exposure		
Silver salmon, *Oncorhynchus kisutch*; acute single exposure		
Early embryonic stages, 0.3-0.6 Gy	LD50 at hatch	13
Later embryonic stages, 9.2-18.7 Gy	LD50 at hatch	13
Rainbow trout, *Oncorhynchus mykiss*		
Embryos, acute single exposure		
0.6 Gy, 1-cell stage	LD50 by end of yolk resorption	10
0.8 Gy, 1-cell stage	LD50 at hatch	3
3.1 Gy, 32-cell stage	LD50 by end of yolk resorption	10
4.1 Gy, early eyed stage	LD50 by end of yolk resorption	3
4.6 Gy, 32-cell stage	LD50 by hatch	3
9.0 Gy, late eyed stage	LD50 by end of yolk resorption	3
Embryos held in water containing 370 million Bq/L of ^{3}H from immediately after fertilization through hatching	No effect on hatching abnormalities	10
Embryos held in water containing 37 million Bq/L of ^{3}H from 6 h after fertilization through hatch	Suppressed immune response of fry	10
Immatures, single acute exposure of 0.2 Gy	Growth stimulation	1
Juveniles exposed for 27 days to radioneptunium isotopes and analyzed 2-15 days postexposure	Maximum BCF values were 8.7 for whole fish, 1.1 for skin, and 0.34 for muscle	14
Yearlings, force-fed 185,000, 1.85 million, or 18.5 million Bq ^{90}Sr-^{90}Y/kg BW daily for 21 weeks	At highest dose, adverse effects on growth (week 12) and survival (week 15); survivors had leucopenia and gut histopathology, and concentrations of 9.2 billion Bq/kg FW in bone and 9.99 million Bq/kg FW in muscle. Residues in the 1.85 million group were 1.04 billion Bq/kg in bone and 2.96 million Bq/kg in muscle. For the 185,000 group, these values were 77.7 million Bq/kg in bone and 74,000 Bq/kg in muscle	11,15
Yearlings force-fed 370,000, 3.7 million, or 37 million Bq ^{65}Zn/kg BW daily for 17 weeks, or 370 million Bq ^{65}Zn/kg BW daily	Adverse effects on growth, survival, or gut histology at any dose; leucopenia evident at week 10 at the highest dose. Residues, in Bq/kg FW,	11,15

Table 21. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
for 10 weeks	in the 37 million group at 17 weeks were 148 million in bone and 12.9 million in muscle	
Yearlings force-fed 222,000, 2.2 million, or 22.2 million Bq ^{32}P/kg BW daily for as long as 25 weeks	At highest dose tested, adverse effects on growth, survival, and gut histology between day 17 and 77. In the intermediate 2.2 million group, adverse effects on growth at 17 weeks; residues (Bq/kg FW) were 66.6 million in bone and 8.5 million in muscle. The 220,000 group had no adverse effects in 25 weeks on growth, survival, or tissue alterations	11
Gametes of adults, single acute exposure of 0.5-1.0 Gy	50% reduction in fecundity	3
Adults, single acute exposure of 15 Gy	LD50	3
Chinook salmon, *Oncorhynchus tshawytscha*		
0.0004 Gy/h, eggs, 81-day exposure, total dose of 0.78 Gy	Significant adverse effects on survival and development	21
0.005 Gy daily, continuous exposure from egg fertilization through yolk sac absorption; total dose of 0.35 Gy	No adverse effects on growth and survival or on numbers of returning adults after seaward migration	22
0.028 Gy daily, continuous exposure from egg fertilization through yolk sac absorption; total dose of 1.99 Gy	No adverse effects observed prior to seaward migration	22
0.2 Gy, single acute exposure	Growth increase	1
10 Gy, eyed eggs, single acute exposure	LD50	3
12.5-25 Gy, fingerlings, single acute exposure	LD50	3
Medaka, *Oryzias latipes*; adult males receiving single acute exposure of 0.64,4.75, or 9.5 Gy	Dose-dependent increase in total mutations in sperm, spermatids, and spermatogonia	16
Sea lamprey, *Petromyzon marinus*; males captured during spawning run, single acute exposure		
20 Gy	LD50, 45 days postexposure; survivors sterile	17

Table 21. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
30 Gy	All died before spawning,	17
Fathead minnow, *Pimephales promelas*; developing eggs, continuous exposure		
4,440 Bq ^{144}Ce-^{144}Pr/L	No effect on embryonic development or hatch	10
9.6 million Bq ^{238}Pu/L	Increased abnormalities	10
48.1 million Bq ^{238}Pu/L	Decreased hatch	10
7.4 million Bq ^{232}U/L	Increased abnormalities	10
18.5 million Bq ^{232}U/L	Decreased hatch	10
Atlantic salmon, *Salmo salar*; fertilized eggs, continuous immersion in 92.5 Bq ^{137}Cs/L or 185 Bq ^{90}Sr/L	Increased mortality of embryos and fry	10
Brown trout, *Salmo trutta*		
Fertilized eggs continuously immersed in water containing 3.7 million Bq/L of ^{90}Sr-^{90}Y through hatch	No effect on hatch or developmental abnormalities	10
Juveniles held in water containing 30,000 Bq ^{110m}Ag/L for 57 days, then transferred to uncontaminated media for 28 days	At day 57, whole trout contained 105,000 Bq ^{110m}Ag/kg FW; about 70% was in liver. No detectable radioactivity after depuration for 28 days	18
Juveniles fed diet containing 3,343,000 Bq ^{110m}Ag/kg for 1 week (5 times weekly), then 269,000-296,000 Bq ^{110m}Ag/kg diet between weeks 2 and 5. Depuration for 28 days	At end of exposure, whole trout contained 27,400 Bq ^{110m}Ag/kg, equivalent to 11.7% of ingested radioactivity; liver accounted for 63%. No detectable radioactivity after depuration for 28 days	19
Integrated study		
Artificial stream simulating outfall from Czechoslovakian nuclear power plant, 28-day exposure, strontium-90		
Water	894 Bq/L	20
Sediments	1,589-2,288 Bq/kg FW	20
Alga, *Cladophora glomerate*	Max. 22,106 Bq/kg FW	20
Snail, *Planorbis corneus*, shell vs. soft parts	760,588 Bq/kg FW vs. 27,468 Bq/kg FW	20
Common carp, *Cyprinus carpio*		
Bone	29,144 Bq/kg FW	20
Muscle	580 Bq/kg FW	20

Table 21. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
Scales	13,101 Bq/kg FW	20
Uncontaminated site		
Water	0.002-0.005 Bq/L	20
Common carp, internal organs vs. scales	0.1-0.5 Bq/kg FW vs. 1.5-9.3 Bq/kg FW	20

[a] l, Rose 1992; 2, Havlik and Robertson 1971; 3, Donaldson and Foster 1957; 4, Prokopchak et al. 1990; 5, Gaubin et al. 1990; 6, Engel and Davis 1976; 7, Su et al. 1990; 8, Guary and Fowler 1990; 9, S. L. Anderson et al. 1990; 10, Whicker and Schultz 1982b; 11, Templeton et al. 1971; 12, Ulrickson 1971; 13, Bonham and Welander 1963; 14, Poston et al. 1990; 15, IAEA 1976; 16, Shima and Shimada 1991; 17, Hanson 1990; 18, Garnier et al. 1990; 19, Garnier and Baudin 1990; 20, Stanek et al. 1990; 21, National Council on Radiation Protection and Measurements (NCRP) 1991; 22, Donaldson and Bonham 1970.

Adverse effects on the fecundity of sensitive aquatic vertebrates were detected at dose rates as low as 0.4 mGy/h; adverse effects on fecundity were measured only at dose rates of greater than 1.0 mGy/h. Thus, deleterious effects in populations of aquatic vertebrates are probably not detected until the 0.4-1.0 mGy/h dose rate is exceeded (NCRP 1991). Organisms such as estuarine organisms that are exposed to variable physicochemical conditions are more radioresistant than those in buffered environments, and this may be due to a higher degree of genetic polymorphism in species of fluctuating environments (IAEA 1976). Estimated dose effects from the induction of chromosomal aberrations in polychaete annelid worms were dependent on cell stage at time of irradiation (S.L. Anderson et al. 1990). For reproduction, the estimated dose effects were dependent on the potential regeneration of gonadal tissue (S.L. Anderson et al. 1990). Radiation causes dominant lethal mutations in the medaka (*Oryzias latipes*; Shima and Shimada 1991). Ionizing radiation at low-level chronic exposure reportedly has no deleterious genetic effects on aquatic populations because exposure is compensated by density-dependent responses in fecundity (IAEA 1976); however, this needs verification.

Accumulation of radionuclides from water by aquatic organisms varies substantially with ecosystem, radionuclide, and trophic level (Tables 22-24); with numerous biological, chemical, and physical variables; and with proximity to sources of radiation (Bowen et al. 1971; Lowman et al. 1971; Templeton et al. 1971; Mo and Lowman 1976; Shure and Gottschalk 1976; Whicker and Schultz 1982b; Becker 1990; Poston et al. 1990; Joshi 1991). Accumulated radionuclides inside embryos of the scorpionfish (*Scorpaena porcus*) and the turbot (*Scopthalmus maeoticus maeoticus*) increased the frequency of nuclear disruptions in these species; ^{90}Sr-^{90}Y and ^{91}Y had greater cytogenetic effects than other tested radionuclides (Polikarpov 1973). In the absence of site-specific data, the U.S. Nuclear Regulatory Commission recommends the use of listed concentration ratios--the concentration of the element in the organism (in mg/kg FW) divided by the concentration in the medium (in mg/L)—for various elements in marine and freshwater fishes and invertebrates (Whicker and Schultz 1982b). However, the commission clearly indicates that these values are only approximations.

Table 22. Concentration factors[a] for cesium-137 and strontium-90 in aquatic organisms (Whicker and Schultz 1982a).

Radionuclide and ecosystem	Molluscs, whole	Crustaceans, whole	Fishes, muscle
Cesium-137			
Freshwater	600	4,000	3,000
Marine	8	23	15
Strontium-90			
Freshwater	600	200	200
Marine	1	3	0.1

[a] Bq per gram fresh weight sample/Bq per mL medium.

Table 23. Maximum concentration factors[a] reported for selected elements in marine organisms at various trophic levels (Bowen et al. 1971).

Element	Algae	Grazers	Predators
Ag	1,000	20,000	3,000
Cd	6,000	2,000,000	10,000
Ce	4,500	300	12
Co	1,000	10,000	50,000
Cr	600	300,000	3,900
Cs	50	15	10
Fe	70,000	300,000	30,000
I	7,000	70	10
Mo	200	175	200
Mn	20,000	60,000	100,000
Ni	1,000	10,000	80
Pb	3,000,000	2,000,000	200,000
Ru	1,000	16	10
Sr	90	85	5
Ti	30,000	20,000	3,000
Zn	3,000	100,000	20,000
Zr	20,000	30,000	40,000

[a] Bq per gram fresh weight tissue/ Bq per mL seawater.

Table 24. Approximate maximum concentration factors[a] for selected transuranics in marine sediments, macroalgae, and fishes (Morse and Choppin 1991).

	Concentration factor		
Transuranic nuclide	Sediments	Macroalgae	Fish
Neptunium	1,000	5,000	10
Plutonium	100,000	2,000	40
Americium, curium, berkelium, californium	2,000,000	8,000	50

[a] Bq per gram fresh weight sample/Bq per mL water.

After more than 400 atmospheric nuclear test explosions and the fallout from Chernobyl, ^{137}Cs became the most frequently released nuclear fission product throughout central Europe (Jandl et al. 1991). Cesium behaves like potassium; it has a ubiquitous distribution inside the body, especially in soft tissues. In the common snail *Helix pomatia*, the biological half-time after a single 24-h dietary dose was 2.5 days by the short-lived component and 28.5 days by the long-lived component (Jandl et al. 1991). Concentration factors (CF) of ^{137}Cs in muscle (ratio of Bq/kg FW muscle:Bq/L filtered seawater) of marine fishes from the North Sea between 1978 and 1985 ranged from a low of 39 in the plaice (*Pleuronectes platessa*) to a high of 150 in the whiting (*Merlangius merlangius*); CF values were intermediate in the haddock (*Merlanogrammus aeglifinus*; CF of 58) and in the Atlantic cod (*Gadus morhua*; CF of 92). These data seem to support the use of a CF of 100 for ^{137}Cs in muscle of marine fishes in generalized assessments, although some adjustment is necessary when particular species, such as whiting, form the bulk of a consumer's diet (Steele 1990). In the Great Lakes, the maximum CF values of ^{137}Cs range from 1,000 to 10,000 in algae, amphipods, and fishes and from 100 to 1,000 in zooplankton (Joshi 1991). Maximum concentration factors of ^{137}Cs in a contaminated creek in South Carolina were 4,243 in suspended particulates, 938 in detritus, 4,496 in algae and macrophytes, 997 in omnivores, 1,292 in primary carnivores, and 1,334 to 2,595 in top carnivores such as the redbreast sunfish (*Lepomis auritis*), largemouth bass (Mi*cropterus salmoides*), and water snakes (*Natrix* spp.; Shure and Gottschalk 1976). Cesium

uptake by oligochaete worms (*Limnodrilus hoffmeisteri*) *is* inhibited by low temperatures, potassium concentrations of greater than 1 mg/L and the presence of bacteria (*Escherichia coli*) that compete with the worms for ^{137}Cs (Steger and Goodnight 1976).

Atmospheric fallout from nuclear testing is the main pathway by which transuranic nuclides such as Np, Pu, Cm, and Am enter the aquatic environment (Guary and Fowler 1990). In general, transuranics are strongly partitioned onto particulates. Living organisms are less enriched than particulate matter by as much as 1,000 times, and concentration factors by marine biota are similar for transuranics beyond neptunium (Morse and Choppin 1991). The uptake of ^{241}Am and ^{244}Cm from contaminated sediments by a freshwater amphipod (*Hyalella* sp.) and oligochaete (*Tubifex* sp.) is reported, presumably by way of adsorption, and this is considered the principal uptake pathway by benthic organisms in freshwater and in marine ecosystems (Sibley and Stohr 1990). Transuranics that were ingested with food by various crabs were initially excreted with feces; the remaining transuranics entered a soluble radionuclide pool inside the animal that was slowly excreted. Decapod crustaceans assimilate and retain 10-40% of the tranuranic nuclides in their diets. Initially, absorbed radionuclides accumulate in the hepatopancreas but are then translocated to other tissues, particularly to tissues of the exoskeleton; accordingly, molting strongly influences elimination in crustaceans (Guary and Fowler 1990). Neptunium isotopes have a higher potential for environmental transport in aquatic systems and in groundwater than other tested actinides. Laboratory studies with ^{235}Np and ^{237}Np, for example, showed concentration factors between 275 and 973 in a green alga (*Selenastrum capricornutum*), 32 and 72 in a daphnid (*Daphnia magna*), 2 in an amphipod (*Gammarus* sp.) and in juvenile rainbow trout, 8.7 in carcass, 1.1 in skin, and 0.3 in muscle during a 96-h period (Poston et al. 1990). When the much higher biological effectiveness of alpha than of beta or gamma radiation is considered, plutonium isotopes may contribute more artificial radiation dose equivalent to marine invertebrates than either ^{90}Sr or ^{137}Cs. Concentration factors of ^{239}Pu and marine organisms ranged from 300 to 100,000 in seaweeds, 250 to 690 in molluscs, 760 to 1,020 in echinoderms, 2,100 in sponges, and as much as 4,100 in worms (Noshkin et al. 1971). Concentration factors of $^{239+240}Pu$ in Lake Michigan were between 1 and 10 in predatory salmonids, 10 and 300 in nonpredatory fishes, 900 and 1,200 in amphipods and shrimp, about 200 in zooplankton, and about 6,000 in algae (Joshi 1991).

Iodine-131 (half-life of 8 days) may cause deleterious effects in marine teleosts--although ^{131}I concentrations in tissues were not detectable. In one case, coral reef fishes from Eniwetok Atoll collected as long as 8 months after a nuclear explosion had thyroid necroalteration, suggesting a thryotoxic level of ^{131}I in the environment. Laboratory studies with teleosts injected with ^{131}I showed similar signs of histopathology. Herbivorous fishes and species that habitually consumed bivalve molluscs were most severely affected (Gorbman and James 1963).

Strontium-90 is an anthropogenic radionuclide in liquid effluents from some European nuclear power plants. Algae and sediments are the most important accumulators of ^{90}Sr, although levels in gastropods and fish bone and scales are also elevated, suggesting piscine uptake through gills and skin (Stanek et al. 1990). Fishes tend to accumulate calcium more than strontium, even when Ca levels in food and water were low. Gill tissue was the most and gut the least discriminatory against Sr. Strontium assimilation was linked to the Sr:Ca ratio in food and water, amounts of Ca derived from each source, and biological discrimination against Sr relative to Ca (Ophel and Judd 1976). The ability of organisms to discriminate between strontium radioisotopes is also documented. In one case, ^{85}Sr was taken up rapidly in bluegill (*Lepomis macrochirus*) muscle and blood and quickly exchanged with stable strontium; however, ^{90}Sr was retained longer than 35 days in these tissues (Reed and Nelson 1969).

Ruthenium-106 appeared in clams from North Carolina within 2 weeks after the third and fifth Chinese nuclear tests in 1965-67. Its retention was resolved into two rate functions with apparent effective half-lives of 40 days and 7 days (Wolfe and Jennings 1971). Iron-55 is a neutron-activation product produced in large quantities from ferrous materials in the immediate vicinity of a nuclear detonation. Concentration factors of ^{55}Fe and plankton in Bikini Atoll ranged from 15,000 to 25,000 (Schell 1976). Silver-110m has been detected in marine organisms after atmospheric weapon tests in the Pacific, in fishes from the Rhone River after the Chernobyl

accident, and in fishes near reactor-waste outfalls (Gamier et al. 1990). Silver-110m is depurated rapidly by brown trout (*Salmo trutta*) after high intake exposures in the water or diet (Gamier et al. 1990; Gamier and Baudin 1990). Radiotungsten is produced in quantity by certain types of nuclear devices. In one case tungsten was the most abundant radionuclide in the environment, accounting for about 90% of the total fallout activity 167 days after the detonation (Reed and Martinedes 1971). Tungsten-181 tended to concentrate in the hepatopancreas and gut of the crayfish (*Cambarus longulus longerostris*); whole body elimination consisted of two components: a rapid 1-day component and a second slower component with a biological half-time of 12.2 days (Reed and Martinedes 1971). Benthic organisms take up limited amounts of heavy metals and radionuclides from bottom sediments and recycle them to benthic and pelagic food webs. For example, polychaete worms (*Nereis diversicolor*) in contact with ^{65}Zn-contaminated sediments for 5 days lost 50% of accumulated ^{65}Zn in about 19 days on transfer to uncontaminated sediments (Renfro and Benayoun 1976).

Amphibians and Reptiles

Radiation adversely affects limb regeneration of amphibians, alters DNA metabolism, and increases the frequency of chromosomal aberrations and liver lesions (Table 25). In some species of amphibians and reptiles as in many mammals, mortality rates after acute exposure to radiation do not stabilize within 30 days--effectively invalidating the conventional LD50 (30-day postexposure) value. In the rough-skinned newt (*Taricha granulosa*), for example, the minimal LD50 dose was 2.5 Gy at 200 days after irradiation but 350 Gy at 30 days (Willis and Lappenbusch 1976). Low temperatures seem to prolong the survival of amphibians that are exposed to ionizing radiation. The survival was greater of leopard frogs (*Rana pipiens*) held at low temperatures (5-6° C) after total-body exposure to lethal doses of X-rays than of frogs held at higher temperatures. Prolonged survival at low temperatures was due to a prolongation of the latent period rather than to appreciable recovery (Patt and Swift 1948).

Table 25. Radiation effects on selected amphibians and reptiles.

Table 25. Species, dose, and other variables	Effect	Reference[a]
Leopard lizard, *Crotaphytus wislizenii*; chronic field exposure of 0.04-0.06 Gy daily (4-5 Sv yearly) for 3 to 6 years	No female reproduction in years 3 and 4. In year 5, males were sterile and females had complete regression of ovaries, undeveloped oviducal walls, and hypertrophied fat bodies. In year 6, 75% of females lacked ovaries and 25% had normal ovaries with signs of recent egg deposition; males appeared normal	1
Mud puppy, *Necturus maculosus*; 1.1 Gy, single acute exposure	LD50, 30 days postexposure	2
Salamander, *Necturus sp*.; 0.8 Gy, single acute exposure	LD50, 200 days postexposure	3
Eastern newt, *Notophthalmus viridescens*; adults, single acute exposure of 20Gy, one limb shielded; or 22 Gy, whole body, no limbs shielded	Forelimb regeneration completely suppressed when limbs to be amputated were irradiated directly. Irradiated limbs had severe and protracted inflammation, with total resorption of the affected limbs in 85% of the cases. Shielded limbs subsequently amputated had	4

Table 25. Species, dose, and other variables	Effect	Reference[a]
	delays-but not suppression-in rate of forelimb regeneration and skin graft rejection	
Frog, *Rana sp*., single acute exposure		
7.0-7.2 Gy	LD50, 730 days after exposure	3
7.8 Gy	LD50, 150 days after exposure	3
Snakes, 2 species, 3 to 4 Gy, single acute exposure	LD50, 90 days after exposure	3
Rough-skinned newt, *Taricha granulosa*; single acute exposure		
2.5 Gy	LD50, 200 days after exposure; skin lesions and depigmentation	5
>6.5 Gy	Progressive anemia over 6-week postirradiation period; reduction in erythrocyte numbers and weight of spleen	5
80 Gy	LD50, 100 days after exposure	5
350 Gy	LD50, 30 days after exposure	5
Turtles, 4 species, <8 to 15 Sv, single acute exposure	LD50, 120 days postexposure	3
Common slider, *Trachemys scripta*; inhabiting a radioactive reservoir, in Aiken, South Carolina. Radionuclide concentrations, in Bq/kg, whole body fresh weight, (FW) were 1,002 for ^{137}Cs and 550 for ^{90}Sr. For controls, these values were 2 for ^{137}Cs and 260 for ^{90}Sr	Contaminated turtles, when compared with controls, had greater variation in DNA content of red blood cell nuclei, suggesting genetic damage. The biological half-life of ^{137}Cs in soft tissues was 64 days; for ^{90}Sr in shell and bone, it was 364 days	6
Spiny tailed lizard, *Urornastix hardwickii*; single acute exposure, held for up to 14 days after irradiation		
2.25 Gy	No lesions in liver	7
4.5 Gy	No liver lesions, but swollen hepatocytes, increases in bile pigmentation, and altered cytoplasmic degranulation; normal after 14 days	7
9.0 Gy	Some liver lesions, but all livers normal 14 days postexposure	7
Side-blotched lizard, *Uta stansburiana*; 10-22 Gy, single acute exposure	LD50, 30 days postexposure	3

[a] 1,Turner et al. 1971; 2, Rose 1992; 3, Hinton and Scott 1990; 4, Sicard and Lombard 1990; 5, Willis and Lappenbusch 1976; 6, Lamb et al. 1991; 7, Gupta and Umadevi 1990.

The South African clawed frog (*Xenopus laevis*) was a suggested bioindicator of radioactive contamination because of the greater radiosensitivity of amphibians than fishes, the ease of maintaining *Xenopus* in the laboratory, and the sensitivity of the *Xenopus* liver to radioactive contamination--including ^{45}Ca, which does not accumulate in the liver (Giannetti et al. 1990). *Xenopus* oocytes exposed to X-rays showed single- and double-strand breaks in DNA and oxidative-type base lesions at a frequency between 85% and 95%. *Xenopus* oocytes repaired X-ray induced damage in plasmid DNA; however, some X-ray lesions can stimulate homologous recombination in these cells (Sweigert and Carroll 1990). Common slider turtles (*Trachemys scripta*) in a radioactive reservoir show evidence of genetic damage, and this was attributed to long-term exposure of low concentrations of long-lived radionuclides, including ^{137}Cs and ^{90}Sr (Lamb et al. 1991). Natural populations of gulf coast toads (*Bufo valliceps*) reportedly can survive genetically damaging doses of ionizing radiation without impairment of population integrity (Whicker and Schultz 1982b). Toads and many other species share a high attrition on the large numbers of young produced each generation, and this provides an agency for intensive selection. Also under this regime, recessive mutants are eliminated as they are exposed through inbreeding in future generations (Whicker and Schultz 1982b). Sterility in field collections of the leopard lizard (*Crotaphytus wislizenii*) and the western whiptail lizard (*Cnemidophorus tigris*) was reported after long-term exposure of 3 to 5 years to various doses of gamma radiation, that is, 4-5 Sv annually in *Crotaphytus* and 2.0-2.5 Sv annually in *Cnemidophorus* (Turner et al. 1971). However, a third species of lizard in the study area (side-blotched lizard, *Uta stansburiana*) reproduced normally (Turner et al. 1971).

The retention of selected isotopes by amphibians and reptiles is quite variable. For example, whole-body retention of ^{131}I after intraperitoneal injection in the rough-skinned newt showed 2 distinct loss components with biological half-lives of 2 and 210 days; the slower component accounted for 26% of the administered activity; thyroid contained 78% of the total ^{131}I and clearly accounted for the long-term component (Willis and Valett 1971). However, similar studies with ^{131}I and the leopard frog showed three distinct loss components (0.1 day; 1.4-2.9 days; 44.3-69.4 days); loss of each component was greater at 25° C than at 10° C; also, the fast component probably represented plasma clearance through urinary excretion (Willis and Valett 1971).

Birds

Among birds, as in most other tested species, there is a direct relation between dose and mortality at single high doses of ionizing radiations (Whicker and Schultz 1982b; Table 26). For any given total dose, the survival of a bird is higher if the dose is delivered at a lower rate or over a longer period of time and suggests that biological repair processes compensate for radiation-induced cellular and tissue damage over a prolonged period or at a comparatively low dose rate (Brisbin 1991). Nestling bluebirds (*Sialia sialis*) were more resistant to gamma radiation than young domestic chickens (*Gallus* sp.), and nestling greatcrested flycatchers (*Myiarchus crinitus*) were more sensitive than bluebirds (Willard 1963). Passerine nestlings are more resistant to radiation stress than adults of larger-bodied precocial species (Brisbin 1991). But the comparatively resistant passerine nestlings frequently show a disproportional disturbance in radiation-induced growth, resulting in a reduction of overall survival. For example, if feather growth is stunted, death results from the inability to escape predators because of impaired flight (Brisbin 1991).

Table 26. Radiation effects on selected birds.

Table 26. Species, dose, and other variables	Effect	Reference[a]
Green-winged teal, *Anas carolinensis*; 4.8 Gy, single acute exposure	LD50, 30 days postexposure	1
Northern shoveler, *Anas clypeata*; 8.9 Gy, single acute exposure	LD50, 30 days postexposure	1
Blue-winged teal, *Anas discors*; 7.2 Gy, single acute exposure	LD50, 30 days postexposure	1

Table 26. Species, dose, and other variables	Effect	Reference[a]
Birds		
Eggs, passerine species, single acute exposure, 5-10 Gy	LD100	2
Nestlings, various species, 1 Gy daily	Growth retardation	3
Common quail, *Coturnix coturnix*; fertilized eggs, exposed first 9 days of incubation, single acute exposure		
5 Gy	Negligible effect on survival	4
7 Gy	Mortality >50%	4
9 Gy	All dead before hatch	4
Domestic chicken, *Gallus sp*.		
Single acute exposure		
Eggs of broilers exposed to 0.05-2.1 Gy before incubation	No adverse effects on embryonic development at 1.6 Gy and lower; at 2.1 Gy, adverse effects on development, survival, and body weight of hatched chicks	5
Chicks, age 15 days		
2.1 Gy	Reversible changes in blood chemistry within 60 days; no deaths	6
6.6 Gy	Irreversible and permanent damage to red blood cells, hemoglobin, and hematocrit; all dead within 7 days	6
Dietary exposure		
Laying hens fed diet containing 400 Bq ^{137}Cs/kg ration for 4 weeks	Of total ^{137}Cs ingested, 3% was distributed in egg contents (29-33 Bq/kg egg; 2 Bq egg); 9% in muscle (171 Bq/kg FW); and 81% in excreta	7
Broiler chickens fed diets containing 400 Bq ^{137}Cs/kg ration for 40 days; some diets contained up to 5% bentonite	Feeding with bentonite reduced ^{137}Cs concentration in muscle by 32% from 155 to 105 Bq/kg FW	7
Common black-headed gull, *Larus ridibundus ridibundus*; eggs, 9.6 Gy over 20 days	LD50	3
Great crested flycatcher, *Myiarchus crinitus*; nestlings, single acute exposure >8 Gy	All dead by fledging	8
Eastern bluebird, *Sialia sialis*, single acute exposure		
Nestlings, age 2 days		
3 Gy	Reduced growth after 16 days	8
3-5 Gy	Reduced growth and shorter primary feathers at fledging	8
4-12 Gy	Developed normally and	2

Table 26. Species, dose, and other variables	Effect	Reference[a]
	fledged successfully	
5-6 Gy	LD50, nestling to fledgling	8
25 Gy	LD50, 16 days postexposure	8
30 Gy	All dead 4 days postexposure	2,8
Fertilized eggs, 6 Gy	All dead before hatch	2
European starling, *Sturnus vulgaris*; >2 Gy, single exposure	Fatal	9
Tree swallow, *Tachycineta bicolor*		
0.006 mGy/h during breeding season, equivalent to annual dose of about 50 mSv	No adverse effects on breeding performance of adults or growth performance of nestlings	10
0.9-4.5 Gy, single acute exposure, nestlings	Adverse effects on growth, survival or both	2
1.0 Gy daily, chronic	Reduced hatch, depressed growth	2
House wren, *Troglodytes aedon*; fledglings, 0.9 Gy, single acute exposure	Growth reduction	9

a 1, Hinton and Scott 1990; 2, Millard and Whicker 1990; 3, Lowe 1991; 4, Wetherbee 1966; 5, Zakaria 1991; 6, Malhotra et al. 1990; 7, Andersson et al. 1990; 8, Willard 1963; 9, Rose 1992; 10, Zach et al. 1993.

Free-living, resident bird populations in the vicinity of sites contaminated with low levels of ionizing radiations generally have negligible genotoxic effects (George et al. 1991). However, 14% of mallards (*Anas platyrhynchos*) from an abandoned South Carolina reactor cooling reservoir heavily contaminated with ^{137}Cs (mallards contained an average of 2,520 Bq ^{137}Cs/kg whole body FW) had abnormal chromosome numbers and unusual variability in the concentration of erythrocyte DNA (George et al. 1991). Contaminated waterfowl rapidly eliminate accumulated radionuclides, suggesting inconsequential long-term damage to the birds and little hazard to human consumers of waterfowl flesh (Halford et al. 1983). This conclusion was from a study of mallards that were held for 68 to 145 days on liquid radioactive waste ponds in southeastern Idaho before they were transferred to an uncontaminated environment for 51 days. The biological half-life in mallards under these conditions was 10 days at ^{131}I and ^{134}Cs, 11 days at ^{137}Cs, 22 days at ^{140}Ba, 26 days at ^{75}Se, 32 days at ^{58}Co, 67 days at ^{6O}Co and ^{65}Zn, and 86 days at ^{51}Cr. At the time of removal from the waste ponds, radionuclide concentrations were highest in gut, then in feather, liver, and muscle, in that order. After 51 days in a radionuclide-free environment, the decreasing order of radionuclide concentrations was feather, liver, muscle, and gut (Halford et al. 1983).

Zinc-65 in trace amounts is accumulated by migratory waterfowl in the Pacific Flyway of North America from ^{65}Zn discharged into the Columbia River from water-cooled reactors at Hanford, Washington (Curnow 1971). The retention of ^{65}Zn in mallards was affected by sex and season but not by the age of the duck. Biological retention of ^{65}Zn was greater in males (Tb½ of 34.7 days) than in females (29.8 days) and greater in October (38 days) than in spring (32 days). Egg production accounted for the elimination of 25% of the ^{65}Zn and feather molt of 2-8% (Curnow 1971). Retention of ^{60}Co and ^{137}Cs--but not ^{109}Cd--in the Northern bobwhite (*Colinus virginianus*) after either acute or chronic exposure to contaminated food is similar. The biological half-life in bobwhites during exposure for 21 days was 8 days at ^{109}Cd, 11 days at ^{137}Cs, and 13 days at ^{60}Co. When radioisotopes were administered during a single 4-h feeding, Tb½ values were 3 days at ^{109}Cd, 10 days at ^{137}Cs, and 15 days at ^{60}Co (Anderson et al. 1976). The biological half-life of ^{137}Cs in avian tissues is about 6.0 days in the domestic chicken (Andersson et al. 1990), 6.7 days in the blue jay (*Cyanocitta cristata*); Levy et al. 1976), 5.6 days in the American wood duck (*Aix sponsa*) and 11.7 days in the mallard (Cadwell et al. 1979). Domestic poultry seem to accumulate a higher fraction of the daily ingested ^{137}Cs/kg muscle than mammals, but levels were effectively reduced by feeding an uncontaminated ration for at least 10 days prior to slaughter

(Andersson et al. 1990).

Mammals

The mammalian sensitivity to acute and chronic exposures of ionizing radiation, ability to retain selected radionuclides, and effect of biological and abiotic variables on these parameters are briefly summarized in Table 27. These data clearly indicate a dose-dependent effect of radiation on growth, survival, organ development, mutagenicity, fatal neoplasms, kidney failure, skeletal development, behavior, and all other investigated parameters. In general, fetuses and embryos were most sensitive to ionizing radiation, and acute or chronic exposures between 0.011 and 0.022 Gy were demonstrably harmful to mice, rats, and guinea pigs.

Table 27. Radiation effects on selected mammals.

Table 27. Species, dose, and other variables	Effect	Reference[a]
Short-tailed shrew, *Blarina brevicauda*; 7.8 Gy, single acute exposure	LD50, 30 days postexposure	1
Cow, *Bos sp*.		
Oral intake of 0.89 Bq ^{129}I, whole animal	Thyroid contained 0.97 Bq ^{129}I/kg fresh weight (FW) vs. <0.0012 Bq/kg FW for all other tissues	2
Fed 6.4 Bq ^{129}I daily for 8 days	After 8 days, 22% of total dose of 51.2 Bq was in thyroid; after 63 days, thyroid contained 1 Bq/kg FW and other tissues <0.01 Bq/kg FW	3
Dog, *Canis familiaris*		
Beagle embryos age 55 days, or pups 2 days old, given single acute exposure of 0.16, 0.83, or 1.25 Gy	Dose-dependent increase in immature dysplastic glomeruli and other signs of progressive renal failure	4
Beagles, prenatal and early neonatal stages, given single acute dose of 0.2-1.0 Gy, then observed over 11-year life span	Irradiation at all ages was associated with increased risk: decreased fertility; inhibited growth and development; lower brain weight; and increase in fatal neoplasms	5
Beagle embryos or pups As above, 2.24-3.57 Gy	Reduction in total number of nephrons and progressive renal failure	4
Beagles, 17-20 months old, single intravenous injection of 200-440,000 Bq ^{226}Ra/kg body weight (BW)	Dose-dependent increase in skeletal malignancies in 36% of dogs during lifetime	6
Beagles, age 5 years, given single injection of ^{226}Ra, in Bq/kg BW, of 39,000, 116,000, or 329,000. Injected ^{226}Ra solutions also contained ^{210}Po, ^{210}Pb, and ^{210}Bi	At lowest dose of 39 kBq/kg BW, kidney was normal, death after 2,032 days. At intermediate dose, death in 1, 210 days; at high dose, death in 581 days. Tubular degeneration and necrosis of kidney at 116 and 329 kBq	7
Beagles, age 7 years, single	No kidney damage with ^{226}Ra, but	7

Table 27. Species, dose, and other variables	Effect	Reference[a]
injection of ^{226}Ra (no contaminating ^{210}Po, ^{210}Pb, or ^{210}Bi) at 45,000 Bq/kg BW, or 122,000 Bq ^{210}Po/kg BW	kidney damage with ^{210}Po	
Beagles, age 7 years given single injection of 1,629,000 Bq ^{226}Ra/kg BW, equivalent to 1.89 Gy (from ^{210}Po contaminants), or 4,831,000 Bq ^{226}Ra/kg BW = 5.15 Gy from ^{210}Po	At low dose, all dead after 516 days; at high dose, all dead in 266 days. Death was from renal failure	7
Guinea pig, *Cavia* sp.; chronically irradiated daily during 8-h exposure. Daily dose, in Gy		
0.000	Mean survival time of 1,372 days	8
0.001	50% dead in 1,457 days	8
0.011	50% dead in 1,224 days	8
0.022	50% dead in 978 days; anemia	8
0.044	50% dead in 653 days; anemia	8
0.088	50% dead in 187 days; anemia	8
Monkey, *Cebus apella*; 1 Gy, whole body, single acute exposure	Leucocyte reduction in 6 days; blood chemistry normal after 90 days	9
Chinese hamster, *Cricetus* sp.; ovary cells, single acute dose ranging between 0.005 and 0.06 Gy	Increased frequency of sister chromatid exchange at 0.005 Gy; increased numbers of chromosomal aberrations at >0.02 Gy; no significant increase in cell death	10
Syrian hamster, *Cricetus* sp.; 0.12-2 Gy, single acute exposure	Genes modifying cytoskeletal development adversely affected at all doses within 3 h by both high LET (neutrons) and low LET (gamma rays, X-rays) radiations	11
Human, *Homo sapiens*		
Developing forebrain, 0.18-0.55 Gy (estimated dose to prenatally exposed Japanese atomic bomb survivors)	Seizures in childhood; reduced school performance at least through age 11 years; some cases of severe mental retardation by age 17 years	12
Fetus, 1 Sv, 8-15 weeks of gestation	40% probability of severe mental retardation; IQ score lowered 30 points	13
Sperm chromosomes, 0.23, 0.45, 0.91, or 1.82 Gy, single acute exposure	Chromosomal aberrations increased linearly from 6.1% at 0.23 Gy to 62% at 1.82 Gy	14
Thyroid, single acute exposure 0.065 Gy	Minimum dose for induction of thyroid carcinoma	15

Table 27. Species, dose, and other variables	Effect	Reference[a]
3-5 Gy	5% increase in thyroid malignancies 20 years after exposure, with tumors appearing 4-5 years after exposure	16
7-10 Gy	Linear dose relation to thyroid cancer, and pathology in adjacent parathyroid and salivary glands	16
Whole body		
Single brief exposure		
0.05-0.11 Sv	Doubles rate of cancers	17
0.15 Sv	Temporary sterility, males	13
0.18-0.29 Sv	Doubles rate of pregnancy complications	17
0.5-2.0 Sv	Opacity of lens; depression of hematopoiesis	13
0.68-1.10 Sv	Doubles rate of F1 generation mortality	17
1 Sv, adults	1% probability of hereditary effects; 4% probability of fatal cancer in occupational workers	13
2.5-6.0 Sv	Sterility, females	13
3.5-6.0 Sv	Permanent sterility, males	13
5.0 Sv	Cataracts	13
<1 Gy	Survival almost certain	18
1-2 Gy	Survival probable	18
1-2 Gy	About 5% mortality in several months from infection and hemorrhage	19
2-5 Gy	Survival possible	18
2-7.5 Gy	Hematopoietic syndrome characterized by bone marrow damage, anemia, lowered immune response, hemorrhage, and sometimes death	20
3-5 Gy	Death in 30-60 days, bone marrow damage	13
5-10 Gy	100% adversely affected within weeks with bone marrow abnormalities; about 45% mortality	19
5-15 Gy	Death in 10-20 days; GI tract and lung damage	13
5-20 Gy	Survival improbable	18
7.5-30 Gy	Gastrointestinal damage: nausea, vomiting, anorexia, diarrhea, lethargy, weight loss, dehydration, exhaustion, and death	20
10-15 Gy	All adversely affected with intestinal problems within 30 min; 95% dead in 2 weeks from enterocolitis shock	19
>15 Gy	Death in 1-5 days, nervous	13

Table 27. Species, dose, and other variables	Effect	Reference[a]
	system damage	
>50 Gy	All dead in 48 h, usually from cerebral edema	19
Annual dose rate or protracted annual exposure for many years		
>0.1 Sv	Lens opacity	13
>0.15 Sv	Cataracts	13
>0.2 Sv	Sterility, females	13
0.4 Sv	Temporary sterility, males; hematopoiesis depression	13
2.0 Sv	Permanent sterility, males	13
Rhesus monkey, *Macaca mulatta*		
Females, single acute dose of 0.25 to 6.5 Gy, observed over a 17-year postexposure period	At doses >2 Gy, 53% developed endometriosis (abnormal uterine growth) vs. 26% in controls; irradiated monkeys weighed 43% less than controls, 35% were anorexic, 89% had abnormal uterine anatomy, and histopathology in most tissues exceed 50% frequency	21
Exposed to single brief whole body proton irradiation (protons in the energy range encountered by astronauts) ranging between 0.25 and 12 Gy and observed for 24 years until death	Dose-dependent life shortening of at least 40 months at doses >4.5 Gy; mean life shortening was 200-500 monkey days per Gy, equivalent to 500-1,250 human days. Brain cancer first observed in 8 Gy group after 13 months. Monkeys receiving between 3 and 8 Gy had a significantly higher proportion of cancer deaths than those receiving 0.25-2.8 Gy. Latent period for cancer in animals receiving 4-8 Gy ranged between 13 months and 20 years	22
Mammals		
10 species, 2.8-8.05 Gy, single acute exposure	LD50, 30 days after exposure	23
Various species, bioconcentration factors (BCF) of selected radionuclides		
^{60}Co		
Herbivores	Whole body BCF of 0.3	24
Caribou, *Rangifer tarandus*		
Bone vs. kidney	BCF of 0.5 vs. 0.4	24
Liver vs. muscle	BCF of 0.9 vs. 0.02	24
$^{134+137}Cs$		
Herbivores	Whole body BCF of 0.3-2.0	24
Omnivores	Whole body BCF of 1.2-2.0	24

Table 27. Species, dose, and other variables	Effect	Reference[a]
Carnivores	Whole body BCF of 3.8-7.0	24
^{131}I		
Herbivores	Whole body BCF of 0.05	24
Omnivores	Whole body BCF of 0.2	24
Carnivores	Whole body BCF of 0.1	24
^{90}Sr, caribou, muscle vs. bone	BCF of 0.02 vs. 7.0	24
Various species, biological half-life of selected radionuclides		
^{241}Am		
Bone	27.4 years	25
Gonads	>27.4 years	25
Kidney, liver	11 years	25
Muscle	4 years	25
Serum	5 days	25
^{137}Cs, kidney, liver, and muscle	30 to 50 days	25
$^{238+239+240}Pu$		
Bone	49 years	25
Gonads	>49 years	25
Kidney, liver	19 years	25
Muscle	5.5 years	25
Serum	5 days	25
Singing vole, *Microtus miurus*; 8.46 Gy, single acute dose	LD50, 30 days after exposure	26
Creeping vole, *Microtus oregoni*; 6.51 Gy, single acute dose	LD50, 30 days after exposure; sensitivity may be associated with low chromosome complement	26
Meadow vole, *Microtus pennsylvanicus*; single brief exposure		
7.04 (6.35-7.98) Gy, irradiated in November	LD50, 30 days after exposure; irradiated voles released into environment	27
7.67 (7.01-8.39) Gy, irradiated in May	LD50, 30 days after exposure; irradiated voles released into environment	27
8.44 (8.17-8.77) Gy	LD50, 30 days after exposure; irradiated voles held in laboratory	7
Pine vole, *Microtus pinetorum*; single brief exposure		
7 Gy	None dead 30 days after exposure; weight normal	28
8.8 Gy, males	LD50, 30 days after exposure; weight loss in survivors	28
10.0 Gy, females	LD50, 30 days postexposure; weight loss in survivors	28
House mouse, *Mus museulus*;		

Table 27. Species, dose, and other variables	Effect	Reference[a]
single brief exposure		
7.5-8.8 Gy	LD50, 30 days postexposure	26,29
7.8, 8.1, 8.3, and 9.8 Gy	LD50, 30 days after exposure; four different strains	1
Mouse, *Mus* sp.		
Intraperitoneal injection		
Single injection of 850 Bq ^{227}Ac/kg BW alone or in combination with ^{227}Th at 18,500, 74,000, or 185,000 Bq/kg BW	The highest bone cancer incidence was observed at the highest doses of ^{227}Th. The addition of ^{227}Ac resulted in an additional osteosarcoma incidence only at 18,500 Bq ^{227} Th/kg BW	30
Single injection of ^{241}Am at concentrations-in Bq/kg BW-of 0.02, 0.06, 0.19, 0.37, or 1.2	Survival time decreased from 594 days for controls and 0.02 group to 135 days in the 1.2 group; increased frequency of tumors in bone, liver and lymph	31
Adult males, 84 days old, given 2 to 64 Bq ^{224}Ra/mouse, either as single injection, or 8 injections at 3.5 day intervals over 4 weeks; observed for 24 months	No difference in single or multiple injection effects. No effect at 16 Bq and lower, At 32 and 64 Bq, reduction in bone growth and osteonecrosis of mandible ("radium jaw")	32
Oocytes given single exposures of 0.1, 0.15, or 0.25 Gy; immature oocytes examined 8-12 weeks later	Controls had 100% survival and zero chromosome aberrations; the 0.1 Gy group had 30% survival and 2% chromosome aberrations; 0.15 Gy had 17% survival and 6% chromosome aberrations; 0.25 Gy had 5% survival and 23% chromosomal aberrations	33
Whole body, single brief exposure		
1 Gy	Acute exposure may extend life span	34
1.35 Gy	Doubles mutation rate of spermatogonia	17
7.6 Gy	LD50, 30 days postexposure	35
9.5 Gy	LD100, 30 days postexposure	35
10.0 Gy, adult males, 16-20 weeks old, observed for 7 days	At 90 min after irradiation, locomotor activity was suppressed and remained depressed; at 4 days, body weight decreased; at day 7, offensive aggressive behavior	20
12.5 Gy	LD100, days 3-7 postexposure	35
0.12-2.5 Sv	Doubles rate of heritable translocations in males	17
0.25-2.5 Sv	Doubles rate of congenital malformations in females	17
0.4-1.0 Sv	Doubles frequency of dominant	17

Table 27. Species, dose, and other variables	Effect	Reference[a]
	lethal mutations	
0.5-1.0 Sv	Doubles rate of heritable translocations in females	17
0.8-2.5 Sv	Doubles rate of congenital malformations in males	17
1.5-3.0 Sv	Doubles rate of recessive lethal mutations	17
Chronic exposure, daily dose over 8-h period, in Gy		
0.0	Mean survival time of 703 days	8
0.001	Mean survival of 761 days	8
0.011	Mean survival time of 684 days; 50% weight gain over controls	8
0.022	50% dead in 630 days	8
0.044	50% dead in 591 days	8
0.088	50% dead in 488 days	8
Total yearly dose, chronic exposure, 16 Gy (about 0.044 Gy daily)	Tolerated	34
Domestic ferret, *Mustela putorius*; 2, 4, or 6 Gy; single brief exposure; adult males	All doses depressed locomotion; vomiting in 22 min at 2 Gy, 13 min at 4 Gy, and 11 min at 6 Gy. Various substituted benzamides reduced vomiting	36
Marsh rice rat, *Oryzomus palustris*; 5.25 Gy, single acute exposure	LD50, 30 days after exposure; this species was the most sensitive of 10 rodent species tested	1
Domestic sheep, *Ovis aries*		
Ewes fed hay containing 9,000 Bq ^{137}Cs/kg DW for 50-60 days, then 40 days on uncontaminated hay; some diets contained 30 or 60 g of vermiculite daily, or 2 g of ammonium ferricyanoferrate (AFCF) daily	Maximum levels of ^{137}Cs were reached in 10 days in milk and 35-40 days in muscle. Radionuclide transfer to milk and meat was reduced 2.5 times at daily intakes of 30 g vermiculite, and 8 times at 60 g vermiculite or 2 g AFCF	37
Ewes given oral dose of 74,000 Bq ^{137}Cs, observed for 76 days	At 76 days, only 26% of ^{137}Cs remained; tissue concentrations, in Bq ^{137}Cs/kg FW, were 77,000 in salivary gland; 42,000 in muscle; 24,000-36,000 in pancreas, liver, and kidney; 14,000-17,000 in spleen and lung; and <8,000 in other tissues	38
Lambs fed 21 kg of vegetation containing 16,600 Bq of	Of the Pu ingested, 46% was in liver, 30% in bone, 12% in muscle, and 2% in	39

Table 27. Species, dose, and other variables	Effect	Reference[a]
$^{238+239+240}Pu$ and 14,400 Bq of ^{241}Am over a 14-day period, followed by 4 days on uncontaminated hay	lung; for ^{241}Am, these values were 19% in liver, 15% in bone, bone, 6% in meat, and 0.5% in lungs	
Lamb given single intravenous injection of 23 Bq ^{238}Pu plus 27 Bq ^{241}Am and held for 11 days	Liver retained up to 44% of the injected ^{238}Pu and 28% of the ^{241}Am; bone had 21% of the ^{238}Pu and 20% of the ^{241}Am	39
Great Basin pocket mouse, *Perognathus parvus*; 8.56 Gy, single exposure	LD50, 30 days after exposure; hair loss within 7 days	26
White-footed mouse, *Permoyscus leucopus*; whole body, single brief exposure		
9.5 Gy, both sexes irradiated	No reproduction	40
9.5 Gy, males only irradiated	91% of pairs successful in producing young	40
9.5 Gy, females only irradiated	40% of pairs reproduced successfully	40
10.7 Gy	LD50, 30 days postexposure; this species was the most radioresistant of 10 species of rodents tested	1
Deer mouse, *Peromyscus maniculatus*; 9.19 Gy, single brief exposure	LD50, 30 days after irradiation	26
Oldfield mouse, *Peromyscus polionotus*; 11.25 Gy, single exposure	LD50, 30 days after exposure	29
Norway rat, *Rattus norvegicus*; 8.67 Gy, single exposure	LD50, 30 days postexposure	1
Laboratory white rat, *Rattus* spp.		
0.001, 0.01, or 0.1 Gy; single acute whole body exposure; adult males; killed up to 180 days after exposure	Fertility reduction was zero in the low-dose group, 25% at 0.01 Gy, and 66% at 0.1 Gy. Primary sites of damage were tubuh of the testes and spermatogonia. The high-dose group also had altered serum hormone chemistry after 30 days that persisted for 180 days	41
Pregnant rats given single brief exposure to 0.25, 0.5, 0.75, or 1 Gy on gestational day 15; fetuses examined 24 h after irradiation	No effect at 0.5 Gy and lower on cerebral mantle of developing brain; however, dose- related increase in pyknotic cells and macrophages in cortical mantle of fetus for all doses	42
Pregnant females exposed on day 15 of gestation	Rats irradiated in utero had impaired gait, slower motor	43

Table 27. Species, dose, and other variables	Effect	Reference[a]
to 0.75 Gy; fetuses examined 1-3 months after birth	behavior, difficulty in learning motor tasks, reduced growth rate, and reduced thickness of the cerebral cortex	
<1 Gy, whole body, single exposure	No brain pathology	44
2 Gy, whole body, single exposure	Brain pathology	44
Adult males conditioned to avoid electric shock by pressing a lever were subjected to various whole body acute exposures		
1.5 Gy daily for 5 consecutive days (total 7.5 Gy)	No significant change in performance over 8 weeks	45
4.5 Gy, single exposure	No effect on performance for at least 6 weeks	45
7.5 Gy, single exposure	Significantly decreased response rate over the first 4 weeks; performance normal during weeks 5-6; 9% reduction in body weight	45
9.5 Gy, single exposure	LD100, 30 days postexposure	45
Single local dose of 5 to 20 Gy to various salivary glands	Dose-dependent decrease in salivary flow rate and sodium composition of saliva; at 10 Gy and higher, changes were irreversible	46
25 Gy, single whole body exposure	50% dead 30-60 days postirradiation from fatal stomach damage; significant liver damage in survivors	47
Eastern harvest mouse, *Reithrodontomys humulis*; 9.5 Gy, single exposure	LD50, 30 days after exposure	1
Rodents, single brief exposure		
3.8-13.3 Gy, 13 species	LD50, 30 days postexposure; females more sensitive than males	48
4-8 Gy, 5 species	Dead rodents had histopathology of lymph nodes, thymus, bone marrow, liver, lung, and gonads; male survivors had atrophied testes	26
5.3-10.7 Gy, 10 species	Range of LD50 values (30 days after exposure); survivors showed conjunctivitis, ataxia, diarrhea, passiveness, cessation of feeding, aggressiveness, and graying of pelage	1
Squirrel monkey, *Saimiri* spp.; fetuses, 80-90 days postconception; given 0.1 or 1.0 Gy, single acute	No effect on behavior at 0.1 Gy. At 1 Gy, emotional stability and vision impaired at age 30 days,	44

Table 27. Species, dose, and other variables	Effect	Reference[a]
exposure; young observed from birth to age 2 years	learning impaired at 1 year; normal at 2 years	
Cotton rat, *Sigmodon hispidus*		
Females given 5, 7.5, 9, 10.5, or 12 Gy whole body once a month for 4 months, then released into a 0.4 ha-impoundment with unirradiated males and females for 15 days	Survival was 91% at 5 Gy and 25% at 12 Gy; intermediate doses had intermediate survival	49
9.58 Gy, single brief exposure	LD50, 30 days after exposure	1
11.2 Gy, single acute exposure, adult females	LD50, 30 days after exposure	49
11.3 Gy, single exposure, adult females	LD50, 15 days postexposure	49
Eastern chipmunk, *Tamias striatus*		
2-4 Gy, single exposure	Irreversible injury throughout life, but lifespan was increased	50
Given single exposure of 2 or 4 Gy, then released into environment	Irradiated chipmunks had consistently smaller home ranges and moved shorter distances than did controls	51
Iodine-131, half-time release rate from thyroid; females vs. males		
Summer	2.3 h vs. 263 h	52
Spring	156 h vs. 217 h	52
Autumn	126 h vs. 129 h	52

[a] 1, Dunaway et al. 1969; 2, Handl et al. 1990; 3, Handl and Pfau 1989; 4, Jaenke and Angleton 1990; 5, Benjamin et al. 1990; 6, Lloyd et al. 1991; 7, Bruenger et al. 1990; 8, Lorenz et al. 1954; 9, Egami et al. 1991; 10, Nagasawa et al. 1990; 11, Woloschak et al. 1990a; 12, Mole 1990; 13, ICRP 1991a; 14, Kamiguchi et al. 1990; 15,Kim et al. 1990; 16, Refetoff 1990; 17, Saknaranarayanan 1991c; 18, McLean 1973; 19, United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1988; 20, Maier and Landauer 1990; 21, Fanton and Golden 1991; 22, Wood 1991; 23, Hobbs and McClellan 1986; 24, Kitchings et al. 1976; 25, Gilbert et al. 1989; 26, O'Farrell 1969; 27, Iverson and Turner 1976; 28, Dunaway et al. 1971; 29, Golley and Gentry 1969; 30, Muller et al. 1990; 31, Schoeters et al. 1991; 32, Robins 1990; 33, Straume et al. 1991; 34, Rose 1992; 35, Cronkite et al. 1955; 36, King and Landauer 1990; 37, Daburon et al. 1991; 38, Vandecasteele et al. 1989; 39, Ham et al. 1989; 40, Di Gregorio et al. 1971; 41, Canfi et al. 1990; 42, Norton and Kimler 1990; 43, Norton et al. 1991; 44, Mole 1990; 45, Mele et al. 1990; 46, Vissink et al. 1990; 47, Geraci et al. 1991; 48, Whicker and Schultz 1982b; 49, Pelton and Provost 1969; 50, Thompson et al. 1990; 51, Snyder et al. 1976; 52, Kodrich and Tryon 1971.

Survival

Survival time is inversely related to dose in whole-body, acute exposures to ionizing radiation (Fig. 9). In general, hematopoietic organs are most sensitive and gastrointestinal tract and central nervous system are next most sensitive (UNSCEAR 1988). Body weight is an important modifier, and heavier mammals are usually most sensitive to radiation (Fig. 10). Feral rodent populations are at risk from ionizing radiation through the reduction in numbers from direct kill and indirectly from the radiation-caused diminution of reproduction (Di Gregorio et al. 1971).

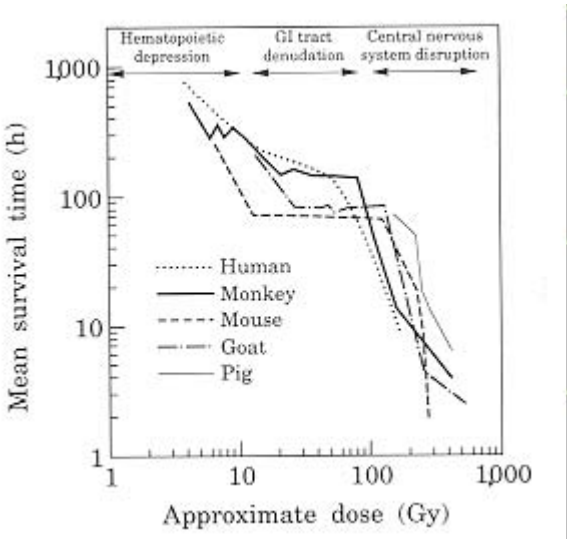


Fig. 9. Survival time and associated mode of death of selected mammals after whole-body doses of gamma radiation (modified from Hobbs and McClellan 1986; UNSCEAR 1988).

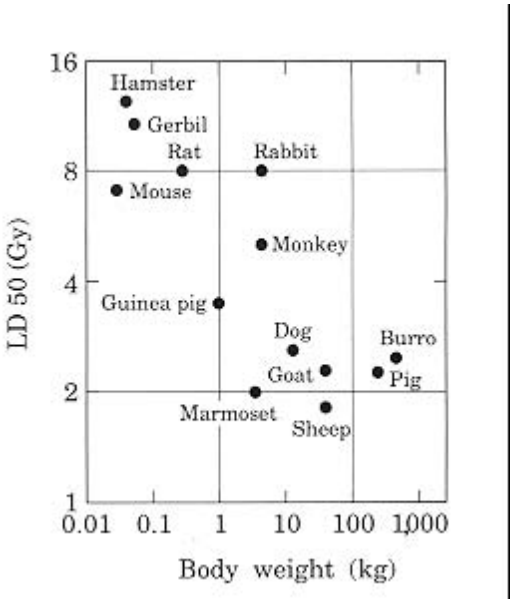


Fig. 10. Relation between body weight and radiation-induced LD50 (30 days postexposure) for selected mammals (modified from UNSCEAR 1988).

Low doses of ionizing radiation are beneficial to many species of mammals; effects of radiation hormesis include increased survival and longevity, lowered sterility, increased fecundity, and accelerated wound healing (Luckey 1980). Low doses of gamma irradiation cause irreversible injury to the eastern chipmunk (*Tamias striatus*), although the life span was significantly longer (Thompson et al. 1990). Acquired radioresistance after exposure to a low dose of ionizing radiation has been described in rats, mice, and yeast (Yonezawa et al. 1990). In mice, for example, low doses of X-irradiation (not higher than 0.15 Gy) enhanced 30-day survival if given 2-months prior to a dose of 7.5 Gy. The low-dose exposure seems to stimulate the recovery of blood-forming stem cells after the second irradiation and favors a decrease in the incidence of bonemarrow death. The exact mechanisms of radiation hormesis are unknown because effects are not related to and not predictable from the high-dose exposure (Yonezawa et al. 1990).

Irradiated small mammals that were released into the environment had a lower survival rate than laboratory populations, suggesting that the extrapolation from laboratory results may overestimate the radioresistance of free-ranging voles and other small animals because of the general level of stress in the population (Iverson and Turner 1976). The opposite was observed in eastern chipmunks after high sublethal doses of X-rays. Chipmunks had an overall reduction in mobility when they were released into the environment and a higher survival rate than controls (Snyder et al. 1976), possibly because of increased predation on the more mobile controls.

Carcinogenicity

The risk of the induction of cancer is a recognized somatic effect of low doses of ionizing radiation, as judged by epidemiological studies of Japanese survivors of the U.S. nuclear bombs (Coggle and Williams 1990) and of Marshall Islanders, underground miners, and radium watchdial workers (Bowden et al. 1990). Yoshimoto et al. (1990), however, conducted a study on the occurrence of malignant tumors in Japanese children that were older than 10 years and born between 1946 and 1982 to survivors of the atomic bombings in 1945 and in a suitable control group. They found no statistically significant increase in malignant tumors in the children of parents who had been exposed to more than 0.01 Sv whole-body radiation (mean gonadal exposure of 0.43 Sv) at the time of the atomic bombings. Nutritional status is important when treating malignant tumors. Unlike tumors of nonanemic individuals, tumors in anemic mice and humans frequently do not satisfactorily respond to radiotheraphy (McCormack et al. 1990).

Ionizing radiation induces basal-cell carcinomas in skin and is active in the initiation of malignant tumors and in the progression of benign to malignant tumors (Bowden et al. 1990). Skin has been widely used in studies of carcinogens because of its accessibility and the visibility of its tumors. All data on experimental radiogenic skin cancer in mice are on a relatively narrow and well defined response curve; however, mouse skin is about 100 times more sensitive than human skin (Coggle and Williams 1990), strongly suggesting that appropriate animal models are necessary in the extrapolation of results to another species.

Thyroidal cancer in dogs and sheep has been induced with repeated administrations of ^{131}I, although single injections of ^{131}I failed to induce thyroid cancer in adult animals except in some strains of laboratory rodents (Walinder 1990). Humans with a prior history of ^{131}I and other radiation exposure in childhood are at a significantly higher risk of thyroid carcinogenesis, and females are at higher risk than males. The minimum latent period in humans is about 4 years, and neoplastic lesions may develop as late as 40 years after irradiation (Kim et al. 1990). Historically, the human thyroid received radiation from irradiation of the scalp for epilation (as much as 0.5 Gy), thymus (as much as 5 Gy), tonsils and adenoids (8 Gy), and facial acne (15 Gy). Higher doses of external irradiation (as much as 50 Gy) were used during 1920-40 for the treatment of hyperthyroidism in adults and are still used for the treatment of cervical malignancies in people of all ages (Refetoff 1990).

Radium-induced bone malignancies after exposure to ^{226}Ra are similar in beagles and humans, and the tibia in dogs is especially sensitive (Lloyd et al. 1991). *Radium jaw* has been described in humans as a late effect of accidental ingestion or therapeutic administration of long-lived radium isotopes such as ^{216}Ra and ^{228}Ra and is characterized by bone tumors, spontaneous fractures, and osteosclerosis (Robins 1990). However, the short-lived ^{224}Ra (Tb½ of 3.6 days) produces similar effects in mice, suggesting that the events that trigger radium-induced bone disorders occur within days of incorporation, even though the consequence is a late effect (Robins 1990).

Aerosol exposures of mice, rats, dogs, and hamsters to radon and its decay products resulted in lifetime shortening, pulmonary emphysema, pulmonary fibrosis, and respiratory tract carcinoma; damages to the skin and kidney were also reported, but the lung seems to be the primary organ that is affected (Cross 1990). Radon and ^{222}Rn daughters have caused problems to miners who work underground in uranium mines. These miners had an excessive incidence of disease of the respiratory system, including lung cancer. The problem is related to the emanation of radon into the mines and the decay of the radon, the short-lived radioactive daughters (^{216}Po, ^{214}Pb, ^{214}Bi, ^{214}Po), which attach to dust particles, eventually resulting in alpha-radiation exposure of the respiratory airways (Hobbs and McClellan 1986). A similar pattern was evident in rats exposed to ^{239}Pu.

Rats exposed to $^{239}PuO_2$ aerosol of about 3,700 Bq/lungs and examined 8 to 18 months after exposure had a high frequency (as much as 80%) of malignant pulmonary neoplasms; genetic mutations were evident in 46% of the radiation-induced tumors (Stegelmeier et al. 1991).

The incidence of ovarian tumors in mice, guinea pigs, and rabbits increased after 3 years of chronic irradiation at doses as low as 1.1 mGy daily (Lorenz et al. 1954). Unlike other tumors, the induction of ovarian tumors depended on a minimum total dose and seemed to be independent of a daily dose (Lorenz et al. 1954). Radiation-induced neoplastic transformation of hamster cells may be associated initially with changes in expression of the genes modifying cytoskeletal elements (Woloschak et al. 1990b).

Mutagenicity

In general, ionizing radiation has produced mutations in every studied plant and animal species. Some genetic risks are associated with exposures, but the risk of inducing a dominant genetic disease is small because radiation-induced mutations are primarily recessive and usually lethal (Sankaranarayanan 1991c).The genetic doubling dose of radiation is the amount of acute or chronic radiation that doubles the naturally occurring spontaneous mutation rate in each generation. For mice, the estimated genetic doubling-dose equivalent is 1.35 Sv from acute exposures and 4.0 Sv from chronic exposures to radiation (Neel and Lewis 1990). For protection from radiation, the estimated genetic risks to humans have largely been based on data from mice (Straume et al. 1991). Studies of children of Japanese survivors of nuclear bomb explosions revealed that the genetic doubling dose equivalent of acute gonadal radiation is about 2.0 Sv (1.69-2.23); from chronic radiation, this value is about 4.0 Sv (Neel and Lewis 1990). Based on results of the study of Japanese survivors of the nuclear explosions, Yoshimoto et al. (1990) and Sankaranarayanan (1991c) concluded that the spontaneous mutation rate did not increase after parents were exposed. The high doubling dose of about 4 Sv estimated from these data is another way of stating that, relative to the assumed spontaneous rates, the rate of induction of mutations that leads to the measured effects is too small (Sankaranarayanan 1991c). The transmission of radiation-induced genetic effects to offspring has not yet been demonstrated in any human population (Straume et al. 1991).

Specific point mutations were identified in ^{239}Pu-induced preneoplastic lesions and in malignant neoplasms in the lungs of rats (Stegelmeier et al. 1991). Mice exposed to a single whole-body dose of 3 Gy produced a radiation-induced mutation that simultaneously generated distinct alleles of the limb deformity and agouti (grizzled fur color) loci, 2 developmentally important--but not adjoining--regions on a single chromosome. This phenomenon was probably associated with DNA breaks that were caused by inversion of a segment in another chromosome (Woychik et al. 1990). The plasma membrane in immature oocytes of mice is the hypersensitive lethal target in producing radiation-induced genetic damage (Straume et al. 1991).

Organ and Tissue Damage

In the abdomen, the kidneys are one of the most sensitive organs to serious or fatal radiation-induced damage (Jaenke and Angleton 1990). The relatively high incidence of kidney disease among mature beagles that were injected with ^{226}Ra and its accompanying ^{210}Bi and ^{210}Po were from alpha irradiation of the kidneys by the substantial amount of ^{210}Po that was in the injected solution (Bruenger et al. 1990). Hepatic injury that was induced by ionizing radiation can be a life-threatening complication. The main responses of the liver to acute radiation exposure include enlargement, dilation of blood vessels, fluid accumulation, and histopathology (Geraci et al. 1991). Damaging effects of ionizing radiation on the fetal cerebral cortex has been recognized for many years (Norton and Kimler 1990). The deleterious effects of ionizing radiation on the developing-brain are prolonged and progressive. Less than 2-Gy doses of gamma radiation are harmful to the developing brain, and mental retardation in humans may occur from doses as low as 0.2 Gy between week 8 and 15 of gestation (Norton et al. 1991).

Irradiated white-footed mice (*Peromyscus leucopus*) frequently had atrophied gonads, degenerating fetuses in the uterus, and greying hair (Di Gregorio et al. 1971). High sublethal doses (7 Gy) of radiation to the pine vole (*Microtus pinetorum*) caused pelage graying wherein unpigmented hair from damaged follicles replaces molted pigmented hair. Pelage graying may decrease survival from increased predation (Dunaway et al 1971), although this needs verification.

Human sperm chromosomes retain a high fertilizing ability after a high dose of X-irradiation, although mammalian spermatozoa have little capacity to repair DNA damage that is induced by radiation (Kamiguchi et al. 1990). Radiation-induced deaths of lymphoid cells in rats are associated with damage to the cell itself but may also be due to secretions from irradiation-activated natural killer cells, which induce pycnosis and interphase death in lymphoid cells (Eidus et al. 1990).

Behavior

Numerous behavioral measures have been evaluated for their usefulness as sensitive indexes of exposure to ionizing radiation. Radiation-related mental retardation is the most likely type of behavioral abnormality in humans; sensitivity peaked between 8 and 15 weeks of conception and doses that were greater than 0.4 Gy (UNSCEAR 1988). No specific mechanism for the production of mental retardation has been established, although proposed mechanisms include the loss of cells, migration of neurons, and failure of synaptogenesis (Norton and Kimler 1990). In studies with rats, operant responses decreased (maintained by positive reinforcement such as food or water) at sublethal radiation doses (3.0-6.75 Gy) under various schedules of reinforcement (Mele et al. 1990). Disrupted operant responses under shock avoidance at greater than LD100 levels are reported in pigs and rhesus monkeys (Mele et al. 1990).

Absorption and Assimilation

The absorption, bioavailability, and retention of radionuclides in mammals are modified by age, sex, species, and diet of the organism; season of collection; the chemical form of the radionuclide in tissue and blood; residence time in the digestive tract; preferential accumulation by selected organs and tissues; and many other variables (Kitchings et al. 1976; Whicker and Schultz 1982a, 1982b; Richmond 1989; Desmet et al. 1991; Harrison 1991). Recommended assimilation fractions of various elements by the International Commission on Radiological Protection are presented in detail by Whicker and Schultz (1982b).

Many radionuclides preferentially accumulate in certain organs or tissues, but the critical organ is different for different radionuclides: liver for ^{54}Mn, erythrocytes and spleen for ^{55}Fe, liver and kidney for cobalt nuclides, liver and prostate for ^{65}Zn, skeletal muscle for ^{137}Cs, and GI tract for ^{95}Zr (Whicker and Schultz 1982a). The persistence of radionuclides in mammals varies with the chemical form, kinetics, species, and other variables. For example, the time for 50% persistence of selected radionuclides in whole-animal studies ranged from 19 h to 14 days at ^{134}Cs; 4 to 35 days at ^{137}Cs; 5 to 12 h at the short-lived component of ^{60}Co, and 5 to 21 days at the long-lived component; 25 to 593 days at ^{90}Sr; and 4 to 26 days at ^{131}I (Kitchings et al. 1976; Whicker and Scultz 1982b).

Some radionuclides act antagonistically when administered together. The combined incorporation of ^{227}Ac and ^{227}Th at tested levels in mice showed a lower biological effect than the sums of the effects of the components administered singly. The less-than-additive effect is in good agreement with experiments with the incorporation of a mixture of β emitters, in which the effects are also less than additive (Muller et al. 1990). Uptake and retention characteristics of essential biological nutrients (i.e., H, C, P, I, K, Ca, Mn, Fe, Co, Zn) are largely controlled by biological processes (Whicker and Schultz 1982a). For example, ^{131}I regardless of route of administration is rapidly absorbed into the bloodstream and concentrated in the thyroid. Ionizing radiation from high levels of ^{131}I destroys the thyroid and affects the thyroid hormone production (Hobbs and McClellan 1986).

Alkali metals (K, Rb, Cs) behave similarly and sometimes one is accumulated preferentially when another is deficient; a similar case is made for Sr and Ca (Whicker and Schultz 1982a). The most important alkali-metal isotope is ^{137}Cs because of its long physical half-life (30 years) and its abundance as a fission product in fallout from nuclear weapons and in the inventory of a nuclear reactor or a fuel-reprocessing plant. Cesium behaves much like potassium. It is rapidly absorbed into the bloodstream and distributes throughout the active tissues of the body, especially muscle. The β and radiation from the decay of ^{137}Cs and its daughter, ^{137}Ba, result in essentially whole-body irradiation that harms bone marrow (Hobbs and McClellan 1986).

Because ^{226}Ra and ^{90}Sr are metabolic analogs of calcium, they are deposited in the skeleton; both isotopes are associated with bone cancers (Hobbs and McClellan 1986). In pregnant rats, the total amount of

^{226}Ra that is transferred from the dam to the 8-10 fetuses in a litter was low after a single injection and did not exceed 0.3% of the maternal content; the retained whole-body burden in dams was 53% at the first, 48% at the second, and 44% at the third pregnancy, mostly in the skeletal system (Kshirsagar 1990). The rare earths (i.e., ^{144}Ce, ^{152}Eu, ^{140}La, ^{147}Pr, ^{151}Sm) are usually not absorbed from the GI tract, and elimination is rapid (Palumbo 1963). Cerium-144 is one of the more biologically hazardous radionuclides in this group because of its half-life (285 days) and the energetic β emissions from it and its daughter, ^{144}Pr (Hobbs and McClellan 1986).

The greatest uncertainty in dose estimates from the ingestion of long-lived alpha emitters is the values used for their fractional absorption from the GI tract (Harrison 1991). For transuranic elements, the fraction of the ingested material that was assimilated by the whole organism was always less than 0.01% and usually nearer 0.003% (Whicker and Schultz 1982b). The major hazard of plutonium nuclides to terrestrial organisms comes from inhalation; uptake by plants is low, and further uptake by humans through the gut is low (Noshkin et al. 1971). Americium-241 is an artificial, toxic bone-seeking radionuclide produced by beta decay of ^{241}Pu (Schoeters et al. 1991). Because of its long half-life, its high-energy alpha irradiation, and its accumulation in the liver and skeleton, consideration should be given to ^{241}Am in risk estimates of latent effects such as induction of liver cancers, bone cancers, and leukemias. In comparison with ^{226}Ra, ^{241}Am is 20 times more effective in reducing the life-span in mice and 13 times more effective in the rate of death from bone cancer (Schoeters et al. 1991).

Although radon has long been known as a health hazard to miners in the uranium industry, global radon contamination of buildings was not recognized before the 1980's; however, years of exposure are required before a health problem develops (Majumdar et al. 1990). Exposure to radon-decay products can be expressed in two different ways: the amount of inhaled decay products (taking into account their potential emission of radiation energy) or the product of the time during which the decay products were inhaled and their concentration in the inhaled air. The potential alpha energy of the inhaled decay products may be expressed in joules (J). The potential alpha energy concentration in air is expressed in joules per cubic meter; for radon in equilibrium with its decay product, this corresponds to 3,700 Bq/m^3 (UNSCEAR 1988).

Rodents that were dosed with tungsten-185 excreted 80% in 24 h; bone was the major retention site; the half-time persistence ranged from 5.7 days in femurs of mice to 86 days in femurs of rats; some components in the bone of rats persisted with a half-time of longer than 3 years (Reed and Martinedes 1971). Niobium-95 is produced directly by nuclear fission and indirectly by decay of ^{95}Zr. Routine discharges of ^{95}Nb from a nuclear fuel-reprocessing plant in the United Kingdom in 1970 contributed about 5% of the bone-marrow dose to a 10-year-old child that resided in the vicinity (Harrison et al. 1990). Gastrointestinal absorption of ^{95}Nb by adult guinea pigs was about 1.1% and supports the now-used values of 1% absorption in adults and 2% in infants to calculate percentage absorption of niobium isotopes by humans (Harrison et al. 1990).

Proposed Criteria and Recommendations

For the protection from radiation, effects of radiation have been characterized as stochastic or nonstochastic. The probability of a stochastic effect--and not its severity--varies as a function of dose in the absence of a threshold, that is, hereditary effects or carcinogenesis. The probability and severity of nonstochastic effects vary with dose, and a threshold for the dose exists, that is, cataract of lens, nonmalignant damage to the skin, cell depletion in the bone marrow that causes hematological deficiencies, gonadal cell damage that leads to impairment of fertility, or pneumotis and pulmonary fibrosis after lung irradiation (ICRP 1977; Hobbs and McClellan 1986; UNSCEAR 1988). Nonstochastic effects can be prevented by setting dose-equivalent limits at sufficiently low levels so that no threshold dose is reached, not even after exposure for the whole of a lifetime or for the total period of a working life (ICRP 1977, 1991a, 1991b). Guides for the protection from radiation are also predicated on the effective half-life of each isotope, the critical organ, the fraction that reaches the critical organ by ingestion and inhalation, and the maximum tolerable whole-body burdens, as judged by radionuclide concentrations in air, water, and diet (Palumbo 1963).

At present, no radiological criteria or standards have been recommended or established for the protection of fishes, wildlife, or other natural resources. All radiological promulgated or proposed criteria are directed towards the protection of human health. It is generally assumed that humans are comparatively radiosensitive and that

guides probably also protect sensitive natural resources (UNSCEAR 1988; ICRP 1991a, 1991b; NCRP 1991; IAEA 1992; Zach et al. 1993), although this needs verification. Numerous radiological criteria exist for the protection of human health (Table 28). Most authorities agree that some adverse effects to humans are probable under the following conditions: more than 5 mSv whole-body exposure of women during the first 2 months of pregnancy; more than 50 mSv whole-body exposure in any single year or more than 2,000 mSv in a lifetime; an annual inhalation intake by a 60 kg individual--in Bq/kg BW--that exceeds 0.67 ^{232}Th, 3.3 ^{241}Am, 3.3 ^{239}Pu, 16 ^{252}Cf, 33 ^{235}U, 1,666 ^{90}Sr, 16,666 ^{60}Co, or 166,666 ^{32}P; an annual ingestion intake by a 60 kg individual--in Bq/kg BW--that exceeds 3,333 ^{129}I, 16,666 ^{125}I, 16,666 ^{131}I, or 66,666 ^{137}Cs; or a total annual intake from all sources--in Bq/kg BW by a 60 kg person--that exceeds 66 ^{210}Pb, 166 ^{210}Po, 333 ^{226}Ra, 666 ^{230}Th, 833 ^{228}Th, or 1,333 ^{238}U (Table 28).

Table 28. Recommended radiological criteria for the protection of human health.

Table 28. Criterion and other variables	Concentration or dose	Reference[a]
Air		
United States; radon-222		
Average	<0.0555 Bq (<1.5 pCi)/L or <55 Bq/m^3	1
Acceptable	<0. 148 Bq (<4.0 pCi)/L	1,2
Allowable emission discharge	<0.74 Bq (<20 pCi)/m^2/s; should not increase the radon 222 concentration in air at or above any location outside the disposal site by >0.0185 Bq (>0.5 pCi)/L or >18 Bq (>500 pCi)/m^3	3
Unacceptable	>0.185 Bq (>5 pCi)/L	2
Astronauts		
Age 25-55 years; expected whole body career dose; females vs. males	1.0-3.0 Sv (100-300 rem) vs. 1.5-4.0 Sv (150-400 rem)	4
Adverse effects expected; lifetime exposure	>2.0 Sv (>200 rem)	4
Cancer risk and birth defects		
Projected 0.04% increase in cancers; 0.01% increase in birth defects	0.11 mSv (0.011 rem) whole body maximum /year; 0.69 mSv (0.069 rem) whole body over 30 years; or 1.00 mSv (0.1 rem) bone marrow over 30 years	5
Projected 0.18% increase in cancers; 0.07% increase in birth defects	0.51 mSv (0.05 rem) whole body maximum/year; 3.30 mSv (0.33 rem) whole body over 30 years; or 4.60 mSv (0.46 rem) bone marrow over 30 years	5
Projected 0.92% increase in cancers; 0.38% increase in birth defects	3.03 mSv (0.3 rem) whole body maximum/year; 19.0 mSv (1.9 rem) whole body over 30 years; or 23.0 mSv (2.3 rem) bone marrow over 30 years	5
Projected 4.4% increase in cancers; 1.8% increase in birth defects	20.1 mSv (2.0 rem) whole body maximum/year; 91.0 mSv (9.1 rem) whole body over 30 years; or 110.0 mSv (11 rem)	5

Table 28. Criterion and other variables	Concentration or dose	Reference[a]
	bone marrow over 30 years	
Diet		
All foods; maximum recommended values		
Adults, Italy	600 Bq (16,200 pCi) cesium-134 + 137/kg fresh weight (FW)	6
Children, Italy	370 Bq (10,000 pCi) cesium-134 + 137/kg FW	6
Sweden, pre-Chernobyl	300 Bq (8,100 pCi) cesium-134 + 137/kg FW	6
Caribou; muscle; North America	<2,260 Bq (<61,000 pCi) cesium-137/kg FW	8
Fish; Great Lakes; muscle	Dose of <0.02 Sv (0.00002 rem)/kg FW fish flesh equivalent to consumers	9
Fish; Sweden	<1,500 Bq (<40,500 pCi) cesium-137/kg FW	10
Fraction of ingested dose absorbed; recommended maximum; selected isotopes		
Americium, curium, neptunium, plutonium, thorium	<0.05%	11
Americium, plutonium	<0.1%	12
Californium, and higher mass radionuclides	<0.1%	11
Uranium	<5.0%	11
Milk; maximum values		
Italy	370 Bq (10,000 pCi) cesium-134 + 137/L	6
Japan	370 Bq (10,000 pCi) cesium-137/L	13
Sweden	300 Bq (8,100 pCi) cesium-137/L	14
Meat and fish; Sweden; maximum values	1,500 Bq (40,500 pCi) cesium-137/kg FW	14
Reindeer meat, game, animal meat, fish, berries, mushrooms; Sweden; post-Chernobyl; maximum values	1,500 Bq (40,500 pCi) cesium-137/kg FW	15
Sheep, muscle	<1,000 Bq (<27,000 pCi) cesium 134 + 137/kg FW	16
Sheep, muscle	<1,000 Bq (<27,000 pCi) cesium-137/kg FW	17
Drinking water		
Natural radioactivity; maximum allowed		
Radium-226 + 228	0.185 Bq (5 pCi)/L	18
Gross alpha	0.555 Bq (15 pCi)/L	18
Artificial radioactivity; maximum		

Table 28. Criterion and other variables	Concentration or dose	Reference[a]
allowed		
Gross beta	1.85 Bq (50 pCi)/L	18
Tritium (Hydrogen-3)	740 Bq (20,000 pCi)/L	18
Strontium-90	0.296 Bq (8 pCi)/L	18
Great Lakes; maximum dose to consumers	10 mSv (0.001 rem)/year	9
General public		
Annual effective dose[b]	<1 mSv (<0.1 rem)	19,29
Cesium-137; total intake		
Sweden	<50,000 Bq (<1,350,000 pCi)/year, equivalent to <1 mSv (<0.l rem)	15
North America	<300,666 Bq (<8,100,000 pCi)/year	8
United Kingdom	<400,000 Bq (<10,800,000 pCi)/year, equivalent to 5 mSv (0.5 rem)	20
Maximum permissible dose		
Eye lens	<15 mSv (<1.5 rem)/year	19
Skin	<50 mSv (<5 rem)/year	19
Whole body		
Individual, except students and pregnant women	<5 mSv (<0.5 rem)/year	9,21,22,23
Students	<1 mSv (<0.1 rem)/year	21
Pregnant women	<5 mSv (<0.5 rem) during the first 2 months of pregnancy	22
Population dose limits, genetic or somatic	<1.7 mSv (<0.17 rem) yearly average	21
Groundwater, maximum allowed		
Radium-226 + 228	0.185 Bq (5 pCi)/L	3
Alpha-emitting radionuclides-including radium-226 + 228, but excluding radon isotopes	0.555 Bq (15 pCi)/L	3
Total beta and gamma radiation	Total annual whole body dose equivalent, or dose to any internal organ, <0.04 mSv (<0.004 rem), based on individual consumption of 2 L daily of drinking water from a groundwater source	3
Radioactive wastes		
Dose limits from spent nuclear fuel or transuranic radioactive wastes		
Whole body	<0.25 mSv (<0.025 rem)/year	3,24
Thyroid	<0.75 mSv (<0.075 rem)/year	3,24
Any other critical organ	<0.25 mSv (<0.025 rem)/year	3,24
Stored for 10,000 years; maximum cumulative release allowed to the accessible environment per 1,000 metric tons of heavy metal during storage		
Americium-241	3.7 trillion (T) Bq (100 TpCi)	3
Americium-243	3.7 TBq (100 TpCi)	3

Table 28. Criterion and other variables	Concentration or dose	Reference[a]
Any alpha emitter with physical half-life >20 years	3.7 TBq (100 TpCi)	3
Any non-alpha emitter radionuclide with physical half-life >20 years	37.0 TBq (1,000 TpCi)	3
Carbon-14	3.7 TBq (100 TpCi)	3
Cesium-135	37.0 TBq (1,000 TpCi)	3
Cesium-137	37.0 TBq (1,000 TpCi)	3
Iodine-129	3.7 TBq (100 TpCi)	3
Neptunium-237	3.7 TBq (100 TpCi)	3
Plutonium-238	3.7 TBq (100 TpCi)	3
Plutonium-239	3.7 TBq (100 TpCi)	3
Plutonium-240	3.7 TBq (100 TpCi)	3
Plutonium-242	3.7 TBq (100 TpCi)	3
Radium-226	3.7 TBq (100 TpCi)	3
Strontium-90	37.0 TBq (1,000 TpCi)	3
Thorium-230	0.37 TBq (10 TpCi)	3
Thorium-232	0.37 TBq (10 TpCi)	3
Tin-126	37.0 TBq (1,000 TpCi)	3
Uranium-233	3.7 TBq (100 TpCi)	3
Uranium-234	3.7 TBq (100 TpCi)	3
Uranium-235	3.7 TBq (100 TpCi)	3
Uranium-236	3.7 TBq (100 TpCi)	3
Uranium-238	3.7 TBq (100 TpCi)	3
Uranium byproduct materials; maximum discharge rates allowed into water		
Radium-226 + 228	0.185 Bq (5 pCi)/L	24
Gross alpha-particle activity, excluding radon and uranium isotopes	0.555 Bq (15 pCi)/L	24
Wastes from uranium fuel cycle entering the environment per billion watts/year of electrical energy produced by the fuel cycle; maximum allowed		
Krypton-85	1.85 TBq (50 TpCi)	24
Iodine-129	185 million Bq (5 billion pCi)	24
Plutonium-239 and other alpha emitting transuranics with Tb1/2 >1 year	2.69 million Bq (72.6 million pCi)	24
Occupational workers		
Annual limit of intake[b] Inhalation vs. oral		
Americium-241	200 Bq (5,400 pCi) vs. 50,000 Bq	25
Californium-252	1,000 Bq (27,000 pCi) vs. 200,000 Bq	25
Cesium-137	6 million Bq (162 million pCi) vs. 4 million Bq	
Cobalt-60	1 million Bq (27 million	25

Table 28. Criterion and other variables	Concentration or dose	Reference[a]
	pCi) vs. 7 million Bq	
Hydrogen-3	3 billion Bq (81 billion pCi) vs. 3 billion Bq	25
Iodine-125	2 million Bq (54 million pCi) vs. 1 million Bq	25
Iodine-129	300,000 Bq (8,100,000 pCi) vs. 200,000 Bq	25
Iodine-131	2 million Bq (54 million pCi) vs. 1 million Bq	25
Phosphorus-32	10 million Bq (270 million pCi) vs. 20 million Bq	25
Plutonium-239	200 Bq (5,400 pCi) vs. 200,000 Bq	25
Polonium-210	20,000 Bq (540,000 pCi) vs. 100,000 Bq	25
Radium-226	20,000 Bq (540,000 pCi) vs. 70,000 Bq	25
Strontium-90	0.1 million Bq (2.7 million pCi) vs. 1.0 million Bq	25
Thorium-232	40 Bq (1,000 pCi) vs. 30,000 Bq	25
Uranium-235	2,000 Bq (54,000 pCi) vs. 500,000 Bq	25
Total intake from all sources; Canada		
Lead-210	<4,000 Bq (<108,000 pCi)	26,27
Polonium-210	<10,000 Bq (<270,000 pCi)	26,27
Radium-226	<20,000 Bq (<540,000 pCi)	26,27
Thorium-228	<50,000 Bq (<1.35 million pCi)	26,27
Thorium-230	<40,000 Bq (<1.08 million pCi)	26,27
Thorium-232	<7,000 Bq (<189,000 pCi)	26,27
Uranium-238	<80,000 Bq (<2.1 million pCi)	26,27
Effective dose[b]		
Average annual	20 mSv (2 rem), not to exceed 50 mSv (5 rem)	28
Five-year maximum	<100 mSv (<10 rem), not to exceed 50 mSv (5 rem) in any year	28
Maximum permissible dose		
Whole body	50 mSv (5 rem) in any 1 year	21,22,29
Long-term accumulation to age N years	(N-18) x 50 mSv (5 rem)	21
Skin	150 mSv (15 rem) in any 1 year	21
Hands	750 mSv (75 rem) in any 1 year; not to exceed 250 mSv (25 rem) in 3 months	21
Forearms	300 mSv (30 rem) in any 1 year; not to exceed 100 mSv (10 rem) in 3 months	21
Skin and hands	500 mSv (50 rem) annually	19,28
Other organs	150 mSv (15 rem) in any 1 year; not to exceed 50	21

Table 28. Criterion and other variables	Concentration or dose	Reference[a]
	mSv (5 rem) in 3 months	
Pregnant women	5 mSv (0.5 rem) in gestation period	21
Eye lens	150 mSv (15 rem) annually	19,28
Soil		
Radium-226; maximum allowed	<185 Bq (<5,000 pCi)/kg over background in top 15 cm; <555 Bq (<15,000 pCi)/kg in soils at depth >15 cm.	3
Total gamma; maximum allowed	<0.2mSv (<0.00002 rem)/h over background	3

[a] 1, Gangopadhyay and Majumdar 1990; 2, Oge and Dickson 1990; 3, United States Code of Federal Regulations (CFR) 1990; 4, Wood 1991; 5, Bair et al. 1979; 6, Battiston et al. 1991; 7, Andersson et al. 1990; 8, Allaye-Chan et al. 1990; 9, Joshi 1991; 10, Hakanson and Andersson 1992; 11, Harrison 1991; 12, Gilbert et al. 1989; 13, Aii et al. 1990; 14, Johanson et al. 1989; 15, Johanson 1990; 16, Moss et al. 1989; 17, Crout et al. 1991; 18, Rose et al. 1990; 19, International Commission on Radiological Protection (ICRP) 1991a; 20, Lowe and Horrill 1991; 21, Hobbs and McClellan 1986; 22, ICRP 1977; 23, Gray et al. 1989; 24, CFR 1991; 25, Mefer 1990; 26, Clulow et al. 1991; 27, Clulow et al. 1992; 28, ICRP 1991b; 29, National Council on Radiation Protection and Measurements (NCRP) 1991.

[b] The Annual Limit of Intake (ALI) for any radionuclide is obtained by dividing the annual average effective dose limit (20 mSv) by the committed effective dose (E) resulting from the intake of 1 Bq of that radionuclide. ALI data for individual radionuclides are given in ICRP (1991b).

Astronauts between 25 and 55 years of age usually receive an average career dose of 2.0 Sv (1.0-3.0 Sv in females; 1.5-4.0 Sv in males), and this theoretically may cause a life shortening of 2,000 to 3,000 days (Wood 1991). Other environmental variables also shorten lives and include cigarette smoking (2,250 days), coal mining (1,100 days), and being 30% overweight (1,300 days); thus, models that assess the harm of a single variable such as radiation on life expectancy have to incorporate all known data and their interacting effects (Wood 1991).

Environmental dose-response models and animal epidemiological data are most frequently used to assess the risk from ionizing radiation. In its ideal form, a risk assessment should clearly present the rationale for an estimate of risk and should include the recognition of the roles of assumptions, approximations, data, theories, models, and deductions in arriving at an inference and a discussion of the involved uncertainties (Cothern et al. 1990). Current risk assessments of ionizing radiation hazards to all living organisms--not just humans--clearly require additional data and reinterpretation of existing data. Specifically, more effort is needed in the following areas: (1) measurement of concentrations of naturally occurring radionuclides and natural background doses in the environment as a baseline for studies of radiation effects (Templeton et al. 1971); (2) refinement of models of radionuclide transfer in food chains to aid in the assessment of radioactive releases from nuclear reactors and other point sources--including possible biomagnification by trophic components and turnover rates by receptor organisms (Kitchings et al. 1976); (3) continuance of protracted exposure studies to measure carcinogenesis in animal and human cell lines and the role of secondary factors--especially chemical agents--in radiation carcinogenesis (Little 1990); (4) research on radiation-induced recessive lethal mutations--the predominant type of radiation-induced mutation--and dominant mutation systems (Sankaranarayanan 1991c); (5) long-term studies to establish sensitive indicators of radiation stress on individuals and communities, including effects on growth and reproduction (Templeton et al. 1971); (6) clarification of the role of enzymes and proteins in repair of radiation-damaged cellular DNA and of mechanisms of enzymatic reactions leading to altered nucleotide sequences (Hagen 1990); (7) reinterpretation of low-level chronic irradiation effects on developing embryos under rigorously controlled conditions (Templeton et al. 1971); and (8) resolution of mathematical shape(s) of radiation dose-response curve(s; Hobbs and McClellan 1986).

Conclusions

Nuclear explosions and nuclear power production are the major sources of human radioactivity in the environment. Other sources include radionuclide use in medicine, industry, agriculture, education, and production; transport and disposal from these activities present opportunities for wastes to enter the environment. Dispersion of radioactive materials is governed by a variety of biogeochemical factors including winds, water currents, and biological vectors. Living organisms normally receive most of their external exposure to radiation from naturally occurring electromagnetic waves and their internal exposure from naturally occurring radionuclides such as potassium-40. Radiation exposure doses from natural sources of radiation are significantly modified by altitude, amount and type of radionuclides in the immediate vicinity, and route of exposure.

Radionuclide concentrations in representative field collections of biota tend to be elevated in the vicinity of nuclear fuel reprocessing, nuclear power production, and nuclear waste facilities; in locations that receive radioactive fallout from nuclear accidents and atmospheric nuclear tests; and near sites of repeated nuclear detonations. Radionuclide concentrations in field collections of living organisms vary significantly with organism age, size, sex, tissue, diet, and metabolism; season of collection; proximity to point source; and other biological, chemical, and physical variables. To date, no extinction of any animal population has been linked to high background concentrations of radioactivity.

The accident at the Chernobyl, Ukraine, nuclear reactor on 26 April 1986 contaminated much of the northern hemisphere, especially Europe, by releasing large amounts of radiocesium-137 and other radionuclides into the environment. In the immediate vicinity of Chernobyl, at least 30 people died, more than 115,000 others were evacuated, and the consumption of locally produced milk and other foods was banned because of radiocontamination. The most sensitive local ecosystems were the soil fauna and pine forest communities. Elsewhere, fallout from Chernobyl measurably contaminated freshwater, marine, and terrestrial ecosystems, including flesh and milk of domestic livestock. Reindeer (*Rangifer tarandus*) calves in Norway showed an increasing frequency of chromosomal aberrations that seemed to correlate with cesium-137 tissue concentrations; tissue concentrations in turn were related to cesium-137 in lichens, an efficient absorber of airborne particles that contain radiocesium and the main food source of reindeer during winter. A pattern similar to that of reindeer was documented in moose (*Alces alces*) in Scandinavia.

A dose and dose-rate dependent radiation effect on growth, survival, organ development, mutagenicity, fatal neoplasms, and other parameters exists for almost all organisms that were tested under laboratory conditions. Some discoveries suggest that low acute exposures of ionizing radiation may extend the life-span of certain species, although adverse genetic effects may occur under these conditions. In living organisms, the sensitivity to radiation is governed by ontogeny and phylogeny. Thus, rapidly dividing cells that are characteristic of embryos and fetuses are most radiosensitive, and evolutionarily advanced organisms such as mammals are more radiosensitive than primitive organisms. Between species in each taxonomic grouping are large variations in sensitivity to acute and chronic exposures of ionizing radiation and in ability to retain selected radionuclides; these processes are modified by many biological and abiotic variables.

Radiosensitive terrestrial plants are adversely affected at single exposures of 0.5-1.0 gray (Gy) and at chronic daily exposures of 0.2-0.65 Gy. Terrestrial insects are comparatively resistant to ionizing radiation; some species show growth stimulation and development at acute doses of 2 Gy--a demonstrably harmful dose for many species of vertebrates. Among aquatic organisms, the developing eggs and young of freshwater fishes are among the most sensitive tested organisms; death was observed at acute doses of 0.3-0.6 Gy and adverse effects on physiology and metabolism at chronic daily exposure rates of 0.01 Gy. The ability of aquatic organisms to concentrate radionuclides from the medium varies substantially with ecosystem, trophic level, radionuclide, proximity to radiation point source, and many other biological, chemical, and physical modifiers. In amphibians, radiation adversely affects limb regeneration, alters DNA metabolism, causes sterility, and increases the frequency of chromosomal aberrations.

Mortality patterns in some species of amphibians begin to stabilize about 200 days after exposure to a single acute dose of ionizing radiation and cannot be evaluated satisfactorily in the typical 30-day postexposure period. In birds, adverse effects on growth were noted at chronic daily exposures as low as 0.9-1.0 Gy and on survival and metabolism at single exposures to 2.1 Gy. Genotoxic effects were associated with whole-body loadings of 2,520 becquerels (Bq) of cesium-137/kg in mallards (*Anas platyrhynchos*). The radionuclide

retention in birds was modified by sex, season, and reproductive state. In mammals, embryos and fetuses of sensitive species were adversely affected at acute doses of 0.011-0.022 Gy. Humans exposed as fetuses to 0.18-0.55 Gy scored significantly lower on tests of intelligence.

No radiological criteria now exist for the protection of fishes, wildlife, or sensitive other natural resources. All current guides for protection from radiation target human health and are predicated on the assumption that protection of comparatively radiosensitive humans confers a high degree of protection to other life forms. Most authorities agree that significant harmful effects on humans occur under the following conditions: exposure of the whole body of women during the first 2 months of pregnancy to more than 5 millisieverts (mSv); exposure of the whole body to more than 50 mSv in any single year or to more than 2,000 mSv in a lifetime; annual inhalation intake by a 60-kg individual, in Bq/kg body weight (BW), of more than 0.7 of thorium-232, 3.3 of americium-241, 3.3 of plutonium-239, 16 of californium-252, 33 of uranium-235, 1,670 of strontium-90, 16,670 of cobalt-60, or 166,670 of phosphorus-32; annual ingestion intake by a 60-kg individual, in Bq/kg BW, of more than 3,330 of iodine-129, 16,670 of iodine-125, 16,670 of iodine-131, or 66,670 of cesium-137; or total annual intake, in Bq/kg BW, from all sources by a 60-kg person exceeds 66 of lead-210, 166 of polonium-210, 333 of radium-226, 670 of thorium-230, 830 of thorium-228, or 1,330 of uranium-238.

Current risk assessments of ionizing radiation hazards to living organisms require additional data and reinterpretation of existing data. Specifically, more effort seems needed in eight areas: (1) establishing a baseline for studies of radiation through measurement of naturally occurring radionuclides and natural background radiation doses; (2) refining radionuclide food-chain transfer models; (3) measuring the role of chemical agents in radiation-induced carcinogenesis; (4) accelerating research on radiation-induced lethal mutations; (5) initiating long-term studies to establish sensitive indicators of radiation stress on individuals and ecosystems; (6) clarifying the role of enzymes and proteins in repair of radiation-damaged cellular DNA; (7) reinterpreting embryotoxic effects of low-level chronic irradiation; and (8) resolving the mathematical shapes of radiation dose-response curves.

Acknowledgments

I greatly appreciate the scientific and technical input of E. K. Block, I. L. Brisbin, Jr., S. W. Fowler, J. B. Hunn, J. F. Moore, S. N. Wiemeyer, and several anonymous reviewers. I also thank L. J. Garrett and P. W. Manning for library services, M. G. Holmes for secretarial assistance, J. Hamilton for illustrations, and E. D. Rockwell for editorial services.

Cited Literature

Aarkrog, A. 1990. Environmental radiation and radiation releases. International Journal of Radiation Biology 57:619-631.

Abrahamson, S. 1990. Risk estimates: past, present, and future. Health Physics 59:99-102.

Ahman, B., S. Forberg, and G. Ahman. 1990a. Zeolite and bentonite as caesium binders in reindeer feed. Rangifer, Special Issue 3:73-82.

Ahman, G., B. Ahman, and A. Rydberg. 1990b. Consequences of the Chernobyl accident for reindeer husbandry in Sweden. Rangifer, Special Issue 3:83-88.

Aii, T., S. Kume, S. Takahashi, M. Kurihara, and T. Mitsuhashi. 1990. The effect of the radionuclides from Chernobyl on iodine-131 and cesium-137 contents in milk and pastures in south-western Japan. Japanese Society of Zootechnical Science 61:47-53.

Allaye-Chan, A. C., R. G. White, D. F. Holleman, and D. E. Russell. 1990. Seasonal concentrations of cesium-137 in rumen content, skeletal muscles and feces of caribou from the Porcupine herd: lichen ingestion rates and implications for human consumption. Rangifer, Special Issue 3:17-24.

Al-Izzi, M. A. J., S. K. Al-Maliky, and N. F. Jabbo. 1990. Effect of gamma rays on males of *Ectomylelois ceratoniae* Zeller (Lepidoptera: Pyralidae) irradiated as pupae or adults. Annales de la Societe Entomologique de France 26:65-69.

Ananthaswamy, H. N., and W. E. Pierceall. 1990. Molecular mechanisms of ultraviolet radiation carcinogenesis. Photochemistry and Photobiology 52:1119-1136.

Anderson, D. E., and M. Badzioch. 1991. Association between solar radiation and ocular squamous cell carcinoma in cattle. American Journal of Veterinary Research 52:784-788.

Anderson, L. E. 1990. Biological effects of extremely low-frequency and 60 Hz fields. Pages 196-235 *in* O. P. Ghandi, editor. Biological effects and medical applications of electromagnetic energy. Prentice Hall, Englewood Cliffs, N.J.

Anderson, S. H., G. J. Dodson, and R. I. Van Hook. 1976. Comparative retention of ^{60}Co, ^{109}Cd and ^{137}Cs following acute and chronic feeding in bobwhite quail. Pages 321-324 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Anderson, S. L., F. L. Harrison, G. Chan, and D. H. Moore 11. 1990. Comparison of cellular and whole-animal bioassays for estimation of radiation effects in the polychaete worm *Neanthes arenaceodentata* (Polychaeta). Archives of Environmental Contamination and Toxicology 19:164-174.

Anderson, S. S., F. R. Livens, and D. L. Singleton. 1990. Radionuclides in grey seals. Marine Pollution Bulletin 21:343-345.

Andersson, I., B. Teglof, and K. Elwinger. 1990. Transfer of ^{137}Cs from grain to eggs and meat of laying hens and meat of broiler chickens, and the effect of feeding bentonite. Swedish Journal of Agricultural Research 20:35-42.

Anspaugh, L. R., R. J. Catlin, and M. Goldman. 1988. The global impact of the Chernobyl reactor accident. Science 242:1513-1519.

Assimakopoulos, P. A., K. G. Ioannides, and A. A. Pakou. 1989. The propagation of the Chernobyl ^{131}I impulse through the air-grass-animal-milk pathway in northwestern Greece. The Science of the Total Environment 85:295-305.

Baeza, A., M. del Rio, C. Miro, A. Moreno, E. Navarro J. M. Paniagua, and M. A. Peris. 1991. Radiocesium and radiostrontium levels in song-thrushes (*Turdus philomelos*) captured in two regions of Spain. Journal of Environmental Radioactivity 13:13-23.

Bagshaw, C., and I. L. Brisbin, Jr. 1984. Long-term declines in radiocesium of two sympatric snake populations. Journal of Applied Ecology 21:407-413.

Bai, D. H. 1969. Radioactive contamination of the atmosphere, soils, and agricultural products in Korea, 1961-66. Pages 587-596 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from the Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Bair, W. J., J. W. Healy, and B. W. Wachholz. 1979. The Enewetak Atoll today. U.S. Department of Energy, Washington, D.C. 25 pp.

Barendsen, G. W. 1990. Mechanisms of cell reproductive death and shapes of radiation dose-survival curves of mammalian cells. International Journal of Radiation Biology 57:885-896.

Bastian, R. K., and W. B. Jackson. 1976. ^{137}Cs and ^{60}Co in a terrestrial community at Enewetok Atoll. Pages 314-320 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of American, Special Publication 1.

Battiston, G. A., S. Degetto, R. Gerbasi, G. Sbrignadello, R. Parigi-Bini, G. Xiccato, and M. Cinetto. 1991. Transfer of Chernobyl fallout radionuclides feed to growing rabbits: cesium-137 balance. The Science of the Total Environment 105:1-12.

Becker, C. D. 1990. Aquatic bioenvironmental studies: the Hanford experience 1944-84. Studies in Environmental Science 39. Elsevier Science Publishers, New York. 306 pp.

Beach, H. 1990. Coping with the Chernobyl disaster: a comparison of social effects in two reindeer-herding areas. Rangifer, Special Issue 3:25-34.

Belli, M., A. Drigo, S. Menegon, A. Menin, P. Nazzi, U. Sansone, and M. Toppano. 1989. Transfer of Chernobyl fall-out caesium. radioisotopes in the cow food chain. The Science of the Total Environment 85:169-177.

Benjamin, S. A., G. M. Angleton, A. C. Lee, W. J. Saunders, and J. S. Williams. 1990. Health effects from whole-body irradiation during development in beagles: studies at Colorado State University. Radiation Research 124:366-368.

Beresford, N. A. 1989. The transfer of Ag-110m to sheep tissues. The Science of the Total Environment 85:81-90.

Billen, D. 1990. Spontaneous DNA damage and its significance for the "negligible dose" controversy in radiation protection. Radiation Research 124:242-245.

Boag, T. S., G. I. Johnson, M. Izard, C. Murray, and K. C. Fitzsimmons. 1990. Physiological responses of mangoes cv. Kensington Pride to gamma irradiation treatment as affected by fruit maturity and ripeness. Annals of Applied Biology 116:177-187.

Bonham, K., and A. D. Welander. 1963. Increase in radioresistance of fish to lethal doses with advancing embryonic development. Pages 353-358 *in* V. Schultz and A.W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Book, S. A. 1969. Fallout cesium-137 accumulation in two subpopulations of black-tailed deer (*Odocoileus hemionus columbianus*). M. A. Thesis, University of California, Berkeley. 61 pp.

Bothmer, S. V., K. J. Johanson, and R. Bergstrom. 1990. Cesium-137 in moose diet; considerations on intake and accumulation. The Science of the Total Environment 91:87-96.

Bowden, G. T., D. Jaffe, and K. Andrews. 1990. Biological and molecular aspects of radiation carcinogenesis in mouse skin. Radiation Research 121:235-241.

Bowen, V. T., J. S. Olsen, C. L. Osterberg, and J. Ravera. 1971. Ecological interactions of marine radioactivity. Pages 200-222 *in* National Academy of Sciences. Radioactivity in the marine environment. National Academy of Sciences, Panel on radioactivity in the marine environment. Washington, D.C.

Brisbin, I. L., Jr. 1991. Avian radioecology. Pages 69-140 *in* D. M. Power, editor. Current ornithology, Volume 8. Plenum Press, New York.

Brisbin, I. L., Jr., D. D. Breshears, K. L. Brown, M. Ladd, M. H. Smith, M. W. Smith, and A. L. Towns. 1989. Relationships between levels of radiocaesium in components of terrestrial and aquatic food webs of a contaminated streambed and floodplain community. Journal of Applied Ecology 26:173-182.

Brisbin, I. L., Jr., M. A. Staton, J. E. Pinder III, and R. A. Geiger. 1974. Radiocesium concentrations of snakes from contaminated and non-contaminated habitats of the AEC Savannah River Plant. Copeia 1974:501-506.

Brittain, J. E., A. Storruste, and E. Larsen. 1991. Radiocesium in brown trout (*Salmo trutta*) from a subalpine lake ecosystem after the Chernobyl reactor accident. Journal of Environmental Radioactivity 14:181-191.

Brown, B. 1966. Long-term radiation damage evaluation of life-span studies. Memorandum RM-5083-TAB. The Rand Corporation, Santa Monica, Calif. 66 pp.

Bruenger, F. W., R. D. Lloyd, G. N. Taylor, S. C. Miller, and C. W. Mays. 1990. Kidney disease in beagles injected with polonium-210. Radiation Research 122:241-251.

Cadwell, L. L., R. G. Schreckhise, and R. E. Fitzner. 1979. Cesium-137 in coots (*Fulica americana*) on Hanford waste ponds: contribution to population dose and offsite transport estimates. Pages 485-491 *in* Low-level radioactive waste management: proceedings of Health Physics Society twelfth midyear topical symposium, 11-15 February 1979, Williamsburg, Va.

Calamosca, M., P. Pagano, F. Trent, L. Zaghini, G. Gentile, G. Tarroni, and L. Morandi. 1990. A modelistic approach to evaluate the factors affecting the ^{137}Cs transfer from mother to fetus in cattle. Deutsche Tieraerztliche Wochenschrift 97:452-456.

Canfi, A., R. Chayoth, S. Weill, and E. Bedrak. 1990. The reproductive system of male rats exposed to very low doses of ionizing radiation, 1: hormonal profile of animals exposed after sexual maturity. Andrologia 22:129-136.

Carlson, L., and B. Erlandsson. 1991. Seasonal variation of radionuclides in *Fucus vesiculosus* L. from the Oresund, southern Sweden. Environmental Pollution 73:53-70.

Cecil, L. D., and T. F. Gesell. 1992. Sampling and analysis for radon-222 dissolved in ground water and surface water. Environmental Monitoring and Assessment 20:55-66.

Chakravarti, D., and R. Eisler. 1961. Strontium-90 and gross beta activity in the fat and nonfat fractions of the liver of the coconut crab (*Birgus latro*) collected at Rongelap Atoll during March 1958. Pacific Science 15:155-159.

Clark, M. J., and F. B. Smith. 1988. Wet and dry deposition of Chernobyl releases. Nature 332:245-249.

Cleary, S. F. 1990. Cellular effects of radiofrequency electro-magnetic fields. Pages 339-356 *in* O. P. Ghandi, editor. Biological effects and medical applications of electromagnetic energy. Prentice Hall, Englewood Cliffs, N.J.

Clooth, G., and D. C. Aumann. 1990. Environmental transfer parameters and radiological impact of the Chernobyl fallout in and around Bonn (FRG). Journal of Environmental Radioactivity 12:97-119.

Clulow, F. V., T. P. Lim, N. K. Dave, and R. Avadhanula. 1992. Radium-226 levels and concentration ratios between water, vegetation, and tissues of ruffed grouse (*Bonasa umbellus*) from a watershed with uranium tailings near Elliot Lake, Canada. Environmental Pollution 77:39-50.

Clulow, F. V., M. A. Mirka, N. K. Dave, and T. P. Lim. 1991. ^{226}Ra and other radionuclides in water, vegetation, and tissues of beavers (*Castor canadensis*) from a watershed containing U tailings near Elliot Lake, Canada. Environmental Pollution 69:277-310.

Coggle, J. E., and J. P. Williams. 1990. Experimental studies of radiation carcinogenesis in the skin: a review. International Journal of Radiation Biology 57:797-808.

Conkic, L., M. Ivo, S. Lulic, K. Kosatic, J. Simor, P. Vancsura, J. Slivka, and I. Bikit. 1990. The impact of the Chernobyl accident on the radioactivity of the River Danube. Water Science and Technology 22:195-202.

Cothern, C. R., D. J. Crawford-Brown, and M. E. Wrenn. 1990. Application of environmental dose-response models to epidemiology and animal data for the effects of ionizing radiation. Environment International 16:127-140.

Coughtrey, P. J., J. A. Kirton, and N. G. Mitchell. 1989. Caesium transfer and cycling in upland pastures. The Science of the Total Environment 85:149-158.

Coulton, L. A., and A. T. Barker. 1991. The effect of low-frequency pulsed magnetic fields on chick embryonic growth. Physics in Medicine and Biology 36:369-381.

Crete, M., M. A. Lefebvre, M. B. Cooper, H. Marshall, J. L. Benedetti, P. E. Carriere, and R. Nault. 1990. Contaminants in caribou tissues from northern Quebec. Rangifer, Special Issue 3:289.

Cristaldi, M., E. D'Arcangelo, L. A. Ieradi, D. Mascanzoni, T. Mattei, and I. V. A. Castelli. 1990. ^{137}Cs determination and mutagenicity tests in wild *Mus musculus domesticus* before and after the Chernobyl accident. Environmental Pollution 64:1-9.

Cristaldi, M., L. A. Ieradi, D. Mascanzoni, and T. Mattei. 1991. Environmental impact of the Chernobyl accident: mutagenesis in bank voles from Sweden. International Journal of Radiation Biology 59:31-40.

Cronkite, E. P., V. P. Bond, W. H. Chapman, and R. H. Lee. 1955. Biological effect of atomic bomb gamma radiation. Science 122:148-150.

Cross, F. T. 1990. Health effects and risks of radon exposure. Pages 223-237 *in* S. K. Majumdar, R. F. Schmalz, and E. W. Miller, editors. Environmental radon: occurrence, control and health hazards. The Pennsylvania Academy of Science, Easton, Pa.

Crout, N. M. J., N. A. Beresford, and B. J. Howard. 1991. The radioecological consequences for lowland pastures used to fatten upland sheep contaminated with radiocaesium. The Science of the Total Environment 103:73-87.

Crowley, M., P. I. Mitchell, J. O'Grady, J. Vires, J. A. Sanchez-Cabeza, A. Vidal-Quadras, and T. P. Ryan. 1990. Radiocaesium and plutonium concentrations in *Mytilus edulis* (L.) and potential dose implications for Irish critical groups. Ocean and Shoreline Management 13:149-161.

Cummings, S. L., J. H. Jenkins, T. T. Fendley, L. Bankert, P. H. Bedrosian, and C. R. Porter. 1971. Cesium-137 in white-tailed deer as related to vegetation and soils of the southeastern United States. Pages 123-128 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from the National Technical Information Service, Springfield, Va.

Curnow, R. D. 1971. Assimilation and retention of zinc-65 by the mallard duck (*Anas platyrhynchos*). Pages 381-384 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from the National Technical Information Service, Springfield, Va.

Curtis, E. J. C., D. S. Popplewell, and G. J. Ham. 1991. Radioactivity in environmental samples taken in the Sellafield, Ravenglass and Morecambe Bay areas of west Cumbria. The Science of the Total Environment 105:211-231.

Cushing, C. E., editor. 1976. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1. 401 pp.

Daburon, F., Y. Archimbaud, J. Cousi, G. Fayart, D. Hoffschir, I. Chevallereau, and H. Le Creff. 1991. Radiocaesium transfer to ewes fed contaminated hay after the Chernobyl accident: effect of vermiculite and AFCF (ammonium ferricyanoferrate) as counter-measures. Journal of Environmental Radioactivity 14:73-84.

Daburon, F., G. Fayart, and Y. Tricaud. 1989. Caesium chronic administration. The Science of the Total Environment 85:253-261.

Dahlman, R. C., and P. V. Voris. 1976. Cycling of ^{137}Cs in soil and vegetation of a flood plain 30 years after initial contamination. Pages 291-298 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Davidson, S. F., S. K. Brantley, and S. K. Das. 1991. The effects of ultraviolet radiation on wound healing. British Journal of Plastic Surgery 44:210-213.

Desmet, G. M., L. R. Van Loon, and B. J. Howard. 1991. Chemical speciation and bioavailability of elements in the environment and their relevance to radioecology. The Science of the Total Environment 100:105-124.

Di Gregorio, D., P. B. Dunaway, and G. E. Cosgrave., 1971. Effect of acute gamma irradiation on the reproduction of *Peromyscus leucopus*. Pages 1076-1081 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 2. Available from the National Technical Information Service, Springfield, Va.

Donaldson, L. R., and K. Bonham. 1970. Effects of chronic exposure of chinook salmon eggs and alevins to gamma irradiation. Transactions of the American Fisheries Society 99:112-119.

Donaldson, L. R., and R. F. Foster. 1957. Effects of radiation on aquatic organisms. Pages 96-102 *in* National Academy of Sciences. The effects of atomic radiation on oceanography and fisheries. Publication 551. National Academy of Sciences-National Research Council, Washington, D.C.

Douka, C. E., and A. C. Xenoulis. 1991. Radioactive isotope uptake in a grass-legume association. Environmental Pollution 73:11-23.

Dunaway, P. B., L. L. Lewis, J. D. Story, J. A. Payne, and J. M. Inglis. 1969. Radiation effects in the soricidae, cricetidae, and muridae. Pages 173-184 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from the Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Dunaway, P. B., J. D. Story, and J. T. Kitchings. 1971. Radiation effects and radionuclide excretion in a natural population of pine voles. Pages 1055-1064 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 2. Available from the National Technical Information Service, Springfield, Va.

Egami, M. I., C. Segreto, J. Kerbauy, and Y. Juliano. 1991. Effects of whole-body X-irridation on the peripheral blood of primate *Cebus apella*. Brazilian Journal of Medical and Biological Research 24:271-274.

Eidus, L. K., Y. N. Korystov, O. R. Dobrovinskaja, and V. V. Shaposhnikova. 1990. The mechanism of radiation-induced interphase death of lymphoid cells: a new hypothesis. Radiation Research 123:17-21.

Eikelmann, I. M. H., K. Bye, and H. D. Sletten. 1990. Seasonal variation of cesium 134 and cesium 137 in semidomestic reindeer in Norway after the Chernobyl accident. Rangifer, Special Issue 3:35-38.

Eisler, R. 1961. Effects of visible radiation on salmonoid embryos and larvae. Growth 25:281-346.

Ekker, M., B. M. Jenssen, and K. Zahlsen. 1990. Radiocesium in Norwegian carnivores following the Chernobyl fallout. Page 275 *in* S. Myrberget, editor. Volume 1: population dynamics. Transactions of the XIXth IUGB Congress. The International Union of Game Biologists, September 1989, Trondheim, Norway.

Emery, R. M., D. C. Klopfer, T. R. Garland, and W. C. Weimer. 1976. The ecological behavior of plutonium and americium in a freshwater pond. Pages 74-85 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Engel, D. W., and E. M. Davis. 1976. The effects of gamma radiation on the survival and growth of brine shrimp, *Artemia salina*. Pages 376-380 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Eriksson, O. 1990. ^{137}Cs in reindeer forage plants 1986-88. Rangifer, Special Issue 3:11-14.

Evans, H. H. 1990. Ionizing radiation mutagenesis in mammalian cells. Pages 211-219 *in* UCLA symposia colloquium. Ionizing radiation damage to DNA: molecular aspects, Wiley-Liss, N.Y.

Fanton, J. W., and J. G. Golden. 1991. Radiation-induced endometriosis in *Macaca mulatta*. Radiation Research 126:141-146.

Farris, G. C., F. W. Whicker, and A. H. Dahl. 1969. Strontium-90 levels in mule deer and forage plants. Pages 602-608 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Folsom, T. R., and J. H. Harley. 1957. Comparisons of some natural radiations received by selected organisms. Pages 28-33 *in* National Academy of Sciences. The effects of atomic radiation on oceanography and fisheries. Publication 551, National Academy of Sciences-National Research Council, Washington, D.C.

Folsom, T. R., D. R. Young, V. F. Hodge, and R. Grismore. 1971. Variations of ^{54}Mn, ^{60}Co, ^{65}Zn, ^{110m}Ag, and ^{108m}Ag in tunas. Pages 721-730 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 2. Available from The National Technical Information Service, Springfield, Va.

Fowler, S. W., P. Buat-Menard, Y. Yokoyama, S. Ballestra, E. Holm, and H. Van Nguyen. 1987. Rapid removal of Chernobyl fallout from Mediterranean surface waters by biological activity. Nature 329:56-58.

Fry, R. J. M. 1991. Radiation carcinogenesis in the whole-body system. Radiation Research 126:157-161.

Gangopadhyay, A., and S. K. Majumdar. 1990. Radon and health consequences: an overview. Pages 209-237 *in* S. K. Majumdar, R. F. Schmalz, and E. W. Miller, editors. Environmental radon: occurrence, control and health hazards. The Pennsylvania Academy of Science, Easton.

Garaj-Vrhovac, V., D. Horvat, and Z. Koren. 1990. The effect of microwave radiation on the cell genome. Mutation Research 243:87-93.

Garnier, J., and J. P. Baudin. 1990. Retention of ingested ^{110m}Ag by a freshwater fish, *Salmo trutta* L. Water, Air, and Soil Pollution 50:409-421.

Garnier, J., J. P. Baudin, and L. Folquier. 1990. Accumulation from water and depuration of ^{110m}Ag by a freshwater fish, *Salmo trutta* L. Water Research 24:1407-1414.

Gaubin, Y., M. Depoux, B. Pianezzi, G. Gasset, C. Heilmann, and H. Planel. 1990. Investigations on the effects of cosmic rays on *Artemia* cysts and tobacco seeds; results of Exobloc II experiment, flown aboard Biocosmos 1887. International Journal of Radiation Applications and Instrumentation 17:133-144.

George, L. S., C. E. Dallas, I. L. Brisbin, Jr., and D. L. Evans. 1991. Flow cytometric DNA analysis of ducks accumulating ^{137}Cs on a reactor reservoir. Ecotoxicology and Environmental Safety 21:337-347.

Geraci, J. P., M. S. Mariano, and K. L. Jackson. 1991. Hepatic radiation injury in the rat. Radiation Research 124:65-72.

Ghandi, O. P. 1990. Electromagnetic energy absorption in humans and animals. Pages 174-194 *in* O. P. Ghandi, editor. Biological effects and medical applications of electromagnetic energy. Prentice Hall, Englewood Cliffs, N.J.

Giannetti, M., A. Trux, B. Giannetti, and Z. Zubrzycki. 1990. *Xenopus laevis* South African clawed toad--a potential indicator for radioactive contamination in ecological systems? Pages 279-285 *in* First international symposium on biology and physiology of amphibians. Karlsruhe, Federal Republic of Germany, 31 August-3 September 1988. Gustav Fischer, Stuttgart.

Gilbert, R. O., D. W. Engel, and L. R. Anspaugh. 1989. Transfer of aged $^{239+240}Pu$, ^{238}Pu, ^{241}Am, and ^{137}Cs to cattle grazing a contaminated arid environment. The Science of the Total Environment 85:53-62.

Glasstone, S. 1958. Sourcebook on atomic energy. Second edition. Van Nostrand, Princeton, N.J. 641 pp.

Godoy, J. M., J. R. D. Guimaraes, J. C. A. Pereira, and M. A. Pieres do Rio. 1991. Cesium-137 in the Goiania waterways during and after the radiological accident. Health Physics 60:99-103.

Golley, F. B., and J. B. Gentry. 1969. Response of rodents to acute gamma radiation under field conditions. Pages 166-172 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Gorbman, A., and M. S. James. 1963. An exploratory study of radiation damage in the thyroids of coral reef fishes from the Eniwetok Atoll. Pages 385-399 *in* V. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Gray, R. H., R. E. Jaquish, P. J. Mitchell, and W. H. Rickard. 1989. Environmental monitoring at Hanford, Washington, USA: a brief site history and summary of recent results. Environmental Management 13:563-572.

Grzybowska, D. 1989. Concentration of ^{137}Cs and ^{90}Sr in marine fish from the southern Baltic Sea. Acta Hydrobiologica 31:139-147.

Guary, J. C., and S. W. Fowler. 1990. Experimental study of the transfer of transuranium. nuclides in marine decapod crustaceans. Marine Ecology Progress Series 60:253-270.

Gupta, M. L., and P. Umadevi. 1990. Response of reptilian liver to external gamma irradiation. Radiobiologica Radiotherapia 31:285-288.

Gustafson, P. F. 1969. Cesium-137 in freshwater fish during 1954-1965. Pages 249-257 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Hader, D. P., and M. Hader. 1991. Effects of solar and artificial U.V. radiation on motility and pigmentation in the marine *Cryptomonas maculata*. Environmental and Experimental Botany 31:33-41.

Hader, D. P., S. M. Liu, M. Hader, and W. Ullrich. 1990. Photoorientation, motility and pigmentation in a freshwater *Peridinium* affected by ultraviolet radiation. General Physiology and Biophysics 9:361-371.

Hagen, U. 1990. Molecular radiation biology: future aspects. Radiation and Environmental Biophysics 29:315-322.

Hakanson, L., and T. Andersson. 1992. Remedial measures against radioactive caesium. in Swedish lake fish after Chernobyl. Aquatic Sciences 54:141-164.

Halford, D. K., O. D. Markham, and G. C. White. 1983. Biological elimination rates of radioisotopes by mallards contaminated at a liquid radioactive waste disposal area. Health Physics 45:745-756.

Ham, G. J., J. D. Harrison, D. S. Popplewell, and E. J. C. Curtis. 1989. The distribution of ^{137}Cs, plutonium and americium in sheep. The Science of the Total Environment 85:235-244.

Handl, J., and A. Pfau. 1989. Long-term transfer of I-129 into the food chain. The Science of the Total Environment 85:245-252.

Handl, J., A. Pfau, and F. W. Huth. 1990. Measurements of ^{129}I into the food chain. Health Physics 58:609-618.

Hanson, L. H. 1990. Sterilizing effects of cobalt-60 and cesium-137 radiation on male sea lampreys. North American Journal of Fisheries Management 10:352-361.

Hanson, W. C. 1976. Studies of transuranic elements in Arctic ecosystems. Pages 28-39 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national Symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Harrison, F. L., K. M. Wong, and R. E. Heft. 1976. Role of solubles and particulates in radionuclide accumulation in the oyster *Crassostrea gigas* in the discharge canal of a nuclear power plant. Pages 9-20 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Harrison, J. D. 1991. The gastrointestinal absorption of the actinide elements. The Science of the Total Environment 100:43-60.

Harrison, J. D., J. W. Haines, and D. S. Popplewell. 1990. The gastrointestinal absorption and retention of niobium in adult and newborn guinea pigs. International Journal of Radiation Biology 58:177-186.

Hatfield, T. W., D. M. Skauen, and J. S. Rankin, Jr. 1963. Gross beta radioactivity in marine organisms. Pages 141-143 *in* V. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Havlik, B., and E. Robertson. 1971. Radium uptake by freshwater algae. Pages 372-380 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Hetherington, J. A., D. F. Jefferies, N. T. Mitchell, R. J. Pentreath, and D. S. Woodhead. 1976. Environmental and public health consequences of the controlled disposal of transuranic elements to the marine environment. Pages 139-154 *in* Transuranium nuclides in the environment. IAEA-SM-199/11, International Atomic Energy Agency, Vienna.

Hinton, T. G., and D. E. Scott. 1990. Radioecological techniques for herpetology, with an emphasis on freshwater turtles. Pages 267-7287 *in* J. W. Gibbons, editor. Life history and ecology of the slider turtle. Smithsonian Institution Press, Washington, D.C.

Hobbs, C. H., and R. O. McClellan. 1986. Toxic effects of radiation and radioactive materials. Pages 669-705 *in* C. D. Klaassen, M. O. Amdur, and J. Doull, editors. Casarett and Doull's toxicology. Third edition. Macmillan, New York.

Holcomb, C. M., C. G. Jackson, Jr., M. M. Jackson, and S. Kleinbergs. 1971. Occurrence of radionuclides in the exoskeleton of turtles. Pages 385-389 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Holleman, D. F., R. G. White, and A. C. Allaye-Chan. 1990. Modelling of radiocesium transfer in the lichen-reindeer/caribou-wolf food chain. Rangifer, Special Issue 3:39-42.

Holtzman, R. B. 1969. Concentrations of the naturally occurring radionuclides ^{226}Ra, ^{210}Pb and ^{210}Po in aquatic fauna. Pages 535-546 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Hopewell, J. W. 1990. The skin: its structure and response to ionizing radiation. International Journal of Radiation Biology 57:751-774.

Hove, K., O. Pederson, T. H. Garmo, H. S. Hansen, and H. Staaland. 1990a. Fungi: a major source of radiocesium contamination of grazing ruminants in Norway. Health Physics 59:189-192.

Hove, K., H. Staaland, O. Pedersen, and H. D. Sletten. 1990b. Effect of Prussian blue (ammonium-iron-hexacyanoferrate) in reducing the accumulation of radiocesium in reindeer. Rangifer, Special Issue 3:43.

Imanaka, T., and H. Koide. 1990. Radiocesium concentration in milk after the Chernobyl accident in Japan. Journal of Radioanalytical and Nuclear Chemistry 145:151-158.

International Atomic Energy Agency (1AEA). 1976. Effects of ionizing radiation on aquatic organisms and ecosystems. Technical Reports Series 172. International Atomic Energy Agency, Vienna, Austria. 131 pp.

International Atomic Energy Agency (IAEA). 1992. Effects of ionizing radiation on plants and animals at levels implied by current radiation protection standards. Technical Reports Series 332. International Atomic Energy Agency, Vienna, Austria. 74 pp.

International Commission on Radiological Protection (ICRP). 1977. Recommendations of the international commission on radiological protection. ICRP publication 26. Annals of the ICRP 1(3):1-53.

International Commission on Radiological Protection (ICRP). 1991a. 1990 recommendations of the international commission on radiological protection. ICRP publication 60. Annals of the ICRP 21(1-3):1-201.

International Commission on Radiological Protection (ICRP). 1991b. Annual limits on intake of radionuclides by workers based on the 1990 recommendations. ICRP publication 61. Annals of the ICRP 21(4):1-41.

Ioannides, K. G., and A. A. Pakou. 1991. Radioiodine retention in ovine thyroids in northwestern Greece following the reactor accident at Chernobyl. Health Physics 60:517-521.

Iverson, S. L., and B. N. Turnea. 1976. Effects of acute irradiation on survival of captive and free-ranging meadow voles. Pages 359-362 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Jaenke, R. S., and G. M. Angleton. 1990. Perinatal radiation-induced damage in the beagle. Radiation Research 122:58-65.

Jandl, J., H. Prochazka, and D. Luks. 1991. The biological half-life of ^{137}Cs in snails. Journal of Radioanalytical and Nuclear Chemistry 153:327-332.

Jenkins, J. H., and T. T. Fendley. 1971. Radionuclide biomagnification in coastal-plain deer. Pages 116-122 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Jenkins, J. H., J. R. Monroe, and F. B. Golley. 1969. Comparison of fallout ^{137}Cs accumulation and excretion in certain southeastern mammals. Pages 623-626 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Johanson, K. J. 1990. The consequences in Sweden of the Chernobyl accident. Rangifer, Special Issue 3:9-10.

Johanson, K. J., G. Karlen, and J. Bertilsson. 1989. The transfer of radiocesium from pasture to milk. The Science of the Total Environment 85:73-80.

Jones, B. 1990. Radiation effects in reindeer. Rangifer, Special Issue 3:15-16.

Jones, B. E. V., O. Eriksson, and M. Nordkvist. 1989. Radiocesium uptake in reindeer on natural pasture. The Science of the Total Environment 85:207-212.

Jordan, C. F. 1969. Recovery of a tropical rain forest after gamma irradiation. Pages 88-109 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Joseph, A. B., P. F. Gustafson, I. R. Russell, E. A. Schuert, H. L. Volchok, and A. Tamplin. 1971. Sources of radioactivity and their characteristics. Pages 6-41 *in* National Academy of Sciences. Radioactivity in the marine environment. National Academy of Sciences, panel on radioactivity in the marine environment, Washington, D.C.

Joshi, S. R. 1991. Radioactivity in the Great Lakes. The Science of the Total Environment 100:61-104.

Kahn, B. 1971. Radionuclides in the environment at nuclear power stations. Pages 30-36 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Kalas, J. A., S. Bretten, I. Byrkjedal, and O. Njastad. 1994. Radiocesium (^{137}Cs) from the Chernobyl reactor in Eurasian woodcock and earthworms in Norway. Journal of Wildlife Management 58:141-147.

Kamiguchi, Y., H. Tateno, and K. Mikamo. 1990. Types of structural chromosome aberrations and their incidences in human spermatozoa X-irradiated in vitro. Mutation Research 228:133-140.

Karu, T. I. 1990. Effects of visible radiation on cultured cells. Photochemistry and Photobiology 52:1089-1098.

Kaye, S. V., and P. B. Dunaway. 1963. Estimation of dose rate and equilibrium state from bioaccumulation of radionuclides by mammals. Pages 107-111 *in* V. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Kedhi, M. 1990. Aerosol, milk and wheat flour radioactivity in Albania caused by the Chernobyl accident. Journal of Radioanalytical and Nuclear Chemistry 146:115-124.

Kershaw, P. J., and D. S. Woodhead, editors. 1991. Radionuclides in the study of marine processes. Elsevier, N.Y. 393 pp.

Kiefer, J. 1990. Biological radiation effects. Springer-Verlag, Berlin. 444 pp.

Kim, J. H., L. R. Mandell, and R. Leeper. 1990. Radiation effects on the thyroid gland. Advances in Radiation Biology 14:119-156.

King, G. L., and M. R. Landauer. 1990. Effects of zacopride and BMY25801 (batanopride) on radiation-induced emesis and locomotion behavior in the ferret. The Journal of Pharmacology and Experimental Therapeutics 253:1026-1033.

Kitchings, T., D. DiGregorio, and P. V. Voris. 1976. A review of the ecological parameters of radionuclide turnover in vertebrate food chains. Pages 304-313 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Kligman, L. H., and A. M. Kligman. 1990. Ultraviolet radiation-induced skin aging. Skinscreens: Development, Evaluation, and Regulatory Aspects 10:55-72.

Kliment, V.1991. Contamination of pork by caesium radioisotopes. Journal of Environmental Radioactivity 13:117-124.

Kodrich, W. R., and C. A. Tryon. 1971. Effects of season on thyroid release of iodine-131 in free-ranging eastern chipmunks (*Tamias striatus*). Pages 260-264 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Korhonen, R. 1990. Modeling transfer of ^{137}Cs fallout in a large Finish watercourse. Health Physics 59:443-454.

Kshirsagar, S. G. 1990. The metabolism of radium-226 during pregnancy in the rat. Radiation Research 122:294-300.

Kudo, A., Y. Mahara, T. Kauri, and D. C. Santry. 1991. Fate of plutonium released from the Nagasaki A-bomb, Japan. Pages 291-300 *in* P. Grau, W. Gujer, K. J. Ives, D. Jenkins, H. Kroiss, A. C. Di Pinto, M. Suzuki, D. F. Torien, A. Milburn, E. J. Izod, and P. T. Nagle, editors. Water pollution research and control, Kyoto, 1990. Part 1. Proceedings of the fifteenth biennial conference of the international association on water pollution research and control, held in Kyoto, Japan, 29 July-3 August 1990. Pergamon Press, Oxford, England.

Lamb, T., J. W. Bickman, J. W. Gibbons, M. J. Smolen, and S. McDowell. 1991. Genetic damage in a population of slider turtles (*Trachemys scripta*) inhabiting a radioactive reservoir. Archives of Environmental Contamination and Toxicology 20:138-142.

Landesman, R. H., and W. S. Douglas. 1990. Abnormal limb regeneration in adult newts exposed to a pulsed electromagnetic field. Teratology 42:137-145.

League of Women Voters Education Fund (LWV) 1985. The nuclear waste primer. Nick Lyons Books, New York. 90 pp.

Lesser, M. P., and J. M. Shick. 1990. Effects of visible and ultraviolet radiation on the ultrastructure of zooxanthellae (*Symbiodinium sp.*) in culture and in situ. Cell and Tissue Research 261:501-508.

Lett, J. T. 1990. Damage to DNA and chromatin structure from ionizing radiations, and the radiation sensitivities of mammalian cells. Progress in Nucleic Acid Research and Molecular Biology 39:305-352.

Levy, C. K., K. A. Youngstrom, and C. J. Maletskos. 1976. Whole-body gamma-spectroscopic assessment of environmental radionuclides in recapturable wild birds. Pages 113-122 *in* C.E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Little, J. B. 1990. Low-dose radiation effects: interactions and synergism. Health Physics 59:49-55.

Lloyd, R. D., F. W. Bruenger, S. C. Miller, W. Angus, G. N. Taylor, W. S. S. Jee, and E. Polig. 1991. Distribution of radium-induced bone cancers in beagles and comparison with humans. Health Physics 60:435-438.

Lorenz, E., L. O. Jacobson, E. W. Heston, M. Shimkin, A. B. Eschenbrenner, M. K. Deringer, J. Doniger, and R. Schweisthal. 1954. Effects of long-continued total-body gamma irradiation on mice, guinea pigs, and rabbits. III. Effects on life span, weight, blood picture, and carcinogenesis and the role of the intensity of radiation. Pages 24-148 *in* R. E. Zirkle, editor. Biological effects of X and gamma radiation. McGraw-Hill, New York.

Lowe, V. P. W. 1991. Radionuclides and the birds at Ravenglass. Environmental Pollution 70:1-26.

Lowe, V. P. W., and A. D. Horrill. 1991. Caesium concentration. factors in wild herbivores and the fox (*Vulpes vulpes* L). Environmental Pollution 70:93-107.

Lowman, F. G., T. R. Rice, and F. A. Richards. 1971. Accumulation and redistribution of radionuclides by marine organisms. Pages 161-199 *in* National Academy of Sciences. Radioactivity in the marine environment. National Academy of Sciences, panel on radioactivity in the marine environment. Washington, D.C.

Lucke-Huhle, C., B. Gloss, and P. Herrlich. 1990. Radiation-induced gene amplification in rodent and human cells. Acta Biologica Hungarica 41:159-171.

Luckey, T. D. 1980. Hormesis with ionizing radiation. CRC Press, Boca Raton, Fla. 222 pp.

Maier, M. A., and M. R. Landauer. 1990. Onset of behavioral effects in mice exposed to 10 Gy ^{60}Co radiation. Aviation Space and Environmental Medicine 61:893-898.

Majundar, S. K., R. F. Schmalz, and E. W. Miller, editors. 1990. Environmental radon: occurrence, control, and health hazards. The Pennsylvania Academy of Science, Easton. 436 pp.

Malhotra, N., N. Rani, K. Rana, and R. K. Malhotra. 1990. Radiation induced blood pathology in chick erythrocytes and related parameters. Experimental Pathology 38:241-248.

Markham, O. D., T. E. Hakonson, and J. S. Morton. 1983. Iodine-129 in mule deer thyroids in the Rocky Mountain west. Health Physics 45:31-37.

Mascanzoni, D., S. V. Bothmer, T. Mattei, and M. Cristaldi. 1990. Small mammals as biological indicators of radioactive contamination of the environment. The Science of the Total Environment 99:61-66.

Mathiesen, S. D., L. M. Nordoy, and A. S. Blix. 1990. Elimination of radiocesium in contaminated adult Norwegian reindeer. Rangifer, Special Issue 3:49.

McCormack, M., A. H. W. Nias, and E. Smith. 1990. Chronic anemia, hyperbaric oxygen and tumour radiosensitivity. The British Journal of Radiology 63:752-759.

McCormick, J. F. 1969. Effects of ionizing radiation on a pine forest. Pages 78-87 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

McInnes, D. O., and T. T. Y. Wong. 1990. Mediterranean fruitfly: interference of oviposition by radiation-sterilized females in field cages. Entomologia Experimentalis et Applicata 56:125-130.

McKay, W. A., and N. J. Pattenden. 1990. The transfer of radionuclides from sea to land via the air: a review. Journal of Environmental Radioactivity 12:49-77.

McLean, A. S. 1973. Early adverse effects of radiation. British Medical Journal 29:69-73.

Mele, P. C., C. G. Franz, and J. R. Harrison. 1990. Effects of ionizing radiation on fixed-ratio escape performance in rats. Neurotoxicology and Teratology 12:367-373.

Miettinen, J. K. 1969. Enrichment of radioactivity by Arctic ecosystems in Finnish Lapland. Pages 23-31 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Millard, J. B., and F. W. Whicker. 1990. Radionuclide uptake and growth of barn swallows nesting by radioactive leaching ponds. Health Physics 58:429-439.

Mo, T., and F. G. Lowman. 1976. Laboratory experiments on the transfer of plutonium from marine sediments to seawater and to marine organisms. Pages 86-95 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Mole, R. H. 1990. The effect of prenatal radiation exposure on the developing human brain. International Journal of Radiation Biology 57:647-663.

Monte, L. 1990. Evaluation of the environmental transfer parameters for ^{137}Cs using the contamination produced by the Chernobyl accident at a site in central Italy. Journal of Environmental Radioactivity 12:13-22.

Morse, J. W., and G. R. Choppin. 1991. The chemistry of transuranic elements in natural waters. Reviews in Aquatic Sciences 4:1-22.

Moss, B. W., E. F. Unsworth, C. H. McMurray, J. Pearce, and D. J. Kilpatrick. 1989. Studies on the uptake, partition and retention of ionic and fallout radiocaesium by suckling and weaned lambs. The Science of the Total Environment 85:91-106.

Mufson, S. 1992. G-7 eyes aid for ex-Soviet nuclear plants. Washington Post (newspaper), Washington, D.C. 22 May 1992:Fl-F3.

Muller, W. A., A. B. Murray, U. Linzner, and A. Luz. 1990. Osteosarcoma risk after simultaneous incorporation of the long-lived radionuclide ^{227}Ac and the short-lived radionuclide ^{227}Th. Radiation Research 121:14-20.

Nagasawa, H., J. B. Little, W. C. Inkret, S. Carpenter, K. Thompson, M. R. Raju, D. J. Chen, and G. F. Strniste. 1990. Cytogenetic effects of extremely low doses of plutonium-238 alpha-particle irradiation in CHO K-1 cells. Mutation Research 244:233-238.

National Academy of Sciences (NAS). 1957. The effects of atomic radiation on oceanography and fisheries. Publication 551. National Academy of Sciences-National Research Council, Washington, D.C. 137 pp.

National Academy of Sciences (NAS). 1971. Radioactivity in the marine environment. National Academy of Sciences, Panel on radioactivity in the marine environment. Washington, D.C. 272 pp.

National Council on Radiation Protection and Measurements (NCRP). 1991. Effects of ionizing radiation on aquatic organisms. NCRP Report 109.115 pp. Available from NCRP Publications, 7910 Woodmont Ave., Bethesda, Md.

Neel, J. V., and S. E. Lewis. 1990. The comparative radiation genetics of humans and mice. Annual Review of Genetics 24:327-362.

Neel, J. W., and K. H. Larson. 1963. Biological availability of strontium-90 to small native animals in fallout patterns from the Nevada test site. Pages 45-49 *in* V. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Nelson, D. J. 1963. The strontium and calcium relationships in Clinch and Tennessee River mollusks. Pages 203-211 *in* V. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Nelson, D. J., editor. 1971. Radionulides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May, 1971, Oak Ridge, Tenn. Vol 1:1-678; Volume 2:679-1268. Available from the National Technical Information Service, Springfield, Va., as CONF 710501-P1 and CONF 710501-P2.

Nelson, D. J., and F. C. Evans, editors. 1969. Symposium on radioecology. Proceedings of the second national symposium. 774 pp. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield Va.

Nelson, W. C., and F. W. Whicker. 1969. Cesium-137 in some Colorado game fish, 1965-66. Pages 258-265 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Newman, M. C., and I. L. Brisbin, Jr. 1990. Variation of ^{137}Cs levels between sexes, body sizes and collection localities of mosquitofish, *Gambusia holbrooki* (Girard 1859), inhabiting a reactor cooling reservoir. Journal of Environmental Radioactivity 12:131-144.

Norton, S., and B. F. Kimler. 1990. Early effects of low doses of ionizing radiation on the fetal cerebral cortex in rats. Radiation Research 124:235-241.

Norton, S., B. F. Kimler, and P. J. Mullenix. 1991. Progressive behavioral changes in rats after exposure to low levels of ionizing radiation in utero. Neurotoxicology and Teratology 13:181-188.

Noshkin, V. E., V. T. Bowen, K. M. Wong, and J. C. Barke. 1971. Plutonium in North Atlantic ocean organisms: ecological relationships. Pages 681-688 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn. Volume 2. Available from the National Technical Information Service, Springfield, Va.

Nozaki, Y. 1991. The systematics and kinetics of U/Th decay series nuclides in ocean water. Reviews in Aquatic Sciences 4:75-105

O'Connor, M. E. 1990. Teratogenesis: nonionizing electromagnetic fields. Pages 357-372 *in* O. P. Ghandi, editor. Biological effects and medical applications of electromagnetic energy. Prentice Hall, Englewood Cliffs, N.J.

O'Farrell, T. P. 1969. Effects of acute ionizing radiation in selected Pacific northwest rodents. Pages 157-165 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va. 22151.

O'Farrell, T. P., and R. O. Gilbert. 1975. Transport of radioactive materials by jackrabbits on the Hanford Reservation. Health Physics 29:9-15.

Oge, M., and M. Dickson. 1990. The Environmental Protection Agency's radon action program. Pages 331-341 *in* S. K. Majumdar, R. F. Schmalz, and E. W. Miller, editors. Environmental radon: occurrence, control, and health hazards. The Pennsylvania Academy of Science, Easton.

Ophel, I. L., and J. M. Judd. 1976. Strontium and calcium accumulation in fish as affected by food composition. Pages 221-225 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Osburn, W. S., Jr. 1963. Influence of four Rocky Mountain regional environments on pea plants grown from irradiated seeds. Pages 319-324 *in V*. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Othman, I. 1990. The impact of the Chernobyl accident on Syria. Journal of Radiological Protection 10:103-108.

Palo, R. T., P. Nelin, T. Nylen, and G. Wickman. 1991. Radiocesium levels in Swedish moose in relation to deposition, diet, and age. Journal of Environmental Quality 20:690-695.

Palumbo, R. F. 1963. Factors controlling the distribution of the rare earths in the environment and in living organisms. Pages 533-537 *in V*. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Patt, H. M., and M. N. Swift. 1948. Influence of temperature on the response of frogs to X irradiation. American Journal of Physiology 155:388-393.

Pearce, J., C. H. McMurray, E. F. Unsworth, B. W. Moss, F. J. Gordon, and D. J. Kilpatrick. 1989. Studies of the transfer of dietary radiocaesium from silage to milk in dairy cows. The Science of the Total Environment 85:267-278.

Pelton, M. R., and E. E. Provost. 1969. Effects of radiation on survival of wild cotton rats (*Sigmodon hispidus*) in enclosed areas of natural habitat. Pages 39-45 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Pentreath, R. J., D. S. Woodhead, and D. F. Jefferies. 1971. Radioecology of the plaice (*Pleuronectes platessa* L.) in the northeast Irish Sea. Pages 731-737 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn. Volume 2. Available from the National Technical Information Service, Springfield, Va.

Plummer, G. L., T. M. Pullen, Jr., and E. E. Provost. 1969. Cesium-137 and a population of Georgia white-tailed deer. Pages 609-615 *in* D. J. Nelson and F. C. Evans, editors. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Poinsot-Balaguer, N., R. Castel, and E. Tabone. 1991. Impact of chronic gamma irradiation on a Mediterranean forest ecosystem in Cadarache (France). Journal of Environmental Radioactivity 14:23-36.

Polikarpov, G. G., editor. 1973. Artificial and natural radionuclides in marine life. Academy of Sciences of the Ukranian SSR, A. O. Kovalevskii Institute of the Biology of the Southern Seas. 115 pp. Available from the U.S. Department of Commerce, National Technical Information Service, Springfield, Va.

Poston, T. P., D. C. Klopfer, and M. A. Simmons. 1990. Short-term bioconcentration studies of Np in freshwater biota. Health Physics 59:869-877.

Prokopchak, M. J., D. P. Spangenberg, and J. Shaeffer. 1990. The effects of X irradiation on the metamorphosis and budding of *Aurelia aurita*. Radiation Research 124:34-42.

Raabe, O. G., L. S. Rosenblatt, and R. A. Schlenker. 1990. Interspecies scaling of risk for radiation-induced bone cancer. International Journal of Radiation Biology 57:1047-1061.

Reed, J. R., and B. A. Martinedes. 1971. Uptake and retention of tungsten-181 by crayfish (*Cambarus longulus longerostris* Ort.). Pages 390-393 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971. Available from The National Technical Information Service, Springfield, Va.

Reed, J. R., and D. J. Nelson. 1969. Radiostrontium uptake in blood and flesh in bluegills (*Lepomis macrochirus*). Pages 226-233 *in* D. J. Nelson, and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-370503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Refetoff, S. 1990. A review of risks of external irradiation of the thyroid gland. Pages 101-103 *in* Iodine prophylaxis following nuclear accidents: proceedings of the Joint WHO/CEC workshop, July 1988. Pergamon Press, New York.

Renfro, W. C., and G. Benayoun. 1976. Sediment-worm interaction: transfer of ^{65}Zn from marine silt by the polychaete *Nereis diversicolor*. Pages 250-255 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Renn, C. E. 1957. Physical and chemical properties of wastes produced by atomic power industry. Pages 26-27 *in* National Academy of Sciences. The effects of atomic radiation on oceanography and fisheries. Publication 551, National Academy of Sciences-National Research Council, Washington, D.C.

Richmond, C. R. 1989. Transfer of radionuclides to animals-an historical perspective of work done in the United States. The Science of the Total Environment 85:1-15.

Rickard, W. H., and K. R. Price. 1990. Strontium-90 in Canada goose eggshells and reed Canary grass from the Columbia River, Washington. Environmental Monitoring and Assessment 14:71-76.

Rissanen, K., and T. Rahola. 1989. Cs-137 concentration in reindeer and its fodder plants. The Science of the Total Environment 85:199-206.

Rissanen, K., and T. Rahola. 1990. Radiocesium in lichens and reindeer after the Chernobyl accident. Rangifer, Special Issue 3:55-61.

Robins, M. W. 1990. ^{224}Ra-induced osteopenia in male CBA mice. Calcified Tissue International 46:94-100.

Roed, K. H., I. M. H. Eikelmann, M. Jacobsen, and O. Pedersen. 1991. Chromosome aberrations in Norwegian reindeer calves exposed to fallout from the Chernobyl accident. Hereditas 115:201-206

Romney, E. M., W. A. Rhoads, A. Wallace, and R. A. Wood. 1971. Persistence of radionuclides in soil, plants, and small mammals in areas contaminated with radioactive fallout. Pages 170-176 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Romney, E. M., A. Wallace, and J. D. Childress. 1971a. Revegetation problems following nuclear testing activities at the Nevada test site. Pages 1015-1022 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Ronai, Z. A., M. E. Lambert, and I. B. Weinstein. 1990. Inducible cellular responses to ultraviolet light irradiation and other mediators of DNA damage in mammalian cells. Cell Biology and Toxicology 6:105-126.

Rose, A. W., W. A. Jester, and B. C. Ford. 1990. Radioactive elements in Pennsylvania waters. Pages 91-109 *in* S. K. Majumdar, R. F. Schmalz, and E. W. Miller, editors. Environmental radon: occurrence, control, and health hazards. The Pennsylvania Academy of Science, Easton.

Rose, K. S. B. 1992. Lower limits of radiosensitivity in organisms, excluding man. Journal of Environmental Radioactivity 15:113-133.

Sankaranarayanan, K. 1991a. Ionizing radiation and genetic risks II. Nature of radiation-induced mutations in experimental mammalian in vivo systems. Mutation Research 258:51-73.

Sankaranarayanan, K. 1991b. Ionizing radiation and genetic risks III. Nature of spontaneous and radiation-induced mutations in mammalian in vitro systems and mechanisms of induction of mutations by radiation. Mutation Research 258:75-97.

Sankaranarayanan, K. 1991c. Ionizing radiation and genetic risks IV. Current methods, estimates of risk of Mendelian disease, human data and lessons from biochemical and molecular studies of mutations. Mutation Research 258:99-122.

Sawada, M., J. C. Carlson, and H. E. Enesco. 1990. The effects of UV radiation and antioxidants on life span and lipid peroxidation in the rotifer *Asplanchna brightwelli*. Archives of Gerontology and Geriatrics 10:27-36.

Sawidis, T. 1988. Uptake of radionuclides by plants after the Chernobyl accident. Environmental Pollution 50:317-324.

Schell, W. R. 1976. Concentrations and physical-chemical states of ^{55}Fe in Bikini Atoll lagoon. Pages 271-276 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Schoeters, G. E. R., J. R. Maisin, and O. L. V. Vanderborght. 1991. Toxicity of ^{241}Am in male C57BL mice: relative risk versus ^{226}Ra. Radiation Research 126:198-205.

Schreckhise, R. G., and F. W. Whicker. 1976. A model for predicting strontium-90 levels in mule deer. Pages 148-156 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Schultz, V., and A. W. Klement, Jr., editors. 1963. Radioecology. Reinhold, N.Y. 746 pp.

Schultz, V., and W. M. Longhurst. 1963. Accumulation of strontium-90 in yearling Columbian black-tailed deer, 1950-1960. Pages 73-76 *in* V. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Severa, J., and J. Bar. 1991. Handbook of radioactive contamination and decontamination. Studies in Environmental Science 47. Elsevier, N.Y. 363 pp.

Shadley, J. D., J. L. Whitlock, J. Rotmensch, R. W. Atcher, J. Tang, and J. L. Schwartz. 1991. The effects of radon daughter α-particle irradiation in K1 and xrs-5 CHO cell lines. Mutation Research 248:73-83.

Shick, J. M., M. P. Lesser, and W. R. Stochaj. 1991. Ultraviolet radiation and photooxidative stress in zooxanthellate anthozoa: the sea anemone *Phyllodiscus semoni* and the octocoral *Clavularia* sp. Symbiosis 10:145-173.

Shields, L. M., and P. V. Wells. 1963. Recovery of vegetation on atomic target areas at the Nevada test site. Pages 307-310 *in* V. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Shima, A., and A. Shimada. 1991. Development of a possible nonmammalian test system for radiation-induced germ-cell mutagenesis using a fish, the Japanese medaka (*Oryzias latipes*). Proceedings of the National Academy of Sciences of the United States of America 88:2545-2549.

Shure, D. J., and M. R. Gottschalk. 1976. Cesium-137 dynamics within a reactor effluent stream in South Carolina. Pages 234-241 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Sibley, T. H., and J. S. Stohr. 1990. Accumulation of Am-241 and Cm-244 from water and sediments by *Hyalella* sp. and *Tubifex* spp. Bulletin of Environmental Contamination and Toxicology 44:165-172.

Sicard, R. E., and M. F. Lombard. 1990. Putative immunological influence upon amphibian forelimb regeneration II. Effects of X-irradiation on regeneration and autograft rejection. Biological Bulletin 178:21-24.

Sivinski, J., and B. Smittle. 1990. Effects of gamma radiation on the development of the Caribbean fruit fly (*Anastrepha suspensa*) and the subsequent development of its parasite *Diachasmimorpha longicaudata*. Entomologia Experimentalis et Applicata 55:295-297.

Skogland, T., and I. Espelien. 1990. The biological effects of radiocesium contamination of wild reindeer in Norway following the Chernobyl accident. Pages 276-279 *in* S. Myrberget, editor. Volume 1: populations dynamics. Transactions of the XIXth IUGB Congress. The International Union of Game Biologists, September 1989, Trondheim, Norway.

Slovic, P., J. H. Flynn, and M. Layman. 1991. Perceived risk, trust, and the politics of nuclear waste. Science 254:1603-1607.

Smedile, E., and G. Queirazza. 1976. Uptake of ^{60}Co and ^{137}Cs in different components of a river ecosystem connected with discharges of a nuclear power station. Pages 1-8 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Smith, F. B., and M. J. Clark. 1986. Radionuclide deposition from The Chernobyl cloud. Nature 322:690-691.

Snyder, D. P., C. A. Tryon, and D. L. Graybill. 1976. Effect of gamma radiation on range parameters in the eastern chipmunk, *Tamias striatus*. Pages 354-358 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Sokolov, V. E., D. A. Krivolutzky, I. N. Ryabov, A. E. Taskaev, and V. A. Shevchenko. 1990. Bioindication of biological after-effects of the Chernobyl atomic power station accident in 1986-1987. Biology International 18:6-11.

Spezzano, P., and R. Giacomelli. 1991. Transport of ^{131}I and ^{137}Cs from air to cow's milk produced in northwestern Italian farms following the Chernobyl accident. Journal of Environmental Radioactivity 13:235-250.

Staaland, H., K. Hove, and O. Pedersen. 1990. Transport and recycling of radiocesium in the alimentary tract of reindeer. Rangifer, Special Issue 3:63-72.

Stanek, Z., M. Penaz, and E. Wohlgemuth. 1990. Accumulation and kinetics of ^{90}Sr in fishes and other components of an artificial aquatic system. Folia Zoologica 39:375-383.

Steele, A. K. 1990. Derived concentration factors for caesium-137 in edible species of North Sea fish. Marine Pollution Bulletin 21:591-594.

Stegelmeier, B. L., N. A. Gillett, A. H. Rebar, and G. Kelly. 1991. The molecular progression of plutonium-239-induced rat lung carcinogenesis: Ki-ras expression and activation. Molecular Carcinogenesis 4:43-51.

Steger, W., and C. J. Goodnight. 1976. The influence of environmental factors on the accumulation and retention of cesium-137 by the worm *Limnodrilus hoffineisteri* (Oligochaeta). Pages 242-249 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Straume, T., T. C. Kwan, L. S. Goldstein, and R. L. Dobson. 1991. Measurement of neutron-induced genetic damage in mouse immature oocytes. Mutation Research 248:123-133.

Su, R. Z., M. Kost, and J. Kiefer. 1990. The effect of krypton ions on *Artemia* cysts. Radiation and Environmental Biophysics 29:103-107.

Sweigert, S. E., and D. Carroll. 1990. Repair and recombination of X-irradiated plasmids in *Xenopus laevis* oocytes. Molecular and Cellular Biology 10:5849-5856.

Templeton, W. L., R. E. Nakatani, and E. E. Held. 1971. Radiation effects. Pages 223-229 *in* National Academy of Sciences. Radioactivity in the marine environment. National Academy of Sciences, panel on radioactivity in the marine environment, Washington, D.C.

Thacker, J. 1990. Molecular nature of ionizing radiation-induced mutations of native and introduced genes in mammalian cells. Pages 221-230 *in* Ionizing radiation damage to DNA: molecular aspects. Proceedings of a Radiation Research Society-UCLA Symposia Colloquium held at Lake Tahoe, Calif., 16-21 January 1990. Wiley-Liss, N.Y.

Thompson, G. A., J. Smithers, and H. Boxenbaum. 1990. Biphasic mortality response of chipmunks in the wild to single doses of ionizing radiation: toxicity and longevity hormesis. Drug Metabolism Reviews 22:269-289.

Tonelli, D., E. Gattavecchia, S. Ghini, C. Porrini, G. Celli, and A. M. Mercuri. 1990. Honey bees and their products as indicators of environmental radioactive pollution. Journal of Radioanalytical and Nuclear Chemistry 141:427-436.

Trnovec, T., Z. Kallay, and S. Bezek. 1990. Effects of ionizing radiation on the blood brain barrier permeability to pharmacologically active substances. International Journal of Radiation Oncology, Biology, Physics 19:1581-1587.

Turner, F. B., P. Licht, J. D. Thrasher, P. A. Medica, and J. R. Lannom, Jr. 1971. Radiation-induced sterility in natural populations of lizards (*Crotaphytus wislizenii* and *Cnemidophorus tigris*). Pages 1131-1143 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Ulrikson, G. U. 1971. Radiation effects on serum proteins, hematocrits, electrophoretic patterns and protein components in the bluegill (*Lepomis macrochirus*). Pages 1100-1105 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 1988. Sources, effects and risks of ionizing radiation. United Nations, New York. 647 pp.

United States Code of Federal Regulations (CFR). 1990. Subchapter F - Radiation protection programs. 40:6-23.

United States Code of Federal Regulations (CFR). 1991. Subchapter F - Radiation protection programs. 40:6-23.

U.S. Environmental Protection Agency (EPA). 1975. Environmental radiation data, report 2. U.S. Environmental Protection Agency, Office of Radiation Programs, Washington, D.C. 51 pp.

U.S. Environmental Protection Agency (EPA). 1977. Environmental radiation data, report 11. U.S. Environmental Protection Agency, Office of Radiation Programs, Washington, D.C. 37 pp.

U.S. Environmental Protection Agency (EPA). 1979. Environmental radiation data, report 15, January 1979. U.S. Environmental Protection Agency, Office of Radiation Programs, Washington, D.C. 57 pp.

U.S. Environmental Protection Agency (EPA). 1982a. Environmental radiation data, report 28, October-December 1981. U.S. Environmental Protection Agency 520/1-83-002. 98 pp.

U.S. Environmental Protection Agency (EPA). 1982b. Environmental radiation data, report 30, April-June 1982. U.S. Environmental Protection Agency 520/5-6-83-006. 90 pp.

U.S. Environmental Protection Agency (EPA). 1989a. Environmental radiation data, report 55, July-September 1988. U.S. Environmental Protection Agency 520/5-89-011. 37 pp.

U.S. Environmental Protection Agency (EPA). 1989b. Environmental radiation data, report 56, October-December 1988. U.S. Environmental Protection Agency 520/5-89-013. 32 pp.

U.S. Environmental Protection Agency (EPA). 1989c. Environmental radiation data, report 57, January-March 1989. U.S. Environmental Protection Agency 520/5-89-021. 41 pp.

U.S. Environmental Protection Agency (EPA). 1989d. Environmental radiation data, report 58, April-June 1989. U.S. Environmental Protection Agency 520/5-89-034. 35 pp.

U.S. Environmental Protection Agency (EPA). 1990a. Environmental radiation data, report 59, July-September 1989. U.S. Environmental Protection Agency 520/5-90-003. 46 pp.

U.S. Environmental Protection Agency (EPA). 1990b. Environmental radiation data, report 60, October-December 1989. U.S. Environmental Protection Agency 520/5-90-018. 33 pp.

U.S. Environmental Protection Agency (EPA). 1990c. Environmental radiation data, report 61, January-March 1990. U.S. Environmental Protection Agency 520/5-90-031. 32 pp.

U.S. Environmental Protection Agency (EPA). 1990d. Environmental radiation data, report 62, April-June 1990. U.S. Environmental Protection Agency 520/5-91-013. 41 pp.

U.S. Environmental Protection Agency (EPA). 1991. Environmental radiation data, report 63, July-September 1991. U.S. Environmental Protection Agency 520/5-91-025. 34 pp.

Van Den Hoek, J. 1989. European research on the transfer of radionuclides to animals--a historical perspective. The Science of the Total Environment 85:17-27.

Vandecasteele, C. M., M. Van Hees, J. P. Culot, and J. Vankerkom. 1989. Radiocaesium. metabolism in pregnant ewes and their progeny. The Science of the Total Environment 85:213-223.

Veskovic, M. M., and G. Djuric. 1990. Game as a bioindicator of radiocontamination. Acta Veterinaria (Beograd) 40:229-234.

Vissink, A., E. J. 's-Gravenmade, E. E. Ligeon, and A. W. T. Konings. 1990. A functional and chemical study of radiation effects on rat parotid and submandibular/sublingual glands. Radiation Research 124:259-265.

Voors, P. I., and A. W. Van Weers. 1989. Transfer of Chernobyl ^{134}Cs and ^{137}Cs in cows from silage to milk. The Science of the Total Environment 85:179-188.

Voors, P. I., and A. W. Van Weers. 1991. Transfer of Chernobyl radiocaesium (^{134}Cs and ^{137}Cs) from grass silage to milk in dairy cows. Journal of Environmental Radioactivity 13:125-140.

Vreman, K., T. D. B. Van Der Struijs, J. Van Den Hoek, D. L. M. Berende, and P. W. Goedhart. 1989. Transfer of Cs-137 from grass and wilted grass silage to milk of dairy cows. The Science of the Total Environment 85:139-147.

Walinder, G. 1990. A review of risks of internal irradiation of the thyroid gland-in utero, neonatally, adults. Pages 105-110 *in* Iodine prophylaxis following nuclear accidents. Proceedings of the joint WHO/CEC Workshop, July 1988. Pergamon Press, New York.

Weast, R. C., editor. 1985. CRC handbook of chemistry and physics. CRC Press, Boca Raton, Fla. Pages B233-B454 and F65-F108.

Welander, A. D. 1969. Distribution of radionuclides in the environment of Eniwetok and Bikini Atolls, August 1964. Pages 346-354 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-370503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Wetherbee, D. K. 1966. Gamma irradiation of birds' eggs and the radiosensitivity of birds. Massachusetts Agricultural Experiment Station, Bull. 561, University of Massachusetts, Amherst. 103 pp.

Whicker, F. W., J. E. Pinder III, J. W. Bowling, J. J. Alberts, and I. L. Brisbin, Jr. 1990. Distribution of long-lived radionuclides in an abandoned reactor cooling reservoir. Ecological Monographs 60:471-496.

Whicker, F. W., and V. Schultz. 1982a. Radioecology: nuclear energy and the environment. Volume I. CRC Press, Boca Raton, Fla. 212 pp.

Whicker, F. W., and V. Schultz. 1982b. Radioecology: nuclear energy and the environment. Volume II. CRC Press, Boca Raton, Fla. 228 pp.

Whitehead, N. E., S. Ballestra, E. Holm, and L. Huynh-Ngoc. 1988a. Chernobyl radionuclides in shellfish. Journal of Environmental Radioactivity 7:107-121.

Whitehead, N. E., S. Ballestra, E. Holm, and A. Walton. 1988b. Air radionuclide patterns observed at Monaco from the Chernobyl accident. Journal of Environmental Radioactivity 7:249-264.

Wiklund, K., L. E. Holm, and G. Eklund. 1990. Cancer risks in Swedish Lapps who breed reindeer. American Journal of Epidemiology 132:1078-1082.

Willard, W. K. 1963. Relative sensitivity of nestlings of wild passerine birds to gamma radiation. Pages 345-349 *in V*. Schultz and A. W. Klement, Jr., editors. Radioecology. Reinhold, N.Y.

Willis, D. L., and W. L. Lappenbusch. 1976. The radiosensitivity of the rough-skinned newt (*Taricha granulosa*). Pages 363-375 *in* C. E. Cushing, editor. Radioecology and energy resources. Proceedings of the fourth national symposium on radioecology, 12-14 May 1975, Oregon State University, Corvallis. The Ecological Society of America, Special Publication 1.

Willis, D. L., and B. B. Valett. 1971. Metabolism of iodine-131 in two amphibian species (*Tarichagranulosa* and *Rana pipiens*). Pages 394-400 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Witherspoon, J. P. 1969. Radiosensitivity of forest tree species to acute fast neutron radiation. Pages 120-126 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-370503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Wolfe, D. A., and C. D. Jennings. 1971. Iron-55 and ruthenium-103 and -106 in the brackish-water clam *Rangia cuneata*. Pages 783-790 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Wolfe, D. A., and C. L. Schelske. 1969. Accumulation of fallout radioisotopes by bivalve molluscs from the lower Trent and Neuse Rivers. Pages 493-504 *in* D. J. Nelson and F. C. Evans, editors. Symposium on radioecology. Proceedings of the second national symposium. Available as CONF-670503 from The Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Va.

Woloschak, G. E., C. M. Chang-Liu, and P. Shearin-Jones. 1990a. Regulation of protein kinase C by ionizing radiation. Cancer Research 50:3963-3967.

Woloschak, G. E., P. Shaearin-Jones, and C.M. Chang-Liu. 1990b. Effects of ionizing radiation on expression of genes encoding cytoskeletal elements: kinetics and dose effects. Molecular Carcinogenesis 3:374-378.

Wood, D. H. 1991. Long-term mortality and cancer risk in irradiated rhesus monkeys. Radiation Research 126:132-140.

Woychik, R. P., W. M. Generoso, L. B. Russell, K. T. Cain, N. L. A. Cacheiro, S. J. Bultman, P. B. Selby, M. E. Dickinson, B. L. M. Hogan, and J. C. Rutledge. 1990. Molecular and structural rearrangement in mouse chromosome 2 causing mutations at the limb deformity and agouti loci. Proceedings of the National Academy of Sciences of the United States of America 87:2588-2592.

Wrenn, M. E., J. W. Lentsch, M. Eisenbud, G. J. Lauer, and G. P. Howells. 1971. Radiocesium distribution in water, sediment, and biota in the Hudson River estuary from 1964 through 1970. Pages 334-343 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Yasuhira, S., H. Mitani, and A. Shima. 1991. Enhancement of photorepair of ultraviolet-damage by preillumination with fluorescent light in cultured fish cells. Photochemistry and photobiology 53:211-215.

Yathom, S., R. Padova, S. Tal, and I. Ross. 1990. Effects of gamma radiation on the immature stages of *Liriomyza trifolii*. Photoparasitica 18:117-124.

Yonezawa, M., A. Takeda, and J. Misonoh. 1990. Acquired radioresistance after low dose X-irradiation in mice. Journal of Radiation Research 31:256-262.

Yoshimoto, Y., J. V. Neel, W. J. Schull, H. Kato, M. Soda, R. Eto, and K. Mabuchi. 1990. Malignant tumors during the first 2 decades of life in the offspring of atomic bomb survivors. The American Journal of Human Genetics 46:1041-1052.

Yusifov, N. I., A. M. Kuzin, F. A. Agaev, and S. G. Alieva. 1990. The effect of low level ionizing radiation on embryogenesis of silkworm, *Bombyx mori* L. Radiation and Environmental Biophysics 29:323-327.

Zach, R., J. L. Hawkins, and S. C. Sheppard. 1993. Effects of ionizing radiation on breeding swallows at current radiation protection standards. Environmental Toxicology and Chemistry 12:779-786.

Zakaria, A. H. 1991. Effect of low doses of gamma irradiation prior to egg incubation on hatchability and body weight of broiler chickens. British Poultry Science 32:103-107.

Zavitkovski, J., and T. D. Rudolph. 1971. Predicted effects of chronic gamma irradiation of northern forest communities. Pages 1007-1014 *in* D. J. Nelson, editor. Radionuclides in ecosystems. Proceedings of the third national symposium on radioecology, 10-12 May 1971, Oak Ridge, Tenn., Volume 1. Available from The National Technical Information Service, Springfield, Va.

Glossary[1]

Actinides Elements of atomic numbers 89 to 103 (Ac, Th, Pa, U, Np, Pu, Am, Cm, Bk, Cf, Es, Fm, Md, No, Lw).

Activity The activity of a radioactive material is the number of nuclear disintegrations per unit time. Until 1977, the accepted unit of activity was the curie (Ci), equivalent to 37 billion disintegrations/s—a number that approximated the activity of 1 g of radium-226. The present unit of activity is the becquerel (Bq), equivalent to 1 disintegration/s.

Alpha (α) particles An α particle is composed of 2 protons and 2 neutrons and has a charge of +2; essentially, it is a helium nucleus without orbital electrons. Alpha particles usually originate from the nuclear decay of radionuclides of atomic number >82 and are detected in samples that contain U, Th, or Ra. Alpha particles react strongly with matter and consequently produce large numbers of ions per unit length of their paths; as a result, they are not very penetrating and traverse only a few centimeters of air. Alpha particles are unable to penetrate clothing or the outer layer of skin; however, when internally deposited, α particles are often more damaging than most other types of radiations because comparatively large amounts of energy are transferred in a small volume of tissue. Alpha particle absorption involves ionization and orbital electron excitation. Ionization occurs whenever the particle is sufficiently close to an electron to pull it from its orbit. The α also loses kinetic energy by exciting orbital electrons with interactions that are insufficient to cause ionization.

Atom The smallest part of an element that has all the properties of that element. An atom consists of one or more protons and neutrons (in the nucleus) and of one or more electrons.

Atomic number The number of electrons outside the nucleus of a neutral (nonionized) atom plus the number of protons in the nucleus.

Becquerel (Bq) The present accepted unit of activity is the becquerel, equivalent to 1 disintegration/s. About 0.037 Bq = 1 picocurie.

Beta (β) particles Beta particles are electrons that are spontaneously ejected from the nuclei of radioactive atoms during the decay process. They may be either positively or negatively charged. A positively charged beta (β), called a *positron, is* less frequently encountered than its negative counterpart, the *negatron* (β). The *neutrino,* a small particle, accompanies beta emission. The neutrino has little mass and is electrically neutral. But neutrinos conduct a variable part of the energy of transformation and account for the variability in kinetic energies of beta particles that are emitted from a given radionuclide. Positrons (β^+) are emitted by many of the naturally and artificially produced radionuclides; they are considerably more penetrating than α particles but less penetrating than X-rays and rays. Beta particles interact with other electrons and with nuclei in the travel medium. The ultimate fate of a beta particle depends on its charge. Negatrons, after their kinetic energy is spent, combine with a positively charged ion or become free electrons. Positrons also dissipate kinetic energy through ionization and excitation; the collision of positrons and electrons causes annihilation and release of energy that is equal to the sums of their particle masses.

Breeder reactor A nuclear chain reactor in which transmutation produces a greater number of fissionable atoms than the number of consumed parent atoms.

Cosmic rays Highly penetrating radiations that originate in outer space.

Curie (Ci) The Curie is equal to that quantity of radioactive material that produces 37 billion nuclear transformations/s. One millicurie (Ci) = 0.001 Ci; 1 microcurie (Ci) = 1 millionth of a Ci; 1 picocurie (pCi) = 1 millionth of a millionth Ci = 0.037 disintegrations/s. About 27 pCi = 1 becquerel (Bq).

Decay Diminution of a radioactive substance because of nuclear emission of α or β particles or of rays.

Decay product A nuclide resulting from the radioactive disintegration of a radionuclide and found as the result of successive transformations in a radioactive series. A decay product may be either radioactive or stable.

Effective dose equivalent The weighted sum, in sieverts, of the radiation dose equivalents in the most radiosensitive organs and tissues, including gonads, active bone marrow, bone surface cells, and the lung.

Electron An electron is a negatively charged particle with a diameter of 10^{-12} cm. Every atom consists of one nucleus and one or more electrons. Cathode rays and negatrons are electrons.

Electron-volt (eV) Energy acquired by any charged particle that carries unit electronic charge when it falls through a potential difference of 1 volt. One eV = 1.602×10^{-19} joule.

Fission The splitting of an atomic nucleus into two fragments that usually releases neutrons and rays. Fission may occur spontaneously or may be induced by capture of bombarding particles. Primary fission products usually decay by β particle emission to radioactive daughter products. The chain reaction that may result in controlled burning of nuclear fuel or in an uncontrolled nuclear weapons explosion results from the release of 2 or 3 neutrons/fission. Neutrons cause additional fissile nuclei in the vicinity to fission, which produces still more neutrons that in turn produce still more fissions. The speed of the chain reaction is governed by the density and geometry of fissile nuclei and of materials that slow or capture the neutrons. In nuclear reactors, neutron-absorbing rods are inserted to various depths into the reactor core. A nuclear explosion is not physically possible in a reactor because of fuel density, geometry, and other factors.

Fusion A nuclear reaction in which smaller atomic nuclei or particles combine to form larger nuclei or particles with the release of energy from mass transformation.

Gamma ( ) rays Gamma rays have electromagnetic wave energy that is similar to but higher than the energy of X-rays. Gamma rays are highly penetrating and able to traverse several centimeters of lead. See *Photons.*

Genetically significant dose (GSD) A radiation dose that, if received by every member of the population, would produce the same total genetic injury to the population as the actual doses that are received by the various individuals.

Grey(Gy) 1 Gy = 1 Joule/kg = 100 rad.

Half-life The average time in which half the atoms in a sample of radioactive element decay.

Hertz (Hz) A measure of frequency equal to 1 cycle/s.

Indirectly ionizing particles Uncharged particles such as neutrons or protons that directly liberate ionizing particles or initiate nuclear transformations.

Ion An atomic particle, atom, or chemical radical with an either negative or positive electric charge.

Ionization The process by which neutral atoms become either positively or negatively electrically charged by the loss or by the gain of electrons.

Isomer One of two or more radionuclides with the same mass number and the same atomic number but with different energies and radioactive properties for measurable durations.

Isotope One of several radionuclides of the same element (i.e., with the same number of protons in their nuclei) with different numbers of neutrons and different energy contents. A single element may have many isotopes. Uranium, for example, may appear naturally as ^{234}U (142 neutrons), ^{235}U (143 neutrons), or ^{238}U (148 neutrons); however, each uranium isotope has 92 protons.

Joule (J) 1 J = 10^7 ergs.

Latent period Period of seeming inactivity between time of exposure of tissue to an acute radiation dose and the onset of the final stage of radiation sickness.

Linear energy transfer (LET) A function of the capacity of the radiation to produce ionization. LET is the rate at which charged particles transfer their energies to the atoms in a medium and a function of the energy and velocity of the charged particle. See *Radiation dose.*

Linear hypothesis The assumption that any radiation causes biological damage in the direct proportion of dose to effect.

Mass number The total number of neutrons and protons in the nucleus of the element, which is equal to the sum of the atomic number and the number of neutrons.

Meson Particles of mass that are intermediate between the masses of the electron and proton.

Neutrinos Neutrinos and antineutrinos are formed whenever a positron particle is created in a radioactive decay; they are highly penetrating.

Neutrons Neutrons are electrically neutral particles that consist of an electron and a proton and are not affected by the electrostatic forces of the atom's nucleus or orbital electrons. Because they have no charge, neutrons readily penetrate the atom and may cause a nuclear transformation. Neutrons are produced in the atmosphere by cosmic ray interactions and combine with nitrogen and other gases to form carbon-14, tritium and other radionuclides. A free neutron has a life time of about 19 minutes, after which it spontaneously decays to a proton, a β particle, and a neutrino. A high energy neutron that encounters biological material is apt to collide with a proton with sufficient force to dislodge the proton from the molecule. The recoil proton may then have sufficient energy to cause secondary damage through ionization and excitation of atoms and molecules along its path.

Nucleus The dense central core of the atom in which most of the mass and all of the positive charge is concentrated. The charge on the nucleus distinguishes one element from another.

Photons X-rays and gamma ( ) rays, collectively termed photons, are electromagnetic waves with shorter wavelengths than other members of the electromagnetic spectrum such as visible radiation, infrared radiation, and radiowaves. X- and photons have identical properties, behavior, and effects. Gamma rays originate from atomic nuclei, but X-rays arise from the electron shells. All photons travel at the speed of light, but energy is inversely proportional to wavelength. The energy of a photon directly influences its ability to penetrate matter. Many types of nuclear transformations are accompanied by ray emission. For example, α and β decay of many radionuclides is frequently accompanied by photons. When a parent radionuclide decays to a daughter nuclide, the nucleus of the daughter frequently contains excess energy and is unstable; stability is usually achieved through release of one or more photons, a process called isometric transition. The daughter nucleus decays from one energy state to another without a change in atomic number or weight. The most probable fate of a photon with an energy higher than the binding energy of an encountered electron is photoelectric absorption, in which the photon transfers its energy to the electron and photon existence ends. As with ionization from any process, secondary radiations that are initiated by the photoelectron produce additional excitation of orbital electrons.

Planck's constant (h) A universal constant of nature that relates the energy of a photon of radiation to the frequency of the emitting oscillator. Its numerical value is about 6.626 X 10^{-27} ergs/s.

Positron A positively charged particle of equal mass to an electron. Positrons are created either by the radioactive decay of unstable nuclei or by collision with photons.

Proton A positively charged subatomic particle with a mass of 1.67252×10^{-24} g that is slightly less than the mass of a neutron but about 1,836 times greater than the mass of an electron. Protons are identical to hydrogen nuclei; their charge and mass make them potent ionizers.

Radiation The emission and propagation of energy through space or through a material medium in the form of waves. The term also includes subatomic particles such as α, β, and cosmic rays and electromagnetic radiation.

Radiation absorbed dose (rad) Radiation-induced damage to biological tissue results from the absorption of energy in or around the tissue. The amount of energy absorbed in a given volume of tissue is related to the types and numbers of radiations and the interactions between radiations and tissue atoms and molecules. The fundamental unit of the radiation absorbed dose is the rad; 1 rad = 100 erg (absorbed)/g material. In the latest nomenclature, 100 rad = 1 grey (Gy).

Radiation dose The term radiation dose can mean several things, including absorbed dose, dose equivalent, or effective dose equivalent. The absorbed dose of radiation is the imparted energy per unit mass of the irradiated material. Until 1977, the *rad* was the unit of absorbed dose, wherein 1 rad = 0.01 joule/kg. The present unit of absorbed dose is the grey (Gy), equivalent to 1 joule/kg. Thus, 1 rad = 0.01 joule/kg = 0.01 Gy. Different types of radiation have different Relative Biological Effectiveness (RBE). The RBE of one type of radiation in relation to a reference type of radiation (usually X or) is the inverse ratio of the absorbed doses of the two radiations needed to cause the same degree of the biological effect for which the RBE is given. Regulatory agencies have recommended certain values of RBE for radiation protection and absorbed doses of various radiations are multiplied by these values to arrive at radioprotective doses. The unit of this weighted absorbed dose is the roentgen equivalent man (rem). The dose equivalent is the product of the absorbed dose and a quality factor (Q), and its unit is the rem. The quality factor is a function of the capacity to produce ionization, expressed as the linear energy transfer (LET). A Q value is assigned to each type of radiation: 1 to X-rays, rays, and β particles; 10 to fast neutrons; and 20 to α particles and heavy particles. The new unit of the effective dose equivalent is the sievert (Sv), replacing rem, where 1 Sv = 100 rem. In addition to absorbed dose and dose equivalent, there is also the exposure. Exposure is the total electrical charge of ions of one sign produced in air by electrons liberated by X or gamma rays per unit mass of irradiated air. The unit of exposure is Coulomb/kg, but the old unit, the roentgen (R) is still in use. One roentgen = 2.58×10^{-4} Coulomb/kg.

Radioactivity The process of spontaneous disintegration by a parent radionuclide, which releases one or more radiations and forms a daughter nuclide. When half the radioactivity remains, that time interval is designated the half-life (Tb ½). The Tb ½ value gives some insight into the behavior of a radionuclide and into its potential hazards.

Radionuclide An atom that is distinguished by its nucleus composition (number of protons, number of neutrons, energy content), atomic number, mass number, and atomic mass.

Relative biological effectiveness (RBE) The biological effectiveness of any type of ionizing radiation in producing a specific damage (i.e., leukemia, anemia, carcinogenicity). See *Radiation dose.*

Roentgen (R) 1 R = 2.58×10^{-4} Coulombs/kg air = production by X or rays of 1 electrostatic unit of charge/cm^3 of dry air at 0° C and 760 mm Hg = 0.87 rad in air.

Roentgen equivalent man (rem) The amount of ionizing radiation of any type that produces the same damage to humans as 1 roentgen of radiation. One rem = 1 roentgen equivalent physical (rep)/ relative biological effectiveness (RBE). In the latest nomenclature, 100 rem = 1 Sievert (Sv).

Roentgen equivalent physical (rep) One rep is equivalent to the amount of ionizing radiation of any type that results in the absorption of energy of 93 ergs/g and is approximately equal to 1 roentgen of X-radiation in soft tissue.

Shell Extranuclear electrons are arranged in orbits at various distances from the nucleus in a series of concentric spheres called shells. In order of increasing distance from the nucleus the shells are designated the K, L, M, N, O, P, and Q shells; the number of electrons that each shell can contain is limited.

Sievert (Sv) New unit of dose equivalent. One Sv = 100 rem = 1 J/kg. See *Radiation dose.*

Specific activity The ratio between activity (in number of disintegrations/m) and the mass (in grams) of material giving rise to the activity. Biological hazards of radionuclides are directly related to their specific activity and are expressed in Bq/kg mass.

Threshold hypothesis A radiation-dose-consequence hypothesis that holds that biological radiation effects occur only above some minimum dose.

Transmutation A nuclear change that produces a new element from an old one.

Transuranic elements Elements of atomic number >92. All are radioactive and produced artificially; all are members of the actinide group.

X-rays See *Photons.*

[1]Whicker and Schultz 1982a; League of Women Voters (LWV) 1985; Weast 1985; Hobbs and McClellen 1986; United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1988; U.S. Code of Federal Regulations (CFR) 1990.

Biological Report 27
February 1995

Contaminant Hazard Reviews
Report No. 30

SODIUM MONOFLUOROACETATE (1080) HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Environmental Science Center
U.S. National Biological Service
Laurel, MD 20708

TABLES

SODIUM MONOFLUOROACETATE (1080) HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Environmental Science Center
U.S. National Biological Service
Laurel, MD 20708

Abstract. Sodium monofluoroacetate ($CH_2FCOONa$), also known as 1080, was first used in the United States to control gophers (*Geomys* spp.), squirrels (*Sciurus* spp., *Spermophilus* spp.), prairie dogs (*Cynomys* spp.), other rodents (Rodentia), and coyotes (*Canis latrans*); 1080 domestic use is currently restricted to livestock-protection collars on sheep and goats to selectively kill depredating coyotes. However, Australia, New Zealand, and some other nations continue to use 1080 to control rabbits, possums, deer, foxes, feral pigs and cats, wild dogs, wallabies, rodents, and other mammals. The chemical is readily absorbed by ingestion or inhalation. At lethal doses, metabolic conversion of fluoroacetate to fluorocitrate results in the accumulation of citrate in the tissues and death within 24 h from ventricular fibrillation or from respiratory failure; no antidote is available. At sublethal doses, the toxic effects of 1080 are reversible. Primary and secondary poisoning of nontarget vertebrates may accompany the use of 1080. Sensitive mammals including representative species of livestock, marsupials, felids, rodents, and canids died after receiving single doses of 0.05-0.2 mg 1080/kg body weight (BW); most tested species died after a single dose of 1-3 mg/kg BW. High residues were measured in some poisoned target mammals, and this contributed to secondary poisoning of carnivores that ingested poisoned prey. Sublethal effects occurred in sensitive mammals at greater than 2.2 mg 1080/L in drinking water or at 0.8-1.1 mg 1080/kg in the diet. Sensitive species of birds died after a single 1080 dose of 0.6-2.5 mg/kg BW, after daily doses of 0.5 mg/kg BW for 30 days, after 47 mg/kg in diets for 5 days, or after 18 mg/L in drinking water for 5 days. Adverse effects occurred in birds at dietary loadings as low as 10-13 mg 1080/kg ration. Amphibians and reptiles were more resistant to 1080 than birds and mammals. LD50 values were greater than 44 mg/kg BW in tested amphibians and greater than 54 mg/kg BW in tested reptiles; resistance to 1080 was attributed to their reduced ability to convert fluoroacetate to fluorocitrate and their increased ability to detoxify fluoroacetate by defluorination. Mosquito larvae reportedly died at 0.025-0.05 mg 1080/L, but fishes seemed unaffected at 13 mg/L; however, data on 1080 in aquatic ecosystems are incomplete. Acute LD50 values in terrestrial insects ranged from 1.1-3.9 mg/kg BW to 130.0 mg/kg BW in larvae feeding on fluoroacetate-bearing vegetation. Residues of 1080 in exposed insects were usually low (<4 mg 1080/kg fresh weight) or negligible and were usually eliminated completely within 6 days, suggesting low risk to insectivorous birds. Loss of 1080 from baits occurs primarily from microbial defluorination and secondarily from leaching by rainfall and consumption by insect larvae; leachates from 1080 baits are probably held in the upper soil layers. The use of 1080 seems warranted in the absence of suitable alternative control methods.

Key words: Sodium monofluoroacetate, 1080, organofluorines, pesticide, predacide, toxicity, wildlife, livestock, invertebrates.

Sodium monofluoroacetate ($CH_2FCOONa$), also known as 1080 or Compound 1080, belongs to the class of chemicals known as fluoroacetates (Pattison 1959). It is a tasteless and odorless, water-soluble poison of extraordinary potency that has been used widely against rodents and other mammalian pests (Anonymous 1946; Negherbon 1959; Rammell and Fleming 1978; McIlroy 1981a; Hornshaw et al. 1986; Aulerich et al. 1987; Connoly and Bums 1990). The widespread use of 1080 in pest control has caused accidental deaths of livestock, wildlife, pets (cats and dogs), and humans (Anonymous 1946; Chenoweth 1949; Sayama and Brunetti 1952; Negherbon 1959; U.S. Environmental Protection Agency [EPA] 1976; McIlroy 1982a), and several suicides in Asia from drinking 1080 rat poison solutions (Howard 1983). There is no effective antidote to 1080 (Mead et al. 1991). When consumed, fluoroacetate is converted to fluorocitrate that inhibits the enzymes aconitase and succinate dehydrogenase; the accumulated citrate interferes with energy production and cellular function (Aulerich et al. 1987).

Monofluoroacetic acid (CH_2FCOOH) was first synthesized in Belgium in 1896 but attracted little attention from chemists and pharmacologists at that time (Chenoweth 1949; Atzert 1971). In 1927, sodium monofluoroacetate was patented as a preservative against moths (Sayama and Brunetti 1952). The toxic nature of monofluoroacetate compounds was first noted in Germany in 1934 (Atzert 1971). In the late 1930's and early 1940's, Polish scientists conducted additional research on the toxic properties of fluoroacetate compounds, especially the methyl ester of fluoroacetic acid that they had synthesized (Anonymous 1946; Chenoweth 1949). In 1942, British scientists further refined this compound to the sodium salt that became known as 1080 (Anonymous 1946). In 1944, potassium monofluoroacetate (CH_2FCOOK) was isolated from *Dichapetalum cymosium*, a South African plant, and was the first known example of a naturally occurring organic fluoride; the plant, known locally as Gifblaar, caused many deaths of livestock (Chenoweth 1949) and was recognized by Europeans as poisonous as early as 1890 (Peacock 1964). Fluoroacetate compounds have since been isolated from poisonous plants in Australia (*Acacia georginae*, *Gastrolobium* spp.), in Brazil (rat weed, *Palicourea marcgravii*), and in Africa (*Dichapetalum* spp; Atzert 1971). Ratsbane (*Dichapetalum toxicarium*), an African plant, was known to contain a poison--subsequently identified as a fluoroacetate--that was lethal to rats, livestock, and humans and reportedly was used by African natives during the 1800's to poison the wells and water supplies of hostile tribes (Anonymous 1946).

During World War II (1939-45), as a result of acute domestic shortages of common rodenticides such as thallium, strychnine, and red squill, testing for alternative chemicals was initiated (Anonymous 1946). In June 1944, the U.S. Office of Scientific Research and Development supplied the Patuxent Wildlife Research Center--then a laboratory of the U.S. Fish and Wildlife Service--with sodium monofluoroacetate and other chemicals for testing as rodenticides (Atzert 1971). The center gave sodium monofluoroacetate the acquisition number 1080, which subsequently was adopted as its name by the chemical's manufacturer. Samples of 1080 were also shipped to the Denver Wildlife Research Center, another former laboratory of the U.S. Fish and Wildlife Service, for testing on additional species. Results of these tests gave evidence of the value of 1080 as an effective control of animal predators of livestock and other animal pests (Atzert 1971). During World War II, 1080 protected allied troops in the Pacific Theater against scrub typhus, also known as tsut sugamushi, a louse-borne rickettsial disease with rodents as vectors (Peacock 1964). In the United States, 1080 was first used in 1945 to control rodents, and later coyotes (*Canis latrans*) and rabbits (*Lepus* spp.; *Sylvilagus* spp.; Hornshaw et al. 1986; Aulerich et al. 1987). Between 1946 and 1949, at least 12 humans died accidentally in the United States from 1080 poisoning when used as a rodenticide; a child became ill but recovered after eating the cooked flesh of a 1080-poisoned squirrel (EPA 1976). Since 1955, 1080 has been used extensively in a variety of baits--especially in Australia and New Zealand--to control European rabbits (*Oryctolagus cuniculus*), dingoes (*Canis familiaris dingo*), feral pigs (*Sus scrofa*), brush-tailed possums (*Trichosurus vulpecula*), and various species of wallabies (McIlroy 1981a, 1981b, 1982a, 1984; Twigg and King 1991). In Australia, vegetable baits are sometimes eaten by nontarget herbivores such as sheep (*Ovis aries*), cattle (*Bos taurus*), and various species of wildlife and cause primary and secondary poisoning of nontarget animals (McIlroy 1982a). In the United States, most uses of 1080 were canceled in 1972 because, in part, of deaths of nontarget animals (Balcomb et al. 1983). At present, the use of 1080 in the United States is restricted to livestock-protection collars on sheep and goats (*Capra hircus*) against predation by coyotes (Palmateer 1989,1990).

Useful reviews of ecotoxicological aspects of 1080 include those by Chenoweth (1949), Peacock (1964), Atzert (1971), Kun (1982), Twigg and King (1991), and Seawright and Eason (1994). I prepared my account in response to requests for information on 1080 from environmental contaminant specialists of the U.S. Fish and

Wildlife Service. It is part of a continuing series of brief reviews of chemicals in the environment with an emphasis on hazards to plants and animals.

Uses of 1080

The use of 1080 in the United States is now restricted to the protection of livestock--collars on sheep and goats--from predation by coyotes. Other countries, most notably Australia and New Zealand, use 1080 extensively in a variety of baits to control many species of vertebrate pests.

Domestic Use

Compound 1080 is highly poisonous to all tested mammals and to humans (Green 1946). There is no known antidote to 1080, and it has been impossible to resuscitate any animal or human during the final stages of 1080 poisoning (Kalbach 1945; Green 1946; Connolly 1989, 1993a). In the United States, 4 suicides and at least 12 accidental human deaths occurred in 25 years of use of 1080 between 1959 and 1969 and 37 known incidents of domestic animal poisoning resulted from federal use of 1080 (Atzert 1971). Compound 1080 is not recommended for use in residential areas or for distribution where the public may be exposed (Green 1946); only licensed pest control operators can use 1080 (Green 1946; Peacock 1964; EPA 1985; Murphy 1986). Tull Chemical in Oxford, Alabama, is the sole domestic producer of 1080; none is imported (EPA 1985). Operators who handle 1080 should wear protective clothing, including gloves and a respirator; extreme caution is recommended at all times (Green 1946). During attaching, removing, or disposing of livestock-protection collars, each applicator must carry syrup of ipecac to induce vomiting in case of accidental poisoning (Connolly 1989, 1993a).

Compound 1080 was first used in the United States in the late 1940's to control gophers (*Geomys* spp.), ground squirrels (*Spermophilus* spp.), prairie dogs (*Cynomys* spp.), field mice (Muridae), commensal rodents, and coyotes (Chenoweth 1949; Fry et al. 1986). Annual damage from coyotes to livestock in California alone is an estimated $75 million (Howard 1983). Yearly amounts of 1080 used in the United States for predator control were 23 kg in the early 1960's, 7,727 kg in the late 1960's, and only 8 kg in 1971 (Connolly 1982). The total annual production of 1080 in the United States between 1968 and 1970 averaged about 1,182 kg (Atzert 1971). In 1977, 277,545 kg of 1080-containing baits (272 kg of 1080) were used to control ground squirrels (76%), prairie dogs (7%), and mice, rats, chipmunks (*Tamias* spp.), and other rodents (17%); California used 83% of all 1080 baits, Colorado 12%, and Nevada and Oregon 5% (EPA 1985). About 0.3 kg of 1080/year are used in the livestock-protection collars but only about 35 g/year is released into the environment (Connolly 1993b). In March 1972, the use of 1080 for predator control was prohibited on federal lands. Later that year, all uses of 1080 for predator control were banned in the United States because of adverse effects on nontarget organisms including endangered species (Palmateer 1989, 1990). Since 1080 was banned, the number of grazing livestock reported lost to predation in western national forests has increased. Between 1960 and 1971, 1.42% (range 1.0-1.9%) of all grazed sheep and goats were lost to predators versus 2.17% (1.7-2.5%) in 1970-78 (Lynch and Nass 1981). Until it was banned in 1972, the use of 1080 as a control agent of predators in the United States was strictly controlled. The chemical was registered under the Federal Insecticide, Fungicide and Rodenticide Act (61 Stat 163; 7 U.S.C. 135-135K) for use only by governmental agencies and experienced pest-control operators (Atzert 1971). The use of 1080 as a rodenticide was disallowed in 1985 for three reasons; (1) lack of emergency treatment, namely a viable medical antidote; (2) high acute toxicity to nontarget mammals and birds; and (3) a significant reduction in populations of nontarget organisms and fatalities to endangered species (EPA 1985). In 1985, 1080 use was conditionally permitted in livestock-protection collars and in single lethal dose baits; a registration of the livestock-protection collar was issued to the U.S. Department of the Interior on 18 July 1985 (EPA 1985). On 21 February 1989, the registration of 1080 was cancelled, prohibiting all uses. In June 1989, however, technical 1080 was conditionally approved for use only in the livestock-protection collar. The 30-mL collar is registered for use by the U.S. Department of Agriculture; by the states of Montana, Wyoming, South Dakota, and New Mexico; and by Rancher's Supply, Alpine, Texas (Palmateer 1989, 1990).

Compound 1080 was highly effective against all species of rats, prairie dogs, and ground squirrels and satisfactory for the control of mice (Peacock 1964). The chemical was formulated in grain baits or chopped greens for crop and range rodents and in water bait stations to control rats (EPA 1985). The concentration of 1080 in baits was lowered to 0.02% in the range of the California condor (*Gymnogyps californianus*) and for prairie dog control because of possible harm to the endangered black-footed ferret (*Mustela nigripes*; EPA 1985). Commercial 1080 was commonly colored with 0.5% nigrosine and sold as a compound containing

greater than 90% sodium monofluoroacetate, to be mixed with foods at 2,226 mg/kg in preparing baits or to be dissolved in water at 3,756 mg/L for poisoning drinking water in indoor control of rodents (Anonymous 1946; Green 1946; Negherbon 1959). Bait acceptance by rats was not significantly reduced by the dye (Peacock 1964). Compound 1080 was adequately accepted by rats and mice when present in water; solid food baits poisoned with 1080 were not always accepted as readily and sometimes required special preparation to insure the ingestion of lethal amounts (Green 1946). A water solution of 1080 was the most effective tested rodenticide for rat control in southern states, and 1080-grain baits were the most effective field rodenticides against ground squirrels, prairie dogs, and mice in California, South Dakota, and Colorado (Kalmach 1945). Seeds and cereal grains were the most effective baits for small rodents: 1 kg of 1080 was sufficient to kill 3.96 million squirrels (Peacock 1964). Grain baits were colored brilliantly yellow or green to heighten the repellency of birds; coloring did not affect the acceptance of baits by rodents (Peacock 1964; Atzert 1971). Rats did not develop a significant tolerance to 1080 from ingestion of sublethal doses; although rats that survived poisoning may develop an aversion to 1080 (Green 1946; Peacock 1964).

To kill coyotes and gray wolves (*Canis lupus*) in the United States and in Canada, meat baits containing 35 mg 1080/kg were recommended--usually an injected water solution of 1080 into horsemeat baits; only 28-56 g of a poisoned bait was sufficient to kill (Peacock 1964). Meat baits were usually placed in fall in areas with maximum coyote use and minimum use by most nontarget carnivores (Atzert 1971). The most widely publicized technique for poisoning predators was the 1080 large bait station: a 22-45 kg livestock meat bait injected with 35 mg 1080/kg bait (Connolly 1982). The use of 1080 stations peaked in the early 1960's, at which time 15 to 16 thousand stations were placed each winter in the western United States. After 1964, the number of stations declined annually to 7,289 stations in 1971 (Connolly 1982). Against canine predators of livestock, 1080 was more selective and less hazardous than strychnine or traps to nontarget species (Peacock 1964). Meat baits for the control of coyotes were seldom fatal to hawks, owls, and eagles (Falconiformes), even when these birds gorged themselves on the poisoned baits (Peacock 1964). In addition to the large bait stations, an unknown number of U.S. Government hunters used 1080 in smaller baits at various stations (Connolly 1982).

The introduction of 1080-livestock-protection collars to protect goats and sheep against coyote depredation was initiated in 1985; its use was limited to certified applicators (Burns et al. 1991). The 1080-filled rubber collars are attached to the throats of sheep and goats; 1080 is released when coyotes attack collared livestock with characteristic bites to the throat (Walton 1990; Burns et al. 1991). The livestock-protection collars contain 30 mL of a 1% 1080 solution (Walton 1990) and tartrazine (Burns and Savarie 1989; Connolly 1993a) as a marker. The livestock-protection collar may not be used in areas known to be frequented by endangered species of wildlife, and these include various geographic areas in California, Michigan, Minnesota, Montana, Washington, Wisconsin, and Wyoming (Connolly 1989, 1993a). In livestock-protection collars, Compound 1080 is reportedly more effective and safer than sodium cyanide, diphacinone, or methomyl (Connolly 1982). Pen tests with compound 1080 in livestock-protection collars began late in 1976 and field tests in 1978 (Connolly and Burns 1990). In the field, 1080 livestock-protection collars on sheep seem to protect selectively against predation by coyotes; no adverse effects on humans, domestic animals, and nontarget wildlife were recorded (Connolly and Burns 1990). The decision to permit limited use of 1080 in livestock-protection collars is now being contested by at least 14 conservation groups because of its alleged hazard to nontarget organisms (bears, *Ursus* spp.; badgers, *Taxidea taxus*; dogs, *Canis* spp.; eagles, *Aquila chrysaetos*, *Haliaeetus leucocephalus*) and to human health, and to the availability of alternate and more successful methods of coyote control (Sibbison 1984). In Texas, for example, the annual cost from losses of sheep and goats to coyotes are an estimated $5 million. But few Texas ranchers have taken advantage of the opportunity to use livestock-protection collars, and only 23 coyotes were killed in 1989 by the collars versus 473 by cyanide, snares, aerial gunning, and other measures (Walton 1990). Toxic livestock-protection collars in full operation would probably kill fewer than 1,000 coyotes annually versus 1 million coyotes killed annually from hunting and other measures (Sibbison 1984).

Compound 1080 was also effective against jackrabbits, foxes, and moles. Baits containing 0.05-0.1% of 1080 on vegetables were used in California to kill jackrabbits (*Lepus* spp.) and various rodents (Schitoskey 1975). The Arctic fox (*Alopex lagopus*), intentionally introduced onto the Aleutian Islands in 1835 (Bailey 1993), almost eliminated the Aleutian Canada goose (*Branta canadensis leucopariea*) by 1967; 1080-tallow baits were successfully used to control fox populations (Byrd et al. 1988; Tietjen et al. 1988; Bailey 1993). Earthworm baits are used to kill moles (Talpidae). The earthworms are soaked for 45 min in a 2.5% solution of 1080 and placed

in mole burrows. The solution can be used several times for additional lots of worms; however, the use of the manure worm (*Eisenia foetida*) should be avoided because it is seldom eaten by moles (Peacock 1964).

Secondary poisoning of domestic cats and dogs from consumption of 1080-poisoned rodents was frequently noted (Anonymous 1946). Cats and dogs are highly susceptible to 1080 and may die after eating freshly poisoned rodents, dried carcasses, or 1080-baits or after drinking 1080-poisoned water (Green 1946). All pets should be confined or removed from the area to be poisoned and released after the entire control is completed. Pigs and carnivorous wildlife are also at risk from consumption of 1080-poisoned rodents (Peacock 1964). Secondary poisoning of kit foxes (*Vulpes macrotis*) is theoretically possible after eating a single kangaroo rat (*Dipodomys* sp.) that swallowed or stuffed its cheeks with 1 g of a 0.1% vegetable/cereal bait and contained a total whole-body burden of about 1 mg of 1080/rat (Schitoskey 1975). To prevent secondary poisoning, all uneaten baits and carcasses of poisoned rodents should be recovered and incinerated (Green 1946), and no 1080-contaminated animal should be eaten by humans or be fed to animals (Connolly 1989, 1993a).

Nondomestic Use

Compound 1080 has had limited use as a vertebrate pesticide in Canada, India, Mexico, and South Africa and extensive use in Australia (Calver et al. 1989b) and New Zealand (Rammell and Fleming 1978). In Canada, 1080 was first used in 1950-51 in British Columbia to control wolves and coyotes preying on livestock (Peacock 1964). Poisoned 1080 baits were used in India to control (67-100% effective) populations of the Indian crested porcupine (*Hystrix indica*) throughout its range because of porcupine-caused damage and losses to agricultural crops; however, control of this species with 1080 baits was not as effective as fumigants (Khan et al. 1992). In Mexico, 1080 was used against rabid coyotes, although many domestic dogs were also killed (Peacock 1964). Beginning in 1961 in South Africa, 1080 was used to control the black-backed jackal (*Canis mesomelas*) that preyed on livestock, and baboons (*Papio anubis*) and moles that consumed agricultural crops (Peacock 1964). Livestock-protection collars containing 30 mL of a 1% solution of 1080 are now used in South Africa to combat predation by the Asiatic jackal (*Canis aureus*; Walton 1990).

Compound 1080 was first used in Australia in the 1950's to kill the introduced European rabbit (*Oryctolagus cuniculus*). Principal target species in Australia now include other introductions such as dingoes, red foxes (*Vulpes vulpes*), feral pigs (*Sus scrofa*), feral cats (*Felis cattus*) as well as native brush-tailed possums (*Trichosurus vulpecula*), red-necked wallabies (*Macropus rufogriseus*), and pademelons (*Thylogale billardierii*; McIlroy 1981a, 1981b, 1982,1984; Calver et al. 1989a, 1989b; Wong et al. 1991). In Australia, different baits contained different concentrations of 1080; meat baits contained 144 mg/kg, grain baits 288-300 mg/kg, fruits and vegetables 330 mg/kg, and pellets 500 mg/kg (McIlroy 1983a).

One method of killing rabbits in many areas of Australia is to apply 1080-poisoned bait (carrots, oat grains, pellets of bran or pollard) to furrows made in the earth or to broadcast baits across the area from the air or on the ground (McIlroy 1984; McIlroy and Gifford 1991). Aerial dropping of diced carrots treated with 1080 was almost 100% effective against rabbits (Anonymous 1964). In Victoria, more than 6.5 million ha were treated with 1080 poisoned carrots. To attract rabbits to the kill area, nonpoisoned carrots were applied to rabbit trails at more than 8.3 kg/km; nonpoisoned baits were offered twice, 3 days apart, before 1080-poisoned carrots were offered 1 week later (Woodfield et al. 1964). Bait avoidance is reported in some populations of European rabbits exposed repeatedly to 1080 baits during sustained control. Behavioral resistance may reduce the effectiveness of sustained control and should be considered in pest management (Hickling 1994). Individuals--but not populations--of some native species of Australian animals and birds face a greater risk of poisoning by 1080 during rabbit-poisoning campaigns than rabbits, particularly herbivorous macropodids, rodents, and bird species with no prior exposure to naturally occurring fluoroacetates (McIlroy 1992). Foxes, dingoes, dogs, and cats seem to be at greater risk of secondary poisoning than native birds and mammals, particularly from eating muscle from poisoned rabbits that contained as much as 5 mg of 1080/rabbit (McIlroy 1992).

The injection of fresh meat baits for the control of dingoes produced more uniform amounts of 1080 in the baits than tumbling mixed baits in 1080 solutions. Both techniques, however, produced baits containing variable quantities of 1080 (Kramer et al. 1987). Use of 1080-poisoned baits to control wild dogs (*Canis familiaris familiaris*) and dingoes were not as successful as traps: 22% control from 1080 versus 56% control with traps. Factors that reduced the success of poisoned baits included rapid loss in toxicity after distribution of the baits; the rapid rate at which they were removed by other animals, particularly foxes and birds; and the dogs' apparent preference for natural prey (McIlroy et al. 1986a).

Feral pigs in Australia damage crops, degrade pastures, kill and eat lambs, and are potential vectors and reservoirs of exotic pathogens (O'Brien et al. 1986; O'Brien 1988). Control of feral pigs with poisoned baits, including 1080 bait, is difficult because most pigs regurgitate these baits shortly after ingestion (O'Brien et al. 1986). The vomitus may cause secondary poisoning of nontarget species, and pigs surviving sublethal exposure to 1080 from vomiting may develop an aversion to 1080 and thus decrease their susceptibility to subsequent poisoning programs. The incorporation of antiemetics into 1080 baits should reduce or prevent vomiting, but those tested were not completely successful (O'Brien et al. 1986). Feral cats altered ecosystems and depleted populations of indigenous lizards and birds in Australia and in New Zealand and in numerous island habitats throughout the world. Fresh fish baits injected with 2 mg of 1080 per bait are used as a humane and lethal poison for feral cats (Eason and Frampton 1991).

The use of 1080 in New Zealand is restricted to licensed operators of pest-destruction boards and government departments (Temple and Edwards 1985). In Australia and in other locations, the addition of dye to identify toxic baits is standard practice (Temple and Edwards 1985; Statham 1989). The main purpose of such addition is to reduce the unintentional poisoning of birds; birds eat significantly less blue- or green-dyed feed than undyed feed (Statham 1989). Although birds prefer undyed baits to those dyed green, Canada geese (*Branta canadensis*) when feeding at night are unable to distinguish between dyed and undyed baits and consume both with equal frequency (Temple and Edwards 1985). Carrots used as wallaby baits in New Zealand are dyed with special green or blue pigments: however, the red-necked wallaby (*Macropus rufogriseus*) equally accepted dyed and undyed carrots (Statham 1989). Mice (*Mus* spp.) readily consumed dyed wheat (Twigg and Kay 1992). Compound 1080 is used in jam-type baits to control brush-tailed possums. These baits contained 1080 at concentrations as high as 1,500 mg 1080/kg FW bait and were dyed green to protect birds. Cinnamon was added to mask the flavor of the 1080 poison, and 800 mg potassium sorbate/kg was added as an antifungal preservative (Goodwin and Ten Houten 1991).

The Norway rat (*Rattus norvegicus*) had a severe effect on island populations of birds, reptiles, and invertebrates in New Zealand (Moors 1985). In one case, rats on the Big South Island exterminated five species of native forest birds within 3 years, including the last known population of the bush wren (*Xenicus longipes*). A paste containing petroleum jelly, soya oil, sugar, green dye, and 800 mg 1080/kg remained toxic for 6 to 9 months to rats that prey on grey-faced petrels (*Pterodroma macroptera*) and on other birds. Because 1080 produces a poison-shyness in any Norway rat that eats a sublethal dose, complete eradication of this species by 1080 is improbable (Moors 1985). The use of anticoagulants--such as warfarin (multiple doses needed), brodifacoum. (single dose) or coumatetralyl--seems more promising than 1080 for the control of rats (Moors 1985), although secondary poisoning of owls and hawks may occur (Hegdal and Colvin 1988).

In New Zealand, compound 1080 in a gel carrier is sometimes applied to the leaves of broadleaf (*Griselinia littoralis*) to poison red deer (*Cervus elephus*), feral goats, white-tailed deer (*Odocoileus virginianus*) and red-necked wallabies (Batcheler and Challies 1988). Use of 1080-gel baits reduced feral goat populations by 90% (Parkes 1983). Wallaby populations were reduced 87-91% with a 1080 gel applied to the foliage of palatable plants, and this compares favorably to reductions with aerially sown baits (Warburton 1990). The gel carrier was an effective phytotoxin, causing withering, death, or loss of chlorophyll from leaves within 10 days and sometimes within 24 h (Parkes 1983).

Feral pigs are sometimes poisoned by inserting as many as 10 gelatin capsules (each containing 100 mg of 1080) into carcasses or offal baits. Poisoned carcasses may remain edible for more than 2 months during fall and winter when poisoning campaigns are conducted; the 1080 is leached out when the carcass disintegrated (McIlroy 1983a). Other techniques to control feral pigs include injection of 1080 gel into beef-lung baits or insertion of capsules containing 1080 into apple, potato, or other fruit and vegetable baits. However, these techniques are potentially the most dangerous to applicators because 1080 powder, rather than a diluted solution, is used; also, the baits are lethal to nontarget scavengers (McIlroy 1983a).

Environmental Chemistry

General

Sodium monofluoroacetate is a whitish powder that is soluble in water to at least 263 mg/L but relatively insoluble in organic solvents. Some aqueous solutions of 1080 retain their rodenticidal properties for at least 12 months, but others lose as much as 54% of their toxicity after 24 days. Compound 1080 is unstable at more than 110° C and decomposes at more than 200° C, although 1080 in baits or poisoned carcasses is comparatively stable. Losses of 1080 from meat baits are due primarily to microbial defluorination and also to leaching from rainfall and consumption by maggots. Leachates from 1080 baits are probably not transported long distances by groundwater because they tend to be held in the upper soil layers. Compound 1080 can be measured in water at concentrations as low as 0.6 m/L and in biological samples at 10-15 m/kg. As discussed later, 1080 is readily absorbed through the gastrointestinal tract, mucous membranes, and pulmonary epithelia; once absorbed, it is uniformly distributed in the tissues. Metabolic conversion of high concentrations of fluoroacetate to fluorocitrate results in large accumulations of citrate in the tissues and eventual death from ventricular fibrillation or respiratory failure. Regardless of dose and tested species, no signs or symptoms of 1080 poisoning were evident during a latent period of 30 min to 2 h; however, death usually occurred within 24 h of exposure. Repeated sublethal doses of 1080 have increased the tolerance of some species of tested birds and mammals to lethal 1080 doses. Because of their low facility to convert fluoroacetate to fluorocitrate and their high defluorination capability, reptiles are more resistant to 1080 than mammals. No effective antidote is now available to treat advanced cases of fluoroacetate poisoning; accidental poisoning of livestock and dogs by 1080 is probably fatal. Partial protection against 1080 poisoning in mammals has been demonstrated with glycerol monoacetate, a sodium acetate-ethanol mixture, and with a calcium glutonate-sodium succinate mixture.

Chemical Properties

Compound 1080 is relatively soluble in water but not in organic solvents (Table 1). In water, trace amounts (0.6 m/L) of 1080 were detected during gas chromatography (GC) with electron capture detection; recoveries from environmental water spiked at 5-10 mg/L ranged from 93 to 97% (Ozawa and Tsukioka 1987). Recent advances make it possible to measure 1080 in solutions at concentrations as low as 0.2 mg/L (Kimball and Mishalanie 1993). In biological tissues, various methods have been used to determine fluoroacetic acid, including colorimetry, fluoride-ion electrodes, gas-liquid chromatography, and high-pressure chromatography; however, these methods involve lengthy extraction procedures, have low recoveries, or show lack of selectivity (Allender 1990). A sensitive gas chromatographic technique was developed and used successfully to determine fluoroacetate levels in organs from a magpie (*Gymnorhina tibicen*) that had ingested a bait containing 1080 poison. The procedure involved extraction of 1080 with acetone:water (8:1) followed by derivatization with pentafluorobenzyl bromide. Bait samples were initially screened by thin-layer chromatography, and identification of derivatized extracts was confirmed by gas chromatography/mass spectrometry = GC/MS (Allender 1990). A new method for fluoroacetate determination in biological samples requires the isolation of fluoroacetate as its potassium salt by ion-exchange chromatography and conversion to its dodecyl ester. The ester is quantified by capillary GC with a flame ionization detector for the range 1-10 mg/kg and by selected ion monitoring with GC/MS for the range 0.01-1.00 mg/kg (Burke et al. 1989). The detection limit for 1080 in tissues and baits is 15 mg/kg by a reaction-capillary GC procedure with photo-ionization detection; the detection limit is 100 mg/kg with flame-ionization procedures. The detection limit with these procedures is less sensitive than GC/MS; however, GC/MS is not normally available in veterinary diagnostic laboratories (Hoogenboom and Rammell 1987).

Table 1. Some properties of sodium monofluoroacetate.[a]

Variable	Datum
Alternate names	1080; Compound 1080; fratol; monosodium fluoroacetate; sodium fluoacetate; sodium fluoroacetate; ten-eighty
Chemical formula	$CH_2FCOONa$
Molecular weight	100.03
Physical state	White, odorless, almost tasteless, hygroscopic powdery salt, resembling powdered sugar or baking powder
Primary use	Rodenticide; mammal control agent
Purity	96.0-98.6%
Solubility	
Water	263 mg/L
Acetone, alcohol, animal and vegetable fats, kerosene, oils	Relatively insoluble
Stability	Unstable at > 110 and decomposes at >200° C. Hydrogen fluoride (20% by weight) is a decomposition product that readily reacts with metals or metal compounds to form stable inorganic fluoride compounds

[a]Chenoweth 1949; Negherbon 1959; Peacock 1964; Tucker and Crabtree 1970; Atzert 1971; Hudson et al. 1984.

Persistence

Significant water contamination is unlikely after aerial distribution of 1080 baits (Eason et al. 1993a). In one field trial in New Zealand in which more than 20 metric tons of 1080 baits were aerially sown over a 2,300-ha island to control brushtail possums (*Trichosurus vulpecula*) and rock wallabies (*Petrogale penicillata*), no 1080 was detected in surface or ground water of the island for at least 6 months after baits were dropped. A similar case was made for streams and rivers after 100 metric tons of 1080 baits were sown by airplane over 17,000 ha of forest (Eason et al. 1992, 1993b). Laboratory studies on 1080 persistence in solutions suggested that degradation to nontoxic metabolites is most rapid at elevated temperatures and in biologically conditioned media but is highly variable. In general, aqueous solutions of the salt or esters decrease in toxicity over time through spontaneous decarboxylation to sodium bicarbonate and to the highly volatile, relatively nontoxic methyl fluoride. Solutions refrigerated at 5° C lost about 54% of their initial toxicity to laboratory rats after 24 days and about 40% after 7 days at room temperature, but 1080 solutions remained toxic to yeast for at least 1 month after storage at 3-5° C (Chenoweth 1949). In an aquarium with plants and invertebrates and 0.1 mg 1080/L, the water concentration of 1080 declined 70% in 24 h and was not detectable after 100 h; residues in plants were not detectable after 330 h (Eason et al. 1993b). In a distilled water aquarium without biota, 1080 residues declined only 16% in 170 h (Eason et al. 1993b). In another study, 1080 solutions prepared in distilled water and stored at room temperature for 10 years showed no significant breakdown; moreover, solutions of 1080 prepared in stagnant algal-laden water did not lose biocidal properties during 12 months (McIlroy 1981a). More research on 1080 persistence in aquatic environments seems needed.

In soils, 1080 is degraded to nontoxic metabolites by soil bacteria and fungi, usually through cleavage of the carbon-fluoride bond (Eason et al. 1991, 1993a). Soil microorganisms capable of defluorinating 1080 include *Aspergillus fumigatus*, *Fusarium oxysporum*, at least 3 species of *Pseudomonas*, *Nocardia* spp., and 2 species of *Penicillium* (Wong et al. 1992a). When grown in solution with 1080 as the sole carbon source and in autoclaved soil, these microorganisms can defluorinate 1080; the amount of defluorination ranged from 2 to 89% in soils and from 2 to 85% in 1080 solutions. Some indigenous soil microflora were able to defluorinate 50-87% of the 1080 within 5-9 days in soil at 10% moisture and 15-28° C. The most effective defluorinaters in solution and in soils were certain strains of *Pseudomonas*, *Fusarium*, and *Penicillium* (Wong et al. 1991, 1992a; Walker 1994). *Pseudomonas cepacia*, for example, isolated from the seeds of various fluoroacetate-accumulating plants can grow and degrade fluoroacetate in fluoroacetate concentrations as high as 10,000

mg/kg (Meyer 1994). Biodefluorination of 1080 by soil bacteria was maximal under conditions of neutral to alkaline pH, at fluctuating temperatures between 11 and 24° C, and at soil moisture contents of 8-15%; biodefluorination of 1080 by soil fungi was maximal at pH 5 (Wong et al. 1992b).

Losses of 1080 from meat baits were probably due to consumption of the bait by blowfly maggots, leaching by rainfall, defluorination by microorganisms, and leakage from baits during decomposition (McIlroy et al. 1988), The 1080 in baits will persist under hot and dry conditions where leaching from rain is unlikely (Wong et al. 1992a). Baits remained toxic to dogs for more than 32 days during winter when maggots were absent and for 6-31 days during summer when maggots were present. Baits contained an average LD50 dose to tiger quolls (*Dasyurus maculatus*)—a raccoon-like marsupial--for 4-15 days in winter and for 2-4 days in summer (McIlroy et al. 1988). Meat baits that initially contained 4.6 mg of 1080 retained 62% after 3 days, 29% after 6 days, and 28% after 8 days (McIlroy et al. 1986a). The persistence of 1080 in fatty meat baits for control of wild dogs in Australia was measured during 226 days (Fleming and Parker 1991). Baits that initially contained 5.4 mg of 1080 retained 73% at day 7, 64% at day 20, 25% at day 48, and 15% at day 226. These baits retained LD50 kill values after 52 days to wild dogs, 93 days to cattle dogs, and 171 days to sheep dogs. In that study, loss of 1080 from the baits did not correlate with rainfall, temperature, or humidity. Losses were attributed to metabolism of 1080 bound to the fatty meat bait, leaching, consumption by maggots, and bacterial defluorination (Fleming and Parker 1991). When it is desirable for baits to remain toxic for long periods, the defluorination activity and microbial growth can be reduced significantly by incorporating bacteriostats and fungistats; conversely, inoculations with suitable defluorinating microbes rapidly detoxify 1080-poisoned baits (Wong et al. 1991).

Compound 1080 was highly persistent in diets formulated for the mink (*Mustela vison*). Mink diets analyzed 30 months after formulation lost 19-29% of the 1080 when the initial concentration was between 0.9 and 5.25 mg 1080/kg; loss was negligible at 0.5 mg 1080/kg ration (Hornshaw et al. 1986). A paste containing 0.08% 1080 and petroleum jelly, soya oil, sugar, and green dye retained its rodenticidal properties for 6 to 9 months. But a rolled oats-cat food 1080 bait, because of its moistness, became fly-infested in warm weather, tended to rot, and lost its rodenticidal properties in a few days (Moors 1985). Gel baits set to kill deer were sampled after 45 days of weathering; only 10% of the 1080-treated leaves retained toxic gel after 45 days (Batcheler and Challies 1988). About 1.4% of 1080/mm rainfall was lost from the leaves; about 90% was lost in 2 trials in which 81 and 207 mm of rainfall were recorded. Compound 1080 decreased from 604 mg/bait at the start to 76 mg/bait after 30 days and to 5 mg/bait after 45 days. Significant losses of compound 1080 also resulted from biodegradation in storage. *Penicillium* spp. from broadleaf samples degraded 1080 at pH 5.4 and 23° C and grew vigorously on 1080-poisoned gels; other species of microorganisms can also degrade 1080 (Batcheler and Challies 1988).

Leachates from 1080-poisoned baits are probably not transported long distances by the leaching water because they are held in the upper soil layers (Atzert 1971). This statement is predicated on the facts that (1) salts of monofluoroacetic acid rapidly adsorb to plant tissues and other cellulosic materials; (2) some plants can decompose 29% of the adsorbed 1080 in 48 h; and (3) 1080 in soils is decomposed by soil microorganisms (Atzert 1971). The percent of 1080 defluorinated from various bait materials after 30 days as a result of microbial action ranged from 0.0 to 7.2% in cereals, eggs, horse meat, and beef and was 14% in kangaroo meat and 71% in oats (Wong et al. 1991). The defluorinating ability of fungi and bacteria was low when 1080 was the sole carbon source and high when alternative carbon sources such as peptone-meat extracts were present. The extent of defluorination varied among the different types of organisms in the baits. Microorganisms isolated from oats and kangaroo meat had the highest defluorinating activity and those from cereals and eggs, the lowest (Wong et al. 1991).

Metabolism

Sodium monofluoroacetate is absorbed through the gastrointestinal tract, open wounds, mucous membranes, and the pulmonary epithelium; it is not readily absorbed through intact skin (Negherbon 1959; Atzert 1971). Once absorbed, it seems to be uniformly distributed in the tissues including the brain, heart, liver, and kidney (Peacock 1964). All tested routes of 1080 administration are equally toxic; there is no noteworthy difference in the acute toxicity of 1080 when administered orally, subcutaneously, intramuscularly, intraperitoneally, or intravenously (Chenoweth 1949; Peacock 1964; Atzert 1971). Moreover, the oral toxicity of

1080 is independent of the carrier, including water, meat, grain, oil, gum acacia suspension, or gelatin capsule carriers (Atzert 1971).

All students of the action of fluoroacetate have been impressed with the unusually long and variable latent period between administration and response. This latent period occurred in all studied species regardless of route of administration (Chenoweth 1949; Negherbon 1959; Peacock 1964; Tucker and Crabtree 1970; Atzert 1971; Hudson et al. 1984). With few exceptions, the latent period ranges from 30 min to 2 h and massive doses—such as 50 times an LD95 dose—do not elicit immediate responses. The time between 1080 treatment and death was relatively constant in all tested species and usually ranged from 1 h to 1 day. The latent period associated with 1080 may result from 3 major factors: (1) the time required for hydrolysis of monofluoroacetate to monofluoroacetic acid and its subsequent translocation and cell penetration; (2) the time required for biochemical synthesis of a lethal quantity of fluorocitrate; and (3) the time required for the fluorocitrate to disrupt intracellular functions on a large enough scale to induce gross signs of poisoning (Chenoweth 1949; Atzert 1971).

Many authorities agree that the toxicity of 1080 to mammals is due to its conversion to fluorocitrate, a fluorotricarboxylic acid (Gal et al. 1961; Atzert 1971; Roy et al. 1980; McIlroy 1981b; Kun 1982; Mead et al. 1985a, 1985b; Hornshaw et al. 1986; Twigg et al. 1986, 1988a, 1988b; Murphy 1986). These authorities concur that enzymatic conversion of fluoroacetate via fluoroacetyl coenzyme A plus oxalacetate in mitochondria is the metabolic pathway that converts the nontoxic fluoroacetate to fluorocitrate. Fluorocitrate blocks the Krebs cycle, also known as the tricarboxylic acid cycle, which is the major mechanism for realizing energy from food. Fluorocitrate inhibits the enzyme aconitase and thereby inhibits the conversion of citrate to isocitrate. Fluorocitrate also inhibits succinate dehydrogenase, which plays a key role in succinate metabolism. The inhibition of these two enzymes results in large accumulations of citrate in the tissues, blocking glucose metabolism through phosphofructokinase inhibition, and eventually destroys cellular permeability, cell function, and finally the cell itself. The classical explanation of fluorocitrate toxicity through aconitase inhibition has been questioned (Kun 1982; Savarie 1984). A more recent explanation is that fluorocitrate binds with mitochondrial protein, thereby preventing citrate transport and its utilization by cells for energy production, although the underlying biochemical mechanisms are not completely understood (Kun 1982). Based on calculated metabolic rates of fluorocarboxylic acids, secondary poisoning of animals that have consumed 1080-poisoned prey is probably due to unmetabolized fluoroacetate rather than to fluorocitric acid (Kun 1982).

Dogs, rats, and rabbits metabolize fluoroacetate compounds to nontoxic metabolites and excrete fluoroacetate and fluorocitrate compounds; the rate of excretion peaks during the first day after dosing and drops shortly thereafter. Rats dosed with radiolabeled 1080 at 5 mg/kg BW had 7 different radioactive compounds in their urine. Monofluoroacetate comprised only 13% of the urinary radioactive material, fluorocitrate only 11%, and an unidentified toxic metabolite, 3%; 2 nontoxic metabolites accounted for almost 73% of the urinary radioactivity (Atzert 1971). Animal muscle usually contained nondetectable residues of any 1080 component within 1 to 5 days of treatment (Marsh et al. 1987; Eason et al. 1993c). Defluorination occurred in the liver by way of an enzymic glutathione-dependent mechanism, which in the brush-tailed opossum resulted in the formation of S-carboxymethylcysteine and free fluoride ion (Twigg et al. 1986). A rapid rate of defluorination together with a low reliance on aerobic respiration favored detoxification of fluoroacetate rather than its conversion into fluorocitrate and may account for the greater resistance of 1080 by reptiles than by mammals (Twigg et al. 1986).

Sublethal doses of 1080 led to a tolerance to subsequent challenging doses in certain animals; in other species, however, lethal concentrations accumulated after repeated sublethal doses (Atzert 1971). Repeated sublethal doses of 1080 increased the tolerance of some eagles, rats, mice, and monkeys but not of dogs. Conversely, repeated sublethal doses of 1080 accumulated to lethal levels in dogs, guinea pigs, rabbits, and mallards. Continued sublethal doses of 1080 to rats caused regressive changes in the germinal epithelium of the seminiferous tubules (Atzert 1971). Altered behavior in mice after high sublethal doses of 1080 were probably caused by neuronal damage from concurrent energy deficiency that was further accentuated by the CNS stimulant action of fluoroacetate/fluorocitrate and the brain anoxia that occurred during 1080-induced intermittent convulsions; a similar pattern was observed in two human patients (Omara and Sisodia 1990). Anuria in some 1080-dosed mice were probably caused by renal shutdown from hypocalcemic tension (Omara and Sisodia 1990). Tolerance to 1080 is a time-related phenomenon (Atzert 1971). Laboratory rats that were pretreated with 0.5 mg 1080/kg BW 4-24 h prior to a dose of 5.0 mg/kg BW were more resistant than rats that

were not similarly pretreated (Atzert 1971). Accumulation of 1080 is also a time-related phenomenon (Chenoweth 1949; Atzert 1971). Domestic dogs given 25 mg 1080/kg BW daily were unaffected until the fifth dose, when they went into convulsions and died. Also, larger sublethal doses could be administered to dogs on alternate days without adverse effects (Atzert 1971).

Fishes, amphibians, and reptiles are usually less sensitive to 1080 than warm-blooded animals (Atzert 1971). Reptiles, for example, are more resistant to 1080 than mammals (Twigg et al. 1986). The relatively small elevation of plasma citrate levels in skinks (*Tiliqua rugosa*) given 100 mg 1080/kg BW reflects the exceptional tolerance of this lizard species. The minimal effect of fluoroacetate on aerobic respiration in *T*. *rugosa* could be explained by a low conversion of fluoroacetate into fluorocitrate or by a low susceptibility of aconitase to the fluorocitrate formed. Although defluorination in skinks helped to minimize the immediate effects of fluoroacetate in aerobic respiration, it resulted in rapid depletion of liver glutathione levels (Twigg et al. 1986).

The breakdown in intracellular processes from fluorocitrate or from decreased energy production may cause death from gradual cardiac failure or ventricular fibrillation, death from progressive depression of the CNS with either cardiac or respiratory failure, or death from respiratory arrest after severe convulsions; signs of 1080 intoxication included labored breathing, vomiting, lethargy, muscular incoordination, weakness, and tremors (Chenoweth 1949; Negherbon 1959; Tucker and Crabtree 1970; Atzert 1971; Hudson et al. 1984; Murphy 1986; Eason and Frampton 1991). Among herbivores, 1080-induced deaths were due primarily to cardiac disorders; among carnivores, deaths were from CNS disorders; and among omnivores, deaths were from both cardiac and CNS disorders (Atzert 1971). Other signs of 1080 intoxication included kidney and testicular damage (Savarie 1984) and altered blood chemistry, specifically, elevated concentrations of citrate (Twigg et al. 1986), glucose, lactic acid, pyruvic acid, acetate, inorganic phosphate, potassium, and fluorine (Negherbon 1959). Some mammals also displayed parasympathetic nervous system effects including increased salivation, urination, and defecation and eventual cardiac failure (Hudson et al. 1984).

Vomiting probably evolved among carrion eaters as a natural protective mechanism, but it does not necessarily ensure survival from 1080 poisoning (McIlroy 1981b). For example, even though 90% of eastern native quolls (*Dasyurus viverrinus*) and 95% of tasmanian devils (*Sarcophilus harrisii*) vomited within 26-55 min after ingesting 1080, this time was still sufficient for many to absorb a lethal dose. Loud sounds, sudden movements of an observer, or convulsions by another animal nearby sometimes stimulated convulsions; however, intraspecific and interspecific variability was great. Signs preceding convulsions usually included restlessness; hyperexcitability or increased response to stimuli; trembling; rapid, shallow breathing; incontinence or diarrhea; excessive salivation; twitching of facial muscles; abnormal eye movements; incoordination; vocalization; and sudden bursts of violent activity. All affected animals subsequently fall to the ground in a tetanic seizure; their hind limbs or all four limbs and sometimes the tail extend rigidly from their arched bodies. This tonic phase is followed by a clonic phase in which the animals kick with the front legs and eventually begin to relax. After this phase, animals either recover gradually, die shortly afterwards, experience additional seizures and then die or recover, or remain comatose until death as many as 6 days later (McIlroy 1981b).

Antidotes

No highly effective treatment of well established fluoroacetate poisoning is available (Chenoweth 1949; Peacock 1964; Atzert 1971), and accidental poisoning of livestock and domestic dogs is probably fatal (Mead et al. 1991). The following compounds were tested and had no effect on ameliorating 1080 intoxication: salts of fatty acids, anticonvulsants, vitamins, metabolic intermediates (Chenoweth 1949), and nonphysiological sulfhydryl compounds such as N-acetylcysteine and cysteamine (Mead et al. 1985a). As discussed later, sodium-acetate/ethanol mixtures, barbituates, glycerol monoacetate, calcium glutonate/sodium succinate mixtures, and 4-methylpyrazole offer partial protection to 1080-poisoned mammals, possibly because they compete with fluoroacetate in the Krebs cycle.

Sodium acetate and ethanol partially protect mice against 1080. Ethanol and sodium acetate administered together are twice as effective as either alone, suggesting a synergistic effect (Chenoweth 1949). Mixtures of acetate and ethanol reduced mortality of 1080-poisoned mice (given 2 times an LD50 dose) from 80% to 30% (Tourtellotte and Coon 1950). Mortality was reduced by 90% in mice given 170 mg 1080/kg BW (about 10 times an LD50 dose) and an intraperitoneal injection of sodium acetate (2-3 g/kg BW) dissolved in ethanol (1.6 g/kg BW). But the beneficial effect of the acetate-ethanol treatment to mice decreased rapidly with increasing time after the administration of 1080. Ethanol-acetate mixtures had some antidotal effect on 1080-poisoned dogs

provided that treatment was administered within 30 min of poisoning (Tourtellette and Coon 1950). A mixture of 2 g sodium acetate/kg BW and 2 g ethanol/kg BW is recommended for treatment of 1080-poisoned monkeys (Peacock 1964).

Barbituates were marginally effective in protecting domestic dogs but not laboratory mice against fluoroacetate poisoning (Chenoweth 1949; Peacock 1964). Barbituates administered to dogs within 30 min of 1080 poisoning (4 times an LD50 dose) resulted in 80% survival; when therapy was given 3 h after poisoning, survival was 17% (Tourtellette and Coon 1950). At higher 1080 doses (i.e., 6 times the LD50 value), barbiturates were ineffective. Repeated intravenous injections of 20 mg pentobarbital/kg BW to a 1080-poisoned dog (0.3 mg 1080/kg BW) prevented death when administered within 8.5 h of poisoning (Tourtellette and Coon 1950).

Glycerol monoacetate at 2 to 4 g/kg BW partially protects 1080-poisoned rats, rabbits, dogs, and rhesus monkeys (Chenoweth 1949; Peacock 1964; Murphy 1986). But its effectiveness is apparent only when administered intramuscularly in large amounts immediately after 1080-ingestion (Mead et al. 1991). A single dose of magnesium sulphate at 800 mg/kg BW given intramuscularly as a 50% solution shortly after 1080 exposure prevented death of rats dosed with marginally lethal amounts of 1080 (Peacock 1964).

A reduced level of blood calcium is one explanation for the toxic effects of fluoroacetate and may account for the gap between chemical manifestations and the biochemistry of 1080 poisoning (Roy et al. 1980). Cats poisoned with 1080 showed a 27% drop in blood calcium levels within 40 min; intravenous administration of calcium chloride prolonged the life of treated cats from 94 min to 167 min (Roy et al. 1980). In a search for effective antidotes to fluoroacetate poisoning, calcium gluconate was chosen to antagonize hypocalcemia, and sodium alpha ketoglutarate and sodium succinate were selected to revive the TCA cycle (Omara and Sisodia 1990). Effectiveness of each of these antidotes individually and in certain combinations was tested in laboratory mice exposed to lethal doses (15 mg/kg BW, intraperitoneal injection) of 1080. Antidotal treatments were administered from 15 min to 36 h after dosing. All three of the antidotes alone, and a combination of calcium glutonate with sodium alpha ketoglutarate were ineffective in reducing mortality in treated mice. However, a combination of calcium glutonate (130 mg/kg BW) and sodium succinate (240 mg/kg BW) was effective if the two solutions were either injected at separate sites or mixed in the same syringe just prior to injection. Increasing the dose of sodium succinate to 360 or 480 mg/kg BW with calcium glutonate (130 mg/kg BW) was unrewarding. Additional studies are needed to confirm the efficacy and mechanisms of action of this combination (Omara and Sisodia 1990).

Intraperitoneal injection of 4-methylpyrazole to rats at 90 mg/kg BW, given 2 h prior to 1080 administration, offered partial protection against accumulations of citrate or fluorocitrate in the kidney (Feldwick et al. 1994). The antidotal effects of 4-methylpyrazole are attributed to its inhibition of NAD^+-dependent alcohol dehydrogenase that converts 1,3-difluoro-2-propanol to difluoroacetone, an intermediate in the pathway of erythrofluorocitrate metabolism (Feldwick et al. 1994). A disadvantage of 4-methylpyrazole is that it needs to be administered before significant exposure to fluoroacetate.

First-aid treatment of humans accidentally poisoned with 1080 includes immediate emesis and gastric lavage followed by an oral dose of magnesium sulfate or sodium sulfate to remove the poison from the alimentary tract before absorption of lethal quantities can occur (Peacock 1964; Atzert 1971). When the stomach is emptied, oral administration of ethanol may be beneficial (Temple and Edwards 1985). The patient should be put at complete rest and given barbituates with moderate duration of action, such as sodium amytol, to control convulsions (Anonymous 1964; Atzert 1971). Intramuscular injections of undiluted glycerol monoacetate at 0.5 mg/kg BW are recommended every 30 min for several hours and then at a reduced level for at least 12 h (Atzert 1971; Temple and Edwards 1985). If intramuscular administration is not feasible, a mixture of 100 mL of undiluted glycerol monoacetate in 500 mL of water can be given orally and repeated in an hour (Atzert 1971). If glycerol monoacetate is not available, acetamide or a combination of sodium acetate and ethanol may be given in the same dose (Atzert 1971). If ventricular fibrillation occurs, the heroic treatment of 5 mL of a 1% procaine hydrochloride by intracardiac puncture is justified (Anonymous 1964). Intravenous administration of procainamide is also effective in the restoration of normal rhythm in ventricular fibrillations (Atzert 1971). Symptoms of 1080 poisoning usually subside in 12 to 24 h, but the patient should be kept in bed for at least 3 days (Anonymous 1946).

Lethal and Sublethal Effects

General

Mammals were the least resistant tested group against 1080; individuals of sensitive species died after receiving a single dose of 0.05-0.2 mg/kg BW. As discussed later, adverse sublethal effects included testicular damage in rats (*Rattus* spp.) after drinking water containing 2.2-20.0 mg 1080/L for 7 days (0.07-0.71 mg/kg BW daily), impaired reproduction in the mink on diets containing 0.8 mg 1080/kg ration for 60 days, and altered blood chemistry in European ferrets on diets containing 1.1 mg 1080/kg feed for 28 days. Elevated fluoroacetate residues of 34 mg/kg DW muscle and 423 mg/kg DW liver were measured in some 1080-poisoned mammals, notably in European rabbits. Sensitive species of birds died after a single 1080 dose of 0.6-2.5 mg/kg BW, daily doses of 0.5 mg/kg BW for 30 days, 47 mg/kg diet for 5 days, or 18 mg/L drinking water for 5 days.

Accumulation and adverse sublethal effects in birds occurred at dietary loadings of 10-13 mg 1080/kg ration. The risk to human consumers of cooked meat from 1080-poisoned waterfowl seems negligible. Amphibians and reptiles were more resistant to 1080 than mammals and birds because of their greater ability to detoxify fluoroacetate by defluorination, a reduced ability to convert fluoroacetate to fluorocitrate, and an aconitase hydratase enzyme that is comparatively insensitive to fluorocitrate inhibition. LD50 values in amphibians were greater than 44 mg 1080/kg BW; in reptiles, this value was greater than 54 mg 1080/kg BW. Other studies with 1080 and sensitive species showed death of mosquito larvae at water concentrations of 0.025-0.05 mg/L, death of terrestrial beetle and lepidopteran larvae at 1.1-3.9 mg/kg BW, no phytotoxicity to terrestrial flora at water concentrations of 10 mg/L, and--based on limited data--no adverse effects on freshwater fishes at 370 mg/L.

Terrestrial Plants and Invertebrates

Fluoroacetate was first isolated in South Africa in 1944 from the gifblaar plant (*Dichapetalum cymosum*; Negherbon 1959). Seeds of the South African *D*. *braunii* may contain as much as 8,000 mg fluoroacetate/kg DW (Meyer 1994). Several other species of *Dichapetalum* and *Palicourea marcgravii*, a South American poisonous species, produce fluoroacetate (Twigg et al. 1986; Twigg and King 1991). In Australia, fluoroacetate occurs naturally in the leaves, flowers, and seeds of more than 35 species of leguminous plants of the genera *Gastrolobium* and *Acacia* (Mead et al. 1985; Twigg et al. 1986, 1988, 1990; Twigg and King 1991; McIlroy 1992). All but two of these species are confined to the southwestern corner of Western Australia; the other two species occur in northern and central Australia. Fluoroacetate concentrations varied regionally, seasonally, among species, and among parts of the plants. The fluoroacetate content of these plants is usually greatest in flowers, seeds, and young leaves, and this is consistent with chemically mediated defense strategies in which plants use poisonous compounds to protect their most essential parts (Twigg and King 1991). In Australia, the highest measured fluoroacetate concentrations were in air-dried leaves and seeds of two species from Western Australia: concentrations reached 2,650 mg/kg in leaves and 6,500 mg/kg in seeds of *Gastrolobium* spp. Air-dried samples of the two species from northern and central Australia, *Acacia georginae* and *Gastrolobium grandiflorum*, contained as much as 25 mg fluoroacetate/kg leaf and 185 mg/kg seed (Twigg and King 1991).

Economic losses of domestic livestock were significant in Africa and Australia after ingestion of fluoroacetate-bearing vegetation (Twigg and King 1991). Herbivores that have had evolutionary exposure to this vegetation are much less susceptible to fluoroacetate intoxication than geographically separate, unchallenged species (Mead et al. 1985; Twigg et al. 1986). The development of tolerance to fluoroacetate by insects, reptiles, birds, and mammals has evolved on at least three continents where indigenous plants produce fluoroacetate that protects them against herbivory (Twigg and King 1991). In Australia, for example, animal populations that have coexisted with fluoroacetate-bearing vegetation for at least several thousands of years have developed varying degrees of tolerance to this potent toxin. Tolerance depends on their diets and habitats, sizes of their home ranges, mobility, and length of evolutionary exposure to fluoroacetate-bearing vegetation. Once developed, this tolerance is retained by animal populations even after isolation from the toxic vegetation for 70 to 100 centuries. Biochemical mechanisms responsible for the large toxicity differential between conspecifics with and without exposure to fluoroacetate-bearing vegetation are poorly understood (Twigg and King 1991).

Fluoroacetate and fluorocitrate have also been isolated from forage crops grown in an environment that is rich in atmospheric or inorganic fluoride (Lovelace et al. 1968; Ward and Huskisson 1969; Atzert 1971; Savarie 1984; Twigg and King 1991). For example, soybeans (*Glycine max*) can synthesize fluoroacetic acid when

grown in an atmosphere with elevated levels of hydrogen fluoride or in media containing high levels of sodium fluoride. Forage crops, including alfalfa (*Medicago sativa*) and crested wheat grass (*Agropyron cristatum*) grew near a phosphate plant that discharged inorganic fluoride with as much as 179 mg fluoroacetate/kg DW, 896 mg fluorocitrate/kg DW, and 1,000 mg total fluoride/kg. The plants were not adversely affected, but horses (*Equus caballus*) that grazed on these crops showed signs of fluoride poisoning, suggesting that the toxic effect of inorganic fluoride adsorbed or absorbed by plants and not incorporated into monofluoroacetic acid was greater than the toxic effect of monofluoroacetic acid synthesized by the plants (Lovelace et al. 1968; Atzert 1971). Lettuce (*Lactuca sativa*) that absorbed radiolabeled 1080 through its roots or leaves had elevated citrate concentrations and retained radioactivity (Ward and Huskisson 1969). Plants can degrade 1080 by cleaving the carbon-fluorine bond, as judged by studies with germinating seeds of the peanut *Arachis hypogea* (Atzert 1971).

Compound 1080 in gels, pastes, or grease carriers and smeared on leaves of palatable plants has been used to control ungulate and marsupial pests in New Zealand, including feral goats (*Capra* sp.), red deer (*Cervus elephus*), and white-tailed deer (*Odocoileus virginianus*; Parkes 1991). The effectiveness of 1080 in carbopol gel or in petrolatum grease on leaves of the mahoe (*Melicytus ramiflorus*) was significantly modified by the phytotoxicity of these carriers. Both carriers caused baited leaves to absciss, and the rate of abscission increased when 1080 was included. Petrolatum was one-third as phytotoxic as carbopol and retained 1080 for longer periods--at least 1 year. Carbopol lost about 95% of its 1080 after 64 days of exposure and 100 mm of rain but only 22% in petrolatum under similar conditions. Carbopol with 1080 is recommended for use where its distribution is sufficient to place goats and other target species at immediate risk; petrolatum can be used where a long-lasting bait is needed (Parkes 1991).

Compound 1080 has systemic insecticidal properties against insects feeding on treated plants. Cabbage (*Brassica oleracea capitata*) that had accumulated 1080 through its roots from solution or from soil cultures after application on leaves was toxic by contact to eggs and larvae of the large white butterfly (*Pieris brassicae*) and to various species of aphids (Negherbon 1959). Compound 1080 was not phytotoxic at 10 mg/L or at several times the concentration necessary for insecticidal action, but its use as an insecticide is not recommended because of its high toxicity in mammals (Negherbon 1959; Spurr 1991).

At least nine groups of terrestrial invertebrates are adversely affected by 1080-poisoned baits, by contaminated habitats with residues that leach from 1080 baits, or by the consumption of animal byproducts and carcasses contaminated with 1080 (Chenoweth 1949; Notman 1989). Lethal effects are reported in houseflies, moths, aphids, ants, bees, and mites that ate 1080-poisoned baits and in fleas that ingested 1080-poisoned rats (Notman 1989). Cockroaches, collembolids, and slugs that ate poisoned baits experienced adverse effects. Egg production in wasps was disrupted after a single sublethal dose of 1080, and mortality of larvae from butterfly eggs treated with 1080 was 98% (Notman 1989). Harvester ants (*Pogonomyrtnex* sp.) and darkling ground beetles (Tentyridae) removed and consumed 1080 bait, leaving bait and dead ants concentrated on the ground near the nest (Hegdal et al. 1986). In a control program, German wasps (*Vespula germanica*) and common wasps (*Vespula vulgaris*) fed 1080-poisoned canned sardines in aspic jelly were not affected at concentrations of less than 100 mg 1080/kg bait (Spurr 1991). At 1,000 mg/kg, however, wasp traffic at nest entrances was reduced by 17%; at 5,000-10,000 mg/kg, traffic was reduced by 78-89%, and almost all wasps died within 100 m of bait stations after 6 h (Spurr 1991). Honeybees (*Apis mellifera*) feed readily on 1080-jam baits that are used to control opossums (*Trichosurus vulpecula*) in New Zealand (Goodwin and Ten Houten 1991). Bee kills have been documented in the vicinity of jam baits, and dead bees contained 3.1 to 10.0 mg 1080/kg whole bee. The oral LD50 in the honey bee is 0.8 mg/bee. Because no deaths occur within 2 h after feeding, poisoned bees may make several foraging trips before dying. Molasses or oxalic acid is now added to 1080-jam baits to repel bees (Goodwin and Ten Houten 1991). Poisoned insects may cause secondary poisoning of insectivores. Accordingly, 1080 should not be used in the vicinities of susceptible nontarget invertebrates or endangered insectivores (Notman 1989).

Variability in sensitivity to 1080 after abdominal injection in tested insect larvae was great (Twigg 1990). The LD50 value in mg 1080/kg BW--administered by fluoroacetate-bearing vegetation--was 1.05 in *Perga dorsalis* (Hymenoptera); in Lepidoptera, these values were 3.9 in *Mnesampla privata*, 42.7 in *Spilosoma* sp., and about 130.0 in *Ochrogaster lunifer*. In all tested species, death occurred within 2 to 48 h after injection, and total body citrate concentrations were significantly higher in the poisoned than in the unpoisoned conspecifics. Tolerance to 1080 was enhanced in larvae of Western Australian insects that consumed fluoroacetate-bearing vegetation (Twigg 1990).

Populations of terrestrial invertebrates including populations of amphipods, ants, beetles, collembolids, millipedes, mites, weevils, slugs, spiders, and snails were not adversely affected by 1080 poisoning in operations to control brushtail possums in New Zealand (Spurr 1994). Residues of 1080 in nontarget terrestrial invertebrates were low or negligible after aerial applications (Eason et al. 1993b). Residues of 1080 were measured in various species of terrestrial invertebrates in New Zealand before and after aerial application of possum baits with 800 mg 1080/kg and sown at 5 kg/ha. No residues of 1080 were found in spiders, beetles, millipedes, centipedes, or earthworms at any stage. Residues of 1080 were detectable in some orthopteran insects (2 mg/kg FW) and in some cockroaches (4 mg/kg FW). Laboratory studies indicated that 90% of all 1080 was eliminated from insects within 4-6 days after dosing, suggesting a low risk to insectivorous birds (Eason et al. 1993b).

Aquatic Organisms

Despite an intensive literature search, very little data were found on the toxicity of 1080 to aquatic life. King and Penfound (1946) reported that fingerling bream and bass (species unidentified) tolerated 370 mg of 1080/L without apparent discomfort for an indefinite period. Deonier et al. (1946) aver that fourth-instar larvae of the mosquito *Anopheles quadrimaculatas* were comparatively sensitive to 1080 and that 1080 was among the most toxic 3% of 6,000 organic compounds screened against this life stage. In 48 h, concentrations of 0.025 mg 1080/L were fatal to 15% of these larvae, 0.05 mg 1080/L to 40%, and 0.1 mg 1080/L to 65%. The common duckweed (*Spirodela oligorrhiza*) seems to be unusually sensitive to 1080. Growth of duckweed was inhibited at 0.5 mg/L (Walker 1994), but this needs verification.

Recent unpublished data (as quoted in Fagerstone et al. 1994) on the acute toxicity of 1080 to rainbow trout (*Oncorhynchus mykiss*), bluegills (*Lepomis macrochirus*), and daphnids (*Daphnia magna*) suggested that these organisms are comparatively tolerant to 1080. For example, bluegills exposed to 970 mg 1080/L for 96 h showed no observable adverse effects; in rainbow trout, the no-observable-effect concentration during a 96-h exposure was 13 mg 1080/L, and the LC50 (96 h) value was 54 mg/L with a 95% confidence interval of 39-74 mg/L; in *Daphnia*, no adverse effects were noted at 130 mg 1080/L during an exposure for 48 h, although 50% were immobilized at 350 mg/L in 48 h (Fagerstone et al. 1994). No data were available on effects of 1080 to aquatic biota during a life cycle or during long-term exposures. The effects of chronic exposure to 1080 on nontarget species of aquatic arthropods and macrophytes require study.

Amphibians and Reptiles

In general, the onset of action and time to death or to recovery was slowest in amphibians and reptiles, which were among the most resistant to 1080 of all tested vertebrate animals (McIlroy et al. 1985; McIlroy 1986). LD50 values in representative species of amphibians ranged from 54 to 2,000 mg 1080/kg BW and in reptiles from 44 to 800 mg/kg BW (Table 2). Frogs and lizards given a lethal oral dose of 1080 did not show signs of poisoning for 22 to 56 h and survived for 78 to 131 h (McIlroy et al. 1985). Frogs seem to be more sensitive to 1080 in summer than in winter (Chenowith 1949). Unlike mammals, amphibians and reptiles possess an innate tolerance to 1080 because of their greater ability to detoxify fluoroacetate by defluorination, a reduced ability to convert fluoroacetate to fluorocitrate, and an aconitase hydratase enzyme system that is less sensitive to inhibition by fluorocitrate (Twigg and Mead 1990).

One of the most tolerant tested reptiles was the shingle-back lizard (*Tiliqua rugosa*; McIlroy 1986), but populations of *T. rugosa* from Western Australia that coexist with fluoroacetate-bearing vegetation were much less sensitive to 1080 intoxication than conspecifics from South Australia not exposed to the toxic plants (Table 2; McIlroy et al. 1985; Twigg et al. 1988a; Twigg and Mead 1990). The shingle-back lizard is an omnivore that feeds on flowers, leaves, and seeds and probably evolved an increased tolerance to fluoroacetate through feeding on toxic plants such as *Gastrolobium* and *Oxylobium* that are abundant in southern Western Australia (McIlroy et al. 1985).

Reptiles are probably not affected by either primary or secondary poisoning during 1080-poisoning campaigns (McIlroy 1992). In Australia, 1080-poisoned baits contained 330 mg 1080/kg in carrot baits for rabbits and in oat baits for pigs, 400 mg 1080/kg in oat baits for rabbits, 500 mg 1080/kg in pellet baits for rabbits and pigs, 14 mg 1080/kg in meat baits for dingoes, and 144 mg/kg in meat baits for pigs (McIlroy et al. 1985). These data indicate that most species of tested reptiles must ingest unrealistic quantities of bait to be adversely affected by 1080. Most lizards, for example, must eat 43-172% of their body weight of poisoned rabbit

baits and 143 to 393% of their body weight of meat baits intended for pigs. However, Gould's monitor (*Varanus gouldi*) may ingest lethal amounts of meat baits intended for pigs after eating 31% of its body weight of poisoned baits. By comparison, a large pig (130 kg) must eat about 2 kg of meat baits (1.6% of its body weight) for an LD99 dose (McIlroy et al. 1985).

Birds

Laboratory studies with birds (Table 3) revealed several trends: (1) death occurred in orally dosed sensitive species after a single dose of 0.6-2.5 mg 1080/kg BW, after daily doses of 0.5 mg 1080/kg BW for 30 days, after 47 mg/kg diet for 5 days, or after 18 mg/L drinking water for 5 days; (2) single doses of more than 10 mg/kg BW were usually fatal; (3) 1080 toxicity was enhanced at lower temperatures; (4) younger birds were more sensitive than older birds; (5) birds tended to avoid diets and drinking water with high sublethal concentrations of 1080; (6) accumulations and adverse effects were noted at dietary concentrations of 10-13 mg 1080/kg feed; and (7) birds with prior or continuing exposures to naturally occurring fluoroacetates were more resistant to 1080 than conspecifics without such exposures. Drinking-water-LC50 values were about 10 times higher (i.e., 10 times less toxic) than dietary LC50s in mallards (*Anas platyrhynchos*) and in northern bobwhites (*Colinus virginianus*); however, both species of birds consumed 5 to 10 times more water than food on a daily mg/kg BW basis (Kononen et al. 1991). The minimum repeated daily oral dosage that was lethal to mallards in 30-day tests was 0.5 mg/kg BW, suggesting a high degree of cumulative action by this species (Tucker and Crabtree 1970). But European starlings (*Sturnus vulgaris*) tolerated 13.5 mg 1080/kg diet for extended periods without significant adverse effects (Balcomb et al. 1983). Studies with the galah (*Cacatua roseicapilla*) showed that 1080 lethality was not affected by the age or sex of the bird or by the route of administration (McIlroy 1981a). But breeding adult female Pacific black ducks (*Anas superciliosa*) were more sensitive to 1080 than either males or nonbreeding females (McIlroy 1984).

The most common external signs of 1080 poisoning in birds included depression, fluffed feathers, a reluctance to move, and convulsions (McIlroy 1984). Signs of 1080 poisoning first appeared 1 to 60 h after dosing, and deaths occurred 1 h to almost 11 days after dosing (McIlroy 1984). Death of 1080-poisoned California quail (*Callipepla californica*) usually occurred within 3 h, although birds were inactive within 2 h of dosing and comatose until death (Sayama and Brunetti 1952). The most common internal sign of 1080 poisoning was a dose-related increase in plasma citrate concentration, and this was a useful indicator of fluoroacetate sensitivity among birds of similar metabolic rates and phylogenetic affinities (Twigg and King 1989).

Table 2. Effects of 1080 on representative amphibians and reptiles.

Table 2. Group, species, dose, And other variables	Effects	Reference[a]
Amphibians		
Spotted grass frog, *Limnodynastes tasmaniensis*; 60 mg/kg body weight (BW); single dose	LD50, adults	1
Bullfrog, *Rana catesbeiana*; 54.4 (95% confidence interval [=CI] of 25.6-115.0) mg/kg BW; single dose	LD50	2, 6
Frogs, various; 1,000-2,000 mg/kg BW; single dose	LD50	7, 8
Leopard frog, *Rana pipiens*; 150 mg/kg BW; single dose	LD50	2, 9
South African clawed frog, *Xenopus laevis*; >500 mg/kg BW; single dose	LD50	2, 9

Table 2.

Group, species, dose, And other variables	Effects	Reference[a]
Reptiles		
Australian reptiles 163 (44-336) mg/kg BW	LD50 mean and range for five species with no previous exposure to naturally occurring fluoroacetates	10
250 and 800 mg/kg BW	LD50 for two species with prior or continuing exposure to naturally occuring fluoroacetates	10
Gopher snake, *Pituophis catenifer*; fed dead or moribund rodents poisoned with high concentrations of 1080	In 21 separate trials, 14 snakes regurgitated rodents and 7 had no significant effects within 5 days of ingestion	11
Bearded dragon, *Pogona barbatus*; <110 mg/kg BW; single dose	LD50	1
Blotched blue-tongued lizard, *Tiliqua nigrolutea*; 336 (95% CI of 232-487) mg/kg BW; single dose	LD50	1, 5
Shingle-back lizard, *Tiliqua rugosa*; single dose 25 mg/kg BW	No effect on plasma testosterone concentration	3
100 mg/kg BW	Plasma testosterone concentration decreased 52%	3
100 mg/kg BW	Plasma citrate levels increased 3.4 times after 48 h	4
206 (95% CI of 147-289) mg/kg BW	LD50; nontolerant populations from South Australia	1,5
300 mg/kg BW	Oxygen consumption reduced 2.5-11.0% over a 22-h postdosing observation period	4
525 (95% CI of 487-589 mg/kg BW)	LD50; tolerant populations from Western Australia	1
Gould's monitor, *Varanus gouldi* 43.6 (95% CI of 27.5-69.2) mg/kg BW; single dose	LD50	1,5
Lace monitor, *Varanus varius*; <119 mg/kg BW; single dose	LD50	1

[a]1, McIlroy et al. 1985; 2, Atzert 1971; 3, Twigg et al. 1988a; 4, Twigg et al. 1986; 5, McIlroy and Gifford 1992; 6, Tucker and Crabtree 1970; 7, Negherbon 1959; 8, Anonymous 1946; 9, Chenoweth 1949; 10, McIlroy 1992; 11, Brock 1965.

Table 3. Effects of 1080 on representative birds.

Table 3. Species, dose, and other variables	Effects	Reference[a]
Chukar, *Alectoris graeca*; 3.5 (95% confidence interval [=CI] of 2.6-4.8) mg/kg body weight (BW); single dose	LD50	1, 2, 3, 4
Northern pintail, *Anas acuta*; 8-10 mg/kg BW; single dose	50-100% dead	2, 5
American wigeon, *Anas americana*; single dose		
4.0 mg/kg BW; males	LD100	5
11.0 mg/kg BW; females	LD100	5
Mallard, *Anas platyrhynchos*		
0.5 mg/kg BW; daily oral dose for 30 days	Some deaths in 30 days, but less than 50%	3, 4
3.7 (95% CI of 21.5-5.5) mg/kg BW; single dose; age 7 days	LD50	6
4.8 (95% CI of 2.6-9.0) mg/kg BW; single dose; age 6 months	LD50	6
6.0 (95% CI of 4.2-8.4) mg/kg BW; single dose; ducklings	LD50	3, 4
7.0-7.5 mg/kg BW; single dose	LD75-LD100	5
8.0 mg/kg BW; adult females; single dose	LD50	2
9.1 (95% CI of 5.6-14.6) mg/kg BW; single dose; adults	LD50	1, 3, 4
10.0 mg/kg BW; adult males; single dose	LD50	2
13-24 mg/L drinking water for 5 days plus 3-day observation period; age 10 days	Avoidance of water containing 1080 when given choice	7
18-24 mg/L drinking water for 5 days plus 3-day observation period; age 10 days	50-90% dead	7
≥236 mg/kg diet fresh weight (FW) for 5 days plus 3-day observation period; age 10 days	Avoidance of diets containing 1080 when given choice	7
527 mg/kg diet FW for 5 days plus 3-day observation period; age 10 days	50% dead	7
Pacific black duck, *Anas superciliosa*; single dose		
10.0 (95% CI of 7.4-13.5) mg/kg BW;	LD50	8

Table 3. Species, dose, and other variables	Effects	Reference[a]
adult breeding females		
18.9 (95% CI of 16.3-219) mg/kg BW; adult males	LD50	8, 9
23.8 (95% CI of 15.3- 37.0) mg/kg BW; adult nonbreeding females	LD50	8
Wedge-tailed eagle *Aquila audax*; 9.5 (95% CI of 7.2-12.5) mg/kg BW; single dose	LD50	8, 10
Golden eagle, *Aquila chrysaetos*; single dose		
1.25-5.00 mg/kg BW	LD50	2, 3, 5, 26
3.5 (95% CI of 0.5-25.1) mg/kg BW	LD50	4, 11
Australian birds; various species; single dose		
7.8 (0.6-25.0) mg/kg BW	LD50 mean and range for 45 species with no known past exposure to naturally occurring fluoroacetates	27
28.4 (1.8-102.0) mg/kg BW	LD50 mean and range for 14 species with prior or continuing exposure to naturally occurring fluoroacetates	27
Australian birds, 41 species; single dose		
0.6-0.99 mg/kg BW	LD50, 2 species	8
1.0-9.9 mg/kg BW	LD50, 27 species	8
20.0-49.9 mg/kg BW	LD50, 11 species	8
>200 mg/kg BW	LD50, 1 species	8
Port Lincoln parrot, *Barnardius zonarius*; 11.5 (95% CI of 9.6-13.7) mg/kg BW; single dose	LD50	9, 12
Great horned owl, *Bubo virginianus*; 20 mg/kg BW; single dose	LD50	5
Rough-legged hawk, *Buteo lagopus*; 10 mg/kg BW; single dose	LD50	5
Ferruginous hawk, *Buteo regalis*; 10 mg/kg BW; single dose	LD50	5
Sulphur-crested cockatoo, *Cacatua galerita*; 3.5 (95% CI of 2.9-4. 1) mg/kg BW; single dose	LD50	8, 13
Galah, *Cacatua roseicapilla*; ~5.6 (95% CI of 3.1-10.5) mg/kg BW; single dose	LD50	8, 14
California quail, *Callipepla californica*		
0.5 or 1.0 mg/kg BW; single dose	No deaths	15
0.5 or 1.0 mg/kg BW on day 1; 2.5 mg/kg BW on days 2, 3, and 4	All dead	15

Table 3. Species, dose, and other variables	Effects	Reference[a]
4.6 (95% CI of 2.7-8.1) mg/kg BW; single dose	LD50	4
>5.0 mg/kg BW; single dose	All dead	15
Turkey vulture, *Cathartes aura*; single dose		
20 mg/kg BW	Lethargy and wing-drooping at 13° C	24
30 mg/kg BW	Tremors, lethargy, ataxia, incoordination at 11-17° C	24
40 mg/kg BW	Lethal at 7-9° C; lethargy, ataxia, and incoordination at 15° C	24
60 mg/kg BW	Tremors, lethargy, and wing-droop at 15-20° C	24
80 mg/kg BW	All dead within 4 h at 20° C; no regurgitation	24
100 mg/kg BW	75% dead at 23-28° C	24
Maned duck, *Chenonetta jubatta*; 12.6 (95% CI of 10.1-15.7 mg 1080/kg BW); single dose	LD50	8, 9
Northern harrier, *Circus cyaneus*; 10 mg/kg BW; single dose	LD50	5
Northern bobwhite, *Colinus virginianus*		
>9 mg/L drinking water daily for 5 days plus 3-day observation period	Avoidance of water containing 1080 when given choice	7
31 mg/L drinking water daily for 5 days plus 3-day observation period	50% dead	7
93 mg/L drinking water daily for 5 days plus 3-day observation period	All dead	7
>95 mg/kg diet daily for 5 days plus 3-day observation period	Avoidance of 1080 diets when given choice	7
385 mg/kg diet daily for 5 days plus 3-day observation period	50% dead	7
Grey shrike thrush, *Colluricincla harmonica*; ~ 12.0 mg/kg BW; single dose	LD50	13
Rock dove, *Columba livia*; 4.2 (95% CI of 3.4-5.3) mg/kg BW; single dose	LD50	1, 2, 3
Black vulture, *Coragyps atratus*; 15 mg/kg BW; single dose	LD50	2, 5
Little crow, *Corvus bennetti*; 13.4 (95% CI of 11.7-15.2) mg/kg BW; single dose	LD50	8, 10, 13

Table 3. Species, dose, and other variables	Effects	Reference[a]
Australian raven, *Corvus coronoides*; 5.1 mg/kg BW; single dose	LD50	10, 13
Little raven, *Corvus mellori*; 3.1 (95% CI of 2.7-3.6) mg/kg BW; single dose	LD50	8
Japanese quail, *Coturnix japonica*; 16.2 (95% CI of 7.2-28.7) mg/kg BW; single dose	LD50	2, 4
Laughing kookaburra, *Dacelo novaeguineae*;~6.0 mg/kg BW; single dose	LD50	10, 13
Emu, *Dromaius novaehollandiae*; 102-278 mg/kg BW; single dose	LD50	8, 12, 13
Red-browed firetail, *Emblema temporalis*; 0.6 (95% CI of 0.4-1.0) mg/kg BW; single dose	LD50	8
Brewer's blackbird, *Euphagus cyanocephalus*; 2.5-3.0 mg/kg BW; single dose	LD33-LD50	2,5
Finches, 7 species; 2.7 (95% CI of 0.8-4.6) mg/kg BW; single dose	LD50	16
Flycatchers, 4 species; 13.2 (95% CI of 8.7-20.0) mg/kg BW; single dose	LD50	16
Domestic chicken, *Gallus* spp.; 5.0-18.0 mg/kg BW; single dose	LD50-LD100	2, 5, 15, 17, 18, 19, 25, 26
Gamebirds, 8 species; 7.3 (95% CI of 0.0-16.4) mg/kg BW; single dose	LD50	16
Australian magpie-lark, *Grallina cyanoleuca*; 8.8 (95% CI of 4.0-13.5) mg/kg BW; single dose	LD50	8, 13
Australian magpie, *Gymnorhina tibicen*; 9.9 (95% CI of 7.6 12.9) mg/kg BW; single dose	LD50	8, 10, 13
Honeyeaters, 5 species; 8.1 (95% CI of 6.9-9.5) mg/kg BW; single dose	LD50	16
Gambel's quail, *Callipepla gambeli*; 20 mg/kg BW; single dose	LD50-LD57	2, 5, 26
Turkey, *Meleagris gallopavo*; 4.8 (95% CI of 1.2-19.0) mg/kg BW; single dose	LD50	4
Black kite, *Milvus migrans*; 18.5 (95% CI of 15.0-23.2) mg/kg BW; single dose	LD50	8, 10, 13
Parrots, single dose 8 species; 4.0 (95% CI of 0.0-9.3) mg/kg BW	LD50	16

Table 3. Species, dose, and other variables	Effects	Reference[a]
5 species; 5-75 mg/kg BW	LD50	9
House sparrow, *Passer domesticus*; single dose		
2.5 mg/kg BW	LD43	5
3.0 (95% CI of 2.4-3.8) mg/kg BW	LD50-LD100	1, 2, 3, 4, 20, 26
Zebra finch, *Peophila guttata*; fed diet containing 10 mg 1080/kg; equivalent to 11-15 mg/kg BW daily	Maximum fluoroacetate concentrations, in mg/kg FW, were 12.6 in crop, 2.0 in stomach, 2.0 in liver, 6.0 in heart, 3.9 in intestine, and 1.2 in muscle; mean concentrations were about 1 mg/kg FW for all tissues except heart (2.0 mg/kg FW)	21
Ring-necked pheasant, *Phasianus colchicus*; 6.5 (95% CI of 3.9-10.8) mg/kg BW; single dose	LD50	1, 2, 3, 4
Black-billed magpie, *Pica pica*; single dose		
0.67 mg/kg BW	No deaths	5
1.3 mg/kg BW	LD100	5
1.6 mg/kg BW; survivors sacrificed at 24 h	Residues of 1080, in mg/kg FW, in survivors were 0.05-0.34 in muscle and 0.07-0.49 In stomach. Dead birds contained 0.2 mg/kg FW in muscle and 0.25 in stomach	22
2.0, 2.5, or 3.2 mg/kg BW	All dead within 24 h. Mean (max.) 1080 residue concentrations, in mg/kg FW, were 0.4 (0.6),0.7 (1.0) and 0.9 (1.4) in muscle, respectively; for stomach, these values were 0.4 (0.9), 0.7 (1.1), and 1.0 (1.5), respectively	22
Pigeons and doves, single dose		
3 species; 10.6 (6-40) mg/kg BW	LD50	9
5 species; 10.6 (95% CI of 1.9-60.9) mg/kg BW	LD50	8, 16, 26
Red-rumped parrot, *Psephotus haematonotus*; ~5.3 mg/kg BW; single dose	LD50	13
Raptors, 5 species; 9.1 (95% CI of 5.1-13. 1) mg/kg BW; single dose	LD50	16
Seed-eating birds; 4 species; single dose; from Western Australia, exposed to fluoroacetate-bearing vegetation; 25-75 mg/kg BW	LD50	12
Pied currawong, *Strepera graculina*; 13.1 (95% CI of 10.9-15.7)	LD50	8

Table 3. Species, dose, and other variables	Effects	Reference[a]
mg/kg BW; single dose		
Laughing dove, *Streptopelea senegalensis*; 5.9 (95% CI of 4.2-8.2) mg/kg BW; single dose	LD50	9
European starling, *Sturnus vulgaris*		
13.5 mg 1080/kg diet for 4 weeks	Treated birds had slightly lower body weight and testes weight than controls, but differences were not statistically significant	23
27 mg 1080/kg diet	No deaths in 5 days	23
47 (95% CI of 27-108) mg 1080/kg diet for 5 days	50% dead	23
54 mg 1080/kg diet for 5 days	67% dead	23
108 mg 1080/kg diet for 3 days	50% dead	23
198 (95% CI of 119-400) mg 1080/kg diet for 24 h	50% dead	23
432 mg 1080/kg diet for 48 h	All dead	23
Waterfowl, 7 species; 7.1 (95% CI of 1.9-25.6) mg/kg BW; single dose	LD50	16
Mourning dove, *Zenaida macroura*; 8.6-14.6 mg/kg BW; single dose	LD25-LD50	1, 2, 4, 5, 20

[a] 1, Tucker and Haegele 1971; 2, Atzert 1971; 3, Tucker and Crabtree 1970; 4, Hudson et al. 1984; 5, Peacock 1964; 6, Hudson et al. 1972; 7, Kononen et al. 1991; 8, McIlroy 1984; 9, Twigg and King 1989; 10, McIlroy and Gifford 1992; 11, Burns et al. 1991; 12, Twigg et al. 1988b; 13, McIlroy 1983a; 14, McIlroy 1981a; 15, Sayama and Brunetti 1952; 16, McIlroy 1986; 17, Anonymous 1946; 18, Kalmbach 1945; 19, Negherbon 1959; 20, Green 1946; 21, Burke et al. 1989; 22, Okuno et al. 1984; 23, Balcomb et al. 1983; 24, Fry et al. 1986; 25, Robison 1970; 26, Chenoweth 1949; 27, McIlroy 1992.

Some birds poisoned with 1080 either vomited (little crow, *Corvus bennetti*; emu, *Dromaius novaehollandiae*; wedge-tailed eagle, *Aquila audax*; sulphur-crested cockatoo, *Cacatua galerita*) or had saliva or fluid dripping from their beaks (Pacific black duck, *Anas superciliosa*; McIlroy 1984). Early signs of poisoning, such as vomiting, were seen at oral doses of 10 mg/kg BW in various raptors including the rough-legged hawk (*Buteo lagopus*), the ferruginous hawk (*Buteo regalis*), the northern harrier (*Circus cyaneus*), and the great horned owl (*Bubo virginianus*; Atzert 1971). The onset of convulsions was preceded by rapid panting, squawking, shrieking or other vocalizations and then a brief period (5-120s) of violent wing flapping, loss of balance, or paddling or running motions with the feet. Birds then fell to the ground while undergoing tetanic seizures, breathing slowly and laboriously, and having wings and tail outstretched (McIlroy 1984). Turkey vultures (*Cathartes aura*) fatally poisoned by 1080 died 4-32 h after dosing; prior to death, birds displayed tremors, ataxia, lethargy, wing drooping and emesis. Turkey vultures were more sensitive to 1080 at colder temperatures of 8-9° C than at 23-28° C; this may be due to inhibition by 1080 of mitchondrial oxidative phosphorylation at colder temperatures that make animals more sensitive at times of increased metabolic demand (Fry et al. 1986).

Some bird species probably developed a tolerance to 1080 from eating plants that contain fluoroacetate or insects and other organisms that fed on such plants (McIlroy 1984). Birds indigenous to geographic areas of Australia where fluoroacetate-bearing vegetation is abundant were more tolerant to 1080 than birds distributed outside the range of the toxic plants. Fluoroacetate tolerance in birds is postulated to increase with increasing evolutionary exposure to the toxic plants and decreasing mobility (Twigg and King 1989). In the low-nutrient environment of Western Australia, fluoroacetate-tolerant herbivores clearly have a potential advantage over nontolerant herbivores in their broadened choice of fluoroacetate-bearing vegetation in the diet (Twigg et al.

1988b). The most sensitive tested Australian bird was the red-browed firetail (*Emblema temporalis*) with an LD50 of 0.63 mg 1080/kg BW (0.007 mg/whole bird); the most resistant tested bird was the emu with an LD50 of about 250 mg 1080/kg BW or about 8,000 mg/whole bird (McIlroy 1983a, 1984, 1986). Emus in the southwestern portion of Western Australia with evolutionary exposure to fluoroacetate-bearing vegetation unusually have a high tolerance to 1080. The tolerance in emus was attributed to (1) their ability to detoxify fluoroacetate by defluorination; (2) a limited ability to convert fluoroacetate into fluorocitrate; and (3) possession of an aconitase hydratase enzyme that is relatively insensitive to fluorocitrate (Twigg et al. 1988b).

Nontarget species of birds have died after eating 1080-poisoned baits (Spurr 1979; McIlroy 1984; Fry et al. 1986; Hegdal et al. 1986; McIlroy et al. 1986a), although population effects have not yet been demonstrated. Dead birds of several species were found after 1080 baits were applied to kill California ground squirrels (*Spermophilus beecheyi*), but only Brewer's blackbirds (*Euphagus cyanocephalus*) contained measurable 1080 residues. Nontarget seed-eating birds that died after eating 1080-poisoned baits included sparrows, blackbirds, towhees (*Pipilo* spp.), horned larks (*Eremophila alpestris*), McCown's longspurs (*Calcarius mccownii*), chestnut-collared longspurs (*Calcarius ornatus*), and western meadowlarks (*Sturnella neglecta*; Hegdal et al. 1986). Individuals of at least 20 species of Australian birds are at risk from dingo and pig poisoning campaigns with meat baits that contain 14-140 mg 1080/kg bait, and 39 species are at risk from rabbit and pig poisoning campaigns with vegetable baits that contain 330-500 mg 1080/kg bait. The extent of bird mortality and possible population effects depend on several factors: bait palatability to each species; availability of other foods; the amount of ingested 1080; the number of birds in each population that consumes baits before the target species or other nontarget groups; and the rate of 1080 leaching from baits by dew or rainfall (McIlroy 1984). Birds that fed on 1080-poisoned baits for control of wild dogs included the pied currawong (*Strepera graculina*), the Australian raven (*Corvus coronoides*), the Australian magpie, (*Gymnorhina tibicen*), and the wedge-tailed eagle (*Aquila audax*; McIlroy 1981b; McIlroy et al. 1986a). Avian scavengers such as vultures, condors, hawks, and ravens probably find poisoned food items as they search for carcasses (Fry et al. 1986).

Secondary 1080 poisoning of birds is documented. Australian birds that died after eating 1080-poisoned carcasses of pigs (*Sus* sp.) included kites (whistling kite, *Haliastur sphenurus*; black kite, *Milvus migrans*), eagles (Australian little eagle, *Hieraaetus morphnoides*; wedge-tailed eagle), the brown falcon (*Falco bevigora*), the Australian kestrel (*Falco cenchroides*), the brown goshawk (*Accipiter fasciatus*), the Australian magpielark (*Grallina cyanoleuca*), the Australian raven, and crows (Australian crow, *Corvus orru*; little crow, *Corvus bennetti*; McIlroy 1983a). Insectivorous birds that may have died after eating 1080-poisoned ants (*Veromessor andrei*, *Liometopum occidentale*) in the United States included acorn woodpeckers (*Melanerpes formicivorus*), the white-breasted nuthatch (*Sitta carolinensis*), and the ash-throated flycatcher (*Myiarchus cinerascens*; Hegdal et al. 1986).

Little or no secondary hazards were evident--as judged by the absence of carcasses--to raptors (hawks, harriers, eagles, ravens, vultures, and condors) from 1080 poisoning of ground squirrels. However, some species of owls including burrowing owls (*Athene cunicularia*) and barn-owls (*Tyto alba*; Hegdal et al. 1986) were comparatively susceptible to 1080. Raptors are less susceptible to secondary poisoning from 1080 than mammalian predators because birds have higher LD50 values, refuse to eat large amounts of 1080-poisoned meats, and sometimes regurgitate poisoned baits (Hegdal et al. 1986). The reduced hazard of acute 1080 poisoning of raptors from secondary sources is illustrated by the golden eagle (*Aquila chrysaetos*), a bird that normally consumes the internal organs of its prey before consuming other portions of the carcass (Atzert 1971). All golden eagles on diets with 7.7 mg 1080/kg diet--about 3 times the highest concentration of 1080 detected in carcasses of coyotes killed by 1080 in livestock-protection collars--survived, although some eagles showed signs of 1080 intoxication such as loss of strength and coordination, lethargy, and tremors (Bums et al. 1991). A 3.2 kg golden eagle must consume the internal organs of 7 to 30 coyotes killed by 1080 to obtain an LD50 dose (1.25-5.00 mg 1080/kg BW), assuming that each coyote ingested 0.1 mg 1080/kg BW and did not excrete, detoxify, or regurgitate any of the toxicant and that, as in rats, about 40% of the dose is present in the internal organs at death (Atzert 1971). Because the internal organs of a coyote account for 20-25% of its live weight or 2.7-3.2 kg/coyote, and a golden eagle's daily consumption of food is about 30% of its live weight or 0.9 kg (Atzert 1971), raptors are probably not at great risk from consuming coyotes killed by 1080 in livestock-protection collars (Burns et al. 1991).

Human consumers of meat from 1080-killed ducks would probably not be adversely affected after eating an average cooked portion (Temple and Edwards 1985). Moreover, oven-baking or grilling at temperatures of

greater than 200° C causes breakdown of 1080. For example, if a mallard received a triple lethal dose of 1080, then a 1-kg mallard would contain an estimated 14.4 mg of 1080. A 70-kg human must consume 25.4 kg of poisoned duck flesh to receive a lethal dose, as judged by LD50 values of 4.8 mg/kg BW in mallards and 5 mg/kg BW in humans; theoretically, consumption of only two whole ducks poisoned by 1080 may cause transient toxicity (Temple and Edwards 1985).

Bird populations that were reduced in numbers during 1080 poisoning of possums usually recovered quickly if they had a high potential for reproduction and dispersal (Spurr 1979). Birds from Australia or New Zealand with poor reproductive potential and poor dispersal had a high risk of nonrecovery; this group includes the three species of kiwi (*Apteryx* spp.), the takake (*Notornis mantelli*), kakapo (*Strigops habroptilus*), laughing owl (*Sceloglaux albifacies*), bush wren (*Xenicus longipes*), rock wren (*Xenicus gilviventris*), fernbird (*Bowdleria punctata*), yellowhead (*Mohoua ochrocephala*), stitchbird (*Notiomystis cincta*), saddleback (*Philesturnus carunculatus*), kokako (*Callaeas cinera*), and New Zealand thrush (*Turnagra capensis*; Spurr 1979, 1993). Control of wild dogs, dingoes, and their hybrids with 1080 meat baits did not significantly affect nontarget populations of birds in the treated areas (McIlroy et al, 1986b). Baiting with 1080 to control rabbits and foxes in Australia usually had no significant permanent adverse effects on nontarget birds, although the abundances of 15 of the 30 bird species in the treated areas tended to decline during the poisoning campaign, especially welcome swallows (*Hirundo neoxena*), tree martins (*Hirundo nigricans*), and crimson rosellas (*Platycercus elegans*; McIlroy and Gifford 1991). Aerial drops of 1080-laced pellets (11.8 kg/ha) to control brushtail possums and rock wallabies (*Petrogale penicillata*) on Rangitoto Island, New Zealand, had no observed effect on island bird populations during the next 12 months (Miller and Anderson 1992). No species of bird showed a population decline and several showed significant increases in numbers, including the greenfinch (*Carduelis chloris*), Australian harrier hawk (*Circus approximans*), and tui (*Prosthemadera novae-seelandiae*). Increases were attributed to the reduction in numbers of mammalian browsers that increased vegetation and improved habitat for nontarget bird species (Miller and Anderson 1992).

The mortalities of nontarget birds from 1080 poisonings may be underreported because many die in their nests or roosts and are never found (Koenig and Reynolds 1987). Dead raptors of several species were found shortly after application of 1080 baits; however, no 1080 residues were detected in any of these birds and the causes of death were not established (Hegdal et al. 1986). Application of 1080 baits to control California ground squirrels was associated with deaths of yellow-billed magpies (*Pica nuttalli*) that contained about 1.02 mg 1080/kg FW of internal organs (Koenig and Reynolds 1987) in contrast to 0.6-0.7 mg 1080/kg FW in stomachs of black-billed magpies (*Pica pica*) that were treated with lethal doses of 1.6-3.2 mg 1080/kg BW (Okuno et al. 1984). Whether *P. nutalli* ingested the 1080 bait directly, ate other poisoned animals, or both is not known (Koenig and Reynolds 1987). Risks of 1080 poisoning to birds can be reduced by (1) setting meat baits out just before sunset and removing them early next morning; (2) burying baits for pigs below ground; (3) using baits that only the target animals prefer; (4) reducing the number of available small bait fragments; and (5) masking the appearance of baits and enhancing their specificity with dyes--although some birds in Australia seem to prefer green-dyed meat baits (McIlroy 1984; McIlroy et al. 1986a).

Mammals

Studies with mammals (Table 4) showed several trends: (1) individuals of sensitive species including species of livestock, marsupials, felids, rodents, and canids died after receiving a single dose between 0.05 and 0.2 mg/kg BW; (2) most individuals of tested species died after a single dose between 1 and 3 mg/kg BW; (3) a latent period was evident between exposure and signs of intoxication; (4) mortality patterns usually stabilized within 24 h after exposure; (5) species from fluoroacetate-bearing vegetation areas were more resistant than conspecifics from nonfluoroacetate vegetation areas; (6) the route of administration had little effect on survival patterns; (7) younger animals were more sensitive than adults; (8) high residues were in some 1080-poisoned animals, notably rabbits with 34 mg/kg DW muscle and 423 mg/kg DW liver; (9) secondary poisoning was evident among carnivores after eating 1080-poisoned mammals; and (10) sublethal effects included testicular damage in rats after drinking water containing 2.2-20.0 mg 1080/L for 7 days (0.07-0.71 mg/kg BW daily), impaired reproduction in mink on diets containing 0.8 mg 1080/kg ration for 60 days, and altered blood chemistry in ferrets on diets containing 1.1 mg 1080/kg ration for 28 days.

Table 4. Effects of 1080 on representative mammals.

Table 4. Species, dose, and other variables	Effects	Reference[a]
Arctic fox, *Alopex lagopus*		
Fed a single bait containing 4 mg of 1080	Muscle contained 0.39 (0.24-0.65) mg 1080/kg fresh weight (FW)	1
Muscle from 66 foxes found dead on Kiska Island, Alaska, after 1080 poisoning. Analysis 60 days after collection	Muscle from males contained 0.7 (0.12-2.2) mg 1080/kg FW; for females, it was 0.81 (0.09-2.8) mg/kg FW	1
Brown antechinus, *Antechinus stuartii*		
1.1-3.5 mg/kg body weight (BW)	LD50, from nonfluoroacetate-bearing vegetation area	2, 3, 4
11.0 mg/kg BW	LD50, from fluoroacetate vegetation area	4
Dusky antechinus, *Antechinus swainsonii*; 3.2 (95% confidence interval [=CI] of 2.4-4.2) mg/kg BW	LD50	3
Black-handed spider monkey, *Ateles geoffroyi*; 10.0-15.0 mg/kg BW	LD50	5, 6, 7, 8
Australian mammals, various; 1.6-20.0 mg/kg BW	Lethal to 8 species of marsupials and 5 species of rodents	9
Australian rodents		
3.1 (0.7-9.0) mg/kg BW	LD50 mean (range) for 10 species with no known exposure to naturally occurring fluoroacetates	10
21.6 (3.5-80.0) mg/kg BW	LD50 mean (range) for 10 species with known past or continuing exposure to naturally occurring fluoroacetates	10
Burrowing bettong, *Bettongia*. *leseuer*; 10-20 mg/kg BW	LD50	11
Cow, *Bos* spp; single dose		
0.078 mg/kg BW	Not fatal to calves and adults	12
0.156 mg/kg BW	Not fatal to cows; LD20 for calves	12
0.22 (95% CI of 0.15-0.33) mg/kg BW	LD50 for steers and calves	5, 11, 12
0.312 mg/kg BW	LD67 for cows; LD80 for calves	12
0.39 (95% CI of 0.25-0.63) mg/kg BW	LD50 for Hereford cows	5, 11
0.624 mg/kg BW	LD100 for cows and calves	12
Canids, 6 species; 0.15 (95% CI of <0.1-0.3) mg/kg BW	LD50	13
Dog, *Canis familiaris*		
0.06 mg/kg BW, single oral dose	LD50; death in 5-9 h	6, 14
0.1-0.35 mg/kg BW, single oral dose	LD100; death in 4-6 h	6, 7, 14, 15, 16
Ingested about 1.96 mg of 1080 (56 g of a 1080-poisoned bait containing 35 mg 1080/kg horse meat)	Vomiting at 1.75 h postingestion; seizure and a short yip 20 min later; seizures and exhaustion for the next 50 min; death at about	16

Table 4. Species, dose, and other variables	Effects	Reference[a]
	3 h after ingestion	
Dingo, *Canis familiaris dingo*		
0.11 (95% CI of 0.09-0.15) mg/kg BW	LD50	3
0.123 (95% CI of 0.110-0.137) mg/kg BW	LD99	13
Coyote, *Canis latrans*		
Fed 1080-poisoned ground squirrels (*Spermophilus* sp.); that contained 0.01-0.09 mg fluoroacetate/kg FW	Maximum residues in dead coyotes, in mg 1080/kg FW, were 0.14 in large intestine, 0.09 in kidney, 0.07 in brain, 0.05 in stomach, and 0.03 in liver	17
0.1-0.2 mg/kg BW	LD50	5, 6, 7, 8, 16
0.13-0.16 mg/kg BW by gavage	Muscle residues were 0.10-0.11 mg/kg FW	18
0.23-0.5 mg/kg BW; poisoned bait	Muscle residues of 0.08-0. 15 mg/kg FW	18
0.5-1.0 mg/kg BW by gavage	Muscle residue of 0.08-0.15 mg/kg FW	18
1 mg/kg BW; poisoned bait	Muscle residue of 0.21 mg/kg FW	18
Ingestion of bait containing 5 mg 1080 (about 2.28 mg 1080/kg BW)	Signs of poisoning noted in 17-18 min after bait ingestion; death in 243 to 313 min after ingestion	19
Single lethal oral dose of 5 mg/kg BW		
Nonrefrigerated muscle tissue	Muscle contained 2.3 mg/kg FW <3 h after death; 1.5 mg/kg FW at 7 days	18
Frozen muscle tissue	Residue of 2.3 mg/kg FW after 30 days, 2.1 mg/kg FW after 60 days	18
Room temperature, muscle tissue	Residues ranged from 1.8-2.0 mg/kg FW between <3 h and 28 days	18
<3 h after death	Residues, in mg/kg FW, were 11.0 in stomach; 2.1-2.4 in heart, muscle, kidney and intestine; and 1.2 in liver	18
30.0 mg/kg BW by gavage	19.5 mg/kg FW in muscle	18
In pen tests, 25 coyotes were offered lambs with collars containing 5 or 10 mg 1080/mL	A total of 23 coyotes attacked and 21 died after collars were punctured in their first (n = 17), second (n = 3), or fifth (n = 1) tests. The average time to death was 217 min (range 115-436 min)	20
Goat, *Capra* sp.		
0.1 mg/kg BW; single oral dose	Half-time persistence of 5.4 h in plasma	21
0.3-0.7 mg/kg BW	LD50	5, 6, 7, 8, 11, 16
Guinea pig, *Cavia* spp.		
0.18 mg/kg BW	LD50 at 4° C	22

Table 4. Species, dose, and other variables	Effects	Reference[a]
0.23 mg/kg BW	LD50 at 32° C	22
0.38 mg/kg BW	LD50 at 17° C	22
0.39 mg/kg BW	LD50 at 24° C	22
Ground squirrels, *Citellus* spp.; 0.3-0.9 mg/kg BW	LD50	5, 6, 7, 15, 16
Hamsters, *Cricetus* spp.; 3.0 mg/kg BW	LD50	6
Black-tailed prairie dog, *Cynomys ludovicianus*		
0.125 mg/kg BW	No deaths	7, 23
0.17-0.3 mg/kg BW	LD50	5, 8, 23, 50
0.4-2.5 mg/kg BW	LD50-LD100	15, 16, 50
Dasyurids, 11 species; 3-12 mg/kg BW	LD50	24
Kowari, *Dasyuroides byrnei*; ~2.8 mg/kg BW	LD50	3
Northern native cat, *Dasyurus hallucatus*; 5.7 (95% CI of 3.9- 8.2) mg/kg BW	LD50	3
Tiger cat, *Dasyurus* *maculatus*; 1.8 (95% CI of 1.3-2.7) mg/kg BW	LD50	3
Quolls, *Dasyurus* spp.		
1.5 mg/kg BW	LD50, nontolerant population from southeastern Australia	4
7.5 mg/kg BW	LD50, tolerant populations from Western Australia	4
Eastern native cat, *Dasyurus viverrinus*; 3.7 (95% CI of 3.2- 4.4) mg/kg BW	LD50	3
Opposum, *Didelphis* *virginana*; 60.0 mg/kg BW	LD50	5
Kangaroo rats, *Dipodomys* spp.		
0.1-0.2 mg/kg BW	LD47-LD85	5, 6, 16
0.2-1.0 mg/kg BW	LD100	16
Mule, *Equus asinus* X *E. caballus*; 0.22-0.44 mg/kg BW	LD50	5, 11, 25
Horse, *Equus caballus*; 0.32-1.00 mg/kg BW	LD50	5, 6, 7, 8, 11, 12, 16, 25
North American porcupine, *Erethizon dorsatum*; ~1.0 mg/kg BW	LD50	5
Eutherian mammals, Australia		
0.36 (95% CI of 0.04- 3.5) mg/kg BW	LD50, 13 species of carnivores	13
0.44 (95% CI of 0.21- 0.60) mg/kg BW	LD50, 7 species of herbivores	13
Feral cat, *Felis cattus*		
0.1-0.19 mg/kg BW	No deaths using poisoned fish baits	26

Table 4. Species, dose, and other variables	Effects	Reference[a]
0.2-0.3 mg/kg BW	LD50, intravenous injection	26
0.28 (95% CI of 0.07-0.49) mg/kg BW	LD50, poisoned fish baits	26
0.35 mg/kg BW	LD50, acute oral route	26
0.35 mg/kg BW	LD90, poisoned fish baits	26
0.4 (95% CI of 0.31-0.52) mg/kg BW	LD50, oral intubation	3
1.3 mg/kg BW	All dead within 24 h when ingested as a fish bait	26
Domestic cat, *Felis cattus*		
0.2-0.3 mg/kg BW	LD50	5, 6, 7, 8, 16
0.5 mg/kg BW	LD100	16
Breviceps pocket gopher, *Geomys breviceps*		
<0.05 mg/kg BW	LD50	5, 6
0.05 mg/kg BW	LD100	16
Tuza pocket gopher, *Geomys floridanus*		
0.2 mg/kg BW	LD50	5, 6
0.25-0.5 mg/kg BW	LD60-LD100	16
Human, *Homo sapiens*		
0.7-2.1 mg/kg BW	LD50 (estimated)	5
2.0 mg/kg BW	LD100 (estimated) for children	16
2.0-10.0 mg/kg BW	LD50 (estimated) for adults	6, 27
Water-rat, *Hydromys chrysogaster*, 2.9 mg/kg BW	LD50	28, 29
Golden bandicoot, *Isoodon auratus barrowensis*; 8.9 (95% CI of 7.2-11.0) mg/kg BW	LD50	30
Northern brown bandicoot, *Isoodon macrourus*; 3.5 mg/kg BW	LD50	30, 31
Southern brown bandicoot, *Isoodon obesulus*		
7.0-8.0 mg/kg BW	LD50; maximum latent period, 183 h; time until death, 7-206 h; time for survivors to recover, 27 h	30, 31
20.0 mg/kg BW; from area of fluoroacetate-bearing vegetation	Tolerated	30
Southern hairy-nosed wombat, *Lasiorhinus latifrons*; 0.21 (95% CI of 0.15-0.29) mg/kg BW	LD50	11
Black-tailed jack rabbit, *Lepus californicus*; 5.6 mg/kg BW	LD50	5, 11
Bobcat, *Lynx rufus*; 0.67 mg/kg BW	LD50-LD100	7, 8, 16
Rhesus monkey, *Macaca mulatta*; 4-12 mg/kg BW	LD50	5, 6, 7, 16
Macropodids, 7 species; 0.23 (95% CI of 0.1-0.6) mg/kg BW	LD50	13
Agile wallaby, *Macropus agilis*; 0.22 mg/kg BW	LD50	11

Table 4. Species, dose, and other variables	Effects	Reference[a]
Tammar wallaby, *Macropus eugenii*		
0.15 mg/kg BW	LD50, pouch young	11
0.27 mg/kg BW vs. 2.0-10.0 mg/kg BW	LD50, adults from nonfluoroacetate- vs. fluoroacetate-vegetation areas	11
Gel containing 12.5 mg 1080 applied to a single leaf of edible foliage	Population reduced 91% in North Island, New Zealand field trial	32
Marsupials		
Various species; fatally poisoned with 1080 under laboratory conditions	Mean residue concentrations, in mg 1080/kg FW, were 0.2 in muscle, 6.1 in viscera, and 29.7 in stomach and contents	33
0.25 (95% CI of 0.1-0.7) mg/kg BW; 10 species of herbivores	LD50, eastern Australia (nonfluoroacetate-vegetation area)	10, 13
2.6 (95% CI of 0.9-7.6) mg/kg BW; 9 species of carnivores	LD50	13
24.2-42.0 (95% CI of 1.5-389.4) mg/kg BW; 10 species of herbivores	LD50, Western Australia (fluoroacetate-vegetation area)	10, 13
From area of fluoroacetate-bearing vegetation		
Red kangaroo, *Macropus rufus*; 2.0-4.4 mg/kg BW	LD50	11
Western brush wallaby, *Macropus irma*; 5-10 mg/kg BW	LD50	11
Western gray kangaroo, *Macropus fuliginosus*; 40-60 mg/kg BW	LD50	11
Brush-tailed bettong, *Bettongia penicillata* and banded hare-wallaby, *Lagostrophus fasciatus*; 100-200 mg/kg BW	LD50	11
Eastern gray kangaroo, *Macropus giganteus*; 0.1-0.4 mg/kg BW	LD50	11
Bennett's wallaby, *Macropus rufogriseus*		
0.2 mg/kg BW	LD50	11
Gel containing about 25 mg 1080 applied to single leaf of edible foliage	Population reduced 87% in South Island, New Zealand, field trial	32
Greater bilby (bandicoot), *Macrotus lagotis*; 15 mg/kg BW; from area of fluoroacetate-bearing vegetation	Tolerated	30
Marten, *Martes martes*; ~1.0 mg/kg BW	LD50	5
Grassland melomys rat, *Melomys burtoni*; 2.6 (95% CI of 2.2-3.1) mg/kg BW	LD50	28

Table 4. Species, dose, and other variables	Effects	Reference[a]
Striped skunk, *Mephitis mephitis*		
Diet		
Fed diet containing 4.1 mg 1080 kg/ration for 5 days (about 2 times level found in 1080-poisoned coyotes)	No deaths or signs of poisoning other than reduced feeding and loss in body weight	35
Fed coyote muscle for 14 to 35 days; coyote had been poisoned with massive (400 mg) dose of 1080	Fatal to all 3 skunks tested	19
Single dose		
0.125 mg/kg BW	No deaths in 7 days	34
0.25 mg/kg BW	LD40	34
0.35 (95% CI of 0.21-0.54) mg/kg BW	LD50	34
0.75 mg/kg BW	LD100	34
Tristram jird, *Meriones tristrami*; fed wheat grain baits		
0.38-0.47 mg/kg BW	50% dead in 3 days	36
1.7-2.5 mg/kg BW	All dead within 24 h	36
Levant vole, *Microtus guentheri*; fed wheat grain baits		
0.24-0.43 mg/kg BW	LD50	36
0.44 mg/kg BW	LD73	36
2.0-2.5 mg/kg BW	All dead within 24 h	36
Meadow mouse, *Microtus haydeni*; 0.3-0.5 mg/kg BW	LD33-LD100	16
Meadow vole, *Microtus pennsylvanicus*; 0.92 mg/kg BW	LD50	5
House mouse, *Mus musculus*		
2.6 mg/kg BW	LD50 at 12.2° C	22
4.5 mg/kg BW	LD50 at 33° C	22
5.8 mg/kg BW	LD50 at 17.9° C	22
7.4 mg/kg BW	LD50 at 30° C	22
8.3 (95% CI of 6.3-11.0) mg/kg BW	LD50	28
10.0 mg/kg BW	LD66	16
12.8 mg/kg BW	LD50 at 24° C	22
Mice, *Mus* spp.		
5.0-19.3 mg/kg BW	LD50	6, 14
13.5 (95% CI of 11.0-16.6) mg/kg BW	LD50; survivors exhibited persistent abnormal behavior ranging from circling to resting with their heads tucked under the abdomen or brisket	37
15 mg 1080/kg BW alone, or followed by intraperitoneal injection of mixture of 130 mg calcium glutonate/kg BW plus 240 mg sodium succinate/kg BW	Alone, 1080 resulted in 80% dead in 48 h and 100% in 120 h. If antidote is administered within 15 min of 1080 exposure, survival increased to 70% at 48 h and 50% at 120 h after 1080 treatment; antidote survivors	37

Table 4. Species, dose, and other variables	Effects	Reference[a]
	recovered much earlier and resumed feeding within 3 days of 1080 injection	
150 mg 1080/kg bait	In pen tests, population numbers were reduced 88% in 20 days	38
Domestic ferret, *Mustela putorius*		
1.41 (95% CI of 1.00-2.00) mg/kg BW	LD50	39
Fed one 1080-poisoned white-footed mouse (*Peromyscus leucopus*) equivalent to 1, 2, 4, or 8 mg/kg BW ferret	All died at all doses except 1 ferret at 2 mg/kg BW	39
European ferret, *Mustela putorius furo*		
Fed internal organs for 3 days of 1080-killed black-tailed prairie dogs	1 of 10 ferrets died and 5 others showed signs of 1080 poisoning; all affected ferrets recovered 24-48 h after exposure	50
Fed ground whole carcasses (less skin, skull, and feet) of black-tailed prairie dogs that died of 1080 poisoning. Carcasses contained 0.05-0.1 mg fluoroacetate/kg FW and composed 90% of diet	No adverse effects after 28 days	23
1.1 mg/kg diet for 28 days	Reduction in red and white blood cell numbers	40
1.2-1.4 mg/kg BW, single dose	LD50	5, 25, 40, 50
9.4 mg/kg diet for 28 days	LD50	40
Mink, *Mustela vison*		
0.1 mg/kg BW	No deaths in 3 days	40
0.25 mg/kg BW	50% dead in 3 days	40
0.5 mg/kg BW	2.5 to 2.8 h to death	40
0.8 mg/kg diet for 2 months prior to breeding	Impaired reproduction	40
1.0 mg/kg BW	1.5 h to death	40
2.9 mg/kg diet for 28 days	40% dead	40
3.2 (95% CI of 2.4-4.5) mg/kg diet for 28 days	50% dead	40
5.25 mg/kg diet for 28 days	Partial paralysis of hind limbs and reduced feed intake by day 5; 90% dead at 28 days	40
Nutria, *Myocastor coypus*; 0.6 mg/kg BW	LD50	5
White-throated wood rat, *Neotoma albigula*		
<0.8 mg/kg BW	LD50	5
0.8 mg/kg BW	LD100	16
Wood rat, *Neotoma intermedia*		
1.0 mg/kg BW	LD20	16
1.5 mg/kg BW	LD50	5
2.0 mg/kg BW	LD100	16

Table 4. Species, dose, and other variables	Effects	Reference[a]
Spinifex hopping mouse, *Notomys alexis*; 32.7 (95% CI of 27.4-39.3) mg/kg BW	LD50	28
Mitchell's hopping mouse, *Notomys mitchelli*; 19.4 (95% CI of 15.8-23.9) mg/kg BW	LD50	28
Mule deer, *Odocoileus hemionus hemionus*; 0.3-1.0 mg/kg BW	LD50, 8-11 months of age	5, 11, 25, 39
European rabbit, *Oryctolagus cuniculus*		
Found dead after consuming 1080-treated carrots; New South Wales, Australia; February 1986	Maximum concentrations of 1080, in mg/kg DW, were 263 in kidney, 423 in liver, 151 in heart, 34 in muscle, 136 in stomach, and 243 in stomach contents. Total 1080 content was 7.04 mg whole body and 4.87 mg in whole body less stomach and contents	33
0.36 (95% CI of 0.30-0.42) mg/kg BW	LD50, immatures	
0.42 (95% CI of 0.26-0.58) mg/kg BW	LD50, adults	
0.51 (95% CI of 0.44-0.58) mg/kg BW	LD90	
Fed pellets containing 10 mg 1080/kg pellet	All dead within 6 h	41
Sheep, *Ovis aries*		
0.1 mg/kg BW; single oral dose	Residues after 2.5 h, in mg/kg, were 0.1 in plasma and 0.02-0.06 in other tissues; after 96 h the maximum value in any tissue was 0.003 mg/kg. Half-time persistence of 1080 in plasma was 10.8 h	21
0.25-0.64 mg/kg BW	LD50	5, 11
2.0 mg/kg BW	LD50	6, 12
Gunn's bandicoot, *Perameles gunni*; 5.4 mg/kg BW	LD50; latent period, 2-6 h; time until death, 4-86 h	31
Long-nosed bandicoot, *Perameles nasuta*; 7.7 (95% CI of 5.3-11.2) mg/kg BW	LD50; maximum latent period, 6.4 h; time until death 4-56 h; time for survivors to recover, 26-42 h	3, 31
Pocket mouse, *Perognathus inornatus*; 1.0 mg/kg BW	LD100	16
Deer mouse, *Peromyscus sp*.		
2.0-4.0 mg/kg BW	LD39-LD50	16
4.0-5.0 mg/kg BW	LD50	5, 6, 15
Raccoon, *Procyon lotor*; single oral dose		
Ambient air temperature of 23-27° C vs. 13-23° C		
0.5 mg/kg BW	LD40 vs. none dead	42

Table 4. Species, dose, and other variables	Effects	Reference[a]
1.0-1.85 mg/kg BW	LD60 vs. LD20	42
2.45 mg/kg BW	LD80 vs. LD60	42
2.82 mg/kg BW	LD100 vs. LD75	42
3.24 mg/kg BW	All dead	42
Plains mouse, *Pseudomys australis*; 1.2 (95% CI of 1.1-1.4) mg/kg BW	LD50	28
Sandy inland mouse, *Pseudomys hermannsburgensis*		
1.6 (95% CI of 1.3-2.0) mg/kg BW	LD50, New Zealand	9
39.3 (95% CI of 23.6-65.4) mg/kg BW	LD50, Australia	28
Long-tailed mouse, *Pseudomys higginsi*; 9.0 (95% CI of 6.2-13.1) mg/kg BW	LD50	28
Western chestnut mouse, *Pseudomys nanus*; 14.7 (95% CI of 13.7-15.9) mg/kg BW	LD50	28
Alexandrine rat, *Rattus alexandricus*		
0.5 mg/kg BW	LD50	5, 6
1.0-2.0 mg/kg BW	LD92-LD100	16
Bush rat, *Rattus fuscipes*; 1.1 (95% CI of 0.9-1.5) mg/kg BW	LD50	28, 29
Swamp rat, *Rattus lutreolus*; 1.7 (95% CI of 1.4-2.1) mg/kg BW	LD50	28
Norway rat, *Rattus norvegicus*		
0.22-3.0 mg/kg BW	LD50, wild strains	6, 43
2.0 mg/kg BW	Oxygen consumption reduced 28-57% in 24 h	43
2.1-2.2 mg/kg BW	LD50, laboratory strains	5
3.0 mg/kg BW	5-fold increase in plasma citrate levels in 4 h	43
4.0-8.0 mg/kg BW	LD72-LD100	16
Black rat, *Rattus rattus*; 1.7 (95% CI of 1.2-2.4) mg/kg BW	LD50	28
Canefield rat, *Rattus sordidus*; 1.3 (95% CI of 1.0-1.6) mg/kg BW	LD50	28, 29
Laboratory white rat, *Rattus* sp.		
Single dose		
0.2 mg/kg BW	LD50	27
4.0 mg/kg BW	LD60	16
7.5 mg/kg BW	LD100	16
10.53 mg radiolabelled 1080/kg BW	After 4 h, radioactivity was highest in carcass (60%), liver (12%), intestine and stomach (10%) and brain, kidney, testes, and spleen (2-3% each)	5
Multiple doses		
Males given drinking water containing 2.2, 6.6, or 20 mg	No overt signs of acute toxicity in any group. However, all groups	44

Table 4. Species, dose, and other variables	Effects	Reference[a]
1080/L for 7 days then observed for 21 days. Daily dose rates, in mg/kg BW, were 0.07 (2.2 mg/L), 0.18 and 0.71 (20 mg/L), respectively	had testes damage (altered appearance, decreased number of spermatids, formation of spermatid and spermatocyte giant cells). The two high dose groups had reduction in testicular weight and seminiferious tubule atrophy; regeneration of tubules was incomplete at day 21 postexposure	
Tunney's rat, *Rattus tunneyi*; 2.6 (95% CI of 2.2-2.9) mg/kg BW	LD50	9
Rodents, 32 species		
<0.1 mg/kg BW	LD50, 4 species	28
0.1-0.25 mg/kg BW	LD50, 6 species	28
0.26-1.0 mg/kg BW	LD50, 15 species	28
>1.0 mg/kg BW	LD50, 7 species	28
Rodents, various, single dose		
0.83 (95% CI of 0.1-6.3) mg/kg BW	LD50, 11 species of cricetids	13
1.05 (95% CI 0.02-2.1) mg/kg BW	LD50, 5 species of *Rattus*	13
2.0-20.0 mg/kg BW	Lethal, 8 species	24
19.4 (95% CI <0.05-48.1) mg/kg BW	LD50, 6 species of pseudo-mice	13
Tasmanian devil, *Sarcophilus harrisii*; 4.2 (95% CI of 2.8-6.6) mg/kg BW	LD50	3
Quokka (kangaroo), *Setonix brachyurus*		
3.5 mg/kg BW	Nontolerant populations had significantly increased plasma citrate levels in 12 h, but none died	45
10-40 mg/kg BW	10 mg/kg BW killed 50% of a nontolerant population; tolerant populations survived	45
60 mg/kg BW	All populations dead within 12 h; plasma citrate levels elevated	45
Cotton rat, *Sigmodon hispidus*		
0.1 mg/kg BW	LD50	5, 6, 16
5.0 mg/kg BW	LD100	16
Fat-tailed dunnart, *Sminthopsis crassicaudata*; 2.1 (95% CI of 1.6-2.7) mg/kg BW	LD50	3
Stripe-faced dunnart, *Sminthopsis macroura*; 0.9 (95% CI of 0.6-1.6) mg/kg BW	LD50	3
Ground squirrel, *Spermophilus beecheyi*; fatally poisoned with 1080		
0.8 mg/kg BW	Tissue residues, in mg fluoroacetate/kg FW, were	17

Table 4. Species, dose, and other variables	Effects	Reference[a]
	0.2-0.7 in brain, kidney, liver, muscle, and lung; 1.0 in caecum; 1.3 in spleen; and 11.8 in stomach	
4.8 mg/kg BW	Tissue residues, in mg fluoroacetate/kg FW, were 0.5-0.7 in brain and muscle; 1.1-1.8 in caecum, kidney, liver, and lung; 9.7 in spleen; and 55.9 in stomach	17
Feral pig, *Sus scrofa*		
0.4 mg/kg BW	LD50, juveniles	46
<1.0 mg/kg BW	LD50, adults	46
1.0 (95% CI of 0.8-1.3) mg/kg BW	LD50	29
1.8 (95% CI of 1.3-185.9) mg/kg BW	LD95	29
2.3 (95% CI of 1.6-3,381) mg/kg BW	LD99	29
4.3 mg/kg BW	LD28 with pellet baits; LD60 with wheat baits	47
21.3 mg/kg BW	LD100; median time to death of 244 min (range 131-7,200 min)	47
Domestic pig, *Sus* sp.		
0.3-0.4 mg/kg BW	LD50, juveniles	5, 7, 8, 16
<1.0 mg/kg BW	LD50, adults	5
Badger, *Taxidea taxus*; 1.0-1.5 mg/kg BW	LD50-LD100	5, 16
Red-bellied pademelon, *Thylogale billardierii*; 0.13 (95% CI of 0.09-0.19) mg/kg BW	LD50	11, 31
Brush-tailed possum, *Trichosurus vulpecula*		
0.3-1.0 mg/kg BW	LD50, from nonfluoroacetate vegetation area	2, 11
16.9 (95% CI of 11.6-24.7) mg/kg BW	LD50 at 10.5° C	22
41.2 (95% CI of 30.2-56.1) mg/kg BW	LD50 at 23.5° C	22
>100->125 mg/kg BW	LD50, from fluoroacetate-bearing vegetation area	11, 45
Gray fox, *Urocyon cinereoargenteus*; 0.3 mg/kg BW	Lethal	5, 16
Bears, *Ursus* spp.; 0.5-1.0 mg/kg BW	LD50	5
Common wombat, *Vombatus ursinus*		
0.15 (95% CI of 0.12-0.19) mg/kg BW	LD50, free-ranging	11
0.22 (95% CI of 0.18-0.27) mg/kg BW	LD50, captive wombats	11
Desert kit fox, *Vulpes*		

Table 4. Species, dose, and other variables	Effects	Reference[a]
macrotis arsipus		
0.22 (95% CI of 0.15-0.34) mg/kg BW; single dose	LD50	48
Fed a 1080-poisoned kangaroo rat (*Dipodomys* sp.). Approximate dose to fox of 0.434 mg/kg BW	Death within 12 h	48
Red fox, *Vulpes vulpes*		
0.08-0.10 mg/kg BW	No deaths	49
0.125-0.15 mg/kg BW	All dead	49
Thick-tailed rat, *Zyzomys argurus*; 3.2-5.8 mg/kg BW	LD50	9

[a] 1,Tietjen et al. 1988; 2, McIlroy 1981a; 3, McIlroy 1981b; 4, King et al. 1989; 5, Atzert 1971; 6, Chenoweth 1949; 7, Anonymous 1946; 8, Negherbon 1959; 9, Calver et al. 1989b; 10, McIlroy 1992; 11, McIlroy 1982a; 12, Robison 1970; 13, McIlroy 1986; 14, Tourtellotte and Coon 1950; 15, Kalmbach 1945; 16, Peacock 1964; 17, Casper et al. 1986; 18, Okuno et al. 1984; 19, Burns et al. 1986; 20, Connolly and Bums 1990; 21, Eason et al. 1994; 22, Oliver and King 1983; 23, Hugghins et al. 1988; 24, Calver et al. 1989a; 25, Tucker and Crabtree 1970; 26, Eason and Frampton 1991; 27, Murphy 1986; 28, McIlroy 1982b; 29, McIlroy 1983a; 30, Twigg et al. 1990; 31, McIlroy 1983b; 32, Warburton 1990; 33, McIlroy and Gifford 1992; 34, Eastland and Beasom 1987; 35, Burns et al. 1991; 36, Moran 1991; 37, Omara and Sisodia 1990; 38, Twigg and Kay 1992; 39, Hudson et al. 1984; 40, Hornshaw et al. 1986; 41, Aulerich et al. 1987; 42, Eastland and Beasom 1986b; 43, Twigg et al. 1986; 44, Sullivan et al. 1979; 45, Mead et al. 1985b; 46, Rathore 1985; 47, O'Brien et al. 1988; 48, Schitoskey 1975; 49, McIlroy and King 1990; 50, Savarie et al. 1994.

The most sensitive tested mammal was the Texas pocket gopher (*Geomys personatus*) with an LD50 of less than 0.05 mg 1080/kg BW (McIlroy 1986). In general, carnivorous eutherian mammals were most sensitive to 1080 and amphibians were most resistant; intermediate in sensitivity were (in that order) herbivorous eutherian mammals and marsupials, carnivorous marsupials, herbivorous-granivorous rodents, omnivorous mammals, and birds (McIlroy 1992). Very young mammals seemed more sensitive to 1080 than other members of their populations (McIlroy 1981a); no other differences in sensitivity to 1080 were found that could be related to sex, age, or nutritional status (McIlroy 1981a, 1981b; O'Brien 1988; O'Brien and Lukins 1988). Route of administration had little effect on 1080 toxicity. Oral dosages were as toxic as subcutaneous, intramuscular, intravenous, and intraperitoneal dosages (Negherbon 1959; McIlroy 1981a, 1983a). There are as yet unexplained species differences in fatal 1080 poisonings: dogs died of convulsions or respiratory paralysis, but monkeys, horses, rabbits, and humans died of ventricular fibrillations (Murphy 1986). Individuals of most species dosed with 1080 died within 7 days, but feral pigs and wedge-tailed eagles took longer (McIlroy 1981a). Ambient air temperatures in the range of 4-33° C modified the sensitivity of small mammals to 1080. In mice (*Mus* spp.) and guinea pigs (*Cavia* spp.), sensitivity was greatest at the extremes of the tested thermal regimes and not at intermediate temperatures (McIlroy 1981b; Oliver and King 1983). Raccoons (*Procyon lotor*) and feral pigs were more sensitive at elevated ambient temperatures (Eastland and Beasom 1986b; O'Brien 1988), but possums and domestic sheep were more sensitive at low temperatures (McIlroy 1982a; Eastland and Beasom 1986b). At elevated temperatures, 1080 was more toxic to feral pigs when administered in drinking water than in oat baits and, in wheat baits than in pellet baits (O'Brien 1988).

Warm-blooded species varied considerably in response to sodium fluoroacetate; primates were more resistant, and rodents and carnivores were more susceptible. Based on fatal or near-fatal cases of human poisonings, the dangerous dose for humans is 0.5-2.0 mg/kg BW (Negherbon 1959). Among the 171 species of tested mammals, for which there are data, variability was considerable in the time until signs of poisoning became apparent (0.1 h to greater than 7 days), the time to death (0.1 h to greater than 21 days), and the time until animals began to show signs of recovery (2 h to 18 days; McIlroy 1986). Signs of poisoning among herbivorous species of marsupials first appeared 1-39 h after dosing; death followed 3-156 h after dosing

(McIlroy 1982a). Australian carnivores did not show signs of 1080 poisoning for 0.6-4.8 h; first deaths occurred between 1.6 and 21 h and recovery in 0.4 to longer than 26 h (McIlroy 1981b). Marsupial carnivores generally showed signs of 1080 poisoning earlier and died or recovered quicker than marsupial herbivores and placental mammals (McIlroy 1986). After the latent period, common signs of 1080 poisoning in caged mammals included hyperexcitation, rapid breathing, and trembling. Some animals then recovered, whereas others began to vomit, convulse, or both (McIlroy 1981b). The most common signs of 1080 poisoning in 14 species of Australian rodents were depression, hypersensitivity to stimuli, respiratory distress, and convulsions; signs usually appeared 0.4-38.1 h after dosing; deaths occurred 0.7-206 h after dosing. Some species were more tolerant, perhaps because of evolutionary exposure to indigenous plants that contained fluoroacetate (McIlroy 1982b). Rabbits (*Oryctolagus* sp.) poisoned by 1080 showed increased sensitivity to noise or disturbance; those surviving high sublethal doses began recovering 5-23 h after dosing (McIlroy 1982a). Cows (*Bos* spp.) showed no signs of fatal 1080 poisoning until shortly before death; signs appeared in the following sequence: urination, staggering, falling down, slight spasms, and death 1.5-29 h after treatment (Robison 1970). Prairie dogs showed no signs of 1080 poisoning for several hours after consuming a fatal dose; death occurred 8-13 h after dosing and was preceded by a rapid respiratory rate, hyperactivity, and convulsions (Hugghins et al. 1988). In feral pigs, signs of poisoning such as vomiting, increasing lethargy, and labored breathing appeared about 6.2 h after dosing (range 1.9-47.3 h) and death, after 16.1 h (range 2.8-80 h) of dosing (McIlroy 1983a). Vomiting occurred in 98% of poisoned pigs but was unrelated to dose (O'Brien 1988) or bait type (O'Brien et al. 1988). In some animals, particularly the eastern native cat (*Dasyurus viverrinus*), the tiger cat (*Dasyurus maculatus*), and the tasmanian devil, the first sign of 1080 poisoning is the sudden onset of vomiting. Vomiting was independent of the ingested dose or mode of administration. Thereafter, animals may either recover or experience hyperexcitation, convulsions, and death (McIlroy 1981b).

Many 1080 control programs had high effectiveness without significant effects on nontarget species. Australian baits for the control of various mammalian pests usually contain 15-110 mg 1080/kg bait, although concentrations as high as 1,200 mg/kg bait are documented (McIlroy 1981b). Baiting with 1080 to control European rabbits and red foxes (*Vulpes vulpes*) in New South Wales, Australia, caused a 90% reduction in numbers of rabbits and 75%, of foxes; populations of both species began to recover soon after the campaign ended, indicating the need for continued control. Populations of nontarget birds and mammals did not seem to be affected, and no dead birds or nontarget mammals were found (McIlroy and Gifford 1991). Reports of 1080 control in Australia of wild dogs, dingoes, and their hybrids are similar (McIlroy et al. 1986b). In Tasmania, deliberate poisoning of forest-browsing pests with carrot baits containing 0.014% of 1080—the same concentration used elsewhere in Tasmania for rabbit control—resulted in 94% mortality of brushtail possum populations, 96% mortality of red-bellied pademelons, and 86% mortality of Bennett's wallabies (McIlroy 1982a). McIlroy (1982a) suggested the use of 1080 to protect island-dwelling rare or endangered species of herbivorous marsupials--a comparatively tolerant group--during control of more sensitive introduced competitors or predators such as rabbits, foxes, and feral cats.

Compound 1080 is highly toxic to some species of nontarget mammals, including domestic cats and dogs (Kalmbach 1945). Baiting of California ground squirrels with 1080 reduced squirrel populations by 85% but also killed individuals of the Heermann's kangaroo rat (*Dipodomys heermanni*), the little pocket mouse (*Perognathus longimembris*), the desert woodrat (*Neotoma lepida*), the deer mouse (*Peromyscus* sp.), and the western harvest mouse (*Reithrodontomys megalotis*); poisoned rodents contained between 5.2 and 23.1 mg 1080/kg BW and 1080-poisoned desert cottontails (*Sylvilagus audubonii*) contained 8.2 mg 1080/kg stomach content (Hegdal et al. 1986). Dead nontarget animals found in New South Wales State forests after 22 rabbit-poisoning operations between 1971 and 1975 included in decreasing order of frequency foxes, wallabies, possums, gray kangaroos, wombats, rats, hares, birds, cats, sheep, and dogs. This pattern may reflect each species' relative abundance in the target areas, access to and acceptance of baits, and ease of detectability after death by forestry personnel (McIlroy 1982a). In Australia, the animals alleged to be most at risk during rabbit or pig-poisoning campaigns with pellet, grain, or carrot baits are the kangaroos, wallabies, and wombats. For example, common wombats (*Vombatus ursinus*) and hairy-nosed wombats (*Lasiorhinus latifrons*) must consume only 10-16 g of pellet, grain or carrot baits containing 0.33 to 0.5 mg of 1080 to receive an LD50. Hairy-nosed wombats eat 120-570 g of food daily, and common wombats can eat more than 500 g of unpoisoned carrots daily, indicating that both species could easily consume lethal quantities of bait. Next at risk in descending order are livestock, brushtail possums, pigs, and various rodents and birds (McIlroy 1986). More data are needed on bait consumption rates by nontarget mammals to assess the risk from 1080 poisoning campaigns.

Laboratory studies may overestimate the risk to nontarget species from 1080 baiting. The northern quoll (*Dasyurus hallucatus*), for example, was at highest theoretical risk from aerial baiting as judged by LD50 laboratory studies with 15 species of rodents and dasyurids. But no dead quolls were found during aerial baiting to control dingoes, and all radio-tagged quolls seemed to have normal movements (King 1989). Alternatives to LD50 testing now include tissue culture, monitoring of metabolite levels in blood or tissues, and estimation of the lowest lethal dose (Calver et al. 1989a). Monitoring the level of citrate in blood plasma of animals that received a sublethal dose of 1080 has been successful with species that are large enough to provide adequate samples of blood plasma during a 24-h period but have not been attempted on Australian fauna (Calver et al. 1989a).

Because 1080 acts as an emetic, especially in coyotes and feral pigs, nontarget animals are at risk of primary poisoning from eating the vomitus (Atzert 1971; McIlroy 1983a; Rathmore 1985; O'Brien et al. 1986, 1988). Wild pigs poisoned by carrot baits for European rabbits left trails of vomitus with carrots and other ingested foods (Rathore 1985). The antiemetic compound metoclopramide (Maxolon) prevents vomiting in pigs by blocking dopamine receptors in the chemoreceptor trigger zones. The addition of metoclopramide to 1080 poison baits for wild pigs reduces vomiting and thereby reduces the poisoning risk to nontarget species. The addition of metoclopramide improves the efficiency and percentage of the kill of wild pigs because they do not develop a taste aversion to the baits. Similarly, baits containing this antiemetic at an effective concentration of 1 mg/kg BW shortened the median time for death in dogs from 151 min postdose in 1080 baits without metoclopramide to 132 min (Rathore 1985). At tested doses (1-16 mg/kg BW), metoclopramide did not decrease the frequency of vomiting by dogs but decreased the amount of vomitus (O'Brien et al. 1986).

Secondary poisoning is probable among carrion eaters feeding on rabbits and other herbivores poisoned with 1080-treated carrots, especially foxes and dingoes (secondary target species) and dogs and cats (McIlroy 1981b; McIlroy and Gifford 1992). Secondary poisoning was experienced by dogs that fed on 1080-treated rodents and prairie dogs and by cats that consumed treated rats and mice (Anonymous 1946). Some dead domestic dogs and cats were found within 450 m of a 1080-treatment area; signs of 1080 poisoning were evident, but no 1080 residues were detected by chemical analyses (Hegdal et al. 1986). Ground squirrel control with 1080 baits caused secondary poisoning of dogs, cats, coyotes, bobcats (*Lynx rufus*), skunks, and kit foxes (Hegdal et al. 1986). The high susceptibility of threatened and endangered populations of the kit fox to 1080 rodenticides, as judged by studies with nonthreatened populations of the kit fox, suggested that 1080 is a factor in their population decline (Schitoskey 1975). Sodium monofluoroacetate has a high degree of secondary toxicity in mammals, as evidenced by deaths of domestic ferrets that ate 1080-poisoned white-footed mice (*Peromyscus leucopus*; Hudson et al. 1984). Similarly, coyotes died after ingestion of 1080-poisoned ground squirrels that contained 3-6 mg of 1080 equivalent to 0.24-0.63 mg/kg BW coyote (Casper et al. 1986; Marsh et al. 1987). Coyotes that ate a single 1080-poisoned squirrel daily for 5 days or an estimated total dose of 0.12-0.27 mg/kg BW usually survived, suggesting that there is little secondary hazard from multiple small doses (Marsh et al. 1987). Carcasses and viscera from coyotes that died after ingesting 5-15 mg of 1080 were fed for 14-35 days to other coyotes, domestic dogs, striped skunks (*Mephitis mephitis*), and black-billed magpies; no evidence of secondary poisoning was seen in any tested species. Maximum residues of 1080 in dead coyote tissues in mg/kg FW were 0.66 in muscle, 0.79 in the small intestines, and 0.76 in stomach tissue (Burns et al. 1986). Tissues of 1080-poisoned coyotes did not produce secondary poisoning in Virginia opossums (*Didelphis virginiana*; Eastland and Beasom 1986a), striped skunks (Eastland and Beasom 1986a; Burns et al. 1991), raccoons (Eastland and Beasom 1986a; Hegdal et al. 1986), or badgers (*Taxidea taxus*; Hegdal et al. 1986). The hazard of secondary poisoning to predators is minimal after consuming tissues of 1080-killed black-tailed prairie dogs (*Cynomys ludovicianus*) because their tissues contained less than 0.1 mg fluoroacetate/kg FW (Hugghins et al. 1988). No mink died when fed 1080-poisoned rabbits at 40% of the total diet if the rabbit gastrointestinal tract had been removed from the carcass. This suggests that secondary toxicity from 1080 is due primarily to consumption of the unmetabolized compound from the gut of prey species (Aulerich et al. 1987). The risk to different individuals or populations depends on the species' sensitivity to 1080, the number of consumed poisoned animals, and the amounts of different consumed tissues or organs (McIlroy and Gifford 1992).

The sensitivity to 1080 poison by animals in Australia varies greatly; known LD50 values range from 0.11 to more than 800 mg/kg BW. Many native species, particularly in Western Australia, have evolved tolerances to 1080 through ingestion of native plants that contain fluoroacetate or prey that consume these plants (McIlroy 1982a; McIlroy 1992). The degree to which this tolerance is developed depends on the extent of the toxic plants in the microhabitat, the need of each species to include food species that contain fluoroacetate in its diet, and

the length of evolutionary exposure to the toxic plants (Twigg et al. 1988b; King et al. 1989; Twigg and Mead 1990). This naturally occurring resistance to the toxins allows control with 1080 to be more specific for introduced test species (Mead et al. 1985). Tolerance to fluoroacetate is present in insects, reptiles, mammals, and birds and descends in magnitude from herbivores to carnivores (Twigg and King 1991). Mammals with lower metabolic rates--such as marsupial carnivores--seem to be more tolerant than mammals with a higher metabolism--such as eutherian carnivores--to a poison such as 1080 that interferes with the metabolism (McIlroy 1981a, 1981b). Tolerance to gradually increasing doses of fluoroacetate can be induced in the mouse, rat, and rhesus monkey but not in the dog or rabbit; however, the protective effect of prior exposure to 1080 seldom persisted for more than 48 h (Chenoweth 1949). Laboratory white rats may acquire tolerances to 1080 by the ingestion of sublethal doses for a period of 5-14 days; cessation of dosing for 7 days caused a loss of tolerance (Kalmbach 1945). Some species acquired tolerances to 1080 after repeated sublethal doses, and others accumulated the chemical until a lethal threshold was reached (McIlroy 1981a). Both phenomena were unpredictable if 1080 residues in the tissues remained between doses. The required time for complete elimination of 1080 from tissues varied among species: dogs required 2-3 days, rats 36 h, and sheep as long as 1 month (McIlroy 1981a).

Sublethal concentrations of 1080 may adversely affect reproduction, growth, and behavior. In rats (*Rattus* sp.), the most vulnerable organ to 1080 poisoning is the testes and this is consistent with 1080-impaired energy production from blockage of the Krebs cycle and subsequent impairment of the carbohydrate metabolism (Sullivan et al. 1979). Subacute dietary exposure to 1080 caused dose-dependent decreases in body weights and feed consumption in mink and in European ferrets (Hornshaw et al. 1986). Toxic 1080 meat baits were usually avoided by tested, nontarget dasyurids and rodents when alternative foods were available; 12 of the 24 tested groups did not sample meat baits under these conditions (Calver et al. 1989a). Adult wild pigs given a sublethal dose of 1080 (0.5 mg/kg BW) in apple baits vomited within 30 min after eating the treated bait and avoided apple baits in future tests (Rathore 1985). Caged wild Norway rats (*Rattus norvegicus*) and black rats (*Rattus rattus*) developed a gradually increasing aversion to drinking water solutions of 1080, although this aversion was not sufficient to disrupt growth and reproduction (Kalmbach 1945).

Recommendations

It is emphasized that 1080 is a restricted pesticide that can only be used by certified applicators who received special training (Green 1946; Negherbon 1959; EPA 1985; Connolly 1993a) and that all organisms that died from 1080 poisoning must be buried or incinerated (EPA 1985). Some authorities aver that continued use of 1080 is justified and desirable and that risk is minimal to nontarget organisms. As discussed earlier, 1080 is a natural plant product, is generally highly toxic to most pests at low concentrations, is readily lost from baits after heavy dews or rainfall, is biodegraded by fungi and bacteria, and does not persist in soil or water. In New Zealand, 1080 has been used since 1954 and is still considered an essential pesticide for limiting forest and crop damage and for containing the spread of tuberculosis to livestock by brush-tailed possums (Eason et al. 1993b). It has been used to control isolated island populations of mammals that prey on endangered or threatened species of birds, for example, Arctic foxes that preyed on Aleutian Canada geese in the Aleutian Islands (Tietjen et al. 1988; Bailey 1993). In Australia and New Zealand, results of field studies suggested that 1080 poisoning campaigns had no significant effect on almost all populations of common nontarget species (McIlroy 1982a, 1992; McIlroy et al. 1986b; McIlroy and Gifford 1991; Spurr 1994), although more studies of vulnerable, rare, endangered, or uncommon species are recommended (McIlroy 1992).

However, a growing body of information questions the usefulness of 1080 in the United States. This database includes adverse effects on some nontarget organisms and endangered species; the confounding effects of the latent period, behavioral alterations, and application routes; and the development of suitable alternative chemicals. On the basis of acute oral toxicity tests, sensitive nontarget mammals and birds may consume lethal quantities of 1080 from poisoned baits or from consumption of organisms fatally poisoned with 1080 (EPA 1985). Field studies showed deaths among sensitive nontarget species that ate 1080 baits, including bees (Goodwin and Ten Houten 1991), insectivorous birds, (McIlroy 1982a; Hegdal et al. 1986), rabbits, rodents (Hegdal et al. 1986), cats, dogs (Kalmbach 1945; Green 1946; Hegdal et al. 1986), and live-stock (McIlroy 1982a, 1986). Carrion eaters and mammalian predators--especially canids and felines—experience secondary poisoning after feeding on 1080-poisoned prey (Hegdal et al. 1986; McIlroy and Gifford 1992). Sublethal effects of 1080 on growth in ferrets and on reproduction in mink are reported (Hudson et al. 1984; Hornshaw et al. 1986). Some endangered species are at risk from direct consumption of the 1080 baits or from secondary

poisoning (EPA 1985). In general, the use of 1080 in the geographic range of any endangered species is discouraged or disallowed outright in the ranges of the California condor, the San Joaquin kit fox (*Vulpes macrotis mutica*), the Aleutian Canada goose; the Morro Bay kangaroo rat (*Dipodomys heermanni morroensis*), and the salt marsh harvest mouse (*Reithrodontomys raviventris*). When exceptions are made or when 1080 use is permitted in an area known to be frequented by an endangered species, restrictions are placed on the maximum concentration of 1080 in the baits (EPA 1985).

Human consumers of meat from 1080-killed ducks are probably not adversely affected after eating an average cooked portion (Temple and Edwards 1985). The risk to humans from eating meat of domestic animals accidentally poisoned with high sublethal concentrations is minimal to low because 1080 is cleared rapidly from domestic animals--usually within a few days (Eason et al. 1994). In the absence of additional data, a minimal 3-week postponement of the slaughter or marketing of livestock that survived 1080 exposure seems prudent. No livestock in the United States contaminated with 1080 are marketed (Connolly 1993a).

No effective antidote to 1080 is currently available, and accidental poisoning of livestock and dogs is probably fatal (Green 1946; Chenoweth 1949; Peacock 1964; Atzert 1971; Mead et al. 1991). The lack of emergency treatment of 1080-poisoned humans and the unavailability of monoacetin--potentially the most effective medication for compound 1080 poisoning--in a pharmaceutical grade (EPA 1985) strongly indicate the need for a viable 1080 antidote. The search for an effective 1080 antidote is ongoing, and some candidate compounds that offer partial protection are mixtures of sodium acetate and ethanol, barbituates (Tourtellotte and Coon 1950; Peacock 1964), glycerol monoacetate (Peacock 1964; Murphy 1986), a mixture of calcium glutonate and sodium succinate (Roy et al. 1980; Omara and Sisodia 1990), and 4-methylpyrazole (Feldwick et al. 1994). The development and availability of an effective 1080 antidote should be of high priority. Until this antidote is distributed, it seems reasonable to use 1080 in the United States only after other alternatives were considered.

The interval between 1080 dosage and signs of intoxication is at least 30 min, regardless of dose or tested species, and must be considered in the evaluation of the efficacy of 1080. Coyotes, for example, may continue to kill livestock after receiving a lethal dose (Connolly and Burns 1990). And coyotes may travel some distance from their prey prior to incapacitation, making carcass recovery and program evaluation difficult--as was the case of 1080-poisoned quolls in Australia (King 1989). Similarly, many 1080-poisoned nontarget animals may have left the treated area before succumbing, thus leading to underestimation of mortality among this group (Collins 1965). Tolerance to fluoroacetates and avoidance of 1080 baits should also be considered in future 1080 poisoning campaigns by wildlife managers and by animal damage-control operators. Avoidance of 1080 toxic baits by target mammals is documented when alternative foods are available (Calver et al. 1989a) and by pigs and rats surviving sublethal exposures (Kalmbach 1945; Rathore 1985). Indigenous populations of mammals, birds, and reptiles that coexist with fluoroacetate-bearing vegetation are much less sensitive to 1080 poisoning, perhaps by as much as 2 orders of magnitude, than conspecifics lacking such exposure (Twigg et al. 1988; King et al. 1989; Twigg and Mean 1990).

The timing of application of 1080 baits is critical. In one mishap, baits were dropped from aircraft while many ground squirrels--the targeted species--were still in hibernation underground for the winter and had not emerged (Collins 1965). Aerial application of 1080 baits in a ground squirrel control program in California, although effective in controlling the squirrels, resulted in great overuse of the baits. As many as 70-77% of the poisoned baits were not eaten by the squirrels and were not recovered. Also, the yellow dye to color the baits--as a deterrent to birds--faded rapidly (Collins 1964, 1965). To protect migratory waterfowl, 1080 baits should not be applied immediately preceding or during the main waterfowl hunting season or whenever birds are abundant (Temple and Edwards 1985). To protect honeybees, 1080-poisoned jam baits should be deposited more than 400 m from apiary sites. If 1080 baits are dispersed less than 400 m from apiary sites, beekeepers should remove their hives to a more distant site (Goodwin and Ten Houten 1991). The 1080 toxicity database on aquatic organisms is insufficient for practicable formulation of criteria to protect this ecosystem. This seems to be a high-priority research need in geographic areas of intensive 1080 application.

Potential replacement chemicals for 1080 include PAPP (*para*-aminopropiophenome), DFP (1,3-difluoro-2-propanol), and various anticoagulant and nonanticoagulant toxins. PAPP is highly toxic to coyotes and domestic cats (each with LD50s of 5.6 mg/kg BW) and lethal to rats (LD50 of 177 mg/kg BW) and mice (LD50 of 233 mg/kg BW); intermediate in toxicity to bobcats (10.0) and to kit foxes (14.1 mg/kg BW; Savarie et al. 1983). DFP

is under investigation in Australia as an alternative to 1080 for management of fauna because it has a mode of action similar to that of 1080 and has an antidote in pyrazole (Mead et al. 1991). DFP is the major ingredient of the pesticide gliftor used in Russia to control rodents, particularly voles of the genus *Microtus*. Also deserving of evaluation are 4-methylpyrazole and related compounds to function as antidotes to DFP intoxication (Mead et al, 1991). In New Zealand, alternatives to 1080 under evaluation include several nonanticoagulant toxins (gliftor, cholecalciferol, calciferol, alpha-chloralase, nicotine, malathion) and anticoagulants including brodifacoum and pindone (Eason et al. 1993a).

Acknowledgments

I thank L. J. Garrett and P. W. Manning for literature search and retrieval services; M. G. Holmes for secretarial assistance; D. R. Clark, C. T. Eason, D. R. King, P. G. Livingstone, P. Nelson, M. C. Perry, R. Sadleir, P. J. Savarie, E. B. Spurr, L. E. Twigg, and two anonymous referees for scientific and technical reviews of the manuscript; and E. D. Rockwell for editorial services.

Cited Literature

Allender, W. J. 1990. Determination of sodium fluoroacetate (compound 1080) in biological tissues. Journal of Analytical Toxicology 14:45-49.

Anonymous. 1946. Compound 1080 as a rodenticide. U.S. Fish and Wildlife Service, Denver Wildlife Research Laboratory. Mimeographed. 7 pp.

Anonymous. 1964. Operation extinction. Aerial poisoning with 1080. Forest and Timber 2:8-9.

Atzert, S. P. 1971. A review of sodium monofluoroacetate (compound 1080). Its properties, toxicology, and use in predator and rodent control. U.S. Bureau of Sport Fisheries and Wildlife, Special Scientific Report—Wildlife 146. 34 pp.

Aulerich, R. J., R. K. Ringer, and J. Safronoff. 1987. Primary and secondary toxicity of warfarin, sodium monofluoroacetate, and methyl parathion in mink. Archives of Environmental Contamination and Toxicology 16:357-366.

Bailey, E. P. 1993. Introduction of foxes to Alaskan islands--history, effects on avifauna, and eradication. U.S. Fish and Wildlife Service Resource Publication 193.53 pp.

Balcomb, R., C. A. Bowen II, and H. O. Williamson. 1983. Acute and sublethal effects of 1080 on starlings. Bulletin of Environmental Contamination and Toxicology 31:692-698.

Batcheler, C. L., and C. N. Challies. 1988. Loss of compound 1080 (sodium monofluoroacetate) from carbopol gel smeared on foliage to poison deer. New Zealand Journal of Forestry Science 18:109-115.

Brock, E. M. 1965. Toxicological feeding trials to evaluate the hazard of secondary poisoning to gopher snakes, *Pituophis catenifer*. Copeia 1965:244-245.

Burke, D. G., D. K. T. Lew, and X. Cominos. 1989. Determination of fluoroacetate in biological matrixes as the dodecyl ester. The Journal of the Association of Official Analytical Chemists 72:503-507.

Burns, R. J., G. E. Connolly, and I. Okuno. 1986. Secondary toxicity of coyotes killed by 1080 single-dose baits. Pages 324-329 *in* T. P. Salmon, editor. Proceedings twelfth vertebrate pest conference. University of California, Davis.

Burns, R. J., and P. J. Savarie. 1989. Persistence of tartrazine in marking sheep wool. Pages 95-100 *in* Proceedings of the Fourth Eastern Wildlife Damage Control Conference, 25-28 September 1989, Madison, Wis.

Burns, R. J., H. P. Tietjin, and G. E. Connolly. 1991. Secondary hazard of livestock protection collars to skunks and eagles. Journal of Wildlife Management 55:701-704.

Byrd, G. V., G. T. McClellan, and J. P. Fuller. 1988. To determine the efficacy and environmental hazards of compound 1080 (sodium fluoroacetate) as a control agent for Arctic fox (*Alopex lagopus*) on Kiska Island, Aleutians Islands unit-Alaska Maritime National Wildlife Refuge (AIU-AMNWR) (Field Investigations). Unpublished final progress report by AIU-AMNWR. 22 pp.

Calver, M. C., D. R. King, J. S. Bradley, J. L. Gardner, and G. Martin. 1989a. An assessment of the potential target specificity of 1080 predator baiting in Western Australia. Australian Wildlife Research 16:625-638.

Calver, M. C., J. C. McIlroy, D. R. King, J. S. Bradley, and J. L. Gardner. 1989b. Assessment of an approximate lethal dose technique for determining the relative susceptibility of non-target species to 1080 toxin. Australian Wildlife Research 16:33-40.

Casper, H. H., M. E. Mount, R. E. Marsh, and R. H. Schmidt. 1986. Fluoroacetate residues in ground squirrel and coyote tissues due to primary or secondary 1080 poisoning. Journal of the Association of Official Analytical Chemists 69:441-442.

Chenoweth, M. B. 1949. Monofluoroacetic acid and related compounds. Pharmacological Reviews 1:383-424.

Collins, B. D. 1964. An evaluation of an experimental aerial application of toxic baits for squirrel control—Kern County. California Department of Fish and Game, Pesticides Investigations. Mimeographed. 10 pp.

Collins, B. D. 1965. Fish and Game's view on aerial application of 1080 baits for squirrel control. County Agricultural Commissioners meeting, Bijou, Calif., 18 May 1965. Mimeographed. 4 pp.

Connolly, G. 1982. U.S. Fish and Wildlife Service coyote control research. Pages 132-149 *in* Proceedings Fifth Great Plains Wildlife Control Workshop, Lincoln, Nebr., 13-15 October 1981.

Connolly, G. 1989. Technical bulletin for the sodium fluoroacetate (compound 1080) livestock protection collar. U.S. Department of Agriculture, Animal Damage Control, Denver Wildlife Research Center, Denver, Colo. 25 pp.

Connolly, G. 1993a. Technical bulletin for the sodium fluoroacetate (compound 1080) livestock protection collar. U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Denver Wildlife Research Center, Denver, Colo. 37 pp.

Connolly, G. 1993b. Livestock protection collars in the United States, 1983-1993. Pages 25-33 *in* Eleventh Great Plains Wildlife Damage Control Workshop Proceedings, Kansas City, Mo., 26-29 April 1993.

Connolly, G., and R. J. Burns. 1990. Efficacy of compound 1080 livestock protection collars for killing coyotes that attack sheep. Pages 269-276 *in* L. R. Davis and R. E. Marsh, editors. Proceedings 14th vertebrate pest conference, University of California, Davis.

Deonier, C. C., H. A. Jones, and H. H. Incho. 1946. Organic compounds effective against larvae of *Anopheles quadrimaculatus*--laboratory tests. Journal of Economic Entomology 39:459-462.

Eason, C. T., and C. M. Frampton. 1991. Acute toxicity of sodium monofluoroacetate (1080) baits to feral cats. Australian Wildlife Research 18:445-449.

Eason, C. T., C. M. Frampton, R. Henderson, M. D. Thomas, and D. R. Morgan. 1993a. Sodium monofluoroacetate and alternative toxins for possum control. New Zealand Journal of Zoology 20:329-334.

Eason, C. T., R. Gooneratne, H. Fitzgerald, G. Wright, and C. Frampton. 1994. Persistence of sodium monofluoroacetate in livestock animals and risk to humans. Human and Experimental Toxicology 13:119-122.

Eason, C. T., R. Gooneratne, G. R. Wright, R. Pierce, and C. M. Frampton. 1993b. The fate of sodium monofluoroacetate (1080) in water, mammals, and invertebrates. Proceedings 46th New Zealand Plant Protection Conference 1993:297-301.

Eason, C. T., G. R. Wright, and H. Fitzgerald. 1992. Sodium monofluoroacetate (1080) water-residue analysis after large-scale possum control. New Zealand Journal of Ecology 16:47-49.

Eastland, W. G., and S. L. Beasom. 1986a. Potential secondary hazards of compound 1080 to three mammalian scavengers. Wildlife Society Bulletin 14:232-233.

Eastland, W. G., and S. L. Beasom. 1986b. Effects of ambient temperature on the 1080-LD_{50} of raccoons. Wildlife Society Bulletin 14:234-235.

Eastland, W. G., and S. L. Beasom. 1987. Acute toxicity of sodium monofluoroacetate to the striped skunk. Bulletin of Environmental Contamination and Toxicology 38:934-936.

Fagerstone, K. A., P. J. Savarie, D. J. Elias, and E. W. Schafer, Jr. 1994. Recent regulatory requirements for pesticide registration and the status of compound 1080 studies conducted to meet EPA requirements. Pages 33-38 *in* A. A. Seawright and C. T. Eason, editors. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28.

Feldwick, M. G., R. J. Mead, and P. J. Kostyniak. 1994. Biochemical effects of fluoroacetate and related pesticides: the potential of 4-methylpyrazole as an antidote. Pages 74-81 *in* A. A. Seawright and C. T. Eason, editors. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28.

Fleming, P. J. S., and R. W. Parker. 1991. Temporal decline of 1080 within meat baits used for control of wild dogs in New South Wales. Australian Wildlife Research 18:729-740.

Fry, D. M., G. Santolo, and C. R. Grau. 1986. Final report for interagency agreement: effects of compound 1080 poison on turkey vultures. Department of Avian Sciences, University of California, Davis. 44 pp.

Gal, E. M., P. A. Drewes, and N. F. Taylor. 1961. Metabolism of fluoroacetic acid-2-C^{14} in the intact rat. Archives of Biochemistry and Biophysics 93:1-14.

Goodwin, R. M., and A. Ten Houten. 1991. Poisoning of honey bees (*Apis mellifera*) by sodium fluoroacetate (1080). New Zealand Journal of Zoology 18:45-51.

Green, D. D. 1946. Service policy on the use of compound 1080 (sodium fluoroacetate). U.S. Fish and Wildlife Service, Division of Predator and Rodent Control, Memorandum No. 121, Supplement No. 1 (Revised). Mimeographed. 6 pp.

Hegdal, P. L., and B. A. Colvin. 1988. Potential hazard to eastern screech-owls and other raptors of brodifacoum bait used for vole control in orchards. Environmental Toxicology and Chemistry 7:245-260.

Hegdal, P. L., K. A. Fagerstone, T. A. Gatz, J. F. Glahn, and G. H. Matschke. 1986. Hazards to wildlife associated with 1080 baiting for California ground squirrels. Wildlife Society Bulletin 14:11-21.

Hickling, G. J. 1994. Behavioral resistance by vertebrate pests to 1080 toxin: implications for sustainable pest management in New Zealand. Pages 151-158 *in* A. A. Seawright and C. T. Eason, editors. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28.

Hoogenboom, J. J. L., and C. G. Rammell. 1987. Determination of sodium monofluoroacetate (compound 1080) in tissues and baits as its benzyl ester by reaction-capillary gas chromatography. Journal of Analytical Toxicology 11:140-143.

Hornshaw, T. C., R. K. Ringer, R. J. Aulerich, and H. H. Casper. 1986. Toxicity of sodium monofluoroacetate (compound 1080) to mink and European ferrets. Environmental Toxicology and Chemistry 5:213-223.

Howard, W. E. 1983. Viewpoint: the coyote-1080 conspiracy--an aborted attempt to drive livestock off Federal lands. Rangelands 5:134-135.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1972. Effect of age on sensitivity: acute oral toxicity of 14 pesticides to mallard ducks of several ages. Toxicology and Applied Pharmacology 22:556-561.

Hudson, R. H., R. K. Tucker, and M. A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. U.S. Fish and Wildlife Service Resource Publication 153. 90 pp.

Hugghins, E. J., H. H. Casper, and C. D. Ward. 1988. Tissue fluoroacetate residues in prairie dogs dosed with low-level sodium monofluoroacetate. Journal of the Association of Official Analytical Chemists 71:579-581.

Kalmbach, E. R. 1945. "Ten-eighty," a war-produced rodenticide. Science 102:232-233.

Khan, A. A., M. Ahmad, S. Ahmad, and S. W. A. Rizvi. 1992. Evaluation of the comparative efficacy of fumigants and acute poison baits against Indian crested porcupine, *Hystrix indica*. Forest Ecology and Management 48:295-303.

Kimball, B. A., and E. A. Mishalanie. 1993. Gas chromatographic determination of sodium monofluoroacetate as the free acid in an aqueous solvent. Journal of Chromatography 634:289-296.

King, D. R. 1989. An assessment of the hazard posed to northern quolls (*Dasyurus hallucatus*) by aerial baiting with 1080 to control dingoes. Australian Wildlife Research 16:569-574.

King, D. R., L. E. Twigg, and J. L. Gardner. 1989. Tolerance to sodium monofluoroacetate in dasyurids from Western Australia. Australian Wildlife Research 16:131-140.

King, J. E., and W. T. Penfound. 1946. Effects of new herbicides on fish. Science 103:487.

Koening, W. D., and M. D. Reynolds. 1987. Potential poisoning of yellow-billed magpies by compound 1080. Wildlife Society Bulletin 15:274-276.

Kononen, D. W., J. R. Hochstein, and R. K. Ringer. 1991. Mallard and northern bobwhite exposure to compound 1080: acute toxicity and food avoidance behavior. Chemosphere 22:655-663.

Kramer, H. L., P. W. Merrell, and B. J. Burren. 1987. Use of sodium fluoroacetate (compound 1080) in the control of dingoes. I. Meat preparation techniques. Australian Wildlife Research 14:65-68.

Kun, E. 1982. Monofluoroacetic acid (compound 1080), its pharmacology and toxicology. Pages 34-41 *in* R. E. Marsh, editor. Proceedings Tenth Vertebrate Pest Conference. University of California, Davis.

Lovelace, J., G. W. Miller, and G. W. Welkie. 1968. The accumulation of fluoroacetate and fluorocitrate in forage crops collected near a phosphate plant. Atmospheric Environment 2:187-190.

Lynch, G. W., and R. D. Nass. 1981. Sodium monofluoroacetate (1080): relation of its use to predation on livestock in western national forests. Journal of Range Management 34:421-423.

Marsh, R. E., R. H. Schmidt, and W. E. Howard. 1987. Secondary hazards to coyotes of ground squirrels poisoned with 1080 or strychnine. Wildlife Society Bulletin 15:380-385.

McIlroy, J. C. 1981a. The sensitivity of Australian animals to 1080 poison. I. Intraspecific variation and factors affecting acute toxicity. Australian Wildlife Research 8:369-383.

McIlroy, J. C. 1981b. The sensitivity of Australian animals to 1080 poison. II. Marsupial and eutherian carnivores. Australian Wildlife Research 8:385-399.

McIlroy, J. C. 1982a. The sensitivity of Australian animals to 1080 poison. III. Marsupial and eutherian herbivores. Australian Wildlife Research 9:487-503.

McIlroy, J. C. 1982b. The sensitivity of Australian animals to 1080 poison. IV. Native and introduced rodents. Australian Wildlife Research 9:505-517.

McIlroy, J. C. 1983a. The sensitivity of Australian animals to 1080 poison. V. The sensitivity of feral pigs, *Sus scrofa*, to 1080 and its implications for poisoning campaigns. Australian Wildlife Research 10: 139-148.

McIlroy, J. C. 1983b. The sensitivity of Australian animals to 1080 poison. VI. Bandicoots. Australian Wildlife Research 10:507-512.

McIlroy, J. C. 1984. The sensitivity of Australian animals to 1080 poison. VII. Native and introduced birds. Australian Wildlife Research 11:373-385.

McIlroy, J. C. 1986. The sensitivity of Australian animals to 1080 poison. IX. Comparisons between the major groups of animals and the potential danger non-target species face from 1080-poisoning campaigns. Australian Wildlife Research 13:39-48.

McIlroy, J. C. 1992. The effect on Australian animals of 1080-poisoning campaigns. Pages 356-359 *in* J. E. Borrecco and R. E. Marsh, editors. Proceedings Fifteenth Vertebrate Pest Conference. University of California, Davis.

McIlroy, J. C., R. J. Cooper, E. J. Gifford, B. F. Green, and K. W. Newgrain. 1986a. The effect on wild dogs, *Canis f. familiaris*, of 1080-poisoning campaigns in Kosciusko National Park, N.S.W. Australian Wildlife Research 13:535-544.

McIlroy, J. C., and E. J. Gifford. 1991. Effects on nontarget animal populations of a rabbit trail-baiting campaign with 1080 poison. Australian Wildlife Research 18:315-325.

McIlroy, J. C., and E. J. Gifford. 1992. Secondary poisoning hazards associated with 1080-treated carrot-baiting campaigns against rabbits, *Oryctolagus cuniculus*. Australian Wildlife Research 19:629-641.

McIlroy, J. C., E. J. Gifford, and S. M. Carpenter. 1988. The effect of rainfall and blowfly larvae on the toxicity of '1080'-treated meat baits used in poisoning campaigns against wild dogs. Australian Wildlife Research 15:473-483.

McIlroy, J. C., E. J. Gifford, and R. J. Cooper. 1986b. Effects on non-target animal populations of wild dog trail-baiting campaigns with 1080 poison. Australian Wildlife Research 13:447-453.

McIlroy, J. C., and D. R. King. 1990. Appropriate amount of 1080 poison in baits to control foxes, *Vulpes vulpes*. Australian Wildlife Research 17:11-13.

McIlroy, J. C., D. R. King, and A. J. Oliver. 1985. The sensitivity of Australian animals to 1080 poison. VIII. Amphibians and reptiles. Australian Wildlife Research 12:113-118.

Mead, R. J., M. G. Feldwick, and J. T. Bunn. 1991. 1,3-difluoro-2-propanol: a potential replacement for 1080 in fauna management programs in Australia. Australian Wildlife Research 18:27-37.

Mead, R. J., D. L. Moulden, and L. E. Twigg. 1985a. Significance of sulfhydryl compounds in the manifestation of fluoroacetate toxicity to the rat, brush-tailed possum, woylie and western grey kangaroo. Australian Journal of Biological Sciences 38:139-149.

Mead, R. J., L. E. Twigg, D. R. King, and A. J. Oliver. 1985b. The tolerance to fluoroacetate of geographically separated populations of the quokka (*Setonix brachyurus*). The Australian Zoologist 21:503-511.

Meyer, J. J. M. 1994. Fluoroacetate metabolism of *Pseudomonas cepacia*. Pages 54-58 *in* A. A. Seawright and C. T. Eason, editors. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28.

Miller, C. J., and S. Anderson. 1992. Impacts of aerial 1080 poisoning on the birds of Rangitoto Island, Hauraki Gulf, New Zealand. New Zealand Journal of Ecology 16:103-107.

Moors, P. J. 1985. Eradication campaigns against *Rattus norvegicus* on the Noises Islands, New Zealand, using brodifacoum and 1080. Pages 143-155 *in* P. J. Moors, editor. Conservation of island birds. Case studies for the management of threatened island species. ICBP Technical Publication No. 3, Cambridge, England.

Moran, S. 1991. Toxicity of sodium fluoroacetate and zinc phosphide wheat grain baits to *Microtus guentheri* and *Meriones tristrami*. Bulletin OEPP/EPPO Bulletin 21:73-80.

Murphy, S. D. 1986. Toxic effects of pesticides. Pages 519-581 *in* C. D. Klaassen, M. O. Amdur, and J. Doull, editors. Casarett and Doull's toxicology. Third edition. Macmillan, New York.

Negherbon, W. O. 1959. Sodium fluoroacetate. Pages 694-695 *in* W. O. Negherbon, editor. Handbook of toxicology. Volume III. Insecticides. A Compendium. WADC Technical Report 55-16. Aero Medical Laboratory, Wright Air Development Center, Air Research and Development Command, United States Air Force, Wright-Patterson Air Force Base, Ohio. Available from the Armed Services Technical Information Agency. Arlington Hall Station, Arlington, Va.

Notman, P. 1989. A review of invertebrate poisoning by compound 1080. New Zealand Entomologist 12:67-71.

O'Brien, P. H. 1988. The toxicity of sodium monofluoroacetate (compound 1080) to captive feral pigs, *Sus scrofa*. Australian Wildlife Research 15:163-170.

O'Brien, P. H., R. E. Kleba, J. A. Beck, and P. J. Baker. 1986. Vomiting by feral pigs after 1080 intoxication: nontarget hazard and influence of anti-emetics. Wildlife Society Bulletin 14:425-432.

O'Brien, P. H., and B. S. Lukins. 1988. Factors influencing the intake of sodium monofluoroacetate (compound 1080) by free-ranging feral pigs. Australian Wildlife Research 15:285-291.

O'Brien, P. H., B. S. Lukins, and J. A. Beck. 1988. Bait type influences the toxicity of sodium monofluoroacetate (compound 1080) to feral pigs. Australian Wildlife Research 15:451-457.

Okuno, I., G. E. Connolly, P. J. Savarie, and C. P. Breidenstein. 1984. Gas chromatographic analysis of coyote and magpie tissues for residues of compound 1080 (sodium fluoroacetate). Journal of the Association of Official Analytical Chemists 67:549-553.

Oliver, A. J., and D. R. King. 1983. The influence of ambient temperatures on the susceptibility of mice, guinea-pigs and possums to compound 1080. Australian Wildlife Research 10:297-301.

Omara, F., and C. S. Sisodia. 1990. Evaluation of potential antidotes for sodium fluoroacetate in mice. Veterinary and Human Toxicology 32:427-431.

Ozawa, H., and T. Tsukioka. 1987. Gas chromatographic determination of sodium monofluoroacetate in water by derivatization with dicyclohexylcarbodiimide. Analytical Chemistry 59:2914-2917.

Palmateer, S. D. 1989. Status of strychnine, compound 1080, and registered alternatives. Pages 14-16 *in* Ninth Great Plains Wildlife Damage Control Workshop proceedings. U.S. Department of Agriculture Forest Service General Technical Report RM-171 (also published as Great Plains Agricultural Council Publication 127).

Palmateer, S. D. 1990. Registration status of vertebrate pesticides with emphasis on 1080 and strychnine. Pages 113-115 *in* L. R. Davis and R. E. Marsh, editors. Proceedings 14th Vertebrate Pest Conference. University of California, Davis.

Parkes, J. P. 1983. Control of feral goats by poisoning with compound 1080 on natural baits and by shooting. New Zealand Journal of Forestry Science 13:266-274.

Parkes, J. P. 1991. Phytotoxicity, poison retention, palatability, and acceptance of carriers used in compound-1080-foliage baits for control of feral goats. Australian Wildlife Research 18:687-694.

Pattison, F. L. M. 1959. Toxic aliphatic fluorine compounds. Elsevier, N.Y. 227 pp.

Peacock, E. A. 1964. Sodium monofluoroacetate (compound 1080). U.S. Bureau of Sport Fisheries and Wildlife, Division of Predator and Rodent Control, Circular Letter dated 1 July 1964. Mimeographed. 26 pp.

Rammell, C. G., and P. A. Fleming. 1978. Compound 1080. Properties and use of sodium monofluoroacetate in New Zealand. New Zealand Ministry of Agriculture and Fisheries, Animal Health Division, Wellington, New Zealand. 112 pp.

Rathore, A. K. 1985. Use of metoclopramide to prevent 1080-induced emesis in wild pigs. Journal of Wildlife Management 49:55-56.

Robison, W. H. 1970. Acute toxicity of sodium monofluroacetate to cattle. Journal of Wildlife Management 34:647-648.

Roy, A. S., V. Taitelman, and S. Bursztein. 1980. Evaluation of the role of ionized calcium in sodium fluoroacetate ("1080") poisoning. Toxicology and Applied Pharmacology 56:216-220.

Savarie, P. J. 1984. Toxic characteristics of fluorocitrate, the toxic metabolite of compound 1080. Pages 132-137 *in* D. O. Clark, editor. Proceedings Eleventh Vertebrate Pest Conference. University of California, Davis.

Savarie, P. J., G. H. Matschke, R. M. Engeman, and K. A. Fagerstone. 1994. Susceptibility of prairie dogs to compound 1080 (sodium monofluoroacetate) baits and secondary poisoning effects in European ferrets under laboratory conditions. Pages 134-143 *in* A. A. Seawright and C. T. Eason, editors. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28.

Savarie, P. J., H. P. Pan, D. J. Hayes, J. D. Roberts, G. J. Dasch, R. Felton, and E. W. Schafer, Jr. 1983. Comparative acute oral toxicity of *para*-aminopropiophenone (PAPP) in mammals and birds. Bulletin of Environmental Contamination and Toxicology 30:122-126.

Sayama, K., and O. Brunetti. 1952. The effects of sodium fluoroacetate (1080) on California quail. California Fish and Game 38:295-300.

Schitoskey, F., Jr. 1975. Primary and secondary hazards of three rodenticides to kit fox. Journal of Wildlife Management 39:416-418.

Seawright, A. A., and C. T. Eason, editors. 1994. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28. 178 pp.

Sibbison, S. 1984. EPA and the politics of poison: the 1080 story. Defenders 59:4-15.

Spurr, E. B. 1979. A theoretical assessment of the ability of bird species to recover from an imposed reduction in numbers, with particular reference to 1080 poisoning. New Zealand Journal of Ecology 2:46-63.

Spurr, E. B. 1991. Reduction of wasp (Hymenoptera: Vespidae) populations by poison-baiting; experimental use of sodium monofluoroacetate (1080) in canned sardine. New Zealand Journal of Zoology 18:215-222.

Spurr, E. B. 1993. Feeding by captive rare birds on baits used in poisoning operations for control of brush-tail possums. New Zealand Journal of Ecology 17:13-18.

Spurr, E. B. 1994. Impacts on non-target invertebrate populations of aerial application of sodium monofluoroacetate (1080) for brushtail possum control. Pages 116-123 *in* A. A. Seawright and C. T. Eason, editors. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28.

Statham, M. 1989. The use of dyes in bait for wallaby control. Australian Wildlife Research 16:421-424.

Sullivan, J. L., F. A. Smith, and R. H. Garman. 1979. Effects of fluoroacetate on the testis of the rat. Journal of Reproduction and Fertility 56:201-207.

Temple, W. A., and I. R. Edwards. 1985. Toxic ducks--1080 residues in game birds. An exercise in applied toxicology. Veterinary and Human Toxicology 27:20-21.

Tietjen, H., F. Deines, and W. Stephensen. 1988. Sodium monofluoroacetate (1080): a study of residues in Arctic fox muscle tissue. Bulletin of Environmental Contamination and Toxicology 40:707-710.

Tourtellotte, W. W., and J. M. Coon. 1950. Treatment of fluoroacetate poisoning in mice and dogs. The Journal of Pharmacology and Experimental Therapeutics 101:82-91.

Tucker, R. K., and D. G. Crabtree. 1970. Handbook of toxicity of pesticides to wildlife. U.S. Bureau of Sport Fisheries and Wildlife, Resource Publication No. 84. 131 pp.

Tucker, R. K., and M. A. Haegele. 1971. Comparative acute oral toxicity of pesticides to six species of birds. Toxicology and Applied Pharmacology 20:57-65.

Twigg, L. E. 1990. The sensitivity of some Western Australian caterpillars to fluoroacetate. Malga Research Centre Journal 10:14-18.

Twigg, L. E., and B. J. Kay. 1992. Evaluation of Quintox for control of feral house mice. Journal of Wildlife Management 56:174-185.

Twigg, L. E., and D. R. King. 1989. Tolerance to sodium fluoroacetate to some Australian birds. Australian Wildlife Research 16:49-62.

Twigg, L. E., and D. R. King. 1991. The impact of fluoroacetate-bearing vegetation on native Australian fauna: a review. Oikos 61:412-430.

Twigg, L. E., D. R. King, and A. J. Bradley. 1988a. The effect of sodium monofluoroacetate on plasma testosterone concentration in *Tiliqua rugosa* (Gray). Comparative Biochemistry and Physiology 91C:343-347.

Twigg, L. E., D. R. King, H. M. Davis, D. A. Saunders, and R. J. Mead. 1988b. Tolerance to, and metabolism of, fluoroacetate in the emu. Australian Wildlife Research 15:239-247.

Twigg, L. E., D. R. King, and R. J. Mead. 1990. Tolerance to fluoroacetate of populations of *Isoodon* spp. and *Macrotis lagotis* and its implications for fauna management. Pages 185-192 *in* J. H. Seebeck, P. R. Brown, R. L. Wallis, and C. M. Kemper. Bandicoats and bilbies. Surrey Beatty, Sydney, Australia.

Twigg, L. E., and R. J. Mead. 1990. Comparative metabolism of, and sensitivity to, fluoroacetate in geographically separated populations of *Tiliqua rugosa* (Gray) (Scincidae). Australian Journal of Zoology 37:617-626.

Twigg, L. E., R. J. Mead, and D. R. King. 1986. Metabolism of fluoroacetate in the skink (*Tiliqua rugosa*) and the rat (*Rattus norvegicus*). Australian Journal of Biological Sciences 39:1-15.

U.S. Environmental Protection Agency (EPA). 1976. Episode summary for reports involving sodium fluoroacetate. Pesticide Episode Review System Report No. 69. Mimeographed. 11 pp.

U.S. Environmental Protection Agency (EPA). 1985. Compound 1080 special review position document 4. U.S. Environmental Protection Agency, Office of Pesticides and Toxic Substances, Washington, D.C. 75 pp.

Walker, J. R. L. 1994. Degradation of sodium monofluoroacetate by soil microorganisms. Pages 50-53 *in* A. A. Seawright and C. T. Eason, editors. Proceedings of the science workshop on 1080. The Royal Society of New Zealand, Miscellaneous Series 28.

Walton, M. T. 1990. Rancher use of livestock protection collars in Texas. Pages 277-280 *in* L. R. Davis and R. E. Marsh, editors. Proceedings 14th Vertebrate Pest Conference. University of California, Davis.

Warburton, B. 1990. Control of Bennett's and tammar wallabies in New Zealand using compound 1080 gel on foliage baits. Australian Wildlife Research 17:541-546.

Ward, P. F. V., and N. S. Huskisson. 1969. The metabolism of fluoroacetate by plants. The Biochemical Journal 113:9P.

Wong, D. H., W. E. Kirkpatrick, D. R. King, and J. E. Kinnear. 1992a. Defluorination of sodium monofluoroacetate (1080) by microorganisms isolated from western Australian soils. Soil Biology & Biochemistry 24:833-838.

Wong, D. H., W. E. Kirkpatrick, D. R. King, and J. E. Kinnear. 1992b. Environmental factors and microbial inoculum size, and their effect on biodefluorination of sodium monofluoroacetate (1080). Soil Biology & Biochemistry 9:838-843.

Wong, D. H., W. E. Kirkpatrick, J. E. Kinnear, and D. R. King. 1991. Defluorination of sodium monofluoroacetate (1080) by microorganisms found in bait materials. Australian Wildlife Research 18:539-549.

Woodfield, B. R. G., I. Nolan, and J. E. Wright. 1964. Rabbit control. Latest methods applied through regional control schemes. The Journal of Agriculture (Victoria, Australia) 62:107-113.

Biological Report 31
August 1996

Contaminant Hazard Reviews
Report No. 31

PLANAR PCB HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler and André A. Belisle

Patuxent Wildlife Research Center
U.S. National Biological Service
Laurel, MD 20708

TABLES

FIGURES

PLANAR PCB HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler and André A. Belisle

Patuxent Wildlife Research Center
U.S. National Biological Service
Laurel, MD 20708

Abstract

Ecological and toxicological aspects of polychlorinated biphenyls (PCBs) in the environment are reviewed with emphasis on biologically active congeners and fish and wildlife. Subtopics include sources and uses, chemical and biochemical properties, concentrations in field collections, lethal and sublethal effects, and recommendations for the protection of sensitive resources. All production of PCBs in the United States ceased in 1977. Of the 1.2 million tons of PCBs manufactured to date, about 65% are still in use in electrical equipment and 31% in various environmental compartments, and 4% were degraded or incinerated. The 209 PCB congeners and their metabolites show wide differences in biological effects. A significant part of the toxicity associated with commercial PCB mixtures is related to the presence of about 20 planar congeners, i.e., congeners without chlorine substitution in the *ortho* position. Toxic planar congeners, like other PCB congeners, have been detected in virtually all analyzed samples, regardless of collection locale. Planar PCB concentrations were usually highest in samples from near urban areas and in fat and liver tissues, filter-feeding bivalve molluscs, fish-eating birds, and carnivorous marine mammals. Adverse effects of planar PCBs on growth, survival, and reproduction are highly variable because of numerous biotic and abiotic modifiers, including interaction with other chemicals. In general, embryos and juveniles were the most sensitive stages tested to planar PCBs, and the chinook salmon (*Oncorhynchus tshawytscha*), domestic chicken (*Gallus* sp.), mink (*Mustela vison*), rhesus macaque (*Macaca mulatta*), and laboratory white rat (*Rattus* sp.) were among the most sensitive species. For protection of natural resources, most authorities now recommend (1) analyzation of environmental samples for planar and other potentially hazardous congeners; (2) exposure studies with representative species and specific congeners, alone and in combination with other environmental contaminants; (3) clarification of existing structure-induction-metabolism relations; and (4) more research on physiological and biochemical indicators of PCB-stress.

Key Words: Polychlorinated biphenyls, PCBs, planar PCBs, ecotoxicology, fish, wildlife, invertebrates

---

Polychlorinated biphenyls (PCBs), a group of 209 synthetic halogenated aromatic hydrocarbons, are used extensively in the electricity generating industry as insulating or cooling agents in transformers and capacitors. Because of human activities and the chemical characteristics of the products, PCBs are now distributed worldwide, and measurable concentrations occur in aquatic organisms and wildlife from North America, Europe, the United Kingdom, and the Atlantic and Pacific Oceans. PCBs elicit a variety of effects including death, birth defects, reproductive failure, liver damage, tumors, and a wasting syndrome. They bioaccumulate and biomagnify in the food chain. Legislation has prohibited virtually all uses of PCBs and their manufacture in the United States since 1979; the ban has been accompanied by declines in PCB residues in fishes and wildlife. But the current environmental burden of PCBs in water, sediments, disposal sites, deployed transformers, and other PCB containers—now estimated at more than 374 million kg, much of it localized—continues to represent a potential hazard to associated natural resources (Pal et al. 1980; Eisler 1986; Hansen 1987; Parkinson and Safe 1987; Safe 1987a, 1990, 1994; Huckins et al. 1988; Tanabe 1988; Skaare et al. 1991; Hoffman et al. 1995).

In this report we summarize the recent technical literature on PCB hazards to fishery and wildlife resources, and place special emphasis on the biologically active planar PCBs. This report is part of a continuing series of brief reviews prepared in response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service and other requestors.

Sources and Uses

The Monsanto Industrial Chemical Company, the principal domestic manufacturer of PCBs, began PCB production in 1929; commercial mixtures of PCBs were also produced in Western Europe and Japan. PCBs have been used in dielectric fluids; in waxes for metal castings; as heat transfer agents; as plasticizers in paints, coatings, and carbonless copy paper; in cutting oils; in sealants and caulking compounds; and as pesticide extenders (Eisler 1986). The use of PCBs was curtailed in the United States in 1971, and sales were limited to manufacturers of capacitors and transformers; all new uses were banned in 1976 (U.S. National Oceanic and Atmospheric Administration [NOAA] 1991). In 1977, all production of PCBs was halted and no shipments were made after October. Direct and indirect sources of PCB contamination may include aerial transport of combustion products, vaporization from continental and marine areas, current and historic industrial and municipal waste discharges, precipitation, land runoff, concealed dumping, transformer fires, and accidental spills (NOAA 1991; U.S. Environmental Protection Agency [USEPA] 1992a).

The ubiquity of PCBs is indicated by their presence in environmental samples from the polar regions of air, snow, ice, water, and in living organisms (Norstrom et al. 1988; Hargrave et al. 1989; Larsson et al. 1992; Tanabe et al. 1993). The presence of PCBs in such remote areas suggests the importance of atmospheric transport. The Committee on the Assessment of Polychlorinated Biphenyls in the Environment estimated that 50-80% of the PCBs derived from the United States were now in sediments and waters of the north Atlantic Ocean (National Academy of Sciences [NAS] 1979). Of the estimated total world PCB production of 1.2 million tons to date, about 374,000 tons are now in various portions of the terrestrial, coastal, and open ocean ecospheres (Table 1). Another 783,000 tons are still in use in electrical equipment and other products or deposited in landfills and dumps (Tanabe 1988) and represent a potential source of environmental contamination. An additional 43,000 tons have been degraded or incinerated (Tanabe 1988). Long range atmospheric and oceanic transport seem to be the primary mechanism of global PCB dispersal (Kannan et al. 1989).

Chemical and Biochemical Properties

General

Polychlorinated biphenyls, a highly lipophilic group of global pollutants, consist of 209 congeners (Fig. 1) with widely different toxicity and other biological effects (Kannan et al. 1989). In vertebrates, toxicological effects of PCBs have been related to their ability to induce the cytochrome P450-dependent monooxygenase system (P450). This varies with the degree of chlorination and the arrangement of chlorine atoms on the biphenyl molecule (Skaare et al. 1991). Transformation of PCBs to hydroxylated metabolites by the cytochrome P450 system is the major pathway of PCB metabolism (Sipes and Schnellmann 1987) and occurs mainly in the liver. The rate of cytochrome P450-catalyzed hydroxylation of PCBs decreases as the number of chlorines increases and as the number of unsubstituted adjacent carbon atoms decreases. Some animals metabolize PCBs at different rates, and this is related in part to differences in the basal level of particular isozymes of cytochrome P450 present in liver. For example, the dog eliminates PCBs more rapidly than other species because it has higher levels of a constitutive isozyme of cytochrome P450 with activity toward the slowly metabolized, bioaccumulated 2,2',4,4',5,5'-hexachlorobiphenyl (Hansen 1987; Sipes and Schnellmann 1987). The reactive arene oxides formed during biotransformation can bind covalently to tissue macromolecules or conjugate with glutathione. Derivatives of glutathione conjugates and glucuronides of the hydroxylated products are major PCB metabolites. Biotransformation of xenobiotics by cytochrome P450 is not always beneficial to the organism because metabolites can be more toxic or biologically active than the parent compound (Parkinson and Safe 1987). The carcinogenic effect of certain xenobiotics depends on the conversion by cytochrome P450 to a reactive carcinogenic metabolite (Parkinson and Safe 1987). Metabolites and possible degradation pathways of selected PCBs in mammals are presented in detail by Sipes and Schnellmann (1987).

Sedimentation and volatilization are the dominant processes that determine the fate of PCBs in lakes. Both processes remove PCBs from the water, but the relative importance of the transferred amount is influenced by particulate dissolved-phase partitioning that determines the relative size of the particulate pool for sedimentation and the soluble pool for volatilization of PCBs (Millard et al. 1993). High productivity of algae increased the proportion of added PCBs that is absorbed to particulate matter and sedimented. In general, PCB volatilization losses increase under conditions of high mixing and low productivity (Millard et al. 1993).

Table 1. Estimated PCB loads in the global environment (Tanabe 1988).

Ecosystem	PCB loads, in metric tons
Terrestrial and Coastal	
Air	500
River and Lakewater	3,500
Seawater	2,400
Soil	2,400
Sediment	130,000
Biota	4,300
Open Ocean	
Air	790
Seawater	230,000
Sediment	110
Biota	270
Total (rounded)	374,000

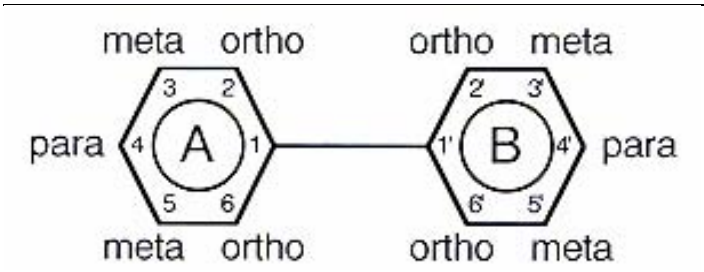


Figure 1. Structure of biphenyl (National Academy of Sciences 1979; U.S. Environmental Protection Agency 1980; Safe 1984, 1994; Eisler 1986). Polychlorinated biphenyls (PCBs) are commercially produced by chlorination of a biphenyl with anhydrous chlorine in the presence of iron filings or ferric chloride as the catalyst. Depending on the conditions under which chlorination occurred, the purified product is a complex mixture of chlorobiphenyls containing 18 to 79% chlorine. Ten possible degrees of chlorination of the biphenyl group produce 10 PCB congener groups: mono-, di-, tri-, tetra-, penta-, hexa-, hepta-, octa-, nona-, and decachlorobiphenyl. Within any congener group, a number of positional isomers are possible. For example, the tetrachlorobiphenyl group consists of 30 possible isomers and the pentachlorobiphenyl congener group contains 46 possible isomers. Not all of the 209 possible isomers are likely to be formed during the manufacturing process. In general, the most common PCB isomers formed have either an equal number of chlorine atoms on both rings, or a difference of one chlorine atom between rings. Chlorine substitution is favored at the ortho and para positions; however, commercial products are complex mixtures of isomers and congeners with no apparent positional preference for halogen substitution.

Physical Properties

Mullin et al. (1984) synthesized and determined the retention times and response factors relative to a reference standard (octachloronaphthalene) of all 209 congeners (Table 2) by using temperature-programmed, high resolution gas chromatography, and electron-capture detection methods (HRGC/ECD). The relative retention times (the ratio of congener retention time/reference standard retention time) of 187 of the 209 congeners differed and permitted HRGC column identification contingent on full or partial separation. Eleven congener pairs had the same retention times and coeluted: 60/56, 70/76, 94/61, 95/80, 133/122, 140/139, 144/135, 145/81, 163/160, 202/171, and 203/196. Of the 209 congeners, 20 can assume a planar configuration (Creaser and Al-Haddad 1989) because of the absence of chlorine substitution in the *ortho* positions (Hong et al. 1992; Fig. 1). Approximately 1% of the non-*ortho*-substituted biphenyl molecules adopt the planar configuration (Safe 1987a). Among the isomers of each homolog, the planar PCBs had the longest retention times. The presence of *ortho*-chloro substituents reduces planarity of the rings. However, congeners with 1 or 2

ortho chlorines can also assume a planar ring position (Safe 1990). Although peak resolution is greatly improved by substitution of high resolution capillary columns for packed columns, more than one candidate congener may occur at many GC peaks. Using a narrow bore column, Duinker et al. (1988a) found only 17 PCB congeners that were fully separated without potential interference from coeluting congeners.

Table 2. Polychlorinated biphenyls: structure, retention times, response factors, and octanol-water partition coefficients (log K_{OW}).[a]

Isometric group and PCB number	Structure (chlorine-filled)	Relative retention time	Relative response factor	Log K_{OW}
Monochlorobiphenyls				
1	2	0.0997	0.0251	4.601
2	3	0.1544	0.0393	4.421
3	4	0.1937	0.04	4.401
Dichlorobiphenyls				
4	2,2'	0.2245	0.0374	5.023
5	2,3	0.2785	0.119	--e
6	2,3'	0.2709	0.38	5.021
7	2,4	0.2566	0.69	5.15
8	2,4'	0.2783	0.206	5.301
9	2,5	0.257	0.388	5.18
10	2,6	0.2243	0.262	5.311
11	3,3'	0.3238	0.0449	5.343
12	3,4	0.3298	0.179	5.295
13	3,4'	0.3315	0.2	--e
14	3,5	0.2373	0.3047	5.404
15	4,4'	0.3387	0.107	5.335
Trichlorobiphenyls				
16	2,2',3	0.3625	0.447	5.311
17	2,2',4	0.3398	0.412	5.761
18	2,2',5	0.3378	0.313	5.551
19	2,2',6	0.3045	0.3037	5.481
20	2,3,3'	0.417	0.7238	5.577
21	2,3,4	0.4135	1.0598	5.517
22	2,3,4'	0.4267	1.0935	5.421
23	2,3,5	0.377	0.5	5.577
24	2,3,6	0.3508	0.793	5.671
25	2,3',4	0.3937	0.5	5.677
26	2,3',5	0.3911	0.603	5.667
27	2,3',6	0.3521	0.495	5.447
28	2,4,4'	0.4031	0.854	5.691
29	2,4,5	0.382	0.6339	5.743
30	2,4,6	0.3165	0.8202	5.504
31	2,4',5	0.4094	0.562	5.677
32	2,4',6	0.3636	0.278	5.751
33	2',3,4	0.4163	0.447	5.572
34	2',3,5	0.3782	0.6092	5.667
35	3,3',4	0.4738	0.3746	5.827
36	3,3',5	0.4375	0.2948	4.151
37	3,4,4'	0.4858	0.58	4.941
38	3,4,5	0.5102	0.722	5.767
39	3,4',5	0.4488	0.347	5.897
Tetrachlorobiphenyls				
40	2,2',3,3'	0.5102	0.722	5.561

Isometric group and PCB number	Structure (chlorine-filled)	Relative retention time	Relative response factor	Log K_{OW}
41	2,2',3,4	0.499	0.5469	6.111
42	2,2',3,4'	0.487	0.792	5.767
43	2,2',3,5	0.4587	0.503	5.757
44	2,2',3,5'	0.4832	0.524	5.811
45	2,2',3,6	0.4334	0.54	5.537
46	2,2',3,6'	0.445	0.468	5.537
47	2,2',4,4'	0.4639	0.848	6.291
48	2,2'4,5	0.4651	0.556	5.787
49	2,2',4,5'	0.461	0.648	6.221
50	2,2',4,6	0.4007	0.6817	5.637
51	2,2',4,6'	0.4242	0.6	5.637
52	2,2',5,5'	0.4557	0.418	6.091
53	2,2',5,6'	0.4187	0.3606	5.627
54	2,2',6,6'	0.38	0.3643	5.904
55	2,3,3',4	0.5562	0.829	6.117
56	2,3,3',4'	0.5676	0.829	6.117
57	2,3,3',5	0.5515	0.6	6.177
58	2,3,3',5'	0.5267	0.609	6.177
59	2,3,3',6	0.486	0.6	5.957
60	2,3,4,4'	0.5676	1.0164	5.452
61	2,3,4,5	0.5331	1.2227	5.943
62	2,3,4,6	0.4685	1.1478	5.897
63	2,3,4',5	0.529	0.728	6.177
64	2,3,4',6	0.4999	0.607	5.957
65	2,3,5,6	0.4671	0.8408	5.867
66	2,3',4,4'	0.5447	0.646	5.452
67	2,3',4,5	0.5214	0.6	6.207
68	2,3',4,5'	0.504	0.726	6.267
69	2,3',4,6	0.451	0.8024	6.047
70	2,3',4',5	0.5407	0.658	6.231
71	2,3',4',6	0.4989	0.468	5.987
72	2,3',5,5'	0.4984	0.5515	6.267
73	2,3',5',6	0.4554	0.5805	6.047
74	2,4,4',5	0.5341	0.671	6.671
75	2,4,4',6	0.4643	0.6461	6.057
76	2',3,4,5	0.5408	0.5795	6.137
77	3,3',4,4'	0.6295	0.3812	6.523
78	3,3',4,5	0.6024	1.1151	6.357
79	3,3',4,5'	0.5894	0.881	6.427
80	3,3',5,5'	0.5464	0.7278	6.583
81	3,4,4',5	0.6149	0.7159	6.367
Pentachlorobiphenyls				
82	2,2',3,3',4	0.6453	0.773	6.142
83	2,2',3,3',5	0.6029	0.6339	6.267
84	2,2',3,3',6	0.5744	0.386	6.041
85	2,2',3,4,4'	0.6224	0.7396	6.611
86	2,2',3,4,5	0.6105	0.7968	6.204
87	2,2',3,4,5'	0.6175	1.021	6.371
88	2,2',3,4,6	0.5486	0.6892	7.516
89	2,2',3,4,6'	0.5779	0.561	6.077
90	2,2',3,4',5	0.5814	0.611	6.367
91	2,2',3,4',6	0.5549	0.571	6.137
92	2,2',3,5,5'	0.5742	0.5375	6.357

Isometric group and PCB number	Structure (chlorine-filled)	Relative retention time	Relative response factor	Log K_{OW}
93	2,2',3,5,6	0.5437	0.6676	6.047
94	2,2',3,5,6'	0.5331	0.4514	6.137
95	2,2',3,5',6	0.5464	0.443	6.137
96	2,2',3,6,6	0.5057	0.4308	5.717
97	2,2',3',4,5	0.61	0.631	6.671
98	2,2',3',4,6	0.5415	0.6246	6.137
99	2,2',4,4',5	0.588	0.613	7.211
100	2,2',4,4',6	0.5212	0.5871	6.237
101	2,2',4,5,5'	0.5816	0.668	7.071
102	2,2',4,5,6'	0.5431	0.4561	6.167
103	2,2',4,5',6	0.5142	0.6068	6.227
104	2,2',4,6,6	0.4757	0.4561	5.817
105	2,3,3',4,4'	0.7049	0.94	6.657
106	2,3,3',4,5	0.668	1.0046	6.647
107	2,3,3',4',5	0.6628	0.8183	6.717
108	2,3,3',4,5'	0.6626	1.0654	6.717
109	2,3,3',4,6	0.6016	0.9625	6.487
110	2,3,3',4',6	0.6314	0.65	6.532
111	2,3,3',5,5'	0.6183	0.6601	6.767
112	2,3,3',5,6	0.5986	0.8286	6.457
113	2,3,3',5',6	0.5862	0.604	6.547
114	2,3,4,4',5	0.6828	1.0261	6.657
115	2,3,4,4',6	0.6171	1.1328	6.497
116	2,3,4,5,6	0.6132	1.3987	6.304
117	2,3,4',5,6	0.615	0.8895	6.467
118	2,3',4,4',5	0.6693	0.87	7.121
119	2,3',4,4',6	0.5968	0.8239	6.587
120	2,3',4,5,5'	0.6256	0.7444	6.797
121	2,3',4,5',6	0.5518	0.7659	6.647
122	2',3,3',4,5	0.6871	0.7247	6.647
123	2',3,4,4',5	0.6658	0.6645	6.747
124	2',3,4,5,5'	0.6584	0.848	6.737
125	2',3,4,5,6'	0.6142	0.556	6.517
126	3,3',4,4'5	0.7512	0.4757	6.897
127	3,3',4,5,5'	0.7078	0.5834	6.957
Hexachlorobiphenyls				
128	2,2',3,3',4,4'	0.7761	1.188	6.961
129	2,2',3,3',4,5	0.7501	0.997	7.321
130	2,2',3,3',4,5'	0.7184	0.952	7.391
131	2,2',3,3',4,6	0.6853	0.8492	6.587
132	2,2',3,3',4,6'	0.7035	0.7303	6.587
133	2,2',3,3',5,5'	0.6871	1.148	6.867
134	2,2',3,3',5,6	0.6796	0.7331	7.304
135	2,2',3,3',5,6'	0.6563	0.7031	7.151
136	2,2',3,3',6,6'	0.6257	0.444	6.511
137	2,2',3,4,4',5	0.7329	1.112	>7.711
138	2,2',3,4,4',5'	0.7403	0.827	7.441
139	2,2',3,4,4',6	0.6707	0.7219	6.677
140	2,2',3,4,4',6'	0.6707	0.6732	6.677
141	2,2',3,4,5,5'	0.720	1.352	7.592
142	2,2',3,4,5,6	0.6848	1.218	6.517
143	2,2',3,4,5,6'	0.6789	0.7088	6.607
144	2,2',3,4,5',6	0.6563	0.8764	6.677

Isometric group and PCB number	Structure (chlorine-filled)	Relative retention time	Relative response factor	Log K_{OW}
145	2,2',3,4,6,6'	0.6149	0.6789	6.257
146	2,2',3,4',5,5'	0.6955	0.728	6.897
147	2,2',3,4',5,6	0.6608	0.6	6.647
148	2,2',3,4',5,6'	0.6243	0.554	6.737
149	2,2',3,4',5',6	0.6672	0.572	7.281
150	2,2',3,4',6,6'	0.5969	0.5676	6.327
151	2,2',3,5,5',6	0.6499	0.785	6.647
152	2,2',3,5,6,6'	0.6062	0.5235	6.227
153	2,2',4,4',5,5'	0.7036	0.688	7.751
154	2,2',4,4',5,6'	0.6349	0.57	6.767
155	2,2',4,4',6,6'	0.5666	0.586	7.123
156	2,3,3',4,4',5	0.8105	1.389	7.187
157	2,3,3',4,4',5'	0.8184	1.1965	7.187
158	2,3,3',4,4',6	0.7429	1.132	7.027
159	2,3,3',4,5,5'	0.7655	0.9934	7.247
160	2,3,3',4,5,6	0.7396	1.1914	6.937
161	2,3,3',4,5',6	0.6968	0.9672	7.087
162	2,3,3',4',5,5'	0.7737	1.0322	7.247
163	2,3,3',4',5,6	0.7396	0.9976	6.997
164	2,3,3',4',5',6	0.7399	0.9848	7.027
165	2,3,3',5,5',6	0.692	1.0777	7.057
166	2,3,4,4',5,6	0.7572	1.0421	6.937
167	2,3',4,4',5,5'	0.7814	1.0658	7.277
168	2,3',4,4',5',6	0.7068	0.8375	7.117
169	3,3',4,4',5,5'	0.8625	0.8355	7.427
Heptachlorobiphenyls				
170	2,2',3,3',4,4',5	0.874	0.75	7.277
171	2,2',3,3',4,4',6	0.8089	1.1712	6.704
172	2,2',3,3',4,5,5'	0.8278	1.172	7.337
173	2,2',3,3',4,5,6	0.8152	2.044	7.027
174	2,2',3,3',4,5,6'	0.7965	0.806	7.117
175	2,2',3,3',4,5',6	0.7611	0.381	7.177
176	2,2',3,3',4,6,6'	0.7305	1.0589	6.767
177	2,2',3,3',4',5,6	0.8031	1.0009	7.087
178	2,2',3,3',5,5',6	0.7537	0.621	7.147
179	2,2',3,3',5,6,6'	0.7205	0.8237	6.737
180	2,2',3,4,4',5,5'	0.8362	1.295	7.367
181	2,2',3,4,4',5,6	0.7968	1.6046	7.117
182	2,2',3,4,4',5,6'	0.7653	1.1272	7.207
183	2,2',3,4,4',5',6	0.772	0.976	7.207
184	2,2',3,4,4',6,6'	0.7016	1.0046	6.857
185	2,2',3,4,5,5',6	0.7848	1.437	7.933
186	2,2',3,4,5,6,6'	0.7416	1.2236	6.697
187	2,2',3,4',5,5',6	0.7654	1.122	7.177
188	2,2',3,4',5,6,6'	0.692	0.7337	6.827
189	2,3,3',4,4',5,5'	0.9142	1.5091	7.717
190	2,3,3',4,4',5,6	0.874	1.31	7.467
191	2,3,3',4,4',5',6	0.8447	1.4741	7.557
192	2,3,3',4,5,5',6	0.8269	1.599	7.527
193	2,3,3',4',5,5',6	0.8397	1.4167	7.527
Octachlorobiphenyls				
194	2,2',3,3',4,4',5,5'	0.962	1.868	8.683
195	2,2',3,3',4,4',5,6	0.9321	0.415	7.567

Isometric group and PCB number	Structure (chlorine-filled)	Relative retention time	Relative response factor	Log K_{ow}
196	2,2',3,3',4,4',5',6	0.8938	1.2321	7.657
197	2,2',3,3',4,4',6,6'	0.8293	0.9522	7.307
198	2,2',3,3',4,5,5',6	0.8845	1.07	7.627
199	2,2',3,3',4,5,6,6'	0.8494	1.1508	7.207
200	2,2',3,3',4,5',6,6'	0.8197	0.369	7.277
201	2,2',3,3',4',5,5',6	0.8875	0.803	7.627
202	2,2',3,3',5,5',6,6'	0.8089	1.165	8.423
203	2,2',3,4,4',5,5',6	0.8938	1.629	7.657
204	2,2',3,4,4',5,6,6'	0.8217	0.8034	7.307
205	2,3,3',4,4',5,5',6	0.9678	1.406	8.007
Nonachlorobiphenyls				
206	2,2',3,3',4,4',5,5',6	1.0103	1.673	9.143
207	2,2',3,3',4,4',5,6,6'	0.9423	1.3257	7.747
208	2,2',3,3',4,5,5',6,6'	0.932	1.1756	8.164
Decachlorobiphenyl				
209	2,2',3,3',4,4',5,5',6,6'	1.0496	1.139	9.603

[a] Ballschmiter and Zell (1980), McDuffie (1981), Bruggeman et al. (1982), Yalkowsky et al. (1983), Mullin et al. (1984), Rapaport and Eisenreich (1984), Shiu and Mackay (1986), Woodburn et al. (1987), Hawker and Connell (1988).

[b] Gas chromatography retention time of PCB congener relative to the retention time of the reference standard octachloronaphthalene on a capillary column of SE-54.

[c] Gas chromatography peak area response of PCB relative to peak area of 1 ng of octachloronaphthalene.

[d] K_{ow} (octanol-water partition coefficient) = C_{ow}/C_{wo}, where C_{ow} is the concentration of the solute in octanol saturated with water, and C_{wo} is the concentration of the solute in water saturated with octanol.

[e] — = no data.

The transport and fate of PCBs in aquatic systems and their partitioning between sediment, water, and organisms depends largely on sorption reactions. In soils, the sorption and retention of PCB congeners is influenced by the number of chlorine atoms in the molecule, and the more highly-chlorinated PCBs tend to be more strongly bound. Relative sorption capacity and other properties of congeners also depend on PCB configuration. The soil sorption capacities of PCB congeners and their bioconcentration factors were related to octanol-water partition coefficients (Connor 1984) as follows:

$$K_{ow} = C_{ow} / C_{wo}$$

where K_{ow} is the octanol-water partition coefficient, C_{ow} the concentration of the solute in octanol saturated with water, and C_{wo} the concentration of the solute in water saturated with octanol.

K_{ow} values are used to estimate bioconcentration factors (bioaccumulation after uptake from water), soil and sediment organic carbon-water partition coefficients, toxicities, and aqueous solubilities (Woodburn et al. 1987; Hawker and Connell 1988). Techniques for measuring the K_{ow} values include the shake-flask method (Shiu and Mackay 1986), the reverse-phase thin-layer chromatography (Bruggeman et al. 1982), reverse-phase high-performance liquid chromatography (Rapaport and Eisenreich 1984), and the generator column technique (Woodburn et al. 1987; Hawker and Connell 1988), or it may be calculated by an estimation technique based on correlation with properties of compounds with known K_{ow} values. From a strong linear relation calculated between known log K_{ow} values and calculated total surface areas (TSA; correlation coefficient of 0.951 for 30 congeners), Hawker and Connell (1988) estimated K_{ow} values of individual congeners from the calculated TSA. Estimated K_{ow} values (Table 2) were previously unavailable of many PCB congeners, including toxic non-*ortho* substituted congeners found only in relatively small amounts in commercial Aroclors. Reported K_{ow} values of

some congeners vary in the literature and may not be comparable when different measuring techniques are used. Reverse-phase thin-layer chromatography (RP-TLC) and high-performance liquid chromatography (RP-HPLC) require empirical correction factors. Discrepancies in K_{OW} values between the generator column and RP-HPLC techniques for *ortho* PCBs relative to the other PCBs were resolved with an *ortho* correction factor (Woodburn et al. 1987). Non-planarity of the *ortho*-substituted PCBs may reduce the ability of the solute to interact with the stationary phase in RP-TLC (Bruggeman et al. 1982). Despite these uncertainties, the K_{OW} is routinely used in hazard evaluation and risk assessment of most organic chemicals.

Toxic Equivalency Factors

A significant part of the toxicity associated with commercial PCB mixtures is related to the presence of the small number of planar congeners. These compounds induce several similar toxic effects in mammals and birds, such as hepatotoxicity, immunotoxicity, and reproductive toxicity (Janz and Metcalfe 1991b; Brunstrom et al. 1995). Planar halogenated aromatic compounds act, in part, by a common mechanism initiated by binding to a cytosolic aryl hydrocarbon receptor. The relative toxicities of planar halogenated hydrocarbons are calculated by expressing their toxicity in relation to 2,3,7,8-TCDD, the most potent compound in this class of chemicals. Toxic equivalency factors (TEFs) are fractional potencies that relate a compound's potency to that of 2,3,7,8-TCDD. The 2,3,7,8-TCDD TEF has been used to estimate the relative toxic potencies of individual planar halogenated hydrocarbons (Safe 1987b; 1990, 1994; Janz and Metcalfe 1991b; Johansen et al. 1993). According to Safe (1990), TEF values should be derived from data on the following effects in descending order of priority: (1) long-term carcinogenicity studies; (2) reproductive studies; (3) subchronic studies that measure Ah receptor-mediated responses, such as thymic atrophy, loss in body weight, and immunotoxicity; (4) acute toxicity studies; and (5) in vivo or in vitro biochemical responses such as enzyme induction and receptor binding. Relative toxic potencies are modified by many variables including age, sex, species, and strain of the animal; the efficiency of the chemical to induce cytochrome P450 and associated monooxygenase enzyme activities, glucuronosyl and glutathione transferases, and other drug-metabolizing enzymes; and the efficiency of the organism to modulate steroid-metabolizing enzymes, induce delta aminolevulinic acid synthetase, inhibit porphyrinogen decarboxylase, decrease Ah receptor binding activity, and alter Vitamin A and thyroid hormone levels (Safe 1990, 1994).

The in vitro induction of the cytochrome P450c-dependent monooxygenases, aryl hydrocarbon hydroxylase, (AHH), or ethoxyresorufin *O*-deethylase, (EROD) by 2,3,7,8-TCDD and related halogenated aryl hydrocarbons in rat liver cells was developed as a short term quantitative bioassay for these chemicals; aromatics that do not fit this correlation are considered as congeners that are readily metabolized in vivo (Safe 1987b). Induction of either AHH or EROD activity in the H4IIE rat hepatoma cell line by PCB, PCDF, and PCDD congeners, either singly or in combination, correlates well with the in vivo toxicity of these compounds to rats (as quoted in Ankley et al. 1991). The proposed mean TEF values range up to 0.1 in non-*ortho* substituted planar PCBs, 0.0005 in mono-*ortho* substituted planar PCBs, and 0.0001 in di-*ortho* substituted planar PCBs (Table 3). Although the concentration of non-and mono-*ortho* substituted PCBs in animal tissues ranges from about 0.01 ug/kg to several micrograms per kg (about 1,000 to 100,000 times lower than the sum of total PCBs), it is significantly higher than the concentration of the highly toxic 2,3,7,8-TCDD and 2,3,4,7,8-pentachloro-dibenzofuran. Accordingly, the non- and mono-*ortho* PCBs—despite their lower toxic potency—often contribute as much or more to the 2,3,7,8-TCDD-like activity than either dioxins or furans (Johansen et al. 1993). However, the overall importance of mono-*ortho* PCBs to the TEF is questioned by Ahlborg et al. (1994), and this must be considered in future risk assessment evaluations.

A note of caution: recent studies revealed that mammal-derived TEFs underestimate the potency of planar PCB mixtures in fish (Newsted et al. 1995). For example, TEFs of non-*ortho* PCB congeners based on mortality of rainbow trout in early life stage are as much as 1,000 times lower than TEFs proposed for human risk assessment (Walker and Peterson 1991, 1994).

Table 3. Proposed toxicity equivalency values (TEF) relative to 2,3,7,8-TCDD of non-*ortho*, mono-*ortho*, and di-*ortho* planar PCBs (Safe 1990, 1994; Ahlborg et al. 1994).

PCB congener	TEF
Non-*ortho* planar PCBs	
PCB 77	0.0005
PCB 126	0.1
PCB 169	0.01
Mono-*ortho* planar PCBs	
PCB 105	0.0001
PCB 114	0.0005
PCB 118	0.0001
PCB 123	0.0001
PCB 156	0.0005
PCB 157	0.0005
PCB 167	0.00001
PCB 189	0.0001
Di-*ortho* planar PCBS	
PCB 170	0.0001
PCB 180	0.00001

Structure-Function Relations

Safe (1984, 1990) described three classes of PCB congeners on the basis of their ability to induce benzo(a)pyrene hydroxylase (also known as aryl hydrocarbon hydroxylase or AHH) and ethoxyresorufin *O*-deethylase (EROD) activities: (1) planar PCBs; (2) mono-*ortho* analogs of the planar PCBs; and (3) di-*ortho* analogs of the planar PCBs. Among the 20 possible planar PCB congeners and their analogs (Fig. 2), the most toxic in rats were PCBs 77, 126, and 169; these three congeners are approximate isostereomers of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) and have similar toxic effects, including induction of 3-methylcholanthrene type drug-metabolizing enzymes, body weight loss, thymic atrophy, dermal disorders, hepatic damage, high binding affinity to hepatic cytosolic receptor proteins, immunotoxicity, reproductive impairment, and teratogenicity (Masse et al. 1986; Parkinson and Safe 1987; Tanabe et al. 1987; Gooch et al. 1989; Kannan et al. 1989; Janz et al. 1992; Himberg 1993; Giesy et al. 1994a). PCBs 77, 126, and 169 have been detected in eggs of terns from Lake Michigan, in marine mammals and humans, and in fish from the Hudson and Ohio Rivers (Huckins et al. 1988). However, they are difficult to detect without proper methods (Tanabe 1988; Schwartz et al. 1993).

The structural characteristics of individual PCB congeners influence their induction of various P450 activities. In mammals, PCB congeners have been characterized as 3-methylcholanthrene-type inducers, phenobarbital-type inducers, or mixed-type inducers of both. AHH and EROD activities (which are preferentially catalyzed by the P450IA gene subfamily) have been induced by planar PCBs in fish and mammals and by some mono-and di-*ortho* analogs of planar PCBs in mammals (Skaare et al. 1991).

The mechanism of toxic action of planar and mono-*ortho* planar PCBs is linked to an interaction with the 2,3,7,8-TCDD (or Ah) receptor protein. But this mechanism does not account for all observed PCB toxicities (Hansen 1987; Safe 1994). Toxic responses unrelated to Ah receptor effects have been reported of PCBs 4, 28, 31, 49, 52, 84, 95, 110, 136, and 153. For example, PCB 153 is less cytotoxic than PCB 169 but is a more effective inhibitor of intercellular communication. PCB 52 caused moderate chick embryotoxicity; however, PCBs 18 and 153 were inactive, and PCBs 84 and 118 were severely toxic but by different mechanisms (Hansen 1987).

Group I planar PCBs are 10 times more toxic and 100 times more effective as inducers of cytochrome P450c dependent monooxygenase and 70 times more effective in competitively displacing 2,3,7,8-TCDD from a rat cytosol receptor protein than Group II planar PCBs (Table 4; Safe 1990; Fig. 2). Mono-*ortho* analogs of the planar PCBs have one substituent in the *ortho* (2 or 2') position; these compounds possess diminished yet

significant EROD- or AHH-inducing capacity and also induce P450 forms that are induced by the phenobarbital class of compounds (Gooch et al. 1989). Mono-*ortho* derivatives (PCBs 105, 118, 156, and 189) may be more important in terms of 2,3,7,8-TCDD-like activity and in occurrence (Hansen 1987). Di-*ortho* analogs of the planar PCBs, that is, those with *ortho*-, *meta*-, and *para*-substituents, possess still weaker but significant AHH-inducing activity (Gooch et al. 1989). Certain di-*ortho* derivatives of the 3,3',4,4' pattern (PCBs 128, 138, 153, 170, 180) are significant components of PCB residues; however, PCBs 128, 138, and 170 have reduced 2,3,7,8-TCDD-like effects (Hansen 1987). In rats, several PCBs (105, 114, 118, 123, 126, 156, 157, 169) produced a linear correlation between the EC50 response (in vitro) of AHH induction against the ED50 (in vivo) of body weight loss, thymic atrophy, hepatic AHH, and EROD induction (Safe 1987b). The planar mono- and di-*ortho* derivatives (PCBs 105, 118, 156, 189, 128, 138, 153, 170, 180) are referred to as mixed inducers because they elicit effects similar to coadministration of phenobarbital plus methylcholanthrene (Hansen 1987).

PCB 156, a mixed inducer of microsomal enzymes, significantly increases the incidences of cleft palates by 2,3,7,8-TCDD in rodents (Birnbaum et al. 1985). Interactions among polychlorinated congeners may range from antagonism to additivity to synergism (Safe 1990), and the toxicity of individual PCBs can be raised by interaction with other PCBs (Table 5).

Quantitation

PCBs are chemically inert, non-polar compounds and relatively stable during collection and storage; however, PCB concentrations in environmental samples vary with different measurement techniques (Kratochvil et al. 1984; Huckins et al. 1990b; Lebo et al. 1992; Prest et al. 1992; Bidleman et al. 1993; Litten et al. 1993), with types of Aroclor standards used for calibration (Table 6), and with oven drying techniques (Table 7). Reports of interlaboratory comparison studies for PCB analysis show wide variations and strongly indicate a need for more rigorous quality control and assurance. In one multilaboratory study (Alford-Stevens 1988)—wherein PCBs were determined in water, soil, and sediments—percent recoveries from analysis of fortified waters averaged 60% in the high concentration sample containing 148 µg/L total PCBs and 55% in the low concentration sample of 37 µg/L. No single combination of extraction and cleanup was best for all solid samples. An analytical intercomparison exercise (International Council for the Exploration of the Sea [ICES] 1992) was conducted on solutions containing 10 PCB congeners. Of the 61 evaluated laboratories, a group of 47 laboratories produced between-group standard deviations of 1.10-1.13 by all PCB congeners except PCB 52; a group of 11 laboratories were identified as an outlier group. Only three laboratories were able to quantify PCBs 110 and 77, which coelute in most GC columns. Peak height measurements gave better reproducibility than peak area methods. In another intercomparison study, the analysis by 11 laboratories of a solution containing 12 pure congeners resulted in a variation of as much as 20% for analysis of a single congener. For the analysis of the same congeners in a fish oil, the coefficient of variation ranged from 17.4 to 132% (66.2% without outliers) and had a median of 47.1% (ICES 1992).

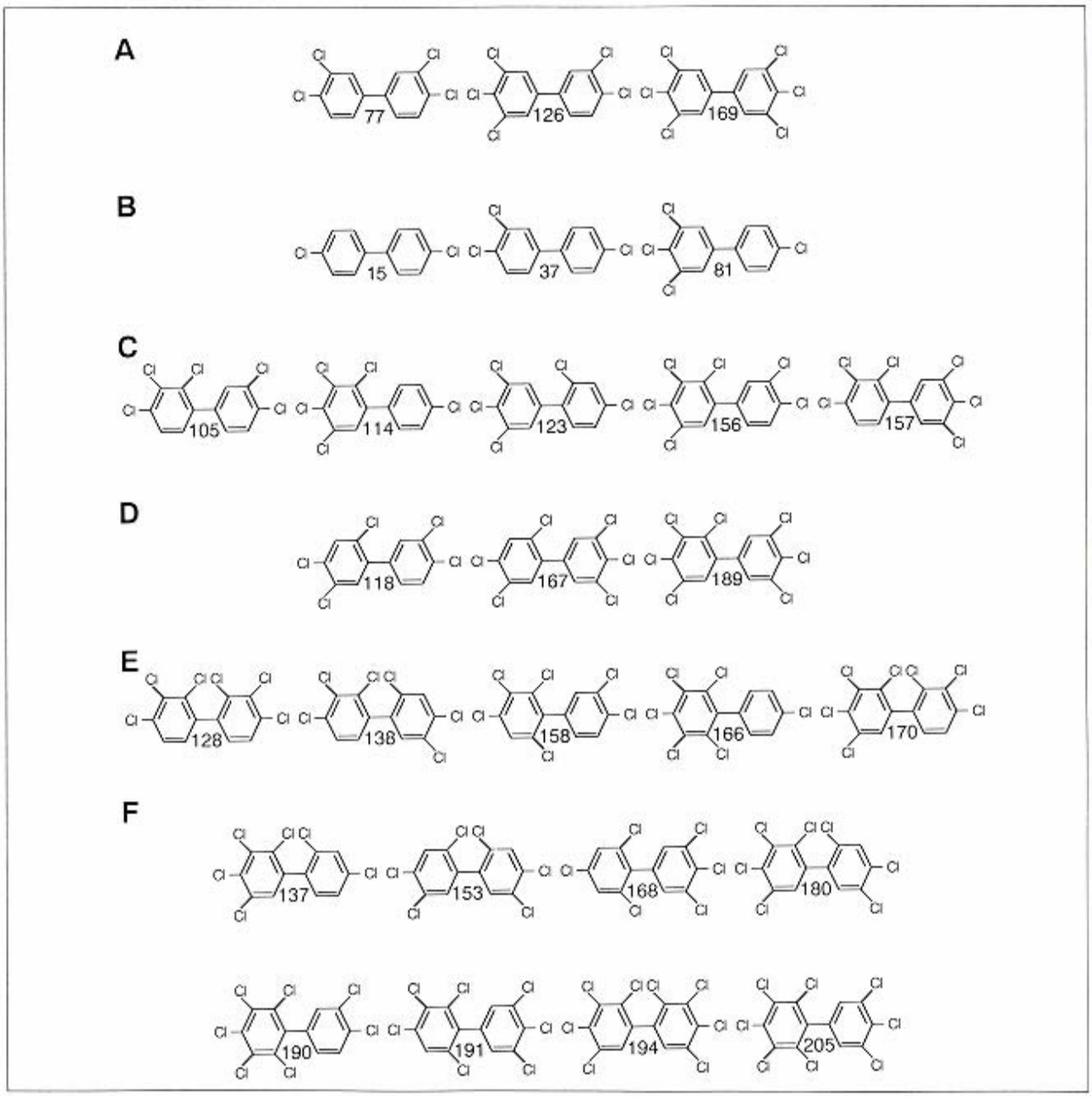


Figure 2. Planar polychlorinated biphenyls and their derivatives (Hansen 1987; Parkinson and Safe 1987; Safe 1987b, 1994; Tanabe et al. 1987; Kannan et al. 1989; de Voogt et al. 1990; Ankley et al. 1991; Sonzogni et al. 1991; Hong et al. 1992; Johansen et al. 1993). The general order of biological activity is: Group I non-*ortho* planar PCBs > Group II non-*ortho* planar PCBs > mono-*ortho* planar PCBs > di-*ortho* planar PCBs. A. Group I. Potent non-*ortho* planar PCBs. This group contains no *ortho*, 2 *para* and at least 2 *meta*-chlorines (PCBs 77, 126, and 169), and are approximate stereoisomers of 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). They are less potent than 2,3,7,8-TCDD but elicit similar biological responses including induction of cytochrome P450 and aryl hydrocarbon hydroxylase (AHH). This group is the most biologically active of all planar PCBs and their derivatives. B. Group II. Less-potent non-*ortho* planar PCBs (PCBs 15, 37, and 81). Group II non-*ortho* planar PCBs, when compared to Group I, were only 0.1 times as toxic, 0.01 times as effective in inducing cytochrome P455c-dependent monooxygenase, and about 0.015 times as effective in competitively displacing 2,3,7,8-TCDD from a cytosol-receptor protein in rat liver. C. Potent mono-*ortho* planar PCBs. The addition of a single *ortho*-

chlorine substituent to non-*ortho* planar PCBs 77, 81, 126, and 169 yields 8 derivatives, of which 5 (PCBs 105, 114, 123, 156, 157) were more potent when the *ortho* chlorine was adjacent to a meta hydrogen. D. Less-potent mono-ortho planar PCBs. The toxicity of non-*ortho* planar PCBs is reduced by the introduction of an *ortho*-chloro substituent, especially when it is adjacent to a *meta*-chlorine (PCBs 118, 167, 189). E. Potent di-*ortho* planar PCBs. The di-*ortho* planar PCBs are less toxic than the mono-*ortho* planar PCBs. At least 5 di-*ortho* derivatives (PCBs 128, 138, 158, 166, 170) compete with 2,3,7,8-TCDD for receptor binding sites in rat liver cytosol to induce cytochrome P450c. F. Less-potent di-*ortho* planar PCBs. These 8 di-*ortho* derivatives (PCBs 137, 153, 168, 180, 190, 191, 194, 205) are less potent than those figured in E.

Table 4. Interactive effects of PCBs on the induction of rat (*Rattus* sp.) liver microsomal cytochrome P450c (Parkinson and Safe 1987).

PCB congener and dose (µmol/kg body weight)	Microsomal enzyme activity, (nmoles product/mg protein/min)	
	Benzo (a)pyrene	Ethoxyresorufin *O*-deethylase
Control, corn oil	0.088	0.277
PCB 153 (300)	0.121	0.530
PCB 126 (0.01)	0.486	3.60
PCB 126 (0.01) plus PCB 153 (300)[a]	0.887	6.03
PCB 169 (125)	0.676	6.89
PCB 169 (125) plus PCB 153 (300)[b]	1.06	10.5

[a] administered 7 days prior to treatment with PCB 126

[b] administered 7 days prior to treatment with PCB 169

PCBs in biological samples are usually extracted by a Soxhlet column and with a nonpolar solvent such as hexane; the sample is first mixed with sodium sulfate to remove moisture. The extraction of PCBs from sediments was tested with sonication, with two sonications interspersed at a 24-h quiescent interval, with steam distillation, or with Soxhlet extraction (Dunnivant and Elzerman 1988). Comparison of the recoveries of various PCB mixtures from dry and wet sediments by the four techniques and the extraction efficiency of four solvents showed that the best overall recoveries were obtained by Soxhlet extraction and the two sonication procedures. In comparisons of solvent systems of acetone, acetonitrile, acetone-hexane (1+1), and water-acetone-isooctane (5+1.5+1), recoveries of lower chlorinated congeners (dichloro- to tetrachloro-) were usually higher with acetonitrile and recoveries of higher chlorinated congeners (tetrachloro- to heptachloro-) extracted with acetone were superior (Dunnivant and Elzerman 1988). The completeness of extraction from a sample matrix does not seem to discriminate against specific isomers; however, discrimination in the cleanup and fractionation process may occur and must be tested (Duinker et al. 1988b).

With most analytical techniques for the quantification of PCB residue levels, chromatographic separations were used, most frequently electron-capture gas chromatography (GC/ECD). With early methods, selected peaks were used to estimate total PCBs. Low resolution separations were satisfactory when packed columns that produced a pattern of peaks with measured areas were used. The patterns were compared with known amounts of Aroclor mixtures. If the Aroclor peaks in a sample closely resembled a particular Aroclor reference mixture of known weight, the total area or peak height of the sample PCBs was compared to those of the reference mixture and the weight of calculated sample PCBs (Kaiser et al. 1980). Other investigators used selected peaks to report Aroclor equivalents (Draper et al. 1991; Turle et al. 1991), but these methods are not useful when samples and Aroclor standards are dissimilar. For another procedure, response factors were used for individual Aroclor peaks as determined by GC and GC-MS procedures (Webb and McCall 1973). The sample peaks were compared with peaks from common Aroclors obtained on packed columns; retention time

windows for the early, middle, and late-eluting peaks were assigned to 3 Aroclors (1242, 1254, 1260) based on the presence or absence of specific peaks. The weight of PCB in the sample peak was calculated by multiplying its peak area by the appropriate response factor; all peaks were added to obtain a total weight of PCB. However, packed columns failed to separate and to identify many congeners because several congeners usually eluted under a single peak of identical retention time. These methods do not account for changes in composition from: interfering compounds; congener changes from hydrolysis, photodegradation, and biodegradation; selective evaporation and adsorption of certain isomers; or solubility differences resulting in different partitioning ratios among the various environmental compartments. Some researchers, who used capillary columns, estimated PCB residues on the basis of a relatively simple cleanup and analysis by high resolution GC-ECD (Duinker et al. 1988b; Maack and Sonzogni 1988; Sericano et al. 1990; Draper et al. 1991) or by HRGC/MS (Porte et al. 1988; Niimi and Oliver 1989; Harrad et al. 1992); others emphasized total PCBs, homolog subgroups, or individual congeners present in substantial amounts in the sample or in commercial mixtures (Maack and Sonzogni 1988; Niimi and Oliver 1989). And still others used total PCBs derived from the sum of homolog subgroup concentrations (Gebhart et al. 1985; Sericano et al. 1990), concentrations of individual subgroups (Gebhart et al. 1985), or the contribution of all congeners in each subgroup (Niimi and Oliver 1989).

Table 5. Summary of PCB structure-function relations in rats, *Rattus* sp. (Parkinson and Safe 1987).

	Cytochrome P450 induction (% of controls)		Relative activity (% of controls)		
			AHH induction		
PCB structure	P450c + P450d	P450b + P450e	In vivo	In vitro	Receptor binding
Planar PCBs: Group I	1,800-4,100	None	+++	1-100	35-100
Planar PCBs: Group II	1,100-1,500	600-1,400	++	0.03	0.5
Mono-*ortho* planars	750-2,400	2,600-4,700	++	0.00002-0.3	1.5-6
Di-*ortho* planars	250-900	1,000-6,300	+	Inactive	<0.3
PCB 153	None	7,300	Inactive	Inactive	<0.3
2,3,7,8-TCDD	3,500	None	+++++	400	2,500

Table 6. PCB congeners in Aroclor 1254 and 1260.[a]

Table 6	Average percent in Aroclor	
PCB Number	1254	1260
16	--[b]	0.04
17	0.19	0.05
18	0.41	0.12
21	--	0.01
22	--	0.01
24	--	0.01
26	--	0.02
28	0.25	0.045
29	--	0.02
31	0.22	0.05

Table 6	Average percent in Aroclor	
PCB Number	1254	1260
33	0.14	0.09
37	--	0.04
40	0.20	0.03
41	0.64	0.20
42	--	0.04
43	--	0.02
44	2.03	0.11
45	--	0.07
46	--	0.02
47	0.17	0.11
48	0.14	0.19
49	1.64	0.06
52	5.18	0.41
53	0.09	0.04
56/60	0.56	0.14
63	0.05	--
64	0.45	--
66	0.59	--
67	0.09	--
70	3.21	0.12
74	0.78	0.03
82	0.95	0.112
83	0.45	0.04
84	1.95	0.45
85	1.66	0.09
87	3.78	0.61
90	0.93	0.56
91	0.83	0.07
92	1.58	0.59
95	6.02	2.87
96	0.08	--
97	2.55	0.34
99	3.60	0.12
100	0.10	0.02
101	7.94	3.82
105	3.83	0.07
107	0.72	0.03
110	5.85	1.80
115	0.30	0.05
118	6.39	0.53
119	0.14	--
122	0.50	0.21
123	0.81	--
128	2.07	0.76
129	0.23	0.66
130	0.63	0.08
132	1.98	3.69
134	0.49	0.35
135	1.62	2.56
136	1.12	1.82
137	0.25	0.14

Table 6	Average percent in Aroclor	
PCB Number	1254	1260
138	3.20	6.31
141	1.04	2.53
144/135	--	1.5
146	0.83	1.39
149	2.21	7.61
151	1.17	3.08
153	4.26	10.20
156	1.62	0.66
157	--	0.14
158	0.77	0.70
160	--	0.05
167	0.21	0.21
169	--	0.05
170	0.31	5.36
171/202	0.05	1.65
172	0.05	0.78
173	0.09	0.21
174	0.34	4.68
175	0.05	0.36
176	0.32	0.64
177	0.21	2.06
178	1.35	1.41
180	0.38	8.11
183	0.17	2.03
185	--	2.72
187	0.32	4.24
189	--	0.13
190	0.08	0.79
191	--	0.18
193	--	0.57
194	--	1.50
195	--	0.38
196	--	1.90
197	--	0.12
198	--	0.09
199	--	0.82
200	--	0.62
201	0.68	1.95
203	--	2.05
205	--	0.13
206	--	0.65
207	--	0.07
208	--	0.17
209	--	0.05
Total (%)	96.25	105.55

[a] Bush et al. (1985), Safe et al. (1985), Schulz et al. (1989), Smith et al. (1990).

[b] -- = no data.

Table 7. Effect of oven drying of sediments on percent loss of selected PCB congeners present at >0.1 mg/kg fresh weight (Bush et al. 1987). Mean loss of these congeners is 56 percent.

PCB number	Percent loss	PCB number	Percent loss
1	65	42	0
4	61	44	0
6	50	46	46
8	50	47	43
9	50	49	47
10	62	51	53
15	100	52	44
16	43	59	50
17	43	60	33
18	57	64	45
19	53	66	50
22	50	70	32
25	40	82	40
26	50	84	50
28	43	94	34
31	33	136	0
40/41	50	151	0

Gas chromatography/ mass spectrometry in the electron ionization mode (GC/MS-EI) has been used to a more limited extent for routine analysis of PCBs (Alford-Stevens et al. 1985; Kuehl et al. 1991). Some interference with quantification ions can occur with EI when compounds such as PCBs 77 and 110 coelute. GC/MS has also been operated in the negative chemical ionization mode (NCI) for PCB determinations (Guevremont et al. 1987; Swackhammer et al. 1987; Erhardt-Zwabik et al. 1990). Increased selectivity is observed in the NCI mode, although interference from other compounds that readily form stable negative ions may be observed. Improvements have also been made in capillary column separations. However, the application of single long, narrow bore capillary columns does not enable investigators to attain full separation of PCB congeners (Ballschmiter and Zell 1980; Bush et al 1983; Mullin et al. 1984; Duinker et al. 1988b). Multidimensional GC (MDGC) analysis of PCBs drastically improved congener separations and the analysis of all sample constituents. Schomburg et al. (1985) connected two capillary columns of different polarities in a double oven instrument; the first column was temperature programmed, and the second was operated isothermally. Congeners of Clophen A 50 were separated by valveless flow switching. Using MDGC techniques, Duinker et al. (1988a, 1988b) analyzed PCBs 28, 52, 101, 138, 153, and 180 and positively identified PCBs 52, 101, and 180 as well as coeluting peaks of PCBs 24, 26, 29, 44, 49, 81, 84, 114, 128, 151, 169, 177, 183, 187, 189 and 194. In a following paper, Schultz et al. (1989) used the same MDGC technique to fully resolve all congeners in commercial PCB mixtures of Clophen A30, A40, A50, A60 and in Aroclors 1221, 1016, 1242, 1254, and 1260. A column of SE-54 with ECD was used to monitor the eluate, and a second, more polar column (usually OV-210) with ECD was used to obtain fully resolved single peaks. The procedure required exact timing of cuts based on retention time but fully separated the PCB congeners by gas chromatography for the first time. A total of 132 congeners at concentrations above 0.05% (w/w) were eluted as fully resolved single peaks and measured (Schultz et al. 1989).

Pattern recognition techniques that incorporate statistical methods have been used to determine spatial and temporal patterns in PCB residue data. Stalling et al. (1980, 1987), for example, characterized sample PCB profiles from 105 individual congeners, measured parameters of similarity between sample and standard mixtures, and determined whether the sample residue pattern corresponded to an Aroclor mixture. Modeling environmental samples with the individual congener concentrations provided more accurate estimations of Aroclor profiles than homolog concentrations. Intact commercial Aroclors have been characterized by automated mass spectrometric determination of weight percent distribution by homolog groups (Alford-Stevens

1986). One isomer from each level of chlorination was normally used to calibrate the MS response to all measurable isomers in that group. In another example, Macdonald et al. (1992) applied pattern recognition techniques to assess biomagnification and to characterize source patterns of multicomponent pollutants such as PCBs, PCDDs, and PCDFs in eggs of the herring gull (*Larus argentatus*) from the Great Lakes between 1983 and 1990. Turle et al. (1991) fitted a linear regression to PCB concentrations in herring gull eggs from the Great Lakes during 1970-85 and from more recent measurements. Aroclor equivalents in eggs were determined with PCB 138 as a single peak estimate for the older data and more recent PCB data as the sum of 41 congeners. The earlier choice of PCB 138 for quantitation seemed fortunate; uptake of heptachloro isomers maintained a stable percentage of total PCB egg residues over time, whereas less chlorinated congeners generally declined and more chlorinated congeners increased over time (Turle et al. 1991).

Methods were developed for routine analysis of AHH-inducing and other PCB congeners in fish by using a comparatively simple gel permeation chromatography (GPC) cleanup and GC/MS-NCI (Schmidt and Hesselberg 1992). Methane was used as the reagent gas for NCI, source temperature and pressure were optimized (1100 C and 0.9 Torr), and fragmentation of the major ions was reduced as much as 10%. A peak area correction factor for interfering ion fragmentation was obtained by instrument calibration with standards and manually applied to coeluting ions as needed (Schmidt and Hesselberg 1992). Additional methods were developed for the analysis of planar congeners. Using a carbon foam adsorbent, Huckins et al. (1978, 1980, 1988) devised procedures for the analysis of toxic non-*ortho*-chloro substituted PCB congeners and trace planar impurities in Aroclors. With carbon-foam chromatography (carbon particles suspended on a polyurethane substrate), concentrations of planar PCB congeners in Aroclors 1016, 1242, 1248, 1254, and 1260 were detected by high resolution electron capture gas chromatography (HRGC/ECD). With current chemical methods for analysis of non-*ortho*-chloro substituted planar PCBs, extraction and a preliminary clean-up, carbon chromatography, and HRGC/ECD or HRGC/MS are generally used (Feltz et al. 1995). The brands of carbon available for isolating planar PCBs include Amoco AX-21 (PX-21), Alltech SK-4, Serva SP-1, and Wako active carbon (Storr-Hansen and Cederberg 1992). All methods shared at least three characteristics: (1) they require some form of adsorption chromatography (usually with carbon) to isolate planar compounds; (2) they include several clean-up steps; and (3) they are complicated.

A semipermeable membrane device (SPMD) with a nonpolar, low density polymeric film is used to separate PCBs from large amounts (20-50 g) of lipids by dialysis in an organic solvent prior to chemical analysis (Huckins et al. 1990a; Meadows et al. 1993). Liquid-liquid phase partitioning of extracts in organic solvent with sulfuric acid has been used to convert fats and pigments into water-soluble compounds that can be separated and removed from the target analytes with water rinses. Fats may be removed by refluxing or partitioning extracts with alcoholic potassium hydroxide to form water soluble hydrolysis products. For example, Tanabe et al. (1987) and Kannan et al. (1987b) combined alkali digestion, active carbon column chromatography, fuming sulfuric acid clean-up, HRGC/ECD, and HRGC/MS confirmation for the analysis of PCBs 77, 126, and 169 in porpoise blubber. Measurement of these three highly toxic PCBs in Aroclor and Kanechlor mixtures is reported by Kannan et al. (1987a). Creaser and Al-Haddad (1989) separated five non-*ortho* substituted PCBs from a synthetic mixture containing Aroclors, organochlorine and organophosphorus pesticides, dioxins, and dibenzofurans on an HPLC column packing of porous graphite carbon (PGC). Soil samples required prior cleanup to remove coextracted organics, and elution from a multilayered column containing acid, base, and silica was followed by elution from Florisil.

Procedures are available for separating mono- and non-*ortho* chloro PCBs. Hong and Bush (1990) used sulfuric acid cleanup, low-pressure liquid chromatography with activated carbon/silica gel and HRGC/ECD to analyze four non-*ortho* and eight mono-*ortho* substituted PCBs. Haglund et al. (1990) used a non-carbon HPLC column of 2-(1-pyrenyl)ethyldimethylsylated silica (PYE) column to isolate mono- and non-*ortho* chloro PCBs from tissue samples. Isolation with this column required almost complete prior removal of lipids by sulfuric acid partitioning and subsequent gel permeation chromatography (GPC) with Bio-Beads S-X3 to remove remaining lipids. Ford et al. (1993) adapted an automated dioxin analysis system with programmable pump and valve setup for the sequential processing of non-*ortho* substituted PCBs in five blubber samples. The procedure included ball/mill tissue extraction, preliminary GPC separation and cleanup, silica gel chromatography, and automated separation of non-*ortho* substituted PCBs on AX21 activated carbon/glass fiber with three solvent systems and was followed by GC-ECD and GC/MS-EI analysis with selected ion monitoring (SIM). The application of high resolution capillary column techniques combined with the development of carbon adsorbents for the separation of planar aromatics has become a powerful tool for the identification and measurement of

single congeners in complex PCB mixtures and have facilitated the resolution and more accurate quantification of individual congeners and the correction of the presence of non-PCB interferences. But the introduction of such methods in long-term monitoring programs, where one, several, or all peaks in Aroclor standard mixtures were used to estimate total PCBs, raises the problem of comparing results among the data sets. For such purposes a value for total Aroclor can also be reported (Porte et al. 1988; Turle et al. 1991).

Concentrations in Field Collections

General

An increasing number of reports indicate the widespread presence of toxic planar PCB congeners such as the non-*ortho* substituted planar PCBs 77, 126, and 169. These PCB congeners were detectable in all Finnish food commodities of animal origin sold in Helsinki (Himberg 1993); in all samples of salmon muscle, cod liver, and seal blubber from the Baltic Sea and environs in the 1980s (Koistinen 1990); and at concentrations between 0.03-30 µg/kg fat fresh weight (FW) in a wide variety of vertebrates, including fish, marine mammals, dogs, cats, and humans (Tanabe et al. 1987). These and other planar congeners contribute the majority of the toxic potency to PCB mixtures as judged by their ability to induce AHH and EROD (Kannan et al. 1989; Ankley et al. 1991; Sonzogni et al. 1991). Detection of these toxic residues in field collections from remote areas suggests that planar PCBs are now as widely distributed as other PCB isomers (Tanabe et al. 1987). The clear positive correlation between concentrations of total PCBs and PCBs 77, 126, and 169 in all analyzed mammals suggest that the sources of planar PCB contamination to the environment are mainly commercial PCB formulations (Tanabe et al. 1987).

Nonbiological Materials

Relatively little contamination from PCBs was found in sediments from riverine and pothole wetlands at national wildlife refuges and waterfowl production areas (WPA) in the north central United States in 1980-82. PCBs were above detection levels (20 µg/kg) in less than 4% of the sediments; a similar case was recorded in fish from WPAs (Martin and Hartman 1985). Maximum total PCB concentrations in field collections of nonbiological materials were 0.000028 µg/kg in ice, 0.000125 µg/kg in snow, 12.3 µg/m^3 in air, 233 µg/L in seawater, 3,860 µg/L in sediment interstitial waters, and 1,800 mg/kg in sediments. Concentrations were comparatively elevated in urban areas, near anthropogenic activities, and at known sites of PCB contamination (Table 8).

Atmospheric transport is a major route in PCB distribution (Swackhammer et al. 1988). Deposition and evaporation studies of 17 PCB congeners in Siskiwit Lake on Isle Royale, Michigan, showed that PCB input fluxes to the lake from rain, snow, and aerosol equalled output fluxes from sedimentation and evaporation. The magnitude of the net vapor flux, calculated by difference and with the assumption that inputs equal outputs, was large and positive for almost all 17 congeners (Swackhammer et al. 1988). Low but measurable PCB concentrations (measured as Aroclor 1254) were found in air, snow, ice, seawater, and sediment in the Arctic Ocean north of Axel Heiberg Island off Canada's northern outer coast (Hargrave et al. 1989). PCB residues were relatively high in melted snow (8-125 pg/L), indicating efficient scavenging from air. The ice island area from which surface seawater samples were collected was well removed from any direct influence of river drainage, and PCB concentrations probably reflect those over much of the Arctic Ocean (Hargrave et al. 1989). PCBs were also monitored in the atmosphere of Ross Island, Antarctica, from March 1988 to January 1990 (Larsson et al. 1992). The geometric mean of total PCBs in air during this period was 15.2 pg/m^3 and the maximum concentration was 12,300 pg/m^3. The geometric mean during the Antarctic summers of 1988-89 and 1989-90 was 21 pg/m^3. During one sampling period (16-28 December 1988), PCB levels were about 100 times higher than during any other period, suggesting either irregular, long-range transport of atmospheric pollutants or volatilization of PCBs from a local dumpsite at McMurdo Base on Ross Island. PCB levels did not correlate with seasonal temperature changes, although changes in atmospheric levels were recorded. The absence of seasonal differences may be due to the cold climate and the low vapor pressure of PCBs (Bidleman et al. 1983).

Table 8. PCB concentrations in field collections of selected nonbiological materials. Concentrations are in ug/kg fresh weight (FW) or dry weight (DW) unless indicated otherwise

Table 8. Material	Concentration[a]	Reference[b]
Air (ug/m^3)		
Antarctica, Ross Island; 1988-90		
PCB 95	Max. 0.000415 FW	1
PCB 101	Max. 0.000574 FW	1
PCB 110	Max. 0.000444 FW	1
PCB 138	Max. 0.00181 FW	1
PCB 149	Max. 0.00161 FW	1
PCB 153	Max. 0.00128 FW	1
Total PCBs	0.015 FW; Max. 12.3 FW	1
Arctic Ocean; 1986-87;total PCB's	<0.00001 FW	2
Ice		
Arctic Ocean; 1986-87;total PCBs	Max. 0.000028 FW	2
Seawater		
Arctic Ocean; 1986-87; total PCBs; water column vs. particulates under ice	Max. 0.00001 FW vs. 2-99 DW	2, 3
Massachusetts; New Bedford Harbor (PCB-contaminated); 1986; total PCBs; bedded phase vs. suspended phase	15 FW vs. 233 FW	4
New York Bight dumpsite; 1970s-1980s; total PCBs	Max. 0.04 FW	5
Sediment interstitial waters		
New Bedford Harbor; 1986; total PCBs	3,860 FW	4
Sediments		
Arctic Ocean; 1986-87; total PCBs	<0.05 DW	2
Canada, Lake Ontario		
Cores; total PCBs		
1940	0-10 FW	6
1966-69	470-880 FW	6
1980	250-290 FW	6
Surficial sediments; 1981		
Total PCBs	(71-1,200) FW	7
Tri-CBs	(11-22) FW	7
Tetra-CBs	(77-200) FW	7
Penta-CBs	(76-180) FW	7
Hexa-CBs	(41-93) FW	7
Hepta-CBs	(20-48) FW	7
Octa-CBs	(11-22) FW	7
Nona-CBs	(2.4-5.7) FW	7
Deca-CB	(5.3-9.4) FW	7
Settling sediments; total PCBs		
1982-83	1,300-1,900 FW	7
1983-84	350-500 FW	7
1984-85	410-680 FW	7
1985-86	80-290 FW	7
Sweden, Eman River; near paper recycling plant		
PCB 77	30.0 DW	8
PCBs 126, 169	Nondetectable	8
Switzerland, Lake Zurich; total PCBs		

Table 8. Material	Concentration[a]	Reference[b]
1929-34	<0.5 DW	9
1960-65	210 DW	9
1975-80	70 DW	9
United States		
California; total PCBs		
Hunter's Point	40 DW	10
Islais Creek	164 (57-255) DW	11
Long Beach; 1984-89	>200,000 DW	12
Oakland Bay	30-61 DW	10, 11
Palos Verdes; 1984-89	>200,000 DW	12
San Diego Bay; 1984-89	>200,000 DW	12
San Francisco Bay	Max. 1,400 DW	13
San Pablo Bay	11.4 (5.7-17.5) DW	10, 11
San Pedro Bay; 1984-89	>200,000 DW	12
Santa Monica Bay; 1984-89	>200,000 DW	12
Southampton Shoal	12 DW	10
Connecticut; 1984-89; total PCBs		
Connecticut River	>200,000 DW	12
Long Island Sound	>200,000 DW	12
Florida; 1984-89; total PCBs		
Choctawhatchee Bay	>200,000 DW	12
St. Andrews Bay	>200,000 DW	12
Tampa Bay	>200,000 DW	12
Illinois, Waukegan Harbor; 1978		
PCB 77	1.05 (0.005-27.5) DW	14
PCB 105	0.86 (0.10-131.0) DW	14
Total PCBs	515 (11-13,360) DW	14
Maryland; 1984-89; total PCBs		
Baltimore Harbor	>200,000 DW	12
Upper Chesapeake Bay	>200,000 DW	12
Michigan		
Raisin River; 1983		
PCB 77	0.6 DW	15
PCB 126	0.28 DW	15
PCB 169	0.07 DW	15
Total PCBs	40,000 DW	15
Saginaw River; 1984		
PCB 77	0.017 DW	15
PCB 126	<0.015 DW	15
PCB 169	ND	15
Massachusetts; total PCBs		
Boston Harbor and Buzzards Bay; 1984-89	>200,000 DW	12
New Bedford Harbor; 1986	1,800,000 FW	4
Salem Harbor; 1984-89	>200,000 DW	12
Nebraska; waterfowl production areas; 1980-82; total PCBs	ND	16
New Jersey; Raritan Bay; total PCBs		
1970s	(3-2,035) DW	17
1984-89	>200,000 DW	12
New York		
Hudson-Raritan estuary and Long Island Sound; 1984-89; total PCBs	>200,000 DW	12
Upper Hudson River; anoxic sediments		

Table 8. Material	Concentration[a]	Reference[b]
PCB 1	200,000 DW	18
PCB 4	160,000 DW	18
PCBs 6/19	40,000 DW	18
PCB 8	33,000 DW	18
PCB 10	75,000 DW	18
PCB 18	7,800 DW	18
PCB 31	12,000 DW	18
PCB 32	12,000 DW	18
PCB 47	12,000 DW	18
PCB 49	21,000 DW	18
PCB 50	9,200 DW	18
PCB 52	30,000 DW	18
PCB 64	11,000 DW	18
PCBs 82/85/110	12,000 DW	18
PCB 92	5,500 DW	18
Others	52,000 DW	18
Ohio, Cuyahoga River; 1984		
PCB 77	0.09 DW	15
PCB 126	0.011 DW	15
PCB 169	<0.01 DW	15
Rhode Island, Narragansett Bay; 1984-89; total PCBs	>200,000 DW	12
South Carolina, Lake Hartwell; total PCBs		
Cores; 1984-87	Max. 153,840 DW	19
Cores; distance from source, in km		
33.2	40,500 DW;Max. 88,500 DW	20
78.2	380 DW; Max. 1,100 DW	20
South Dakota; waterfowl production areas; 1980-82; total PCBs	ND	16
U.S. National Wildlife Refuges; North Central area; 1980-82; total PCBs	ND-1 DW	16
Virginia; Elizabeth River; 1984-89; total PCBs	>200,000 DW	12
Washington; total PCBs		
Elliot Bay; 1984-89	>200,000 DW	12
Puget Sound; 1980s		
Main basin	93 DW	21
Nonurban bays	15-34 DW	21
Urban bays	750 DW	21
Wisconsin		
Fox River; 1984		
PCB 77	1.4 DW	15
PCBs 126, 169	ND	15
Fox River; 1988		
Total PCBs	22,000-41,450 DW	15, 22
Total AHH-active PCBs	710 DW	15
PCB 77	8.5 DW	15
PCB 105	6 DW	15
PCB 118	17 DW	15
PCB 128	13 DW	15
PCB 138	87 DW	15
PCB 156	2 DW	15
PCB 158	1.5 DW	15

Table 8. Material	Concentration[a]	Reference[b]
PCB 170	31 DW	15
Green Bay; 1984		
PCB 77	0.94 DW	15
PCB 126	0.024 DW	15
PCB 169	<0.005 DW	15
Lake Pepin; 1983		
PCBs 77, 126, 169	<0.002-0.002 DW	15
Total PCBs	56 DW	15
Menominee River; 1984		
PCB 77	0.1 DW	15
PCB 126	0.04 DW	15
PCB 169	0.003 DW	15
Snow		
Arctic Ocean; 1986-87; total PCBs	Max. 0.000125 FW	2

[a] Concentrations are shown as mean, range (in parentheses), maximum (Max.), and nondetectable (ND).

[b] 1, Larsson et al. 1992; 2, Hargrave et al. 1989; 3, Hargrave et al. 1992; 4, Burgess et al. 1993; 5, Boehm 1981; 6, Eisenreich et al. 1989; 7, Oliver et al. 1989; 8, Asplund et al. 1990; 9, Buser and Muller 1986; 10, NOAA 1987; 11, Chapman et al. 1986; 12, NOAA 1991; 13, Law and Goerlitz 1974; 14, Huckins et al. 1988; 15, Smith et al. 1990; 16, Martin and Hartman 1985; 17, Stainken and Rollwagen 1979; 18, Rhee et al. 1989; 19, Elzerman et al. 1991; 20, Dunnivant et al. 1989; 21, Ginn and Pastorok 1992; 22, Ankley et al. 1992.

PCB concentrations in sediment cores from Lake Ontario were similar to production and sales data of PCBs in the United States (Eisenreich et al. 1989). Annual PCB accumulation rates in the sediments rose from about 2 ng/cm^2 in 1950 to about 40 ng/cm^2 in the 1966-69 peak years and declined in 1980 to 10-20 ng/cm^2; about 50% of the 1966-69 load was attributed to the upward mixing by oligochaete worms (Eisenreich et al. 1989). Each of several PCB congeners in Lake Ontario sediments contributed 5.7 to 7.9% of the total PCBs (PCBs 66, 110, and 56/60) and others (including PCBs 44, 52, 70/76, 101, and 153) contributed 4.0-4.7% (Oliver and Niimi 1988; Oliver et al. 1989). Surficial sediments of Lake Ontario in 1981-86 contained elevated concentrations of organochlorine compounds, including mirex, chlorobenzenes, octachlorostyrenes, DDT, 2,3,7,8-TCDD, fluorinated aromatic compounds, and PCBs (Oliver et al. 1989). Among the identified congeners, PCBs 60 (5.7%) and 118 (2.6%) are AHH-active (Smith et al. 1990). The frequency of isomers of low chlorination decreased with core depth in sediments, remained fairly stable of hexa isomers, and increased with core depth of the more highly chlorinated congeners. This pattern with depth reflects the change in use pattern over time to less highly chlorinated PCBs such as Aroclor 1016. The more highly chlorinated congeners that are disproportionately present in deeper sediments may be due to stronger partitioning to sediment and higher hydrophobicity than those of less chlorinated congeners and to the positive correlation with their high octanol-water partition coefficients (Karickoff 1981). Anaerobic dechlorination was not evident in these sediments. This contradicts the findings of others who maintain that relatively high levels of less-chlorinated PCBs in the bottom (anaerobic) core sections of Hudson River sediments were due to anaerobic dechlorination (Brown et al. 1985). Oliver et al. (1989) concluded that the total mass of PCBs in Lake Ontario sediments was about 50 tons and sufficient to impact Lake Ontario for many years. Lake Michigan sediments, analyzed for 18 planar AHH-active PCBs, total PCBs, 2,3,7,8-TCDD, and 2,3,7,8 tetrachloro-*p*-dibenzofuran (2,3,7,8-TCDF), had elevated levels of PCBs 77, 126, and 169 (Smith et al. 1990). Results suggest that the contribution of toxic equivalents—that is, the sums of congeners after the raw congener concentrations were normalized by the TEF—was greater from PCBs 77, 126, and 169 than from 2,3,7,8-TCDD and 2,3,7,8-TCDF, even in environments with significant concentrations of dioxins and dibenzofurans (Smith et al. 1990). Sediments from the Waukegan Harbor, Illinois, in 1978 contained weathered mixtures of Aroclors 1242, 1248, and 1254. Total PCB concentrations were variable between stations and ranged from 10.6 mg/kg to 13,360 mg/kg DW; 3,3',4,4'-TCB residues ranged from 5 to 27,500 µg/kg DW, or about 0.16% of the total PCBs; concentrations were higher of 2,3,3',4,4'-PCB (102 to 131,000 µg/kg DW, or 0.66%; Huckins et al. 1988).

PCB homologs and total PCBs in water, sediments, and biota were measured in Hamilton Harbor on Lake Ontario and Wheatley Harbor on Lake Erie. Hamilton Harbour receives inputs from steel mills and an incinerator plant; Wheatley Harbour receives fish-processing plant wastes. Total PCBs in sediments ranged from 608 to 14,185 µg/kg DW in Hamilton Harbour and from 166 to 1,177 µg/kg DW in Wheatley Harbour (Mudroch et al. 1989). The high PCB value in Hamilton Harbor is similar to values reported earlier in Lake Erie sediments (Frank et al. 1977). Concentrations of lower chlorinated homologs were greater in water than in sediment in both harbors (Mudroch et al. 1989). Homolog patterns in biota (oligochaetes, snails, isopods, and fish) reflected patterns in sediments but not in water. Concentrations of penta- and hexachlorobiphenyls were dominant in the oligochaetes and sediment samples from Wheatley Harbour; concentrations of these homologs also predominated in Hamilton Harbour, but the differences were less pronounced. Particle size distribution of 82-98% silt and clay (63 µm) was similar in both harbors. The concentrations of several metals (Zn, Pb, Cu, and Cr) were much higher in Hamilton Harbor, but their effect on PCB bioaccumulation is unknown (Mudroch et al. 1989).

Contaminated sediments are a major source of PCBs in aquatic environments (Dillon and Burton 1992). PCB discharges prior to 1977 from capacitor manufacturing plants on the Hudson River at Ft. Edward and Harbor Falls, New York (14 kg PCBs daily for 30 years, mostly Aroclors 1242 and 1016), contaminated 306 km of river bed between Hudson Falls and New York Harbor. By 1978, an estimated 63,500 kg of PCBs were in the river bank deposits, 134,000 kg in the upper river, and 91,000 kg in the lower river (Brown et al. 1985; Eisler 1986; Bush et al. 1987; Kennish 1992). PCB concentrations in biota and the water column are largely controlled by PCB concentrations in surficial sediments. Declines in PCB levels in Hudson River sediments corresponded to decreased use of PCBs at local capacitor-manufacturing plants (Brown et al. 1985; Kennish 1992). The stabilization of highly contaminated upper stream banks and reduced PCB releases from bed sediments contributed to lower concentrations in the water column. A model of the fate and accumulation of 7 PCB homologs in the Hudson River estuary showed that 66% of the 270,454 kg of total PCBs discharged into the estuary between 1947 and 1987 had volatilized, 6% was stored in sediments, and the rest was either dredged or lost by boundary transport to the New York Bight and Long Island Sound (Thomann et al. 1991). Total PCBs peaked in the mid-1970s and upstream loading now has a relatively small effect. The upstream PCB load above Troy, New York, accounts for about 20% of the PCB concentrations in striped bass. A steady decline of Aroclors 1016 and 1254 in upstream contribution was projected to the year 2005 and suggests that 95% of 3-6 year old striped bass in the lower Hudson would have residues below the USFDA action level of 2 mg/kg FW by the year 2004 (Thomann et al. 1991). PCB congener patterns in Hudson River sediments differed from the Aroclors discharged into the river. Sediments had comparatively enriched concentrations of certain lower-chlorinated congeners, especially *ortho*-substituted congeners, and some congeners not usually detected in commercial Aroclor mixtures. Changes in PCB composition of sediments were greater in lower portions of sediment cores than in surficial sediments (Brown et al. 1987). Two dechlorination mechanisms seemed to be operating: *meta*, *para*-dechlorinations with stepwise, selective dechlorination at the *meta* and *para* positions of certain *ortho*-substituted di- through tetra-*ortho* chlorinated biphenyls; and *ortho*, *meta*, *para*-dechlorinations, in which the dechlorinations occur at *ortho*, *meta*, or *para* positions and reactivity is favored by increasing electron affinity and relatively positive reduction potential. Both mechanisms preferentially removed toxic congeners (Brown et al. 1987). Residues of individual PCB congeners in the upstream water were similar to residues in caddisfly larvae from that system (Bush et al. 1985), although residues in the larvae were enriched with lower chlorinated congeners. Because of their relatively high water solubility and low affinity for sediment, higher concentrations of lower chlorine homologs were expected to preferentially dissolve in water. But PCB profiles of dissolved residues transported downstream in the water samples during low flow season were dominated by only three low chlorinated PCBs; more than half of the residues consisted of 2-chlorobiphenyl and 2,2'- and 2,6' dichlorobiphenyl congeners (Bush et al. 1985).

Anoxic Hudson River sediments contaminated with PCBs and dredged sediments in clay encapsulation were treated to induce or raise anaerobic biodegradation of PCBs (Rhee et al. 1989). Variations in sediment type, bacterial flora, and treatment influenced dechlorination. The addition of biphenyl under anoxic nitrogen was the most effective treatment for raising biodegradation. Unlike the findings of Brown et al. (1987), no evidence was found of accumulation of less chlorinated PCBs from biodegradation of more highly chlorinated congeners, although a faster degradation rate of less chlorinated congeners than the more highly substituted PCBs would have allowed this phenomena to occur unobserved. Hudson River sediments incubated at room temperature (25°C) under a nitrogen atmosphere or incubated with biphenyl enrichment under nitrogen for 7 months

decreased significantly in chlorobiphenyl compounds of 33 to 65%. In general, mono- and dichlorobiphenyl congeners from Hudson River sediments were not significantly degraded by the biphenyl, but biphenyl addition significantly decreased the higher chlorinated congeners (Rhee et al. 1989). In earlier studies with the same mixed bacterial culture without biphenyl addition, significant reductions were evident in Hudson River sediments of PCB congeners with as many as three chlorines (Chen et al. 1988).

Sediments in oceans, estuaries, rivers, and lakes concentrate PCBs. Organisms accumulate PCBs by way of the water column, from interstitial sediment waters, and from consumption of contaminated prey by predator species. Coastal sediments with the highest total PCB concentrations between 1984 and 1989 are usually within 20 km of population centers of more than 100,000 people (NOAA 1991) and directly correlate with sediment content of total organic carbon (Karickoff 1981). Variability in PCB content of sediments is great, and large differences between adjacent stations is not uncommon (NOAA 1988). The approximate percent PCB distribution in sediments by level of chlorination was di-3.9%, tri- 11%, tetra- 20%, penta- 24%, hexa- 21%, hepta-12%, octa- 3.9%, and nona- 1.3%. The mean PCB concentration in sediments at 233 sites was 39 µg/kg, and concentrations greater than 200,000 µg/kg were considered elevated (NOAA 1988; Table 8). In most regions of New Jersey, for example, PCB contamination of sediments and water column was negligible (Kennish 1992). But PCBs in estuarine and coastal locations of New Jersey showed elevated sediment contamination in the northeastern region—an area that included the Hudson-Raritan estuary and adjacent ocean waters of the New York Bight—where direct discharges from capacitor manufacturing plants on the upper Hudson River, dredged material, and sewage-sludge dumping were the principal sources of PCB contamination. PCB levels in teleosts from the northeastern region in 1986-87 exceeded the USFDA action level of 2,000 µg/kg and were consistent with data from previous years. Action levels were also exceeded in fishes from Camden and from the northern coast regions (Kennish 1992). PCB sediment residues in Raritan Bay in the 1970s averaged 100 µg/kg DW in a range of 3.4 to 2,035 µg/kg (Stainken and Rollwagen 1979). Water column concentrations were usually not detectable but approached 0.04 µg/L in parts of the New York Bight after sewage sludge and dredged material were deposited in the 1970s and early 1980s (Boehm 1981). Sediments near dumpsites in the New York Bight contained as many as 15,000 µg/kg PCBs (MacLeod et al. 1981), and bottom sediments in the upper Hudson River had localized contaminated areas containing more than 50,000 µg/kg (Brown et al. 1985). Nation-wide, PCB loadings in surficial sediments and mussels (*Mytilus edulis*) in the Long Island Sound were greater than in other sites (Robertson et al. 1991).

Surficial stream sediments in the San Francisco estuarine system during 1972 had high residues (350-1,400 µg/kg DW) at several locations (Phillips and Spies 1988); however, residues were highly variable between sites (Law and Goerlitz 1974). In 1984, low to intermediate concentrations of PCBs (9-60 µg/kg DW) were measured at four locations in the San Francisco Bay. Overall, congener profiles resembled Aroclor 1254 and were dominated by pentachlorobiphenyl isomers (NOAA 1987). The patterns of the 11 reported congeners were variable between areas, indicating many sources of different PCB mixtures.

Lake Hartwell in South Carolina received Aroclor 1016 and 1254 discharges for 21 years from a capacitor manufacturing plant (Elzerman et al. 1991). Analysis of sediment cores collected between 1984 and 1987 showed that samples nearest the source were relatively high in lower chlorinated PCB congeners, and downstream samples were enriched with the higher congeners; in all samples, total PCB concentrations decreased with increasing distance from the point source. The estimated total remaining PCBs was 41,000 kg (Elzerman et al. 1991). The highest PCB concentrations were in subsurface sediments, although PCB levels in surficial sediments were also elevated (Dunnivant et al. 1989). A survey of total PCBs in sediments and invertebrates in major estuaries of South Carolina showed no significant contamination. PCBs were found only in sediments (622 µg/kg) and in oysters (87 µg/kg) from the Wando River near a large ship repair and retrofitting facility; PCB residues in crabs, when present, ranged from 95 to 375 µg/kg (Marcus and Renfrow 1990).

Aquatic Organisms

Marine mammals are the most vulnerable and most probable target organisms to PCBs (Tanabe 1988). The metabolic potential to degrade organochlorine contaminants and therefore accumulate relatively high concentrations of persistent PCBs is lower in marine mammals, particularly in cetaceans, than in terrestrial mammals (Tanabe et al. 1987; Kannan et al. 1989, 1993). Dead harbour porpoises (*Phocoena phocoena*) along the Dutch coast contained 51,350-139,790 µg total PCBs/kg blubber; 35-50% of the total PCBs were PCBs 138 and 153 (Duinker et al. 1988a); a similar pattern was noted in harbour porpoises from Scandinavia in 1987-91

(Kleivane et al. 1995). The intrinsic toxicity of PCBs mainly resulted from the planar PCB congeners that imposed a greater toxic threat to marine mammals than chlorinated dioxins and furans (Tanabe 1988; Tanabe et al. 1989; Daelemans et al. 1993; Falandysz et al. 1994b). The toxic threat of planar PCBs to higher aquatic predators was primarily assessed by 2,3,7,8-tetracholoridobenzo-*p*-dioxin toxic equivalent analysis, which is based on the induction of arylhydrocarbon hydroxylase (AHH) and ethoxyresorufin *O*-deethylase (EROD; Kannan et al. 1989). The concentrations of planar PCBS in marine mammals were higher (in the order of di-*ortho* mono-*ortho* non-*ortho* congeners) and significantly higher than the levels of toxic dioxins and furans (Tanabe 1988; Tanabe et al. 1989; Kannan et al. 1989). In particular, the accumulation of PCBs 105 and 126 in carnivorous aquatic mammals is cause for considerable concern (Tanabe et al. 1987, 1989; Kannan et al. 1989; Daelamans et al. 1993; Storr-Hansen and Spliid 1993).

Declines in total PCB levels in blubber of marine mammals between the late 1960s and 1990-92 have been noted worldwide (Muir et al. 1988; Lake et al. 1995a), possibly because of the PCB ban in the mid-1970s. PCB levels in animal tissues will probably not decline in the near future because of the greater quantities of PCBs still in use than the quantity that already escaped into the open environment (Tanabe 1988). Temporal changes of PCBs in remote marine waters are slow and could be attributable to the large PCB load in the marine environment (Loganathan et al. 1990). The geographical distribution of planar PCBs with reference to total PCBs did not vary in terrestrial, coastal, and open ocean mammals, whereas those of dioxins and furans decreased from land to ocean (Tanabe et al. 1989). PCB concentrations—including planar PCBs—in blubber of striped dolphins (*Stenella coeruleoalba*) from the Mediterranean Sea in 1990 are among the highest reported in the literature (Table 9; Kannan et al. 1993). Striped dolphins affected by the western Mediterranean morbillivirus epizootic also contained extremely high concentrations of PCBs (including non-and mono-*ortho* planar congeners) and low immune suppression, suggesting that PCBS were a major factor in this epizootic; however, this needs verification. Planar PCBs in blubber of striped dolphins accounted for about 53% of total PCBs and for virtually all of the potential toxicity. Di-*ortho* planar PCBs accounted for 93.7% of all planar PCB residues in striped dolphins and for 21% of the potential toxicity, mono-*ortho* planars for 6.3% of the residues and 70.8% of the potential toxicity, and non-*ortho* planars for 0.03% of the residues and 8.2% of the potential toxicity (Kannan et al. 1993). Concentrations of PCBs in tissues of adult male striped dolphins of the same age from the Pacific coast of Japan did not change between 1979 and 1986 (Loganathan et al. 1990).

White whales (*Delphinapterus leucas*) of the St. Lawrence estuary were severely contaminated by DDT metabolites and PCBs; the highest residues were in blubber (Masse et al. 1986). Several PCB congeners known to be AHH inducers—including PCBs 138 and 153— were among the major PCB congeners detected in tissues of white whales. Because these compounds are not metabolized and persist indefinitely in tissues of the white whale, the integrated total exposure to these AAH inducers may be significant. Considerable variations by sex, age, and lipid content of the tissues in PCB concentrations were observed in white whales. Qualitative and quantitative differences in the PCB profiles of white whales were not solely related to the respective lipid content of the tissues but also to the specific nature of the lipids, which varied from one tissue to the other. The major PCB components in various tissues of white whales were PCBs 52, 99, 129, 137, 141, 153, 165, 180, and 185. Organ-specific retention of some PCB congeners occurs in white whales. PCBs 165 and 179, which were minor in blubber, were more abundant in kidney, liver, and lung. PCB 129 was more abundant in kidney and liver than in lung. Atlantic cod (*Gadus morhua*) composed a minor part of the white whale diet; however, PCB patterns in cod positively correlated with those in white whale tissues, suggesting a common source of intake. PCB congeners 52, 91, 99, 108, 118, 128, 138, 144, 149, 153, 163, and 180 were among the most abundant chlorinated biphenyls in cod liver oil and in the white whale blubber, liver, lung, kidney, and milk (Masse et al. 1986).

Table 9. PCB concentrations in field collections of selected aquatic organisms. Concentrations are in micrograms PCBs per kilogram (ppb) fresh weight (FW), dry weight (DW), or lipid weight (LW).

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Invertebrates		
Bivalve molluscs (*Mytilus, Tapes, Ostrea, Crassostrea*; Catalonia, Spain, 1989-90; soft parts		
Sum of PCBs 28, 52, 101, 118, 138, 153, 180	1.4-596.0 DW	1
Crabs; southern Norway, 1990-92; hepatopancreas		
PCBs 28, 52, 66, 74, 99, 101, 110, 157	ND	2
PCB 77	Max 3.4 LW	2
PCB 126	Max 2.5 LW	2
PCB 169	Max. 1.1 LW	2
PCB 209	Max 2,600 LW	2
Total of PCBs 105, 118, 128, 138, 149, 153, 156, 170, 180, 187, 194, 206	600-2,050 LW	2
Eastern oyster, *Crassostrea virginica*; soft parts; 1990-1991; Galveston Bay, Texas vs. Tampa Bay Florida; maximum values		
PCB 77	2.0 DW vs. 1.5 DW	45
PCB 105	39.0 DW vs. 7.6 DW	45
PCB 118	48.0 DW vs. 36.0 DW	45
PCB 126	2.2 DW vs. 0.3 DW	45
PCB 128	4.4 DW vs. 2.0 DW	45
PCB 138	50.0 DW vs. 8.9 DW	45
PCB 169	0.79 DW vs. 0.28 DW	45
Mayfly, *Hexagenia bilineata*; upper Mississippi River, summer 1988; total PCBs (sum of 125 congeners)	210-4,100 DW;1,200-29,000 LW	46
Mayfly, *Hexagenia limbata*; Lake St.Clair, July 1987,sediments vs. whole adults		
PCB 87	1.2 DW vs. 0.7 FW	34
PCB 101	2.9 DW vs. 1.7 FW	34
PCB 118	2.1 DW vs. 0.9 FW	34
PCB 138	2.4 DW vs. ND	34
PCB 153	1.8 DW vs. 0.9 FW	34
PCB 180	0.8 DW vs. 0.6 FW	34
Burrowing mayfly, *Hexagenia* sp., adults; summer 1987; contaminated sites on Detroit and St. Clair rivers		
PCB 18	Max 7.6 DW	35
PCB 31	Max. 2.8 DW	35
PCB 52	Max. 10.9 DW	35
PCB 66	Max 4.6 DW	35
PCB 87	Max. 6.5 DW	35
PCB 97	Max 3.5 DW	35
PCB 101	Max. 16.6 DW	35

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
PCB 110	Max. 6.0 DW	35
PCB 118	Max. 13.6 DW	35
PCB 138	Max. 18.1 DW	35
PCB 141	Max. 6.1 DW	35
PCB 153	Max. 23.2 DW	35
PCB 170	Max. 4.8 DW	35
PCB 180	Max. 10.4 DW	35
PCB 182	Max. 7.3 DW	35
PCB 194	Max. 4.7 DW	35
Squid, *Illex illecebrosus argentinus*; near Falkland Islands, March 1988; muscle		
PCBs 28, 31, 44, 47, 49, 52, 66, 87, 97, 101, 105, 110, 118, 128, 138, 141, 149, 151, 153, 170, 180, 184, 187, 206	ND (= nondetectable)	3
Common mussel, *Mytilus edulis* German Bight, 6 locations; 1993; extractable organic matter; spring vs. autumn		
PCB 77	33-50 DW vs. 4-8 DW	49
PCB 81	5-7 DW vs. 2-4 DW	49
PCB 105	45-60 DW vs. 37-130 DW	49
PCB 114	Max. 1.1 DW vs. Max. 0.5 DW	49
PCB 118	75-97 DW vs. 65-520 DW	49
PCB 123	9-150 DW vs. 0.2-4 DW	49
PCB 126	4-15 DW vs. 6-12 DW	49
PCB 138	280-420 DW vs. 83-210 DW	49
PCB 156	Max. 3.9 DW vs. Max. 1.4 DW	49
PCB 169	0.0-2.1 DW vs. 0.4-4.1 DW	49
PCB 170	0.0-7.9 DW vs. 2.2-4.1 DW	49
PCB 180	18-43 DW vs. 9-23 DW	49
PCB 189	0.5-1.7 DW vs. 0.1-0.4 DW	49
Long Island Sound, New York vs. freshwater mussels (species unknown) from a contaminated site near Troy, New York; soft parts		
Total PCBs	247 DW vs. 2,734 DW	4
Total planar PCBs	11.9 DW vs. 112.9 DW	4
PCB 77	0.4 DW vs. 6.9 DW	4
PCB 81	ND vs. 0.9 DW	4
PCB 105	3.3 DW vs 27.0 DW	4
PCB 114	ND vs. 4.0 DW	4
PCB 118	8 DW vs. 53 DW	4
PCB 123	ND vs. ND	4
PCB 126	ND vs. 0.6 DW	4
PCB 156	ND vs. 1.8 DW	4
PCB 157	ND vs. 0.6 DW	4
PCB 167	0.2 DW vs. 18.6 DW	4
PCB 169	ND vs. 0.1 DW	4
PCB 189	ND vs. 0.1 DW	4
Fishes		
Bloater, *Coregonus hoyi*; whole; Lake Michigan; total PCBs		

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
1972 vs. 1975	5,700 FW vs. 4,500 FW	5
1978 vs. 1982	3,100 FW vs. 2,100 FW	5
1986	1,600 FW	5
Margined flyingfish, *Cypselurus cyanopterus*; near Falkland Islands, March 1988; muscle		
PCBs 28, 31, 44, 47, 49, 52, 66, 87, 97, 101, 105, 110, 128, 141, 151, 170, 194, 206	0.01-0.1 FW	3
PCBs 118, 138, 180, 187	0.14-0.31 FW	3
PCB 153	0.45 FW	3
Fish liver oil; various species; Finland		
PCB 77	2.7 LW	6
PCB 105	30.0 LW	6
PCB 126	0.62 LW	6
PCB 169	0.13 LW	6
Fish muscle; various species sold for human consumption; Finland		
PCB 77	0.006-0.153 FW	6
PCB 105	0.113-2.7 FW	6
PCB 126	0.002-0.035 FW	6
PCB 169	ND-0.012 FW	6
Fish, 14 species, muscle; Wisconsin, 1986-87; total PCBs	1,300 (700-7,000) FW	7
Freshwater fishes; USA; nationwide; whole: adults; total PCBs measured as Aroclors 1248, 1254, and 1260; noncontaminated sites		
1976-77	Max. 70.6 FW	48
1978-79	Max. 92.8 FW	48
1980-81	Max. 11.3 FW	48
1984	Max. 6.7 FW	48
Freshwater fishes; USA; nationwide; whole; 1986-87; mostly contaminated sites		
Median	209 FW	52
Mean	1,890 FW	52
Maximum	124,000 FW	52
Atlantic cod, *Gadus morhua*		
Liver; Norway, 1988		
PCB 28	19 (0.5-64) FW	8
PCB 52	31 (0.5-144) FW	8
PCB 101	78 (0.5-533) FW	8
PCB 118	170 (1.1-653) FW	8
PCB 138	283 (1.4-918) FW	8
PCB 153	363 (1.3-1,175) FW	8
PCB 170	28 (0.4-163) FW	8
PCB 180	68 (1.1-391) FW	8
PCB 209	7 (0.3-35) FW	8
Liver; Norway 1989		
PCB 77	Max. 4.8 LW	9
PCB 105	Max. 39.0 LW	9
PCB 126	Max. 1.0 LW	9
PCB 169	Max. 0.3 LW	9

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Muscle; Baltic Sea, 1988		
PCB 77	Max. 4.2 LW	9
PCB 105	Max. 36.0 LW	9
PCBs 126, 169	ND	9
Ictalurids, 4 species (blue catfish, *Ictalurus furcatus*; black bullhead, *Ameiurus melas*; channel catfish, *Ictalurus punctatus*; flathead catfish, *Pylodictis olivaris*); whole; 1,944 km stretch of Mississippi River; July-August 1987		
Total PCBs	Max. 138 FW; Max. 2,910 LW	10
Tetrachlorobiphenyls	Max. 21 FW; Max. 671 LW	10
Pentachlorobiphenyls	Max. 56 FW; Max. 1,230 LW	10
Hexachlorobiphenyls	Max. 67 FW; Max. 870 LW	10
Heptachlorobiphenyls	Max. 12 FW; Max. 140 LW	10
Dab, *Limanda limanda* German Bight; December 1988-May 1989; total of 35 PCB congeners		
Females		
Liver (mostly PCBs 77, 138, and 153)	1,200-16,200 LW	36
Ovaries (mostly PCBs 77, 138, and 153)	2,600-4,300 LW	36
Males		
Liver	900-24,400 LW	36
Testes (mostly PCBs 15, 13, 52)	1,900-11,800	36
North Sea; January-March 1987; total PCBs		
Liver, Females	1,450 FW	11
Liver, Males	2,000 FW	11
Ovaries	2,600 FW	11
Tilefish, *Lopholatilus chamaeleonticeps*; 1981-1982; New Jersey vs. Georges Bank		
Total PCBs		
Gonad	3,373 DW vs. 1,004 DW	12
Liver	4,693 DW vs. 1,002 DW	12
Muscle	435 DW vs. 190 DW	12
Dichlorobiphenyls		
Gonad	196 DW vs. 15 DW	12
Liver	258 DW vs. 42 DW	12
Muscle	9 DW vs. 5 DW	12
Trichlorobiphenyls		
Gonad	164 DW vs. 11 DW	12
Liver	278 DW vs. 35 DW	12
Muscle	11 DW vs. 7 DW	12
Tetrachlorobiphenyls		
Gonad	1,176 DW vs. 192 DW	12
Liver	789 DW vs. 151 DW	12
Muscle	62 DW vs. 25 DW	12
Pentachlorobiphenyls		
Gonad	806 DW vs. 463 DW	12
Liver	1,273 DW vs. 358 DW	12
Hexachlorobiphenyls		
Gonad	664 DW vs. 191 DW	12
Liver	1,290 DW vs. 221 DW	12
Muscle	112 DW vs. 46 DW	12

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Heptachlorobiphenyls		
Gonad	158 DW vs. 27 DW	12
Liver	109 DW vs. 27 DW	12
Muscle	14 DW vs. 3 DW	12
Nonochlorobiphenyls		
Gonad	62 DW vs. 6 DW	12
Liver	22 DW vs. 13 DW	12
Muscle	3 DW vs. 0.5 DW	12
Decachlorobiphenyl		
Gonad	45 DW vs. 6 DW	12
Liver	24 DW vs. 16 DW	12
Muscle	2 DW vs. 0.7 DW	12
PCB 77		
Gonad	48 DW vs. 19 DW	12
Liver	86 DW vs. 45 DW	12
Muscle	62 DW vs. ND	12
PCB 126		
Gonad	ND vs. 27 DW	12
Liver	214 DW vs. 33 DW	12
Muscle	19 DW vs. 4 DW	12
Argentinian hake, *Merluccius merluccius hubbsi*; near Falklands Islands, March 1988; muscle		
PCBs 28, 31, 44, 47, 49, 87, 97, 105, 128, 141, 151, 194, 206	0.01-0.04 FW	3
PCBs 52, 66, 101, 110, 170	0.05-0.1 FW	3
PCBs 118, 138, 149, 153, 180, 187	0.11-0.28 FW	3
Striped bass, *Morone saxatilis*; muscle, New York, Long Island Sound, 1985		
Total PCBs	5,500 FW; Max. 15,000 FW	13
PCBs 48, 52, 82, 101, 118, 138, 153	Contributed at least 28% of total PCB concentration	13
New York, various locations		
Total PCBs	1,100-24,100 FW	4
Total planar PCBs	100-2,020 FW	4
PCB 77	Max. 37 FW	4
PCB 81	Max. 5 FW	4
PCB 105	Max. 562 FW	4
PCB 114	Max. 112 FW	4
PCB 118	Max. 779 FW	4
PCB 126	Max. 8 FW	4
PCB 156	Max. 202	4
PCB 157	Max. 68 FW	4
PCB 167	Max. 232 FW	4
PCB 169	Max. <0.1 FW	4
PCB 189	Max. 19 FW	4
Striped mullet, *Mugil cephalus*; Japan, May 1976; muscle		
Total PCBs	1,200 (220-3,200) FW	14
PCB 77	2.1 (0.6-4.8) FW	14
PCB 126	0.1 (0.03-0.23) FW	14
PCB 169	0.002 (0.001-0.004) FW	14

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Rainbow trout, *Oncorhynchus mykiss*;		
Lake Ontario, 1989; liver vs. muscle		
PCB 77	2.9 FW, 78 LW vs.3.3 FW, 85 LW	31
PCB 126	0.7 FW, 18 LW vs. 0.9 FW, 22 LW	31
PCB 169	0.3 FW, 8 LW vs. 0.3 FW, 9 LW	31
Red mullet, *Mullus barbatus*; Spain,		
Mediterranean coast, summers 1989, 1990; muscle		
Sum of PCBs 28, 52, 101, 118, 138, 153, 180	21.2 (7.4-33.2) FW	33
Sum of PCBs 18, 31, 44, 97, 99, 105, 110, 128, 134, 146, 149, 151, 170, 174, 177, 183, 187, 194, 201	38.4 (15.5-61.4) FW	33
Chinook salmon, *Oncorhynchus tshawytscha*;		
Lake Michigan, 1986; eggs		
Total PCBs	7,020 FW	32
PCBs 77, 105, 118, 126	0.2-12 FW	32
Fathead minnow, *Pimephales promelas*; upper Hudson River, 1985; caged juveniles exposed for 3 to 42 days during the year; whole fish	Regardless of exposure duration or season, the consistently most abundant congeners in caged fish were PCBs 37, 42, 44, 47, 48, 49, 52, 59, 61, 66, 70, 73, 75, 76, 93, 95, and 104	15
European flounder, *Platichthys flesus;*		
Norway, 1988; liver		
PCB 28	7 (0.3-68) FW	8
PCB 52	21 (0.7-609) FW	8
PCB 101	44 (1.1-1,452) FW	8
PCB 118	77 (3.2-1,693) FW	8
PCB 138	90 (1.1-1,960) FW	8
PCB 153	95 (5.7-2,088) FW	8
PCB 170	7 (0.4-158) FW	8
PCB 180	16 (1.2-296) FW	8
PCB 209	4 (0.4-88) FW	8
Paddlefish, *Polyodon spathula*;		
Ohio River, Kentucky; 1988-89;		
total PCBs; males vs. females		
Gonads	16,200 (5,600-23,000) FW vs. 7,300 (50-18,700) FW	16
Red muscle (females only)	4,200 (2,000-6,300) FW	16
White muscle	700(50-3,300) FW vs. 400 (50-1,000) FW	16
Winter flounder, *Pleuronectes americanus*		
Long Island Sound, New York, 1984-86;		
total PCBs		
Liver	420-2,400 FW	17
Ovaries	30-730 FW	17
Testes	50-190 FW	17
New Bedford Harbor, Massachusetts vs. two control sites in Rhode Island; spring, 1988; liver		
Planar PCBs		
PCB 77	391 DW vs. 4.6 DW	38
PCB 126	49 DW vs. 1.8 DW	38
PCB 169	3.7 DW vs 0.4 DW	38

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Nonplanar PCBs		
PCB 47	2,530 DW vs. 14 DW	38
PCB 52	1,100 DW vs. 6.5 DW	38
PCB 101	2,450 DW vs. 49 DW	38
PCB 105	2,200 DW vs. 92 DW	38
PCB 118	12,800 DW vs. 239 DW	38
PCB 128	1,370 DW vs. 47 DW	38
PCB 138	7,070 DW vs. 286 DW	38
PCB 151	422 DW vs. 19 DW	38
PCB 153	11,000 DW vs. 441 DW	38
PCB 180	1,010 DW vs. 141 DW	38
PCB 194	79 DW vs. 23 DW	38
PCB 195	32 DW vs. 1.4 DW	38
PCB 206	33 DW vs. 33 DW	38
PCB 209	3.1 DW vs. 20.5 DW	38
Total PCBs		
Gravid females	333,000 DW vs. 3,900 DW	38
Spent females	132,000 DW vs. 4,000 DW	38
Ripe males	124,000 DW vs. 13,300 DW	38
Sediments	8,000 DW vs. 500 DW	38
Atlantic salmon, *Salmo salar*;		
Baltic Sea and environs		
Eggs, 1988		
PCB 77	Max. 28 LW	9
PCB 105	Max. 90 LW	9
PCB 126	Max. 2.4 LW	9
PCB 169	Max. 0.6 LW	9
Muscle, 1985		
Total PCBs	Max. 332 FW	18
PCB 77	Max. 1.1 FW	18
PCBs 126, 169	ND	18
Muscle, 1988		
PCB 77	Max. 34 LW	9
PCB 105	Max. 170 LW	9
PCB 126	Max. 3.8 LW	9
PCB 169	Max. 0.8 LW	9
Brown trout, *Salmo trutta*; Catalonia, Spain; isolated mountain lakes; summers 1989, 1990; muscle		
Sum of PCBs 28, 52, 101, 118, 138, 153, 180	2.5 (1.3-3.8) FW	33
Sum of PCBs 18, 31, 44, 97, 99, 105, 110, 128, 134, 146, 149, 151, 170, 174, 177, 183, 187, 194, 201	4.8 (2.7-7.5) FW	33
Lake trout, *Salvelinus namaycush*		
Lake Ontario; total PCBs; whole fish		
1977 vs. 1978	6,800 FW vs. 8,000 FW	19
1979 vs. 1980	3,700 FW vs. 3,900 FW	19
1981 vs. 1982	2,900 FW vs. 5,300 FW	19
1983 vs. 1984	4,500 FW vs. 4,800 FW	19
1985 vs. 1986	2,500 FW vs. 3,100 FW	19
1987 vs. 1988	3,400 FW vs. 2,500 FW	19
Lake Michigan		

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Adult females; total PCBs		
1985	4,900-10,100 FW	47
1986	6,100-6,800 FW	47
1987	3,500-13,900 FW	47
Adult females; 1987; whole fish vs. eggs		
PCB 77	9.7 FW vs. 2.1 FW	47
PCB 126	4.0 FW vs. 0.65 FW	47
PCB 169	<0.4 FW vs. <0.4 FW	47
Marine Mammals		
Giant bottlenosed whale, *Berardius bairdii*; blubber		
Japan, July 1985		
Total PCBs	2,300 (1,800-2,800) FW	20,21
Di-*ortho* planars		
PCB 128	54 (36-70) FW	20,21
PCB 138	460 (260-810) FW	20,21
Mono-*ortho* planars		
PCB 105	5 (2-8) FW	20,21
PCB 118	47 (15-94) FW	20,21
PCB 156	23 (6-50) FW	20,21
Non-*ortho* planars		
PCB 77	1.3 (0.7-1.9) FW	20,21
PCB 126	0.35 (0.1-0.57) FW	20,21
PCB 169	0.24 (0.09-0.45) FW	20,21
Northern north Pacific, July 1985		
Total PCBs	2,600 (2,400-2,800) FW	14
PCB 77	1.6 (1.3-1.9) FW	14
PCB 126	0.48 (0.39-0.57) FW	14
PCB 169	0.31 (0.17-0.45) FW	14
Beluga whale, *Delphinapterus leucas*;		
Canada, St. Lawrence estuary; November 1983-December 1984; beach-stranded whales; total PCBs		
Blubber	Max. 72,200 FW	22
Kidney	Max. 10,000 FW	22
Liver	Max. 2,500 FW	22
Lung	Max. 560 FW	22
Milk	Max. 1,720 FW	22
Dolphins and toothed whales; blubber; total PCBs		
Atlantic Ocean, 1980-88; 15 species	130-190,000 FW	23
Indian Ocean, 1980-91; 5 species	520-7,900 FW	23
Pacific Ocean, 1980-86; 7 species	190-40,000 FW	23
Gray seal, *Halichoerus grypus*		
Baltic Sea and environs; 1981-87; blubber		
PCB 77	Max. 10 LW	9
PCB 105	Max. 180 LW	9
PCB 126	Max. 3 LW	9
PCB 169	Max. 2 LW	9
Nova Scotia, 1984-85; total PCBs; mother vs. pups		
Blood	6,080 LW vs. 6,240 LW	24
Blubber	16,200-30,300 LW vs. 8,800-10,400 LW	24
Milk (mother)	7,480-10,120 LW	24
Serum	10,210 LW vs. 11,840 LW	24

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Pacific white-sided dolphin, *Lagenorhynchus obliquidens*; Japan, 1981; blubber		
Total PCBs	53,00 (40,000-71,000) FW	14
PCB 77	27 (14-38) FW	14
PCB 126	3.8 (3.2-4.4) FW	14
PCB 169	1.2 (0.9-1.4) FW	14
Finless porpoise, *Neophocaena phocaenoides*; Japan, July 1985; blubber		
Total PCBs	320,000 FW	20,21
Di-*ortho* planars		
PCB 128	3,500 FW	20,21
PCB 138	35,000 FW	20,21
Mono-*ortho* planars		
PCB 105	1,200 FW	20,21
PCB 118	11,000 FW	20,21
PCB 156	160 FW	20,21
Non-*ortho* planars		
PCB 77	14 FW	14,20,21
PCB 126	0.9 FW	14,20,21
PCB 169	0.6 FW	14,20,21
Killer whale, *Orcinus orca*; blubber Died after 2 years in captivity		
Total PCBs	160,000 FW	14
PCB 77	42.0 FW	14
PCB 126	4.0 FW	14
PCB 169	3.6 FW	14
Pacific coast of Japan; July 1985		
Total PCBs	370,000 (350,000- 410,000) FW	20,21
Di-*ortho* planars		
PCB 128	8,000 (3,200-12,000) FW	20,21
PCB 138	65,000 (24,000-85,000) FW	20,21
Mono-*ortho* planars		
PCB 105	3,000 (2,300-3,600) FW	20,21
PCB 118	11,000 (6,700-14,000) FW	20,21
PCB 156	1,900 (950-3,100) FW	20,21
Non-*ortho* planars		
PCB 77	48 (39-55) FW	14,20,21
PCB 126	3.7 (2.4-4.4) FW	14,20,21
PCB 169	7.7 (2.3-12.0) FW	14,20,21
Ringed seal, *Pusa hispida*; Norway, March-April, 1990		
Blubber		
PCBs 77, 126, 169	ND-0.19 LW	25
PCBs 66, 110, 149	20-22 LW	25
PCBs 52, 61, 105, 180	40-52 LW	25
PCBs 101, 118, 138	108-188 LW	25
PCB 153	280 LW	25
Kidney		
PCBs 77, 126, 169	ND	25
PCBs 66, 110, 149, 180	12-14 LW	25
PCBs 52, 61, 105	21-28 LW	25
PCBs 101, 118, 138	49-67 LW	25
PCB 153	95 LW	25
Liver		

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
PCBs 77, 126, 169	ND-0.78 LW	25
PCBs 61, 66, 105, 110, 149, 180	18-43 LW	25
PCBs 52, 101, 118	57-71 LW	25
PCBs 138, 153	115-188 LW	25
Harbor seal, *Phoca vitulina*; northeast coast of USA; 1980-92		
Blubber; 1980 vs. 1990-92		
Total	12,000 (7,300-24,300) FW vs. 6,660 (2,610-11,300) FW	51
PCB 8	ND vs. 0.9 FW	51
PCB 18	26 FW vs. 2 FW	51
PCB 28	99 FW vs. 16 FW	51
PCB 44	105 FW vs. 17 FW	51
PCB 52	661 FW vs. 213 FW	51
PCBs 66 + 95	192 FW vs. 29 FW	51
PCB 77	0.36 FW vs. 0.07 FW	51
PCB 101	897 FW vs. 500 FW	51
PCB 105	205 FW vs. 82 FW	51
PCBs 118+ 149	615 FW vs. 279 FW	51
PCB 126	1.45 FW vs. 0.53 FW	51
PCB 128	459 FW vs. 244 FW	51
PCB 138	2,990 FW vs. 1,650 FW	51
PCB 153	3,040 FW vs. 1,880 FW	51
PCB 169	0.019 FW vs. 0.013 FW	51
PCBs 170 + 190	458 FW vs. 266 FW	51
PCB 180	1,210 FW vs. 713 FW	51
PCB 187	865 FW vs. 601 FW	51
PCB 195	67 FW vs. 56 FW	51
PCB 206	72 FW vs. 79 FW	51
PCB 209	22 FW vs. 34 FW	51
Liver; 1980 vs. 1990-92		
Total	9,860 (6,290-16,000) FW vs. 6,260 (528-25,300) FW	51
PCB 8	ND vs. 1.2 FW	51
PCB 18	8.2 FW vs. 0.5 FW	51
PCB 28	27 FW vs. 10 FW	51
PCB 44	42 FW vs. 8 FW	51
PCB 52	343 FW vs. 145 FW	51
PCBs 66 + 95	127 FW vs. 9 FW	51
PCB 101	523 FW vs. 371 FW	51
PCB 105	345 FW vs. 26 FW	51
PCBs 118 + 149	470 FW vs. 196 FW	51
PCB 128	385 FW vs. 232 FW	51
PCB 138	2,250 FW vs. 1,550 FW	51
PCB 153	2,040 FW vs. 1,690 FW	51
PCBs 170 + 190	476 FW vs. 253 FW	51
PCB 180	1,160 FW vs. 696 FW	51
PCB 187	1,450 FW vs. 904 FW	51
PCB 195	85 FW vs. 60 FW	51
PCB 206	97 FW vs. 80 FW	51
PCB 209	41 FW vs. 36 FW	51

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Common porpoise, *Phocoena phocoena*		
Found dead along Dutch coast, 1971- 81		
Blubber vs. liver		
PCB 44	530 FW vs. 1 FW	26
PCB 49	900 FW vs. 5 FW	26
PCB 52	10,000 FW vs. 80 FW	26
PCB 101	3,200 FW vs. 20 FW	26
PCB 118	8,200 FW vs. 35 FW	26
PCB 138	28,900 FW vs. 280 FW	26
PCB 149	16,700 FW vs. 140 FW	26
PCB 153	32,600 FW vs. 340 FW	26
PCB 172	530 FW vs. 5 FW	26
PCB 174	3,700 FW vs. 40 FW	26
PCB 177	6,200 FW vs. 60 FW	26
PCB 180	4,000 FW vs. 80 FW	26
PCB 183	3,700 FW vs. 50 FW	26
PCB 194	700 FW vs. 10 FW	26
PCB 201	1,200 FW vs. 20 FW	26
PCB 206	360 FW vs. 7 FW	26
PCB 209	40 FW vs. 10 FW	26
Total PCBs (from above congeners)		
Blubber	51,350-139,790 FW	26
Heart	1,410-4,900 FW	26
Kidney	860-3,970 FW	26
Liver	1,190-17,400 FW	26
Muscle	960-3,990 FW	26
Three females found dead in fishing nets;		
Baltic Sea, 1989-90		
Blubber, maximum concentrations		
PCB 77	3.6 FW	37
PCB 126	1.4 FW	37
PCB 169	2.1 FW	37
PCB 60	15 FW	37
PCB 105	150 FW	37
PCB 118	1,100 FW	37
PCB 156	ND	37
PCB 137	730 FW	37
PCB 138	7,700 FW	37
PCB 153	9,600 FW	37
PCB 170	380 FW	37
PCB 180	1,500 FW	37
PCB 194	84 FW	37
Liver vs. muscle		
PCB 77	0.2 FW vs. ND	37
PCB 126	0.05 FW vs. ND	37
PCB 169	0.02 FW vs. ND	37
PCB 118	63 FW vs. 120 FW	37
PCB 138	250 FW vs. 350 FW	37
PCB 153	320 FW vs. 500 FW	37
PCB 170	33 FW vs. 64 FW	37
PCB 180	110 FW vs. 220 FW	37
Scandinavia; 1987-91; blubber; males; total of 47 detected PCB congeners	23,300 (3,710-65,260) LW	50

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Dall's porpoise, *Phocoenoides dalli*; northern North Pacific, 1980-85; blubber		
Total PCBs		
Females	1,500 (1,000-2,000) FW	14
Males	12,000 (7,100-18,000) FW	14
All samples	8,600 (1,000-18,000) FW	20,21
Di-*ortho* planars		
PCB 128	480 (110-1,100) FW	20,21
PCB 138	970 (160-2,000) FW	20,21
Mono-*ortho* planars		
PCB 105	100 (30-200) FW	20,21
PCB 118	280 (90-450) FW	20,21
PCB 156	11 (5-15) FW	20,21
Non-*ortho* planars		
PCB 77	2.3 (0.4-3.5) FW	14,20,21
PCB 126	0.16 (0.08-0.25) FW	14,20,21
PCB 169	0.11 (0.04-0.2) FW	14,20,21
Ringed seal, *Pusa hispida*; Baltic Sea and environs, 1981-87; blubber		
PCB 77	Max. 9 LW	9
PCB 105	Max. 1,100 LW	9
PCB 126	Max. 4 LW	9
PCB 169	Max. 0.3 LW	9
Striped dolphin, *Stenella coeruleoalba*; blubber		
Japan; 1978-79 vs. 1986; adult males; total PCBs	29,000 (15,000-46,000) FW vs. 28,000 (17,000-38,000) FW	27
Total PCBs		
Alive vs. dead	480,000 FW vs. 340,000 FW	28
Males vs. females	430,000 FW vs. 94,000 FW	28
Matures vs. immatures	430,000 FW vs. 380,000 FW	28
Healthy vs. emaciated	480,000 FW vs. 340,000 FW	28
Di-*ortho* planars		
PCB 137	5,500 FW	28
PCB 138	60,000 FW	28
PCB 153	73,000 FW	28
PCB 170	12,000 FW	28
PCB 180	39,000 FW	28
PCB 194	4,000 FW	28
Mono-*ortho* planars		
PCB 60	160 FW	28
PCB 105	2,000 FW	28
PCB 118	7,900 FW	28
PCB 156	3,000 FW	28
Non-*ortho* planars		
PCB 77	43 (16-85) FW	28
PCB 126	6.8 (2.4-13.0) FW	28
PCB 169	7.8 (1.9-15.0) FW	28
Goosebeaked whale, *Ziphius cavirostris*; Bermuda, 1981; beached		
Blubber vs. liver		
PCB 44	5 FW vs. 0.4 FW	26
PCB 49	6 FW vs. 0.4 FW	26
PCB 52	36 FW vs. 4 FW	26

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
PCB 101	47 FW vs. 6 FW	26
PCB 118	74 FW vs. 13 FW	26
PCB 138	153 FW vs. 19 FW	26
PCB 149	73 FW vs. 15 FW	26
PCB 153	186 FW vs. 21 FW	26
PCB 172	14 FW vs. 2 FW	26
PCB 174	32 FW vs. 6 FW	26
PCB 177	24 FW vs. 5 FW	26
PCB 180	92 FW vs. 11 FW	26
PCB 183	37 FW vs. 6 FW	26
PCB 194	20 FW vs. 3 FW	26
PCB 201	64 FW vs. 10 FW	26
PCB 206	26 FW vs. 5 FW	26
PCB 209	6 FW vs. 0.5 FW	26
Total PCBs (from above congeners)		
Blubber	720-1,450 FW	26
Heart	18 FW	26
Kidney	26-78 FW	26
Liver	98-127 FW	26
Muscle	6-138 FW	26
Integrated Studies		
Freshwater lake near Amsterdam, the Netherlands; near dredged materials discharge site		
Sediments		
PCB 28	1.4 DW	29
PCB 52	2.3 DW	29
PCB 101	4.1 DW	29
PCB 138	13.7 DW	29
PCB 153	7.2 DW	29
PCB 180	3.4 DW	29
Plankton, 2 species vs. zebra mussel, *Dreissena polymorpha*		
PCB 28	0.2 FW, 68 LW vs. 0.5 FW, 36 LW	29
PCB 52	0.3 FW, 102 LW vs. 0.9 FW, 57 LW	29
PCB 101	0.5 FW, 206 LW vs. 3.8 FW, 220 LW	29
PCB 138	0.7 FW, 259 LW vs. 4.5 FW, 258 LW	29
PCB 153	0.5 FW, 209 LW vs. 5.8 FW, 322 LW	29
PCB 180	0.2 FW, 60 LW vs. 1.2 FW, 75 LW	29
Crustaceans, 3 species vs. European eel, *Anguilla* sp.		
PCB 28	3 FW, 362 LW vs. 4 FW, 21 LW	29
PCB 52	3 FW, 400 LW vs. 15 FW, 83 LW	29
PCB 101	4 FW, 532 LW vs. 28 FW, 186 LW	29
PCB 138	4 FW, 529 LW vs. 97 FW, 986 LW	29
PCB 153	4 FW, 505 LW vs. 89 FW, 932 LW	29
PCB 180	0.8 FW, 107 LW vs. 41 FW, 436 LW	29
Gulf of Mexico; 1986-87; coastal sediments vs. oyster soft parts		
Di-CBs	0.08-0.6 DW vs. 0.4-1.6 DW	39
Tri-CBs	0.6-2.6 DW vs. 7.6-8.3 DW	39
Tetra-CBs	1.8-11.0 DW vs. 26-38 DW	39
Penta-CBs	3.1-13.4 DW vs. 66-78 DW	39
Hexa-CBs	2.7-15.6 DW vs. 26-42 DW	39
Hepta-CBs	1.3-9.5 DW vs. 5-6 DW	39
Octa-CBs	0.3-2.6 DW vs. 0.4-1.0 DW	39

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
Nona-CBs	0.06-0.4 DW vs. 0.3-0.4 DW	39
Total PCBs	9.8-55.7 DW vs. 134-1,734 DW	39
Hudson River (upper), New York; 1983; total PCBs; water column vs. fish muscle	0.14 FW vs. 3,800 FW	40
Lake Clear (PCB-contaminated), Canada; 1986-87; vs. Lake Scugog (noncontaminated); total of 19 PCB congeners		
Sediments	571 DW vs. 22 DW	41
Crayfish	73 FW vs. 9 FW	41
Plankton	59 FW vs. ND	41
Fish	90-153 FW vs. 6-27 FW	41
Lake Erie, Hamilton Harbour; 1984; water column vs. sediments		
Tri-CBs	0.04 FW vs. 244 FW	42
Tetra-CBs	0.07 FW vs. 405 FW	42
Penta-CBs	0.07 FW vs. 1,025 FW	42
Hexa-CBs	0.02 FW vs. 982 FW	42
Hepta-CBs	0.01 FW vs. 983 FW	42
Octa-CBs	0.002 vs. 246 FW	42
Total PCBs	0.22 vs. 3,927 FW; Max.14,185 FW	42
Oligochaetes		
Tri-CBs	33 FW	42
Tetra-CBs	39 FW	42
Penta-CBs	54 FW	42
Hexa-CBs	45 FW	42
Hepta-CBs	31 FW	42
Octa-CBs	5 FW	42
Total PCBs	207 FW	42
Lake Ontario, Wheatley Harbour; 1984; sediments vs. oligochaetes		
Tri-CBs	14 FW vs. 22 FW	42
Tetra-CBs	53 FW vs. 40 FW	42
Penta-CBs	133 FW vs. 102 FW	42
Hexa-CBs	141 FW vs. 72 FW	42
Hepta-CBs	69 FW vs. 23 FW	42
Octa-CBs	6 FW vs. 3 FW	42
Puget Sound, Washington; total PCBs		
Sediments	270-380 DW	43
Crab hepatopancreas	32,000 DW	43
English sole (*Pleuronectes vetulus*); liver	35,000 DW	43
Rainy River, Ontario; 1988; total PCBs		
Mill effluent, water vs. suspended solids	86-334 FW vs. 131-414 FW	44
Fish, two species; upstream vs. downstream	ND vs. 149-229 FW	44
Marine mammals (4 species; blubber) vs. terrestrial mammals (human, dog, cat; adipose or intestinal fat)		
Total PCBs	2,300-370,000 FW vs. 100-2,000 FW	20
Di-*ortho* planars		
PCB 128	54-8,000 FW vs. 1.2-72 FW	20
PCB 138	460-65,000 FW vs. 6.2-360 FW	20
Mono-*ortho* planars		
PCB 105	5-3,000 FW vs. 0.6-46 FW	20
PCB 118	47-11,000 FW vs. 2-160 FW	20

Table 9. Taxonomic group, organism, PCB congener, and other variables	Concentration (ug/kg)[a]	Reference[b]
PCB 156	11-1,900 FW vs. 1-22 FW	20
Non-*ortho* planars		
PCB 77	1.3-48.0 FW vs. 0.03-0.37 FW	20
PCB 126	0.16-3.7 FW vs. 0.007-0.33 FW	20
PCB 169	0.11-7.7 FW vs. 0.03-0.09 FW	20
Waukegan Harbor, Illinois, Lake Michigan;		
August 1978; heavily contaminated by PCBs		
Sediments, samples from 5 locations		
Total PCBs	10,600-6,996,000 DW	30
PCB 77	10-390 DW	30
PCB 105	70-43,400 DW	30
PCBs 126, 169	ND	30
Fish		
White sucker, *Catostomus commersoni*; whole		
Total PCBs	41,400 FW	30
PCB 77	50 FW	30
PCB 105	483 FW	30
PCBs 126, 169	ND	30
Black bullhead, *Ameiurus melas*; whole		
Total PCBs	49,400 FW	30
PCB 77	89 FW	30
PCB 105	352 FW	30
PCBs 126, 169	ND	30
Largemouth bass, *Micropterus salmoides*; offal		
Total PCBs	56,600 FW	30
PCB 77	86 FW	30
PCB 105	290 FW	30
PCBs 126, 169	ND	30
Coho salmon, *Oncorhynchus kisutch*; whole		
Total PCBs	2,400 FW	30
PCB 77	2 FW	30
PCB 105	45 FW	30
Yellow perch, *Perca flavescens*; whole		
Total PCBs	11,200 FW	30
PCB 77	23 FW	30
PCB 105	80 FW	30
White crappie, *Pomoxis annularis*; whole		
Total PCBs	40,300 FW	30
PCB 77	24 FW	30
PCB 105	242 FW	30
Black crappie, *Pomoxis nigromaculatus*; whole		
Total PCBs	32,200 FW	30
PCB 77	43 FW	30
PCB 105	114 FW	30

[a]Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

[b]1, Galceran et al. 1993; 2, Johansen et al. 1993; 3, de Boer and Wester 1991; 4, Hong et al. 1992; 5, Hesselberg et al. 1990; 6, Himberg 1993; 7, Maack and Sonzogni 1988; 8, Marthinsen et al. 1991; 9, Koistinen 1990; 10, Leiker et al. 1991; 11, Knickmeyer and Steinhart 1989; 12, Steimle et al. 1990; 13, Bush et al. 1990; 14, Tanabe et al. 1987; 15, Jones et al. 1989; 16, Gundersen and Pearson 1992; 17, Greig and Sennefelder 1987; 18, Tarhanen et al. 1989; 19, Borgmann and Whittle 1991; 20, Kannan et al. 1989; 21, Tanabe et al. 1989; 22, Masse et al. 1986; 23, Tanabe et al. 1993; 24, Addison and Brodie 1987; 25, Daelemans et al. 1993; 26, Duinker et al. 1988b; 27, Loganathan et al. 1990; 28, Kannan et al. 1993; 29, Van der Oost et al. 1988; 30

Huckins et al. 1988; 31, Janz et al. 1992; 32, Williams and Giesy 1992; 33, Sanchez et al. 1993; 34, Gobas et al. 1989; 35, Kovats and Ciborowski 1989; 36, Kammann et al. 1993; 37, Falandysz et al. 1994b; 38, Elskus et al. 1994; 39, Sericano et al. 1990; 40, Brown et al. 1985; 41, Macdonald and Metcalfe 1989; 42, Mudroch et al. 1989; 43, Long 1982; 44, Merriman et al. 1991; 45, Sericano et al. 1994; 46, Steingraeber et al. 1994; 47, Mac et al. 1993; 48, Schmitt et al. 1990; 49, Huhnerfuss et al. 1995; 50, Kleivane et al. 1995; 51, Lake et al. 1995a; 52, USEPA 1992a.

In gray seals (*Halichoerus grypus*), PCBs were transferred from blubber to milk by way of the circulatory system. Of the total concentration of PCBs in various tissues of maternal gray seals, PCB 153 accounted for about 30% in blubber, 20% in serum, and 30% in milk; PCB 180 accounted for 20% in blubber, 20% in serum, and 10% in milk; PCB 77 accounted for 20% in serum (Addison and Brodie 1987). In whales (*Ziphius* sp.), the dominant PCB congeners in blubber had 5-8 chlorines; PCBs 138, 153, 149, 180, and 201 accounted for about 70% of the total PCBs (Duinker et al. 1988b). In the Canadian Arctic food chain of Arctic cod (*Boreogadus saida*) to ringed seal (*Phoca hispida*) to polar bear (*Ursus maritimus*), the total PCB concentrations in µg/kg FW ranged from 4 in cod muscle to 680 in seal blubber to 4,500 in bear fat. The hexachlorobiphenyl PCB 153 accounted for 42% of the total PCBs in bear fat and for only 20% in seal blubber and 7% in cod muscle. Tri- and tetrachlorobiphenyl homologs predominated in cod, penta- and hexachlorobiphenyl congeners predominated in seal blubber, and hexa- and heptachlorobiphenyl congeners in fat of polar bears (Muir et al. 1988).

In comparison to conspecifics from noncontaminated sites, aquatic invertebrates from PCB-contaminated sites contained elevated concentrations of PCBs in tissues (Table 9). Adult aquatic insects are one of the groups considered useful and reliable indicators of PCB contamination (Wood et al. 1987; Kovats and Ciborowski 1989). Mayflies (*Hexagenia* spp.) from Lake St. Clair had PCB concentrations that reflected sediment PCB concentrations (Table 9). Observed mayfly sediment concentration ratios from PCBs linearly correlated with K_{ow} when expressed on a logarithmic basis (Gobas et al. 1989). PCB congener distributions in lake biota showed that no particular trophic level consistently accumulated the highest PCB concentrations and suggest that accumulations were associated with the organism's lipid concentrations (Table 9). A relation was consistent between the concentration of dissolved PCBs and tissue concentrations in mussels from PCB-contaminated sites, such as New Bedford Harbor, Massachusetts. Uptake of PCB congeners in blue mussels (*Mytilus edulis*) from the dissolved phase of seawater was predictable from the log of the bioconcentration factor and the log K_{ow} of the congeners (Bergen et al. 1993). Eastern oysters (*Crassostrea virginica*) from Galveston Bay, Texas, contained as much as 1,100 µg/kg total PCBs DW soft parts, whereas conspecifics from Tampa Bay, Florida contained only 580 µg/kg DW soft parts; most (54-94%) of the relative toxicity in both groups was due to PCBs 77, 126, and 169 (Sericano et al. 1994).

The partitioning of individual, highly chlorinated PCB congeners with small differences in K_{ow} values may not adequately explain the accumulations in aquatic organisms (van der Oost et al. 1988). Hydrophobic chemicals, such as PCBs, are accumulated as a consequence of chemical partitioning between the water column, the organic phase of sediment, and biotic lipids or from biomagnification, a process reflecting the ratio between uptake rate from food and elimination rate from the organism. Accumulations of six PCB congeners (PCBs 28, 52, 101, 138, 153, 180) in surficial sediments (0-20 cm) and in an aquatic food chain in Lake Nieuwe Meer—a freshwater lake near Amsterdam containing contaminated dredged materials discharged over 30 years—were low in sediments; elevated in carnivores, plankton, molluscs, crustaceans, and eels; and independent of fat content (van der Oost et al. 1988). With concentrations in organisms expressed on the basis of lipid content (C_{org}) and concentrations in sediments expressed on the basis of organic carbon (C_{sed}) the median C_{org}/C_{sed} PCB accumulation patterns in aquatic organisms showed significant differences and indicated that mechanisms other than partitioning were operating. In plankton and mollusks, C_{org}/C_{sed} ratios seemed to be independent of hydrophobicity of PCB congeners. But with ascending trophic level from plankton to molluscs to crustaceans to eels, the median C_{org}/C_{sed} ratios of higher chlorinated congeners (PCBs 138, 153, 180) increased. Differences in accumulations of individual congeners were attributed to (1) increased biomagnification of higher chlorinated congeners because increasing hydrophobicity decreased elimination rates but not uptake efficiency; (2) greater mobility of eels and different feeding habits of eels and crustaceans that impact accumulation patterns because of biomagnification and partitioning; (3) variability in the time period (limited by lifespan) available in a particular trophic level for equilibration between uptake and clearance; and (4) the tendency of equilibrium to be established at faster rates in less chlorinated congeners. In crustaceans,

C_{org}/C_{sed} ratios decreased with decreasing hydrophobicity; the opposite occurred in eels and is attributed to differences in uptake efficiencies and low elimination rates of lower chlorinated congeners in crustaceans (van der Oost et al. 1988).

A correlation exists between the concentration of lipophilic, hydrophobic, chlorinated hydrocarbons in benthic fishes and the concentration of these compounds in sediments. The correlation is affected by the solubility of the contaminants, as reflected by the octanol/water partition coefficient K_{ow} and the carbon content of the sediment (Connor 1984; Breck 1985). Connor (1984) suggested that surface sediments, which change more slowly than the water column, are useful for averaging spatial and temporal contaminant inputs; however, correlations between PCB concentrations in sediment and those in nonbenthic carnivores with limited home ranges are extremely variable.

Concentrations of total PCBs—measured as Aroclors 1248, 1254, and 1260—in adult freshwater fishes in the United States from noncontaminated sites declined between 1976 and 1984 (Table 9), and more than 90% of all analyzed samples contained measurable quantities of PCBs during this period (Schmitt et al. 1990). Total PCB concentrations in domestic freshwater fishes in 1986-87 from contaminated sites were as high as 124,000 µg/kg FW (USEPA 1992a). In general, total PCB concentrations in domestic freshwater fishes sampled between 1976 and 1984 were highest in the industrialized regions of the northeast, the Great Lakes, the upper Mississippi River, and the Ohio River (Schmitt et al. 1990). Phillips and Birchard (1990) reviewed PCB concentrations (as judged by residues of Aroclors 1016, 1221, 1232, 1242, 1248, 1254, and 1260) in sediments and fish tissues in the United States during 1978-87. During 1978-81, total PCB concentration rankings in sediments were highest in the lower Mississippi, Tennessee, South Atlantic-Gulf of Mexico, and lower Colorado regions and lowest in the Great Lakes, Arkansas, mid-Atlantic, Pacific Northwest, and Rio Grande regions. During this same period, PCB concentrations in fish tissues were highest in the Missouri, upper Colorado, California, and the Great Lakes regions and lowest in the upper Mississippi, New England, Ohio, Pacific Northwest, Tennessee, lower Mississippi, and Rio Grande regions. Sediment PCB rankings during 1982-87 were highest in the Arkansas, California, Ohio, and Missouri regions and lowest in the South Atlantic-Gulf, and Colorado regions. Total PCBs were highest in fish tissues in the upper Mississippi Region during 1982-87. The fish tissue rankings in descending order assigned to 12 regions with sufficient total PCB data were the upper Mississippi and Missouri regions, Ohio, south Atlantic-Gulf, Arkansas, Great Basin, lower Colorado, California, Pacific Northwest, Ohio, upper Colorado, and lower Mississippi. PCB rankings between fish tissues and sediments were not necessarily comparable because high levels in sediment do not necessarily result in high levels in fishes if bioconversion was significant (Phillips and Birchard 1990). Total PCB concentrations in coastal sediments and fish liver in the United States were highest in the Boston Harbor (17.1 mg/kg DW sediment, 10.5 mg/kg in liver of winter flounder, *Pleuronectes americanus*), San Diego Harbor (O.42 mg/kg DW sediment, 19.7 mg/kg in barred sand bass, *Paralbrax nebulifer*), and Elliot Bay, Washington (0.33 mg/kg sediment, 14.7 mg/kg in flathead sole, *Hippoglossoides elassodon*). Trichloro PCBs were in sediments at many sites but did not accumulate in fish livers except in the Boston Harbor. Sediments in the Boston Harbor, western Long Island Sound, and Raritan Bay were contaminated with PCB mixtures that were relatively high in tri- and tetrachlorobiphenyl isomers, although penta- and particularly hexachlorobiphenyls were the dominant isomers at most sediment sites. As expected, levels of hexachlorobiphenyls in fish livers were dominant because of the more persistent and lipophilic characteristics of increasingly chlorinated PCBs (NOAA 1987).

Variations in PCB concentrations in sediment and water in the Great Lakes can largely account for the variability between different bodies of water in fish PCB residues. Other variables include fish lipid content, position of the fish species in the food web, and trophic structure of the food chain. Collectively, these variables explain 72% of the variation in PCB concentrations of 25 species of Great Lakes fishes (Rowan and Rasmussen 1992). Tissue concentrations of PCBs in benthic and lower trophic organisms in lakes can be estimated by assuming equal lipid-normalized concentrations in biota and sediment; however, food chain transport had a greater effect on PCB concentrations in higher trophic levels (Macdonald et al. 1993). Total PCB concentrations in whole body of lake fishes were higher among older piscivores and higher with increasing lipid concentration and seemed to reflect exposure conditions at the capture site (Southworth 1990).

Eggs of chinook salmon (*Oncorhynchus tshawytscha*) from Lake Michigan in 1986 contained AHH-active PCB congeners—including PCBS 77, 105, 118, and 126—at concentrations from 0.9 to 262 µg/kg FW; concentrations of these congeners did not correlate with survival (Williams and Giesy 1992). Mortality of chinook

salmon eggs was not related to total PCB concentrations as high as 7,020 µg/kg FW (Williams and Giesy 1992). In Lake Ontario, the overall trend in total PCB concentrations in whole lake trout (*Salvelinus namaycush*) between 1977 and 1988 was a gradual decline with a half-time persistence of about 10 years (Borgmann and Whittle 1991). In Lake Michigan, total PCB concentrations declined 64% in bloaters (*Coregonus hoyi*) from 5,700 µg/kg FW in 1972 to 1,600 µg/kg FW in 1986 (Hesselberg et al. 1990). In Lake Superior, the PCB congener fingerprint in eggs of the lake trout differed from that of lake trout eggs of other Great Lakes (Mac et al. 1993). A difference between residue patterns was also identified between eggs and the parent fish, suggesting preferential deposition of congeners other than AHH-active congeners. Concentrations of individual congeners in lake trout have been declining at similar rates in the Great Lakes during a 10-year period (Mac et al. 1993).

Distribution patterns of PCB congeners in water, sediment, and four groups of biota from two lakes in Ontario contaminated by known point sources of PCBs (Lake Clear, Rice Lake) were compared with the congener distribution in Lake Scugog, a relatively clean control lake exposed only to atmospheric inputs of PCBs (Macdonald and Metcalfe 1989). Samples were analyzed for 19 PCBs. Those from Lake Clear had a distribution pattern similar to Aroclor 1254 and dominant concentrations of congeners 87, 101, and 118; this lake was contaminated with a PCB mixture similar to Aroclor 1254 in the mid to late 1970s. The sources to Rice Lake were less clear. Lake Scugog contained a higher proportion of less chlorinated PCBs, in agreement with another study of atmospheric deposition to isolated lakes (Swackhammer et al. 1988). Because the sediments contained elevated levels of organic carbon, the sediments were expected to also hold relatively large concentrations of the higher, more hydrophobic PCBs, in accord with previous reports (Karickoff 1981; Formica et al. 1988). But this was not the case; subsequent deposition of total and higher chlorinated congeners into the bottom sediments (organic carbon basis) was unexpectedly low. The proportion of higher chlorinated congeners in sediments were also lower than in biota (lipid weight basis) in all three lakes. Because dissolved organic carbon (DOC) increases the solubility of PCBs in water (Gschwend and Wu 1985), the high DOC levels may have caused partitioning of more PCBs into the water and less sorbed onto sediments. The sediments were not efficient at accumulating PCBs, although bottom sediment concentrations were higher in contaminated lakes. Adsorption of PCBs on suspended particles occurred, as anticipated; PCBs on total suspended solids were higher in contaminated lakes (978 µg/kg) than in the control lake (49 µg/kg) and reflected lake concentrations (Gschwend and Wu 1985). In a related study, Macdonald and Metcalfe (1991) analyzed the concentration and distribution of 19 PCB congeners in biota, sediments, water, and suspended solids of isolated oligotropic lakes in central Ontario that were contaminated by atmospheric deposition. The range of the total congener concentrations was 1-2 ng/L dissolved in water, 10-50 µg/kg DW in sediment, 5-10 µg/kg FW in lower trophic levels, and 10-30 µg/kg in fishes from upper trophic levels. The high proportion of trichlorobiphenyls previously reported in vapor (Duinker and Bouchertall 1989; Baker and Eisenreich 1990) and hexachlorobiphenyl congeners 153 and 138 in particulate-bound PCBs (Swackhammer et al. 1988; Duinker and Bouchertall 1989; Baker and Eisenreich 1990) were reflected in the four study lakes. PCB concentrations (lipid basis) were higher in teleosts than they were in invertebrate prey organisms.

Winter flounder from the PCB-contaminated harbor in New Bedford, Massachusetts, had grossly elevated concentrations of PCBs in their livers (as high as 333,000 µg/kg DW); concentrations were about 5 times higher than in any other fish sample collected worldwide (Table 9; Elskus et al. 1994). PCB patterns in the New Bedford Harbor showed high agreement between the exposure environment (water and sediments) and ribbed mussels (*Geukensia demissa*) and mummichogs (*Fundulus heteroclitus*); however, agreements with American eels (*Anguilla rostrata*) or grass shrimp (*Palaemonetes pugio*) were poor because, in part, of differential metabolism of PCBs by these species (Lake et al. 1995b). PCB concentrations in four species of catfishes from the Mississippi River and its tributaries in summer 1987 were highest from the Illinois River; the Ohio River at Olmsted; and the Mississippi River at Helena, Arkansas, and Arkansas City, Arkansas. These sites seem to be point sources of PCB pollution because PCB residues in catfishes above and below these sites were lower. Although PCBs were banned in 1978, the elevated levels in catfishes suggests PCB leakage from hazardous waste sites with transformer and hydraulic fluids and flame-resistant plasticizers (Leiker et al. 1991). Findings of high (greater than 4,000 µg/kg FW) total PCB levels in mature roe samples of the paddlefish (*Polyodon spathula*) from the Ohio River warranted warnings of the general public about consuming this domestic caviar (Gundersen and Pearson 1992).

The upper Hudson River was massively contaminated with PCBs from an industrial plant for several decades prior to 1975. All fishing in this section in 1976 was banned because of PCB contamination. The

prohibition is still in effect because, in part, of measurable PCB residues in caged fishes from this area (Table 9; Jones et al. 1989). Striped bass (*Morone saxatilis*) collected near Troy and Albany, New York, contained higher concentrations in muscle of PCB 77 (37 µg/kg FW) and PCB 126 (8 µg/kg FW) than conspecifics from other locations in New York (Hong et al. 1992). Almost all (99%) the PCB toxicity in muscle of striped bass was attributed to PCBs 77, 105 (62 µg/kg FW), and 126 (Hong et al. 1992).

The most prominent PCB congeners in muscle from 14 species of Wisconsin fishes in 1986-87 were PCBs 28/31, 66/95, 70/76, 101, 105, 110, 118, 138, 146, 149 and 180 (Maack and Sonzogni 1988). Congeners 105 and 118 were found in the greatest amount in fishes at 1 to 5% of the total PCB concentration of each. Congeners with responses similar to 2,3,7,8-TCDD, that is, the planar PCBs, were seldom present above detection levels. The sum of the individual congeners measured in Wisconsin fish muscle were similar to total recorded PCB values (Maack and Sonzogni 1988). Increased fish consumption by Wisconsin anglers in 1985 positively correlated with increased human serum PCB concentrations (Sonzogni et al. 1991). Human consumers of Wisconsin game fishes (chinook salmon, *Oncorhynchus tshawytscha*; yellow perch, *Perca flavescens*; walleye, *Stizostedion vitreum*) in 1986 contained various PCB congeners in their sera. PCB 153 (78% frequency of occurrence) was present at 1.46 (0.6-7.3) µg/L human serum, PCB 138 (56%) at 1.32 (0.6-6.0) µg/L, PCB 180 (42%) at 1.06 (0.6-3.5) µg/L, PCB 118 (34%) at 1.12 (0.6-5.7) µg/L, PCB 187 (11%) at 0.98 (0.6-2.2) µg/L, PCB 170 (5.8%) at 0.86 (0.6-1.4) µg/L, PCB 28 (1.2%) at 0.8 µg/L, PCB 101 (0.58%) at 0.8 µg/L, PCB 70 (0.58%) at 0.7 µg/L, and a single planar PCB—PCB 77—(0.58% frequency of occurrence) at 1.3 µg/L. PCBs 118, 138, and 180 are potentially most toxic to human consumers, as judged by the concentrations of these congeners in human sera (Sonzogni et al. 1991).

Concentrations of PCBs in female northern pikes (*Esox lucius*) from a Scandinavian lake decreased with increasing age, weight, or body length (Larsson et al. 1993). Seasonal elimination of the lipophilic contaminants in roe—which contained as much as 10 times more fat than muscle and more than 10 times the amount of pollutants than muscle—is the major route of PCB loss. Male northern pikes contained higher concentrations of PCBs than females because of the lower elimination by way of gonadal products; males showed no significant relation between age and PCB burdens in tissues (Larsson et al. 1993). Total PCB levels of 7,700 to 34,000 µg/kg LW in eggs of the Arctic char (*Salvelinus alpinus*) from Lake Geneva, Switzerland, correlated with a mortality rate of 29 to 100% (Gundersen and Pearson 1992).

On the Pacific coast and in adjacent areas of Mexico, data from more than 150 survey and monitoring programs were summarized on contamination of sediments, invertebrates, and fishes (Mearns 1992). PCBs in sediments seem to be reflected in mussels, and PCB residues from mussels collected at harbor entrances remained unchanged or were increasing. The harbors in Los Angeles-Long Beach and San Diego remained contaminated with PCBs, and PCB concentrations in sediments were reflected in fish livers. Waste management seems to have been effective in the Palos Verdes outfall area. Sediments and mussel samples in Palos Verdes from 1974-88 showed decreasing PCB levels that reflected a 100-fold reduction in PCB wastewater emissions during that period. Contamination of the coastal zone declined to levels found 30 and 40 years ago. PCB levels had declined at least one order of magnitude in teleosts and shellfish at offshore sites since the 1970s. Bays and harbors were more contaminated than the open coastal zone and must be monitored more closely; lower detection levels (0.001 to 0.01 mg/kg FW versus the current analytical limits of 0.02 mg/kg FW) were proposed to monitor the effectiveness of current source control programs (Mearns 1992).

PCBs in the Puget Sound, Washington, were measured in sediments, fish livers, and benthic invertebrates. Maximum total PCB concentrations were 2,100 µg/kg DW in sediments near Tacoma and 32,000 µg/kg DW in crab hepatopancreas and 35,000 µg/kg DW in fish liver near Seattle (Long 1981). PCB concentrations in sediments of the Puget Sound in May 1988 positively correlated with PCB concentrations in livers of several species of flatfishes in these sediments (Stein et al. 1992). Increased sediment PCB concentrations also correlated well with increased hepatic AHH and EROD activities and with increases in total hepatic GSH, all of which are acknowledged early indicators of chemical contamination by PCBs and other organic contaminants (Gooch et al. 1989; Stein et al. 1992).

PCB residues in liver of the European flounder (*Platichthys flesus*) were extremely variable, but residues of individual congeners were usually higher in fall, higher in females, and higher in flounders captured inland near a PCB point source (Marthinsen et al. 1991); a similar pattern was documented in the Atlantic cod, (*Gadus morhua*; Marthinsen et al. 1991). In the dab (*Limanda limanda*), a marine flatfish, the accumulation of PCBs 128,

138, and 163 differs significantly by sex (Knickmeyer and Steinhart 1989). Depletion of lipids from the liver of female dabs during ovary maturation is an important excretory pathway for PCBs during spawning (Knickmeyer and Steinhart 1989). PCB levels in liver of dabs were higher in spring than in winter; livers and ovaries were dominated by penta-and hexacholorobiphenyls, but the dominant PCBs in testes were tri-and tetrachlorobiphenyls (Kammann et al. 1993).

The most prominent PCB congeners at 280-323 µg/kg DW in the tilefish (*Lopholatilus chamaeleonticeps*) from Georges Bank in 1981-92 were PCBs 138 and 153 in gonad and liver; at 69-82 µg/kg DW the most prominent PCB congeners in the tilefish from New Jersey during this same period were PCBs 138 and 153 in liver (Steimle et al. 1990). Total PCB concentrations in marine coastal fishes were dominated by the hexachlorobiphenyls (Knickmeyer and Steinhart 1989), but trout from isolated mountain lakes had tri-, tetra-, and pentachlorobiphenyls as the major components of total PCBs (Sanchez et al. 1993).

Reptiles

PCBs accumulate in the fat, testes, and brain of snapping turtles *(Chelydra serpentina*), and concentrations seem to reflect the lipoprotein solubility of individual congeners (Bryan et al. 1987a; Table 10). With increasing hydrophobicity (increasing K_{OW}) of PCB congeners, accumulations increased in livers of snapping turtles; total liver PCB concentrations in adults increased with increasing age, length, and weight (Hebert et al. 1993). PCB loadings in snapping turtle eggs were not related to the body size of females or to the number of eggs in the clutch (Bishop et al. 1994). However, a positive relation between PCB loadings in liver of adult female snapping turtles and their eggs was significant (Hebert et al. 1993).

PCB 105 may be an important contributor to the toxic burden of snapping turtle populations (Hebert et al. 1993). Eggs of snapping turtles from the Great Lakes had a lower hatch rate and a significantly increased frequency of deformed hatchlings than eggs from a control site, and this seemed to be strongly associated with total PCB concentrations and PCB 105 (Bishop et al. 1991). Of the 5 toxic PCB congeners measured in the yolks, egg whites, and shells of snapping turtle eggs, PCBs 105 and 167 accounted for more than 99% of the total toxicity—as measured by 2,3,7,8-TCDD TEF equivalents—and 95% of the total toxicity resided in the yolk (Bryan et al. 1987b). Large reserves of fat in eggs of the snapping turtle do not seem to protect against toxic PCB congeners from being dispersed into egg components low in fat (Bryan et al. 1987b).

Birds

In general, total PCB concentrations in birds were usually higher in males and in eggs than in livers, in adipose tissues, in fish-eating species, and at PCB-contaminated sites; PCBs 138 and 153 tended to predominate in all samples (Table 11). The change in PCB content in livers of Norwegian raptors between 1965 and 1983 was not significant despite a marked reduction in the use of these compounds (Froslie et al. 1986). When total PCB concentrations declined, for example, in eggs of red-breasted mergansers (*Mergus serrator*) between 1977 and 1990, the relative potency of the mixture of PCBs—as measured by 2,3,7,8-TCDD equivalents—was unchanged (Williams et al. 1995).

Commercial PCB mixtures frequently contain impurities that may contribute to the 2,3,7,8-TCDD toxic equivalency factor; these impurities may include other PCBs, dioxins, dibenzofurans, naphthalenes, diphenyl ethers and toluenes, phenoxy and biphenyl anisoles, xanthenes, xanthones, anthracenes, and fluorenes (Jones et al. 1993). PCB concentrations in avian tissues sometimes positively correlate with DDE concentrations (Mora et al. 1993). Eggs of peregrine falcons (*Falco peregrinus*) from California, for example, contained measurable quantities of various organochlorine compounds, including dioxins, dibenzofurans, mirex, hexachlorobenzene, and p,p' DDE at 7.1-26.0 mg/kg FW; PCB 126 accounted for 83% of the 2,3,7,8-TCDD equivalents, but its interactions with other detectable organochlorine compounds is largely unknown (Jarman et al. 1993).

There is a relation between PCB uptake and the position of the species in the food chain. In a 3-step central-European oak-forest food chain involving the great tit *(Parus major*), caterpillars (*Tortrix viridana*, *Operophtera brumata, Erannis defoliara*), and leaves of the red oak (*Quercus* sp.), mean concentrations of PCB 153—the most abundant measured congener—rose from about 1 µg/kg DW in leaves to 10 in caterpillars to 170 in bird eggs (Winter and Streit 1992). Older juvenile tits contained 307 µg of PCB 153/kg whole body DW; these birds received PCBs from the mother during egg transfer and from the caterpillar food source during the nesting period. PCBs 101, 138, and 180 were also present in most samples but at lower concentrations than PCB 153.

Populations of *Parus major* in this area declined in recent years, and the influence of anthropogenic contaminants may be a factor (Winter and Streit 1992). Fish-eating waterfowl and seabirds had comparatively high total PCB and high planar PCB concentrations in eggs and tissues; waterfowl and seabirds that feed mainly on invertebrates had lower PCB concentrations (Focardi et al. 1988b; Borlakoglu et al. 1990; Gonzalez et al. 1991; Jones et al. 1993). PCB concentrations were higher in adipose tissues of the Arctic tern *(Sterna paradisaea*) than in those of their fish and invertebrate food items (Scharenberg 1991a). PCB concentrations in adipose tissues of cormorants, when compared to their diet of fishes, were 10 to 100 times higher than marine fishes and 100 to 1,000 times higher than freshwater fishes (Scharenberg 1991b). Double-crested cormorants (*Phalacrocorax auritus*) biomagnify total PCBs from their fish diet to their eggs—based on 2,3,7,8-TCDD equivalents—by a factor of 31.3 (Jones et al. 1994). Higher-chlorinated PCBs accumulated in tissues of the herring gull (*Larus argentatus*) to a greater extent than were present in the alewife (*Alosa pseudoharengus*), a primary food item; lower-chlorinated biphenyls, including the tetra- and penta-CBs, did not biomagnify (Braune and Norstrom 1989).

Table 10. PCB concentrations in field collections of selected reptiles. Concentrations are in ug/kg (ppb) fresh weight (FW) or lipid weight (LW).

Table 10. Species, tissue, PCB congener, and other variables	**Concentration[a] in ug/kg**	**Reference[b]**
American alligator, *Alligator mississippiensis*; total PCBs; Florida		
Eggs, 1984	80-170 FW; Max. 670 FW	1
Muscle, 1985	100-2,100 LW	2
Snapping turtle, *Chelydra serpentina*		
Canada		
Great Lakes (Ontario and Erie) vs. control site in central Ontario; eggs; sum of PCB congeners 105, 118, 138, 153, 170, and 180		
1986-87	2,600-2,700 FW vs. 80 FW	3
1988-89	300-3,300 FW vs. 30 FW	3
Hamilton Harbour; adults; found dead; 1986-87; fat; sum of PCBs 105, 118, 138, 153, 170, and 180	57,700-72,200 LW	3
Lake Ontario; eggs; 1990		
PCB 52	20(10-40) LW	4
PCB 105	1,700 (500-2,900) LW	4
PCB 118	7,300 (2,100-11,700) LW	4
PCB 138	9,300 (2,000-16,200) LW	4
PCB 153	9,300 (2,500-16,200) LW	4
PCB 180	6,400 LW	4
PCB 194	600 LW	4
Total PCBs	54,300 (13,300-96,400) LW	4
Southern Ontario; adults; 1988-89; muscle; sum of Aroclors 1254 and 1260	7-660 FW; Max. 2,120 FW	5
United States		
Contaminated site (South Glen Falls, New York) vs. noncontaminated site (Columbus, New York); adults; total PCBs		
Brain	82,000 LW vs. 1,000 LW	6
Heart	49,000 LW vs. 600 LW	6
Kidney	48,000 LW vs. 1,200 LW	6
Liver	72,000 LW vs. 1,000 LW	6
Lungs	13,000 LW vs. 400 LW	6
Pancreas	48,000 LW vs. 1,200 LW	6
Testes	100,000 LW vs. 1,600 LW	6
Fat	1,600,000 LW vs. 4,200 LW	6
PCB 66	272,000 LW vs. 200 LW	6

Table 10. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
PCB 82	100,000 LW vs. 90 LW	6
PCB 99	166,000 LW vs. 50 LW	6
PCB 105	171,000 LW vs. 160 LW	6
PCB 136	297,000 LW vs. 200 LW	6
PCB 176	152,000 LW vs. 300 LW	6
Upper Hudson River, New York; egg yolk		
PCB 105	700-1,890 FW	7
PCB 118	16-32 FW	7
PCB 120	120-280 FW	7
PCB 167	200-560 FW	7
PCB 189	60-120 FW	7

[a] Concentrations are shown as means, range (in parentheses), and maximum (Max.).

[b] 1, Heinz et al. 1991; 2, Delaney et al. 1988; 3, Bishop et al. 1991; 4, Bishop et al. 1994; 5, Hebert et al. 1993; 6, Bryan et al. 1987a; 7, Bryan et al. 1987b.

Declining populations of Caspian terns (*Sterna caspia*)—especially populations nesting in Green Bay and Saginaw Bay between 1986 and 1990—were associated with elevated PCB concentrations in blood; the frequency of developmental abnormalities and deformities in Caspian tern populations at Saginaw Bay was almost 100 times above that recorded in the same area between 1962 and 1972 (Table 11; Mora et al. 1993). High PCB concentrations in tissues of white-tailed eagles (*Haliaeetus albicilla*) are directly connected to high concentrations in eggs and associated with eggshell thinning and low reproductive success (Falandysz et al. 1994a). A total lack of reproduction among white-tailed sea eagles in the coastal area of the southwestern Baltic Sea in the 1960s and 1970s may be related, in part, to high concentrations of PCBs 105, 118, 126, and 156 in tissues of adult eagles. It is noteworthy that concentrations of planar PCBs in adult white-tailed sea eagles were among the highest reported in wildlife and that total PCB concentrations in this species were similar to those reported in dead eagles from Sweden and Finland in the 1960s and 1970s (Falandysz et al. 1994a).

Table 11. PCB concentrations in field collections of selected birds. Concentrations are in ug/kg (ppb) fresh weight (FW), dry weight (DW), or lipid weight (LW).

Table 11. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
Northern goshawk, *Accipiter gentilis*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	2,000 (<100-1,260,000) FW vs. 12,300 (2,600-53,000 FW	1
Northern sparrow hawk, *Accipiter nisus*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	1,100 (<100-107,000) FW vs. 5,900 (<100-39,000) FW	1
Sharp-shinned hawk, *Accipiter striatus*; blood plasma; total PCBs (as Aroclors 1254 and 1260); Great Lakes, 1985-89	80 (10-190) FW	2
Tengmalm's owl, *Aegolius funereus*; liver vs.eggs; total PCBs; Norway 1965-83; dead on collection	1,000 (<100-9,400) FW vs. 400 (<100-1,300) FW	1 1
Red-winged blackbird, *Agelaius phoeniceus*; eggs (less shell) and chicks (less feathers, feet, beaks, stomach content contents, and wings); total PCBs; Green Bay, Wisconsin, 1989	5,400-8,900 FW	9
Razorbill, *Alca torda*; adipose tissue; males vs. females; England, 1988		
PCBs 3, 8, 18	ND vs. ND	3

Table 11. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
PCB 28	110 FW vs. ND	3
PCB 52	140 FW vs. ND	3
PCB 101	310 FW vs. 32 FW	3
PCB 118	2,500 FW vs. 500 FW	3
PCB 138	6,500 FW vs. 1,600 FW	3
PCB 153	4,400 FW vs. 1,100 FW	3
PCB 180	2,600 FW vs. 600 FW	3
Total PCBs	16,500 FW vs. 4,100 FW	3
Imperial eagle, *Aquila heliaca adalberti*; infertile eggs; Spain, 1986-87		
PCB 101	9-16 FW; Max. 440 FW	4
PCB 118	1-4 FW; Max. 66 FW	4
PCB 138	7-30 FW; Max. 620 FW	4
PCB 153	37-115 FW; Max. 5,300 FW	4
PCB 180	30-110 FW; Max. 4,800 FW	4
Total PCBs	280-820 FW; Max. 28,900 FW	4
Golden eagle, *Aquila chrysaetos*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	2,000 (<100-250,000) FW vs. 1,000 (400-5,700) FW	1
Grey heron, *Ardea cinerea*; total PCBs (35 congeners); England, 1988-90		
Fat	198,000 FW; 226,000 LW	5
Kidney	3,600 FW; 135,000 LW	5
Liver	2,800 FW; 936,000 LW	5
Muscle	8,100 FW; 139,000 LW	5
Great blue heron, *Ardea herodias*; eggs; British Columbia		
PCB 77	0.05-0.2 LW	6
PCB 105	17-31 LW	6
PCB 118	63-116 LW	6
PCB 126	0.1-0.2 LW	6
PCB 169	0.02-0.04 LW	6
Short-eared owl, *Asio flammeus*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	300 (<100-46,000) FW vs. 2,100 (2,000-22,000) FW	1
Greater scaup, *Aythya marila*; total PCBs; carcass; Detroit River, 1981	11,000 FW	25
Eagle owl, *Bubo bubo*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	3,000 (100-550,000) FW vs. 4,000 (2,200-29,000) FW	1
Common buzzard, *Buteo buteo*; infertile eggs; total PCBs; Spain, 1985-86	1,650 (1,600-1,700) FW	7
Rough-legged buzzard, *Buteo lagopus*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	200 (<100-15,000) FW vs. 800 (200-9,300) FW	1
White stork, *Ciconia ciconia*; infertile eggs; total PCBs; Spain, 1985-86	800 (200-2,700) FW	7
Dipper, *Cinclus cinclus*; addled eggs; Wales vs. Ireland, 1990-92		
PCB 101	10-20 LW vs. <10 LW	8
PCB 118	10-70 LW vs. 10-1,280 LW	8
PCB 138	10-380 LW vs. 10-80 LW	8
PCB 153	20-530 LW vs. 10-160 LW	8
PCB 170	10-190 LW vs. 10-30 LW	8

Table 11. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
PCB 180	10-20 LW vs. 10-40 LW	8
Merlin, *Falco columbarius*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	400(<100-41,000) FW vs. 4,500 (2,400-11,000) FW	1
Peregrine, *Falco peregrinus*		
Liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	120,000 FW vs. 43,000 FW	1
Eggs; California, 1983-88		
PCB 37	0.18 FW	10
PCB 77	0.93 FW	10
PCB 126	1.0 FW	10
PCB 138	750 FW; Max. 2,440 FW	10
PCB 153	1,200 FW; Max. 4,400 FW	10
PCB 169	0.14 FW	10
Total PCBs	4,800 (1,400-13,000) FW	10
Gyr falcon, *Falco rusticolus*; liver vs. eggs; total PCBs; Norway 1965-83; dead on collection	5,000 (300-42,000) FW vs. 12,000 FW	1
Kestrel, *Falco tinnunculus*; liver vs. eggs; total PCBs; Norway 1965-83	500 (<100-45,000) FW vs. 600 (<100-1,000) FW	1
Chicken, *Gallus* sp.; fat vs. feather; total of PCBs 118, 138, 153, and 156; PCB-contaminated area	12,800 LW vs. 200 LW	11
Gull-billed tern, *Gelochelidon nilotica*; infertile eggs; Spain, 1988		
PCB 138	Max. 220 FW	12
PCB 153	Max. 90 FW	12
PCB 180	Max. 190 FW	12
White-tailed sea eagle, *Haliaeetus albicilla*		
Liver vs. eggs; total PCBs; Norway 1965-83	5,000 (100-180,000) FW vs. 13,900 (4,200-31,000) FW	1
Breast muscle; Poland, 1982-90		
Non-*ortho* planars		
PCB 77	3-140 FW	13
PCB 126	1-160 FW	13
PCB 169	2-380 FW	13
Mono-*ortho* planars		
PCB 60	5-760 FW	13
PCB 105	110-9,200 FW	13
PCB 118	290-28,000 FW	13
PCB 156	53-9,200 FW	13
Di-*ortho* planars		
PCB 128	ND-600 FW	13
PCB 137	50-6,800 FW	13
PCB 138	930-65,000 FW	13
PCB 153	1,100-92,000 FW	13
PCB 170	100-22,000 FW	13
PCB 180	330-61,000 FW	13
PCB 194	20-8,900 FW	13
Booted eagle, *Hieraaetus pennatus*; infertile eggs; total PCBs; Spain, 1985-86	1,500 (500-8,400) FW	7
Loggerhead shrike, *Lanius ludovicianus*; eggs vs. carcasses; total PCBs; Virginia, 1985-88	940 FW; Max. 1,300 FW vs. <5 FW	14

Table 11. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
Herring gull, *Larus argentatus*		
Eggs; Great Lakes; total PCBs		
Lake Erie		
1972-74 vs. 1977-80	34,700-130,700 FW vs. 14,600-33,100 FW	26
1983 vs. 1987-88	11,800-14,100 FW vs. 5,600-21,900 FW	26
Lake Huron		
1971-77 vs. 1980-83	43,000-59,500 FW vs. 8,800-10,900 FW	26
1987-88	4,500-11,300 FW	26
Lake Ontario		
1971-72 vs. 1974-77	58,800-143,900 FW vs. 36,200-96,600 FW	26
1980-83 vs. 1987	15,900-27,500 FW vs. 14,400-15,800 FW	26
Lake Superior; 1973-77 vs. 1980-87	37,100-46,400 FW vs. 5,500-11,400 FW	26
Eggs; Great Lakes		
PCB 77	0.6-3.0 LW	6
PCB 105	50-860 LW	6
PCB 118	180-2,550 LW	6
PCB 126	2-10 LW	6
PCB 169	0.2-9.0 LW	6
Infertile eggs; Spain, 1988		
PCB 138	Max. 450 FW	12
PCB 153	Max. 400 FW	12
PCB 180	Max. 280 FW	12
Total PCBs	2,000 (1,100-3,600) FW	12
Lake Ontario, 1985		
Adults		
Total PCBs		
Carcass	47,000 FW	15
Diet (fish)	510 FW	15
Liver	12,000 FW	15
Total tetra-chlorobiphenyls (PCBs 56, 60, 66, and 74); carcass vs. liver	1,490 FW vs. 450 FW	15
Total penta-CBs (PCBs 99, 101, 105, 110, and 118); carcass vs. liver	7,440 FW vs. 2,050 FW	15
Total hexa-CBs (PCBs 128, 132, 137, 138, 141, 146, 149, 153); carcass vs. liver	19,900 FW vs. 5,100 FW	15
Total hepta-CBs (PCBs 170, 171, 172, 174, 177, 178, 180, 182, 183, 187, 190, 197); carcass vs. liver	14,400 FW vs. 3,700 FW	15
Total octa-CBs carcass vs. liver	3,400 FW vs. 860 FW	15
Eggs		
Total PCBs	16,000 FW	15
Total tetra-CBs	560 FW	15
Total penta-CBs	2,880 FW	15
Total hexa-CBs	7,250 FW	15
Total hepta-CBs	4,340 FW	15
Total octa-CBs	860 FW	15

Table 11. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
Yellow-legged herring gull, *Larus cachinnans*; eggs; Italy, 1981-86		
Total PCBs (30 congeners)	30,400-56,100 DW	16, 17
PCB 138	4,600-6,800 DW	16
PCB 153	7,800-14,100 DW	16
PCB 180	3,900-7,000 DW	16
Audouin's gull, *Larus audouinii*; eggs		
Italy, 1981-86; total PCBs	28,600-45,900 DW	17
Spain, 1988		
Total PCBs	9,000 (4,700-20,500) FW	12
PCB 138	Max. 1,800 FW	12
PCB 153	Max. 1,600 FW	12
PCB 180	Max. 1,300 FW	12
Red-breasted merganser, *Mergus serrator*, eggs; Michigan; 1977-78 vs. 1990		
Total PCBs	23,000 FW vs. 11,100 FW	28
PCB 77	24 FW vs. 20 FW	28
PCB 81	5 FW vs. 3 FW	28
PCB 126	13 FW vs. 6 FW	28
PCB 169	1.6 FW vs. 0.9 FW	28
PCB 105	454 FW vs. 205 FW	28
PCB 118	847 FW vs. 415 FW	28
PCB 101	246 FW vs. 115 FW	28
PCB 138	1,417 FW vs. 659 FW	28
PCB 153	2,313 FW vs. 1,221 FW	28
PCB 180	641 FW vs. 327 FW	28
Black kite, *Milvus migrans*; infertile eggs; total PCBs; Spain, 1985-86	2,900 (500-18,700) FW	7
Black-crowned night heron, *Nycticorax nycticorax*; embryos; total PCBs		
Control site, Virginia	1,130 (240-4,000) FW	18
Cat Island, Green Bay, Wisconsin	9,300 (2,400-53,000) FW	18
San Francisco Bay	900-2,600 (ND-12,000) FW	18
Osprey, *Pandion haliaetus*; liver vs. eggs; Norway, 1965-83; dead on collection	5,000 (<100-26,000) FW vs. 3,200 (700-8,300) FW	1
Double-crested cormorant, *Phalacrocorax auritus*; eggs; Great Lakes; total PCBs	900-7,300 FW; reduced hatch at >6,500 FW	27
Great cormorant, *Phalacrocorax carbo*; yolk sac; Netherlands		
PCB 105	Max. 25,000 LW	19
PCB 118	Max. 75,000 LW	19
PCB 156	Max. 20,000 LW	19
PCB 157	Max. 10,000 LW	19
PCB 167	Max. 15,000 LW	19
Great cormorant, *Phalacrocorax carbo sinensis*; age <2 years vs. age >2 years; Germany, 1985-86		
Brain		
PCB 28	100 FW vs. 50 FW	20
PCB 52	100 FW vs. 100 FW	20
PCB 101	20 FW vs. 10 FW	20
PCB 138	300 FW vs. 900 FW	20
PCB 153	200 FW vs. 1,500 FW	20
PCB 180	100 FW vs. 600 FW	20

Table 11. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
Liver		
PCB 28	200 FW vs. 100 FW	20
PCB 52	80 FW vs. 100 FW	20
PCB 101	100 FW vs. 50 FW	20
PCB 138	800 FW vs. 2,400 FW	20
PCB 153	800 FW vs. 3,700 FW	20
PCB 180	300 FW vs. 1,000 FW	20
Subcutaneous fat		
PCB 28	1,000 FW vs. 1,400 FW	20
PCB 52	400 FW vs. 1,200 FW	20
PCB 101	800 FW vs. 6,100 FW	20
PCB 138	13,000 FW vs. 85,000 FW	20
PCB 153	20,000 FW vs. 93,000 FW	20
PCB 180	5,800 FW vs. 53,000 FW	20
White spoonbill, *Platalea leucorodia*; infertile eggs; total PCBs; Spain, 1985-86	600 (400-1,300) FW	7
Caspian tern, *Sterna caspia*; blood plasma; total PCBs (Aroclors 1242, 1248, 1254, 1260); Great Lakes, 1990		
Green Bay	3,500 (900-13,800) FW	21
Saginaw Bay	2,500 (1,600-3,800) FW	21
Other locations	900-2,100 (400-3,600) FW	21
Forster's tern, *Sterna forsteri*; whole eggs and chicks; total PCBs; Green Bay, Wisconsin; 1988 vs. 1989	Max. 5,100-9,500 FW vs. Max. 3,800-8,500 FW	9, 22
Common tern, *Sterna hirundo*; eggs and chicks; total PCBs; Green Bay, Wisconsin, 1989	5,000-14,100 FW	9
Arctic tern, *Sterna paradisaea*; prefledgling carcass; German Wadden Sea, 1988; found dead; age 2-14 days vs. age 15-27 days		
PCB 26	2,800 LW vs. 500 LW	23
PCB 44	200 LW vs. 40 LW	23
PCB 49	200 LW vs. 40 LW	23
PCB 128	2,200 LW vs. 400 LW	23
PCB 138	15,800 LW vs. 4,000 LW	23
PCB 153	25,700 LW vs. 5,000 LW	23
PCB 180	8,600 LW vs. 1,700 LW	23
PCB 183	2,200 LW vs. 300 LW	23
PCB 187	3,300 LW vs. 600 LW	23
PCB 194	700 LW vs. 20 LW	23
Tawny owl, *Strix aluco*; liver vs. eggs; total PCBs; Norway, 1965-83; dead on collection	700 (<100-70,000) FW vs. 1,100 (300-6,600) FW	1
Northern gannet, *Morus bassanus*; total PCBs (35 congeners); England, 1988-90		
Fat	14,600 FW; 18,000 LW	5
Liver	700 FW; 184,000 LW	5
Muscle	2,900 FW; 20,000 LW	5
Tree swallow, *Tachycineta bicolor*; eggs and chicks; total PCBs; Green Bay, Wisconsin, 1989	10,800-13,100 FW	9
Guillemot, *Uria aalge*; total PCBs (35 congeners); England, 1988-90		
Brain	Max. 3,200 FW;	5

Table 11. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
Fat	Max. 56,000 LW Max. 450,000 FW;	5
Gizzard and contents	Max. 659,000 LW Max. 137,000 FW;	5
Kidney	Max. 563,000 LW Max. 5,900 FW;	5
Liver	Max. 321,000 LW Max. 1,500 FW;	5
Muscle	Max. 354,000 LW Max. 1,100 FW;	5
Waterfowl, 8 species; eggs; total PCBs;Italy	Max. 67,000 LW 500-24,000 DW	24

[a] Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

[b] 1, Froslie et al. 1986; 2, Elliott and Shutt 1993; 3, Borlakoglu et al. 1991b; 4, Hernandez et al. 1989; 5, Boumphrey et al. 1993; 6, Kennedy et al. 1992; 7, Hernandez et al. 1988; 8, Ormerod and Tyler 1994; 9, Jones et al. 1993; 10, Jarman et al. 1993; 11, Zupancic-Kralj et al. 1992; 12, Gonzalez et al. 1991; 13, Falandysz et al. 1994a; 14, Blumton et al. 1990; 15, Braune and Norstrom 1989; 16, Focardi et al. 1988a; 17, Leonzio et al. 1989; 18, Rattner et al. 1993; 19, van den Berg et al. 1992; 20, Scharenberg 1991b; 21, Mora et al. 1993; 22, Ankley et al. 1993; 23, Scharenberg 1991a; 24, Focardi et al. 1988b; 25, Smith et al. 1985; 26, Turle et al. 1991; 27, Jones et al. 1994; 28, Williams et al. 1995.

PCB 153 is the most widespread PCB in the environment because it is easily stored and retained in adipose tissue; PCB 153 was the main PCB congener in eggs of eight examined species of Italian waterfowl and accounted for 11.4-21.2% of the total PCB concentration (Focardi et al. 1988b). Infertile eggs of the endangered imperial eagle (*Aquila heliaca adalberti*) contained as much as 28.9 mg total PCBs/kg FW; PCB 153 constituted 13.5% of the total PCB loading, PCB 180 13%, PCB 138 3.2%, PCB 101 3.2%, and PCB 118 0.7% (Hernandez et al. 1989). In the endangered Audouin's gull (*Larus audouinii*), most (62%) of the total PCB burden consisted of PCBs 153, 138, 170, and 180; other important congeners were PCBs 118, 194, and 203, and each contributed about 5% (Leonozio et al. 1989). PCBs 138, 153, and 180 comprised more than 50% of the total PCB burden in eggs of the yellow-legged herring gull (*Larus cachinnans*); a similar case is made for eggs of other species of marine birds (Focardi et al. 1988a). PCBs 138, 153, and 180 were also dominant in tissues of most birds collected in Great Britain between 1988 and 1990, although total PCB concentrations ranged from 0.02 to 105 mg/kg FW and also differed considerably in different tissues from individual birds (Boumpherey et al. 1993). PCBs 138 and 153 were the most prominent congeners in eggs of 3 species of gulls collected in Spain during 1988, accounting for 10.5% and 8.7%, respectively, of the total PCB burden; other important congeners were PCBs 180 (7.5%), 170 (3.2%), 101 (1.9%), 151 (1.1%) and 194 (0.9%; Gonzalez et al. 1991).

PCB signatures in bird eggs are not constant. Eggs of the dipper (C*inclus cinclus*) from Wales and Ireland were dominated by PCB 118 in 1990, PCB 170 in 1991, and PCB 153 in 1992; 6 congeners accounted for 26-35% of the total PCBs in Welsh eggs and for 10-26% of the total in eggs from Ireland (Ormerod and Tyler 1992, 1994). In tissues of birds in Great Britain, the mono-*ortho* congeners—PCBs 105 and 118—made a high contribution (70%) to the TEF, whereas the non-*ortho* congeners (PCBs 77, 126, 169) contributed 20%, and the di-*ortho* congeners (PCBs 138, 153, 180) contributed 10% (Boumpherey et al. 1993). Young of all avian species sampled in Wisconsin accumulated PCBs 77, 105, 126, and 169. Chicks of Forster's terns (*Sterna forsteri*) had daily uptakes of 15 µg total PCBs, 0.07 µg PCB 77, 0.2 µg PCB 105, 0.006 µg for PCB 126, and 0.00014 µg PCB 169 (Ankley et al. 1993).

Concentrations of mono-*ortho* PCBs in yolk-sac of cormorants ranged from 10 to 250 mg/kg LW; high PCB residues in yolk were associated with increased cytochrome P450 and EROD activities and decreased thyroid hormone activity (van den Berg et al. 1992). Embryos of the black-crowned night heron (*Nycticorax nycticorax*) with the greatest burdens of total PCBs had increased cytochrome P450-associated monooxygenase activities and cytochrome P450 proteins, which suggests that cytochrome P450 may be a useful biomarker of exposure to

some PCB mixtures (Rattner et al. 1993). The absence of established thresholds for P450 induction indicates that more research is needed (Rattner et al. 1994) to make this a useful technique for evaluating PCB exposure.

Mammals

The highest total PCB concentrations recorded in terrestrial mammalian wildlife occurred in fat and liver tissues of species collected near urban areas; di-*ortho* congeners were the major contributors to PCB tissue burdens (Table 12). Atmospheric transport of PCBs governed uptake in terrestrial mammalian herbivores and predators; for example, PCB residues in tissues of voles and shrews in the Scandinavian peninsula directly correlated with fallout loadings (Larsson et al. 1990). An increase in atmospheric deposition of PCBs increased PCB burdens in plants, herbivores, and predators of the herbivores. But herbivores and predators differentially metabolized PCBs, raising concentrations of highly-chlorinated congeners in predators and concentrations of the more easily metabolized low-chlorinated PCBs in herbivores (Larsson et al. 1990).

Populations of mink (*Mustela vison*) declined in many areas of the world, and the declines were linked to exposures to synthetic halogenated hydrocarbons (Giesy et al. 1994b). In the Great Lakes region, mink density is lower along the shores of the Great Lakes and their tributaries where mink have access to fishes from the Great Lakes. Tissue PCB concentrations and their dioxin TEFs were considered critical in the hazard assessment of PCBs. Mink that consumed fishes below dams in Michigan were 10 to 20 times more likely to suffer PCB damage than mink consuming fishes from above the dams, as judged by the elevated concentrations of total PCBs and dioxin TEFs in fishes from below the dams (Giesy et al. 1994b). European polecats (*Mustela putorius*) collected in the Netherlands between 1985 and 1990 had PCB patterns that were independent of diet and seemed to be controlled by anal gland secretions containing elevated PCB residues (Leonards et al. 1994). Juvenile polecats contained higher PCB concentrations than adult males and females, and this is attributed to an increased elimination of PCBs by adults through anal gland secretions. In all examined polecat tissues, PCB 126 accounted for 63 to 98% of the 2,3,7,8-TCDD toxic equivalents (Leonards et al. 1994).

The use of PCBs in Germany was prohibited in 1989. From 1983 to 1991, the body fat of red foxes (*Vulpes*) in Germany showed a reduction in the mean concentration of highly-chlorinated PCBs (PCBs 138, 153, and 180) but an increase in the lower-chlorinated congeners (PCBs 24, 49, and 52). These findings suggest a trend toward a reduction of environmental contamination with highly-chlorinated biphenyls since 1983, perhaps as a consequence of metabolic degradation, whereas contamination with lower-chlorinated biphenyls from diverse sources is increasing (Georgii et al. 1994). Low-chlorinated congeners that are metabolized via reactive intermediates must be evaluated because they show weak tumor-initiating properties (Georgii et al. 1994).

Populations of bats in Europe have been declining, and PCBs together with pesticides and wood preservatives are the suspected main causes of the decline (Fernandez et al. 1993). Three species of bats collected in Spain in 1988-90 contained only a few dominant PCB congeners; PCBs 138, 153, and 180 accounted for about 80% of the total PCB burden in whole bats (Fernandez et al. 1993). But the most abundant PCB congeners in brain and liver of European otters (*Lutra*) were in the descending order of PCBs 163, 153, 138, and 170, each constituting at least 10% of the total PCB burden (Mason and Ratford 1994).

The PCB composition in tissues of polar bears (*Ursus maritimus*) suggest that polar bears—unlike other mammals—can readily metabolize PCB congeners with unsubstituted *para* positions and unsubstituted adjacent *ortho-meta* positions (Norheim et al. 1992). Six PCB congeners (PCBs 99, 138, 153, 170, 180, 194)—all with a minimum 2,2',4,4'-chlorine substitution—accounted for about 99% of the total PCB content in liver and 87% in fat; PCB 153 accounted for 37% of the total PCB loading in liver and 30% in fat. The PCB congener pattern in polar bear liver and adipose tissue is similar and seems to be independent of sex, age, nutritional status, collection locale, and PCB body burden (Norheim et al. 1992).

Lethal and Sublethal Effects

General

In all tested organisms, PCBs—especially PCBs with 2,3,7,8-TCDD-like activity—adversely affected patterns of survival, reproduction, growth, metabolism, and accumulation. Common manifestations of PCB exposure in animals include hepatotoxicity (hepatomegaly, necrosis), immunotoxicity (atrophy of lymphoid tissues, suppressed antibody responses), neurotoxicity (impaired behavior and development, catecholamine

alterations), increased abortion, low birth weight, embryolethality, teratogenicity, gastrointestinal ulceration and necrosis, bronchitis, dermal toxicity (chloracne, edema, hyperplasia), weak mutagenicity at high doses, and preneoplastic changes at low doses (Hansen 1987). At concentrations above a threshold, PCBs are potent promoters of hepatic carcinogenesis in laboratory rodents; however, there is no clear evidence of carcinogenicity of PCBs to human and animal populations from natural exposure (Hayes 1987). Induction of hepatic microsomal enzymes is one of the earliest and most sensitive responses to PCBs (Hansen 1987).

Table 12. PCB concentrations in field collections of selected mammals. Concentrations are in ug/kg (ppb) fresh weight (FW) or lipid weight (LW).

Table 12. Species, tissue, PCB congener, and other variables	**Concentration[a] in ug/kg**	**Reference[b]**
Bats; whole body less wings, feet, and head; total PCBs; Spain, 1988-90		
Schreiber's bat, *Miniopterus schreibersi*	760 LW	1
Common pipistrelle, *Pipistrellus pipistrellus*	1,290 LW	1
Greater horseshoe bat, *Rhinolophus ferrumequinum*	480 LW	1
All species		
Madrid vs other locations	2,980 LW vs. <560 LW	1
Immatures vs. adults	1,940 LW vs. 800 LW	1
Domestic dog, *Canis familiaris*; muscle fat; Germany, 1987		
PCB 28	<1 LW	2
PCB 49	5 (6-8) LW	2
PCB 52	<1 LW	2
PCB 101	3 (ND-9) LW	2
PCB 138	11 (3-25) LW	2
PCB 153	22 (7-58) LW	2
PCB 180	47 (6-153) LW	2
Human, *Homo sapiens*		
Adipose tissue; United States; 1982 vs. 1986		
Tetra-CBs	16 FW vs. 56 FW	7
Penta-CBs	78 FW vs. 135 FW	7
Hexa-CBs	176 FW vs. 314 FW	7
Hepta-CBs	85 FW vs. 125 FW	7
Total PCBs	407 FW vs. 672 FW	7
Maternal milk; New York State, 1988-90; maximum values		
PCB 77	1.3 LW	3
PCB 81	1.1 LW	3
PCB 105	6.7 LW	3
PCB 114	1.3 LW	3
PCB 118	8.7 LW	3
PCB 123	6.2 LW	3
PCB 126	3.6 LW	3
PCB 156	3.2 LW	3
PCB 157	9.4 LW	3
PCB 167	8.8 LW	3
PCB 169	ND	3
PCB 189	4.7 LW	3
Total PCBs	52.9 (3.4-179) LW; 1.5 FW	3
European otter, *Lutra lutra*; total PCBs		
Ireland; brain vs. liver	4,700 (1,200-14,400) LW vs. 42,800 (18,500- 92,100) LW	4
Denmark; liver	58,000 (22,000-104,000) LW	4

Table 12. Species, tissue, PCB congener, and other variables	Concentration[a] in ug/kg	Reference[b]
England; liver	51,000 (2,000-190,000) LW	4
European polecat, *Mustela putorius*; the Netherlands, 1985-90		
Anal gland		
Total PCBs	32,000 (5,000-104,000) LW	5
Non-*ortho* PCBs	6.9 LW	5
Di-*ortho* PCBs	28,000 (4,000-88,000) LW	5
Mono-*ortho* PCBs	3,700 (700-13,000) LW	5
Fat (mesenteric)		
Total PCBs	51,000 (1,000-370,000) LW	5
Non-*ortho* PCBs	2.7 LW	5
Di-*ortho* PCBs	49,000 (2,000-350,000) LW	5
Mono-*ortho* PCBs	1,800 (100-11,000) LW	5
Kidney		
Total PCBs	22,000 (2,000-114,000) LW	5
Non-*ortho* PCBs	7.6 LW	5
Di-*ortho* PCBs	20,000 (1,000-107,000) LW	5
Mono-*ortho* PCBs	1,100 (200-4,200) LW	5
Liver		
Total PCBs	48,000 (4,000-260,000) LW	5
Non-*ortho* PCBs	5.5 LW	5
Di-*ortho* PCBs	45,000 (4,000-248,000) LW	5
Mono-*ortho* PCBs	1,200 (300-3,400) LW	5
Muscle		
Total PCBs	28,000 (3,000-150,000) LW	5
Non-*ortho* PCBs	2.8 LW	5
Di-*ortho* PCBs	26,000 (3,000-140,000) LW	5
Mono-*ortho* PCBs	1,300 (200-5,700) LW	5
Polar bear, *Ursus maritimus*; total PCBs; Norway, 1978-89; liver vs. fat		
Adults	13,000 FW vs. 31,000 FW	6
Juveniles	12,000 FW vs. 15,000 FW	6
Red fox, *Vulpes vulpes*; muscle fat; Germany, 1983 vs. 1991; maximum values		
PCB 28	160 LW vs. 50 LW	2
PCB 49	<1 LW vs. 30 LW	2
PCB 52	130 LW vs. 50 LW	2
PCB 101	240 LW vs. 90 LW	2
PCB 138	2,720 LW vs. 310 LW	2
PCB 153	4,300 LW vs. 1,000 LW	2
PCB 180	7,890 LW vs. 2,080 LW	2

[a] Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

[b] 1, Fernandez et al. 1993; 2, Georgii et al. 1994; 3, Hong et al. 1994; 4, Mason and Ratford 1994; 5, Leonards et al. 1994; 6, Norheim et al. 1992; 7, USEPA 1994.

PCB-induced toxicity patterns are highly variable. Variability, as discussed later, is attributed in part to differences between species and strains in ability to metabolize PCBs and in primary sites of action; in the age, growth rate, biomass, and lipid content of the species; in dose rate, duration of exposure, route of administration, and tested congeners; in physicochemical characteristics of the habitat during exposure; and in PCB interactions with other PCBs, other organochlorine compounds, and heavy metals. Chinook salmon (*Oncorhynchus tshawytscha*) had decreased hatch when eggs contained the equivalent of 0.1 ug 2,3,7,8-TCDD/kg fresh weight (FW); domestic chickens (*Gallus* sp.) had decreased survival and increased

developmental abnormalities when embryos had 20 µg PCB 77/kg FW; mink (*Mustela vison*) had reduced growth when fed 100 µg Aroclor 1254/kg BW daily and reduced survival at 50 µg PCB 169/kg diet; rhesus macaques (*Macaca mulatta*) had reproductive impairment when fed more than 8 µg Aroclor 1016/kg BW daily; and rats (*Rattus* sp.) had reduced litter sizes and survival when given 10 µg PCB 126/kg BW daily during gestation.

Aquatic Organisms

PCBs influence patterns of survival, reproduction, growth, enzyme activities, and accumulation in representative aquatic organisms (Table 13). Some PCB congeners at laboratory concentrations that were several orders of magnitude higher than those encountered under field conditions killed 47 to 83% of tested freshwater fishes and invertebrates in 24-48 h; however, most PCB tested congeners produced negligible mortality under these conditions (Dillon and Burton 1992; Table 13). Mortality increased when PCB 133 or PCB 177 concentrations in whole guppies (*Poecilia reticulata*) exceeded 1 µmole/g, equivalent to more than 200 mg PCB/kg whole body FW or about 4,000 mg PCB/kg on a lipid weight basis (Opperhuizen and Schrap 1988). PCBs—especially those with TCDD-type activity—adversely affect reproductive success of spawning female chinook salmon. Chinook salmon eggs that contained total PCB concentrations equivalent to 0.1 µg 2,3,7,8-TCDD equivalents/kg eggs and higher had a dose-dependent decrease in hatching success (Ankley et al. 1991). PCBs also impair the reproductive capacities of marine mammals (Kannan et al. 1993).

Table 13. Effects of PCBs on representative aquatic organisms.

Table 13. Taxonomic group, organism, PCB congener, dose, and other variables	**Effect**	**Reference[a]**
Invertebrates		
Daphnid, *Daphnia magna*; early life stages		
PCB 1; 710 ug/L	LC50 (24h)	1
PCB 2; 430 ug/L	LC50 (24h)	1
PCB 3; 420 ug/L	LC50 (24h)	1
PCB 18; 86 ug/L	47% dead in 48 h	
PCBs 28 (1.5 ug/L), 52 (74 ug/L), 77 (0.3 ug/L), 101 (1.2 ug/L), 116 (2.8 ug/L), 128 (0.4 ug/L), 153 (1.3 ug/L), 171 (1.7 ug/L), 194 (3.0 ug/L)	Negligible mortality; 87-100% survival in 48 h	1
PCB 47; 30 ug/L	LC50 (24h)	1
Zebra mussel, *Dreissena polymorpha*		
Fed alga (*Chlorella* sp.) containing 500 mg PCB 77/kg for 32 days	Maximum tissue concentration of 3.4 mg PCB 77/kg fresh weight soft parts reached in about 14 days; concentration dropped to about 2 mg/kg after 32 days	2
Fed *Chlorella* containing 500 mg PCB 169/kg for 50 days, then clean *Chlorella* diet for 45 days	Maximum tissue concentration of 3.7 mg PCB 169/kg soft parts reached in 10 days, then decline during exposure to equilibrium level of about 1 mg/kg soft parts. After 25 days of clearance, soft parts contained 0.1 mg/kg fresh weight	2

Table 13. Taxonomic group, organism, PCB congener, dose, and other variables	Effect	Reference[a]
Amphipod, *Gammarus pseudolimnaeus*		
PCBs 8, 15, 32, 155, 101; initial water concentrations of 70-210 ug/L	LC50 (96h)	1
Mysid, *Mysis relicta*; exposed to radiolabeled PCB 153 for 6 h at 4^{o}C then transferred to clean water for 26 days	Bioconcentration factor from water of 442,230; calculated half-time persistence of 220 days	10
Amphipod, *Pontoporeia hoyi*; exposed to radiolabeled PCB 153 for 6 h at 4^{o}C then transferred to clean water for 26 days	Bioconcentration factor from water of 101,660; calculated half-time persistence of 50 days	10
Vertebrates		
Rainbow trout, *Oncorhynchus mykiss*		
Eggs injected 24 to 50 h after fertilization with graded doses of various PCBs		
PCB 4; >24,200 ug/kg egg fresh weight (FW)	LD50, embryos	13
PCB 28; >24,300 ug/kg egg FW	LD50 embryos	13
PCB 52; >30,400 ug/kg egg FW	LD50, embryos	13
PCB 77		
0.578 ug/kg egg FW	At age 35 days, sac-fry contained 78% of original dose	13
1,348 (1,064-1,621) ug/kg egg FW	LD50, embryos; blue-sac syndrome	13, 14
PCB 81; 549 ug/kg egg FW	LD50, embryos; blue-sac syndrome	13
PCB 105		
67 ug/kg egg FW	At sac-fry stage 78% of original dose remained	13
>6,970 ug/kg egg FW	LD50, embryos	14
PCB 118		
1,330 ug/kg egg FW	About 81% of original dose present in sac-fry	13
>6,970->57,400 ug/kg egg FW	LD50, embryos	13, 14
PCB 126		
74 (44-83) ug/kg egg FW	LD50, embryos	13, 14
1,203 ug/kg egg FW	About 88% recovered from embryos	13
PCBs 128, 138, and 156; >115,000 ug/kg egg FW	LD50, embryos	13
PCB 153; >6,200 ug/kg FW	LD50, embryos	14
PCB 169; 7,110 (5,630-8,090) ug/kg egg FW	LD50, embryos; blue-sac syndrome	13
PCB 170; >41,100 ug/kg egg FW	LD50, embryos	13
Single intraperitoneal (ip) injection; 134 ug/kg BW of PCB 77; or 5.8 ug/kg BW of PCB 126; or 93.7 ug/kg BW of PCB 169; subadults	50% increase in liver EROD activity	12
Single ip injection of 1.0 mg PCB 77/kg BW; livers analyzed 13 days postinjection; subadult	Compared to controls, livers were elevated in levels of cytochrome P-450 (2X), ethoxycoumarin-*O*-deethylase (10X) and ethoxyresorufin-*O*-deethylase (50X)	3
Injected ip with 2,3,7,8-TCDD at 0.00037, 0.0022 or 0.0045 umol/kg BW, or with PCB 77 at 0.2, 1.1, or 2.2 umol/kg BW; subadults	50% induction of AHH (arylhydrocarbon hydroxylase) activity in liver microsomes of sexually immature trout at 0.002 umol/kg for TCDD and 0.37 umol/kg for PCB 77	3

Table 13. Taxonomic group, organism, PCB congener, dose, and other variables	Effect	Reference[a]
Single ip injection of mixture of 0.00018 umol TCDD/kg BW plus 0.1 umol/kg PCB 77; or mixture of 0.0011 umol TCDD/kg BW plus 0.6 umol PCB 77/kg BW; subadults	Mixtures of TCDD and PCB 77 produced greater than additive AHH responses	3
Single ip injection of mixture of 0.0022 umol TCDD/kg BW plus 1.1 umol PCB 77/kg BW; subadults	AHH induction response was less than additive	3
Single ip injection of PCB 77, PCB 126, or 2,3,7,8-TCDD. Liver AHH activity measured 3 days later; subadults	50% AHH induction occurred at 0.005 umol/kg BW for TCDD, 1.0 for PCB 77 and 2.2 for PCB 126. PCB 77 was 1/200 as effective in inducing AHH activity in liver as TCDD, and PCB 126 was 1/500 as effective	4
Single ip injection of 30 mg PCB 118/kg BW to immatures. Fish killed 4 days later and liver analyzed	Liver EROD (7-ethoxyresorufin *O*-deethylase) activity was 5.6 times higher than controls; AHH activity was 2.7 times higher than controls	5
Fingerlings were injected ip with ^{14}C-labeled PCB mixture at 0.3, 1, 3, 10, and 30 mg PCB/kg BW; tissues sampled up to 70 days postinjection.	At 3 days postinjection high doses of 10 and 30 mg PCB/kg BW caused elevation of liver microsomal monooxygenase activity when maximum tissue concentrations, in mg total PCB/kg FW, were 55 in bile, 12 in blood, 8 in muscle, and 8 in liver. Elevated hepatic microsomal monooxygenase activity with muscle and liver PCB concentrations of >0.3 mg/kg FW, but not 0.25 mg/kg FW	6
Fathead minnow, *Pimephales promelas*; fry		
PCB 18; 86 ug/L	83% dead in 48h	1
PCBs 28 (1.5 ug/L), 52 (74 ug/L), 77 (0.3 ug/L), 101 (1.2 ug/L), 116 (2.8 ug/L), 128 (0.4 ug/L), 153 (1.3 ug/L), 171 (1.7 ug/L), 194 (3.0 ug/L)	Negligible mortality; 97-100% survival in 48h	1
Guppy, *Poecilia reticulata*; adult males		
Fed diets containing 6-150 mg PCB 133 or PCB 197/kg diet for 191-247 days, or 550-1,400 mg/kg diet for 65 days	At 6-150 mg/kg diet, uptake efficiency was near 50%; at higher dietary loadings uptake efficiency decreased to 25%. No deaths in controls or at low dietary dosages; 13-25% mortality at 550-1,400 mg/kg diet. Prior to death, guppies were sluggish, uncoordinated, and darkly-colored; fish that died during exposure contained >0.7 umol PCB/g FW	7

Table 13. Taxonomic group, organism, PCB congener, dose, and other variables	Effect	Reference[a]
Fed PCB 133 at 550 mg/kg diet FW or PCB 197 at 530 mg/kg diet FW for 65 days, followed by a clean diet for 89 days, then reexposure to the contaminated diet for another 37 days	No PCB clearance during initial exposure; significant elimination of both PCBs when fed a clean diet. During reexposure, uptake efficiency for both PCBs was significantly higher than during the initial exposure.	8
Scup, *Stenotomus chrysops*		
Injected intraperitoneally with 1,5, or 10 mg/kg BW of PCBs 77, 105, 118, 128, or 138 and examined for increases in ethoxyresorufin *O*-deethylase (EROD) activity, immunodetectable cytochrome P450E (the EROD catalyst in scup) and in vitro translatable MRNA for P450E	Monooxygenase parameters were significantly induced only by PCB 77; translatable MRNA for P450E was induced at all doses; EROD activity and P450E were decreased at the 5 and 10 mg/kg BW doses; a positive correlation was established between PCB 77 residues in liver and decreased EROD activity at the higher doses	9

[a]1, Dillon and Burton 1992; 2, Brieger and Hunter 1993; 3, Janz and Metcalfe 1991b; 4, Janz and Metcalfe 1991a; 5, Skaare et al. 1991; 6, Melancon et al. 1989; 7, Schrap and Opperhuizen 1988; 8, Opperhuizen and Schrap 1988; 9, Gooch et al. 1989, 10, Evans and Landrum 1989; 11, Tyle et al. 1991; 12, Newsted et al. 1995; 13, Zabel et al. 1995; 14, Walker and Peterson 1991.

The relation between PCB accumulation by the freshwater alga *Scenedesmus* sp. and the compound's octanol/water partition coefficient (K_{ow}) was measured with 40 PCB compounds in a log K_{ow} range of 4.46 to 8.18, PCB concentrations between 0.03 and 1.1 µg/L, and exposures between 20 and 30 days (Swackhammer and Skoglund 1993). The accumulation process was consistent with partitioning from water into cell lipids but was slower than the growth of *Scenedesmus* (i.e., no significant uptake of PCBs from congeners with log K_{ow} > 5.0 under conditions of rapid growth or log > 7.0 under conditions of slow growth). Thus, under nonwinter field conditions, many PCB congeners never reached equilibrium concentrations (Swackhammer and Skoglund 1993). Similar results are reported of other species of freshwater algae, including *Selenastrum capricornutum*, *Anabaena* sp., and *Synedra* sp. (Stange and Swackhammer 1994).

Zebra mussels (*Dreissena polymorpha*) accumulated PCB 77 from their diet and from the surrounding lake sediments (Brieger and Hunter 1993). An uptake rate of PCB 77 by zebra mussels followed the descending order of sediment, food, and water. Tissue concentrations in mussels peaked after 10-14 days at 3.4-3.7 mg PCB 77/kg FW soft parts; equilibrium levels of PCB 77 were near 1.0 mg/kg FW. Zebra mussels are more efficient accumulators of PCBs than other bivalve molluscs to which they are attached; accordingly, high densities of zebra mussels probably influence contaminant dynamics (Brieger and Hunter 1993). A freshwater crustacean (*Mysis relicta*) plays an important role in the transfer of PCBs from sediments into the Lake Champlain food web (Lester and McIntosh 1994), and freshwater grazing and shredding benthic invertebrates promote downstream transport of PCB 153 (Sallenave et al. 1994). Marine invertebrates accumulated PCBs 52, 101, 128, 138, 151, 153, 180, 194, 206, and 209 from PCB-contaminated sediments (Pruell et al. 1993). Clams (*Macoma nasuta*) reached a steady state equilibrium in 10 days, but sandworms (*Nereis virens*) took 70-120 days. Clams showed preferential accumulation of lower molecular weight PCB congeners, and this may be due to the comparatively low lipid content in this species. Sandworms and grass shrimp (*Palaemonetes pugio*) metabolized PCBs 52, 101, and 151 (Pruell et al. 1993).

Golden shiners (*Notemigonus crysoleucas*) rapidly accumulated radiolabeled PCBs from water during 96-h exposure (Karara and McFarland 1992). The uptake rate of PCBs from water was controlled by gill blood-flow rate. About 50% of the accumulated PCBs in shiners was eliminated in 4.9 days, and this is similar to PCB elimination rates in striped bass (*Morone saxatilis*) and channel catfish (*Ictalurus punctatus*; Karara and McFarland 1992). In guppies, residual PCB concentrations increased with increasing duration of exposure; however, steady state concentrations did not occur after dietary exposure for 65 days (Schrap and Opperhuizen

1988). PCB congeners with *ortho*-chlorine substitutions (PCBs 77, 105, 118, 128, 138) were effective inducers of EROD (7-ethoxyresorufin *O*-deethylase) and AHH (aryl hydrocarbon hydroxylase) activities in marine mammals (Gooch et al. 1989) and freshwater fishes (Janz and Metcalfe 1991a; Skaare et al. 1992) but were ineffective at doses as high as 10 mg/kg BW in scup (*Stenotomus chrysops*), a marine teleost (Gooch et al. 1989). Industrial mixtures of planar and nonplanar PCBs induced AHH in fishes (Skaare et al. 1991). Mixtures of planar PCBs and dioxins, however, produced synergism of AHH activity in fish liver at low doses and antagonism at high doses; the possible antagonistic effects on nonplanar halogenated compounds may further complicate these interactions (Janz and Metcalfe 1991b). Liver is the primary target organ for the induction of cytochrome P450-dependent monooxygenases by PCBs in fishes, and the most frequently examined organ; however, in salmonids, muscle tissue is also suitable for evaluation of hepatic monooxygenase induction, as judged by PCB concentrations in muscle (Janz et al. 1992).

Birds

PCB 126 is among the most toxic of all PCB congeners to birds and the domestic chicken is the most sensitive tested species (Table 14; Hoffman et al. 1995). However, adverse effects of PCBs in birds vary markedly between species and tissues. And birds react differently to different PCB congeners and to PCB-metal mixtures. American kestrels (*Falco sparverius*) differ from Japanese quail (*Coturnix japonica*) after exposure to PCBs 105, 126, and 153; quail accumulated porphyrins in liver but kestrels did not (Elliott et al. 1991). Japanese quail dosed with PCBs 47 or 77 showed marked differences between the abilities of the small intestines and liver to metabolize porphyrin and the induction of cytochrome P450 isozymes and associated monooxygenases (Miranda et al. 1987). Pure hexachlorobiphenyls (HCBs) caused uroporphyrin accumulations and increased delta-aminolevulinic acid synthetase activity in chicken livers, and some HCBs significantly increased cytochrome P450 and *p*-nitrophenol glucuronyl transferase when given in the feed for 3 weeks at 400 mg/kg ration; however, PCBs 128 and 169 caused grosser accumulations of hepatic porphyrins than PCBs 138, 155, and 156 (Goldstein et al. 1976, 1977). PCBs 77, 136, 153, and 159 produced acute histopathological changes in chick embryo livers and selectively induced cytochrome P448-mediated mixed function oxidases; the degree of histopathologic change produced by each of the tested PCBs positively correlated with the degree of P448 inhibition (Rifkind et al. 1984). Interactions of metals with PCBs are not well documented, although some studies with Japanese quail showed that cadmium raises PCB uptake from the diet. In one study, cadmium fed at high dietary levels of 100 mg/kg ration interfered with high levels of dietary PCBs (100 mg/kg ration). In that study, muscle of treated quails had increased loadings of congeners chlorinated in the 2,4,5 position (such as PCBs 138, 153, 170, and 180), and these are comparatively toxic and resistant to metabolic degradation (Leonzio et al. 1992). More research is needed on variables known to modify PCB uptake, retention, translocation, and toxicity.

Table 14. Effects of PCBs on selected birds.

Table 14. Species, PCB congener, dose, and other variables	**Effect**	**Reference[a]**
Mallard, *Anas platyrhynchos*; PCB 77		
Single injection into egg yolk on day 5 of incubation		
0.1 mg/kg egg fresh weight (FW)	No effect on hatching rate; chicks normal	1
5.0 mg/kg egg FW	No effect on embryo survival and no gross abnormalities	2
Greylag goose, *Anser anser*		
PCB 77; single injection into egg yolk on day 5 of incubation; 1.0 mg/kg egg FW	No effect on survival or development	2
Goldeneye, *Bucephala clangula*	33% hatch vs. 52% hatch in	
PCB 77; single injection into egg yolk; 1.0 mg/kg egg FW	controls; chicks normal	1
Northern bobwhite, *Colinus virginianus*;	LD50 through hatching	16
PCB 126; single injection of egg with 0.04-0.07 mg/kg FW		
Japanese quail, *Coturnix japonica*	All compounds caused a significant	3
Adults given a single oral dose of either PCB 47 at 87.6 mg/kg body weight (BW),	increase in EROD activity and porphyrin content in small intestine	

Table 14. Species, PCB congener, dose, and other variables	Effect	Reference[a]
PCB 77 at 87.6 mg/kg BW, or Aroclor 1242 at 100 to 500 mg/kg BW. Quail were killed 48 h postdosing and liver and intestine analyzed for porphyrins and cytochrome P450 monooxygenases	and liver, and a significant increase in hepatic P450 content	
Adults fed diets for 30 days containing 100 mg cadmium/kg diet, 100 mg Aroclor 1260/kg diet, or mixture of 100 mg cadmium plus 100 mg Aroclor 1260/kg	Quail fed the mixture diet had 3 times more PCBs in muscle than the Aroclor group alone, and 70 times more PCBs than controls. The most dominant PCB congeners were 138, 153, 170, and 180	4
American kestrel, *Falco sparverius*		
Aroclor 1248; fed diets containing 3 mg/kg ration for 6 months; carcasses and egg analyzed for total PCBs (Aroclors 1248, 1254, and 1260)	Carcasses of adults had 18.5 mg total PCBs/kg FW (vs. 3.3 in controls); eggs had 5.6 mg/kg FW vs 1.5 in controls; shell thickness of eggs reduced 5%	5
Fed diets for 4 weeks containing daily doses equivalent to 3 mg PCB 105/kg BW, 0.05 mg PCB 126/kg BW, or 4.0 mg PCB 153/kg BW. Birds were killed 3 days after final treatment and livers analyzed for porphyrins, PCB residues, and activities of ethoxyresorufin *O*-deethylase (EROD), aminopyrine N-demethylase(APND), and aldrin epoxidase (AE)	PCB 105 caused significant APND induction; liver had 182.0 mg PCB 105/kg FW vs. 2.4 in corn oil controls PCB 126 induced hepatic EROD and AE; liver had 3.3 mg PCB 126/kg FW. PCB 153 induced APND and AE; liver contained 119.0 mg PCB 153/kg FW. For all dose groups, liver weights and liver porphyrin levels were normal	6
Nestlings given daily doses of PCBs 77, 105, or 126 for 10 days		
PCB 77; 1.0 mg/kg BW daily	Liver contained 892 ug PCB 77/kg FW; onset of liver necrosis	16
PCB 105; 4.0 mg/kg BW daily	Liver contained 1,677 ug PCB 105/kg FW; liver necrosis	16
PCB 126		
50 ug/kg BW daily	Liver contained 158 (68-563) ug PCB 126/kg FW; pronounced liver enlargement; lymphoid depletion of spleen	16
250 ug/kg BW daily	Liver had 380 ug PCB 126/kg FW	16
1.0 mg/kg BW daily	Liver had 1.1 (0.6-4.5) mg PCB 126/kg FW; decreased body weight	16
Egg injected through air cell with 70-100 ug PCB 126/kg FW	LD50 through hatching	16
Domestic chicken, *Gallus* sp.		
PCB 77; single dose injected into egg yolk on day 4 of fertilization		
0.0006 mg/kg egg FW	50% increase in AHH activity after 48 h	7
0.004 mg/kg egg FW	60% hatch vs. 88% in controls	1, 8
0.010 mg/kg egg FW	17% dead in 18 days; reduced thymus weight	7
0.020 mg/kg egg FW	70-100% dead by day 18; treated embryos had increased frequency of liver lesions, subcutaneous	1, 2, 8

Table 14. Species, PCB congener, dose, and other variables	Effect	Reference[a]
	edema, shortened beaks, and microphthalmia	
0.050 mg/kg egg FW	All dead within 18 days	7
0.100 mg/kg egg FW	Zero hatch; all dead	8
PCB 77; single dose injected into air sac on day 3 of incubation; 0.005 mg/kg egg FW	Whole liver homogenates had increases of 300-fold in 7 -ethoxycoumarin *O*-deethylase and 75-fold in AHH activities between days 5 and 10	15
PCB 77; single dose injected into air sac on day 13 of incubation		
0.045 mg/kg egg FW	Reduction by 50% in lymphoid cells in bursa of Fabricus	9
0.20-0.30 mg/kg egg FW	30-fold increase in AHH activity; bursa almost devoid of lymphoid cells	9
PCBs 77, 136, 153, 169; 17-day old embryos; single injection at 0.5-30,000 nmol/egg; examined for liver histopathology and induction of mixed function oxidases after 24 h	Significant alterations occurred at 0.5 nmol PCB 77/egg (about 0.003 mg/kg egg), at 5 nmol PCB 169/egg , and between 500 and 5,000 nmol PCB 153/egg. PCB 136 had no effect on liver pathology at the highest dose tested of 30,000 nmol/egg	10
Single injection of eggs of PCBs 105 (2.2 mg/kg FW), 126 (0.0006-0.0031 mg/kg FW), 157 (1.5-2.0 mg/kg FW), or 169 (0.17 mg/kg FW	LD50 through hatching	16
PCBs 128, 136, 153, 155, and 169; each was fed in diets to 1-day-old chicks for 21 days at 400 mg/kg ration		
PCB 128	Decrease in weight gain; moderate liver pathology; gross accumulations of hepatic porphyrins and increased delta-amimolevulinic acid synthetase activity	11, 12
PCB 136	Decrease in weight gain; comparatively small increase in liver weight	11
PCB 153	Decrease in weight gain; mild liver pathology	11
PCB 155	Largest increase in liver weight; significant liver pathology	11
PCB 169	All dead in 11 days; thymic involution and edema; gross accumulations of uroporphyrins in liver	11, 12
Herring gull, *Larus argentatus*		
PCB 77; single injection into egg yolk on day 5 of incubation; 1.0 mg/kg egg FW	No effect on survival or development	2
Black-headed gull, *Larus ridibundus*		
PCB 77; single injection into egg yolk of 1.0 mg/kg egg FW	No effect on hatching rate; chicks normal	1

Table 14. Species, PCB congener, dose, and other variables	Effect	Reference[a]
Wild turkey, *Meleagris gallopavo*		
PCB 77; single injection into air sac of 5-day-old embryos		
0.006 mg/kg egg FW	50% increase in AHH activity after 48 h	7
1.0 mg/kg egg FW	60% dead in 24 days	7
Ring-necked pheasant, *Phasianus colchicus*		
PCB 77; single injection into egg yolk		
0.1 mg/kg egg FW	No decrease in hatching rate; chicks normal	1
1.0 mg/kg egg FW	All embryos died	1
Common eider, *Somateria mollissima*; single injection into yolk on day 5 of incubation		
PCB 77; 1.0 mg/kg egg FW	No effect on survival	13
PCB 126; 0.1 mg/kg egg FW	35% dead on day 24 of incubation vs. 20% dead in controls	13
Common tern, *Sterna hirundo;*		
PCB 126; single egg injection with 0.045 mg/kg FW	35% embryo mortality through hatching	16
Ringed-turtle dove, *Streptopelia risoria*; fed iodine-deficient diet		
PCB 77; given 20 mg/kg BW 3 times over a 28-day period	Thyroid hyperplasia caused by low iodine diet was not enhanced by PCB 77	14
PCB 77; single dose of 60 mg/kg BW	Thyroid hyperplasia reversed within 7 days	14

[a] 1, Brunstrom and Reutergardh 1986; 2, Brunstrom 1988; 3, Miranda et al. 1987; 4, Leonzio et al. 1992; 5, Lowe and Stendell 1991; 6, Elliott et al. 1991; 7, Brunstrom and Lund 1988; 8, Brunstrom and Darnerud 1983; 9, Nikolaides et al. 1988; 10, Rifkind et al. 1984; 11, McKinney et al. 1976; 12, Goldstein et al. 1976; 13, Brunstrom et al. 1990; 14, Spear and Moon 1985; 15, Brunstrom 1986; 16, Hoffman et al. 1995.

Embryos of the domestic chicken (*Gallus* sp.) are unusually sensitive to PCB 77. Mortality and a high incidence of developmental abnormalities—including microphthalmia, beak deformities, edema, and retarded growth—were recorded in chicks at 0.02 mg PCB 77/kg egg FW, but no deaths or abnormalities were recorded in embryos of ducks, pheasants, and gulls at 0.1-1.0 mg PCB 77/kg egg FW (Table 14; Brunstrom and Lund 1988). Chicken embryos were 20 to 100 times more sensitive to PCB 77 than embryos of the wild turkey (*Meleagris gallopavo*), and this sensitivity emphasizes the uncertainties of applying toxicity data from one species of bird to predict toxic effects in other avian species (Brunstrom 1988; Brunstrom and Lund 1988). Differences in sensitivity of birds to PCB 77 may be related to differences in metabolism and in the formation of toxic metabolites and to the increased availability of Ah receptors in chicks (Brunstrom and Reutergardh 1986). For example, Ah receptors were detected in livers of 7-day-old chicken embryos but not in livers of 9-day-old turkey embryos (Brunstrom and Lund 1988).

Birds and mammals exposed to PCBs frequently react differently. PCBs generally elicit large-colloid goiters in birds; these goiters are inherently different from hyperplastic goiters produced in mammals exposed to PCBs (Spear and Moon 1985). Fish-eating seabirds, such as the razorbill (*Alca torda*), can rapidly metabolize PCB congeners that have at least one pair of adjacent unsubstituted *meta-para* combinations in the biphenyl moiety (Borlakoglu et al. 1991b). Razorbills metabolized 4-chlorobiphenyl to 4-chloro-4' hydroxybiphenyl; however, mice (*Mus* sp.) metabolized the same compound 15 times faster. PCB-exposed razorbills and rock doves (*Columba livia*) had similar concentrations of cytochrome P450 and glutathione-S-transferase enzymes, but concentrations were significantly higher in rats (*Rattus* sp.) than either avian species (Borlakoglu et al. 1991b). The relative potency of tested PCBs—as measured by EROD activity of microsomal liver enzymes—in fertile eggs of the domestic chicken were 0.02 for PCB 77, and less than 0.001 for PCB 169 (Bosveld et al. 1992); these values differ somewhat from those proposed for mammals of 0.0005 for PCB 77, and 0.01 for PCB 169 (Safe 1990). Lymphoid development in the bursa of Fabricius of the avian embryo is inhibited by TCDD-like congeners. PCB 77, for example, affects the immune system by interacting with the Ah receptor, causing

inhibition of lymphoid development in the mammalian thymus and in the avian bursa of Fabricius (Nikolaides et al. 1988). More research seems needed on the relation of avian Ah receptors to natural physiological processes.

Mammals

Deleterious effects were significant on growth, survival, reproduction, or metabolism from chronic exposures of sensitive species of tested rodents, primates, and mustelids to daily concentrations as low as 0.008 mg/kg BW of Aroclor 1016, 0.01-0.02 mg/kg BW of PCB 126, 0.01-0.05 mg/kg diet or 0.1 mg/kg BW of PCB 169, 0.09 mg/kg BW of Aroclor 1246, 0.1 mg/kg BW of Aroclor 1254, and 0.3-1.0 mg/kg diet or 0.6 mg/kg BW of PCB 77 (Table 15). Several PCBs had negligible adverse effects on tested mammals during chronic daily exposures to doses of at least 5 mg/kg ration or 5 mg/kg BW, specifically, PCBs 4, 15, 47, 52, 80, 136, 153, 155, and 167 (Table 15). Although subhuman primates seem to be more sensitive to reproductive and other adverse effects of PCBs than humans, no clear and convincing evidence associated PCB exposures with human cancers and reproductive problems (Kimbrough 1995). At present, no meaningful reproductive problems have been identified in female capacitor workers and no carcinogenicity was evident in humans having more than 1.0 mg total PCBs/L serum or more than 400 mg total PCBs/kg adipose fat (Kimbrough 1995).

Table 15. Effects of PCBs on selected mammals.

Table 15. Species, PCB congener, dose, and other variables	**Effect**	**Reference[a]**
Cotton top marmoset monkey, *Callithrix jacchus*		
PCB 77; adult females orally dosed with 0.1, 1.0, or 3.0 mg/kg body weight (BW) twice weekly for 18-28 weeks	Severe toxicity in the 3.0 mg/kg group that included body weight loss, hair loss, abnormal nail growth, scaly skin, anemia, elevated blood triglyceride and cholesterol levels, and tissue histopathology. Toxicity was less severe in the 1.0 mg/kg group and minor in the low-dose group	1
Rhesus macaque, *Macaca mulatta*		
Aroclor 1016		
>0.008 mg/kg BW daily via the diet	Adverse effects on reproduction	2
>0.028 mg/kg BW daily	Adverse effects on growth	2
Aroclor 1248; >0.09 mg/kg BW daily	Adverse effects on growth	2
Aroclor 1254; females were fed 0, 5, 20, 40, or 80 ug/kg BW daily for 6 years. During this time females were bred with non-dosed males. Resultant offspring were nursed for 22 weeks and fed no additional PCBs until they were necropsied at age 120 weeks	Total PCB concentrations in all tissues of adult females increased with increasing dosage; highest levels were in adipose tissue (Max. 141 mg/kg fresh weight [FW]; Max. 171 mg/kg lipid weight [LW]) and lowest in brain (1.1 mg/kg FW; 12.9 mg/kg LW). PCB concentrations were higher in infants from dosed dams than those nursed by controls; higher in females having a stillborn infant than those with a viable infant; and higher in those in poor health. The PCB distribution pattern in tissues from a dosed mother/infant pair was different: more hepta-chlorobiphenyls were found in the infant than in the dam	28
PCB 52		
Fed diets containing 3.0-5.0 mg/kg for 180-200 days	No clinical effects or pathologic lesions	3, 4

Table 15. Species, PCB congener, dose, and other variables	Effect	Reference[a]
PCB 77		
Fed diets containing 0.3-3.0 mg/kg ration for 1 to 6 months	Dose-and time dependent increase in chloracne; weight loss; death; and histopathology of sebaceous glands, thymus, and gastric mucosa	3
Fed diet containing 1.0 mg/kg ration for 38 days	Adverse effects on survival	4
Immature males fed diets containing 1.0 or 3.0 mg/kg ration	All were moribund in 7-14 weeks; abnormal gastric histology	5
Adult females received a total of 9 intragastric doses 20-40 days postconception; total doses were 0.6 or 3.15 mg/kg BW	All animals in both dose groups survived, but all aborted	4
Adult females given a single intravenous injection of 0.6 mg/kg BW; blood measured 1 h to 42 days postinjection	As a percentage of the total dose administered, PCB 77 concentrations in blood fell from 4.4% at 1 h to 0.14% at 42 days. About 60% of the total dose was excreted in feces, and 10% in urine	18
PCBs 136, 153, or 155; each fed in diet at 15-65 mg/kg ration for 63-122 days	No discernable deleterious effects	4
PCB 169; fed diet containing 400.0 mg/kg ration for 40 days	Concentrations in body fat increased steadily during exposure; recovery was protracted and incomplete during a 6-month observation period	4
Mouse, *Mus* sp.		
Aroclor 1254		
>1.3 mg/kg BW daily via diet	Adverse effects on reproduction	2
Single intraperitoneal injection of 500 mg/kg BW (a dose that promoted nitrosamine-initiated lung and liver tumors). The amounts of the 9 congeners that made up >90% of the PCBs present 1 day after treatment (PCBs 99, 105, 118, 128, 138, 153, 156, 170, 180) were quantified in liver, lung, and whole body for 112 days after dosing	In carcass fat, net PCB loss was attributed to metabolic loss of PCBs 105 and 138. In lung, all congeners except 153 were retained and decreased only as a function of dilution due to growth. In liver, all congeners were retained and 105 was enriched. Total PCBs in carcass averaged 80.8 mg/kg BW 24 h after treatment and about 10 mg/kg BW after 16 weeks; similar trends occurred in liver and lung. Tb 1/2 for PCB 153 was 81-101 days	6
PCB 15; pregnant mice given daily doses of 16, 32, or 64 mg/kg BW on days 6-15 of gestation and killed on day 18	Toxic to dams at 64 mg/kg BW daily, but no embryotoxicity	7
PCB 77		
Pregnant mice given 1, 2, 4, 8, 16, 32, or 64 mg/kg BW daily on days 6-15 of gestation and killed on day 18	Dose-dependent increase in incidence of malformed fetuses-especially cleft palate and hydronephrosis--at 4 mg/kg BW daily and higher. At 16 mg/kg BW and higher, dams had dose-dependent increase in weight loss, frequency of	7

Table 15. Species, PCB congener, dose, and other variables	Effect	Reference[a]
	vaginal bleeding, and other evidence of abortion	
Pregnant mice given single intravenous injection of 3.5 mg/kg BW of ^{14}C-labeled PCB 77 on days 4-17 of gestation and killed 4-96 h later	Radioactivity levels were elevated in uterine fluid and in fetuses in late gestation. No unmetabolized PCB 77 was detected in fetuses but PCB 77 metabolites (including 3,3',4,4'-tetrachloro-2-biphenylol, and methylsulphonyl- tetrachloro-biphenyl) were found in fetuses in late gestation	8
Strain C57BL/R_{ij} given single intraperitoneal injection		
15 mg/kg BW	30-40% reduction of retinol and retinyl palmitate concentrations in liver within 2-4 days	9
17 mg/kg BW	50% reduction in hepatic retinyl palmitate	9
32 mg/kg BW	50% reduction in hepatic retinol	9
Strain DBA/2; single intraperitoneal injection of 729 mg/kg BW	No reduction in hepatic retinoids	9
Single oral dose of 25, 50, or 100 mg/kg BW given to Ah-responsive pregnant mice on gestation day 11, 12, or 13; mice killed on day 18 of gestation	Dose-dependent increase in embryo deaths, resorption of the conceptus, and frequency of developmental abnormalities (cleft palate, dilated kidney pelvis, thymus hypoplasia). ED50 for cleft palate was about 100 mg PCB 77/kg BW	10
Dams received oral dose of 32 mg/kg BW daily on days 10-16 of gestation	Permanent motor dysfunction in weaning mice characterized by swift circling movements, restlessness, and hyperkinesia; spinal and cranial nerve roots abnormal	11
Ah-responsive and Ah-nonresponsive strains; females, age 10 weeks; given single intraperitoneal injection of 50 mg/kg BW; killed after 7 days	Both groups had increased body weight, increased blood EROD activity, decreased plasma retinol levels, and increased plasma total thyroid hormone levels. The Ah-responsive group also had increased hepatic pentoxyresorufin-*O*-deethylase activity, increased liver cytochrome P450 activity, and increased liver weight	12
PCB 80; pregnant mice given 64 mg/kg BW daily on days 6-15 of gestation and killed on day 18	No effect on maternal or developmental toxicity	7
PCB 169; pregnant mice given daily doses of 0.1, 1, 2, 4, 8, or 16 mg/kg BW by gavage on days 6-15 of gestation; mice killed on day 18 and dams evaluated for reproductive health and fetuses examined on day 19 for malformations	All dams survived all treatments; some lost weight during pregnancy at 8 mg/kg BW and higher. Incidence of malformed fetuses increased from 0.9% in controls, to 3.6-4.3% in the 0.1- 1.0 mg/kg groups, to 37% in the 4 mg/kg group to 61-66% in the 8-16 mg/kg groups. Fetal deaths increased at daily doses of 4 mg/kg BW and	13

Table 15. Species, PCB congener, dose, and other variables	Effect	Reference[a]
	higher, and abortions increased in the 8 and 16 mg/kg groups. Fetal liver discolored at 1 mg/kg BW daily	
Mink, *Mustela vison*		
Aroclor 1254		
0.1 mg/kg BW daily	Adverse effects on growth	2
0.115 mg/kg BW daily (1.64 mg daily)	Adverse effects on reproduction	2, 16
PCB 47; subadult females given daily intraperitoneal injections of 50 mg/kg BW for 3 days and killed 7 days after last dose	No evidence of illness or pathology. PCB 47 residues, in mg/kg FW, were 389 in fat and 38 in liver	14, 15
PCB 77; subadult females given daily intraperitoneal injections of 50 mg/kg BW for 3 days and killed 7 days after last dose	Severe anorexia,diarrhea, and melena. Significant histopathology of mucosa of the small intestine. PCB residues, in mg/kg FW, were 139 in fat and 16 in liver	14, 15
PCBs 136 and 167; each fed to adult females in the diet at 5 mg/kg ration for 3 months	No adverse effects on reproduction	16
PCB 169; fed in diet at concentrations of 0.01-0.5 mg/kg ration for 135 days		
0.01 mg/kg diet	No deaths; some weight loss and liver enlargement	17
0.05 mg/kg diet	50% mortality in 135 days	17
0.1 mg/kg diet	50% dead in 75 days	17
0.5 mg/kg diet	All dead within 73 days	17
Laboratory white rat, *Rattus* sp.		
Aroclor 1254		
Dams and resultant pups fed diets containing 0, 3, 30, or 300 mg Aroclor 1254/kg ration from conception to weaning	Most congeners that accumulated in pup tissues were concentrated in the dam's milk when compared to the feed. PCB uptake by pups was greater during lactation than during gestation. Congeners that accounted for 46% of the brain PCB content and also accumulated in a dose-dependent manner were PCBs 105, 138, 141, 153, 168, 178, 179, and 186	19
0.25 mg/kg BW daily via the diet	Adverse effects on reproduction	2
PCB 4; young males given intraperitoneal injections of 50 mg/kg BW daily for 3 days and killed 4 days after last injection	Negligible morphological effects on liver when compared to PCBs 15, 52, and 77 groups dosed at same regimens	20
PCB 28; dams dosed on days 10 to 16 of gestation by gavage with 8 or 32 mg/kg BW daily; offspring tested in mazes at age 12 to 16 weeks	Birth weight lower in high dose group; female pups--but not males--in the high dose group had learning deficits	27
PCB 47; subadult females given 3 daily injections of 50 mg/kg BW and killed 7 days after last injection	No clinical signs of illness and no significant gross or microscopic lesions. PCB 47 residues, in mg/kg FW, were 747 in fat and 28 in liver	14, 15
PCB 77		
Young adults given single intravenous injection of 0.6 mg/kg BW. Blood and tissue	In males (females), adipose tissue 4 h postinjection contained 23% (12%) of the total dose administered,	18

Table 15. Species, PCB congener, dose, and other variables	Effect	Reference[a]
concentrations analyzed 0.5 h-7 days postinjection	skin 14% (16%), liver 6.8% (8.8%), muscle 6.7% (16.2%), and blood 4.1% (4.0%); after 7 days, adipose tissue contained 2.7% (7.4%) and other tissues 0.5-2.2% (1.0-3.4%)	
Pregnant rats dosed orally on days 6-18 of gestation with 1, 3, or 10 mg/kg BW daily; fetuses were examined on day 19 for developmental abnormalities	A dose-dependent increase in mortality, intestinal histopathology, and external malformations, and decrease in fetal size and length of tibias. A daily dose of 3 mg/kg BW significantly affected fetus growth, bone development, and survival	21
Single intraperitoneal injection of 15 mg/kg BW	Significant reduction in liver and heart retinol and in liver retinylester concentrations	22
Single intraperitoneal injection of 50 mg/kg BW	Metabolites in feces included 5-hydroxy-3,4,3',4'-tetra-chlorobiphenyl, 4-hydroxy-3,5,3'4'-tetra-chlorobiphenyl, and a dihydroxy- and monohydroxy trichlorophenyl. After 5 days, unchanged PCB 77 in feces accounted for 0.8% of the initial dose, but hydroxylated metabolites constituted about 32%	23
Subadult females given 3 daily intraperitoneal injections of 50 mg/kg BW and killed 7 days after last injection	No signs of illness or histopathology. PCB 77 residues, in mg/kg FW, were 148 in fat and 138 in liver	14, 15
Adults injected intra-peritoneally for 3 days at 80 mg/kg BW daily then killed 24 h after last injection	Heme destruction in the P448-containing reconstituted monooxygenase system; reactive epoxide, or possibly nonepoxide, intermediate metabolites may participate in cytochrome P448 destruction	24
PCB 118; dams dosed on days 10 to 16 of gestation by gavage with 4 or 16 mg/kg BW daily; offspring tested in mazes at age 12-16 weeks	Birth weight lower in high-dose group; female offspring, but not males, in high-dose group had learning deficits	27
PCB 126; dams given 0.01 or 0.02 mg/kg BW by gavage every second day from days 9-19 of gestation	Reduction in litter size, body weight, and survival of sucklings; delayed spontaneous movement and neuromuscular maturation. Dams and pups had reduced body weight, and increased cytochrome P4501A1 activity	25
PCB 153		
Dams dosed on days 10 to 16 by gavage with 16 or 64 mg/kg BW daily; offspring tested on mazes at age 12 to 16 weeks	Female offspring from high-dose group had learning deficits; males were not affected	27
Immature female pups given 8, 11, 25, 51, or 59 mg/kg BW on days 20 and 21; killed on day 22	Increased uterine weight at 25 and 51 mg/kg BW, but not in other groups	26

[a] 1, van den Berg et al. 1988; 2, Golub et al. 1991; 3, McNulty et al. 1980; 4, McNulty 1985; 5, Becker and McNulty 1984; 6, Anderson et al. 1993; 7, Marks et al. 1989; 8, Darnerud et al. 1986; 9, Brouwer et al. 1985; 10, d'Argy et al. 1987; 11, Chou et al. 1979; 12, Murk et al. 1991; 13, Marks et al. 1981; 14, Gillette al. 1987a; 15, Gillette et al. 1987b; 16, Kihlstrom et al. 1992; 17, Aulerich et al. 1987; 18, Abdel-Hamid et al. 1981; 19, Shain et al. 1986; 20, Hansell and Ecobichon 1974; 21, Wardell et al. 1982; 22, Brouwer et al. 1988; 23, Yoshimura et al. 1987; 24, Shimada and Sawabe 1983; 25, Bernhoft et al. 1994; 26, Li et al. 1994; 27, Schantz et al. 1995; 28, Mes et al. 1995.

Mink (*Mustela vison*) is among the most sensitive mammals to PCB toxicity (Aulerich et al. 1987; Edqvist et al. 1992; Table 15). Reproductive failure, especially fetal death and resorption, of PCB-fed mink is well documented (Backlin and Bergman 1992; Bergman et al. 1992b; Edqvist et al. 1992; Madej et al. 1992). The mechanisms of intra-uterine death of mink fetuses after PCB exposure are not fully understood (Backlin and Bergman 1992), although planar PCB congeners seem to be implicated (Hakansson et al. 1992). Studies showed that EROD and AHH activities were maximally induced in adult mink by PCB fractions containing non-*ortho* or mono-*ortho* chlorobiphenyls and that mink kits are about 10 times more sensitive to P450-inducers than adults (Brunstrom 1992; Kihlstrom et al. 1992). PCB-dosed mink also show altered blood chemistry (Edqvist et al. 1992), abnormal liver metabolism and histology (Edqvist et al. 1992; Bergman et al. 1992b), raised cortisol excretion (Madej et al. 1992), enhanced EROD activity (Brunstrom 1992), and altered metabolism of Vitamin A (Hakansson et al. 1992). Selective retention of certain PCBs and their hydroxylated metabolites occurred in mink muscle after 3 months of a diet containing a PCB mixture (Bergman et al. 1992a). Retention of PCBs 99, 105, 118, 138, 153, 156, and 180 was high in muscle of mink on the diet. Not retained and presumably metabolized were PCBs 44, 49, 52, 91, 92, 95, 97, 107, 132, 149, and 174 (Bergman et al. 1992a).

Estrogen receptors bind to many compounds other than natural estrogen. Several organochlorine compounds, including certain PCBs, reportedly act as estrogen mimics (Hileman 1994). Many estrogen mimics are persistent, lipid soluble compounds that are defined by their ability to stimulate the proliferation of cells in the uterus of the mouse (*Mus* spp.); in males, these mimics may also inhibit sperm production and testes growth. PCBs and their metabolites may be estrogenic to wildlife, although the evidence is not conclusive (Hileman 1994). PCB mixtures and pure individual chlorobiphenyls with a significant degree of *ortho*-substitution have elevated estrogenic activity; Aroclor 1221, for example, rich in *ortho*-chlorobiphenyl, has estrogenic activity in female rats (Korach et al. 1988). Hydroxylated metabolites of PCBs also show estrogenic hormonal activity (Korach et al. 1988; Li et al. 1994). Hydroxylation of PCBs occurs in amphibians and teleosts but at a much slower rate than that of mammals (Safe et al. 1976). Hydroxylated metabolites of PCB 3 include 4'-chloro-4-biphenylol, 4'-chloro-3,4-biphenyldiol, and 4'-chlor-3-methoxy-4-biphenylol; PCB 15 gave 4,4'-dichloro-3-biphenylol; and Aroclor 1254 yielded mono-, di-, and tri-chlorophenylols (Safe et al. 1976). PCB 77 is detoxified by metabolic hydroxylation to hydroxy biphenyl metabolites (Borlakoglu et al. 1991a). Hydroxylated PCB metabolites may be more toxic than the parent product because of their (1) estrogenic properties (Yoshimura et al. 1987); (2) tendency to accumulate in the fetus (Darnerud et al. 1986), and (3) interference with thyroxin metabolism (Brouwer et al. 1990). The ability of hydroxylated PCB metabolites to bind to the uterine estrogen receptor in rats was in increasing order of effectiveness 4-hydroxy 3,5,4'-trichlorobiphenyl, 4,4'-dihydroxy 3,5,3',5'-tetrachlorobiphenyl, 4-hydroxy 2-chlorobiphenyl, 4-hydroxy 4'-chlorobiphenyl, 4,4'-dihydroxy 2',3',5',6'-tetrachlorobiphenyl, 4,4'-dihydroxybiphenyl, and 4-hydroxybiphenyl; PCB compounds that demonstrated appreciable receptor binding activity were also active in stimulating uterine weight increases (Korach et al. 1988). More research seems needed on the estrogenic properties of hydroxylated PCB metabolites.

Long-term neurobehavioral changes were reported in children, monkeys, and rodents exposed to commercial PCB mixtures during fetal and neonatal development (Schantz et al. 1995). Perinatal exposure of rats (*Rattus* sp.) to *ortho*-substituted PCBs (PCBs 28, 118, 153) can cause long-lasting deficits in learning in females; males were not affected (Table 15).

In comparison to primates and mustelids, rodents are only moderately sensitive to intoxication by most PCBs (Abdel-Hamid et al. 1981). In rodents, PCBs 77 and 169 cause effects that are characteristic of the dioxins and furans, including P450 induction, porphyrin accumulations, and atrophy of the lymphatic organs (Abdel-Hamid et al. 1981), as well as teratogenicity in mice (Darnerud et al. 1986). Exposure of rats to PCB 126 in utero and through lactation produced fetotoxic effects, delayed physical maturation, and induced liver xenobiotic metabolizing enzymes without causing neurobehavioral effects (Bernhoft et al. 1994). In mice, PCBs

77, 126, and 169 were teratogenic in a high percentage of the fetuses from treated dams but without apparent effect on the dams (Marks et al. 1981). PCB 77, for example, was toxic to the conceptus at dose levels below those toxic to the dam when administered to pregnant CD-1 mice on days 6-15 of gestation (Marks et al. 1989). The predominant PCB-induced fetal malformations in mice were cleft palate and hydronephrosis (Marks et al. 1981). PCB 77 also interferes with retinyl ester hydrolase (REH), the enzyme responsible for the hydrolysis of vitamin A into free retinol, lowering levels of vitamin A in liver and decreasing serum concentrations of REH and retinol (Mercier et al. 1990).

Toxicokinetics of PCBs in rodents were altered when administered in mixtures (de Jongh et al. 1992). PCBs 153, 156, and 169 produced biphasic elimination patterns in mice when administered in combinations but single phase elimination when administered alone; elimination of all PCBs was more rapid after coadministration. Mixtures of PCBs 153 and 156 raised EROD activity and lengthened retention of each congener in liver; however, a mixture of PCBs 153 and 169 lowered EROD activity (de Jongh et al. 1992). Selected PCBs of low acute toxicity may increase the toxicity of compounds such as 2,3,7,8-TCDD (Birnbaum et al. 1985). Thus, PCBs 153 or 157 at sublethal dosages (20-80 mg/kg BW) did not produce cleft palate deformities in mouse embryos. But a mixture of PCB 157 and 2,3,7,8-TCDD produced a 10-fold increase in the incidence of palate deformities that were expected of 2,3,7,8-TCDD alone; palate deformities did not increase with a mixture of PCB 153 and 2,3,7,8-TCDD. The widespread environmental occurrence of PCB-PCDD and PCB-PCDF combinations suggests a need for further evaluation of the mechanism of this interaction (Birnbaum et al. 1985).

Intraspecific variability to PCBs was high, especially between genetically inbred AHH-responsive and AHH-nonresponsive strains of mice (Robertson et al. 1984). In mice, PCB 77 was metabolized and excreted more rapidly than 2,3,7,8-TCDD (d'Argy et al. 1987); in rats, PCB 77 was excreted more rapidly than PCB 47 (Shimada and Sawabe 1984). PCBs that lack adjacent hydrogen atoms in at least one of the rings are enriched in rat tissues, indicating that accumulation exceeds elimination by metabolism and excretion. PCBs with a tendency to accumulate were non-*ortho* and mono-*ortho* substituted congeners; however, PCBs with *meta-para* unsubstituted carbon atoms in at least one ring were not enriched in tissues (Borlakoglu et al. 1991a). Uptake and retention of individual PCB congeners in rats are related to properties associated with K_{OW} and high chlorination, especially in the tetra- and penta-chlorobiphenyls (Shain et al. 1986). The highly chlorinated hexa- and octa-chlorobiphenyls produced morphological changes in rats comparable to those produced by DDT, Aroclor 1254, and Aroclor 1260 (Hansell and Ecobichon 1974).

Recommendations

Proposed PCB criteria for the protection of natural resources are predicated on total PCBs and selected Aroclor compounds (Table 16) and offer minimal insight into PCB toxicokinetics. Most authorities now agree that future PCB risk assessments require (1) analysis of non-*ortho* PCBs and selected mono-*ortho* PCBs; (2) exposure studies of individual species to specific congeners alone or in combination with other compounds, including other PCB congeners, dioxins, and dibenzofurans; (3) clarification of existing structure-induction relations, and (4) more refined analytical techniques (Eisler 1986; Maack and Sonzogni 1988; Tanabe 1988; Gooch et al. 1989; Hernandez et al. 1989; Kannan et al. 1989; Tanabe et al. 1989; Borlakoglu et al. 1990; Hebert et al. 1993; Giesy et al. 1994a; Safe 1994; Walker and Peterson 1994). Marked differences between species in their abilities to metabolize specific PCB congeners must be considered in toxicity testing. Foxes and dogs, for example, in contrast to monkeys and rats, can degrade the otherwise highly persistent PCB 153 because they possess an unusual cytochrome P450 isoenzyme that metabolizes PCB 153 (Georgii et al. 1994). Also, low-chlorinated congeners that are metabolized via reactive intermediates must be critically evaluated because they show weak tumor-initiating properties (Georgii et al. 1994).

To complement PCB chemical residue analyses, the rat hepatoma cell bioassay was useful for assessing the toxic potency of PCBs in extracts from environmental samples (Tillitt et al. 1991). This in vitro bioassay of cytochrome P450IA1 catalytic activity in the H4IIE cells in response to planar halogenated hydrocarbons was considered accurate and precise. Comparison of the responses of the H4IIE cells was calibrated against their responses to 2,3,7,8-TCDD (Tillitt et al. 1991). EROD (ethoxyresorufin-*O*-deethylase) and porphyria induction measurements also potentially complement PCB chemical residue analyses and have been used to determine the toxic potencies of complex mixtures of PCBs and other halogenated aromatic hydrocarbons extracted from wildlife tissues (Kennedy et al. 1992). In one case, extracts of PCB-contaminated eggs of herring gulls (*Larus argentatus*) from the Great Lakes and of great blue herons (*Ardea herodias*) from British Columbia induced

EROD and porphyria in primary cultures of chicken embryo hepatocytes (Kennedy et al. 1992). Hepatic cytochrome P450-associated monooxygenases and cytochrome P450 proteins in embryos of the black-crowned night-heron (*Nycticorax nycticorax*) were associated with concentrations of total PCBs and 11 PCB congeners that express toxicity through the Ah receptor, and also should be considered as biomarkers for assessing PCB contamination of wetlands (Rattner et al. 1994).

The interpretation of PCB residue data is challenging from several perspectives, as judged by analysis of eggs of Forster's terns (*Sterna forsteri*) from Wisconsin (Schwartz and Stalling 1991): (1) data from a single analysis frequently contained measurable concentrations of 100 to 150 PCB congeners; (2) a single sample was not sufficient to understand the environmental distribution of PCBs; (3) source profiles of PCB inputs into the environment were poorly characterized; (4) PCB congeners in the original polluting material often merged with congeners from other sources; and (5) the contaminant mixture may have been altered by metabolism and subsequent partition into multiple environmental compartments that may be further changed by weathering or degradation. To understand these processes and to correlate residue profiles with specific toxic responses required congener-specific methods of analysis and complex statistical techniques (principal component analysis). Using these techniques, it was established that eggs of Forster's terns of two colonies differed significantly in PCB composition (Schwartz and Stalling 1991). Similar techniques were used to identify various PCB-contaminated populations of harbor seals (*Pusa vitulina*) in Denmark (Storr-Hansen and Spliid 1993).

Selected congeners should be quantified in human foodstuffs and tissues, as determined from a survey of PCB congener frequency in commercial formulations, environmental and biological samples and human tissues, and a consideration of the relative toxicity and persistence of the congeners (Jones 1988). PCBs 28, 74, 77, 99, 105, 118, 126, 128, 138, 153, 156, 169, 170, 179, and 180 reportedly account for more than 70% of the total PCB burden in any sample and should be quantified. Additionally, PCBs 8, 37, 44, 49, 52, 60, 66, 70, 82, 87, 101, 114, 158, 166, 183, 187, and 189 should be considered for quantification because of their reported occurrence or toxicity. Some PCBs are particularly prevalent in aquatic animals, especially PCBs 95, 101, 110, 118, 138, 149, 153, 180, and 187; also detected in aquatic biota and reported as important components were PCBs 26, 52, 66, 70, 99, 105, 132, 151, 170, 177, 201, and 206.

Table 16. Proposed PCB criteria for the protection of natural resources and human health.

Table 16. Resource, criterion, and other variables	Effective concentration	Reference[a]
Aquatic life protection, total PCBs		
Fish		
Diet	<500 ug/kg fresh weight (FW)	1
Eggs	<300 ug/kg FW	1
Whole body	<400 ug/kg FW	1
Marine mammals, blubber	<70 mg/kg FW	2
Medium		
Freshwater		
Acute	<2.0 ug/L	6
Chronic	<0.014 ug/L	1, 6
Saltwater		
Acute, most species	<10.0 ug/L	6
Chronic, sensitive species	<0.03 ug/L	6
Filter-feeding shellfish	<0.006 ug/L	1
Birds, total PCBs		
Brain	<300 mg/kg FW	3
Mammals		
Aroclor 1016		
Rhesus macaque	<0.008-<0.028 mg/kg body weight (BW) daily	4
Aroclor 1248		
Rhesus macaque	<0.009 mg/kg BW daily	4
Aroclor 1254		
Mink	<0.1-<0.115 mg/kg BW daily	4

Table 16. Resource, criterion, and other variables	Effective concentration	Reference[a]
Mouse	<1.3 mg/kg BW daily	4
Rat	<0.25 mg/kg BW daily	4
Human health protection, total PCBs (unless indicated otherwise)		
Air		
Aroclor 1242	<1.0 mg/m^3	6
Aroclor 1254	<0.5 mg/m^3	6
Reduced risk from cancer	<7.7 mg/kg BW daily	6
Drinking water		
Child	<1.0 ug/L	6
Adult	<4 ug/L	6
Fish, edible portion		
Canada	<2 mg/kg FW	5
United States	<2 mg/kg FW	6
New York State	<2 ug/kg FW	5

[a]1, Eisler 1986; 2, Norheim et al. 1992; 3, Bryan et al. 1987a; 4, Golub et al. 1991; 5, Hebert et al. 1993; 6, USEPA 1992b.

In the Netherlands, maximum PCB limits in fishes as dietary items for human health protection are now derived from the sum of PCBs 28, 95, 101, 138, 149, 153, and 180. From a toxicological viewpoint, other congeners may be more important. These have been identified (on the basis of ability to induce AHH) as the most toxic planars (PCBs 15, 37, 77, 81, 126, and 169), the mono-*ortho* analogues of the planar PCBs (PCBs 105, 114, 123, 156, and 189), and the di-*ortho* analogues (PCBs 128, 138, 158, 166, and 170). Of these compounds, PCBs 37, 105, 114, 128, 138, 156, and 158 occur in human tissues and PCBs 15, 77, 81, 123, 126, 166, and 169 do not occur (Jones 1988).

Acknowledgments

We thank L.J. Garrett and P.W. Manning for library services; J.B. French, Jr., R.W. Greene, T.R. Schwartz, M.J. Melancon, and two anonymous referees for technical and scientific input; K. Boone for the illustrations; and E.D. Rockwell for editorial services.

Cited Literature

Abdel-Hamid, F. M., J. A. Moore, and H. B. Matthews. 1981. Comparative study of 3,4,3',4'-tetrachlorobiphenyl in male and female rats and female monkeys. Journal of Toxicology and Environmental Health 7:181-191.

Addison, R. F., and P. F. Brodie. 1987. Transfer of organochlorine residues from blubber through the circulatory system to milk in the lactating grey seal *Halichoerus grypus*. Canadian Journal of Fisheries and Aquatic Sciences 44:782-786.

Ahlborg, U. G., G. C. Becking, L. S. Birnboum, A. Brouwer, H. J. G. M. Derks, M. Feely, G. Golor, A. Hanberg, J. C. Carsen, A. K. D. Liem, S. H. Safe, C. Schlatter, F. Waern, M. Younes, and E. Yrjanheikke. 1994. Toxic equivalency factors for dioxin-like PCBs. Chemosphere 28:1049-1067.

Alford-Stevens, A. L., T. A. Bellar, J. W. Eichelberger, and W. L. Budde. 1985. Determination of pesticides and PCBs in water and soil/sediment by gas chromatography/mass spectrometry. U.S. Environmental Protection Agency Method 680. 46 pp.

Alford-Stevens, A. L., T. A. Bellar, J. W. Eichelberger, and W. L. Budde. 1986. Characterization of commercial Aroclors by automated mass spectrometric determination of polychlorinated biphenyls by level of chlorination. Analytical Chemistry 58:2014-2022.

Alford-Stevens, A. L., J. W. Eichelberger, and W. L. Budde. 1988. Multilaboratory study of automated determinations of polychlorinated biphenyls and chlorinated pesticides in water, soil, and sediment by gas chromatography/mass spectrometry. Environmental Science & Technology 22:304-312.

Anderson, L. M., S. D. Fox, C. W. Riggs, and H. J. Issaq. 1993. Selective retention of polychlorinated biphenyl congeners in lung and liver after single-dose exposure of infant mice to Aroclor 1254. Journal of Environmental Pathology, Toxicology and Oncology 12:3-16.

Ankley, G. T., P. M. Cook, A. R. Carlson, D. J. Call, J. A. Swenson, and H. F. Corcoran. 1992. Bioaccumulation of PCBs from sediments by oligochaetes and fishes: comparison of laboratory and field studies. Canadian Journal of Fisheries and Aquatic Sciences 49:2080-2085.

Ankley, G. T., G. J. Niemi, K. B. Lodge, H. J. Harris, D. L. Beaver, D. E. Tillett, T. R. Schwartz, J. P. Giesy, P. D. Jones, and C. Hagley. 1993. Uptake of planar polychlorinated biphenyls and 2,3,7,8-substituted polychlorinated dibenzofurans and dibenzo-*p*-dioxins by birds nesting in the lower Fox River and Green Bay, Wisconsin, USA. Archives of Environmental Contamination and Toxicology 24:332-344.

Ankley, G. T., D. E. Tillitt, J. P. Giesy, P. D. Jones, and D. A. Verbrugge. 1991. Bioassay-derived 2,3,7, 8-tetrachlorodibenzo-p-dioxin equivalents in PCB-containing extracts from the flesh and eggs of Lake Michigan chinook salmon *(Oncorhynchus tshawytscha*) and possible implications for reproduction. Canadian Journal of Fisheries and Aquatic Sciences 48:1685-1690.

Asplund, L., A. K. Grafstrom, P. Haglund, B. Jansson, U. Jarnberg, D. Mace, M. Strandell, and C. de Wit. 1990. Analysis of non-ortho polychlorinated biphenyls and polychlorinated naphthalenes in Swedish dioxin survey samples. Chemosphere 20:1481-1488.

Aulerich, R. J., S. J. Bursian, M. G. Evans, J. R. Hochstein, K. A. Koudele, B. A. Olson, and A. C. Napolitano. 1987. Toxicity of 3,4,5,3'4',5'-hexachlorobiphenyl to mink. Archives of Environmental Contamination and Toxicology 16:53-60.

Backlin, B. M., and A. Bergman. 1992. Morphological aspects on the reproductive organs in female mink (*Mustela vison*) exposed to polychlorinated biphenyls and fractions thereof. Ambio 21:596-601.

Baker, J. E., and S. J. Eisenreich. 1990. Concentration, speciation, and fluxes of PAHs and PCB congeners across the air-water interface. Environmental Science & Technology 22:342-352.

Ballschmiter, K., and M. Zell. 1980. Analysis of polychlorinated biphenyls (PCB) by glass capillary gas chromatography. Fresenius Zeitschrift fur Analytische Chemie 302:20-31.

Becker, G. M., and W. P. McNulty. 1984. Gastric epithelial cell proliferation in monkeys fed 3,4,3',4'-tetrachlorobiphenyl. Journal of Pathology 143:267-274.

Bergen, B. J., W. G. Nelson, and R. J. Pruell. 1993. Bioaccumulation of PCB congeners by blue mussels (*Mytilus edulis*) deployed in New Bedford Harbor, Massachusetts. Environmental Toxicology and Chemistry 12:1671-1681.

Bergman, A., M. Athanasiadou, S. Bergek, K. Haraguchi, S. Jensen, and E. K. Wehler. 1992a. PCB and PCB methyl sulfones in mink treated with PCB and various PCB fractions. Ambio 21:570-576.

Bergman, A., B. M. Backlin, B. Jarplid, L. Grimelius, and E. Wilander. 1992b. Influence of commercial polychlorinated biphenyls and fractions thereof on liver histology in female mink (*Mustela vison*). Ambio 21:591-595

Bernhoft, A., I. Nafstad, P. Engen, and J. U. Skaare. 1994. Effects of pre- and postnatal exposure to 3,3',4,4',5-pentachlorobiphenyl on physical development, neurobehavior and xenobiotic metabolizing enzymes in rats. Environmental Toxicology and Chemistry 13:1589-1597.

Bidleman, T. F., N. F. Burdick, J. W. Westcott, and W. N. Billings. 1983. Influence of volatility on the collection of airborne PCB and pesticides with filter-solid adsorbent samplers. Pages 15-48 *in* D. Mackay, S. Paterson, S. J. Eisenreich, and M. S. Simmons, editors. Physical behavior of PCBs in the Great Lakes. Ann Arbor Science, Ann Arbor, Mich.

Birnbaum, L. S., H. Weber, M. W. Harris, J. C. Lamb IV, and J. D. McKinney. 1985. Toxic interaction of specific polychlorinated biphenyls and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin: increased incidence of cleft palate in mice. Toxicology and Applied Pharmacology 77:292-302.

Bishop, C. A., R. J. Brooks, J. H. Carey, P. Ng, R. J. Norstrom, and D. R. S. Lean. 1991. The case for a cause-effect linkage between environmental contamination and development in eggs of the common snapping turtle (*Chelydra s. serpentina*) from Ontario, Canada. Journal of Toxicology and Environmental Health 33:521-547.

Bishop, C. A., G. P. Brown, R. J. Brooks, D. R. S. Lean, and J. H. Carey. 1994. Organochlorine contaminant concentrations in eggs and their relationship to body size and clutch characteristics of the female common snapping turtle (*Chelydra serpentina*) in Lake Ontario, Canada. Archives of Environmental Contamination and Toxicology 27:82-87.

Blumton, A. K., J. D. Fraser, R. W. Young, S. Goodbred, S. L. Porter, and D. Luukkonen. 1990. Pesticide and PCB residues for loggerhead shrikes in the Shenandoah Valley, Virginia, 1985-88. Bulletin of Environmental Contamination and Toxicology 45:697-702.

Boehm, P. D. 1981. Investigations of pollutant organic chemical fluxes in the Hudson-Raritan estuarine and New York Bight coastal systems. Technical Report, Energy Resources Co. (ERCO), Cambridge, Massachusetts. Submitted to the Office of Marine Pollution Assessment, U.S. National Oceanic and Atmospheric Administration, Rockville, Md. 59 pp.

Borgmann, U., and D. M. Whittle. 1991. Contaminant concentration trends in Lake Ontario lake trout (*Salvelinus namaycush*): 1977 to 1988. Journal of Great Lakes Research 17:368-381.

Borlakoglu, J. T., J. P. G. Wilkins, and R. R. Dils. 1991a. Metabolism by rat hepatic microsomes of individual isomers and congeners in Aroclor 1016. Bulletin of Environmental Contamination and Toxicology 46:436-441.

Borlakoglu, J. T., J. P. G. Wilkins, M. P. Quick, C. H. Walker, and R. R. Dils. 1991b. Metabolism of [^{14}C]4-chlorobiphenyl by hepatic microsomes isolated from razorbills, pigeons and rats. Comparative Biochemistry and Physiology 99C:287-291.

Borlakoglu, J. T., J. P. G. Wilkins, C. H. Walker, and R. R. Dils. 1990. Polychlorinated biphenyls (PCBs) in fish-eating seabirds—III. Molecular features and metabolic interpretations of PCB isomers and congeners in adipose tissues. Comparative Biochemistry and Physiology 97C:173-177.

Bosveld, B. A. T. C., M. van den Berg, and R. M. C. Theelen. 1992. Assessment of the EROD inducing potency of eleven 2,3,7,8- substituted PCDD/Fs and three coplanar PCBs in the chick embryo. Chemosphere 25:911-916.

Boumphrey, R. S., S. J. Harrad, K. C. Jones, and D. Osborn. 1993. Polychlorinated biphenyl congener patterns in tissues from a selection of British birds. Archives of Environmental Contamination and Toxicology 25:346-352.

Braune, B. M., and R. J. Norstrom. 1989. Dynamics of organochlorine compounds in herring gulls: III. Tissue distribution and bioaccumulation in Lake Ontario gulls. Environmental Toxicology and Chemistry 8:957-968.

Breck, J. E. 1985. Comment on “fish/sediment concentration ratios for organic compounds.” Environmental Science & Technology 19:198-199.

Brieger, G., and R. D. Hunter. 1993. Uptake and depuration of PCB 77, PCB 169, and hexachlorobenzene by zebra mussels (*Dreissena polymorpha*). Ecotoxicology and Environmental Safety 26:153-165.

Brouwer, A., E. Klasson-Wehler, M. Bokdam, D. C. Morse, and W. A. Traag. 1990. Competitive inhibition of thyroxin binding to transthyretin by monohydroxy metabolites of 3,3’,4,4’-tetrachlorobiphenyl. Chemosphere 20:1257-1262.

Brouwer, A., A. Kukler, and K. J. van den Berg. 1988. Alterations in retinoid concentrations in several extrahepatic organs of rats by 3,4,3’,4’-tetrachlorobiphenyl. Toxicology 50:317-330.

Brouwer, A., K. J. van den Berg, and A. Kukler. 1985. Time and dose responses of the reduction in retinoid concentrations in C57BL/Rij and DBA/2 mice induced by 3,4,3’,4’-tetrachlorobiphenyl. Toxicology and Applied Pharmacology 78:180-189.

Brown, J. F., D. L. Bedard, M. J. Brennan, J. C. Carnahan, H. Feng, and R. E. Wagner. 1987. Polychlorinated biphenyl dechlorination in aquatic sediments. Science 236:709-712.

Brown, M. P., M. B. Werner, R. J. Sloan, and K. W. Simpson. 1985. Polychlorinated biphenyls in the Hudson River. Environmental Science & Technology 19:656-661.

Bruggeman, W. A., J. Van Der Steen, and O. Hutzinger. 1982. Reversed-phase thin-layer chromatography of polynuclear aromatic hydrocarbons and chlorinated biphenyls. Relationship with hydrophobicity as measured by aqueous solubility and octanol-water partition coefficient. Journal of Chromatography 238:335-346.

Brunstrom, B. 1986. Activities in chick embryos of 7-ethoxycoumarin *O*-deethylase and aryl hydrocarbon (benzo[*a*]pyrene) hydroxylase and their induction by 3,3’,4,4’-tetrachlorobiphenyl in early embryos. Xenobiotica 16:865-872.

Brunstrom, B. 1988. Sensitivity of embryos from duck, goose, herring gull, and various chicken breeds to 3,3’-4,4’-tetrachlorobiphenyl. Poultry Science 67:52-57.

Brunstrom, B. 1992. Induction of cytochrome P-450-dependent enzyme activities in female mink (*Mustela vison*) and their kits by technical PCB preparations and fractions thereof. Ambio 21:585-587.

Brunstrom, B., D. Broman, and C. Naf. 1990. Embryotoxicity of polycyclic aromatic hydrocarbons (PAHs) in three domestic avian species, and of PAHs and coplanar polychlorinated biphenyls (PCBs) in the common eider. Environmental Pollution 67:133-143.

Brunstrom, B., and P. O. Darnerud. 1983. Toxicity and distribution in chick embryos of 3,3’,4,4’-tetrachlorobiphenyl injected into the eggs. Toxicology 27:103-110.

Brunstrom, B., M. Engwall, K. Hjelm, L. Lindqvist, and Y. Zebuhr. 1995. EROD induction in cultured chick embryo liver: a sensitive bioassay for dioxin-like environmental pollutants. Environmental Toxicology and Chemistry 14:837-852.

Brunstrom, B., and J. Lund. 1988. Differences between chick and turkey embryos in sensitivity to 3,3’,4,4’-tetrachlorobiphenyl and in concentration/affinity of the hepatic receptor for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Comparative Biochemistry and Physiology 91C:507-512.

Brunstrom, B., and L. Reutergardh. 1986. Differences in sensitivity of some avian species to the embryotoxicity of a PCB, 3,3’,4,4’-tetrachlorobiphenyl, injected into the eggs. Environmental Pollution 42A:37-45.

Bryan, A. M., P. G. Olafsson, and W. B. Stone. 1987a. Disposition of low and high environmental concentrations of PCBs in snapping turtle tissues. Bulletin of Environmental Contamination and Toxicology 38:1000-1005.

Bryan, A. M., W. B. Stone, and P. G. Olafsson. 1987b. Disposition of toxic PCB congeners in snapping turtle eggs: expressed as toxic equivalents of TCDD. Bulletin of Environmental Contamination and Toxicology 39:791-796.

Burgess, R. M., K. A. Schweitzer, R. A. McKinney, and D. K. Phelps. 1993. Contaminated marine sediments: water column and interstitial effects. Environmental Toxicology and Chemistry 12:127-138.

Buser, H. R., and M. D. Muller. 1986. Methythio metabolites of polychlorinated biphenyls identified in sediment samples from two lakes in Switzerland. Environmental Science & Technology 20:730-735.

Bush, B., L. A. Shane, and M. Wahlen. 1987. Sedimentation of 74 PCB congeners in the upper Hudson River. Chemosphere 16:733-744.

Bush, B., K. W. Simpson, L. Shane, and R. R. Koblintz. 1985. PCB congener analysis of water and cadissfly larvae (Insecta:Trichoptera) in the upper Hudson River by glass capillary chromatography. Bulletin of Environmental Contamination and Toxicology 34:96-105.

Bush, B., J. T. Snow, and S. Connor. 1983. High resolution gas chromatographic analysis of nonpolar chlorinated hydrocarbons in human milk. Journal of the Association of Official Analytical Chemists 66:248-255.

Bush, B., R. W. Streeter, and R. J. Sloan. 1990. Polychlorobiphenyl (PCB) congeners in striped bass (*Morone saxatilis*) from marine and estuarine waters of New York State determined by capillary gas chromatography. Archives of Environmental Contamination and Toxicology 19:49-61.

Chapman, P. M., R. N. Dexter, S. F. Cross, and D. G. Mitchell. 1986. A field trial of the sediment quality triad in San Francisco Bay. NOAA Technical Memorandum NOS OPMA 25. U.S. National Oceanic and Atmospheric Administration, Rockville, Maryland. 127 pp. + appendixes.

Chen, M., C. S. Hong, B. Bush, and G. Y. Rhee. 1988. Anaerobic biodegradation of polychlorinated biphenyls by bacteria from Hudson River sediments. Ecotoxicology and Environmental Safety 16:95-105.

Chen, P. R., H. M. Mehendale, and L. Fishbein. 1973. Effect of two isomeric tetrachlorobiphenyls on rats and their hepatic enzymes. Archives of Environmental Contamination and Toxicology 1:36-47.

Chou, S. M., T. Miike, W. M. Payne, and G. J. Davis. 1979. Neuropathology of “spinning syndrome” induced by prenatal intoxication with a PCB in mice. Annals of the New York Academy of Sciences 320:373-395.

Connor, M. S. 1984. Comment on “fish/sediment concentration ratios for organic compounds.” Environmental Science & Technology 19:199.

Creaser, C. S., and A. Al-Haddad. 1989. Fractionation of polychlorinated biphenyls, polychlorinated dibenzo-p-dioxins, and polychlorinated dibenzofurans on porous graphite. Analytical Chemistry 61:1300-1302.

d’Argy, R., L. Denker, E. Klasson-Wehler, A. Bergman, P. O. Darnerud, and I. Brandt. 1987. 3,3’,4,4’-tetrachlorobiphenyl in pregnant mice: embryotoxicity, teratogenicity, and toxic effects on the cultured embryonic thymus. Pharmacology and Toxicology 61:53-57.

Daelemans, F. F., F. Mehlum, C. Lydersen, and P. J. C. Schepens. 1993. Mono-ortho and non-ortho substituted PCBs in Arctic ringed seal (*Phoca hispida*) from the Svalbard area: analysis and determination of their toxic threat. Chemosphere 27:429-437.

Darnerud, P. O., I. Brandt, E. Klasson-Wehler, A. Bergman, R. d’Argy, L. Denker, and G. O. Sperber. 1986. 3,3’,4,4’,-tetrachloro[^{14}C]-biphenyl in pregnant mice: enrichment of phenol and methyl sulfone metabolites in late gestational fetuses. Xenobiotica 16:295-306.

de Boer, J., and P. Wester. 1991. Chlorobiphenyls and organochlorine pesticides in various sub-Antarctic organisms. Marine Pollution Bulletin 22:441-447.

de Jongh, J., F. Wondergem, W. Seinen, and M. Van den Berg. 1992. Toxicokinetic interactions in the liver of the C57BL/6J mouse after administration of a single oral dose of a binary mixture of some PCBs. Chemosphere 25:1165-1170.

Delany, M. F., J. U. Bell, and S. F. Sundlof. 1988. Concentrations of contaminants in muscle of the American alligator in Florida. Journal of Wildlife Diseases 24:62-66.

de Voogt, P., D. E. Wells, L. Reutergaardh, and U. A. T. Brinkman. 1990. Biological activity, determination, and occurrence of planar, mono- and di-ortho PCBs. International Journal of Environmental Chemistry 40:1-46.

Dillon, T. M., and W. D. S. Burton. 1992. Acute toxicity of PCB congeners to *Daphnia magna* and *Pimephales promelas*. Bulletin of Environmental Contamination and Toxicology 46:208-215.

Draper, W. M., D. Wijekoon, and R. D. Stephens. 1991. Speciation and quantitation of Aroclors in hazardous wastes based on congener data. Chemosphere 22:147-163.

Duinker, J. C., and F. Bouchertall. 1989. On the distribution of atmospheric polychlorinated biphenyl congeners between vapor phase, aerosols, and rain. Environmental Science & Technology 22:99-103.

Duinker, J. C., A. H. Knap, K. C. Binkley, G. H. Van Dam, A. Darrel-Rew, and M. T. J. Hillebrand. 1988a. Method to represent the qualitative and quantitative characteristics of PCB mixtures: marine mammal tissues and commercial mixtures as examples. Marine Pollution Bulletin 19:74-79.

Duinker, J. C., D. E. Schulz, and G. Petrik. 1988b. Multidimensional gas chromatography with electron capture detection for the determination of toxic congeners in polychlorinated biphenyl mixtures. Analytical Chemistry 60:478-482.

Dunnivant, F. M., and A. W. Elzerman. 1988. Determination of polychlorinated biphenyls in sediments, using sonication extraction and capillary column gas chromatography-electron capture detection with internal standard calibration. Journal of the Association of Official Analytical Chemists 71:551-556.

Dunnivant, F. M., A. L. Polansky, and A. W. Elzerman. 1989. Persistence and distribution of PCBs in the sediments of a reservoir (Lake Hartwell, South Carolina). Bulletin of Environmental Contamination and Toxicology 43:870-878.

Edqvist, L. E., A. Madej, and M. Forsberg. 1992. Biochemical blood parameters in pregnant mink fed PCB and fractions of PCB. Ambio 21:577-581.

Eisenreich, S. J., P. D. Capel, J. A. Robbins, and R. Bourbonnierre. 1989. Accumulation and digenesis of chlorinated hydrocarbons in lacustrine sediments. Environmental Science & Technology 23:1116-1126.

Eisler, R. 1986. Polychlorinated biphenyl hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85(1.7). 72 pp.

Elliott, J. E., S. W. Kennedy, D. Jeffrey, and L. Shutt. 1991. Polychlorinated biphenyl (PCB) effects on hepatic mixed function oxidases and porphyria in birds—II. American kestrel. Comparative Biochemistry and Physiology 99C:141-145.

Elliott, J. E., and L. Shutt. 1993. Monitoring organochlorines in blood of sharp-shinned hawks migrating through the Great Lakes. Environmental Toxicology and Chemistry 12:241-250.

Elskus, A. A., J. J. Stegeman, J. W. Gooch, D. E. Black, and R. J. Pruell. 1994. Polychlorinated biphenyl congener distributions in winter flounder as related to gender, spawning site, and congener metabolism. Environmental Science & Technology 28:401-407.

Elzerman, A. W., F. M. Dunnivant, and G. G. Germann. 1991. PCBs and related compounds in Lake Hartwell. U.S. Geological Survey. Technical Completion Report Grant No. G1488-04. 232 pp.

Erhardt-Zabik, S., J. T. Watson, and M. J. Zabik. 1990. Selective sensitivity of highly chlorinated species in negative ion mass spectrometry: implications for complex mixture analysis. Biomedical and Environmental Mass Spectrometry 19:101-108.

Evans, M. S., and P. F. Landrum. 1989. Toxicokinetics of DDE, benzo(a)pyrene, and 2,4,5,2',4',5'-hexachlorobiphenyl in *Pontoporeia hoyi* and *Mysis relicta*. Journal of Great Lakes Research 15:589-600.

Falandysz, J., N. Yamashita, S. Tanabe, R. Tatsukawa, L. Rucinska, T. Mizera, and B. Jakuczun. 1994a. Congener-specific analysis of polychlorinated biphenyls in white-tailed sea eagles *Haliaeetus albicilla* collected in Poland. Archives of Environmental Contamination and Toxicology 26:13-22.

Falandysz, J., N. Yamashita, S. Tanabe, R. Tatsukawa, L. Rucinska, and K. Skora. 1994b. Conger-specific data on polychlorinated biphenyls in tissues of common porpoise from Puck Bay, Baltic Sea. Archives of Environmental Contamination and Toxicology 26:267-272.

Feltz, K. P., D. E. Tillitt, R. W. Gale, and P. H. Peterman. 1995. Automated HPLC fractionation of PCDDs and PCDFs and planar and nonplanar PCBs on C_{18}-dispersed PX-21 carbon. Environmental Science and Technology 29:709-718.

Fernandez, M. A., L. M. Hernandez, C. Ibanez, M. J. Gonzalez, A. Guillen, and J. L. Perez. 1993. Congeners of PCBs in three bat species from Spain. Chemosphere 26:1085-1097.

Focardi, S., C. Fossi, M. Lambertini, C. Leonzio, and A. Massi. 1988a. Long term monitoring of pollutants in eggs of yellow-legged herring gull from Capraia Island (Tuscan Archipeligo). Environmental Monitoring and Assessment 10:43-50.

Focardi, S., C. Leonzio, and C. Fossi. 1988b. Variations in polychlorinated biphenyl congener composition in eggs of Mediterranean water birds in relation to their position in the food chain. Environmental Pollution 52:243-255.

Ford, C. A., D. C. G. Muir, R. J. Nostrom, M. Simon, and M. J. Mulvihill. 1993. Development of a semi-automated method for non-ortho PCBs: application to Canadian Arctic marine mammal tissues. Chemosphere 26:1981-1991.

Formica, S. J., J. A. Baron, L. J. Thibodeaux, and K. T. Valsaraj. 1988. PCB transport into lake sediments. Conceptual model and laboratory simulation. Environmental Science & Technology 22:1435-1440.

Frank, R., M. Holdrinet, H. E. Braun, R. Thomas, A. L. W. Kemp, and J. M. Jaquet. 1977. Organochlorine insecticides and PCBs in sediments of Lake St. Clair (1970 and 1974) and Lake Erie (1971). The Science of the Total Environment 8:205-227.

Froslie, A., G. Holt, and G. Norheim. 1986. Mercury and persistent hydrocarbons in owls Strigiformes and birds of prey Falconiformes collected in Norway during the period 1965-1983. Environmental Pollution 11B:91-108.

Galceran, J. T., F. J. Santos, J. Caixach, and J. Rivera. 1993. PCBs and chlorinated pesticides in shellfish of a deltaic environment. Chemosphere 27:1183-1200.

Gebhart, J. E., T. L. Hayes, A. L. Alford-Stevens, and W. L. Budde. 1985. Mass spectrometric determination of polychlorinated biphenyls as isomer groups. Analytical Chemistry 57:2458-2463.

Georgii, S., G. Bachour, K. Failing, U. Eskins, I. Elmadfa, and H. Brunn. 1994. Polychlorinated biphenyl congeners in foxes in Germany from 1983 to 1991. Archives of Environmental Contamination and Toxicology 26:1-6.

Giesy, J. P., J. P. Ludwig, and D. E. Tillitt. 1994a. Dioxins, dibenzofurans, PCBs and colonial, fish-eating water birds. Pages 249-307 *in* A. Schecter, editor. Dioxins and health. Plenum Press, New York.

Giesy, J. P., D. A. Verbrugge, P. A. Othout, W. W. Bowerman, M. A. Mora, P. D. Jones, J. L. Newsted, C. Vandervoort, S. N. Heaton, R. J. Aulerich, S. J. Bursian, J. P. Ludwig, G. A. Dawson, T. J. Kubiak, D. A. Best, and D. E. Tillitt. 1994b. Contaminants in fishes from Great Lakes-influenced sections and above dams of three Michigan rivers. II. Implications for health of mink. Archives of Environmental Contamination and Toxicology 27:213-223.

Gillette, D. M., R. D. Corey, W. G. Helferich, J. M. MacFarland, L. J. Lowenstine, D. E. Moody, B. D. Hammock, and L. R. Shull. 1987a. Comparative toxicology of tetrachlorobiphenyls in mink and rats. I. Changes in hepatic enzyme activity and smooth endoplasmic reticulum volume. Fundamental and Applied Toxicology 8:5-14.

Gillette, D. M., R. D. Corey, L. J. Lowenstine, and L. R. Shull. 1987b. Comparative toxicology of tetrachlorobiphenyls in mink and rats. II. Pathology. Fundamental and Applied Toxicology 8:15-22.

Ginn, T. C., and R. A. Pastorok. 1992. Assessment and management of contaminated sediments in Puget Sound. Pages 371-401 *in* G.A. Burton, Jr., editor. Sediment toxicity assessment. Lewis Publishers, Boca Raton, Florida.

Gobas, F. A. P. C., D. C. Bedard, J. J. H. Cibrowski, and G. D. Haffner. 1989. Bioaccumulation of chlorinated hydrocarbons by the mayfly *(Hexagenia limbata*) in Lake St. Clair. Journal of Great Lakes Research 15:581-588.

Goldstein, J. A., P. Hickman, H. Bergaman, J. D. McKinney, and M. P. Walker. 1977. Separation of pure polychlorinated biphenyl isomers into two types of inducers on the basis of induction of cytochrome P-450 or P-448. Chemical-Biological Interactions 17:69-87.

Goldstein, J. A., J. D. McKinney, G. W. Lucier, P. Hickman, H. Bergman, and J. A. Moore. 1976. Toxicological assessment of hexachlorobiphenyl isomers and 2,3,7,8-tetrachlorodibenzofuran in chicks: II. Effects on drug metabolism and porphyrin accumulation. Toxicology and Applied Pharmacology 36:81-92.

Golub, M. S., J. M. Donald, and J. A. Reyes. 1991. Reproductive toxicity of commercial PCB mixtures: LOAELs and NOAELs from animal studies. Environmental Health Perspectives 94:245-253.

Gonzalez, M. J., M. A. Fernandez, and L. M. Hernandez. 1991. Levels of chlorinated insecticides, total PCBs and PCB congeners in Spanish gull eggs. Archives of Environmental Contamination and Toxicology 20:343-348.

Gooch, J. W., A. A. Elskus, P. J. Kloepper-Sams, M. E. Hahn, and J. J. Stegman. 1989. Effects of *ortho*-and non-*ortho* substituted polychlorinated biphenyl congeners on the hepatic monooxygenase system in scup (*Stenotomus chrysops*). Toxicology and Applied Pharmacology 98:422-433.

Greig, R. A., and G. Sennefelder. 1987. PCB concentrations in winter flounder from Long Island Sound, 1984-1986. Bulletin of Environmental Contamination and Toxicology 39:863-868.

Gschwend, P. M., and S. Wu. 1985. On the constancy of sediment-water partition coefficients of hydrophobic organic pollutants. Environmental Science & Technology 22:1435-1440.

Guevremont, R., R. A. Yost, and W. D. Jamieson. 1987. Identification of PCB congeners by collision-induced dissociation of [M-Cl+]- from oxygen-enhanced negative chemical ionization mass spectrometry. Biomedical and Environmental Mass Spectrometry 14:435-441.

Gundersen, D. T., and W. D. Pearson. 1992. Partitioning of PCBs in the muscle and reproductive tissues of paddlefish, *Polyodon spathula*, at the falls of the Ohio River. Bulletin of Environmental Contamination and Toxicology 49:455-462.

Haglund, P., L. Asplund, U. Jarnberg, and B. Jansson. 1990. Isolation of mono- and non-ortho polychlorinated biphenyls from biological samples by electron donor acceptor high performance liquid chromatography using a 2-(1-pyrenyl)ethyldimethylsilylated silica column. Chemosphere 20:887-894.

Hakansson, H., E. Manzoor, and U. G. Ahlborg. 1992. Effects of technical PCB preparations and fractions thereof on Vitamin A levels in the mink (*Mustela vison*). Ambio 21:588-590.

Hansell, M. M., and D. J. Ecobichon. 1974. Effects of chemically pure chlorobiphenyls on the morphology of rat liver. Toxicology and Applied Pharmacology 28:418-427.

Hansen, L. G. 1987. Environmental toxicology of polychlorinated biphenyls. Pages 15-48 *in* S. Safe, editor. Polychlorinated biphenyls (PCBs): mammalian and environmental toxicology. Environmental Toxin Series 1. Springer-Verlag, New York.

Hargrave, B. T., G. C. Harding, W. P. Vass, P. E. Erickson, B. R. Fowler, and V. Scott. 1992. Organochlorine pesticides and polychlorinated biphenyls in the Arctic Ocean food web. Archives of Environmental Contamination and Toxicology 22:41-54.

Hargrave, B. T., W. P. Vass, P. E. Erickson, and B. R. Fowler. 1989. Distribution of chlorinated hydrocarbon pesticides and PCBs in the Arctic Ocean. Canadian Technical Report of Fisheries and Aquatic Sciences No. 1644. Department of Fisheries and Oceans, Dartmouth, Nova Scotia. 111 pp.

Harrad, S. J., A. S. Stewart, R. Boumphrey, R. Duarte-Davidson, and K. C. Jones. 1992. A method for the determination of PCB congeners 77, 126 and 169 in biotic and abiotic matrices. Chemosphere 24:1147-1154.

Hawker, D. W., and D. W. Connell. 1988. Octanol-water partition coefficients of polychlorinated biphenyl congeners. Environmental Science & Technology 22:382-387.

Hayes, M. A. 1987. Carcinogenic and mutagenic effects of PCBs. Pages 77-95 *in* S. Safe, editor. Polychlorinated biphenyls (PCBs): mammalian and environmental toxicology. Environmental Toxin Series 1. Springer-Verlag, New York.

Hebert, C. E., V. Glooschenko, G. D. Haffner, and R. Lazar. 1993. Organic contaminants in snapping turtles (*Chelydra serpentina*) populations from southern Ontario, Canada. Archives of Environmental Contamination and Toxicology 24:35-43.

Heinz, G. H., H. F. Percival, and M. L. Jennings. 1991. Contaminants in American alligator eggs from Lake Apopka, Lake Griffin, and Lake Okeechobee, Florida. Environmental Monitoring and Assessment 16:277-285.

Hernandez, L. M., M. A. Fernandez, and M. J. Gonzalez. 1989. Total PCBs and PCB congeners in Spanish imperial eagle eggs. Bulletin of Environmental Contamination and Toxicology 43:725-732.

Hernandez, L. M., M. J. Gonzalez, M. C. Rico, M. A. Fernandez, and A. Aranda. 1988. Organochlorine and heavy metal residues in falconiforme and ciconiforme eggs (Spain). Bulletin of Environmental Contamination and Toxicology 40:86-93.

Hesselberg, R. J., J. P. Hickey, D. A. Nortrup, and W. A. Willford. 1990. Contaminant residues in the bloater (*Coregonus hoyi*) of Lake Michigan, 1969-1986. Journal of Great Lakes Research 16:121-129.

Hileman, B. 1994. Environmental estrogens linked to reproductive abnormalities, cancer. Chemical & Engineering News, January 31, 1994:19-23.

Himberg, K. K. 1993. Coplanar polychlorinated biphenyls in some Finnish food commodities. Chemosphere 27:1235-1243.

Hoffman, D. J., C. P. Rice, and T. J. Kubiak. 1995. PCBs and dioxins in birds. Pages 167-209 *in* W. N. Beyer, G. H. Heinz, and A. Redmon, editors. Environmental contaminants in wildlife: interpreting tissue concentrations. Lewis Publishers, Boca Raton, Florida.

Hong, C. S., and B. Bush. 1990. Determination of mono- and non-ortho coplanar PCBs in fish. Chemosphere 21:173-181.

Hong, C. S., B. Bush, and J. Xiao. 1992. Coplanar PCBs in fish and mussels from marine and estuarine waters of New York State. Ecotoxicology and Environmental Safety 23:118-131.

Hong, C. S., J. Xiao, A. C. Casey, B. Bush, E. F. Fitzgerald, and S. A. Hwang. 1994. Mono-ortho- and non-ortho-substituted polychlorinated biphenyls in human milk from Mohawk and control women: effects of maternal factors and previous lactation. Archives of Environmental Contamination and Toxicology 27:431-437.

Huckins, J. N., T. R. Schwartz, J. D. Petty, and L. M. Smith. 1988. Determination, fate, and potential significance of PCBs in fish and sediment samples with emphasis on selected AHH-inducing congeners. Chemosphere 17:1995-2016.

Huckins, J. N., D. L. Stalling, and J. D. Petty. 1980. Carbon-foam chromatographic separation of non-o,o'chlorine substituted PCBs from Aroclor mixtures. Journal of the Association of Official Analytical Chemists 63:750-755.

Huckins, J. N., D. L. Stalling, and W. A. Smith. 1978. Foam-charcoal chromatography for analysis of polychlorinated dibenzodioxins in herbicide orange. Journal of the Association of Official Analytical Chemists 61:32-38.

Huckins, J. N., M. W. Tubergen, J. A. Lebo, R. W. Gale, and T. R. Schwartz. 1990a. Polymeric film dialysis in organic solvent media for cleanup of organic contaminants. Journal of the Association of Official Analytical Chemists 73:290-293.

Huckins, J. N., M. W. Tubergen, and G. K. Manuweera. 1990b. Semipermeable membrane devices containing model lipid: a new approach to monitoring the bioavailability of lipophilic contaminants and estimating their bioconcentration potential. Chemosphere 20:533-552.

Huhnerfuss, H., B. Pfaffenberger, B. Gehrcke, L. Karbe, W. A. Konig, and O. Landgraf. 1995. Stereochemical effects of PCBs in the marine environment: seasonal variation of coplanar and atropisomeric PCBs in blue mussels (*Mytilus edulis* L.) of the German Bight. Marine Pollution Bulletin 30:332-340.

International Council for the Exploration of the Sea (ICES). 1992. Report on the results of the ICES/IOC/OSPARCOM intercomparison exercise on the analysis of chlorobiphenyl congeners in marine media - step 1 and the intercomparison study of the determination of CBs in Baltic herring oil. ICES Cooperative Research Report No. 183.

Janz, D. M., and C. D. Metcalfe. 1991a. Relative induction of aryl hydrocarbon hydroxylase by 2,3,7,8-TCDD and two coplanar PCBs in rainbow trout (*Oncorhynchus mykiss*). Environmental Toxicology and Chemistry 10:917-923.

Janz, D. M., and C. D. Metcalfe. 1991b. Nonadditive interactions of 2,3,7,8-TCDD and 3,3',4,4'-tetrachlorobiphenyl on aryl hydrocarbon hydroxylase induction in rainbow trout (*Oncorhynchus mykiss*). Chemosphere 23:467-472.

Janz, D. M., T. L. Metcalfe, C. D. Metcalfe, and G. D. Haffner. 1992. Relative concentrations of cytochrome P450-active organochlorine compounds in liver and muscle of rainbow trout from Lake Ontario. Journal of Great Lakes Research 18:759-765.

Jarman, W. M., S. A. Burns, R. R. Chang, R. D. Stephens, R. J. Norstrom, M. Simon, and J. Linthicum. 1993. Determination of PCDDs, PCDFs, and PCBs in California peregrine falcons (*Falco peregrinus*) and their eggs. Environmental Toxicology and Chemistry 12:105-114.

Johansen, H. R., O. J. Rossland, and G. Becher. 1993. Congener specific determination of PCBs in crabs from a polluted fjord region. Chemosphere 27:1245-1252.

Jones, K. C. 1988. Determination of polychlorinated biphenyls in human foodstuffs and tissues: suggestions for a selective congener analytical approach. Science of the Total Environment 68:141-159.

Jones, P. A., R. J. Sloan, and M. P. Brown. 1989. PCB congeners to monitor with caged juvenile fish and the upper Hudson River. Environmental Toxicology and Chemistry 8:793-803.

Jones, P. D., J. P. Giesy, J. L. Newsted, D. A. Verbrugge, D. L. Beaver, G. T. Ankley, D. E. Tillett, K. B. Lodge, and G. J. Niemi. 1993. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin equivalents in tissues of birds at Green Bay, Wisconsin, USA. Archives of Environmental Contamination and Toxicology 24:345-354.

Jones, P. D., J. P. Giesy, J. L. Newsted, D. A. Verbrugge, J. P. Ludwig, M. E. Ludwig, H. J. Auman, R. Crawford, D. E. Tillitt, T. J. Kubiak, and D. A. Best. 1994. Accumulation of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin equivalents by double-crested cormorant (*Phalacrocorax auritus*, Pelicaniformes) chicks in the North American Great Lakes. Ecotoxicology and Environmental Safety 27:192-209.

Kaiser, T. E., W. L. Reichel, L. N. Locke, E. Cromartie, A. J. Krynitsky, T. G. Lamont, B. M. Mulhern, R. M. Prouty, and D. M. Swineford. 1980. Organochlorine pesticides, PCB, and PBB residues and necropsy data for bald eagles from 29 states—1975-77. Pesticides Monitoring Journal 13:145-149.

Kammann, U., O. Landgref, and H. Steinhart. 1993. Distribution of aromatic organochlorines in livers and reproductive organs of male and female dabs from the German Bight. Marine Pollution Bulletin 26:629-635.

Kannan, N., S. Tanabe, A. Borrell, A. Aguilar, S. Focardi, and R. Tatsukawa. 1993. Isomer-specific analysis and toxic evaluation of polychlorinated biphenyls in striped dolphins affected by an epizootic in the western Mediterranean Sea. Archives of Environmental Contamination and Toxicology 25:227-233.

Kannan, N., S. Tanabe, M. Ono, and R. Tatsukawa. 1989. Critical evaluation of polychlorinated biphenyl toxicity in terrestrial and marine mammals: increasing impact of non-*ortho* and mono-*ortho* coplanar polychlorinated biphenyls from land to ocean. Archives of Environmental Contamination and Toxicology 18:850-857.

Kannan, N., S. Tanabe, T. Wakimoto, and R. Tatsukawa. 1987a. Coplanar PCBs in Aroclor and Kaneclor mixtures. Journal of the Association of Analytical Chemists 70:451-454.

Kannan, N., S. Tanabe, T. Wakimoto, and R. Tatsukawa. 1987b. A simple method for determining non-ortho substituted PCBs in Kanechlors, Aroclors and environmental samples. Chemosphere 16:1631-1634.

Karara, A. H., and V. A. McFarland. 1992. A pharmacokinetic analysis of the uptake of polychlorinated biphenyls (PCBs) by golden shiners. Environmental Toxicology and Chemistry 11:315-320.

Karickoff, S. W. 1981. Semi-empirical estimation of sorption of hydrophobic pollutants on natural sediments and soils. Chemosphere 10:833-846.

Kennedy, S. W., A. Lorenzen, C. A. James, and R. J. Norstrom. 1992. Ethoxyresorufin-O-deethylase (EROD) and porphyria induction in chicken embryo hepatocyte cultures—a new bioassay of PCB, PCDD, and related chemical contamination in wildlife. Chemosphere 25:193-196.

Kennish, M. J. 1992. Polychlorinated biphenyls in estuarine and coastal marine waters of New Jersey: a review of contamination problems. Reviews in Aquatic Sciences 6:275-293.

Kihlstrom, J. E., M. Olsson, S. Jensen, A. Johansson, J. Ahlbom, and A. Bergman. 1992. Effects of PCB and different fractions of PCB on the reproduction of the mink (*Mustela vison*). Ambio 21:563-569.

Kimbrough, R. D. 1995. Polychlorinated biphenyls (PCBs) and human health: an update. Critical Reviews in Toxicology 25:13-163.

Kleivane, L., J. U. Skaare, A. Bjorge, E. de Ruiter, and P. J. H. Reijnders. 1995. Organochlorine pesticide residue and PCBs in harbour porpoise (*Phocoena phocoena*) incidentally caught in Scandinavian waters. Environmental Pollution 89:137-146.

Knickmeyer, R., and H. Steinhart. 1989. On the distribution of polychlorinated biphenyl congeners and hexachlorobenzene in different tissues of dab (*Limanda limanda*) from the North Sea. Chemosphere 19:1309-1320.

Koistinen, J. 1990. Residues of planar polychloro-aromatic compounds in Baltic fish and seal. Chemosphere 20:1043-1048.

Korach, K. S., P. Sarver, K. Chae, J. A. McLachlan, and J. D. McKinney. 1988. Estrogen receptor-binding of polychlorinated hydroxybiphenyls: conformationally restricted structural probes. Molecular Pharmacology 33:120-126.

Kovats, Z. E., and J. J. H. Ciborowski. 1989. Aquatic insects as indicators of organochlorine contamination. Journal of Great Lakes Research 15:623-634.

Kratochvil, B. 1984. Sampling for chemical analysis. Analytical Chemistry 56:113R-129R.

Kuehl, D. W., B. C. Butterworth, J. Libal, and P. Marquis. 1991. An isotope dilution high resolution gas chromatographic-high resolution mass spectrometric method for the determination of coplanar polychlorinated biphenyls: application to fish and marine mammals. Chemosphere 22:849-858.

Lake, C. A., J. L. Lake, R. Haebler, R. McKinney, W. S. Boothman, and S. S. Sadove. 1995a. Contaminant levels in harbor seals from the northeastern United States. Archives of Environmental Contamination and Toxicology 29:128-134.

Lake, J. L., R. McKinney, C. A. Lake, F. A. Osterman, and J. Heltshe. 1995b. Comparisons of patterns of polychlorinated biphenyl congeners in water, sediment, and indigenous organisms from New Bedford Harbor, Massachusetts. Archives of Environmental Contamination and Toxicology 29:207-220.

Larsson, P., C. Jarnmark, and A. Sodergren. 1992. PCBs and chlorinated pesticides in the atmosphere and aquatic organisms of Ross Island, Antarctica. Marine Pollution Bulletin 25:9-12.

Larsson, P., L. Okla, and L. Collvin. 1993. Reproductive status and lipid content as factors in PCB, DDT, and HCH contamination of a population of pike (*Esox lucius* L.). Environmental Toxicology and Chemistry 12:855-861.

Larsson, P., L. Okla, and P. Woin. 1990. Atmospheric transport of persistent pollutants governs uptake by holarctic terrestrial biota. Environmental Science & Technology 24:1599-1601.

Law, L. M., and D. F. Goerlitz. 1974. Selected chlorinated hydrocarbons in bottom material from streams tributary to San Francisco Bay. Pesticides Monitoring Journal 8:33-36.

Lebo, J. A., J. L. Zajicek, J. N. Huckins, J. D. Petty, and P. H. Peterman. 1992. Use of semipermeable membrane devices for in situ monitoring of polycyclic aromatic hydrocarbons in aquatic environments. Chemosphere 25:697-718.

Leiker, T. J., C. E. Rostad, C. R. Barnes, and W. E. Pereira. 1991. A reconnaissance study of halogenated organic compounds in catfish from the lower Mississippi River and its major tributaries. Chemosphere 23:817-829.

Leonards, P. E. G., B. van Hattum, W. P. Cofino, and U. A. T. Brinkman. 1994. Occurrence of non-ortho-, mono-ortho-, and di-ortho-substituted PCB congeners in different organs and tissues of polecats (*Mustela putorius* L.) from the Netherlands. Environmental Toxicology and Chemistry 13:129-142.

Leonzio, C., M. Lambertini, A. Massi, S. Focardi, and C. Fossi. 1989. An assessment of pollutants in eggs of Audouin's gull, (*Larus audouinii*), a rare species of the Mediterranean Sea. The Science of the Total Environment 78:13-22.

Leonzio, C., L. Marsili, and S. Focardi. 1992. Influence of cadmium on PCB congener accumulation in quail. Bulletin of Environmental Contamination and Toxicology 49:686-693.

Lester, D. C., and A. McIntosh. 1994. Accumulation of polychlorinated biphenyl congeners from Lake Champlain sediments by *Mysis relicta*. Environmental Toxicology and Chemistry 13:1825-1841.

Li, M. H., Y. D. Zhao, and L. G. Hansen. 1994. Multiple dose toxicokinetic influence on the estrogenicity of 2,2',4,4', 6,6'-hexachlorobiphenyl. Bulletin of Environmental Contamination and Toxicology 53:583-590.

Litten, S., B. Mead, and J. Hassett. 1993. Application of passive samplers (PISCES) to locating a source of PCBs on the Black River, New York. Environmental Toxicology and Chemistry 12:639-647.

Loganathan, B. G., S. Tanabe, H. Tanaka, S. Watanabe, N. Miyazaki, M. Amano, and R. Tatsukawa. 1990. Comparison of organochlorine residue levels in the striped dolphin from western North Pacific, 1978-79 and 1986. Marine Pollution Bulletin 21:435-439.

Long, E. R. 1982. An assessment of marine pollution in Puget Sound. Marine Pollution Bulletin 13:380-383.

Lowe, T. P., and R. C. Stendell. 1991. Eggshell modifications in captive American kestrels resulting from Aroclor 1248 in the diet. Archives of Environmental Contamination and Toxicology 20:519-522.

Maack, L., and W. C. Sonzogni. 1988. Analysis of polychlorobiphenyl congeners in Wisconsin fish. Archives of Environmental Contamination and Toxicology 17:711-719.

Mac, M. J., T. R. Schwartz, C. C. Edsall, and A. M. Frank. 1993. Polychlorinated biphenyls in Great Lakes trout and their eggs: relations to survival and congener composition 1979-1988. Journal of Great Lakes Research 19:752-765.

Macdonald, C. R., and C. D. Metcalfe. 1989. A comparison of PCB congener distributions in two point-source contaminated lakes and one uncontaminated lake in Ontario. Water Pollution Research Journal of Canada 24:23-46.

Macdonald, C. R., and C. D. Metcalfe. 1991. Concentration and distribution of PCB congeners in isolated Ontario Lakes contaminated by atmospheric deposition. Canadian Journal of Fisheries and Aquatic Sciences 48:371-381.

Macdonald, C. R., C. D. Metcalfe, G. C. Balch, and T. L. Metcalfe. 1993. Distribution of PCB congeners in seven lake systems: interactions between sediment and food-web transport. Environmental Toxicology and Chemistry 12:1991-2003.

Macdonald, C. R., R. J. Norstrom, and R. Turle. 1992. Application of pattern recognition techniques to assessment of biomagnification and sources of polychlorinate multicomponent pollutants, such as PCBs, PCDDs, and PCDFs. Chemosphere 25:129-134.

MacLeod, W. D., Jr., L. S. Ramos, A. J. Friedman, D. G. Burrows, P. G. Prohaska, D. L. Fisher, and D. W. Brown. 1981. Analysis of residual chlorinated hydrocarbons, aromatic hydrocarbons, and related compounds in selected sources, sinks, and biota of the New York Bight. U.S. National Oceanic and Atmospheric Administration, Technical Memorandum OMPA-6. 128 pp.

Madej, A., M. Forsberg, and L. E. Edqvist. 1992. Urinary excretion of cortisol and oestrone sulfate in pregnant mink fed PCB and fractions of PCB. Ambio 21:582-585.

Marcus, J. M., and R. T. Renfrow. 1990. Pesticides and PCBs in South Carolina estuaries. Marine Pollution Bulletin 21:96-99.

Marks, T. A., G. L. Kimmel, and R. E. Staples. 1981. Influence of symmetrical polychlorinated biphenyl isomers on embryo and fetal development in mice. I. Teratogenicity of 3,3',4,4',5,5'-hexachlorobiphenyl. Toxicology and Applied Pharmacology 61:269-276.

Marks, T. A., G. L. Kimmel, and R. E. Staples. 1989. Influence of symmetrical polychlorinated biphenyl isomers on embryo and fetal development in mice. II. Comparison of 4,4'-dichlorobiphenyl, 3,3'4,4'-tetrachlorobiphenyl, 3,3'5,5'-tetrachlorobiphenyl, and 3,3'4,4'-tetramethylbiphenyl. Fundamental and Applied Toxicology 13:681-693.

Martin, D. B., and W. A. Hartman. 1985. Organochlorine pesticides and polychlorinated biphenyls in sediment and fish from wetlands in the north central United States. Journal of the Association of Official Analytical Chemists 68:712-717.

Marthinsen, L., G. Staveland, J. U. Skaare, K. I. Ugland, and A. Haugen. 1991. Levels of environmental pollutants in male and female flounder (*Platichthys flesus* L.) and cod (*Gadus morhua* L.) caught during the year 1988 near or in the waterway of Glomma, the largest river of Norway. I. Polychlorinated biphenyls. Archives of Environmental Contamination and Toxicology 20:353-360.

Mason, C. F., and J. R. Ratford. 1994. PCB congeners in tissues of European otters (*Lutra*). Bulletin of Environmental Contamination and Toxicology 53:548-554.

Masse, R., D. Martineau, L. Tremblay, and P. Beland. 1986. Concentrations and chromatographic profile of DDT metabolites and polychlorobiphenyl (PCB) residues in stranded beluga whales (*Delphinapterus leucas*) from the St. Lawrence estuary, Canada. Archives of Environmental Contamination and Toxicology 15:567-579.

McDuffie, B. 1981. Estimation of octanol/water partition coefficients for organic pollutants using reverse-phase HPLC. Chemosphere 10:73-83.

McKinney, J. D., K. Chae, B. N. Gupta, J. A. Moore, and J. A. Goldstein. 1976. Toxicological assessment of hexachlorobiphenyl isomers and 2,3,7,8-tetrachlorodibenzofuran in chicks. I. Relationship of chemical parameters. Toxicology and Applied Pharmacology 36:65-80.

McNulty, W. P. 1985. Toxicity and fetotoxicity of TCDD, TCDF, and PCB isomers in rhesus macaques (*Macaca mulatta*). Environmental Health Perspectives 60:77-88.

McNulty, W. P., G. M. Becker, and H. T. Cory. 1980. Chronic toxicity of 3,4,3',4'- and 2,5,2',5'-tetrachlorobiphenyls in rhesus macaques. Toxicology and Applied Pharmacology 56:182-190.

Meadows, J., D. Tillitt, J. Huckins, and D. Schroeder. 1993. Large-scale dialysis of sample liquids using a semipermeable membrane device. Chemosphere 26:1993-2006.

Mearns, A. J. 1992. Contaminant trends in the Southern California Bight: four decades of stress and recovery. Pages 5-25 *in* Perspectives on the marine environment: proceedings from a symposium on the marine environment of southern California, May 10, 1991, Los Angeles, California. USC SG TR ; No. 01 92. National Oceanic and Atmospheric Administration, Seattle, Washington. 130 pp.

Melancon, M. J., K. A. Turnquist, and J. J. Lech. 1989. Relation of hepatic microsomal monooxygenase activity to tissue PCBs in rainbow trout (*Salmo gairdneri*) injected with [^{14}C] PCBs. Environmental Toxicology and Chemistry 8:777-782.

Mercier, M., G. Pascal, and V. Azais-Braesco. 1990. Retinyl ester hydrolase and vitamin A status in rats treated with 3,3',4,4'-tetrachlorobiphenyl. Biochimica et Biophysica Acta 1047:70-76.

Merriman, J. C., D. H. J. Anthony, J. A. Kraft, and R. J. Wilkinson. 1991. Rainy River water quality in the vicinity of bleached kraft mills. Chemosphere 23:1605-1615.

Mes, J., D. L. Arnold, and F. Bryce. 1995. Postmortem tissue levels of polychlorinated biphenyls in female rhesus monkeys after more than six years of daily dosing with Aroclor 1254 and in their non-dosed offspring. Archives of Environmental Contamination and Toxicology 29:69-76.

Millard, E. S., E. Halfon, C. K. Minns, and C. C. Charlton. 1993. Effect of primary productivity and vertical mixing on PCB dynamics in planktonic model ecosystems. Environmental Toxicology and Chemistry 12:931-946.

Miranda, C. L., M. C. Henderson, J. L. Wang, H. S. Nakaue, and D. R. Buhler. 1987. Effects of polychlorinated biphenyls on porphyrin synthesis and cytochrome P-450-dependent monooxygenases in small intestine and liver of Japanese quail. Journal of Toxicology and Environmental Health 20:27-35.

Mora, M. A., H. J. Auman, J. P. Ludwig, J. P. Giesy, D. A. Verbrugge, and M. E. Ludwig. 1993. Polychlorinated biphenyls and chlorinated insecticides in plasma of Caspian terns: relationships with age, productivity, and colony site tenacity in the Great Lakes. Archives of Environmental Contamination and Toxicology 24:320-331.

Mudroch, A., F. I. Onuska, and L. Kalas. 1989. Distribution of polychlorinated biphenyls in water, sediments, and biota of two harbours. Chemosphere 18:2141-2154.

Muir, D. C. G., R. J. Norstrom, and M. Simon. 1988. Organochlorine contaminants in Arctic marine food chains: accumulation of specific polychlorinated biphenyls and chlordane-related compounds. Environmental Science & Technology 22:1071-1079.

Mullin, M. D., C. M. Pochini, S. McCrindle, M. Romkes, S. H. Safe, and L. M. Safe. 1984. High resolution PCB analysis: synthesis and chromatographic properties of all 209 PCB congeners. Environmental Science & Technology 18:468-476.

Murk, A. J., J. H. J. van den Berg, J. H. Koeman, and A. Brouwer. 1991. The toxicity of tetrachlorobenzyltoluenes (Ugilec 141) and polychlorinated biphenyls (Aroclor 1254 and PCB-77) compared in Ah-responsive and Ah-nonresponsive mice. Environmental Pollution 72:57-67.

National Academy of Sciences (NAS). 1979. Polychlorinated biphenyls. National Academy of Sciences, Washington, D.C. 182 pp.

National Oceanic and Atmospheric Administration (NOAA). 1987. National status and trends programs for marine environmental quality. Progress report and preliminary assessment of findings of the benthic surveillance project—1984. NOAA, Rockville, Md. 81 pp.

National Oceanic and Atmospheric Administration (NOAA). 1991. Second summary of data on chemical concentrations in sediments from the National Status and Trends Program. NOAA Technical Memorandum NOS OMA 59. National Oceanic and Atmospheric Administration, Rockville, Md. 29 pp. + appendixes.

Newsted, J. L., J. P. Giesy, G. T. Ankley, D. E. Tillitt, R. A. Crawford, J. W. Gooch, P. D. Jones, and M. S. Denison. 1995. Development of toxic equivalency factors for PCB congeners and the assessment of TCDD and PCB mixtures in rainbow trout. Environmental Toxicology and Chemistry 14:861-871.

Niimi, A. J., and B. G. Oliver. 1989. Distribution of polychlorinated biphenyl congeners and other halocarbons in whole fish and muscle among Lake Ontario salmonids. Environmental Science & Technology 23:83-88.

Nikolaides, E., B. Brunstrom, and L. Dencker. 1988. Effects of the TCDD congeners 3,3',4,4'-tetrachlorobiphenyl and 3,3',4,4'-tetrachloroazoxybenzene on lymphoid development in the bursa of Fabricius of the chick embryo. Toxicology and Applied Pharmacology 92:315-323.

Norheim, G., J. U. Skaare, and O. Wiig. 1992. Some heavy metals, essential elements, and chlorinated hydrocarbons in polar bear (*Ursus maritimus*) at Svalbard. Environmental Pollution 77:51-57.

Norstrom, R. J., M. Simon, D. C. G. Muir, and R. E. Schweinsburg. 1988. Organochlorine contaminants in Arctic marine food chains: identification, geographical distribution, and temporal trends in polar bears. Environmental Science & Technology 22:1063-1071.

Oliver, B. G., M. M. Charlton, and R. W. Durham. 1989. Distribution, redistribution, and geochronology of polychlorinated biphenyl congeners and other chlorinated hydrocarbons in Lake Ontario sediments. Environmental Science & Technology 23:200-208.

Oliver, B. G., and A. J. Niimi. 1988. Trophodynamic analysis of PCB congeners and other chlorinated hydrocarbons in the Lake Ontario ecosystem. Environmental Science & Technology 22:388-397.

Opperhuizen, A., and S. M. Schrap. 1988. Uptake efficiencies of two polychlorobiphenyls in fish after dietary exposure to five different concentrations. Chemosphere 17:253-262.

Ormerod, S. J., and S. J. Tyler. 1992. Patterns of contamination by organochlorines and mercury in the eggs of two river passerines in Britain and Ireland with reference to individual PCB congeners. Environmental Pollution 76:233-243.

Ormerod, S. J., and S. J. Tyler. 1994. Inter- and intra-annual variation in the occurrence of organochlorine pesticides, polychlorinated biphenyl congeners, and mercury in the eggs of a river passerine. Archives of Environmental Contamination and Toxicology 26:7-12.

Pal, D., J. B. Weber, and M. R. Overcash. 1980. Fate of polychlorinated biphenyls (PCBs) in soil-plant systems. Residue Reviews 74:45-98.

Parkinson, A., and S. Safe. 1987. Mammalian biologic and toxic effects of PCBs. Pages 49-75 *in* S. Safe, editor. Polychlorinated biphenyls (PCBs): mammalian and environmental toxicology. Environmental Toxin Series 1. Springer-Verlag, New York.

Phillips, D. J. H., and R. B. Spies. 1988. Chlorinated hydrocarbons in the San Francisco estuarine ecosystem. Marine Pollution Bulletin 19:445-453.

Phillips, L. J., and G. F. Birchard. 1990. An evaluation of the potential for toxics exposure in the Great Lakes region using Store data. Chemosphere 20:587-598.

Porte, C., D. Barcelo, and J. Albaiges. 1988. Quantitation of total versus selected polychlorinated biphenyl congeners in marine biota samples. Journal of Chromatography 442:386-393.

Prest, H. F., W. M. Jarman, S. A. Burns, T. Weismuller, M. Martin, and J. N. Huckins. 1992. Passive water sampling via semipermeable membrane devices (SPMDs) in concert with bivalves in the Sacramento/San Joaquin river delta. Chemosphere 25:1811-1823.

Pruell, R. J., N. I. Rubenstein, B. K. Taplin, J. A. LiVolsi, and R. D. Bowen. 1993. Accumulation of polychlorinated organic contaminants from sediment by three benthic marine species. Archives of Environmental Contamination and Toxicology 24:290-297.

Rapaport, R. A., and S. J. Eisenreich. 1984. Chromatographic determination of octanol-water partition coefficients ($K_{OW'S}$) for 58 polychlorinated biphenyl congeners. Environmental Science & Technology 18:163-170.

Rattner, B. A., J. S. Hatfield, M. J. Melancon, T. W. Custer, and D. E. Tillitt. 1994. Relation among cytochrome P450, Ah-active PCB congeners and dioxin equivalents in pipping black-crowned night-heron embryos. Environmental Toxicology and Chemistry 13:1805-1812.

Rattner, B. A., M. J. Melancon, T. W. Custer, R. L. Hothem, K. A. King, L. J. LeCaptain, J. W. Spann, B. R. Woodin, and J. J. Stegeman. 1993. Biomonitoring environmental contamination with pipping black-crowned night heron embryos: induction of cytochrome P450. Environmental Toxicology and Chemistry 12:1719-1732.

Rhee, G. Y., B. Bush, M. P. Brown, M. Kane, and L. Shane. 1989. Anaerobic biodegradation of polychlorinated biphenyls in Hudson River sediments and dredged sediments in clay encapsulation. Water Research 23:957-964.

Rifkind, A. B., A. Firpo, Jr., and D. R. Alonso. 1984. Coordinate induction of cytochrome P-448 mediated mixed function oxidases and histopathologic changes produced acutely in chick embryo liver by polychlorinated biphenyl congeners. Toxicology and Applied Pharmacology 72:343-354.

Robertson, A., B. W. Gottholm, D. D. Turgeon, D. A. Wolfe. 1991. A comparative study of contaminant levels in Long Island Sound. Estuaries 14:290-298.

Robertson, L. W., A. Parkinson, S. Bandiera, L. Lambert, J. Merrill, and S. H. Safe. 1984. PCBs and PBBs: biologic and toxic effects on C57BL/6J and DBA/2J inbred mice. Toxicology 31:191-206.

Rowan, D. J., and J. B. Rasmussen. 1992. Why don't Great Lakes fish reflect environmental concentrations of organic contaminants?—An analysis of between-lake variability in the ecological partitioning of PCBs and DDT. Journal of Great Lakes Research 18:724-741.

Safe, S. 1984. Polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs): biochemistry, toxicology, and mechanism of action. Critical Reviews in Toxicology 13:319-393.

Safe, S., editor. 1987a. Polychlorinated biphenyls (PCBs): mammalian and environmental toxicology. Environmental Toxin Series 1. Springer-Verlag, New York. 152 pp.

Safe, S. 1987b. Determination of 2,3,7,8-TCDD toxic equivalent factors (TEFs): support for the use of the in vitro AHH induction assay. Chemosphere 16:791-802.

Safe, S. 1990. Polychlorinated biphenyls (PCBs), dibenzo-p-dioxins PCDDs), dibenzofurans (PCDFs), and related compounds: environmental and mechanistic considerations which support the development of toxic equivalency factors (TEFs). Critical Reviews in Toxicology 21:51-88.

Safe, S. H. 1994. Polychlorinated biphenyls (PCBs): environmental impact, biochemical and toxic responses, and implications for risk assessment. Critical Reviews in Toxicology 24:87-149.

Safe, S., D. Jones, J. Kohli, and L. O. Ruzo. 1976. The metabolism of chlorinated aromatic pollutants by the frog. Canadian Journal of Zoology 54:1818-1823.

Safe, S., L. Safe, and M. Mullin. 1985. Polychlorinated biphenyls: congener-specific analysis of a commercial mixture and a human milk extract. Journal of Agricultural and Food Chemistry 33:24-29.

Sallenave, R. M., K. E. Day, and D. P. Kreutzweiser. 1994. The role of grazers and shredders in the retention and downstream transport of a PCB in lotic environments. Environmental Toxicology and Chemistry 13:1843-1847.

Sanchez, J., M. Sole, and J. Albaiges. 1993. A comparison of distributions of PCB congeners and other chlorinated compounds in fishes from coastal areas and remote lakes. International Journal of Environmental Analytical Chemistry 50:269-284.

Schantz, S. L., J. Moshtaghian, and D. K. Ness. 1995. Spatial learning deficits in adult rats exposed to *ortho*-substituted PCB congeners during lactation and gestation. Fundamental and Applied Toxicology 26:117-126.

Scharenberg, W. 1991a. Prefledging terns (*Sterna paradisaea, Sterna hirundo*) as bioindicators for organochlorine residues in the German Wadden Sea. Archives of Environmental Contamination and Toxicology 21:102-105.

Scharenberg, W. 1991b. Cormorants (*Phalacrocorax carbo sinensis*) as bioindicators for polychlorinated biphenyls. Archives of Environmental Contamination and Toxicology 21:536-540.

Schmidt, L. J., and R. J. Hesselberg. 1992. A mass spectroscopic method for analysis of AHH-inducing and other polychlorinated biphenyl congeners and selected pesticides in fish. Archives of Environmental Contamination and Toxicology 23:37-44.

Schmitt, C. J., J. L. Zajicek, and P. H. Peterman. 1990. National Contaminant Biomonitoring Program: residues of organochlorine chemicals in U.S. freshwater fish, 1976-1984. Archives of Environmental Contamination and Toxicology 19:748-781.

Schomburg, G., H. Husmann, and E. Hubinger. 1985. Multidimensional separation of isomeric species of chlorinated hydrocarbons such as PCB, PCDD, and PCDF. Journal of High Resolution Chromatography & Chromatography Communications 8:395-400

Schrap, S. M., and A. Opperhuizen. 1988. Elimination kinetics of two unmetabolized polychlorinated biphenyls in *Poecilla reticulata* after dietary exposure. Bulletin of Environmental Contamination and Toxicology 40:381-388.

Schulz, D. E., G. Petrick, and J. C. Duinker. 1989. Complete characterization of polychlorinated biphenyl congeners in commercial Aroclor and Clophen mixtures by multidimensional gas chromatography-electron capture detection. Environmental Science & Technology 23:852-859.

Schwartz, T. R., and D. L. Stalling. 1991. Chemometric comparison of polychlorinated biphenyl residues and toxicologically active polychlorinated biphenyl congeners in the eggs of Forster's terns (*Sterna forsteri)*. Archives of Environmental Contamination and Toxicology 20:183-199.

Schwartz, T. R., D. E. Tillitt, K. P. Feltz, and P. H. Peterman. 1993. Determination of mono- and non-O,O'-chlorine substituted polychlorinated biphenyls in Aroclors and environmental samples. Chemosphere 26:1443-1460.

Sericano, J. L., E. L. Atlas, T. L. Wade, and J. M. Brooks. 1990. NOAA's Status and Trends Mussel Watch Program: chlorinated pesticides and PCBs in oysters (*Crassostrea virginica*) and sediments from the Gulf of Mexico, 1986-1987. Marine Environmental Research 29:161-203.

Sericano, J. L., S. H. Safe, T. L. Wade, and J. M. Brooks. 1994. Toxicological significance of non-, mono, and di-ortho-substituted polychlorinated biphenyls in oysters from Galveston and Tampa Bays. Environmental Toxicology and Chemistry 13:1797-1803.

Shain, W., S. R. Overmann, L. R. Wilson, J. Kostas, and B. Bush. 1986. A congener analysis of polychlorinated biphenyls accumulating in rat pups after perinatal exposure. Archives of Environmental Contamination and Toxicology 15:687-707.

Shimada, T., and Y. Sawabe. 1983. Activation of 3,4,3',4'-tetrachlorobiphenyl to protein-based metabolites by rat liver microsomal cytochrome P-448 containing monooxygenase system. Toxicology and Applied Pharmacology 70:486-493.

Shimada, T., and Y. Sawabe. 1984. Comparative studies on distribution and covalent tissue binding of 2,4,2',4'- and 3,4,3',4'-tetrachlorobiphenyl isomers in the rat. Archives of Toxicology 55:182-185.

Shiu, W. Y., and D. Mackay. 1986. A critical review of aqueous solubilities, vapor pressures, Henry's Law constants, and octanol-water partition coefficients of the polychlorinated biphenyls. Journal of Physical and Chemical Reference Data 15:911-929.

Sipes, I. G., and R. G. Schnellmann. 1987. Biotransformation of PCBs: metabolic pathways and mechanisms. Pages 97-110 in S. Safe, editor. Polychlorinated biphenyls (PCBs): mammalian and environmental toxicology. Environmental Toxin Series 1. Springer-Verlag, New York.

Skaare, J. U., E. G. Jensen, A. Goksoyr, and E. Egaas. 1991. Response of xenobiotic metabolizing enzymes of rainbow trout (*Oncorhynchus mykiss*) to the mono-ortho substituted polychlorinated PCB congener 2,3',4,4',5-pentachlorobiphenyl, PCB-118, detected by enzyme activities and immunochemical methods. Archives of Environmental Contamination and Toxicology 20:349-352.

Smith, L. S., T. R. Schwartz, K. Felz, and T. J. Kubiak. 1990. Determination and occurrence of AHH-active polychlorinated biphenyls, 2,3,7,8-tetrachloro p-dioxin and 2,3,7,8-tetrachlorodibenzofuran in Lake Michigan sediment and biota. The question of their relative toxicological significance. Chemosphere 21:1063-1085.

Smith, V. E., J. M. Spurr, J. C. Filkins, and J. J. Jones. 1985. Organochlorine contaminants of wintering ducks foraging on Detroit River sediments. Journal of Great Lakes Research 11:231-246.

Sonzogni, W., L. Maack, T. Gibson, D. Degenhardt, H. Anderson, and B. Fiore. 1991. Polychlorinated biphenyl congeners in blood of Wisconsin sport fish consumers. Archives of Environmental Contamination and Toxicology 20:56-60.

Southworth, G. R. 1990. PCB concentrations in stream sunfish (*Lepomis auritus* and *L*. *macrochirus*) in relation to proximity to chronic point sources. Water, Air and Soil Pollution 51:287-296.

Spear, P. A., and T. W. Moon. 1985. Low dietary iodine and thyroid anomalies in ring doves, *Streptopelia risoria*, exposed to 3,4,3'4'-tetrachlorobiphenyl. Archives of Environmental Contamination and Toxicology 14:547-553.

Stainken, D. M., and T. C. Rollwagen. 1979. PCB residues in bivalves and sediments of Raritan Bay. Bulletin of Environmental Contamination and Toxicology 23:690-697.

Stalling, D. L., J. N. Huckins, J. D. Petty, and J. L. Johnson. 1980. Presence and potential significance of o,o' unsubstituted PCB isomers and trace Aroclor 1248 and 1254 impurities. Pages 13-139 *in* B.N. Afgan and D. Mackay, editors. Hydrocarbons and halogenated hydrocarbons in the aquatic environment. Plenum Press, New York.

Stalling, D. L., and T. R. Schwartz. 1987. Classification of polychlorinated biphenyl residues: isomer vs. homologue concentrations in modeling Aroclors and polychlorinated biphenyl residues. Analytical Chemistry 59:1853-1859.

Stange, K., and D. L. Swackhammer. 1994. Factors affecting phytoplankton species-specific differences in accumulation of 40 polychlorinated biphenyls (PCBs). Environmental Toxicology and Chemistry 13:1849-1860.

Steimle, F. W., V. S. Zdanowicz, and D. F. Gadbois. 1990. Metals and organic contaminants in northwest Atlantic deep-sea tilefish tissues. Marine Pollution Bulletin 21:530-535.

Stein, J. E., T. K. Collier, W. L. Reichert, E. Casillas, T. Hom, and U. Varanasi. 1992. Bioindicators of contaminant exposure and sublethal effects: studies with benthic fish in Puget Sound, Washington. Environmental Toxicology and Chemistry 11:701-714.

Steingraeber, M. T., T. R. Schwartz, J. G. Wiener, and J. A. Lebo. 1994. Polychlorinated biphenyl congeners in emergent mayflies from the upper Mississippi River. Environmental Science & Technology 28:707-714.

Storr-Hansen, E., and T. Cederberg. 1992. Determination of coplanar polychlorinated biphenyl (CB) congeners in seal tissues by chromatography on active carbon, dual-column high resolution GC/ECD and high resolution GC/high resolution MS. Chemosphere 24:1181-1196.

Storr-Hansen, E., and H. Spliid. 1993. Coplanar polychlorinated biphenyl congener levels and patterns and the identification of separate populations of harbor seals *(Phoca vitulina*) in Denmark. Archives of Environmental Contamination and Toxicology 24:44-58.

Swackhammer, D. L., M. J. Charles, and R. A. Hites. 1987. Quantitation of toxaphene in environmental samples using negative ion chemical ionization mass spectrometry. Analytical Chemistry 59:913-917.

Swackhammer, D. L., B. D. McVeety, and R. A. Hites. 1988. Deposition and evaporation of polychlorobiphenyl congeners to and from Siskiwit Lake, Isle Royale, Lake Superior. Environmental Science & Technology 22:664-672.

Swackhammer, D. L., and R. S. Skoglund. 1993. Bioaccumulation of PCBs by algae: kinetics versus equilibrium. Environmental Toxicology and Chemistry 12:831-838.

Tanabe, S. 1988. PCB problems in the future: foresight from current knowledge. Environmental Pollution 50:5-28.

Tanabe, S., N. Kannan, M. Ono, and R. Tatsukawa. 1989. Toxic threat to marine mammals: increasing toxic potential of non-*ortho* and mono-*ortho* coplanar PCBs from land to ocean. Chemosphere 18:485-490.

Tanabe, S., N. Kannan, A. Subramanian, S. Watanabe, and R. Tatsukawa. 1987. Highly toxic coplanar PCBs: occurrence, source, persistency and toxic implications to wildlife and humans. Environmental Pollution 47:147-163.

Tanabe, S., N. Kannan, T. Wakimoto, and R. Tatsukawa. 1987. Method for the determination of three toxic non-ortho chlorine substituted coplanar PCBs in environmental samples at part-per-trillion levels. International Journal of Environmental Analytical Chemistry 29:199-213.

Tanabe, S., A. Subramanian, A. Ramesh, P.L. Kumaran, N. Miyazaki, and R. Tatsukawa. 1993. Persistent organochlorine residues in dolphins from the Bay of Bengal, South India. Marine Pollution Bulletin 26:311-316.

Tarhanen, J., J. Koistinen, J. Paasivirta, P. J. Vuorinen, J. Koivusaari, I. Nuuja, N. Kannan, and R. Tatsukawa. 1989. Toxic significance of planar aromatic compounds in Baltic ecosystem -new studies on extremely toxic coplanar PCBs. Chemosphere 18:1067-1077.

Thomann, R. V., J. A. Mueller, R. P. Winfield, and C. R. Huang. 1991. Model of fate and accumulation of PCB homologues in Hudson estuary. Journal of Environmental Engineering 117:161-178.

Tillitt, D. E., J. P. Giesy, and G. T. Ankley. 1991. Characterization of the H4IIE rat hepatoma cell bioassay as a tool for assessing toxic potency of planar halogenated hydrocarbons in environmental samples. Environmental Science & Technology 25:87-92.

Turle, R., R. J. Norstrom, and B. Collins. 1991. Comparison of PCB quantitation methods: re-analysis of archived specimens of herring gull eggs from the Great Lakes. Chemosphere 22:201-213.

Tyle, H., M. Egsmose, and N. Harrit. 1991. Mixed-function oxygenase in juvenile rainbow trout exposed to hexachlorobenzene or 3,3',4,4'-tetrachlorobiphenyl. Comparative Biochemistry and Physiology 100C:161-164.

U.S. Environmental Protection Agency (USEPA). 1980. Ambient water quality criteria for polychlorinated biphenyls. U.S. Environmental Protection Agency Report 440/5-80-068. 211 pp.

U.S. Environmental Protection Agency (USEPA). 1992a. National study of chemical residues in fish. Volume I. U.S. Environmental Protection Agency Report EPA 823-R-92-008a. 304 pp.

U.S. Environmental Protection Agency (USEPA). 1992b. National study of chemical residues in fish. Volume II. U.S. Environmental Protection Agency Report EPA 823-R-92-008b. 459 pp.

U.S. Environmental Protection Agency (USEPA). 1994. Semivolatile compounds in the general U.S. population: NHATS FY86 results. Volumes I and II. U.S. Environmental Protection Agency Report EPA 747-R-94-001. 409 pp.

van den Berg, K. J., C. Zurcher, A. Brouwer, and D. W. van Bekkum. 1988. Chronic toxicity of 3,4,3',4'-tetrachlorobiphenyl in the marmoset monkey (*Callithrix jacchus*). Toxicology 48:209-224.

van den Berg, M., B. L. H. J. Craane, T. Sinnige, I. J. Lutke-Schipholt, B. Spenkelink, and A. Brouwer. 1992. The use of biochemical parameters in comparative toxicological studies with the cormorant (*Phalacrocorax carbo*) in the Netherlands. Chemosphere 25:1265-1270.

Van der Oost, R., H. Heida, and A. Opperhuizen. 1988. Polychlorinated biphenyl congeners in sediments, plankton, mollusks, crustaceans, and eel in a freshwater lake: implications of using reference chemicals and indicator organisms in bioaccumulation studies. Archives of Environmental Contamination and Toxicology 17:721-729.

Walker, M. K., and R. E. Peterson. 1991. Potencies of polychlorinated dibenzo-*p*-dioxin, dibenzofuran, and biphenyl congeners, relative to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, for producing early life stage mortality in rainbow trout (*Oncorhynchus mykiss*). Aquatic Toxicology 21:219-238.

Walker, M. K., and R. E. Peterson. 1994. Aquatic toxicity of dioxins and related chemicals. Pages 347-387 *in* A. Schecter, editor. Dioxins and health. Plenum Press, New York.

Wardell, R. E., N. E. Seegmiller, and W. S. Bradshaw. 1982. Induction of prenatal toxicity in the rat by diethylstilbestrol, zeranol, 3,4,3',4'-tetrachlorobiphenyl, cadmium, and lead. Teratology 26:229-237.

Webb, R. G., and A. C. McCall. 1973. Quantitative PCB standards for electron capture gas chromatography. Journal of Chromatographic Science 11:366-373.

Williams, L. L., and J. P. Giesy. 1992. Relationships among concentrations of individual polychlorinated biphenyl (PCB) congeners, 2,3,7,8-tetrachlorodibenzo-p-dioxin equivalents (TCDD-EQ), and rearing mortality of chinook salmon (*Oncorhynchus tshawytscha*) eggs from Lake Michigan. Journal of Great Lakes Research 18:108-124.

Williams, L. L., J. P. Giesy, D. A. Verbrugge, S. Jurzysta, G. Heinz, and K. Stromborg. 1995. Polychlorinated biphenyls and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin equivalents in eggs of red-breasted mergansers near Green Bay, Wisconsin, USA, in 1977-78 and 1990. Archives of Environmental Contamination and Toxicology 29:52-60.

Winter, S., and B. Streit. 1992. Organochlorine compounds in a three-step terrestrial food chain. Chemosphere 24:1765-1774.

Wood, L. W., G. Y. Rhee, B. Bush, and E. Barnard. 1987. Sediment desorption of PCB congeners and their bio-uptake by dipteran larvae. Water Research 21:875-884.

Woodburn, K. B., W. J. Doucette, and A. W. Andren. 1987. Generator column determination of octanol/water partition coefficients for selected polychlorinated biphenyl congeners. Environmental Science & Technology 18:457-459.

Yalkowsky, S. H., S. C. Valvani, and D. Mackay. 1983. Estimation of the aqueous solubility of some aromatic compounds. Residue Reviews 85:43-55.

Yoshimura, H., Y. Yonemoto, H. Yamada, N. Koga, K. Oguri, and S. Saeki. 1987. Metabolism *in vivo* of 3,4,3',4'-tetrachlorobiphenyl and toxicological assessment of the metabolites in rats. Xenobiotica 17:897-910.

Zabel, E. W., P. M. Cook, and R. E. Peterson. 1995. Toxic equivalency factors of polychlorinated dibenzo-*p*-dioxin, dibenzofuran and biphenyl congeners based on early life stage mortality in rainbow trout (*Oncorhynchus mykiss*). Aquatic Toxicology 31:315-328.

Zupancic-Kralj, L., J. Jan, and J. Marsel. 1992. Assessment of polychlorobiphenyls in human/poultry fat and in hair/plumage from a contaminated area. Chemosphere 25:1861-1867.

Biological Report 32
September 1996

Contaminant Hazard Reviews
Report No. 32

SILVER HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. National Biological Service
Laurel, MD 20708

TABLES

Number

SILVER HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

U.S. Department of the Interior
National Biological Service
Patuxent Wildlife Research Center
Laurel, MD 20708

Abstract. Ecological and toxicological aspects of silver (Ag) and silver salts in the environment are briefly summarized with an emphasis on natural resources. Subtopics include sources and uses, chemistry and metabolism, concentrations in field collections, lethal and sublethal effects, and recommendations for the protection of natural resources. Elevated silver concentrations in biota occur in the vicinities of sewage outfalls, electroplating plants, mine waste sites, and silver-iodide seeded areas; in the United States, the photography industry is the major source of anthropogenic silver discharges into the biosphere. Maximum concentrations recorded in field collections, in milligrams total silver/kilogram dry weight (tissue), were 1.5 in mammals (liver), 6 in fish (bone), 14 in plants (whole), 30 in annelid worms (whole), 44 in birds (liver), 110 in mushrooms (whole), 185 in bivalve mollusks (soft parts), and 320 in gastropods (whole); humans afflicted with silver poisoning (argyria) contained 72 mg total Ag/kg dry weight skin and 1,300 mg total Ag/kg fresh weight whole body. Silver and its compounds are not known to be mutagenic, teratogenic, or carcinogenic. Under normal routes of exposure, silver does not pose serious environmental health problems to humans at less than 50 µg total Ag/L drinking water or 10 µg total Ag/m^3 air. Free silver ion, however, was lethal to representative species of sensitive aquatic plants, invertebrates, and teleosts at nominal water concentrations of 1.2 to 4.9 µg/L; at sublethal concentrations, adverse effects were significant between 0.17 and 0.6 µg/L. No data were found on effects of silver on avian or mammalian wildlife; all studied effects were on poultry, small laboratory animals, and livestock. Silver was harmful to poultry at concentrations as low as 1.8 mg total Ag/kg whole egg fresh weight by way of injection, 100 mg total Ag/L in drinking water, or 200 mg total Ag/kg in diets; sensitive mammals were adversely affected at total silver concentrations as low as 250 µg/L in drinking water, 6 mg/kg in diets, or 13.9 mg/kg whole body. Proposed criteria for the protection of living organisms from silver are listed and discussed.

Key words: Silver, plants, fish, wildlife, invertebrates, mammals, ecotoxicology.

Silver (Ag) found in the body of mammals (including humans) has no known biological purpose and is suspected of being a contaminant (Smith and Carson 1977). Silver, as ionic Ag^+, is one of the most toxic metals known to aquatic organisms in laboratory testing, although large industrial losses to the aquatic environment are probably infrequent because of its economic value as a recoverable resource (National Association of Photographic Manufacturers [NAPM] 1974; Nebeker et al. 1983). Silver, however, is of concern in various aquatic ecosystems because of the severity of silver contamination in the water column, sediments, and biota. San Francisco Bay, for example, is impacted from discharges of silver in wastewater outfalls and from the diagenic remobilization of silver from contaminated sediments in the estuary (Luoma and Phillips 1988; Rivera-Duarte and Flegal 1993).

The principal industrial use of silver is as silver halide in the manufacture of photographic imaging materials; other products include jewelry, coins, indelible inks, and eating utensils (Klaassen et al. 1986). In medicine, silver salts are used as caustics, germicides, antiseptics, and astringents; the use of silver nitrate for prophylaxis of ophthalmia neonatorum in the eyes of newborn infants is a legal requirement in some states (Klaassen et al. 1986). Long-term industrial or medical exposure to silver and its compounds may increase blood concentrations of silver to levels which can have toxic effects, such as induction of sarcomas, anemia, and enlargement of the

heart (Aoki et al. 1993). Repeated occupational handling of silver objects, especially after repeated minor injuries, may result in localized argyria—a bluish-gray discoloration of the skin at the exposed site (Fowler and Nordberg 1986). In humans, the most common noticeable effects of chronic exposure to silver and its compounds are generalized argyria, localized argyria, and argyrosis (argyria of the eye, usually; Smith and Carson 1977). Generalized argyria consists of a slate-gray pigmentation of the skin and hair caused by deposition of silver in the tissues, a silver coloration of the hair and fingernails, and a blue halo around the cornea and in the conjunctiva. Acute toxic effects in humans have resulted only from accidental or suicidal overdoses of medical forms of silver (Smith and Carson 1977).

Ecological and toxicological aspects of silver are reviewed by Smith and Carson (1977), the U.S. Environmental Protection Agency [EPA] (1980, 1987), Lockhart (1983), the U.S. Public Health Service [PHS] (1990), Andren et al. (1993, 1994), and Andren and Bober (1995). The present report is another in a series on hazards of selected contaminants to plants and animals, with an emphasis on fishery and wildlife resources. It was prepared in response to requests for information on silver from environmental specialists of the U.S. Fish and Wildlife Service.

Sources and Uses

General

About 2.47 million kg of silver are lost each year to the domestic biosphere, mostly (82%) as a result of human activities. As discussed later, the photography industry accounts for about 47% of all silver discharged into the environment from anthropogenic sources. In 1990, about 50% of the refined silver consumed domestically was used to manufacture photographic products; 25% in electrical and electronic products; 10% in electroplated ware, sterlingware, and jewelry; 5% in brazing alloys; and 10% in other products and processes.

Sources

Silver is a rare but naturally occurring metal, often found deposited as a mineral ore in association with other elements (PHS 1990). Argentite is the main ore from which silver is extracted by cyanide, zinc reduction, or electrolytic processes (Fowler and Nordberg 1986). Silver is frequently recovered as a byproduct from smelting of nickel ores in Canada, from lead-zinc and porphyry copper ores in the United States, and from platinum and gold deposits in South Africa (Smith and Carson 1977). About 12-14% of the domestic silver output is recovered from lead ores and about 4% from zinc ores. Secondary sources of silver comprise new scrap generated in the manufacture of silver-containing products; coin and bullion; and old scrap from electrical products, old film and photoprocessing wastes, batteries, jewelry, silverware, and bearings (Smith and Carson 1977).

Silver is produced in 68 countries, but most (75%) of the world's silver (excluding the former Soviet bloc) is mined in the United States, Mexico, Canada, Australia, and Japan; the United States produces about 50% of the world's supply of refined silver (Smith and Carson 1977). The primary silver mines of the United States are in the Coeur d'Alene mining district in the northern Idaho panhandle (PHS 1990). Between 1949 and 1970, the United States consistently produced less than 15% of the global silver production and consumed 34-64% (Heyl et al. 1973). Since 1951, silver consumption in the United States has exceeded its extraction from ore (PHS 1990). In 1979, about 95% of the silver in domestic production was from Idaho, Nevada, Arizona, Colorado, Utah, Montana, and Missouri (U.S. Bureau of Mines 1980). End use categories of silver consumed domestically in 1979 included photography (39%), electrical and electronic components (25%), sterlingware and electroplated materials (15%), and brazing alloys and solders (8%). In 1979, the photographic industry was located mainly in New York, and most other end use manufacturers were in Connecticut, New York, Rhode Island, and New Jersey (U.S. Bureau of Mines 1980).

World production of silver increased from 7.40 million kg in 1964 to 9.06 million kg in 1972 and to 9.67 million kg in 1982 (Fowler and Nordberg 1986). In 1986, 13.06 million kg of silver were produced globally; the United States produced 1.06 million kg in 1986 but consumed 3.94 million kg (PHS 1990). In 1990, the estimated world mine production of silver was 14.6 million kg; major producers were Mexico with 17% of the total, the United States with 14%, Peru with 12%, the former Soviet Union with 10%, and Canada with 9% (Reese 1991). In the United States during 1990, about 160 mines produced silver worth an estimated value of $320 million; most (71%) of the 1990 mine production was in Nevada (32%), Idaho (21%), Montana (11%), and Arizona (7%). In 1990, 22 major refiners of commercial grade silver and more than 5,000 silver fabricating and manufacturing firms were located primarily in the northeastern states. Of the silver imported into the United

States in 1990, 44% came from Mexico, 34% from Canada, 5% from Peru, and 4% from Chile. Most was exported after transformation to sterlingware, coinage, and other finished products. Melting and refining old scrap silver in 1990 accounted for 500,000 kg of silver (Reese 1991).

Emissions from smelting operations, manufacture and disposal of certain photographic and electrical supplies, coal combustion, and cloud seeding are some of the anthropogenic sources of silver in the biosphere (Freeman 1979). Fallout from cloud seeding with silver iodide is not always confined to local precipitation; silver residuals have been detected several hundred kilometers downwind of seeding events (Freeman 1979). In 1978, the estimated loss of silver to the environment in the United States was 2.47 million kg, mostly to terrestrial and aquatic ecosystems; the photography industry alone accounted for about 47% of all silver discharged into the environment from anthropogenic sources (Smith and Carson 1977; Table 1). In California, anthropogenic sources contributed 50% more silver to sediments of coastal basins than did natural sources, as judged by sedimentary basin fluxes of 0.09 µg/cm^2 in anthropogenic sources of silver and 0.06 µg/cm^2 in natural sources (Bruland et al. 1974). Sometimes, liquid effluents from the nuclear industry contained significant quantities of radiosilver-110m (Berthet et al.1992). In Lake Michigan, storms contribute a large fraction of the annual load of tributary-derived silver; concentrations of particle-bound silver in many rivers during storms were more than 0.1 µg/L (Shafer et al. 1995).

Table 1. Estimated release of silver to the environment in the United States in 1978 (U.S. Public Health Service 1990).

Compartment and source category	Metric tons[a]
Atmosphere	
Metals production	30
Urban refuse combustion	10
Coal and petroleum combustion	9
Iron and steel production	7
Cloud seeding	3
Cement manufacture	2
Other	30
Aquatic	
Soil erosion (natural source)	438
r uban runoff	72
Sewage treatment plants	70
Photographic developing	65
Photographic manufacture	54
Other	6
Terrestrial	
Photographic industry	630
Urban refuse	445
Sewage treatment	220
Metals production	165
Electrical contacts and conductors	150
Alloys and solders	60
Other	5

[a]Of the total silver released to the domestic environment in 1978 (2,470,700 kg), about 3.7% entered the atmosphere, 28.5% the aquatic environment, and 67.8% the terrestrial ecosystem.

Most of the silver lost to the environment each year enters terrestrial ecosystems where it is immobilized in the form of minerals, metal, or alloys; agricultural lands may receive as much as 80,000 kg of silver from photoprocessing wastes in sewage sludge. An estimated 150,000 kg of silver enter the aquatic environment every year from the photography industry, mine tailings, and electroplating (Smith and Carson 1977). During processing of photographic paper and film, silver is generally solubilized as the tightly bound thiosulfate complex. Silver thiosulfate in secondary biological waste treatment plants is converted to insoluble silver sulfide,

which is removed in the sludge; only trace amounts of complexed and adsorbed silver are discharged into the aquatic environment. The silver incorporated into the sludge is immobile and should not restrict the use of sludge for the enrichment of soils (Dagon 1973; Bard et al. 1976; Cooley et al. 1988). The atmosphere receives 300,000 kg of silver each year from a variety of sources, but atmospheric concentrations are not known to exceed the occupational threshold limit value of 10 µg total Ag/m^3 (Smith and Carson 1977).

Daily intake of total silver from all sources by humans in the United States ranges from 70 to 88 µg; diet accounted for 35-40 µg daily (EPA 1980). Sources of elevated dietary silver include seafood from areas near sewage outfalls or industrial sources and crops grown in areas with high ambient levels of silver in the air or soil (PHS 1990). Most occupational exposures to silver occur through inhalation of silver-containing dusts or dermal exposure to photographic compounds. Dermal routes of human exposure to silver include handling of silver-containing processing solutions used in radiographic and photographic materials, dental amalgams, and silver sulfadiazine cream and solutions for treating burns (PHS 1990).

Uses

Silver has been used for ornaments and utensils for almost 5,000 years, and as a precious metal, a monetary medium, and a basis of wealth for more than 2,000 years. Until the late 1960's, it was used extensively for coinage (Heyl et al. 1973). Since 1970, U.S. coinage has not contained silver, although minting of as many as 45 million silver-clad subsidiary coins has been authorized (Smith and Carson 1977). Industrial consumption of silver in the United States between 1966 and 1972 totaled 4.67 million kg, primarily in the manufacture of photographic materials, electrical contacts and conductors, and sterlingware (Table 2). In 1973, silver was used mainly in photographic materials (29%), electrical and electronic components (22%), sterlingware (20%), electroplated ware (10%), brazing wares (20%), dental and medical products, catalysts, bearings, and jewelry (9%; Heyl et al. 1973). In 1986, photographic materials accounted for 45% of the silver consumption in the United States; electrical and electronic components, 25%; jewelry, sterlingware, and electroplated ware, 11%; alloys and solders, 5%; and mirrors, dental amalgam, medical supplies, chemicals, water purification, and cloud seeding, 14% (PHS 1990). Silver, as silver iodide, is used in the United States for weather modification, including rain and snow making and hail suppression; as much as 3,110 kg of silver is used for this purpose annually (Smith and Carson 1977). Silver nitrate in hair dyes has been in use regularly for almost 200 years (EPA 1980), although its use may lead to argyria (Smith and Carson 1977). In 1990, about 50% of the refined silver consumed domestically was used to manufacture photographic and x-ray products; 25% in electrical and electronic products; 10% in electroplated ware, sterlingware, and jewelry; 5% in brazing alloys; and 10% in other uses (Reese 1991).

Table 2. Industrial domestic use of silver during 1966-72. Total silver used was 4.67 million kg (Smith and Carson 1977).

Category	Approximate percent of total
Photographic materials	28.1
Contacts and conductors	20.2
Sterlingware	17.1
Brazing alloys and solders	10.1
Electroplated ware	10.0
Batteries	5.1
Jewelry	3.3
Miscellaneous	2.4
Dental and medical supplies	1.5
Mirrors	1.2
Bearings	0.4

Because of its bacteriostatic properties, silver compounds are used in filters and other equipment to purify water of swimming pools and drinking water and in the processing of foods, drugs, and beverages (Smith and Carson 1977; EPA 1980; PHS 1990). Activated charcoal filters coated with metallic silver to yield water concentrations of 20-40 µg Ag/L are used in filtering systems of swimming pools to control bacteria (EPA 1980). Silver may also function as an algicide in swimming pools if chlorine, bromine, and iodine are absent; it prevents growth of blue-green algae at 80-140 µg Ag/L (Smith and Carson 1977). Aboard orbiting Russian space stations and spaceships, potable water is routinely treated with 100-200 µg Ag/L to eliminate microorganisms; sterilization is usually complete in 20 min (Smith and Carson 1977). Silver-containing ceramic water filters are used to purify potable water in Swiss ski resorts, German breweries, British ships, oil tankers, drilling rigs, U.S. home consumption, and more than half the world's airlines. Monovalent and metallic silver compounds are considered excellent disinfectants; however, Ag^{2+} and Ag^{3+} are about 50 to 200 times more effective than Ag^{+} or Ag^{o} (Antelman 1994), possibly because of their higher oxidation states (Kirschenbaum 1991).

Silver nitrate was used for many years as eye drops in newborns to prevent blindness caused by gonorrhea (PHS 1990). Laws in many states still require that a few drops of a 1-2% silver nitrate solution be applied to the conjunctiva of the eyes of newborn infants to prevent ophthalmia neonatorum by transmittal of gonorrhea from the mother (EPA 1980; PHS 1990). This treatment is still required in Denmark but not in Japan or Australia (EPA 1980). Silver nitrate is not used in many U.S. hospitals because of the dangers of chemical conjunctivitis and has been replaced by antibiotics (EPA 1980). In the United States, several silver-containing pharmaceuticals were used topically on skin or mucous membranes to assist in healing burn patients and to combat skin ulcers (Smith and Carson 1977; EPA 1980). Oral medicines containing silver include silver acetate-containing antismoking lozenges; breath mints coated with silver; and silver nitrate solutions for treating gum disease (PHS 1990). The widespread medical use of silver compounds for topical application to mucous membranes and for internal use became nearly obsolete in the past 50 years because of the fear of argyria and the development of sulfonamide and antibiotic microbials (Smith and Carson 1977).

Chemistry and Metabolism

General

Silver occurs naturally in several oxidation states, the most common being elemental silver (Ag^{o}) and the monovalent ion (Ag^{+}). Soluble silver salts are in general more toxic than insoluble salts; in natural waters, the soluble monovalent species is the form of environmental concern. Sorption is the dominant process that controls silver partitioning in water and its movements in soils and sediments. As discussed later, silver enters the animal body through inhalation, ingestion, and movement across mucous membranes and broken skin. The interspecies differences in the ability of animals to accumulate, retain, and eliminate silver are large. Almost all of the total silver intake is usually excreted rapidly in feces; less than 1% of the total silver intake is absorbed and retained in tissues, primarily liver, through precipitation of insoluble silver salts. In mammals, silver usually interacts antagonistically with selenium, copper, and vitamin E; in aquatic environments, ionic or free silver interferes with calcium metabolism in frogs and marine annelids and with sodium and chloride uptake in gills of fishes.

Physical and Chemical Properties

Silver is a white, ductile metal occurring naturally in the pure form and in ores (EPA 1980). Silver has the highest electrical and thermal conductivity of all metals. Some silver compounds are extremely photosensitive and are stable in air and water except for tarnishing readily when exposed to sulfur compounds (Heyl et al. 1973). Metallic silver is insoluble in water but many silver salts, such as silver nitrate, are soluble in water to 1,220 g/L (Table 3). In natural environments, silver occurs primarily in the form of the sulfide or is intimately associated with other metal sulfides, especially those of lead, copper, iron, and gold, which are all essentially insoluble (EPA 1980; PHS 1990). Silver readily forms compounds with antimony, arsenic, selenium, and tellurium (Smith and Carson 1977). Silver has two stable isotopes (^{107}Ag and ^{109}Ag) and 20 radioisotopes; none of the radioisotopes of silver occurs naturally, and the radioisotope with the longest physical half-life (253 days) is ^{110m}Ag. Several compounds of silver are potential explosion hazards: silver oxalate decomposes explosively when heated; silver acetylide (Ag_2C_2) is sensitive to detonation on contact; and silver azide (AgN_3) detonates spontaneously under certain conditions (Smith and Carson 1977).

Table 3. Some properties of silver and silver nitrate (Lockhart 1983; U.S. Public Health Service 1990).

Variable	Silver	Silver nitrate
Alternate names	Argentum, argentum crede CI 77820, shell silver, silver atom, silver colloidal, silflake, silpowder, silber	Lunar caustic fused silver nitrate, molded silver nitrate argenti, nitras, nitric acid silver (I) salt, nitric acid silver (1+) salt, silver (1+) nitrate
CAS number	7440-22-4	7761-88-8
Chemical formula	Ag	$AgNO_3$
Molecular weight	107.87	169.89
Physical state	Solid metal	Solid crystalline
Boiling point	2,212° C	Decomposes at 440 C
Solubility	Insoluble in water; soluble in nitric acid but not sulfuric acid	Soluble in water to 1,220 g/L; soluble in ethanol and acetone
Density	10.5	4.35

Silver occurs naturally in several oxidation states, usually as Ag^0 and Ag^+; other possible oxidation states of silver are Ag^{2+} and Ag^{3+} (PHS 1990). In surface fresh water, silver may be found as the monovalent ion; in combination with sulfide, bicarbonate, or sulfate; as part of more complex ions with chlorides and sulfates; and adsorbed onto particulate matter (PHS 1990). Soluble silver salts are more toxic than insoluble salts, and soluble silver ion (Ag^+) is the most toxic chemical species. In natural waters, the soluble monovalent species is the form of environmental concern (EPA 1980). The argentous ion (Ag^+) does not hydrolyze appreciably in solution and is considered to be a mild oxidizing agent (Smith and Carson 1977). Hypervalent silver species, such as Ag^{2+} and Ag^{3+}, are significantly more effective as oxidizing agents than Ag^0 and Ag^+ (Kouadio et al. 1990; Kirschenbaum 1991; Sun et al. 1991) but are unstable in aqueous environments, especially at water temperatures near 100^0 C (Smith and Carson 1977). In natural waters, silver may exist as metalloorganic complexes or adsorb to organic materials (EPA 1980). In fresh water and soils, the primary silver compounds under oxidizing conditions are bromides, chlorides, and iodides; under reducing conditions the free metal and silver sulfide predominate (PHS 1990). In river water, one study showed silver present as the monovalent ion (Ag^+) at 53-71% of the total silver, as silver chloride (AgCl) at 28-45%, and as silver chloride ion ($AgCl_2^-$) at 0.6-2.0% (PHS 1990). Increasing salinity of brackish and marine waters increase concentrations of silver chloro complexes ($AgCl^0$, $AgCl_2^-$, $AgCl_3^{2-}$, $AgCl_4^{3-}$); these chloro complexes retain some silver in dissolved form, and relatively small anthropogenic quantities can substantially enrich the environment (Luoma 1994; Andren et al. 1995). In the open ocean, the principal dissolved form of silver is $AgCl_2^-$, but the most bioavailable form may be the neutral monochloro complex AgCl (Bryan and Langston 1992).

Sorption is the dominant process that controls silver partitioning in water and its movement in soils and sediments (EPA 1980; PHS 1990). Silver may leach from soils into ground water; the leaching rate increases with decreasing pH and increasing drainage (PHS 1990). Silver adsorbs to manganese dioxide, ferric compounds, and clay minerals, and these compounds are involved in silver deposition into sediments; sorption by manganese dioxide and precipitation with halides reduce the concentration of dissolved silver, resulting in higher concentrations in sediments than in the water column (EPA 1980). Under reducing conditions, adsorbed silver in sediments may be released and subsequently reduced to metallic silver or it may combine with reduced sulfur to form the insoluble silver sulfide (EPA 1980). Sediments may be a significant source of silver to the water column. In one study, anoxic sediments containing 1.0-27.0 g Ag/kg dry weight (DW) and 10 mmoles of acid volatile sulfide/kg DW were resuspended in oxygenated seawater for several hours to days. The seawater in contact with sediment containing 10.8 g/kg had 20 µg Ag/L; seawater in contact with sediments containing 27

g Ag/kg had about 2,000 µg Ag/L, which seems to be the solubility of silver in seawater (Crecelius and Phillips 1995).

The global biogeochemical movements of silver are characterized by releases to the atmosphere, water, and land by natural and anthropogenic sources, long-range transport of fine particles in the atmosphere, wet and dry deposition, and sorption to soils and sediments (PHS 1990). The chief source of silver contamination of water is silver thiosulfate complexes in photographic developing solutions that photofinishers discard directly to sewers (Smith and Carson 1977). Secondary waste treatment converts most of the silver thiosulfate complex to insoluble silver sulfide and forms some metallic silver (Lytle 1984). About 95% of the total silver is removed in publicly owned treatment works from inputs containing municipal sewage and commercial photoprocessing effluents, and effluents contain less than 0.07 µg ionic silver/L (Lytle 1984). Silver in sewage treatment plant effluents may be associated with suspended particles or be present as thiosulfate complex, colloidal silver complex, colloidal silver chloride, silver sulfide, or soluble organic complexes (Smith and Carson 1977). Silver on suspended matter and in colloidal forms and insoluble salts ultimately settles out in the sediments. At the water treatment plant, most of the silver is precipitated after treatment with lime or adsorbed after treatment with alum-flocculent. Chlorination converts some silver to silver chloride or to a soluble silver chloride complex (Smith and Carson 1977).

Forms of silver in atmospheric emissions are probably silver sulfide, silver sulfate, silver carbonate, silver halides, and metallic silver (Smith and Carson 1977). About 50% of the silver released into the atmosphere from industrial operations is transported more than 100 km and is eventually deposited in precipitation (PHS 1990). Minute amounts of ^{110m}Ag detected in natural waters are attributed to atmospheric fallout from nuclear explosions (Smith and Carson 1977).

A variety of spectrographic, colorimetric, polarographic, and other analytical techniques are used for routine measurement of silver in biological and abiotic samples. The detection limit of silver in biological tissues with scanning electron microscopy and x-ray energy spectrometry is 0.02 µg/kg and sometimes as low as 0.005 µg/kg. In air, water, and soil samples, the preferred analytical procedures include flame and graphite furnace atomic absorption spectrometry, plasma emission spectroscopy, and neutron activation (Fowler and Nordberg 1986; PHS 1990). Sensitive voltammetry techniques using anodic stripping have recently been developed to measure free silver ion in solution at concentrations as low as 0.1 µg/L (Schildkraut 1993; Song and Osteryoung 1993).

Metabolism

The acute toxicity of silver to aquatic species varies drastically by the chemical form and correlates with the availability of free ionic silver (Wood et al. 1994). In natural aquatic systems, ionic silver is rapidly complexed and sorbed by dissolved and suspended materials that are usually present. Complexed and sorbed silver species in natural waters are at least one order of magnitude less toxic to aquatic organisms than the free silver ion (Rodgers et al. 1994). Thus, silver nitrate—which is strongly dissociated—is extremely toxic to rainbow trout (*Oncorhynchus mykiss*); the 7-day LC50 value is 9.1 µg/L. Silver thiosulfate, silver chloride, and silver sulfide are relatively benign (7-day LC50 values >100,000 µg/L), presumably because of the abilities of the anions to remove ionic silver from solution (Wood et al. 1994, 1996b; Hogstrand et al. 1996). The probable cause of hyperventilation in rainbow trout exposed to silver nitrate was a severe metabolic acidosis manifested in decreased arterial plasma pH and HCO_3^- levels. Lethality of ionic silver to trout is probably due to surface effects at the gills—disrupting Na^+, Cl^-, and H^+—causing secondary fluid volume disturbance, hemoconcentration, and eventual cardiovascular collapse (Wood et al. 1994, 1995, 1996a, 1996b). Morgan et al. (1995) suggest that the sites of action of silver toxicity in rainbow trout may be inside the cells of the gill epithelium rather than at the external surface, and that they are linked to carbonic anhydrase—a gill enzyme involved in Na^+ and Cl^- transport. Silver concentrations and metallothionein levels in gills and livers of rainbow trout increased with increasing exposure to silver; internal toxicity associated with increased silver accumulations may be lessened by the formation of silver-induced metallothioneins (Hogstrand et al. 1996). In seawater, silver nitrate is less toxic to biota than in fresh water (Wood et al. 1995). This difference is probably due to the low concentration of free Ag^+ (the toxic moiety in freshwater) in seawater and to the high levels of chloride and negatively charged Ag-chloro complexes in seawater. However, high levels of silver nitrate are

toxic to marine invertebrates despite the absence of Ag^+, and this is attributed to the bioavailability of Ag-chloro complexes; mechanisms of silver toxicity in marine fishes are still unknown (Wood et al. 1995).

Ionic silver interferes with calcium metabolism of frogs and marine polychaete worms. Silver ions cause muscle fibers of frogs (*Rana* spp.) to deteriorate by allowing excess calcium to enter the cell. Studies with frog skeletal muscle fibers exposed to 1.08 mg/L showed that silver activated the calcium ion channel by acting on sulfhydryl groups in a calcium ion channel protein (Aoki et al. 1993). In marine polychaetes contaminated with silver, the calcium content of nephridial cells was reduced, although silver was not detected in the calcium vesicles (Koechlin and Grasset 1988). Silver binds with protein sulfhydryl groups and this process protects the worm against silver poisoning (Koechlin and Grasset 1988). In marine mollusks, however, sulfide anion was the ligand of silver (Truchet et al. 1990). In marine gastropods (*Littorina littorea*), silver was stored in the basement membranes of the digestive system; in clams (*Scrobicularia plana*), it was stored in the basement membranes of the outer fold of the mantle edge and in the amoebocytes (Truchet et al. 1990). The availability of free silver in marine environments was strongly controlled by salinity because of the affinity of silver for the chloride ion (Sanders et al. 1991). Silver sorbs readily to phytoplankton and to suspended sediments. As salinity increases, the degree of sorption decreases. Nearly 80% of silver sorbed to suspended sediments at low salinities desorbs at higher salinities, but desorption does not occur when silver is associated with phytoplankton. Thus, silver incorporation in or on cellular material increases the retention of silver in the estuary, reducing the rate of transport (Sanders and Abbe 1987).

Silver may enter the body of mammals through inhalation, ingestion, and movement across mucous membranes or broken skin (Smith and Carson 1977; EPA 1980; Klaassen et al. 1986; PHS 1990). In most cases of occupational argyrosis, absorption occurs via the respiratory tract or at the eyes (Smith and Carson 1977; EPA 1980). Silver is retained by all body tissues; tissue concentrations are related to the dose, form of administered silver, and route of exposure. Silver also accumulates in mammalian tissues with increasing age of the individual, even if none is administered intentionally. Inside the body, silver is transported mainly in the protein fractions of plasma, presumably as silver albuminate or silver chloride (Smith and Carson 1977; EPA 1980). In mammals, the highest concentrations of silver are usually found in the liver and spleen and to some extent in the muscles, skin, and brain (Fowler and Nordberg 1986). The primary sites of silver deposition in the human body are the liver, skin, adrenals, lungs, muscle, pancreas, kidney, heart, and spleen; silver is also deposited in blood vessel walls, the trachea, and bronchi (Smith and Carson 1977). Dogs exposed to silver by inhalation accumulated most of the administered dose in the liver; concentrations in the lung, brain, skin, and muscle were lower (EPA 1980; Fowler and Nordberg 1986). Intravenous injection of silver produces accumulations in the spleen, liver, bone marrow, lungs, muscle, and skin (Klaassen et al. 1986). Intestinal absorption of silver by rodents, canids, and primates has been recorded at 10% or less after ingestion of radioactive silver; a value of 18% was estimated in a single human given radiosilver acetate (EPA 1980; Klaassen et al. 1986) and about 3-10% of the absorbed silver is retained in the tissues (Smith and Carson 1977). In a human given radioactive silver, more than 50% of the whole-body burden of silver was found in the liver after 16 days (Fowler and Nordberg 1986)

Deposition of silver in tissues of warm-blooded animals results from precipitation of relatively insoluble silver salts, such as silver chloride and silver phosphate (PHS 1990). These insoluble salts may be transformed into soluble silver sulfide albuminates that bind or complex with RNA, DNA, and proteins, or may be reduced to metallic silver by ascorbic acid or catecholamines. In humans with argyria, the blue or gray skin discoloration is caused by the photoreduction of silver chloride to metallic silver during exposure to ultraviolet light. Metallic silver, in turn, is oxidized and bound as black silver sulfide (PHS 1990). Silver sulfide (Ag_2S) is localized in extracellular structures such as basement membranes and in macrophageous cells (Baudin et al. 1994). Before storage as a stable mineral combination, silver binds to proteins that contain a large proportion of sulfhydryl groups such as metallothioneins (Fowler and Nordberg 1986). The last stage in the catabolic pathway of these proteins leads to storage of silver after reaction with a sulfur ligand (Baudin et al. 1994). These mechanisms explain why the liver, the most important organ for protein synthesis, shows the highest capacity for silver accumulation. High concentrations of silver in the digestive tract are linked to the numerous basement membranes contained in its tissues. Interspecies differences in the ability to accumulate, retain, and eliminate silver are large (Baudin et al. 1994).

The enzyme-inhibiting action of silver ions may be due to the binding of sulfhydryl groups of some enzymes. Binding, in certain enzymes, is probably at a histidine imidazole group; in the case of glucose oxidase, silver ions compete with molecular oxygen as a hydrogen acceptor (Smith and Carson 1977). About 60% of the silver in liver and kidneys of silver-injected rats was in the cytosol fractions bound to the high molecular weight proteins and metallothionein fractions; however, in spleen and brain only 30% of the total tissue silver was found in the cytosol fractions (Fowler and Nordberg 1986). At moderate doses (0.4 mg Ag/kg body weight [BW]) in rats, the liver handles most of the absorbed silver from the body in the bile; at higher doses, silver deposits are markedly increased in the skin (EPA 1980). In house sparrows (*Passer domesticus*), a silver-binding protein was identified in liver after radiosilver-110m injection; the protein was heat-stable, resistant to low pH, and of low molecular weight (Kumar and Bawa 1979). The properties of the hepatic silver-binding protein in birds were similar to other studied metallothioneins, but more research is needed to distinguish differences from mammalian metallothioneins (Kumar and Bawa 1979).

Most absorbed silver is excreted into the intestines by way of the liver into the bile and subsequently excreted in feces; urinary excretion of silver is generally very low (EPA 1980; Fowler and Nordberg 1986; Klaassen et al. 1986; PHS 1990). Rodents, monkeys, and dogs given radioactive silver salts by oral and other routes excreted more than 90% of the absorbed dose in the feces (Fowler and Nordberg 1986). Rats injected intravenously with radioactive silver nitrate excreted silver in bile mainly bound to a low molecular weight complex similar to glutathione (Fowler and Nordberg 1986). Excretion was faster and percentages excreted by mice, rats, monkeys, and dogs were larger when silver was administered orally than by intravenous or intraperitoneal injection (Smith and Carson 1977).

Among mammals, low doses of ingested silver were eliminated from the body within 1 week (PHS 1990). In rats, mice, and rabbits, about 99% of a single oral dose of silver was eliminated within 30 days (EPA 1980). Time for 50% clearance of silver in rats, mice, monkeys, and dogs after oral ingestion was about 1 day; this short half-time is due, in part, to fecal elimination of unabsorbed silver; the half-times were longer (1.8-2.4 days) after intravenous injection (Fowler and Nordberg 1986). Rodents dosed with silver accumulated high initial concentrations in the liver, which greatly decreased within 10 days; however, silver concentrations in spleen and brain were retained for longer periods. The biological half-time of radiosilver in rats given a single intraperitoneal injection was 40 h in whole blood, plasma, kidney, and liver; 70 h in spleen; and 84 h in brain. After exposure by inhalation, dogs cleared 59% of an administered dose of radiosilver-110m from the lungs in 1.7 days and from the liver in 9 days (Fowler and Nordberg 1986). The mean daily intake of silver in humans is about 88 µg; about 60 µg is excreted daily in the feces (Smith and Carson 1977). In humans, the whole-body effective half-time of persistence was 43 days (EPA 1980). The biological half-time of silver in the lungs of an exposed person was about 1 day; in liver it was 52 days (Fowler and Nordberg 1986). In humans, 80% of the retained silver in lung was cleared in about 1 day; 50% of the remainder was usually cleared in 3 days (EPA 1980). In persons who had accidentally inhaled radiosilver-110m, most of the inhaled silver had a half-time persistence of about 1 day, probably because of rapid mucociliary clearance, swallowing, and fecal excretion; most of the absorbed radiosilver translocated to the liver (EPA 1980).

Silver interacts competitively with selenium, vitamin E, and copper and induces signs of deficiency in animals fed adequate diets or aggravates signs of deficiency when diets lack one or more of these nutrients; antagonistic effects of silver have been described in dogs, pigs, rats, sheep, chicks, turkey poults, and ducklings (EPA 1980). Conversely, the addition of selenium, copper, or vitamin E to diets of turkey poults decreased the toxicity of diets containing 900 mg Ag/kg (Fowler and Nordberg 1986). Dietary administration of silver acetate antagonized selenium toxicity; silver prevented growth depression and death in chicks fed diets containing excess selenium (EPA 1980). The addition of selenium to the diets of rats exposed to silver in drinking water prevented growth retardation but increased the concentration of silver in liver and kidneys (Fowler and Nordberg 1986). Silver deposits in rat liver, kidneys, and other internal organs were in the form of sulfides; under high selenium exposure, the sulfur can be replaced with selenium (PHS 1990) and formation of silver selenide deposits in the liver may be considered a silver detoxification process (EPA 1980).

Concentrations in Field Collections

General

Silver is comparatively rare in the earth's crust—67th in order of natural abundance of elements; the crustal abundance is an estimated 0.07 mg/kg and predominantly concentrated in basalt (0.1 mg/kg) and igneous rocks (0.07 mg/kg; Heyl et al. 1973). Silver concentrations in nonbiological materials tend to be naturally elevated in crude oil and in water from hot springs and steam wells. Anthropogenic sources associated with the elevated concentrations of silver in nonliving materials include smelting, hazardous waste sites, cloud seeding with silver iodide, metals mining, sewage outfalls, and especially the photoprocessing industry. Silver concentrations in biota were greater in organisms near sewage outfalls, electroplating plants, mine wastes, and silver-iodide seeded areas than in conspecifics from more distant sites.

Nonbiological Materials

Maximum concentrations of total silver recorded in selected nonbiological materials were 36.5 ng/m^3 in air near a smelter in Idaho; 2.0 µg/m^3 in atmospheric dust; 0.1 µg/L in oil well brines; 4,500 ng/L in precipitation from clouds seeded with silver iodide; 6.0 µg/L in groundwater near a hazardous waste site; 8.9 µg/L in seawater from Galveston Bay, Texas; 260 µg/L in the Genesee River, New York—the recipient of photoprocessing wastes; 300 µg/L in steam wells; 300 ng/L in treated photoprocessing wastewaters; 31 mg/kg in some Idaho soils; 43 mg/L in water from certain hot springs; 50 mg/kg in granite; as much as 100 mg/kg in crude oils; 150 mg/kg in some Genesee River sediments; and 27,000 mg/kg in some solid wastes from photoprocessing effluents (Table 4). It is emphasized that only a small portion of the total silver in each of these compartments is biologically available. For example, typical publicly owned treatment works receiving photoprocessing effluents show silver removal efficiencies greater than 90%; the mean concentration of free silver ion present in the effluents from these plants ranged from 0.001 to 0.07 µg/L (Lytle 1984; Bober et al. 1992).

Table 4. Silver concentrations in representative nonbiological materials.

Table 4. Material, units of concentration, and other variables	**Concentration[a]**	**Reference[b]**
Air, ng/m^3		
Chicago, 1969	4.3	1
Heidelberg, Germany; April 1971	4.2	1
Indiana, industrialized area	1-5	2
Industrialized areas	7.0	3
Kellogg, Idaho, near smelter, 1977	10.5; Max. 36.5	1, 2
Niles, Michigan; June 1969	1.0	1
Rural areas		
Silver-iodide cloud-seeding area	1.0	1
Areas not cloud-seeded	0.04-0.17	2,3
San Francisco, 1970	0.15	1
U.S. national parks	0.012-0.19	2
Vicinity of lead smelters	Max. 175	3
Vicinity of silver iodide ground-based cloud-seeding generator		

Table 4. Material, units of concentration, and other variables	**Concentration[a]**	**Reference[b]**
At generator site	>10,000	1
>50 m from site	0.1	1
Washington, D.C. 1974	1.1	1
Atmospheric dust, µg/m^3		
Northern hemisphere	2.0	4
Drinking water, solid residues, mg/kg		
United States	0.08 (0.01-0.20)	1
Fossil fuels, mg/kg		
Coal fly ash	Max. 10-15	2, 5
Crude oil	Max. 100	3
Fuel oil, residual	Max. 0.12	3
Freshwater, µg/L		
Amazon River, South America	0.23	3
Genesee River, New York; receives photoprocessing wastes; 1973		
June	90-260	1
Winter	20	1
Patuxent River, Maryland	0.08-0.1	6
Rhone River, Europe	0.38	3
United States		
Dissolved	Usually <0.2	1, 3
Rivers	0.3 (0.09-0.55)	1, 3, 5
Surface waters	2.6	3
Tap water	2.2 (0.3-5.0)	1, 5
Tap water	Max. 26	3
Groundwater, µg/L		
Near hazardous waste site	6.0	2
Noncontaminated site	<0.5	4
Hot springs, µg/L	Max. 43,000	1
Oil well brines, µg/L	0.1	1
Precipitation, ng/L		
From seeding clouds with silver iodide	Usually 10-300; Max. 4,500	1, 2
From non-seeded clouds	Usually 0.0-20; Max. 216	1, 2

Table 4. Material, units of concentration, and other variables	**Concentration[a]**	**Reference[b]**
Rock, mg/kg		
Granite, igneous	Max. 50	5
Seawater, µg/L		
Near shore	0.25 (0.06-2.9)	1, 2, 5
Open ocean	0.00004-0.0025	3, 7
Galveston Bay, Texas, 1989		
Dissolved	3.2 (0.2-8.9)	8
Particulate	2.8 (0.7-5.9)	8
Sediments, mg/kg		
Ireland, Cork Harbour; intertidal sites, February 1990	<0.05	9
United Kingdom		
19 estuaries	0.07-4.1	7
Contaminated vs. uncontaminated estuaries	>1 vs. <0.1	7
United States		
Marine sediments, near Pacific coast cities	1.5-3.5	4
New York, Genesee River, 1973; receives photoprocessing effluents	150	1
Puget Sound, Washington, August, 1982		
0-20 cm depth	Max. 0.67	10
51-75 cm depth	Max. 0.55	10
110-175 cm depth	Max. 0.27	10
195-265 cm depth	Max. 0.07	10
San Francisco Bay	Max. >10	7
Southern California coastal basins, contaminated by wastewater	14-20	5
Soils, mg/kg		
Canada	0.l3	2
Earth's crust	0.1	2
Hazardous waste site	4.5	2
Kellogg, Idaho	20.0 (3.2-1.0)	2
Michigan		

Table 4. Material, units of concentration, and other variables	**Concentration[a]**	**Reference[b]**
Agricultural	0.19	2
Industrial	0.37	
Residential	0.13	2
Solid wastes, mg/kg		
Municipal wastes	3.0 (<3-7)	2
Municipal and industrial wastes	15-120	2
Photoprocessing effluents	450-27,000	2
Sewage sludge	225-960	2
Steam wells		
Water, µg/L	Max. 300	1
Residue, mg/L	Max. 13,000	1
Wastewater, µg/L		
Agricultural drainage water	Max. 1	1
Entering southern California coastal basins	Max. 30	5
Municipal wastewater	0.05-45.0	1
Sewage sludge, United States	5-150	5
Photoprocessing wastes, treated	70.0 (20-300)	2, 11

[a]Concentrations are shown as mean, range (in parentheses), and maximum (Max.).

[b]1, U.S. Environmental Protection Agency (EPA) 1980; 2, U.S. Public Health Service (PHS) 1990; 3, Smith and Carson 1977; 4, Freeman 1979; 5, Fowler and Nordberg 1986; 6, Connell et al. 1991; 7, Bryan and Langston 1992; 8, Morse et al. 1993; 9, Berrow 1991; 10, Bloom and Crecelius 1987; 11, National Association of Photographic Manufacturers 1974.

Silver is usually found in extremely low concentrations in natural waters because of its low crustal abundance and low mobility in water (EPA 1980). One of the highest silver concentrations recorded in fresh water, 38 µg/L, occurred in the Colorado River at Loma, Colorado, downstream of an abandoned gold-copper-silver mine, an oil shale extraction plant, a gasoline and coke refinery, and a uranium processing facility (EPA 1980). The maximum recorded value of silver in tap water in the United States was 26 µg/L—significantly higher than finished water from the treatment plant (maximum of 5.0 µg/L)—because of the use of tin-silver solders for joining copper pipes in the home, office, or factory (EPA 1980).

In general, silver concentrations in surface waters of the United States decreased between 1970-74 and 1975-79, although concentrations increased in the north Atlantic, Southeast, and lower Mississippi basins (PHS 1990). About 30 to 70% of the silver in surface waters may be ascribed to suspended particles (Smith and Carson 1977), depending on water hardness or salinity. For example, sediments added to solutions containing 2 µg Ag/L had 74.9 mg Ag/kg DW sediment after 24 h in freshwater, 14.2 mg/kg DW at 1.5% salinity and 6.9 mg/kg DW at 2.3% salinity (Sanders and Abbe 1987). Riverine transport of silver to the ocean is considerable: suspended materials in the Susquehanna River, Pennsylvania—containing as much as 25 mg silver/kg—result in an estimated transport of 4.5 metric tons of silver to the ocean each year (EPA 1980).

Emissions of silver from coal-fired power plants may lead to accumulations in nearby soils (Fowler and Nordberg 1986). Silver in soils is largely immobilized by precipitation to insoluble salts and by complexation or adsorption by organic matter, clays, and manganese and iron oxides (Smith and Carson 1977).

Silver can remain attached to oceanic sediments for about 100 years under conditions of high pH, high salinity, and high sediment concentrations of iron, manganese oxide, and organics (Wingert-Runge and Andren 1994). Estuarine sediments that receive metals, mining wastes, or sewage usually have higher silver concentrations (>0.1 mg/kg DW) than noncontaminated sediments. Silver is tightly bound by sewage sludge, and elevated silver concentrations in sediments are often characteristic of areas near sewage outfalls. In the absence of sewage, silver in oxidized sediments is associated with oxides of iron and with humic substances (Bryan and Langston 1992). Sediments in the Puget Sound, Washington, were significantly enriched in silver, in part from human activities; concentrations were higher in fine-grained particles (Bloom and Crecilius 1987). Marine annelids and clams accumulate dissolved and sediment-bound forms of silver. Uptake of silver from sediments by marine polychaete annelids decreased in sediments with high concentrations of humic substances or copper but increased in sediments with elevated concentrations of manganese or iron (Bryan and Langston 1992).

Plants and Animals

Maximum concentrations of total silver recorded in field collections of living organisms (Table 5), in milligrams silver per kilogram dry weight, were 1.5 in liver of marine mammals, 2 in liver and 6 in bone of trout from ecosystems receiving precipitation from silver-iodide seeded clouds, 7 in kidneys and 44 in liver of birds from a metals-contaminated area, 14 in marine algae and macrophytes, 30 in whole annelid worms from San Francisco Bay, 72 in skin of humans afflicted with argyria, 110 in whole mushrooms, 133 to 185 in soft parts of clams and mussels near sewage and mining waste outfalls, and 320 in whole gastropods from South San Francisco Bay. Silver concentrations in conspecifics from areas remote from anthropogenic contamination were usually lower by one or more orders of magnitude (Table 5).

Silver is a normal trace constituent of many organisms (Smith and Carson 1977). In terrestrial plants, silver concentrations are usually less than 1.0 mg/kg ash weight (equivalent to less than 0.1 mg/kg DW) and are higher in trees, shrubs, and other plants near regions of silver mining; seeds, nuts, and fruits usually contain higher silver concentrations than other plant parts (EPA 1980). Silver accumulations in marine algae (max. 14.1 mg/kg DW) are due mainly to adsorption rather than uptake; bioconcentration factors of 13,000 to 66,000 are not uncommon (PHS 1990).

Silver concentrations in mollusks vary widely between closely related species and among conspecifics from different areas (Bryan 1973; Eisler 1981; Table 5). The inherent differences in ability to accumulate silver among bivalve mollusks are well documented (oysters >> scallops >> mussels; Brooks and Rumsby 1965; Eisler 1981). The highest silver concentrations in all examined species of mollusks were in the internal organs, especially in the digestive gland and kidneys (Eisler 1981; Miramand and Bentley 1992; Table 5). Elevated concentrations of silver (5.3 mg/kg DW) in shells of limpets from uncontaminated sites suggest that silver may actively participate in carbonate mineral formation (Navrot et al. 1974), but this needs verification. In general, silver concentrations were elevated in mollusks collected near port cities and in the vicinities of river discharges (Fowler and Oregioni 1976; Berrow 1991), electroplating plant outfalls (Eisler et al. 1978; Stephenson and Leonard 1994), ocean dump sites (Greig 1979), and urban point sources including sewage outfalls (Alexander and Young 1976; Smith and Carson 1977; Martin et al. 1988; Anderlini 1992; Crecelius 1993) and from calcareous sediments rather than detrital organic or iron oxide sediments (Luoma and Jenne 1977). Season of collection (Fowler and Oregioni 1976; Sanders et al. 1991) and latitude (Anderlini 1974) also influenced silver accumulations. Seasonal variations in silver concentrations of Baltic clams (*Macoma balthica*) were associated with seasonal variations in soft tissue weight and frequently reflected the silver content in the sediments (Cain and Luoma 1990). Oysters from the Gulf of Mexico vary considerably in whole body concentrations of silver and other trace metals. Variables that modify silver concentrations in oyster tissues include the age, size, sex, reproductive stage, general health, and metabolism of the animal; water temperature, salinity, dissolved oxygen, and turbidity; natural and anthropogenic inputs to the biosphere; and chemical species and interactions with other compounds (Presley et al. 1990). Silver concentrations in whole American oysters (*Crassostrea virginica)* from the Chesapeake Bay were reduced in summer, reduced at increasing water salinities, and elevated near sites of human activity; chemical forms of silver taken up by oysters included the free ion (Ag^+) and the uncharged

$AgCl^0$ (Sanders et al. 1991; Daskalakis 1995). Declines in tissue silver concentrations of the California mussel (*Mytilus californianus*) were significant between 1977 and 1990; body burdens decreased from 10-70 mg/kg DW to less than 2 mg/kg DW and seem to be related to the termination of metal plating facilities in 1974 and decreased mass emission rates by wastewater treatment facilities (Stephenson and Leonard 1994).

Table 5. Silver concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in field collections of selected plants and animals.

Table 5. Taxonomic group, organism, and other variables	**Concentration[a] (mg/kg)**	**Reference[b]**
Algae, macrophytes, and higher plants		
Marine algae and macrophytes, 24 species		
9 species	<0.1-2.0 DW	1
11 species	2.1- 10.0 DW	1
4 species	10.1-14.1 DW	1
Higher terrestrial plants	0.2-<1.0 AW	2, 3
Cnidarians		
Corals, 34 species	<1.0 DW	1
Various, 10 species	Max. 0.1 DW	1
Mollusks		
Cephalopods, 7 species; digestive gland	3.0-46.0 DW	4
Cephalopods, French coast of English Channel, October 1987		
Octopus, *Eledone cirrhosa*		
Digestive gland	2.0-4.4 DW	4
Digestive tract	0.5 DW	4
Other tissues	<0.3 DW	4
Whole	0.8 DW	4
Cuttlefish, *Sepia officinalis*		
Digestive gland	4.9-7.4 DW	4
Kidney	0.7 DW	4
Other tissues	<0.3 DW	4
Whole	0.7 DW	4
Clam, *Corbicula* sp.; San Francisco Bay, 1983-86; soft parts	0.07-0.2 DW	5
Eastern oyster, *Crassostrea virginica*; soft parts		
Connecticut	6.1 FW	6

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
East coast	0.3-5.0 DW	7, 55
Georgia	28.0-82.0 DW	8
Gulf coast	0.6-6.0 DW; Max. 7.0 DW	7, 9, 10
Louisiana	5.5 DW	11
Maryland, Chesapeake Bay, 1986-88	2.0-6.0 DW	12
Northeast coast	0.8-2.3 FW	13
Red abalone, *Haliotis rufescens*; California		
Digestive gland	14.0-60.0 DW	14
Foot	1.0-44.0 DW	14
Gills	13.0-129.0 DW	14
Mantle	16.0-54.0 DW	14
Periwinkle, *Littorina littorea*; soft parts; Looe estuary, U.K. vs. uncontaminated site,1988	10.7 (3.1-17.4) DW vs. 4.1 (3.4-5.0) DW	15
Baltic clam, *Macoma balthica*; soft parts; San Francisco Bay		
Near sewage outfall	32.0-133.0 DW	11, 16
Reference site	<1.0 DW	11
Mollusks, marine; edible tissues; 18 species		
10 species	<0.1 FW	17
5 species	0.1-0.3 FW	17
3 species	0.3-0.7 FW	17
Mollusks; south San Francisco Bay, 1982; soft parts		
Mud snail, *Nassarius obsoletus*	Max. 320.0 DW	16
Bent-nose macoma (clam), *Macoma nasuta*	Max. 5.1 DW	16
Softshell clam, *Mya arenaria*	Max. 34.0 DW	16
Clam, *Tapes japonica*	Max. 65.0 DW	16
California mussel, *Mytilus californianus;* soft parts		
Bodega Bay, California; 1976-78 vs. 1986-88	0.15 DW vs. 0.1 DW	18
California coast, 1977-81 vs. 1989-91	Max. 10.0-70.0 DW vs. <2.0 DW	19
San Diego Bay near municipal wastewater outfall vs. reference sites in Baja California and northern California	59.0 DW vs. 0.08-0.22 DW	20
San Francisco Bay, 1982; North Bay vs. South Bay	0.04-0.16 DW vs. 0.7-2.9 DW	16

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
Common mussel, *Mytilus edulis*		
Shell	0.1-6.3 DW	21, 22, 23
Soft parts		
Europe	0.1-6.0 DW	1
Ireland, February 1990; contaminated sites (Cork Harbour) vs. reference sites (east coast of Ireland)	0.8-4.3 DW vs. <0.05-1.0 DW	24
Rhode Island, Narragansett Bay, 1976-78 vs. 1986-88	0.20 DW vs. 0.22 DW	18
United States	0.04-2.3 DW	1
East coast; rural sites vs. urban areas	0.3 DW vs. Max. 2.0 DW	55
West coast; rural sites vs. urban areas	0.1 DW vs. Max. 5.0 DW	55
Mussel, *Mytilus edulis aoteanus*; soft parts; New Zealand, 1986-87; various distances from sewage outfall		
50 m	5.3-7.7 DW	25
100 m	4.2 DW	25
200 m	3.9 DW	25
750 m	3.5-4.1 DW	25
1,500 m	2.9 DW	25
3,000 m	2.7-3.4 DW	25
Oyster, *Ostrea equestris*; soft parts, United States		
East coast	18.9 DW	7
Gulf coast	0.7-1.6 DW	7
Oyster, *Ostrea sinuata*; New Zealand		
Foot, gills, soft parts	0.7-1.1 DW	26
Gonad, mantle	0.2 DW	26
Intestine	2.9 DW	26
Kidney	4.8 DW	26
Muscle, shell	<0.1 DW	26
Limpet, *Patella vulgata*; Israel, 1973; soft parts vs. shell		
Near sewage outfall	6.7 DW vs. 5.7 DW	27
Reference site 80 km north of outfall	1.2 DW vs. 5.3 DW	27

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
Mussel, *Perna canaliculus*; soft parts; New Zealand, 1986-87; distance from sewage outfall		
200 m	35.0-113.0 DW	25
750 m	49.0-85.0 DW	25
1,500-3,000 m	8.0-13.0 DW	25
False quahog, *Pitar morrhuanus* (formerly Widgeon clam, *Pitar morrhuana*); soft parts; near Rhode Island electroplating plant	1.2-4.6 DW	28
Sea scallop, *Placopecten magellanicus*; soft parts		
Ocean disposal site	Max. 9.1 DW	11
Reference site	<0.1 DW	11
Clam, *Potamocorbula amurensis*; San Francisco Bay (0.006 µg Ag/L); 1991-92; soft parts	2.2 (0.3-7.0) DW; BCF of about 366,000	57
Oysters, *Saccostrea* spp.; Australia, 1980-83; soft parts	Max. 0.4 FW	29
Clam, *Scrobicularia plana*		
Digestive gland	0.8 DW	4
Kidney	0.4 DW	4
Soft parts		
Reference sites	0.2-1.5 (0.03-2.1) DW	15, 30
Silver-contaminated estuary	4.0-5.8 (1.1- 185.0) DW	15, 31
Bryozoans		
Bryozoan, *Victorella* sp; whole; Chesapeake Bay, Maryland	11.5 DW	32
Crustaceans		
Amphipods, whole; Antarctica, February- March 1989	1.2 (0.7-1.4) DW	33
Rock crab, *Cancer irroratus*		
Digestive gland	2.1-3.4 FW; 6.3 DW	34, 35
Muscle	0.2-0.8 FW; 0.2 DW	34, 35
Crustaceans, edible tissues, 16 species		
8 species	<0.1 FW	17
5 species	0.1-0.2 FW	17
3 species	0.3-0.5 FW	17
Barnacle, *Elminius modestus*; pyrophosphate granules	10.5 (9.7-11.3) DW	36

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
American lobster, *Homarus americanus*; muscle	0.4-0.5 DW	37
Shrimps, unidentified		
Exoskeleton	1.1 DW	38
Muscle	0.2 DW	38
Annelids		
Polychaete annelid, *Marphysa sanguinea*; whole; San Francisco Bay, 1982	Max. 5.5 DW	16
Sandworm, *Nereis diversicolor*; whole	5.2 (0.7-30.0) DW	31
Echinoderms		
Various, 9 species	Usually <0.3 DW; Max. 0.6 DW	1
Starfish, *Luidia clathrata*; Tampa Bay, Florida vs. Gulf of Mexico; 1992		
Body wall	0.26-0.84 DW vs. 0.67 DW	39
Pyloric caeca	0.4-1.1 DW vs. 0.17 DW	39
Tunicates		
Whole, 2 species; New Zealand	Max. 0.03 DW; Max. 0.005 FW	1
Tunicate, *Cynthia claudicans*; soft parts, Greece	0.9 FW; 4.8 DW	1
Fishes and Elasmobranchs		
Blackfin icefish, *Chaenocephalus aceratus*; Antarctica, February-March 1989		
Liver	0.05 (0.04-0.05) DW	33
Muscle	0.01 (0.008-0.012) DW	33
Freshwater fishes, whole;United States, 1975-79	0.225 (0.004-1.9) FW	11
Atlantic cod, *Gadus morhua*; Newfoundland, November 1990-March 1991; females		
Liver	Max. 1.49 DW; Max. 0.44 FW	40
Muscle	Max. 0.3 DW; Max. 0.02 FW	40
Ovaries	Max. 0.32 DW; Max. 0.04 FW	40
Marine fishes		
Liver		
66 species	<0.01 FW	17
12 species	(0.1-0.3) FW	17
4 species	(0.3-0.6) FW	17
Muscle		

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
158 species	<0.1 FW	17
1 species	(0.1-0.2) FW	17
Scales, 7 species	(0.1-0.3) DW	41
Whole		
10 species	<0.1 FW	17
7 species	(0.1-0.2) FW	17
Striped bass, *Morone saxatilis*		
Liver	0.08 FW	42
Muscle	0.003 FW	42
Smooth dogfish, *Mustelus canis*; New York Bight		
Liver	Max. 0.3 FW	43
Muscle	<0.1 FW	43
Hump rock cod, *Notothenia gibberifrons*; Antarctica, February-March 1989; muscle	0.014 (0.012-0.016) DW	33
Winter flounder, *Pleuronectes americanus*		
Liver	<0.1-0.8 FW	43
Muscle	<0.1 FW	43
Windowpane flounder, *Scophthalmus aquosus*		
Liver	<0.1-0.5 FW	35
Muscle	<0.1 FW	35
Birds		
Antarctica, February-March 1989		
Arctic giant-petrel, *Macronectes giganteus*; muscle	0.018 (0.017-0.02) DW	33
Imperial shag, *Phalacrocorax atriceps*; muscle	0.01 DW	33
Adelie penguin, *Pygoscelis adeliae*		
Liver	0.02 DW	33
Muscle	0.01 DW	33
Chinstrap penguin, *Pygoscelis antarctica*		
Feces	0.18 (0.13-0.22) DW	33
Liver	0.05 DW	33
Muscle	0.009 DW	33

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
Gentoo penguin, *Pygoscelis papua*		
Liver	0.43 (0.41-0.46) DW	33
Muscle	0.01 DW	33
Greater scaup, *Aythya marila*		
San Francisco Bay, March-April 1982; liver	1.0 (0.4-3.1) DW	44, 45
British Columbia, Canada		
Diet	0.006-0.029 FW	46
Liver	0.04-0.32 FW	46
Ruffed grouse, *Bonassa umbellus*; primary feathers; Virginia, 1977-79		
Adults	<0.01 DW	47
Immatures	<0.01 DW	47
Lesser black-backed gull, *Larus fuscus*; Norway; metals-contaminated area		
Kidney	1.0 DW	22
Liver	2.0 DW	22
Muscle	3.0 DW	22
Surf scoter, *Melanitta perspicillata*		
British Columbia		
Diet	0.004-0.026 FW	46
Liver	0.03-0.14 FW	46
San Francisco Bay, March-April 1982		
Kidney	Max. 3.7 DW	44
Liver	0.9 (0.3-3.7) DW	44
Common eider, *Somateria mollissima*; Norway; metals-contaminated area		
Eggs	1.0 DW	22
Kidneys	7.0 DW	22
Liver	44.0 DW	22
Muscle	2.0 DW	22
Mammals		
Human, *Homo sapiens*		
Daily intake, 70-kg individual, whole body		

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
All sources (35-88 µg)	0.0005-0.00125 FW	11
Air (0.023 µg)	0.0000033 FW	11
Drinking water (20-100 µg)	0.00285-0.00143 FW	11
Food (4.5 µg)	0.000064 FW	11
Diet		
Beef liver	0.005-0.194 FW	3
Beef muscle	0.004-0.024 FW	3, 11
Cereals and grains	0.008 (0.0-140.0) FW	11
Cigarettes; filter vs. nonfilter	0.27 FW vs. 0.18 FW	11
Crustaceans	2.0 DW	3
Dairy products	<0.06 FW	11
Fruits	<0.05 FW	11
Leafy vegetables	0.007 (0.0-0.04) FW	11
Meat, fish, poultry	0.01 (0.0-87.0) FW	11
Milk (cow)	0.027-0.059 FW	3, 11
Mushrooms	"Up to several hundred" DW	3
Oils and fats	<0.03 FW	11
Pork and mutton	0.006-0.012 FW	3, 11
Sugar	0.002-0.03 FW	3
Tea	0.2-2.0 DW	3, 11
Trout	0.48-0.68 DW	3
Typical diet	0.0091 DW	11
Wheat	0.5 DW	3
Tissues and organs		
Abnormal (argyria)		
Skin	63.0-72.0 DW	48
Normal		
Kidney	0.001 FW; 0.4 DW	48
Liver	0.006 FW; 0.7 DW	48
Lung	0.0001 FW	48
Skin	0.035 DW	48

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
Spleen	2.7 DW	48
Whole body	0.05 FW; <10.0 DW	2
Leopard seal, *Hydrurga leptonyx*; Antarctic, February-March 1989		
Kidney	0.15 DW; Max. 0.24 DW	49
Liver	0.99 DW; Max. 1.55 DW	49
Muscle	0.01 DW; Max. 0.017 DW	49
Stomach contents	0.22 (0.20-0.24) DW	49
Weddell seal, *Leptonychotes weddelli*; Antarctic, February-March 1989		
Kidney	0.10 DW; Max. 0.29 DW	49
Liver	0.73 DW; Max. 0.94 DW	49
Muscle	Max. 0.012 DW	49
Crabeater seal, *Lobodon carcinophagus*; Antarctic, February-March 1989		
Kidney	0.06 DW; Max. 0.17 DW	49
Liver	0.81 DW; Max. 1.36 DW	49
Muscle	0.01 DW; Max. 0.022 DW	49
Terrestrial mammals, various species, liver	<50.0 AW	2
Polar bear, *Ursus maritimus*; Northwest Territories, Canada, 1984; liver	0.21-0.54 DW	50
California sea lion, *Zalophus californianus*; recent mothers; liver		
Mothers with normal pups	0.5 DW	51
Mothers giving birth to premature pups	0.4 DW	51
Integrated Studies		
Alpine lake, Colorado, 1973-74. Silver iodide (43 kg), equivalent to 19.7 kg silver, released into system from local cloud-seeding practices between 1963 and 1973		
Lake water, 1973 vs. 1974		
Bottom	0.00022 (Max. 0.00063) FW vs. 0.00044 (Max. 0.00122) FW	52
Surface	0.00031 (Max. 0.0009) FW vs. 0.00071 (Max. 0.00134) FW	52
Cutthroat trout, *Oncorhynchus clarki*; age 1year vs. age 3 years		
Bone	5.8 DW vs. 2.6 DW	52

Table 5. Taxonomic group, organism, and other variables	Concentration[a] (mg/kg)	Reference[b]
Liver	2.3 DW vs. 1.4 DW	52
Muscle	0.1 DW vs. 0.4 DW	52
Skin	0.2 DW vs. 0.4 DW	52
Arabian Sea, near Pakistan, 1987-88		
Sediments	0.53 DW	53
Water	0.000015 FW; Max. 0.000033 FW	53
Seaweeds, whole, 4 species	0.40-0.76 FW	53
Shrimps, edible portions, 2 species	0.25-0.29 FW	53
Fish, muscle, 3 species	0.29-0.53 FW	53
Calcasieu River, Louisiana		
Periphyton, whole	2.1 DW	54
Hooked mussel, *Ischadium recurvum* (formerly *Brachidontes exustus)* soft parts	0.4 DW	54
American oyster, *Crassostrea virginica*; soft parts	1.0 DW	54
Zooplankton, whole	0.8 DW	54
Blue crab, *Callinectes sapidus*; muscle	0.1 DW	54
Shrimps, 2 species; muscle	0.04 DW	54
Fish, 7 species: muscle	0.1 DW	54
Poland, 1989-92		
Mushrooms, *Agaricus campestris*, whole	9-62 (6-110) DW	56
Soils	0.1-0.95 DW; Max. 1.4 DW; BCF values for silver by mushrooms from soils ranged between 60 and 330	56

[a]Concentrations are shown as mean, range (in parentheses), and maximum (Max.).

[b]1, Eisler 1981; 2, Smith and Carson 1977; 3, U.S. Environmental Protection Agency 1980; 4, Miramand and Bentley 1992; 5, Luoma et al. 1990; 6, Thurberg et al. 1974; 7, Goldberg et al. 1978; 8, Windom and Smith 1972; 9, Morse et al. 1993; 10, Presley et al. 1990; 11, U.S. Public Health Service 1990; 12, Sanders et al. 1991; 13, Greig and Wenzloff 1978; 14, Anderlini 1974; 15, Truchet et al. 1990; 16, Luoma and Phillips 1988; 17, Hall et al. 1978; 18, Lauenstein et al. 1990; 19, Stephenson and Leonard 1994; 20, Martin et al. 1988; 21, Segar et al. 1971; 22, Lande 1977; 23, Graham 1972; 24, Berrow 1991; 25, Anderlini 1992; 26, Brooks and Rumsby 1965; 27 Navrot et al. 1974; 28, Eisler et al. 1978; 29, Talbot 1985; 30, Bryan and Uysal 1978; 31, Bryan and Hummerstone 1977; 32, Connell et al. 1991; 33, Szefer et al. 1993; 34, Greig et al. 1977a; 35, Greig et al. 1977b; 36, Pullen and Rainbow 1991; 37, Greig 1975; 38, Bertine and Goldberg 1972; 39, Lawrence et al. 1993; 40, Hellou et al. 1992; 41, Papadopoulu and Kassimati 1977; 42, Heit 1979; 43, Greig and Wenzloff 1977a; 44, Ohlendorf et al. 1986; 45, Bryan and Langston 1992; 46, Vermeer and Peakall 1979; 47, Scanlon et al. 1980; 48, Fowler and Nordberg 1986; 49, Szefer et al. 1994; 50, Braune et al. 1991; 51, Martin et al. 1976; 52, Freeman 1979; 53, Tariq et al. 1993; 54, Ramelow et al. 1989; 55, Crecelius 1993; 56, Falandysz and Danisiewicz 1995; 57, Brown and Luoma 1995.

Among arthropods, pyrophosphate granules isolated from barnacles have the capability to bind and effectively detoxify silver and other metals under natural conditions (Pullen and Rainbow 1991). In a Colorado alpine lake, silver concentrations in caddisflies and chironomid larvae usually reflected silver concentrations in sediments; seston, however, showed a high correlation with lakewater silver concentrations from 20 days earlier (Freeman 1979).

In other studies, silver concentrations in fish muscles rarely exceeded 0.2 mg/kg DW and usually were less than 0.1 mg/kg fresh weight (FW); livers contained as much as 0.8 mg/kg FW, although values greater than 0.3 mg/kg FW were unusual; and whole fish contained as much as 0.2 mg/kg FW (Table 5). Livers of Atlantic cod (*Gadus morhua*) contained significantly more silver than muscles or ovaries; a similar pattern was evident in other species of marine teleosts (Hellou et al. 1992; Szefer et al. 1993; Table 5). Accumulations of silver in offshore populations of teleosts is unusual, even among fishes collected near dump sites impacted by substantial quantities of silver and other metals. For example, of seven species of marine fishes from a disposal site in the New York Bight that were examined for silver content, concentrations were highest (0.15 mg/kg FW) in muscle of blue hake (*Antimora rostrata*; Greig et al. 1976). Similarly, the elevated silver concentration of 0.8 mg/kg FW in liver of winter flounder (*Pleuronectes americanus*; Table 5) was from a specimen from the same general area (Greig and Wenzloff 1977b).

Silver concentrations in muscles of Antarctic birds were low (0.01 mg/kg DW) when compared to livers (0.02-0.46 mg/kg DW) or feces (0.18 mg/kg DW; Szefer et al. 1993; Table 5). Silver concentrations in avian tissues, especially in livers, were elevated in the vicinity of metals-contaminated areas and in diving ducks from the San Francisco Bay (Table 5). Birds with elevated concentrations of silver in tissues—as much as 44 mg/kg DW in liver in the common eider (*Somateria mollissima*)—seemed outwardly unaffected (Bryan and Langston 1992).

Silver in mammalian tissues is usually present at low or nondetectable concentrations (Klaassen et al. 1986). The concentration of silver in tissues of three species of seals collected in the Antarctic during 1989 was highest in liver (1.55 mg/kg DW; Table 5) and lowest in muscle (0.01 mg/kg DW); intermediate in value were kidney (0.29 mg/kg DW) and stomach contents (0.24 mg/kg DW; Szefer et al. 1994). The mean concentration of silver in livers from normal female California sea lions (*Zalophus calfornianus*), with normal pups, was 0.5 mg/kg DW (Martin et al. 1976; Table 5). Mothers giving birth to premature pups had only 0.4 mg Ag/kg DW liver. In general, *Zalophus* mothers delivering premature pups had lower concentrations in liver of silver, cadmium, copper, manganese, mercury, and zinc than did mothers delivering normal pups (Martin et al. 1976). Silver concentrations in tissues of Antarctic seals were related to, and possibly governed by, concentrations of other metals (Szefer et al. 1994). In muscle, silver inversely correlated with zinc; in liver, silver positively correlated with nickel, copper, and zinc; and in kidney, correlations between silver and zinc and between silver and cadmium were negative (Szefer et al. 1994). In humans, EPA (1980) states that silver is present in placentas and fetal livers, that silver concentrations in tissues increase with age, and that variations in tissue concentrations of silver are wide. The average maximum daily intake of silver from all sources by humans is 88 µg (Table 5), but very little of the silver ingested from nontherapeutic sources is retained (Smith and Carson 1977).

Lethal and Sublethal Effects

General

As discussed and documented later, free silver ion is lethal to representative species of sensitive aquatic plants, invertebrates, and teleosts at water concentrations of 1.2-4.9 µg/L. Adverse effects occur on development of trout at concentrations as low as 0.17 µg/L and on phytoplankton species composition and succession at 0.3 to 0.6 µg/L. Aquatic organisms accumulate silver from environmental sources. No data were found on effects of silver on avian or mammalian wildlife and all studied effects were on poultry and small laboratory mammals. Silver was not mutagenic, carcinogenic, or teratogenic to tested animals by normal routes of exposure. Adverse effects of silver on poultry occur at 1.8 mg/kg FW whole egg by way of injection (reduced survival), 10 mg/kg in copper-deficient diets (reduced hemoglobin), and 200 mg/kg in copper-adequate diets (growth suppression), or when the birds are given drinking water containing 100 mg Ag/L (liver necrosis). Effects of silver on sensitive species of mammals include death at 13.9-20.0 mg/kg BW by intraperitoneal injection, histopathology of kidney and brain at 250-450 µg Ag/L drinking water, tissue accumulations at 6 mg/kg diet, and

liver necrosis when fed diets containing more than 130 mg/kg. In humans, generalized argyria seems to be declining, which may be due to improved work conditions.

Terrestrial Plants

Smith and Carson (1977) report that sprays containing 9.8 mg dissolved Ag/L kill corn (*Zea mays*), and sprays containing 100-1,000 mg dissolved Ag/L kill young tomato (*Lycopersicon esculentum*) and bean (*Phaseolus* spp.) plants. Hirsch et al. (1993) planted seeds of corn, lettuce (*Lactuca sativa*), oat (*Avena sativa*), turnip (*Brassica rapa*), soybean (*Glycine max*), spinach (*Spinacia oleracea*), and Chinese cabbage (*Brassica* spp.) in soils amended with silver sulfide and sewage sludge to contain 10, 50, or 100 mg Ag/kg DW soil. All plants germinated and most grew normally at the highest soil concentration of silver tested. But growth of Chinese cabbage and lettuce was adversely affected at 10 mg Ag/kg DW soil and higher. Silver concentrations in edible portions from all plants at all soil levels of silver tested, except lettuce, were less than 80 µg/kg DW. Lettuce grown in soil containing 100 mg Ag/kg DW had about 1.2 mg Ag/kg DW (Hirsch et al. 1993).

Aquatic Organisms

In fish and amphibian toxicity tests with 22 metals and metalloids, silver was the most toxic tested element as judged by acute LC50 values (Birge and Zuiderveen 1995). In solution, ionic silver is extremely toxic to aquatic plants and animals (Nehring 1976; Nelson et al. 1976; Calabrese et al. 1977a; Gould and MacInnes 1977; Smith and Carson 1977; EPA 1980; Buhl and Hamilton 1991; Bryan and Langston 1992), and water concentrations of 1.2-4.9 µg/L killed sensitive species of aquatic organisms, including representative species of insects, daphnids, amphipods, trout, flounders, sticklebacks, guppies, and dace (Table 6). At nominal water concentrations of 0.5-4.5 µg/L, accumulations in most species of exposed organisms were high and had adverse effects on growth in algae, clams, oysters, snails, daphnids, amphipods, and trout; molting in mayflies; and histopathology in mussels (Table 6). Among all tested species, the individuals most sensitive to silver were the poorly nourished and young and those exposed to low water hardness or salinity (Smith and Carson 1977; EPA 1980; Le Blanc et al. 1984; Table 6). It is emphasized that silver-induced stress syndromes vary widely among animal classes. Among marine organisms, for example, silver ion was associated with respiratory depression in marine gastropods and cunners (*Tautagolabrus adspersus*), a teleost; however, silver ion increased oxygen consumption in six species of bivalve mollusks (Gould and MacInnes 1977).

Sensitive aquatic plants accumulated silver from water containing as little as 2 µg Ag/L to whole-cell burdens as high as 58 mg Ag/kg DW; grew poorly at 3.3-8.2 µg Ag/L during exposure for 5 days; and died at concentrations greater than 130 µg Ag/L (Table 6). Some metals seem to protect aquatic plants against adverse effects of silver. Algae in small lakes that contained elevated concentrations of metals, especially copper and nickel, had higher tolerances to silver than conspecifics reared in the laboratory under conditions of depressed concentrations of heavy metals (EPA 1980). Species composition and species succession in Chesapeake Bay phytoplankton communities were significantly altered in experimental ecosystems continuously stressed by low concentrations (0.3-0.6 µg/L) of silver (Sanders and Cibik 1988; Sanders et al. 1990). At higher concentrations of 2-7 µg/L for 3 to 4 weeks, silver inputs caused disappearance of *Anacystis marina*, a mat-forming blue-green alga; increased dominance by *Skeletonema costatum*, a chain-forming centric diatom; and increased silver concentrations in various species of phytoplankton to 8.6-43.7 Ag mg/kg DW (Sanders and Cibik 1988). Dissolved silver speciation and bioavailability were important in determining silver uptake and retention by aquatic plants (Connell et al. 1991). Silver availability was controlled by the concentration of free silver ion (Ag^+) and the concentrations of other silver complexes, such as AgCl (Sanders and Abbe 1989). Silver uptake by phytoplankton was rapid, in proportion to silver concentration, and inversely proportional to water salinity. Silver incorporated by phytoplankton was not lost as the salinity increased, and silver associated with cellular material was largely retained in the estuary (Sanders and Abbe 1989). Diatoms (*Thalassiosira* sp.), for example, readily accumulated silver from the medium. Once incorporated, silver was tightly bound to the cell membrane, even after the cells were mechanically disrupted (Connell et al. 1991).

Table 6. Effects of silver on representative aquatic plants and animals. Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
Bacteria, algae, and macrophytes		
Bacteria, freshwater		
Escherichia coli		
1,000-2,000 (as Ag+3)	All dead in 0.5-5.0 min	1
Streptococcus faecalis		
1,000-2,000 (as Ag^{+3})	All dead in 0.5-5.0 min	1
Various species		
100-200	All dead in 15-20 min	2
Bacteria, marine		
Isolated from tubes of deep-sea polychaete annelids		
3,000	Lowest concentration tested that inhibited growth in 50% of strains during 10-day exposure	3
20,000	Silver-resistant strains (55% of all strains tested) survived at least 24 h	3
40,000	Some strains survived during 10-day exposure	3
Alga, *Chlorella* spp.		
50-100	Growth inhibition	4
Waterweed, *Elodea canadensis*		
100	Respiration inhibited	4
Freshwater algae and macrophytes, 13 species		
30-7,500	Adverse effects	4
Freshwater plants		
26	Bioconcentration factor (BCF) of X200	2
Duckweed, *Lemna minor*		
270	Phytotoxic	4
Marine algae, 3 species		
2	After 24 h algae contained 27.8-58.6 mg silver/kg dry weight (DW) at 1% salinity, 16.4-33.4 mg/kg at 1.5% salinity, and 9.8-25.2 mg Ag/kg DW at 2.0% salinity	5

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
Marine algae, 4 species; various concentrations	BCF between X13,000 and X66,000 at equlibrium	40
Freshwater alga, *Phormidium inundatum*		
80-140	Controls growth in swimming pools	2
Marine alga, *Prorocentrum mariae-lebouriae*		
3.3	50% growth reduction in 5 days at 0.75% salinity	6
6.7	50% growth reduction in 5 days at 1.5-2.25% salinity	6
8.2	50% growth reduction in 5 days at 3% salinity	6
Marine algae, various species		
Radiosilver-110m at 3.3 microcuries/L	BCF of X1,600 to X2,800 in 38 days	7
Marine plants		
60	BCF of X200	2
Alga, *Scendesmus* spp.		
100-200	100% growth inhibition	4
Marine diatom, *Skeletonema costatum*		
5.9	50% growth reduction in 5 days at 0.75% salinity	6
15.4	50% growth reduction in 5 days at 1.5% salinity	6
20.0	50% growth reduction in 5 days at 2.25-3.0% salinity	6
130-170	50% reduction in cell numbers in 96 h	4
Protozoans		
Ciliate, *Fabrea salina*; held in seawater solution containing radiosilver-110m	Bioconcentration factor (volume/volume basis) of 7,000 to 40,000 within 24 h	39
Protozoan, *Spirostomum ambiguum*		
8.8	LC50(24 h) at 2.8 mg $CaCO_3$/L	8
15.3	LC50(24 h) at 250 mg $CaCO_3$/L	8
Nematodes		
Free-living nematode, *Caenorhabditis elegans*		
102 (95% confidence interval [CI] of 10 to 4,980)	LC50(96 h)	9
5,000, (95% CI of 3,000 to 10,000)	LC50(96 h)	9

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
Mollusks		
Bay scallop, *Argopecten irradians*, juveniles		
22	Oxygen consumption elevated after 96 h	10
33	LC50(96 h);survivors with elevated silver concentrations	10
Freshwater snail, *Australorbis* sp.		
30-100	Inhibited feeding and coordination	2
Bivalves, 4 species		
10	Elevated oxygen consumption after exposure for 30-90 days	10, 11
Scallop, *Chlamys varia*, adults		
20	After 14 days soft parts contained 18 mg Ag/kg DW vs. 1.7 in controls	12
100	LC50(115 h)	12
Asiatic clam, *Corbicula fluminea*		
4.5	Adverse effects on growth after exposure for 21 days; residues of 1.65 mg Ag/kg FW soft parts were associated with reduced growth	13
7.8	No deaths in 21 days	13
26.0	Some deaths in 21 days	13
155 (116-208); exposed for 96 h then transferred to uncontaminated media for 96 h	LC50 for juveniles at end of observation period	13
Pacific oyster, *Crassostrea gigas*		
2-10	5% to 8% of embryos exposed for 48 h were abnormal (retarded shell growth, reduced size, erratic swimming behavior) vs. 1% in controls; no significant effect on embryogenesis	14
13.5-15.5	Significant effect on embryogenesis; 25-37% of embryos developed abnormally	14
18-32	95-98% of embryos exposed for 48 h were abnormal	14
20	Soft parts of adults exposed for 28 days contained 188.0 mg Ag/kg DW vs. 3.0 mg/kg DW in controls	12
Juveniles held in 20 µg Ag/L for 14 days then transferred to uncontaminated seawater for 23	No histopathology. During exposure, but not depuration, glycogen storage capacity was diminished. During depuration, silver concentrations	15

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
days	decreased from 31.3 mg/kg DW soft parts to 12.8 vs. <10.0 in controls. Most of the insoluble accumulated silver was sequestered as Ag_2S in amoebocytes and basement membranes	
100	LC50(209 h), adults	12
American oyster, *Crassostrea virginica*		
0.1 (controls) vs. 2; adults exposed for 14 days in large enclosures with natural phytoplankton assemblages	In controls, phytoplankton had 0.03 mg Ag/kg DW and oyster soft parts 0.8 mg/kg DW. In the 2.0 µg/L group, phytoplankton had 8.6 mg Ag/kg DW and oysters 2.8 mg/kg DW; oyster growth rate significantly reduced	16
5 or 7; conditions as above	Phytoplankton had 24-44 mg Ag/kg DW and oysters 4.8- 6.6 mg Ag/kg DW	16, 17
5.8	LC50(48 h), embryos	10
10	LC100(48 h), embryos	4
25	LC50(12 days), juveniles	10
500-1,000	Adults exposed for 96 h had 12.4-14.9 mg Ag/kg FW in body and 34-38 mg Ag/kg FW in gills	11
Slipper limpet, *Crepidula fornicata*		
1, 5, or 10; exposed for 24 months and observed for effects on growth, reproduction, histology and accumulations	Growth reduced in the 5 and 10 µg/L groups and reproduction inhibited in the 10 µg/L group. All test groups showed deposition of silver in connective tissues and basement membranes. Maximum silver concentrations (mg/kg FW soft parts) were recorded for the controls at 12 months (2.8), for the 1.0 µg/L group at 12 months (34.0), for the 5.0 µg/L group at 6 months (54.1), and for the 10.0 µg/L group at 6 months (86.7). After 24 months, silver-exposed groups contained between 5.4 and 8 mg Ag/kg FW soft parts	18
Zebra mussel, *Dreissena polymorpha*, adults		
400	No deaths in 28 days; soft parts at 28 days contained 147-184 mg Ag/kg DW vs. 0.02-1.8 mg/kg DW in controls	12
Quahog clam, *Mercenaria mercenaria*		
21.0	LC50(48 h), embryos	10
32.4	LC50(10 days), juveniles	10
500-1,000	Adults exposed for 96 h had 0.8-1.0 mg Ag/kg FW in soft parts and 6.9-7.6 mg Ag/kg FW in gills. Controls	11

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
	(<1.5 µg/L) had 0.4 mg Ag/kg FW soft parts and 1.6 mg/kg FW in gills	
Softshell clam, *Mya arenaria*		
100	Increased oxygen consumption after 96 h	11
500	After exposure for 96 h adults had 10.4 mg Ag/kg FW soft parts vs. 0.3 mg Ag/kg FW in controls	11
1,000	All adults died within 96 h	11
Common mussel, *Mytilus edulis*		
Exposed continuously for 21 months to 0.0 (control), 1, 5, or 10 µg Ag/L from age 2.5 months (4.5 mm in shell length) and observed for growth, accumulations, and histopathology	No effect on growth. Silver concentrations (mg/kg FW soft parts) for controls ranged between 0.2 and 0.7; maximum concentrations in the 1 µg/L group (9.1) occurred at 18 months; for the 5 µg/L group, residues were highest (11.9) at 18 months; for the 10 µg/L group, concentrations were highest (15.3) at 12 months. All silver-exposed groups had histopathology of basement membranes and connective tissues	19
Juveniles (16.1 mm shell length) and adults (53.4 mm shell length) were continuosly exposed for 12 months to 0.0 (control), 5, 25, or 50 µg Ag/L and observed for growth and accumulations	Growth inhibition of the 50 µg/L group after 6 months but growth normal after 12 months; growth of other groups as in controls. At 12 months residues, in mg Ag/kg FW soft parts, for juveniles (adults) were 0.2 (0.1) in controls, 9.9 (2.0) in the 5 µg/L group, 8.0 (2.0) in the 25 µg/L group, and 10.7 (3.0) in the 50 µg/L group	19
100	Increasing oxygen consumption with increasing water salinity	11
500 or 1,000	Adults exposed for 96 h had 3.7-5.2 mg Ag/kg FW soft parts	11
Radiosilver-110m	BCF values after 1 day were X860 in soft parts and X8 in shell; after 9 days these values were X2,550 in soft parts and X11 in shell	20
Mussel, *Mytilus galloprovincialis*, adults		
10	Growth normal after 21-month exposure	12
20	After 28 days soft parts contained 15 mg Ag/kg DW vs. 0.08 mg Ag/kg DW in controls (<0.1 µg Ag/L)	12
25	Growth depressed after 21-month exposure	12
50	Severe tissue histopathology after 14 days	12
100	LC50(110 h)	12
Mud snail, *Nassarius obsoletus*		

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
1.0	Inhibition of embryonic development	21
Clam, *Potamocorbula amurensis*; exposed for 14 days at 1.8% salinity to 0.1, 0.2, 0.5, 1.0, or 2.0 µg Ag^+/L	Silver concentrations in soft parts rose in a dose-dependent manner from <1.0 mg Ag/kg DW to about 14.0 mg/kg Ag/kg DW	42
Clam, *Scrobicularia plana*, adults		
20	Normal after 14 days	12
50	No deaths in 16 days; severe histopathology	12
100	LC50(250 h)	12
200	LC50(96 h)	12
Surf clam, *Spisula solidissima*		
10	Elevated oxygen consumption in juveniles after 96 h	10
14; 1-h exposure 60 min after fertilization	50% of embryos developed abnormally in 48 h	21
100	Lethal to juveniles in 96 h	10
Bryozoans		
Bryozoan, *Victorella* sp.		
0.18 (control), 2, or 10	Silver concentrations, in mg/kg DW whole animal, after 24 h were 11.5 in controls, 38.3 in the 2 µg/L group, and 180.0 in the 10 µg/L group	22
Arthropods		
Copepod, *Acartia tonsa*		
36	LC50(96 h)	4
Daphnid, *Daphnia magna*		
0.4-15.0	LC50(96 h) at 38-75 mg $CaCO_3$/L	4
0.9	50% of starved daphnids immobilized in 48h	23
1.6-19.4	MATC[b]	23
3.5	50% reduction in growth of nonstarved daphnids in 21 days	23
4.1	Reduced survival during 21-day exposure	23
10.5	Reproduction inhibited during 21-day exposure	23
12.5	50% of nonstarved daphnids immobilized in 48 h	23
45-49	LC50(96 h) at 255 mg $CaCO_3$/L	4

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
Daphnids, *Daphnia* spp.		
10 (0.25-49.0)	LC50(96 h)	9
Mayfly, *Ephemerella grandis*		
<1.0	LC50(14 days), naiads	24
4.0-8.8	LC50(7-15 days), adults	4
60 or 120	On death, whole mayflies contained 25.3 and 28.7 mg Ag/kg DW	24
Scud (amphipod), *Gammarus pseudolimnaeus*		
4.5 (3.7-5.5)	LC50(96 h) at 44 mg $CaCO_3$/L	25
American lobster, *Homarus americanus*		
6.0	Altered enzyme activity after 30 days but no effect on survival, oxygen consumption, or osmoregulation	10
Amphipod, *Hyalella azteca*		
0.95	No observable effects after 21-day exposure	13
1.4	Reduced growth after 20 days	13
1.9 (1.4-2.3)	LC50(96 h)	13
Mayfly, *Isonychia bicolor*		
1.6	Molting inhibited after 20 days	13
6.8 (5.5-7.8)	LC50(96 h)	13
Stonefly, *Leuctra* sp.		
0.69	Adverse effects after 12 days	13
2.5 (1.7-3.2)	LC50(96 h)	13
Mysid shrimp, *Mysidopsis bahia*		
250.0	LC50(96 h)	4
Grass shrimp, *Palaemonetes pugio*		
2.0	After 2 weeks whole shrimps contained 0.5 mg Ag/kg DW vs. 0.36 in controls	22
5.0	After 2 weeks whole shrimps had 3.7 mg Ag/kg DW	22
10.0	Whole shrimps contained 4.5 mg Ag/kg DW after exposure for 2 weeks	22
For 2 weeks shrimp ate *Artemia*	Silver concentration (mg/kg DW whole body) in	22

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
nauplii containing 0.72 mg Ag/kg DW, or bryozoans (*Victorella* sp.) containing elevated silver burdens (38-180 mg Ag/kg DW), or control bryozoans (11.5 mg Ag/kg DW)	shrimp on *Artemia* diet was 0.19 vs. 0.09 in silver-free *Artemia* diet; 0.26-0.62 in the high-silver bryozoan diet and 0.36 in the control bryozoan diet	
Stonefly, *Pteronarcys californica*		
4.0-9.0	LC50(96 h)	24
50.0	On death, whole stoneflies contained 9.1 mg Ag/kg DW	24
105.0	Dead stoneflies had 13.2 mg Ag/kg DW	24
Mayfly, *Stenonema* sp.		
3.9 (2.5-5.7)	LC50(96 h)	13
Midge, *Tanytarsus dissimilis*		
3,160 (2,490-4,010)	LC50(48 h) at 44 mg $CaCO_3$/L	25
Annelids		
Marine polychaete, *Sabella pavonina*		
Adults immersed in seawater containing 50 µgAg/L for 8 weeks then transferred to silver-free media for 8weeks	During immersion, the maximum whole-body silver concentration was 22.1 mg/kg DW vs. 0.8 in controls; main sites of accumulation were the connecting tissues of nephridia and gut. No histopathology. A constant elimination of silver in urine occurs simultaneously with silver accumulation. During depuration, new connective tissue formed and silver concentrations were reduced by 88%	26
Echinoderms		
Sea urchin, *Arbacia lixula*		
0.5	Reduced embryo development after 52 h	4
Fishes		
Mottled sculpin, *Cottus bairdi*		
5.3	LC50(96 h) at 30 mg $CaCO_3$/L	4
14.0	LC50(96 h) at 250 mg $CaCO_3$/L	4
Sheepshead minnow, *Cyprinodon variegatus*		
1,400	LC50(96 h), juveniles	4
Common carp, *Cyprinus carpio*		

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
Held in radiosilver-110m solutions for 41 days then transferred to uncontaminated media for 42 days	Whole body BCF during immersion rose rapidly and progressively to X51 at day 19, then more slowly to X73 at day 41. At day 41, BCF for liver was X866, for digestive tract X560, for kidneys X299, for spleen X155, and for air bladder X109. During depuration, 68% of the silver was eliminated-- about 31% during the first 3 days and 37% in the next 39 days. In both uptake and depuration phases, 71-77% of all radiosilver was present in liver and digestive tract	27
Mummichog, *Fundulus heteroclitus*		
30-40	Inhibited liver enzyme activity after 4 days	2, 4
Mosquitofish, *Gambusia affinis*		
23.5 (17.2-27.0)	LC50(96 h), juveniles	13
Threespine stickleback, *Gasterosteus aculeatus*		
3	Lethal in 10-30 days	2
4	Lethal in 7 days	2
10	Lethal in 96 h	2
Flagfish, *Jordanella floridae*		
9.2 (8.0-10.7)	LC50(96 h) at 44 mg $CaCO_3$/L	25
Bluegill, *Lepomis macrochirus*		
31.7 (24.2-48.4)	LC50(96 h)	13
70.0	Survival as in controls after 6 months; whole body contained 0.3 mg Ag/kg ash weight	28
Atlantic silverside, *Menidia menidia*		
110.0	LC50(96 h), larvae	4
400.0	LC50(96 h), juveniles	4
Largemouth bass, *Micropterus salmoides*		
7.0	Survival of young of year as in controls after continuous exposure for 6 months. After 4 months, viscera contained 0.6 mg Ag/kg ash weight, gills 0.38, and carcass 0.016 mg Ag/kg ash weight	28
70.0	All dead within 24 h. Prior to death, bass had reddened gills, body tremors, and erratic swimming	28
Chum salmon, *Oncorhynchus keta*		
Eggs were exposed in freshwater to	At end of study, experimentals had a small, but	29

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
4 µg Ag/L for 14 days prior to hatch. After hatching, larvae were exposed to 4 µg Ag/L in saltwater for 14 days during yolk-sac resorption. Fry were then transferred to uncontaminated saltwater and fed a high metals diet for 64 days (diet contained--in µg metal/kg feed DW--2 Ag, 255 Cd, 6,670 Cu, 1,320 Pb, and 96,000 Zn)	significant, decline in survival. Just prior to transfer to uncontaminated saltwater, experimentals contained 62 µg Ag/kg whole body DW vs. 4 in controls. After 64 days in uncontaminated saltwater, whole alevins contained 18 µg Ag/kg DW vs. 4 in controls	
Coho salmon, *Oncorhynchus kisutch*		
11.1 (7.9-15.7)	LC50(96 h), alevins	30
12.5 (10.7-14.6)	LC50(96 h), juveniles	30
Rainbow trout, *Oncorhynchus mykiss*		
0.03-0.06	MATC[b] after 13-month exposure beginning at eyed embryo stage	4
0.09-0.17	MATC[b] after exposure of eyed eggs and subsequent developmental stages for 18 months in soft water	31
0.18-0.40	MATC[b]; 10-month exposure starting with newly-fertilized embryos	4
0.6	All eyed eggs survived 10-week exposure	31
1.2	40% of eyed eggs dead in 39 days	31
2.0	Inhibition of Na^+ and Cl^- influx across gills in mature trout after 72 h	44
2.2	All eyed eggs dead in 60 days	31
4.8-8.9	LC50(144 h); juveniles	13, 44
5.3-8.1	LC50(96 h); water hardness 20-31 mg $CaCO_3$/L	31
7.6-10.9	LC50(96 h)	4, 23, 41
10.0	LC50(28 days) at 93-105 mg $CaCO^3$/L	4
13.0	LC50(96 h); water hardness 350 mg $CaCO_3$/L	31
16.1 (12.8-20.2)	LC50(96 h); alevins	30
19.2 (16.0-23.1)	LC50(96 h); juveniles	30
Steelhead trout, *Oncorhynchus mykiss*		

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
0.1-1.1	Growth reduced during chronic exposure from egg through swimup fry	23
0.5 and 1.3	Survival reduced at low dose when exposed continuously from egg through swimup; all dead at high dose	23
9.2	LC50(96 h)	23
100.0	LC50(62 h); eyed embryos	32
200.0	LC50(96 h); eyed embryos	32
Chinook salmon, *Oncorhynchus tshawytscha*		
33.0	Fry survived exposure for 48 h	2
40.0-44.0	Lethal to fry in 48 h	2
Summer flounder, *Paralichthys dentatus*		
4.7	LC50(96 h); larvae	4
8.0-48.0	LC50(96 h); embryos	4
Fathead minnow, *Pimephales promelas*		
5.3-20.0	LC50(96 h) at water hardness of 25-75 mg $CaCO_3$/L	4
5.6-7.4	LC50(96 h); flow-through tests	23
9.4-9.7	LC50(96 h); static tests	23
10.7 (10.6-10.8)	LC50(96 h) at 44 mg $CaCO_3$/L	25
29.0	LC100(96 h)	33
110.0-270.0	LC50(96 h) at water hardness of 255 mg $CaCO_3$/L	4
Guppy, p*oecilia reticulata*		
4.3	Lethal	2
Winter flounder, Pleuronectes americanus		
10.0	Depressed liver transaminase activity after 60 days	10
54, 92, 180, or 386	No significant effect of lowest dose on growth or survival during exposure for 18 days of embryo through yolk-sac absorption. At 92 µg/L, 31% died; at 180 µg/L, 97% died; at 386 µg/L, hatch was reduced 24% and all larvae died	34
200.0-450.0	LC50(96 h); embryos	4

Table 6. Taxonomic group, organism, silver concentration (ppb), and other variables	Effects	Reference[a]
Speckled dace, *Rhinichthys osculus*		
4.9	LC50(96 h) in soft water	4
14.0	LC50(96 h) in hard water	4
Brown trout, *Salmo trutta*		
Fingerlings exposed to radiosilver-110m for 57 days then transferred to clean freshwater for 28 days	After 57 days the whole-body BCF was X2.7 with about 70% of total radiosilver concentrated in the liver (BCF for liver was X282); during depuration, 23% of whole fish radiosilver was excreted but concentration in liver was unchanged	35
Fingerlings were fed a diet containing radiosilver-110m for 34 days then fed a clean diet for 27 days	After 34 days, about 12% of the silver fed was retained; liver contained 63% of the total radioactivity. After 27 days of depuration 31% of the radiosilver was lost from whole trout, but liver contained 79% of the total radioactivity	36
Cunner, *Tautogolabrus adspersus*		
120, 250, or 500; after 96 h, gill tissues were excised and gill oxygen consumption monitored for 4 h	Gill-tissue oxygen consumption was significantly lower than controls at all silver concentrations tested in a dose-dependent manner	37
500	After 96 h, gill tissue respiration was reduced and liver enzyme activity altered. Similar effects seen for silver nitrate and silver acetate	38
>500	Lethal after 96 h	37
Arctic grayling, *Thymallus arcticus*		
6.7 (5.5-8.0)	LC50(96 h); alevins	30
11.1 (9.2-13.4)	LC50 (96 h); juveniles	30
Amphibians		
Early life stages exposed to silver nitrate from fertilization through 4 days after hatching		
Leopard frog, *Rana pipiens*		
0.7-0.8	10% mortality or abnormal development of embryos and larvae	43
10.0	50% mortality or gross terata of embryos and larvae	43
5 species		
1-34	10% mortality or gross terata of embryos and larvae	43
10-240	50% mortality or abnormal development of embryos and larvae	43

[a]1, Antelman 1994; 2, Smith and Carson 1977; 3, Jeanthon and Prieur 1990; 4, U.S. Environmental Protection Agency 1980; 5, Sanders and Abbe 1987; 6, Sanders and Abbe 1989; 7, Eisler 1981; 8, Nalecz-Jawecki et al. 1993; 9, Williams and Dusenbery 1990; 10, Calabrese et al. 1977b; 11, Thurberg et al. 1974; 12, Berthet et al. 1992; 13, Diamond et al. 1990; 14, Coglianese and Martin 1981; 15, Berthet et al. 1990; 16, Sanders et al. 1990; 17, Abbe and Sanders 1990; 18, Nelson et al. 1983; 19, Calabrese et al. 1984; 20, Nolan and Dahlgaard 1991; 21, Bryan and Langston 1992; 22, Connell et al. 1991; 23, Nebeker et al. 1983; 24, Nehring 1976; 25, Lima et al. 1982; 26, Koechlin and Grasset 1988; 27, Baudin et al. 1994; 28, Coleman and Cearley 1974; 29, Buell 1991; 30, Buhl and Hamilton 1991; 31, Davies et al. 1978; 32, Rombough 1985; 33, LeBlanc et al. 1984; 34, Klein-MacPhee et al. 1984; 35, Garnier et al. 1990; 36, Garnier and Baudin 1990; 37, Thurberg and Collier 1977; 38, Gould and MacInnes 1977; 39, Fisher et al. 1995; 40, Fisher et al. 1984; 41, Hogstrand et al. 1996; 42, Brown and Luoma 1995; 43, Birge and Zuiderveen 1995; 44, Morgan et al. 1995.

[b]MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable adverse effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

The ability to accumulate dissolved silver from the medium ranges widely between species. Some reported bioconcentration factors (mg Ag per kg FW organism/mg Ag per liter of medium) are 210 in diatoms, 240 in brown algae, 330 in mussels, 2,300 in scallops, and 18,700 in oysters (EPA 1980). Silver is the most strongly accumulated of all trace metals by marine bivalve mollusks (Luoma 1994). Studies with radiosilver-110m suggest that the half-time persistence of silver is 27 days in mussels, 44-80 days in clams, and more than 180 days in oysters (Fisher et al. 1994). In oysters and other bivalve mollusks, the major pathway of silver accumulation was from dissolved silver; uptake was negligible from silver adsorbed onto suspended sediments or algal cells, and oysters eliminated adsorbed silver in the feces (Abbe and Sanders 1990; Sanders et al. 1990). Sometimes, benthic bivalve mollusks accumulated silver from certain sediments. Sediment-bound silver was taken up by the Baltic clam (*Macoma balthica*) at 3.6 to 6.1 times the concentration in calcite sediments but less than 0.85 times from manganous, ferrous, and biogenic $CaCO_3$ sediments (EPA 1980). In oysters, silver associated with food was unavailable for incorporation, which may be due to the ability of silver to adsorb rapidly to cell surfaces and to remain tightly bound despite changes in pH or enzymatic activity (Connell et al. 1991). Silver concentrations in American oysters (*Crassostrea virginica)* held in seawater solutions containing 1.0 mg Ag/L for 96 h rose from 6.1 mg/kg FW soft parts to 14.9 mg/kg FW; in gills, these values were 5.9 and 33.9 mg/kg FW (Thurberg et al. 1974). A similar pattern was evident in common mussels (*Mytilus edulis*) and quahog clams (*Mercenaria mercenaria*; Thurberg et al. 1974). Adults of surf clams (*Spisula solidissima*) immersed for 96 h in seawater containing 10 µg Ag/L had 1.0 mg Ag/kg FW soft tissues versus 0.08 mg/kg in controls (Thurberg et al. 1975). Oysters accumulated radiosilver-110m from the medium by factors of 500 to 32,000 (Pouvreau and Amiard 1974); uptake of dissolved silver by oysters was higher at elevated temperatures in the range of 15-25^{o} C (Abbe and Sanders 1990). American oysters maintained near a nuclear power plant in Maryland that discharged radionuclides on a daily basis into the Chesapeake Bay accumulated radiosilver-110m; accumulations were higher in summer and fall than in winter and spring (Rose et al. 1988).

Marine gastropods exposed to concentrations as low as 1.0 µg Ag/L for as long as 24 months showed histopathology and accumulations as high as 34 mg Ag/kg FW soft parts; higher exposure concentrations of 5 and 10 µg Ag/L were associated with inhibited reproduction and whole-body burdens as high as 87 mg Ag/kg FW (Nelson et al. 1983). Histopathological findings in silver-exposed mussels (*Mytilus edulis*) were typical of argyria in humans and other mammals that have absorbed organic or inorganic silver compounds (Calabrese et al. 1984). Juvenile Pacific oysters (*Crassostrea gigas*) exposed for 2 weeks to solutions containing 20 µg Ag/L had high silver accumulations in tissues and a reduced capacity to store glycogen; however, after 30 days of depuration, glycogen storage capacity was restored and 80% of the soluble silver and 27% of the insoluble forms were eliminated, suggesting recovery to a normal physiological state (Berthet et al. 1990). About 70% of the insoluble silver in Pacific oysters was sequestered as Ag_2S, a stable mineral form that is not degradable, thereby limiting the risk of silver transfer through the food chain (Berthet et al. 1990). Most (69-89%) of the silver accumulated from the medium in soft tissues of oysters and clams was sequestered in amoebocytes and basement membranes; in scallops and mussels, silver was stored in basement membranes and pericardial gland. In all species of bivalve mollusks, sequestered silver was in the form of silver sulfide (Berthet et al. 1992). American oysters excreted about 60% of their accumulated silver in soft tissues within 30 days of transfer to silver-free seawater; soluble forms were preferentially eliminated and insoluble forms retained (Berthet et al.

1992). Interspecies differences in ability to retain silver among bivalve mollusks are large, even among closely related species of crassostreid oysters. For example, the half-time persistence of silver was about 149 days in American oysters but only 26 days in Pacific oysters (PHS 1990).

Among arthropods, grass shrimp (*Palaemonetes pugio*) rapidly incorporate silver dissolved in brackish water in proportion to its concentration but not from planktonic or detrital food sources containing elevated silver burdens (Connell et al. 1991). Variations in ability of decapod crustaceans to accumulate radiosilver-110m from seawater are large, as judged by concentration factors that ranged from 70 to 4,000 (Pouvreau and Amiard 1974). The reasons for this variability are unknown but may be associated with hepatopancreas morphology. It is generally acknowledged that hepatopancreas or digestive gland is the major repository of silver in decapods (Greig 1975; Greig et al. 1977a, 1977b). Aquatic insects concentrate silver in relative proportion to environmental levels (Nehring 1976), and more efficiently than most fish species (Diamond et al. 1990). Whole-body bioconcentration factors (BCF = mg total Ag per kg fresh weight tissue divided by mg total Ag per liter of medium) of silver in three species of aquatic insects ranged from 21 to 240 in water containing 30-65 mg $CaCO_3$/L during exposure of 3-15 days; in bluegill sunfish (*Lepomis macrochirus*), this value was less than 1 after exposure for 28 days (EPA 1980). Molt frequency of a mayfly (*Isonychia bicolor*) was a sensitive indicator of silver stress over time, and 1.6 µg total Ag/L over a 20-day period inhibited molting (Diamond et al. 1990).

Silver ion (Ag^+) was the most toxic chemical species of silver to fishes. Silver ion was 300 times more toxic than silver chloride to fathead minnows (*Pimephales promelas*), 15,000 times more toxic than silver sulfide, and more than 17,500 times more toxic than silver thiosulfate complex; in all cases, toxicity reflected the free silver ion content of tested compounds (LeBlanc et al. 1984); a similar pattern was noted in rainbow trout (Hogstrand et al. 1996). Silver was less toxic to fathead minnows under conditions of increasing water hardness between 50 and 250 mg $CaCO_3$/L, increasing pH between 7.2 and 8.6, and increasing concentrations of humic acid and copper; starved minnows were more sensitive to ionic silver than minnows fed regularly (Brooke et al. 1994). Eggs of rainbow trout exposed continuously to silver concentrations as low as 0.17 µg/L had increased embryotoxicity and hatched prematurely; resultant fry had a reduced growth rate (Davies et al. 1978). Removal of the egg capsule of eyed embryos of steelhead trout (*Oncorhynchus mykiss*) significantly lowered the resistance of the embryos to salts of silver, copper, and mercury but not zinc and lead (Rombough 1985). Silver accumulation in gills of juvenile rainbow trout exposed to 11 µg Ag/L for 2-3 h was significantly inhibited by various cations (Ca^{2+}, Na^+, H^+) and complexing agents (dissolved organic carbon, thiosulfate, chloride); these variables must be considered when constructing predictive models of silver binding to gills (Janes and Playle 1995).

Largemouth bass (*Micropterus salmoides*) and bluegills accumulated silver from the medium; accumulations increased with increasing concentrations of ionic silver and increasing duration of exposure (Coleman and Cearley 1974). Bioconcentration factors of radiosilver-110m for various species of teleosts were as high as 40 after 98 days (Pouvreau and Amiard 1974). However, plaice (*Pleuronectes platessa*; a marine flounder), and thornback rays (*Raja clavata*) fed nereid polychaete worms labeled with radiosilver-110m retained about 4.2% of the ingested dose after 3 days (Pentreath 1977), which suggests that the high silver concentration factors reported by Pouvreau and Amiard (1974) may have been due to loosely bound adsorbed silver. Flounders (*Pleuronectes* sp.) held for 2 months in seawater solutions containing 40 µg Ag/L had elevated silver concentrations in the gut (0.49 mg Ag/kg FW) but less than 0.05 mg/kg in all other examined tissues (Pentreath 1977). Similarly exposed rays (*Raja* sp.) contained 1.5 mg Ag/kg FW in liver, 0.6 in gut, 0.2 in heart, and 0.05-0.18 mg/kg FW in spleen, kidney, and gill filament (Pentreath 1977); liver is usually considered the major repository of silver in teleosts (Garnier et al. 1990).

Food chain biomagnification of silver in aquatic systems is unlikely at silver concentrations normally encountered in the environment (Connell et al. 1991), although regular ingestion of fish from contaminated waters may significantly affect dietary silver intake in humans (EPA 1980). Silver—as thiosulfate-complexed silver at nominal concentrations of 500 or 5,000 µg Ag/L—was concentrated and magnified over a 10-week period in freshwater food chains of algae, daphnids, mussels, and fathead minnows (Terhaar et al. 1977), although the mechanisms of accumulation in this study were imperfectly understood.

Birds and Mammals

No data were found on the effects of silver compounds on avian or mammalian wildlife. All controlled studies with silver were with domestic poultry, livestock, or small laboratory mammals. Signs of chronic silver ion intoxication in tested birds and mammals included cardiac enlargement, vascular hypertension, hepatic necrosis, anemia, lowered immunological activity, altered membrane permeability, kidney pathology, enzyme inhibition, growth retardation, and a shortened life span (Smith and Carson 1977; Freeman 1979; Fowler and Nordberg 1986; PHS 1990).

Silver affects turkeys (*Meleagris gallopavo*) and domestic chickens (*Gallus* spp.). Turkey poults on diets containing 900 mg Ag/kg feed for 4 weeks had enlarged hearts and reduced growth, hemoglobin, and hematocrit (EPA 1980). Chicken eggs injected with silver nitrate at 0.1 mg Ag/egg (equivalent to about 1.8 mg Ag/kg egg FW) had a 50% reduction in survival but no developmental abnormalities (Ridgway and Karnofsky 1952). Adverse effects of silver were reported in normal chicks fed diets containing 200 mg Ag/kg ration (growth suppression) or given drinking water containing 100 mg Ag/L (liver necrosis; Smith and Carson 1977). Chicks on copper-deficient diets had adverse effects at 10 mg Ag/kg ration (reduced hemoglobin; reversible when fed copper-adequate diet) and at 50-100 mg Ag/kg ration (growth suppression and increased mortality). Chicks that were deficient in vitamin E experienced reduced growth when given drinking water containing 1,500 mg Ag/L. Chickens infected with pathogenic strains of *Salmonella* sp. and *Escherichia coli* were cured with aerosol treatments containing 10 µg Ag/L air (Smith and Carson 1977).

Studies with small laboratory mammals—which require verification—show that long-term exposure to high levels of silver nitrate in drinking water may result in sluggishness and enlarged hearts; however, these effects have not been observed in silver-exposed humans (PHS 1990). Concentrations as high as 200 µg Ag/L in drinking water of test animals for 5 months had no significant effect on animal health or metabolism (EPA 1990). But 400 µg Ag/L for 5 months caused kidney damage, and 500 µg/L for 11 months was associated with impaired conditioned-reflex activities, immunological resistance, and altered brain nucleic acid content (EPA 1980). Diets deficient in vitamin E or selenium caused rapidly fatal hepatocellular necrosis and muscular dystrophy to rats if they contained the dietary-intake equivalent of 130 mg Ag/kg BW daily, a comparatively high silver ion intake (Smith and Carson 1977; PHS 1990).

The extent of absorption of an administered dose of silver depends on silver speciation, the presence and extent of silver-binding proteins, and other variables. But absorption is dependent mainly on the transit time through the gastrointestinal tract: the faster the transit time is, the less silver is absorbed. Transit times ranged from about 8 h in mice and rats to about 24 h in monkeys, dogs, and humans (PHS 1990). Route of administration affected the excretion rate of silver. Clearance of silver from mammals 2 days after silver was administered intravenously ranged from 15% in dogs to 82% in mice; clearance rates were intermediate in monkeys and rats. When silver was administered orally, clearance was more rapid, and extended from 90.4% in dogs to 99.6% in mice (PHS 1990). The half-time persistence of silver administered orally to mice was 0.1 day for the short-lived component and 1.6 days for the long-lived component. Other species of tested laboratory animals had biphasic or triphasic whole-body silver-excretion profiles that differed significantly from mice. Monkeys, for example, had a biphasic excretion profile with peaks at 0.3 and 3.0 days; rats had a triphasic profile with peaks at 0.1, 0.7, and 5.9 days; and dogs had half-time persistence peaks at 0.1, 7.6, and 33.8 days (PHS 1990).

Ionic silver is lethal to mice (*Mus* spp.) at 13.9 mg/kg BW by intraperitoneal injection, to rabbits (*Oryctolagus* spp.) at 20 mg/kg BW intraperitoneally, to dogs (*Canis familiaris)* at 50 mg/kg BW by intravenous injection, to humans at greater than 166 mg/kg BW in a single dose, and to rats (*Rattus* spp.) at 1,586 mg/L drinking water for 37 weeks (Table 7). Sublethal effects are reported in rabbits given 250 µg Ag/L drinking water (brain histopathology), in rats given 400 µg Ag/L drinking water for 100 days (kidney damage), in mice given 95 mg Ag/L drinking water for 125 days (sluggishness), in guinea pigs (*Cavia* sp.) given 81 mg Ag/cm^2 skin applied daily for 8 weeks (reduced growth), and in rats given diets containing 6 mg Ag/kg for 3 months (high accumulations in kidneys and liver) or 130-1,110 mg/kg (liver necrosis; Table 7).

The connections between human cancers and silver as a causal agent are tenuous (EPA 1980). All available evidence is negative or inconclusive regarding silver's ability to induce cancer, mutagenicity, or birth defects in animals by normal routes of exposure (EPA 1980; PHS 1990). Silver pellets, however, implanted

under the skin of rodents, have caused sarcomas, malignant fibrosarcomas, fibromas, fibroadenomas, and invasions of muscle with connective tissue; in these cases, silver seems to act as a nonspecific irritant rather than as a specific carcinogen (Smith and Carson 1977; EPA 1980). Intratumoral injections of colloidal silver promotes cancer growth in rats, possibly by producing an area of lowered tissue resistance that allows resistant cancer cells to grow freely (Smith and Carson 1977); however, silver nitrate seems to be a tumor inhibitor in mice (EPA 1980).

In humans, acute toxic effects of silver have resulted only from accidental or suicidal overdoses of medical forms of silver. Symptoms of acute silver poisoning in patients dying after intravenous administration of Collargo (silver plus silver oxide) included gastrointestinal disturbances, pulmonary edema, tissue necrosis, and hemorrhages in bone marrow, liver, and kidney (Smith and Carson 1977; EPA 1980). High sublethal doses of silver nitrate taken orally cause some patients to experience violent abdominal pain, abdominal rigidity, vomiting, and severe shock; systemic effects among recovering patients are unlikely, although degenerative liver changes may occur (EPA 1980). In humans, skin contact with silver compounds may cause mild allergic reactions such as rash, swelling, and inflammation (PHS 1990); industrial and medicinal exposures to silver may cause lesions of the kidneys and lungs, and arteriosclerosis (Klaassen et al. 1986); colloidal silver compounds may interfere with nasal ciliary activity (Smith and Carson 1977); and exposure to dust containing high levels of silver compounds, such as silver nitrate or silver oxide, may cause breathing problems, lung and throat irritation, and stomach pain (PHS 1990).

Table 7. Effects of silver on selected mammals.

Table 7. Organism, route of administration, dose, and other variables	**Effects**	**Reference[a]**
Domestic dog, *Canis familiaris*		
Inhalation route. Anaesthetized dogs exposed to metallic silver particles about 0.5 um in diameter; total dose deposited of 25 µg	About 3% (0.8 µg) of the deposited silver was found in liver and blood 6 h after exposure. Clearance from the lung to the blood was triphasic, with half-times of 1.7, 8.4, and 40 days	1
Intratracheal route. Elemental silver deposited in lungs	After 6 h, 96.9% remained in lungs, 2.4% in liver, 0.35% in blood, 0.14% in gall bladder and bile, 0.1% in intestines, 0.06% in kidneys, and 0.02% in stomach. After 225 days, 0.49% of the initial dose was detected in liver, and 0.01-0.03% each in brain, gall bladder, intestines, lungs and trachea, bone, stomach and contents, heart, and muscle. If lung is excluded, liver contained 77% of the total-silver body burden between 6 h and 225 days postexposure	1
Intravenous injection route		
0.003 µg/kg body weight (BW) daily	15% cleared in 2 days	1
500 mg (estimated at 50 mg/kg BW), single injection	All dead within 24 h with hemolysis and lung edema	2
Oral route; 0.005 µg/kg BW daily	90.4% cleared in 2 days	1

Table 7. Organism, route of administration, dose, and other variables	Effects	Reference[a]
Guinea pig, *Cavia* sp.		
Dermal application of 81 mg silver nitrate to 3.1 cm^2 of skin daily for 8 weeks	Growth rate reduced 10-20%	1
Humans, *Homo sapiens*		
External route		
0.25% silver nitrate solution in eyes for 3 weeks	Argyrosis	2
3-5% colloidal silver compounds in eyes for 5-10 weeks	Argyrosis	2
Inhalation route		
0.25 mg/m^3 air	Possibility of generalized argyria in 20 years	2
1-2 mg/m^3 air; occupational exposure	Argyrosis of cornea and conjunctiva	3
Clearance half-time		
Feces	>300 days	1
Lung	Biexponential profile; 1 day and 52 days	1
Urine	<54 days	1
Oral route		
80 µg/kg BW, single dose	21% of dose retained in body after 1 week	1
0.7 mg silver weekly in diet	Possibility of generalized argyria	2
2-30 g of silver nitrate, single dose	At dosages >10 g (equivalent to >166 mg Ag/kg BW for a 60-kg person), death usually occurs within a few hours to a few days	2, 3
50-260 g of metallic silver	Gastric fullness, anorexia, gastric pain, diarrhea	2, 3
>600 g over 1.2 years; given as silver nitrate to treat epilepsy and GI symptoms	Generalized argyria evident 2 years after last dose	2
Monkeys, various		
Intravenous administration of 0.01 µg/kg BW daily	44.1% excreted in 2 days	1
Oral administration of 0.01 µg/kg BW daily	94.3% cleared in 2 days	1

Table 7. Organism, route of administration, dose, and other variables	Effects	Reference[a]
Domestic mouse, *Mus* spp.		
Drinking water route; 95 mg/L for 125 days	Sluggishness	1
Intraperitoneal route		
13.9 mg/kg BW, single injection	LD50(30 days)	3
35.0 mg/kg BW, single injection; pretreated with single injection of 3.5 mg Ag/kg BW 24 h earlier	Only 3 of 10 pretreated mice died within 7 days vs. 8 of 10 nonpretreated mice	3
Intravenous injection; 1.0 µg/kg BW daily	82% cleared in 2 days	1
Oral route; 1.1 µg/kg BW daily	99.6% cleared in 2 days	1
Rabbit, *Oryctolagus* sp.		
Drinking water route		
Equivalent to 2.5 µg Ag/kg BW daily	No observable adverse effects	2
Equivalent to 25 or 250 µg Ag/kg BW daily for 11 months	Brain histopathology; altered conditioned reflexes	2
Equivalent to 500 or 5,000 µg Ag/kg BW daily for 11 months	Lowered immunological activity; pathology of vascular, nerve, brain, and spinal cord tissues	3
Intraperitoneal injection route; 20 mg/kg BW, single injection	All dead within 2 h. Silver granules in liver parenchyma and kidney tubules	3
Laboratory white rat, *Rattus* spp.		
Diet		
Equivalent to 6 mg/kg BW daily	After 12 weeks, kidneys and liver were impregnated with silver	2
130-1,110 mg/kg ration	Liver necrosis which could be prevented by adding Vitamin E	2
Drinking water route		
50 µg/L (equivalent to 0.0025 mg Ag/kg BW daily) for 11 months	Normal in all variables measured (conditioned reflex activity, gastric secretion, blood serum enzymes, histology)	3
200 µg/L for 6 months	Normal conditioned reflex activity	3
<400, 400, 700, or 1,000 µg/L for 100 days	At <400 µg/L, rats seemed healthy with normal tisssue histology. At 400 µg/L, hemorrhages noted	3

Table 7. Organism, route of administration, dose, and other variables	Effects	Reference[a]
	in kidney. At 700 µg/L, kidney and liver histopathology was evident. At 1,000 µg/L, spleen was pigmented and kidney and liver damage more pronounced	
500 µg/L (equivalent to 0.025 mg Ag/kg BW daily) for 6-11 months	Abnormal conditioned reflex activity; increased liver weight and liver RNA concentration	3
5 mg/L for 6 months	Signs of intoxication beginning at days 25-27	3
20 mg/L for 3 months	Decreased growth; abnormal liver; increased levels of blood amino acids	3
20 mg/L for 5 months	Pathology in stomach, small intestine, and liver; altered blood serum enzyne activity; growth depressed 36%	3
20 mg/L for 6 months	Increased brain DNA and RNA	2
129 mg/L (about 18 mg/kg BW daily) for 17.8 weeks	Silver accumulations in brain and central nervous system; reduced motor activity	1
634 mg/L (89 mg Ag/kg BW daily) for 2 years	No effect on male fertility; no silver deposits in testes	1
635-660 mg/L; lifetime exposure beginning shortly after weaning	Lifespan normal; hypertrophy of left ventricle, suggesting vascular hypertension; skin normal but internal organs and eyes darkened by silver deposits	3
1,200 mg/L for several months	Degenerative kidney changes	3
1,500 mg/L for 2-4 weeks; vitamin E-deficient rats	Liver necrosis and death. Prevented by adding vitamin E	2
1,586 mg/L for 37 weeks	Some deaths beginning at week 23; survivors weighed about 50% less than controls	1
2,500 mg/L for 3 months, then silver-free water for 16 months	At end of exposure livers had 6.7-7.0 mg Ag/kg FW and kidneys 3.7-7.1 mg/kg FW; 16 months after exposure livers had 1.6 mg/kg FW and kidneys 6.0 mg/kg FW	3
2,589 mg/L, (equivalent to 362 mg Ag/kg BW daily) for 2 weeks	25% died; water intake decreased beginning at day 1; survivors poorly groomed and listless	1
Intramuscular injection route		
Given radiosilver-110m alone or in combination with 4.0 mg Ag/kg BW daily for 6 days. Percent of		

Table 7. Organism, route of administration, dose, and other variables	Effects	Reference[a]
tracer dose recovered vs. percent tracer plus 4.0 mg/kg BW		
Blood	0.5 vs. 3.0	1
Bone	0.2 vs. 2.2	1
Feces	96.6 vs. 37.3	1
GI tract	1.1 vs. 8.2	1
Heart, lungs	0.06 vs. 0.6	1
Kidney	0.07 vs. 0.6	1
Liver	0.4 vs. 33.7	1
Muscle	0.2 vs. 2.4	1
Skin	0.2 vs. 7.4	1
Spleen	0.01 vs. 2.7	1
Urine	0.6 vs. 1.8	1
Intravenous injection route		
0.2 µg/kg BW daily	70.7% excreted in 2 days vs. 98.4% in 2 days when administered orally	1
Isolated hepatocytes exposed for 20 h		
<275 µg/L	Not cytotoxic	4
500, 2,000, or 5,000 µg/L	Silver accumulated in nuclear fraction of hepatocytes at all concentrations; DNA repair synthesis was stimulated at 2,000 µg/L; moderately cytotoxic at 5,000 µg/L	5
1,100 µg/L	Protein synthesis activity inhibited 50%	4
1,980 µg/L	Almost complete inhibition of protein synthesis activity	4
Subcutaneous injection route		
7 mg/kg BW, single injection	Adverse effects on spermatogenesis and on testes histology	2,3
Oral route		

Table 7. Organism, route of administration, dose, and other variables	Effects	Reference[a]
123 mg/kg BW, as silver cyanide	Acute oral LD50	6
200-400 mg/kg BW, as silver arsenate	Acute oral LD50	6
500-800 mg/kg BW, as silver nitrate	Acute oral LD50	6
Caribou, *Rangifer tarandus*		
Ratio of silver concentration (mg/kg FW) in tissues to silver concentration (mg/kg FW) in lichen diet		
Bone	Bioconcentration factor (BCF) of 3.0	3
Kidney	BCF of 1.3	3
Liver	BCF of 80.0	3
Muscle	BCF of 0.3	3

[a]1, U.S. Public Health Service 1990; 2, Smith and Carson 1977; 3, U.S. Environmental Protection Agency 1980; 4, Denizeau et al. 1990; 5, Denizeau and Marion 1989; 6, Lockhart 1983.

Chronic exposure of humans to silver or silver compounds has frequently resulted in generalized argyria (slate-gray pigmentation of the skin and hair caused by deposition of silver), localized argyria (limited areas of pigmentation usually associated with medicinal silver applications), or argyrosis (argyria of the eye). Every silver compound in common chemical use has caused generalized argyria, usually from medical and occupational exposures (Smith and Carson 1977; EPA 1980). In generalized argyria, skin pigmentation was highest in light-exposed areas, although silver concentrations in light-exposed and dark-exposed skin were the same (EPA 1980). In severe cases of argyria, the skin may become black with a metallic luster, the eyes affected to the point that vision is disturbed, and the respiratory tract impaired (Klaassen et al. 1986). Individual variability in susceptibility to argyria is great and this is probably explained by the variability in absorption and retention of silver (Smith and Carson 1977). Generalized argyria as an occupational disease is unusual but has been reported in workers that make silver nitrate or are involved in mirror plating, glass bead silvering, silver Christmas cracker manufacturing, photographic plate manufacturing, and silver mining. Generalized argyria was also associated with chronic inhalation or ingestion of silver fulminate, silver nitrate, silver albuminate, and silver cyanide (Smith and Carson 1977). Improved workplace ventilation and sanitation among silver nitrate workers effected a decline in general argyria (EPA 1980).

Localized argyria is rare and usually occurs when silver compounds contact broken skin or mucous membranes (Smith and Carson 1977). Localized argyria has been reported in workers who handle metallic silver in filing, drilling, polishing, turning, engraving, forging, soldering, or smelting operations. Silver polishers exposed for 25 years or more (range 2-38 years) sometimes exhibit increased densities in their lung x-rays due to silver impregnation of the elastic membranes of the pulmonary vessels. In one case, an Italian physician who dyed his facial hair with a silver dye for 25 years developed argyria in the conjunctiva of both eyes (Smith and Carson 1977).

Recommendations

Most measurements of silver concentrations in natural waters prior to the use of clean techniques are considered inaccurate. Until analytical capabilities that exceed the dissolved-particulate classification are developed, it will be necessary to rely on laboratory and theoretical modeling studies to fully understand chemical speciation of silver in natural waters (Andren et al. 1995).

Factors governing the environmental fate of silver are not well characterized, including silver transformations in water and soil and the role of microorganisms (PHS 1990). Food chain transfer of silver requires more current information on sources and forms of silver and data on concentrations in field collections of flora and fauna, especially near hazardous waste sites (PHS 1990). Although silver in sewage sludge is mostly immobilized, data are limited on the uptake by vegetation of silver from soils amended with silver-contaminated sewage sludge and on silver concentrations in flesh and milk of livestock pastured or fed grains raised on soils amended with sewage sludge (Smith and Carson 1977). Data are needed on partition coefficients and vapor pressures of silver compounds (PHS 1990) and on silver concentrations in emissions from cement producers and smelters and refineries of copper, lead, zinc, silver, iron, and steel (Smith and Carson 1977). Also, technology to recapture silver from waste media before it reaches the environment must be improved (PHS 1990).

In aquatic environments, more research is needed on the chemical speciation of silver to evaluate risk to the organism and its consumers (EPA 1987; Berthet et al. 1992). Most silver criteria formulated for the protection of aquatic life are now expressed as total recoverable silver per liter (Table 8). But total silver measurements do not provide an accurate assessment of potential hazard. Silver ion (Ag^{+}), for example, is probably the most toxic of all silver chemical species and must be accurately measured in the assessment of silver risks in aquatic environments (LeBlanc et al. 1984), perhaps as acid-soluble silver (EPA 1987). Little is known of the biocidal properties of Ag^{2+} and Ag^{3+} that are the active ingredients in disinfectants and used increasingly in water purification systems of drinking water and swimming pools (Antelman 1994). The effects of these silver species on organism health clearly must be researched (PHS 1990). Silver interactions with other metals and compounds in solution are not well defined. For example, mixtures of salts of silver and copper markedly increased the survival of oyster embryos, but only when copper concentrations were less than 6 µg/L and total silver less than 11 µg/L (Coglianese and Martin 1981).

Table 8. Proposed silver criteria for the protection of natural resources and human health.

Table 8. **Resource, criterion, and other variables**	**Effective silver concentration**	**Reference[a]**
Agricultural crops		
Soils	<100 mg total silver/kg dry weight soil for most species; <10 mg/kg for sensitive species	7
Freshwater aquatic life protection		
Acute exposure		
Total recoverable silver	<1.32 µg/L	1
Acid-soluble silver[b]	4-day average shall not exceed 0.12 µg/L more than once every three years; 1-h average not to exceed 0.92 µg/L more than once every 3 years	8
Acute exposure		
Total recoverable silver, in µg/L, should not exceed $e^{(1.72[\ln(\text{hardness})]-6.52}$ at any time. Examples follow		
50 mg $CaCO_3$/L	<1.2 µg/L	2

Table 8. Resource, criterion, and other variables	Effective silver concentration	Reference[a]
100 mg $CaCO_3$/L	<4.1 µg/L	2
200 mg $CaCO_3$/L	<13.0 µg/L	2
Chronic exposure	<0.12-<0.13 µg total recoverable silver/L	1, 2
Tissue residues		
Adverse effects on growth of the Asiatic clam, *Corbicula fluminea*	>1.65 mg total silver/kg soft tissues, fresh weight basis	1
Marine life protection		
Acute exposure		
Total recoverable silver	<2.3 µg/L at any time	2
Acid-soluble silver[b]	4-day average concentration not to exceed 0.92 µg/L more than once every 3 years on average and the 1-h concentration not to exceed 7.2 µg/L more than once every 3 years	8
Tissue residues		
Marine clams, soft parts		
Normal	<1 mg total silver/kg dry weight	3
Stressful or fatal	>100 mg total silver/kg dry weight	3
Human health		
Air, United States		
Current level of exposure, nationwide	100 µg total silver daily per person	2
Short-term exposure limit (15 min; up to 4 times daily with 60-min intervals at <0.01 mg Ag/m^3 air)	<0.03 mg total silver/m^3	2
Threshold limit value (8 h daily, 5 days weekly)		
Aerosol silver compounds	<0.01 mg total silver/m^3	2, 4, 5
Metallic silver dust	<0 .1 mg total silver/m^3	5
Diet, United States		
Current level of exposure	35 to 40 µg daily per person	2
Drinking water		
United States		
Long-term exposure (>10 days)	<50 µg total silver/L	2, 5, 6
Proposed long-term exposure	<90 µg total silver /L	5

Table 8. Resource, criterion, and other variables	Effective silver concentration	Reference[a]
Short-term exposure (1-10 days)	<1,142 µg total silver/L	5
California	<10 µg/L	2
Germany	<100 µg/L	2
Space vehicles		
Former Soviet Union	Max. 200 µg total silver/L	2
United States	100 to Max. 200 µg total silver/L	2
Switzerland	<200 µg total silver/L	2
Groundwater	<50 µg total silver/L	5

[a]1, Diamond et al. 1990; 2, U.S. Environmental Protection Agency (EPA) 1980; 3, Bryan and Langston 1992; 4, Smith and Carson 1977; 5, U.S. Public Health Service (PHS) 1990; 6, Fowler and Nordberg 1986; 7, Hirsch et al. 1993; 8, EPA 1987.

[b]Silver that passes through a 0.45-um membrane after the sample has been acidified to a pH between 1.5 and 2.0 with nitric acid.

The proposed human drinking water criteria of 50 to <200 µg total Ag/L do not seem to represent a hazard to human health, although much lower concentrations adversely affect freshwater and marine organisms (Smith and Carson 1977; Table 8). Proposed silver criteria for the protection of freshwater aquatic life during acute exposure now range from 1.2 to 13.0 µg total recoverable silver per liter (Table 8). If all total recoverable silver were in the ionic form, these proposed criteria would overlap the 1.2 to 4.9 µg/L range found lethal to sensitive species of aquatic plants and animals and indicates that the proposed freshwater acute silver criteria need to be reexamined. For freshwater aquatic life protection during chronic exposure, the proposed criterion of less than 0.13 µg total recoverable silver per liter (Table 8) is probably sufficient. But the proposed silver criterion of 2.3 µg total silver/L to protect marine life (Table 8) needs to be reconsidered because phytoplankton species composition and succession are significantly altered at 0.3-0.6 µg total silver/L and because some species of marine algae and mollusks show extensive accumulations at 1.0-2.0 µg total silver/L. Limited but insufficient data were available on correlations between tissue residues of silver with health of aquatic organisms (Table 8); additional research seems needed on the significance of silver residues in tissues.

Silver criteria in aquatic ecosystems are under constant revision by regulatory agencies. For example, total recoverable silver is no longer recommended by the U.S. Environmental Protection Agency in silver criteria formulation and should be replaced by dissolved silver (EPA 1995a). Dissolved silver more closely approximates the bioavailable fraction of silver in the water column than does total recoverable silver (EPA 1995b). Dissolved silver criteria recommended are about 0.85 times those of total recoverable silver under certain conditions but may vary considerably depending on other compounds present in solution (EPA 1995b).

No studies have been conducted with silver and avian or mammalian wildlife, and it is unreasonable to extrapolate the results of limited testing with domestic poultry and livestock to wildlife to establish criteria or administratively enforced standards. Research on silver and avian and terrestrial wildlife merits the highest priority in this subject area. No silver criteria are available for the protection of avian and mammalian health, and all criteria now proposed are predicated on human health (Table 8). As judged by the results of controlled studies with poultry and small laboratory mammals, safe concentrations of silver ion were less than 250 µg/L in drinking water of mammals, less than 100 mg/L in drinking water of poultry, less than 6 mg/kg in diets of mammals, less than 10 mg/kg in copper-deficient diets of poultry, less than 200 mg/kg in copper-adequate diets of poultry, and less than 1.8 mg/kg in chicken eggs. The proposed short-term (10-day) allowable limit of 1,142 µg Ag/L in drinking water for human health protection (Table 8) should be reconsidered because it is 4.6 times higher than the value that produced adverse effects in sensitive laboratory mammals. Additional animal studies

are needed to elucidate the effects of silver and silver compounds on reproduction, development, immunotoxicity, neurotoxicity, absorption, distribution, metabolism, and excretion; and on oral, dermal, and inhalation routes of exposure (PHS 1990). In animals, there is also the need to establish a target organ for intermediate exposures to silver, to establish suitable biomarkers of silver exposures and effects, and to measure effects of chronic silver exposures on carcinogenicity (PHS 1990). These studies should be implemented with suitable sentinel organisms including waterfowl, aquatic mammals, and other species of wildlife.

It is emphasized that silver and its compounds do not pose serious environmental health problems to humans from 50 µg/L in drinking water and 10 µg/m^3 in air (Smith and Carson 1977). The only proven effect of chronic exposure to silver is argyria from occupational or therapeutic exposure to much larger amounts of silver (minimum necessary absorption of 910 µg, equivalent to about 15 µg/kg BW) than can feasibly be ingested or inhaled from environmental sources. Regular ingestion of fish, meat, and plants from silver-contaminated areas probably does not cause argyria (Smith and Carson 1977). Humans at special risk to argyria include those treated with silver-containing medicinals and people marginally deficient or deficient in copper, selenium, or vitamin E (EPA 1980). There is no recognized effective treatment for argyria, although the condition seems to be relatively stationary when exposure to silver is discontinued (Fowler and Nordberg 1986). Absorption and retention of silver from food and medicinals is imperfectly understood (Smith and Carson 1977), suggesting the need for additional animal studies.

Finally, alternatives exist to the use of silver in various materials and processes. These include substitution of aluminum and rhodium for silver in mirrors and other reflecting surfaces; tantalum replacement of silver in surgical plates, pins, and sutures; using stainless steel as an alternative material to silver in the manufacture of table flatware; and, in photography, using film with reduced silver content (Reese 1991).

Acknowledgments

I thank L. J. Garrett and P. W. Manning for library services; D. R. Buckler, D. J. Hoffman, J. F. Moore, and several anonymous referees for technical reviews of the manuscript; M. C. Hager, E. D. Rockwell, and B. A. Vairin for editorial services; and S. M. Lauritzen for layout.

Cited Literature

Abbe, G. R., and J. G. Sanders. 1990. Pathways of silver uptake and accumulation by the American oyster (*Crassostrea virginica*) in Chesapeake Bay. Estuarine, Coastal and Shelf Science 31:113-123.

Alexander, G. V., and D. R. Young. 1976. Trace metals in southern California mussels. Marine Pollution Bulletin 7:7-9.

Anderlini, V. 1974. The distribution of heavy metals in the red abalone, *Haliotis rufescens,* on the California coast. Archives of Environmental Contamination and Toxicology 2:253-265.

Anderlini, V. C. 1992. The effect of sewage on trace metal concentrations and scope for growth in *Mytilus edulis aoteanus* and *Perna canaliculus* from Wellington Harbour, New Zealand. The Science of the Total Environment 125:263-288.

Andren, A. W., and T. W. Bober, organizers. 1995. Transport, fate and effects of silver in the environment. Abstracts of 3rd international conference, 6-9 August, 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison. 35 pp.

Andren, A. W., T. W. Bober, E. A. Crecelius, J. R. Kramer, S. N. Luoma, J. H. Rodgers, and A. Sodergren, organizers. 1993. Proceedings of the first international conference on transport, fate, and effects of silver in the environment. University of Wisconsin Sea Grant Institute, Madison. 120 pp.

Andren, A. W., T. W. Bober, J. R. Kramer, A. Sodergren, E. A. Crecelius, S. N. Luoma, and J. H. Rodgers, organizers. 1994. Transport, fate and effects of silver in the environment. Proceedings of the 2nd international conference. University of Wisconsin Sea Grant Institute, Madison. 223 pp.

Andren, A. W., B. Wingert-Runge, and D. Sedlak. 1995. The occurrence and behavior of silver in natural waters. *In* A. W. Andren and T. W. Bober, organizers. Transport, fate and effects of silver in the environment. Abstracts of 3rd international conference, 6-9 August, 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison.

Antelman, M. S. 1994. Silver (II, III) disinfectants. Soap/Cosmetics/Chemical Specialties 70:52-59.

Aoki, T., K. Nihonyanagi, and T. Oba. 1993. Involvement of thiols in the induction of inward current induced by silver in frog skeletal muscle. Experientia 49:792-794.

Bard, C. C., J. J. Murphy, D. L. Stone, and C. J. Terhaar. 1976. Silver in photoprocessing effluents. Journal Water Pollution Control Federation 48:389-394.

Baudin, J. P., J. Garnier-Laplace, and A. Lambrechts. 1994. Uptake from water, depuration and tissue distribution of ^{110m}Ag in a freshwater fish *Cyprinus carpio* L. Water, Air, and Soil Pollution 72:129-141.

Berrow, S. D. 1991. Heavy metals in sediments and shellfish from Cork Harbour, Ireland. Marine Pollution Bulletin 22:467-469.

Berthet, B., J. C. Amiard, C. Amiard-Triquet, M. Martoja, and A. Y. Jeantet. 1992. Bioaccumulation, toxicity and physico-chemical speciation of silver in bivalve molluscs: ecotoxicological and health consequences. The Science of the Total Environment 125:97-122.

Berthet, B., C. Amiard-Triquet, and R. Martoja. 1990. Effets chimiques et histologiques de la decontamination de l'huitre *Crassostrea gigas* Thurberg prealablement exposee a l'argent. Water, Air, and Soil Pollution 50:355-369.

Bertine, K. K., and E. D. Goldberg. 1972. Trace elements in clams, mussels, and shrimp. Limnology and Oceanography 17:877-884.

Birge, W. J., and J. A. Zuiderveen. 1995. The comparative toxicity of silver to aquatic biota. *In* A. W. Andren and T. W. Bober, organizers. Transport, fate and effects of silver in the environment. Abstracts of 3rd international conference, 6-9 August 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison.

Bloom, N. S., and E. A. Crecilius. 1987. Distribution of silver, mercury, lead, copper and cadmium in central Puget Sound sediments. Marine Chemistry 21:377-390.

Bober, T. W., T. J. Dagon, and H. E. Fowler. 1992.Treatment of photographic processing wastes. Pages 173-227 *in* L. K. Wang and M. H. S. Wang, editors. Handbook of industrial waste treatment. Volume 1. Marcel Dekker, New York.

Braune, B. M., R. J. Norstrom, M. P. Wong, B.T. Collins, and J. Lee. 1991. Geographical distribution of metals in livers of polar bears from the Northwest Territories, Canada. The Science of the Total Environment 100:283-299.

Brooke, L.,R. Erickson, M. Kahl, F. Vande-Venter, S. Harting, T. Markee, C. Stephan, amd R. Spehar. 1994. Effects of laboratory test conditions on the toxicity of silver to aquatic organisms. Pages 119-122 *in* A. W. Andren, T. W. Bober, J. R. Kramer, A. Sodergren, E. A. Crecelius, S. N. Luoma, and J. H. Rodgers, organizers. Transport, fate and effects of silver in the environment. Proceedings of the 2nd international conference. University of Wisconsin Sea Grant Institute, Madison.

Brooks, R. R., and M. G. Rumsby. 1965. The biogeochemistry of trace element uptake by some New Zealand bivalves. Limnology and Oceanography 10:521-527.

Brown, C. L., and S. N. Luoma. 1995. Use of the euryhaline bivalve *Potamocorbula amurensis* as a biosentinel species to assess trace metal contamination in San Francisco Bay. Marine Ecology Progress Series 124:129-142.

Bruland, K. W., K. Bertine, M. Koide, and E. D. Goldberg. 1974. History of metal pollution in southern California coastal zone. Environmental Science and Technology 8:425-432.

Bryan, G. W. 1973. The occurrence and seasonal variation of trace metals in the scallops *Pecten maximus* (L.) and *Chlamys opercularis* (L.). Journal of the Marine Biological Association of the United Kingdom 53:145-166.

Bryan, G. W., and L. G. Hummerstone. 1977. Indicators of heavy metal contamination in the Looe estuary (Cornwall) with particular regard to silver and lead. Journal of the Marine Biological Association of the United Kingdom 57:75-92.

Bryan, G. W., and W. J. Langston. 1992.Bioavailability, accumulation and effects of heavy metals in sediments with special reference to United Kingdom estuaries: a review. Environmental Pollution 76:89-131.

Bryan, G. W., and H. Uysal. 1978. Heavy metals in the burrowing bivalve *Scrobicularia plana* from the Tamar estuary in relation to environmental levels. Journal of the Marine Biological Association of the United Kingdom 58:89-108.

Buell, J. W. 1991. Consequences of episodic exposure of chum salmon eggs/alevins to expected A-J mine tailing pond concentrations of Ag, Cd, Cu, Pb, and Zn. Pages 208-237 *in* P. Chapman, F. Bishay, E. Power, K. Hall, L. Harding, D. McLeary, M. Nassichuk, and W. Knapp, editors. Proceedings of the seventeenth annual aquatic toxicity workshop, 5-7 November 1990, Vancouver, B.C. Volume 1, Canadian Technical Report of Fisheries and Aquatic Sciences No. 1774 (Vol. 1).

Buhl, K. J., and S. J. Hamilton. 1991. Relative sensitivity of early life stages of Arctic grayling, coho salmon, and rainbow trout to nine inorganics. Ecotoxicology and Environmental Safety 22:184-197.

Cain, D. J., and S. N. Luoma. 1990. Influence of seasonal growth, age, and environmental exposure on Cu and Ag in a bivalve indicator, *Macoma balthica,* in San Francisco Bay. Marine Ecology Progress Series 60:45-55.

Calabrese, A., J. R. MacInnes, D. A. Nelson, R.A. Greig, and P. P. Yevich. 1984. Effects of long-term exposure to silver or copper on growth, bioaccumulation and histopathology in the blue mussel *Mytilus edulis.* Marine Environmental Research 11:253-274.

Calabrese, A., J. R. MacInnes, D. E. Nelson, and J. E. Miller. 1977a. Survival and growth of bivalve larvae under heavy-metal stress. Marine Biology 41:179-184.

Calabrese, A., F. P. Thurberg, and E. Gould. 1977b. Effects of cadmium, mercury, and silver on marine animals. Marine Fisheries Review 39:5-11.

Coglianese, M. P., and M. Martin. 1981. Individual and interactive effects of environmental stress on the embryonic development of the Pacific oyster, *Crassostrea gigas.* I. The toxicity of copper and silver. Marine Environmental Research 5:13-27.

Coleman, R. L., and J. E. Cearley. 1974. Silver toxicity and accumulation in largemouth bass and bluegill. Bulletin of Environmental Contamination and Toxicology 12:53-61.

Connell, D. B., J. G. Sanders, G. F. Riedel, and G. R. Abbe. 1991. Pathways of silver uptake and trophic transfer in estuarine organisms. Environmental Science and Technology 25:921-924.

Cooley, A. C., T. J. Dagon, P. W. Jenkins, and K. A. Robillard. 1988. Silver and the environment. Journal of Imaging Technology 14:183-189.

Crecelius, E. A. 1993. The concentration of silver in mussels and oysters from NOAA National Status and Trends Mussel Watch sites. Pages 65-66 *in* A. W. Andren, T. W. Bober, E. A. Crecelius, J. R. Kramer, S. N. Luoma, J. H. Rodgers, and A. Sodergren, organizers. Proceedings of the first international conference on transport, fate, and effects of silver in the environment. University of Wisconsin Sea Grant Institute, Madison.

Crecelius, E., and D. Phillips. 1995. Uptake and release of silver from marine sediment. *In* A. W. Andren and T. W. Bober, organizers. Transport, fate and effects of silver in the environment. Abstracts of 3rd international conference, 6-9 August 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison.

Dagon, T. J. 1973. Biological treatment of photo processing effluents. Journal Water Pollution Control Federation 45:2123-2135.

Daskalakis, K. D. 1995. Silver in oyster soft tissue: relations to site selection and sampling size. *In* A. W. Andren and T. W. Bober, organizers. Transport, fate, and effects of silver in the environment. Abstracts of 3rd international conference, 6-9 August 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison.

Davies, P. H., J. P. Goettl, Jr., and J. R. Sinley. 1978. Toxicity of silver to rainbow trout. Water Research 12:113-117.

Denizeau, F., and M. Marion. 1989. Genotoxic effects of heavy metals in rat hepatocytes. Cell Biology and Toxicology 5:15-25.

Denizeau, F., M. Marion, M. Chtaib, and J. P. Schmit. 1990. Toxicity of heavy metals in cultured hepatocytes. Environmental Toxicology and Chemistry 9:737-743.

Diamond, J. M., D. G. Mackler, M. Collins, and D. Gruber. 1990. Derivation of a freshwater silver criteria for the New River, Virginia, using representative species. Environmental Toxicology and Chemistry 9:1425-1434.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, Elmsford, New York. 687 pp.

Eisler, R., M. M. Barry, R. L. Lapan, Jr., G. Telek, E. W. Davey, and A. E. Soper. 1978. Metal survey of the marine clam *Pitar morrhuana* collected near a Rhode Island (USA) electroplating plant. Marine Biology 45:311-317.

Falandysz, J., and D. Danisiewicz. 1995. Bioconcentration factors (BCF) of silver in wild *Agaricus campestris.* Bulletin of Environmental Contamination and Toxicology 55:122-129.

Fisher, N. S., M. Bohe, and J. L. Teyssie. 1984. Accumulation and toxicity of Cd, Zn, Ag, and Hg in four marine phytoplankters. Marine Ecology Progress Series 18:201-213.

Fisher, N. S., V. T. Breslin, and M. Levandowsky. 1995. Accumulation of silver and lead in estuarine microzooplankton. Marine Ecology Progress Series 116:207-215.

Fisher, N.S., and J.R. Reinfelder. 1995. The trophic transfer of metals in marine systems. Pages 363-406 *in* A. Tessier and D.R. Turner, editors. Metal speciation and bioavailability in aquatic systems. John Wiley & Sons, New York.

Fisher, N. S., W. Wang, J. R. Reinfelder, and S.N. Luoma. 1994. Bioaccumulation of silver in marine bivalves. Pages 139-140 *in* A. W. Andren, T. W. Bober, J. R. Kramer, A. Sodergren, E. A. Crecelius, S. N. Luoma, and J. H. Rodgers, organizers. Transport, fate and effects of silver in the environment. Proceedings of the 2nd international conference. University of Wisconsin Sea Grant Institute, Madison.

Fowler, B. A., and G. F. Nordberg. 1986. Silver. Pages 521-530 *in* L. Friberg, G. F. Nordberg, and V. B. Vouk, editors. Handbook on the toxicology of metals. Volume II: specific metals. Elsevier, New York.

Fowler, S. W., and B. Oregioni. 1976. Trace metals in mussels from the N. W. Mediterranean. Marine Pollution Bulletin 7:26-29.

Freeman, R. A. 1979. Ecological kinetics of silver in an alpine lake ecosystem. Pages 342-358 *in* L. L. Marking and R. A. Kimerle, editors. Aquatic toxicology. Proceedings of the second annual symposium on aquatic toxicology. ASTM Special Technical Publication 667. American Society for Testing and Materials, Philadelphia.

Garnier, J., and J. P. Baudin. 1990. Retention of ingested ^{110m}Ag by a freshwater fish, *Salmo trutta* L. Water, Air, and Soil Pollution 50:409-421.

Garnier, J., J. P. Baudin, and L. Foulquier. 1990. Accumulation from water and depuration of ^{110m}Ag by a freshwater fish, *Salmo trutta* L. Water Research 24:1407-1414.

Goldberg, E. D., V. T. Bowen, J. W. Farrington, G. Harvey, J. H. Martin, P. L. Parker, R. W. Risebrough, W. Robertson, and E. Gamble. 1978. The mussel watch. Environmental Conservation 5:101-125.

Gould, E., and J. R. MacInnes. 1977. Short-term effects of two silver salts on tissue respiration and enzyme activity in the cunner (*Tautoglolabrus adspersus*). Bulletin of Environmental Contamination and Toxicology 18:401-408.

Graham, D. L. 1972. Trace metal levels in intertidal mollusks of California. Veliger 14:365-372.

Greig, R. A. 1975. Comparison of atomic absorption and neutron activation analyses for determination of silver, chromium, and zinc in various marine organisms. Analytical Chemistry 47:1682-1684.

Greig, R. A. 1979. Trace metal uptake by three species of mollusks. Bulletin of Environmental Contamination and Toxicology 22:643-647.

Greig, R. A., A. Adams, and D. R. Wenzloff. 1977a. Trace metal content of plankton and zooplankton collected from the New York Bight and Long Island Sound. Bulletin of Environmental Contamination and Toxicology 18:3-8.

Greig, R. A., and D. R. Wenzloff. 1977a. Final report on heavy metals in small pelagic finfish, euphausid crustaceans and apex predators, including sharks, as well as on heavy metals and hydrocarbons (C_{15+}) in sediments collected at stations in and near deepwater dumpsite 106. Pages 547-564 *in* Vol. III. Contaminant inputs and chemical characteristics. Baseline report of the environmental conditions on deepwater dumpsite 106. U.S. Department of Commerce, NOAA, Rockville, Md.

Greig, R. A., and D. R. Wenzloff. 1977b. Trace metals in finfish from the New York Bight and Long Island Sound. Marine Pollution Bulletin 8:198-200.

Greig, R. A., and D. R. Wenzloff. 1978. Metal accumulation and depuration by the American oyster, *Crassostrea virginica.* Bulletin of Environmental Contamination and Toxicology 20:499-504.

Greig, R. A., D. R. Wenzloff, B. Nelson, and C. Shelpuk. 1977b. Trace metals in organisms from ocean disposal sites of the middle eastern United States. Archives of Environmental Contamination and Toxicology 6:395-409.

Greig, R. A., D. R. Wenzloff, and J. B. Pearce. 1976. Distribution and abundance of heavy metals in finfish, invertebrates, and sediments collected at a deepwater disposal site. Marine Pollution Bulletin 7:185-187.

Hall, R. A., E. G. Zook, and G. M. Meaburn. 1978. National Marine Fisheries Service survey of trace elements in the fishery resources. U.S. Department of Commerce NOAA Technical Report NMFS SSRF-721. 323 pp.

Heit, M. 1979. Variability of the concentrations of seventeen trace elements in the muscle and liver of a single striped bass, *Morone saxatilis.* Bulletin of Environmental Contamination and Toxicology 23:1-5.

Hellou, J., W. G. Warren, J. F. Payne, S. Belkhode, and P. Lobel. 1992. Heavy metals and other elements in three tissues of cod, *Gadus morhua* from the northwest Atlantic. Marine Pollution Bulletin 24:452-458.

Heyl, A. V., W. E. Hall, A. E. Weissenborn, H. K. Stager, W. P. Puffett, and B. L. Reed. 1973. Silver. Pages 581-603 *in* D. A. Brobst and W. P. Pratt, editors. United States mineral resources. U.S. Geological Survey Professional Paper 820.

Hirsch, M., M. Ritter, K. Roser, P. Garrisi, and S. Forsythe. 1993. The effect of silver on plants grown in sludge-amended soils. Pages 69-73 *in* A. W. Andren, T. W. Bober, E. A. Crecelius, J. R. Kramer, S. N. Luoma, J. H. Rodgers, and A. Sodergren, organizers. Proceedings of the first international conference on transport, fate, and effects of silver in the environment. University of Wisconsin Sea Grant Institute, Madison.

Hogstrand, C., F. Galvez, and C. M. Wood. 1996. Toxicity, silver accumulation and metallothionein induction in freshwater rainbow trout during exposure to different silver salts. Environmental Toxicology and Chemistry 15; 1102-1108.

Janes, N., and R. C. Playle. 1995. Modeling silver binding to gills of rainbow trout (*Oncorhynchus mykiss*). Environmental Toxicology and Chemistry 14:1847-1858.

Jeanthon, C., and D. Prieur. 1990. Susceptibility to heavy metals and characterization of heterotrophic bacteria isolated from two hydrothermal vent polychaete annelids, *Alvinella pompejana* and *Alvinella caudata*. Applied and Environmental Microbiology 56:3308-3314.

Kirschenbaum, L. J. 1991. Higher oxidation states in group IB: the chemistry of hypervalent silver. Pages 1-29 *in* C. P. Murthy, editor. T. N. Rao commemorative celebration. Osmania University, Hyderabad, India.

Klaassen, C. D., M. O. Amdur, and J. Doull, editors. 1986. Casarett and Doull's toxicology. The basic science of poisons. Third edition. Macmillan, New York. 974 pp.

Klein-MacPhee, G., J. A. Cardin, and W. J. Berry. 1984. Effects of silver on eggs and larvae of the winter flounder. Transactions of the American Fisheries Society 113:247-251.

Koechlin, N., and M. Grasset. 1988. Silver contamination in the marine polychaete annelid *Sabella pavonina* S.: a cytological and analytical study. Marine Environmental Research 26:249-263.

Kouadio, I., L. J. Kirschenbaum, and R. N. Mehrota. 1990. The oxidation of iodide by the tetrahydroxoargentate (III) ion in aqueous alkaline media. Journal of the Chemical Society, Dalton Transactions 1990:1928-1933.

Kumar, R., and S. R. Bawa. 1979. Hepatic silver binding protein (Ag BP) from sparrow (*Passer domesticus*). Experientia 35:1621-1623.

Lande, E. 1977. Heavy metal pollution in Trondheimsfjorden, Norway, and the recorded effects on the fauna and flora. Environmental Pollution 12:187-198.

Lauenstein, G. G., A. Robertson, and T. P. O'Connor. 1990. Comparison of trace metal data in mussels and oysters from a mussel watch programme of the 1970s with those from a 1980s programme. Marine Pollution Bulletin 21:440-447.

Lawrence, J. M., W. D. Mahon, W. Avery, and M. Lares. 1993. Concentrations of metals in *Luidia clathrata* and *Luidia senegalensis* (Echinodermata: Asteroidea) in Tampa Bay and the nearshore Gulf of Mexico, Florida. Comparative Biochemistry and Physiology 105C:203-206.

LeBlanc, G. A., J. D. Mastone, A. P. Paradice, B. F. Wilson, H. B. Lockhart, Jr., and K. A. Robillard. 1984. The influence of speciation on the toxicity of silver to fathead minnow (*Pimephales promelas*). Environmental Toxicology and Chemistry 3:37-46.

Lima, A. R., C. Curtis, D. E. Hammermeister, D. J. Call, and T. A. Felhaber. 1982. Acute toxicity of silver to selected fish and invertebrates. Bulletin of Environmental Contamination and Toxicology 29:184-189.

Lockhart, H. B., Jr. 1983. Silver compounds. Pages 16-32 *in* Encyclopedia of chemical technology, third edition. John Wiley & Sons, New York.

Luoma, S. N. 1994. Fate, bioavailability and toxicity of silver in estuarine environments. Pages 151-155 *in* A. W. Andren, T. W. Bober, J. R. Kramer, A. Sodergren, E. A. Crecelius, S. N. Luoma, and J. H. Rodgers, organizers. Transport, fate and effects of silver in the environment. Proceedings of the 2nd international conference. University of Wisconsin Sea Grant Institute, Madison.

Luoma, S. N., R. Dagovitz, and E. Axtmann. 1990. Temporally intensive study of trace metals in sediments and bivalves from a large river-estuarine system: Suisan Bay/Delta in San Francisco Bay. The Science of the Total Environment 97/98:685-712.

Luoma, S. N., and E. A. Jenne. 1977. The availability of sediment-bound cobalt, silver, and zinc to a deposit-feeding clam. Pages 213-230 *in* H. Drucker and R. E. Wildung, editors. Biological implications of metals in the environment. ERDA Symposium Series 42. Available as CONF-750929 from the National Technical Information Service, Springfield, Va.

Luoma, S. N., and D. J. H. Phillips. 1988. Distribution, variability, and impacts of trace elements in San Francisco Bay. Marine Pollution Bulletin 19:413-425.

Lytle, P. E. 1984. Fate and speciation of silver in publicly owned treatment works. Environmental Toxicology and Chemistry 3:21-30.

Martin, J. H., P. D. Elliott, V. C. Anderlini, D. Girvin, S. A. Jacobs, R. W. Risebrough, R. L. Delong, and W. G. Gilmartin. 1976. Mercury-selenium bromine imbalance in premature parturient California sea lions. Marine Biology 35:91-104.

Martin, M., M. D. Stephenson, D. R.Smith, E. A. Gitierrez-Galindo, and G. F. Munoz. 1988. Use of silver in mussels as a tracer of domestic wastewater discharge. Marine Pollution Bulletin 19:512-520.

Miramand, P., and D. Bentley. 1992. Concentration and distribution of heavy metals in tissues of two cephalopods, *Eledone cirrhosa* and *Sepia officinalis,* from the French coast of the English Channel. Marine Biology 114:407-414.

Morgan, L. J., F. Galvez, R. F. Munger, C. M. Wood, and R. Henry. 1995. The physiological effects of acute silver exposure in rainbow trout (*Oncorhynchus mykiss*). *In* A. W. Andren and T. W. Bober, organizers. Transport, fate and effects of silver in the environment. Abstracts of 3rd international conference. 6-9 August 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison.

Morse, J. W., B. J. Presley, R. J. Taylor, G. Benoit, and P. Santschi. 1993. Trace metal chemistry of Galveston Bay: water, sediments, and biota. Marine Environmental Research 36:1-37.

Nalecz-Jawecki, G., K. Demkowicz-Dobrzanski, and J. Sawicki. 1993. Protozoan *Spirostomum ambiguum* as a highly sensitive bioindicator for rapid and easy determination of water quality. The Science of the Total Environment, Supplement 2:1227-1234.

National Association of Photographic Manufacturers [NAPM]. 1974. Environmental effect of photoprocessing chemicals. Volumes I and II. NAPM, Harrison, N.Y. 324 pp. plus appendices.

Navrot, J., A. J. Amiel, and J. Kronfeld. 1974. *Patella vulgata*: a biological monitor of coastal metal pollution—a preliminary study. Environmental Pollution 7:303-308.

Nebeker, A. V, C. K. McAuliffe, R. Mshar, and D. G. Stevens. 1983. Toxicity of silver to steelhead and rainbow trout, fathead minnows and *Daphnia magna*. Environmental Toxicology and Chemistry 2:95-104.

Nehring, R. B. 1976. Aquatic insects as biological monitors of heavy metal pollution. Bulletin of Environmental Contamination and Toxicology 15:147-154.

Nelson, D. A., A. Calabrese, R. A. Greig, P. P. Yevich, and S. Chang. 1983. Long-term silver effects on the marine gastropod *Crepidula fornicata*. Marine Ecology Progress Series 12:155-165.

Nelson, D. A., A. Calabrese, B. A. Nelson, J. R. MacInnes, and D. R. Wenzloff. 1976. Biological effects of heavy metals on juvenile bay scallops, *Argopecten irradians*, in short-term exposures. Bulletin of Environmental Contamination and Toxicology 16:275-282.

Nolan, C., and H. Dahlgaard. 1991. Accumulation of metal radiotracers by *Mytilus edulis*. Marine Ecology Progress Series 70:165-174.

Ohlendorf, H. M., R. W. Lowe, P. R. Kelly, and T. E. Harvey. 1986. Selenium and heavy metals in San Francisco Bay diving ducks. Journal of Wildlife Management 50:64-71.

Papadopoulu, C., and E. M. Kassimati. 1977. Stable elements in skeletal formations of fish species from Greek waters. Thalassia Jugoslavica 13:187-192.

Pentreath, R. J. 1977. The accumulation of ^{110m}Ag by the plaice, *Pleuronectes platessa* L. and the thornback ray, *Raja clavata* L. Journal of Experimental Marine Biology and Ecology 29:315-325.

Pouvreau, B., and J. C. Amiard. 1974. Etude experimentale de l'accumulation de l'argent 110m chez divers organismes marine. Commission Energie Atomique France, Report CEA-R-4571. 19 pp.

Presley, B. J., R. J. Taylor, and P. N. Boothe. 1990. Trace metals in Gulf of Mexico oysters. The Science of the Total Environment 97/98:551-593.

Pullen, J. S. H., and P. S. Rainbow. 1991. The composition of pyrophosphate heavy metal detoxification granules in barnacles. Journal of Experimental Marine Biology and Ecology 150:249-266.

Ramelow, G. J., C. L. Webre, C. S. Mueller, J. N. Beck, J. C. Young, and M. P. Langley. 1989. Variations of heavy metals and arsenic in fish and other organisms from the Calcasieu River and Lake, Louisiana. Archives of Environmental Contamination and Toxicology 18:804-818.

Reese, R. G. 1991. Silver. Pages 148-149 *in* Mineral commodity summaries 1991. U.S. Bureau of Mines, Washington, DC 20241.

Ridgway, L. P., and D. A. Karnofsky. 1952. The effects of metals on the chick embryo: toxicity and production of abnormalities in development. Annals of the New York Academy of Sciences 55:203-215.

Rivera-Duarte, I., and A. R. Flegal. 1993. Pore water fluxes of silver in estuaries. Pages 37-39 *in* A. W. Andren, T. W. Bober, E. A. Crecelius, J. R. Kramer, S. N. Luoma, J. H. Rodgers, and A. Sodergren, organizers. Proceedings of the first international conference on transport, fate, and effects of silver in the environment. University of Wisconsin Sea Grant Institute, Madison.

Rodgers, J. H., Jr., E. Deaver, and P. Rogers. 1994. Evaluations of the bioavailability and toxicity of silver in sediment. Pages 131-137 *in* A. W. Andren, T. W. Bober, J. R. Kramer, A. Sodergren, E. A. Crecelius, S. N. Luoma, and J. H. Rodgers, organizers. Transport, fate and effects of silver in the environment. Proceedings of the 2nd international conference. University of Wisconsin Sea Grant Institute, Madison.

Rombough, P. J. 1985. The influence of the zona radiata on the toxicities of zinc, lead, mercury, copper and silver ions to embryos of steelhead trout *Salmo gairdneri.* Comparative Biochemistry and Physiology 82C:115-117.

Rose, K. A., J. K. Summers, R. I. Mclean, and S. L. Domotor. 1988. Radiosilver (Ag-110m) concentrations in Chesapeake Bay oysters maintained near a nuclear powerplant: a statistical analysis. Environmental Monitoring and Assessment 10:205-218.

Sanders, J. G., and G. R. Abbe. 1987. The role of suspended sediments and phytoplankton in the partitioning and transport of silver in estuaries. Continental Shelf Research 7:1357-1361.

Sanders, J. G., and G. R. Abbe. 1989. Silver transport and impact in estuarine and marine systems. Pages 5-18 *in* G. W. Suter II and M. A. Lewis, editors. Aquatic toxicology and environmental fate. Vol. 11. American Society for Testing and Materials, Special Technical Publication 1007, Philadelphia.

Sanders, J. G., G. R. Abbe, and G. F. Riedel. 1990. Silver uptake and subsequent effects on growth and species composition in an estuarine community. The Science of the Total Environment 97/98:761-769.

Sanders, J. G., and S. J. Cibik. 1988. Response of Chesapeake Bay phytoplankton communities to low levels of toxic substances. Marine Pollution Bulletin 19:439-444.

Sanders, J. G., G. F. Riedel, and G. R. Abbe. 1991. Factors controlling the spatial and temporal variability of trace metal concentrations in *Crassostrea virginica* (Gmelin). Pages 335-339 *in* M. Elliott and J. P. Ducrotoy, editors. Estuaries and coasts: spatial and temporal comparisons. ECSA Symposium 19 (University of Caen, France, 1989). Olsen & Olsen, Fredensborg, Denmark.

Scanlon, P. F., R. G. Oderwald, T. J. Dietrick, and J. L. Coggin. 1980. Heavy metal concentrations in feathers of ruffed grouse shot by Virginia hunters. Bulletin of Environmental Contamination and Toxicology 25:947-949.

Schildkraut, D. E. 1993. Application of analytical voltammetric methods to the determination of silver at sub-ng/mL levels. Pages 5-7 *in* A. W. Andren, T. W. Bober, E. A. Crecelius, J. R. Kramer, S. N. Luoma, J. H. Rodgers, and A. Sodergren, organizers. Proceedings of the first international conference on transport, fate, and effects of silver in the environment. University of Wisconsin Sea Grant Institute, Madison.

Segar, D. A., J. D. Collins, and J. P. Riley. 1971. The distribution of the major and some minor elements in marine animals. Part II. Molluscs. Journal of the Marine Biological Association of the United Kingdom 51:131-136.

Shafer, M. M., D. E. Armstrong, and J. T. Overdier. 1995. Silver levels and partitioning in effluent-receiving streams and rivers tributary to Lake Michigan, and a preliminary mass balance for silver in the Lake Michigan basin. *In* A. W. Andren and T. W. Bober, organizers. Transport, fate and effects of silver in the environment. Abstracts of 3rd international conference, 6-9 August 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison.

Smith, I. C., and B. L. Carson. 1977. Trace metals in the environment. Vol. 2: Silver. Ann Arbor Science Publishers, Ann Arbor, Mich. 469 pp.

Song, S., and J. G. Osteryoung. 1993. Determination of silver (I) ion by anodic stripping in flow injection system. Pages 109-111 *in* A. W. Andren, T. W. Bober, E. A. Crecelius, J. R. Kramer, S. N. Luoma, J. H. Rodgers, and A. Sodergren, organizers. Proceedings of the first international conference on transport, fate, and effects of silver in the environment. University of Wisconsin Sea Grant Institute, Madison.

Stephenson, J. D., and G. H. Leonard. 1994. Evidence for the decline of silver and lead and the increase of copper from 1977 to 1990 in the coastal marine waters of California. Marine Pollution Bulletin 28:148-153.

Sun, Y., L. J. Kirschenbaum, and I. Kouadio. 1991. Kinetics and mechanism of the multi-step oxidation of ethylenediaminetetracetate by $[Ag(OH)_4]^-$ in alkaline media. Journal of the Chemical Society, Dalton Transactions 1991:2311-2315.

Szefer, P., J. Pempkowiak, B. Skwarzec, R. Bojanowski, and E. Holm. 1993. Concentration of selected metals in penguins and other representative fauna of the Antarctica. The Science of the Total Environment 138:281-288.

Szefer, P., K. Szefer, J. Pempkowiak, B. Skwarzec, R. Bojanowski, and E. Holm. 1994. Distribution and coassociations of selected metals in seals of the Antarctic. Environmental Pollution 83:341-349.

Talbot, V. 1985. Heavy metal concentrations in the oysters *Saccostrea cucullata* and *Saccostrea* sp. from the Dampier Archipelago, Western Australia. Australian Journal of Marine and Freshwater Research 36:169-175.

Tariq, J., M. Jaffar, M. Ashraf, and M. Moazzam. 1993. Heavy metal concentrations in fish, shrimp, seaweed, sediment, and water from the Arabian Sea, Pakistan. Marine Pollution Bulletin 26:644-647.

Terhaar, C. J., W. S. Ewell, S. P. Dziuba, W. W. White, and P. J. Murphy. 1977. A laboratory model for evaluating the behavior of heavy metals in an aquatic environment. Water Research 11:101-110.

Thurberg, F. P., W. D. Cable, M. A. Dawson, J. R. MacInnes, and D. R. Wenzloff. 1975. Respiratory response of larval, juvenile, and adult surf clams, *Spisula solidissima,* to silver. Pages 41-52 *in* J. J. Cech, Jr., D. W. Bridges, and D. B. Horton, editors. Respiration of marine organisms. TRIGOM Publishers, South Portland, Maine.

Thurberg, F. P., A. Calabrese, and M. A. Dawson. 1974. Effects of silver on oxygen consumption of bivalves at various salinities. Pages 67-78 *in* F. J. Vernberg and W. B. Vernberg, editors. Pollution and physiology of marine organisms. Academic Press, New York.

Thurberg, F. P., and R. S. Collier. 1977. Respiratory response of cunners to silver. Marine Pollution Bulletin 8:40-41.

Truchet, M., R. Martoja, and B. Berthet. 1990. Consequences histologiques de la pollution metallique d'un estuairesur deux mollusques, *Littorina littorea* L. et *Scrobicularia plana* da costa. Comptes rendus de l'Academie des Sciences. Serie III, 311:261-268.

U.S. Bureau of Mines. 1980. Mineral commodity summaries 1980. Available from the U.S. Government Printing Office: 1979-603-002/128.

U.S. Environmental Protection Agency (EPA). 1980. Ambient water quality criteria for silver. U.S. Environmental Protection Agency Report 440/5-80-071. 212 pp.

U.S. Environmental Protection Agency (EPA). 1987. Ambient aquatic life water quality criteria for silver. Draft. Available from the National Technical Information Service, Springfield, Va. 104 pp.

U.S. Environmental Protection Agency (EPA). 1995a. Stay of water quality criteria for metals. Federal Register 60 (86):22227-22229.

U.S. Environmental Protection Agency (EPA). 1995b. Water quality standards; establishment of numeric criteria for priority toxic pollutants; states' compliance—revision of metals criteria. Federal Register 60 (86):22229-22237.

U.S. Public Health Service (PHS). 1990. Toxicological profile for silver. Agency for Toxic Substances and Disease Registry TP-90-24. 145 pp.

Vermeer, K., and D. B. Peakall. 1979. Trace metals in seaducks of the Fraser River delta intertidal area, British Columbia. Marine Pollution Bulletin 10:189-191.

Williams, P. L., and D. B. Dusenbery. 1990. Aquatic toxicity testing using the nematode, *Caenorhabditis elegans*. Environmental Toxicology and Chemistry 9:1285-1290.

Windom, H. L., and R. G. Smith. 1972. Distribution of iron, magnesium, copper, zinc, and silver in oysters along the Georgia coast. Journal of the Fisheries Research Board of Canada 29:450-452.

Wingert-Runge, B., and A. W. Andren. 1994. Desorption behavior of silver from natural sediments under freshwater and marine conditions. Pages 89-93 *in* A. W. Andren, T. W. Bober, J. R. Kramer, A. Sodergren, E. A. Crecelius, S. N. Luoma, and J. H. Rodgers, organizers. Transport, fate and effects of silver in the environment. Proceedings of the 2nd international conference. University of Wisconsin Sea Grant Institute, Madison.

Wood, C. M., C. Hogstrand, F. Galvez, and R. S. Munger. 1996a. The physiology of waterborne silver toxicity in freshwater rainbow trout (*Oncorhynchus mykiss*): 1. The effects of ionic Ag^{+}. Aquatic Toxicology. 35:93-109.

Wood, C. M., C. Hogstrand, F. Galvez, and R. S. Munger. 1996b. The physiology of waterbone silver toxicity in freshwater rainbow trout (*Oncorhynchus mykiss*): 2. The effects of silver thiosulfate. Aquatic Toxicology. 35:111-125.

Wood, C. M., I. Morgan, F. Galvez, and C. Hogstrand. 1995. The toxicity of silver in fresh and marine waters. *In* A. W. Andren and T. W. Bober, organizers. Transport, fate and effects of silver in the environment. Abstracts of 3rd international conference, 6-9 August 1995, Washington, D.C. University of Wisconsin Sea Grant Institute, Madison.

Wood, C. M., S. Munger, F. Galvez, and C. Hogstrand. 1994. The physiology of silver toxicity in freshwater fish. Pages 109-114 *in* A. W. Andren, T. W. Bober, J. R. Kramer, A. Sodergren, E. A. Crecelius, S. N. Luoma, and J. H. Rodgers, organizers. Transport, fate and effects of silver in the environment. Proceedings of the 2nd international conference. University of Wisconsin Sea Grant Institute, Madison.

Biological Science Report USGS/BRD/BSR--1997-0002
January 1998

Contaminant Hazard Reviews
Report No. 33

COPPER HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Geological Survey
Laurel, MD 20708

Suggested citation:
Eisler, R. 1998. Copper hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Geological Survey, Biological Resources Division, Biological Science Report USGS/BRD/BSR--1998-0002.

CONTENTS

TABLES

COPPER HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Geological Survey
Laurel, MD 20708

Abstract. This report is a selective review and synthesis of the technical literature on copper and copper salts in the environment and their effects primarily on fishes, birds, mammals, terrestrial and aquatic invertebrates, and other natural resources. The subtopics include copper sources and uses; chemical and biochemical properties; concentrations of copper in field collections of abiotic materials and living organisms; effects of copper deficiency; lethal and sublethal effects on terrestrial plants and invertebrates, aquatic organisms, birds, and mammals, including effects on survival, growth, reproduction, behavior, metabolism, carcinogenicity, mutagenicity, and teratogenicity; proposed criteria for the protection of human health and sensitive natural resources; and recommendations for additional research.

Key words: Copper, copper sulfate, metals, toxicity, deficiency, criteria, residues, agriculture, nutrition, metallothionein, fish, invertebrates, amphibians, birds, wildlife, livestock, endangered species.

Copper (Cu) is plentiful in the environment and essential for the normal growth and metabolism of all living organisms (Schroeder et al. 1966; Carbonell and Tarazona 1994). Abnormal levels of copper intake may range from levels so low as to induce a nutritional deficiency to levels so high as to be acutely toxic (U.S. Environmental Protection Agency [USEPA] 1980). Copper is probably the first metal worked by humans some 70 to 80 centuries ago (Schroeder et al. 1966). The earliest known artifacts of hammered copper date from about 6000 BCE. After 4000 BCE, melting and casting of copper was common in the Near East. Smelting was developed about 3000 BCE and bronze around 2500 BCE. Brass, a copper alloy, was developed in Roman times. Copper derives from the Latin *cuprum*, a corruption of *cyprium*, Cyprus being the source of Egyptian and Roman copper (Schroeder et al. 1966). Copper was identified in terrestrial plants in 1817 (Gallagher 1979), in marine invertebrates in 1833 (Schroeder et al. 1966), in vertebrates in 1838 (Gallagher 1979), and in hemocyanin—the blue respiratory pigment of mollusks and crustaceans—in 1880 (Schroeder et al. 1966). But the metabolic importance of copper in plants and animals was not suspected until the 1920's when diseases due to copper deficiency began to be recognized (National Academy of Sciences [NAS] 1977; Gallagher 1979). Copper deficiency in vertebrates, for example, is associated with anemia, gastrointestinal disturbances, aortic aneurisms, bone development abnormalities, and death (Aaseth and Norseth 1986).

Copper toxicosis in terrestrial higher plants is rare but occurs on mine spoils and where copper-rich manures or fungicides are used excessively (Schroeder et al. 1966; NAS 1977; Alva et al. 1995; Arduini et al. 1995). Copper is among the most toxic of the heavy metals in freshwater and marine biota (Schroeder et al. 1966; Betzer and Yevich 1975), and often accumulates and causes irreversible harm to some species at concentrations just above levels required for growth and reproduction (Hall et al. 1988). Birds and mammals, when compared to lower forms, are relatively resistant to copper. But diets containing elevated concentrations of copper are sometimes fatal to ducklings (Wood and Worden 1973) and livestock when fed for extended periods. Domestic sheep (*Ovis aries*) are the most susceptible farm animals to chronic copper poisoning and effects include liver damage, impaired reproduction, reduced resistance to diseases, jaundice, and death (Gopinath and Howell 1975; Higgins 1981; Bires et al. 1993).

Many reviews and annotated bibliographies are available on copper ecology and toxicology, including those by Eisler (1973, 1979), Eisler and Wapner (1975), NAS (1977), Eisler et al. (1978, 1979), Nriagu (1979a, 1979b), USEPA (1980), Aaseth and Norseth (1986), and Agency for Toxic Substances and Disease Registry [ATSDR] (1990). I prepared this report at the request of resource contaminant specialists of the U.S Fish and Wildlife Service; it is part of a continuing series of synoptic reviews on contaminant hazards to natural resources.

Sources and Uses

General

The United States is the major world producer and consumer of copper and its compounds. Most of the copper produced is used to manufacture electrical equipment, pipe, and machinery. Copper releases to the global biosphere—which may approach 1.8 million metric tons per year—come mostly from anthropogenic activities such as mining and smelting, industrial emissions and effluents, and municipal wastes and sewage sludge. Copper compounds are widely used as biocides to control nuisance algae and macrophytes, freshwater snails that may harbor schistosomiasis and other diseases, ectoparasites of fish and mammals, marine fouling organisms, and mildew and other diseases of terrestrial crop plants. Copper compounds are also used in agricultural fertilizers, in veterinary and medical products, in the food industry, and as a preservative of wood and other materials.

Sources

Global copper production during the past 60 centuries is estimated at 307 million metric tons, most of which (79%) occurred since 1900; annual global production of copper is now estimated at 13.6 million tons (Nriagu 1979c). Copper occurs naturally in many minerals and as uncombined metal. The three most important sources of copper are chalcocite (Cu_2S), chalcopyrite ($CuFeS_2$), and malachite ($CuCO_3 \cdot Cu(OH)_2$; ATSDR 1990). The United States is the largest global consumer and producer of copper. In 1986, domestic consumption of copper in the United States was 2.14 million metric tons and mine production was 1.14 million metric tons, mostly from mines in Arizona, New Mexico, and Michigan. The major copper deposits in the United States are of hydrothermal origin and uniformly distributed in fractures or veins (ATSDR 1990). Copper is the major toxic component in streams impacted by active placer mines (Buhl and Hamilton 1990). About 60% of copper metal is eventually recycled; in 1986, smelting of scrap copper produced an additional 0.9 million metric tons of copper. Also in 1986, 1.1 million tons of copper were imported into the United States, mostly from Canada, Chile, Peru, and Mexico (ATSDR 1990).

The amount of copper entering the global ecosystem annually is unknown, but estimates range from 211,000 metric tons (Nriagu 1979c) to 1.8 million metric tons (NAS 1977). About 80.7% of this copper is deposited in terrestrial compartments, 15.7% in the hydrosphere, and 3.6% to the atmosphere (Nriagu 1979c). The residence time for copper in the deep ocean is 1,500 years; in soils it may be retained for as long as 1,000 years; in air, copper persists for about 13 days (Nriagu 1979c). Copper in the atmosphere results mainly (73%) from human activities such as copper production and combustion of fossil fuels; the remainder is from natural sources that include seasalt sprays, windblown dusts, volcanogenic particles, and decaying vegetation (Nriagu 1979c, 1979d).

Input of copper into aquatic ecosystems increased sharply during the past century and includes inputs from waste discharges into saline waters, industrial discharges into freshwater, and leaching of antifouling marine paints and wood preservatives (Nriagu 1979c). Present anthropogenic inputs of copper are two to five times higher than natural loadings; the atmosphere is a primary recipient of these inputs (Nriagu 1979d). In mining and industrial areas, precipitation of atmospheric fallout is a significant source of copper to the aquatic environment (USEPA 1980). More than 99.9% of oceanic copper fell as clay and manganese oxide particles in precipitation (NAS 1977). In the lower Great Lakes, direct atmospheric inputs of copper—in metric tons per year—range from 55 to 2,300 for Lake Michigan, 120 to 330 for Lake Erie, and 72 to 123 for Lake Ontario; regional disparities in atmospheric deposition of copper are related to the intensity of industrial activity and to the regional wind systems (Nriagu 1979d).

Copper in soils may come from a variety of anthropogenic sources: mining and smelting activities; other industrial emissions and effluents; traffic; fly ash; dumped waste materials; contaminated dusts and rainfall; sewage and sludge; pig slurry; composted refuse; and agricultural fertilizers, pesticides, and fungicides (Nriagu 1979c; Thornton 1979; Ma 1984; ATSDR 1990; Roncero et al. 1992; Alva et al. 1995). In the case of Florida citrus groves, copper-containing fertilizers applied during the early 1900's accounted for as much as 34 kg Cu/ha annually, and routine fungicidal sprays contributed another 10 kg Cu/ha annually. Surface soils (0-15 cm) from some mature citrus groves contained as much as 540 kg Cu/ha (Alva et al. 1995). Copper deposition rates in soils are higher in cities and near highways, railroads, power plants, and industrial activities (Nriagu 1979d). But a Kansas landfill near a freshwater stream had no significant effect on copper concentrations in water, sediments, crayfish, and sunfish (Morrissey and Edds 1994).

Uses

Metallic copper end uses include electrical (70%), construction (15%), machinery (6%), transportation (4%), and ordinance (2%). The top domestic markets for copper and its alloys in 1986 were, in order of importance, plumbing, building wire, telecommunications, power utilities, in-plant equipment, air conditioning, automotive electrical, automotive nonelectrical, business electronics, and industrial valves and fittings (ATSDR 1990). A small percentage of copper production is used to manufacture chemicals, mainly copper sulfate. Of the copper sulfate used domestically, 65% is used in agriculture for fungicides, algicides, nutritional supplements, insecticides, and repellents; 28% is used industrially in froth flotation production of chromated copper arsenate wood preservatives, in electroplating, and in the manufacture of azo dyes; and 7% is used in water treatment to control nuisance algae (ATSDR 1990).

Copper is widely used to control unwanted species of freshwater algae and macrophytes (Bartley 1967; NAS 1977; USEPA 1980; Rowe and Prince 1983; Havens 1994). Chelated copper products are claimed to be effective algicides in hard water; the chelation of copper by organic compounds, such as ethanolamines or ethanolamine complexes, protects copper from precipitation and complexation (Straus and Tucker 1993). Copper sulfate is approved by the U.S. Environmental Protection Agency (USEPA) as an algicide in waters used to raise fish for human consumption (Straus and Tucker 1993). In algae, copper inhibits photosynthesis, nitrogen fixation, and phosphorus uptake; it selectively eliminates cryptophytes but spares diatoms (Havens 1994). Copper sulfate at low concentrations has been used to control freshwater algae in Wisconsin since 1918 without any conclusively proven effect on diversity or abundance of nontarget species (Mackenthun and Cooley 1952). But reduced abundance of freshwater benthos was noted in Lake Monova, Wisconsin, which received 771 metric tons of copper to control algae over a 26-year period and had sediment levels as high as 1,093 mg Cu/kg DW (Mackenthun and Cooley 1952). Copper sulfate used to control algal blooms in Wisconsin lakes at 1.25 mg Cu/L killed nontarget fishes, crustaceans, snails, and amphibians in 14 days or less; however, 0.25 mg Cu/L was not fatal to these species in 20 days (Hasler 1949). Concentrations as low as 0.03 mg Cu/L inhibited growth in two of four species of nuisance aquatic weeds in Lake Mendota, Wisconsin, and 0.3 mg Cu/L was fatal to all four species (Hasler 1949). Copper sulfate controls algae in cranberry bogs at 0.4 mg Cu/L but this concentration also kills resident fishes (Deubert and Demoranville 1970). Copper was not measurable in the surface waters of cranberry bogs within 10 days of treatment, regardless of initial copper concentration; it is probable that copper was adsorbed onto bog soils (Deubert and Demoranville 1970). In England, copper sulfate was effective at 1.0 mg Cu/L in controlling algae and most species of aquatic weeds for 1.6 km downstream of treatment for 6 months during the summer; only 0.25 mg Cu/L was necessary in autumn and winter for effective aquatic weed control (Chancellor et al. 1960). During copper treatment to control plants, aquatic snails were greatly reduced or eliminated but fishes seemed unaffected. Sensitive aquatic weeds included *Myriophyllum spicatum*, *Elodea canadensis*, *Potamogeton* spp., and *Lemna minor*; sensitive genera of algae included *Oedogonium*, *Spirogyra*, *Enteromorpha*, and *Mougeotia* (Chancellor et al. 1960).

In Iowa lakes, copper sulfate was used to control summer blooms of various species of toxic blue-green algae. Prior to treatment, blooms of *Anabaena flos-aquae*, *Aphanizomenon flos-aquae*, and *Microcystis aeruginosa* were associated with deaths of migratory waterfowl, game birds, songbirds, game, and domestic animals (Rose 1954). Most of these species of algae were controlled within 24 h by 1.0 mg Cu/L as copper sulfate. Copper treatment had no adverse effects on bottom fauna but populations of crustaceans (daphnids, copepods, entomostracans) were reduced. One year after treatment no deaths of birds or mammals were recorded (Rose 1954).

Copper salts are intentionally added to drinking water supplies of some municipalities to control growth of algae; concentrations as high as 59 µg Cu/L are maintained in New York City (USEPA 1980).

Copper compounds are used routinely and widely to control freshwater snails that serve as intermediate vectors of schistosomiasis and other diseases that afflict humans (Hasler 1949; NAS 1977; Rowe and Prince 1983; Winger et al. 1984; Al-Sabri et al. 1993). These compounds include copper sulfate, copper pentachlorophenate, copper carbonate, copper-tartaric acid, Paris green (copper arsenite-acetate), copper oxide, copper chloride, copper acetyl acetonate, copper dimethyl dithiocarbamate, copper ricinoleate, and copper rosinate (Cheng 1979). Also, many species of oyster enemies are controlled by copper sulfate dips. All tested species of marine gastropods, tunicates, echinoderms, and crabs that had been dipped for 5 seconds in a saturated solution of copper sulfate died if held in air for as little as a few seconds to 8 h; mussels, however, were resistant (MacKenzie 1961).

Copper sulfate is used to control protozoan fish ectoparasites including *Ichthyopthirius*, *Trichodina*, and *Costia*; the effectiveness of the treatment diminishes with increasing total alkalinity and total hardness of the water (Straus and Tucker 1993). Copper compounds now used to control protozoan parasites of cultured red drum (*Sciaenops ocellatus*) include copper sulfate, copper sulfate plus citric acid, and chelated copper compounds (forms of copper bound by sequestering agents, such as ethanolamine); chelated copper compounds are considered less toxic to fish than copper sulfate and at least as effective in controlling parasites (Peppard et al. 1991).

Copper is the active agent in many antifouling paints applied to watercraft (Aaseth and Norseth 1986; Hall et al. 1988). The growing use of copper-based paints subsequent to the prohibition in 1982 of tributyltin-based paints (Hall et al. 1988) is associated with elevated copper concentrations in Pacific oysters (*Crassostrea gigas*) farmed in the Bay of Arcachon, France (Claisse and Alzieu 1993).

Copper compounds are used in agriculture to treat mildew and other plant diseases; in the food industry as preservatives, additives, or coloring agents; in preservatives of wood, leather, and fabrics; in coin manufacture; and in water treatment (ATSDR 1990; Roncero et al. 1992). The use of copper-containing pesticides is traditional along the Mediterranean Coast, especially the use of Bordeaux mixture, a copper sulfate-based fungicide that has been widely used for more than a century to prevent mildew on grape vines (Romeu-Moreno et al. 1994). However, at current application rates of about 0.8 mg Cu/cm^2, Bordeaux mixture significantly reduces the life span and breeding rate of the fruit fly (*Drosophila melanogaster*) (Marchal-Segault et al. 1991).

Copper is widely used in veterinary clinics in medical products (Roncero et al. 1992). Copper sulfate is used by veterinarians to treat cattle and sheep for helminthiasis and infectious pododermatitis (NAS 1977). Cuprol (a 1% solution of cupric oleinate) is used to control lice (Aaseth and Norseth 1986). Copper is routinely used as a growth supplement in the diets of swine (*Sus* sp.) in the United Kingdom and elsewhere; diets may contain as much as 250 mg Cu/kg ration (USEPA 1980). The intensity of pig farming within about 10 km from the coast may influence copper content in estuarine sediments. For example, intensive pig farming in coastal Brittany, France, increased soil copper concentrations by 0.6 kg/ha annually and increased coastal sediment copper concentrations to as high as 49.6 mg/kg DW (Arzul and Maguer 1990).

Table 1. Some properties of copper and copper sulfate (ATSDR 1990).

Property	Copper	Copper sulfate
Chemical and other names	Copper	Cupric sulfate, blue vitriol, cupric sulphate, Roman vitriol, Salzburg vitriol, blue copperas, copper (II) sulfate
Chemical formula	Cu	$CuSO_4$
Oxidation state	0	2+
CAS (Chemical Abstract Services) number	7440-50-8	7758-98-7
Molecular weight	63.546	159.60
Color and form	Reddish solid	Blue crystals
Melting point	1,083.4º C	Decomposes slightly at >200º C
Boiling point	2,567º C	Decomposes to CuO at 650º C
Density	8.92	3.603
Solubility		
Water	Insoluble	143 g/L
Organic solvents	Insoluble	Soluble in methanol, slightly soluble in ethanol

In human medicine, metallic copper is used in some intrauterine devices, and various copper compounds are used as emetics and to treat rheumatoid arthritis (USEPA 1980; Aaseth and Norseth 1986). Some individuals wear copper bracelets as treatment for arthritis although its therapeutic value has little support (USEPA 1980).

Chemical and Biochemical Properties

General

This section demonstrates that (1) free ionic copper (Cu^{2+}) is the most toxic chemical species of copper and that copper bioavailability is modified by many biological and abiotic variables; (2) copper metabolism and sensitivity to copper of poikilotherms differs from that of mammals; and (3) copper interactions with inorganic and organic chemicals are substantial and must be considered when evaluating copper hazards to natural resources.

Chemical Properties

Copper is a soft heavy metal, atomic number 29, with a density in elemental form at 20º C of 8.92 g/cc and a melting point of 1,083.4º C (USEPA 1980; Aaseth and Norseth 1986; Table 1). Copper has two natural isotopes: Cu-63 (69.09%) and Cu-65 (30.91%; NAS 1977).

Copper exists in four oxidation states: Cu^0, Cu^{+1}, Cu^{+2}, and Cu^{+3} (ATSDR 1990). Elemental copper (Cu^0) is readily attacked by organic and mineral acids that contain an oxidizing agent and is slowly soluble in dilute ammonia; halogens attack elemental copper slowly at room temperature to yield the corresponding copper halide (USEPA 1980); elemental copper is not oxidized in water (Aaseth and Norseth 1986). Cuprous copper (Cu^{+1}) exists only in water solution when complexed, usually in a tetrahedral form, with affinity for sulfur and nitrogen ligands (Schroeder et al. 1966). Cuprous copper is unstable in aerated aqueous solution over the pH range 6 to 8, and will undergo auto-oxidation-reduction into elemental copper (Cu^0) and cupric ion (Cu^{+2}) (USEPA 1980; Aaseth and Norseth 1986). The only cuprous ion (Cu^{+1}) compounds that are stable in water are extremely insoluble ones such as cuprous chloride (CuCl; ATSDR 1990). Cuprous ion-complexes may be formed in seawater by photochemical processes and persist for several hours. The cupric ion (Cu^{+2}) is the one generally encountered in water. Cupric ions are coordinated with six water molecules in solution (ATSDR 1990). Cupric ion ordinarily forms planar, less stable chelates with nitrogen and oxygen ligands (Schroeder et al.

1966). In seawater and sediment interstitial waters, the free cupric ion (Cu^{+2}) is the most readily available and toxic inorganic species of copper; however, the free ion concentration is sensitive to complexation and is less available to aquatic biota in the presence of natural organic chelators and high salinities (Bryan and Langston 1992). Cupric ions account for about 1% of the total dissolved copper in seawater and less than 1% in freshwater (Boyle 1979). Trivalent copper (Cu^{+3}) probably does not occur naturally (Schroeder et al. 1966). Trivalent copper is strongly oxidizing and occurs only in a few compounds; none of these compounds is currently considered industrially important or environmentally significant (ATSDR 1990).

Copper speciation in freshwater is figured in detail by Leckie and Davis (1979). In freshwater, the solubility of copper salts is decreased under reducing conditions and is further modified by water pH, temperature, and hardness; size and density of suspended materials; rates of coagulation and sedimentation of particulates; and concentration of dissolved organics. The chemical form of copper in freshwater is important in controlling geochemical and biological processes. But the lack of knowledge on the adsorption characteristics of most cupric ion (Cu^{+2}) complexes contributes to uncertainties about the behavior of known copper species (Leckie and Davis 1979). Ionic copper (Cu^{+2}) and some copper hydroxyl species are correlated with high toxicity to aquatic life; however, carbonato species ($CuHCO_3^+$, $CuCO_3$, $Cu(CO_3)_2^{-2}$) are much less toxic than other copper complexes (Meador 1991). The major chemical species of copper in freshwater are $Cu(CO_3)_2^{-2}$ and $CuCO_3$ (Boyle 1979). Cupric ion is the dominant toxic copper species at pH levels less than 6; the aqueous copper carbonate complex is dominant from pH 6.0 to 9.3 (USEPA 1980). This equilibrium is altered in the presence of humic acids, fulvic acids, amino acids, cyanide, certain polypeptides, and detergents (USEPA 1980). Most cupric salts dissolve readily in freshwater to produce the aquo ion, $Cu(H_2O)_6^{+2}$ (Leckie and Davis 1979). Divalent copper chloride, nitrate, and sulfate are highly soluble in water (USEPA 1980; Table 1), but copper carbonate, cupric hydroxide, cupric oxide, and cupric sulfide will precipitate from solution or form colloidal suspensions when excess cupric ions are present (USEPA 1980).

In seawater, the major chemical species of copper are Cu(OH)Cl and $Cu(OH)_2$ and these account for about 65% of the total copper in seawater (Boyle 1979). The levels of copper hydroxide ($Cu(OH)_2$) increase from about 18% of the total copper at pH 7.0 to 90% at pH 8.6; copper carbonate ($CuCO_3$) levels drop from 30% at pH 7.0 to less than 0.1% at pH 8.6 (USEPA 1980). The dominant copper species in seawater over the entire ambient pH range are copper hydroxide, copper carbonate, and cupric ion (USEPA 1980). Bioavailability and toxicity of copper in marine ecosystems is promoted by oxine and other lipid soluble synthetic organic chelators (Bryan and Langston 1992).

Copper concentrations in sediment interstitial pore waters correlate positively with concentrations of dissolved copper in the overlying water column and are now used to predict the toxicity of test sediments to freshwater amphipods (Ankley et al. 1993). Sediment-bound copper is available to deposit-feeding clams, especially from relatively uncontaminated anoxic sediments of low pH (Bryan and Langston 1992). The bioavailability of copper from marine sediments, as judged by increased copper in sediment interstitial waters, is altered by increased acid volatile sulfide (AVS) content (Casas and Crecelius 1994). But acid volatile sulfide is not an appropriate partitioning phase for predicting copper bioavailability of freshwater sediments (Ankley et al. 1993).

Metabolism

Copper is part of several essential enzymes including tyrosinase (melanin production), dopamine beta-hydroxylase (catecholamine production), copper-zinc superoxide dismutase (free radical detoxification), and cytochrome oxidase and ceruloplasmin (iron conversion) (Aaseth and Norseth 1986). All terrestrial animals contain copper as a constituent of cytochrome *c* oxidase, monophenol oxidase, plasma monoamine oxidase, and copper protein complexes (Schroeder et al. 1966). Excess copper causes a variety of toxic effects, including altered permeability of cellular membranes. The primary target for free cupric ions in the cellular membranes are thiol groups that reduce cupric (Cu^{+2}) to cuprous (Cu^{+1}) upon simultaneous oxidation to disulfides in the membrane. Cuprous ions are reoxidized to Cu^{+2} in the presence of molecular oxygen; molecular oxygen is thereby converted to the toxic superoxide radical (O^{-2}), which induces lipoperoxidation

(Aaseth and Norseth 1986).

Aquatic Organisms. Bioavailability and toxicity of copper to aquatic organisms depends on the total concentration of copper and its speciation (Hung et al. 1990). In hard, moderately polluted waters, 43 to 88% of the copper is associated with suspended solids and not available to biota (Shaw and Brown 1974). Copper toxicity to aquatic biota is related primarily to the dissolved cupric ion (Cu^{+2}) and possibly to some hydroxyl complexes (NAS 1977; Hall et al. 1988; Hung et al. 1990). Soluble copper is largely complexed with carbonate, amino acids, or humic substances. Cupric copper—one of the most toxic forms—constitutes 0.1 to 0.2% of this soluble material (Shaw and Brown 1974). The toxicity of copper in its complexed, precipitated, or adsorbed form is less than that of the free ionic form (Hall et al. 1988; Hung et al. 1990). In aquatic invertebrates, copper causes gill damage at high concentrations, and in fishes it interferes with osmoregulation (Hodson et al. 1979). Elevated concentrations of copper interfere with oxygen transport and energy metabolism; tissue hypoxia is the cause of death and is associated with reductions in the activities of regulatory enzymes of ATP-synthesizing pathways (Hansen et al. 1992b).

In freshwater algae, movement of copper into cells occurs mainly by physical transport; the plasmalemma is the initial site of copper binding. Copper on the plasmalemma increases its permeability, as shown by the leakage of potassium and other ions from copper-treated cells and entry of copper into intracellular sites (Stokes 1979).

Marine prosobranch gastropods, like several other groups of mollusks and arthropods, normally accumulate and store copper and use it in the synthesis of hemocyanin, a blood pigment (Betzer and Yevich 1975). In gastropods, copper may elicit secretions of mucus by goblet cells; bind to hydrophilic regions of the external membranes of epithelial cells, altering their biochemical and biophysical properties; or disrupt the normal functioning of peroxidase and ferritin (Cheng 1979). Peroxidation products, such as hydroperoxides and malondialdehyde, are toxic to vital functions of membranes and cells; bivalve mollusks challenged with ionic copper show significant increases in these products (Chelomin and Belcheva 1992). Exposure of gastropods to high sublethal concentrations of copper completely inhibits succinic dehydrogenase activity at whole body concentrations between 4.7 and 11.9 mg Cu/kg DW soft parts, causes a measurable decrease in heart beat rate, and adversely affects surface epithelia, especially those covering the head-foot and rectal ridge, disrupting osmoregulation and producing water accumulation in tissues (Cheng 1979). The primary lethal effect of copper in gastropod mollusks is caused by disruption of the transporting surface epithelium (Cheng 1979).

In crabs, the gills are a major target organ of copper toxicity; waterborne copper decreases hemocyanin-oxygen affinity (Truchot and Boitel 1992). Exposure of shore crabs (*Carcinus maenas*) to lethal concentrations of copper is associated with reductions in activity of glycolytic enzymes but, unlike fishes, did not involve cellular energy deprivation (Hansen et al. 1992b). Copper-tolerant strains of aquatic mayflies (*Baetis thermicus*) have evolved in Japan. Tolerance is attributed to the ability to induce a metal-binding protein that preferentially sequesters copper over cadmium and zinc (Suzuki et al. 1989).

In fishes, the gill surface's low affinity for metal allows greater entry of the metal to the intracellular compartment. Once there, more complex binding sites are present. Binding to these ligands causes one or more of the following toxic mechanisms: (1) blocking of the essential biological functional groups of biomolecules; (2) displacing the essential metal ion in molecules; or (3) modifying the active conformation of biomolecules. These mechanisms may account for the specific inhibition of ion transport from ionic copper (Cu^{+2}) exposure (Reid and McDonald 1991). Studies with radiocopper-64 and rainbow trout (*Oncorhynchus mykiss*) show that the external gill epithelial surface has a relatively low affinity for copper, allowing copper to penetrate intracellular compartments. Copper disrupts gill function of rainbow trout by impairing transepithelial ion exchange, for example, impairing or upsetting electrolyte balance by inhibiting active uptake or stimulating passive loss (Reid and McDonald 1991). Copper toxicity to rainbow trout in hard water is related to the total concentration of soluble copper (copper carbonate, $CuCO_3$; cupric ion, Cu^{+2}) in the test medium rather than to either of these two forms alone (Shaw and Brown 1974). Long-term retention of copper accumulations in fish tissues is characterized by high half-time persistence after copper administration and binding of copper to proteins in a nonexchangeable or slowly exchangeable pool (Carbonell and Tarazona 1994).

Copper detoxifying mechanisms in fishes include the induction of metallothioneins, allowing copper retention for weeks or months after absorption without producing toxic effects (Hogstrand et al. 1991; Hylland et al. 1992; Carbonell and Tarazona 1994; Marr et al. 1995). Hepatic metallothionein contents of individual fishes usually reflect the accumulation of copper in that organ (Hogstrand et al. 1991). This strongly supports the use of metallothionein as an indicator of copper stress (Hogstrand 1991).

In tench (*Tinca tinca*), hepatic alterations observed after exposure to lethal concentrations of copper (75 mg/L for 4 to 12 days) include accumulation of various pigments in Kupffer cells and hepatocytes. Death was attributed to deficient oxygen transport and consumption and to the lytic effect of copper on various cell membranes, eventually causing massive necrosis in large areas of the liver parenchyma (Roncero et al. 1992). In rapidly growing juvenile flounders (*Paralichthys* spp.), copper blocks calcium transport, possibly through interference with gill chloride cells. Copper inhibition of calcium accumulation is alleviated by removing copper from the medium (Dodoo et al. 1992).

Mammals. Copper homeostasis plays an important role in the prevention of copper toxicity. After copper requirements are met, excess copper absorbed into gastrointestinal mucosal cells is bound to metallothionein and excreted when the cell is sloughed. Copper that eludes the intestinal barrier is stored in the liver or incorporated into bile and excreted in feces. The most likely pathway for the entry of toxic amounts of copper would be long term inhalation or entry through the skin. Both of these pathways allow copper to pass unimpeded into the blood (ATSDR 1990). The levels of copper in the mammalian body are held constant by alterations in the rate and amount of copper absorbed, its distribution, and rate and route of excretion (ATSDR 1990). Many factors interfere with copper absorption including competition for binding sites, as with zinc; chelation, as with phytates; and interaction with ascorbic acid, which aggravates copper deficiency by decreasing copper absorption and—with excess copper—reduces the toxic effects (USEPA 1980; ATSDR 1990).

Two inherited human diseases that represent abnormal copper metabolism are Menkes' syndrome and Wilson's disease. Menkes' syndrome, with symptoms similar to those of copper deficiency, is characterized by a progressive brain disease, abnormally low copper concentrations in liver and other tissues, and diminished ability to transfer copper across the absorptive cells of the intestinal mucosa (USEPA 1980; Aaseth and Norseth 1986). Wilson's disease (hepatolenticular degeneration) is the only significant example of copper toxicity in humans. Wilson's disease is an autosomal recessive disorder that affects normal copper homeostasis and is characterized by excessive retention of hepatic copper, decreased concentration of serum ceruloplasmin, impaired biliary copper excretion, and hypercupremia. Systemic manifestations of Wilson's disease are hepatic and renal lesions and hemolytic anemia (Schroeder et al. 1966; Goresky et al. 1968; Baker 1969; USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). Certain strains of mutant rats with reduced excretion of biliary copper spontaneously develop hepatitis because of the extremely gross deposition of copper in the liver (Sugawara et al. 1994). Most humans afflicted with Wilson's disease usually die before puberty, although some survive to age 35 (Schroeder et al. 1966). Postmortems of Wilson's patients show that livers had as much as 7.5% copper and kidney ash had up to 2.7% copper. There is no evidence, however, that persons with normal homeostatic mechanisms are subject to any chronic degenerative disorders resulting from modern exposures to copper (Schroeder et al. 1966). Unusually susceptible human populations to copper poisoning include those afflicted with Wilson's disease, infants and children under age one year, those with liver damage or chronic renal disease, individuals undergoing dialysis (excess copper in the dialysate), and those with an inherited deficiency of the enzyme glucose-6-phosphate dehydrogenase (ATSDR 1990).

Ingested copper travels through the gastrointestinal (GI) tract, where some of it is absorbed into the blood and becomes associated with plasma albumin and amino acids (Sugawara et al. 1994) or is used to maintain copper levels in erythrocytes (USEPA 1980). Albumin-bound copper is eventually transported to the liver; however, minor fractions are transported into the bone marrow, the erythrocytes, or other tissues (Aaseth and Norseth 1986). Most of the circulating copper is translocated within minutes. During the next few hours, blood copper concentrations increase and copper becomes an integral part of the ceruloplasmin molecule (Goresky et al. 1968). Gastrointestinal absorption is normally regulated by the copper status in the body. In general, up to 50% of small doses (i.e., less than 1 µg in rats) are absorbed, whereas large doses are absorbed to a lesser extent (Aaseth and Norseth 1986). In humans, about 40% of the dietary copper is absorbed (USEPA 1980). Absorbed copper is freely exchangeable with copper loosely bound to the alpha-globulin ceruloplasmin where it is exchanged in the cupric form (Schroeder et al. 1966). Copper is stored mainly in liver, brain, heart, kidney, and muscle; in tissues and blood cells, copper is bound to proteins, including many enzymes (Aaseth and

Norseth 1986). Amino acids facilitate the entry of copper into liver cells and a small proportion of copper in serum is bound to amino acids (Goresky et al. 1968). About 80% of the absorbed copper is bound to metallothionein in the liver; the remainder is incorporated into compounds such as cytochrome *c* oxidase (USEPA 1980; ATSDR 1990). Copper accumulations in animals are associated with increased number and increased size of copper-containing lysosomes in hepatocytes. In liver, copper is initially bound to a metallothionein-like, low molecular-weight protein and later it appears in a high-molecular weight protein, ceruloplasmin, which reenters the circulation. Ceruloplasmin transports copper to tissues and also functions as an oxidase (Aaseth and Norseth 1986). The amount of copper absorbed is usually far in excess of metabolic requirements (Sugawara et al. 1994). Of the copper retained in the body, almost all plays a particular physiological role in the function of at least 12 specific copper proteins, such as cytochrome *c* oxidase and tyrosinase. Thus, only extremely small concentrations of free copper ions are normally found in body fluids (NAS 1977).

Retention of radiocopper injected into humans is high; only 10% is excreted within 72 h in urine and feces and 50% in four weeks (Aaseth and Norseth 1986). Most (72%) of the unabsorbed copper is excreted in the feces primarily by way of the biliary duct, the salivary glands, or the intestinal mucosa; a minor portion is excreted by way of sweat and menses (Schroeder et al. 1966; USEPA 1980; ATSDR 1990). In mammals, copper is excreted mainly via the bile in association with glutathione or unidentified high molecular weight molecules; however, the transport mechanisms of copper from liver cells into bile are essentially unknown (Aaseth and Norseth 1986). In rats, biliary excretion of copper is increased by increased flow of bile, increased body temperature, or administration of adrenal steroids (Sugawara et al. 1994).

Mechanisms implicated in copper poisoning include free radical production, alteration in activities of several enzymes, and interference with metallothionein synthesis. At the cellular level, copper has several primary mechanisms of toxicity that alter protein configuration and biological activity. These include the catalysis of peroxidation reactions and subsequent generation of free radicals that damage lipids and proteins, interactions with R groups of proteins—particularly SH groups, and acting as a substituent for other metals in metalloproteins (Sanders et al. 1994). Copper, in relative excess, is a cytotoxic metal with injury related to the process of lipid peroxidation. Isolated rat hepatocytes exposed to copper solutions for as long as 90 min show a concentration- and time-related decrease in cell viability as judged by loss of intracellular potassium and aspartate aminotransferase, an increase in lipid peroxidation, and a decrease in glutathione (Stacey and Klaassen 1981). Falling disease in cattle, dogs, and chickens is associated with a cardiovascular disorder caused by reduced activity of lysal oxidase, a copper-requiring enzyme necessary for elastic tissue formation and maintenance (USEPA 1980). Metallothionein synthesis acts as a protective mechanism against buildup of excessive amounts of the essential, but potentially toxic, copper ions, possibly before the development of other control processes. In livers of newborn lambs, rabbits, mice, and hamsters copper concentrations are usually directly related to the metallothionein content in cytoplasmic fractions (Bakka and Webb 1981). In sheep, elevated serum glutamic oxaloacetic transaminase (SGOT) levels were linked to elevated copper concentrations in blood at least one to six weeks before obvious external signs of copper poisoning. SGOT measurements in sheep serum seem to constitute an adequate early warning of the approach of the hemolytic crisis and eventual death of the animal from chronic copper poisoning (MacPherson and Hemingway 1969).

Interactions

Copper interacts with numerous compounds normally found in natural waters. The amounts of the various copper compounds and complexes present in solution depend on water pH, temperature, and alkalinity and on the concentrations of bicarbonate, sulfide, and organic ligands (USEPA 1980). In animals, copper interacts with essential trace elements such as iron, zinc, molybdenum, manganese, nickel, and selenium and also with nonessential elements including silver, cadmium, mercury, and lead; interactions may be either beneficial or harmful to the organism (Kirchgessner et al. 1979). The patterns of copper accumulation, metabolism, and toxicity from these interactions frequently differ from those produced by copper alone. Acknowledgment of these interactions is essential to understanding copper toxicokinetics.

Aluminum

Mixtures of copper and aluminum (Al) were more than additive in toxicity to ova of brown trout, *Salmo trutta* (Sayer et al. 1991).

Cadmium

Exposure of algae to low sublethal concentrations of copper (0.03 µg/L) increases their sensitivity towards additional copper challenge and to cadmium (Cd) salts (Visviki and Rachlin 1994a). In freshwater clams (*Anodonta cygnea*) exposed for 46 days to a mixture of high concentrations of copper (139 µg/L) and cadmium (122 µg/L), cadmium accumulation is reduced 90% and copper accumulation reduced 50% (Holwerda 1991). Exposure of crayfish (*Cambarus bartoni*) to 12.5 µg Cd/L for 72 h results in significantly increased copper stores in the hepatopancreas; however, isopods similarly exposed had decreased copper stores in antennal glands (Mwangi and Alikhan 1993). In the presence of copper, barnacles tend to accumulate cadmium (Powell and White 1990). In fishes, copper-cadmium interactions occur in Mozambique tilapia (*Oreochromis mossambicus*) during single and combined exposures. Waterborne copper tends to increase whole body cadmium content of tilapia at all tested copper concentrations and exposure durations (as high as 400 µg Cu/L for 96 h); however, cadmium exposure tends to lower copper concentrations in tissues of tilapia (Pelgrom et al. 1994).

In birds, copper concentrations in kidneys of the willow ptarmigan (*Lagopus lagopus*) are positively correlated with concentrations of cadmium (Wren et al. 1994).

In mammals, cadmium inhibits copper absorption across the intestinal mucosa (Aaseth and Norseth 1986). Intercorrelations of copper with cadmium and zinc in livers of polar bears (*Ursus maritimus*) are probably mediated by metallothioneins, which may contain all three metals (Braune et al. 1991). In rats, copper protects against nephrotoxicity induced by cadmium, provided that copper is administered 24 h prior to cadmium insult. Specifically, rats given 12.5 mg Cu/kg BW by way of subcutaneous injection 24 h before receiving 0.4 mg Cd/kg BW—when compared to a group receiving Cd alone—did not have excessive calcium in urine and renal cortex or excessive protein in urine; thus, 2.8 mg Cu/kg BW protects against 0.25 mg Cd/kg BW (Liu et al. 1992).

Iron

Mixtures of copper and iron (Fe) salts were more than additive in toxicity to ova of brown trout (Sayer et al. 1991).

In muscle of Weddell seals (*Leptonychotes weddelli*), copper is positively correlated with iron (Szefer et al. 1994). In general, concentrations of copper in all tissues of all marine vertebrates examined are positively correlated with concentrations of iron (Eisler 1984).

The primary function of the mammalian red blood cell is to maintain aerobic metabolism while the iron atom of the heme molecule is in the ferrous (Fe^{+2}) oxidation state; however, copper is necessary for this process to occur (USEPA 1980). Excess copper within the cell oxidizes the ferrous iron to the ferric (Fe^{+3}) state. This molecule, known as methemoglobin, is unable to bind oxygen or carbon dioxide and is not dissociable (Langlois and Calabrese 1992). Simultaneous exposure of sheep to mixtures of cupric acetate, sodium chlorite, and sodium nitrite produced a dose-dependent increase in methemoglobin formation (Calabrese et al. 1992; Langlois and Calabrese 1992).

The addition of iron to diets of domestic pigs increases their resistance to copper poisoning (USEPA 1980), but this is an exception. High intake of iron, in general, adversely affects copper status in ruminants, guinea pigs, and rats; the mechanisms for this phenomenon are unknown (Yu et al. 1994). Genetically anemic and normal strains of rats fed high iron diets had reduced kidney copper concentrations in both groups; this was associated with decreased absorption and biliary excretion of copper (Yu et al. 1995).

Manganese

Copper in livers and muscles of Weddell seals was positively correlated with manganese (Mn; Szefer et al. 1994). In general, manganese and copper are positively correlated in tissues of marine vertebrates (Eisler 1984). Uptake of copper from copper-contaminated freshwater sediments by annelid worms is related to the amount of reducible manganese oxide in the sediments (Diks and Allen 1983).

Molybdenum

In terrestrial vegetation, molybdenum (Mo) and sulfur interfere with copper-induced deficiencies (Gupta 1979). Copper poisoning in cattle and other ruminants is governed by dietary concentrations of molybdenum and sulfate (Lewis et al. 1967; Todd 1969; Buckley and Tait 1981; Eisler 1989). Molybdenum and sulfur in mammalian diets cause a decrease in the availability of copper because of the formation of the biologically

unavailable copper-thiomolybdate complex (Aaseth and Norseth 1986). Cattle die when grazing for extended periods on pastures where the ratio of copper to molybdenum is less than 3 to 1, or if they are fed low copper diets containing molybdenum at 2 to 20 mg Mo/kg ration (Eisler 1989). Wilson's disease is induced in rabbits by feeding a diet high in molybdates and sulfates, suggesting that the disease is not solely the result of copper intoxication (Goresky et al. 1968).

Zinc

Copper is positively correlated with zinc in gills of two species of fishes from the Mediterranean Sea (Romeo et al. 1994). Mixtures of copper and zinc salts in marine or freshwater fishes are more-than-additive in toxicity, producing more deaths in 96 h than expected on the basis of individual components (Eisler and Gardner 1973; Birge and Black 1979; Hodson et al. 1979). Mixtures of copper and zinc are generally acknowledged to be more-than-additive in toxicity to a wide variety of aquatic organisms (Birge and Black 1979; Hodson et al. 1979; Fernandez and Jones 1990; Eisler 1993). But mixtures of copper (0 to 90 µg/L) and zinc (0 to 1,200 µg/L) are only additive in action to a marine bacterium (*Photobacterium phosphoreum*), decreasing its luminescence after exposure for 30 min (Parrott and Sprague 1993). And sometimes mixtures of copper and zinc salts are less-than-additive in action, as judged by DNA, RNA, and protein contents of newly hatched fathead minnows (*Pimephales promelas*) exposed for 4 days (Parrott and Sprague 1993).

In birds, copper and zinc are positively correlated in kidneys of the willow ptarmigan (*Lagopus lagopus*; Wren et al. 1994) and in kidneys and livers of common murres (*Uria aalge*; Stewart et al. 1994).

In mammals, copper absorption across the intestinal mucosa is inhibited by concomitant high oral intake of zinc (Aaseth and Norseth 1986). In livers from Weddell seals, copper is positively correlated with zinc (Szefer et al. 1994). The addition of zinc to swine diets protects against copper toxicosis caused by eating diets containing 250 mg Cu/kg ration (USEPA 1980).

Other Inorganics

Copper interacts with lead (Pb), magnesium (Mg), silver (Ag), and other elements. In mammals, supplemental copper promotes urinary excretion of lead from the body and loss of lead from tissues (Flora 1991). In shore crabs (*Carcinus maenas*), ionic copper displaces ionic magnesium in gills, leading to inhibition of phosphoryl transfer (Hansen et al. 1992b). In embryos of the Pacific oyster (*Crassostrea gigas*), silver—at 0.5 to 15.5 µg Ag/L—enhances adverse effects when copper concentrations exceed 6.0 µg Cu/L (Coglianse and Martin 1981). Silver positively correlates with copper in livers of Weddell seals, but in muscles the correlation is negative (Szefer et al. 1994).

In fishes, additive or more-than-additive toxicity occurs with mixtures of salts of copper and mercury, copper-zinc-phenol, and copper-nickel-zinc (Birge and Black 1979). Accumulation of copper in gills of fathead minnows during exposure to 16 µg Cu/L is reduced by added ionic calcium, which competes with copper for gill binding sites (Playle et al. 1992).

Organic Compounds

Sequestering agents, increasing salinity, sediments, and other variables all reduce toxicity and accumulation of copper in tested species of aquatic plants and invertebrates. Chelating agents, such as nitrilotriacetic acid, reduce the toxicity of ionic copper to six species of estuarine phytoplankton (Erickson et al. 1970). Sensitivity of freshwater zooplankton communities varies seasonally. Communities are most sensitive to copper stress (20 or 40 µg Cu/L) during exposure for 5 weeks in spring rather than in summer or autumn because, in part, of reduced dissolved organic carbon concentrations in the spring (Winner et al. 1990). Adverse effects of copper on survival of marine copepods are reduced or eliminated by the presence of clay minerals, diatoms, ascorbic acid, sewage effluents, water extracts of humic acids, and certain soil types (Lewis et al. 1972). Chelators, such as EDTA, and more alkaline pH increase the survival and larval developmental rates of copepods challenged with copper through increased complexation of cupric ions (Sunda et al. 1990). Natural fulvic acids, which comprise 75% of dissolved humic substances, reduce the acute toxicity of copper to rotifers (Porta and Ronco 1993). A significant reduction in radiocopper-64 accumulation by clams (*Macoma balthica*) occurs at high concentrations of dissolved organic ligands; reduction is more pronounced at 3.0% salinity than 1.0% salinity (Absil et al. 1993). The presence of sediments in assay containers reduces the toxicity of copper to freshwater gastropods (Winger et al. 1984). Copper uptake by brine shrimp (*Artemia franciscana*) increases with decreasing pH and

decreasing carbonate complexation (Blust et al. 1991). Studies with a freshwater shrimp (*Paratya australiensis*) and copper salts show that uncomplexed cupric ions are the most toxic chemical species in solutions containing nitrilotriacetic acid or glycine; however, the singly charged copper-glycine^{+} complex also appears to be mildly toxic (Daly et al. 1990a). Shrimp (*Paratya* sp.) are more resistant to copper in higher alkalinity waters (Daly et al. 1990b) and under conditions of increasing dissolved organic matter (Daly et al. 1990c).

In freshwater fishes, mixtures of copper with anionic detergents or various organophosphorus insecticides cause more-than-additive toxicity (Hodson et al. 1979). And in marine vertebrates, copper in tissues is positively correlated with metal-binding proteins (Eisler 1984). Accumulations of copper in gills of fathead minnows during exposure to 16 µg Cu/L is reduced by added EDTA, which reduces bioavailability of copper through complexation (Playle et al. 1992). Copper LC50 (96 h) values (i.e., concentrations of ionic copper in solution at the start of the test estimated to kill 50% of the test species in 96 h) to larval fathead minnows range from a low of 2 µg/L at low pH and low dissolved organic carbon to 182 µg/L at pH 6.9 and dissolved organic carbon of 15.6 mg/L (Welsh et al. 1993). Acidification and the removal of dissolved organic carbon increases the toxicity of copper to fathead minnows in natural waters of low alkalinity and explains 93% of the variability in field toxicity data for that species (Welsh et al. 1993).

In mammals, phenobarbital and phenytoin increase serum ceruloplasmin concentrations (Aaseth and Norseth 1986). Chronic copper poisoning in sheep is exacerbated when diets contain heliotrope plants (*Heliotropium* sp., *Echium* spp., *Senecio* sp.). Aggravated effects of the heliotrope plants include reduced survival and a twofold to threefold increase in liver and kidney copper concentrations when compared to control animals fed copper without heliotropes (Howell et al. 1991). Rats given acutely toxic doses of 2,3,7,8-tetrachlorodibenzo-para-dioxin had elevated concentrations of copper in liver and kidney because of impaired biliary excretion of copper (Elsenhans et al. 1991). Morphine increases copper concentrations in the central nervous system of rats, and dithiocarbamates inhibit biliary excretion (Aaseth and Norseth 1986). In human patients, urinary excretion of copper is increased after treatment with D-penicillamine, calcium disodium EDTA, or calcium trisodium diethylenetriamine penta acetic acid (Flora 1991).

Carcinogenicity, Mutagenicity, Teratogenicity

General

No definitive evidence exists demonstrating that copper or copper compounds at environmentally realistic concentrations are the causative agents in the development of carcinogenicity, mutagenicity, or teratogenicity (USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). However, under controlled conditions of grossly elevated exposures, some studies suggest that copper is a potential carcinogen in rodents (USEPA 1980; ATSDR 1990; Toussaint and Nederbragt 1993); mutagen in rodents (Aaseth and Norseth 1986; ATSDR 1990), sheep (Bires et al. 1993), and grasshoppers (Bhunya and Behura 1986); and teratogen in fish (Birge and Black 1979), rodents, and other small laboratory animals (Aaseth and Norseth 1986).

Carcinogenicity

The carcinogenic classification of copper is Group 3 or D; that is, not classifiable as to its carcinogenicity in humans (ATSDR 1990). No definitive evidence exists showing that copper or copper compounds cause cancer in mammals (USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). Although hypercupremia is sometimes associated with neoplasms (USEPA 1980), some copper compounds seem to have an inhibitory effect on the development and growth of malignant tumor cells (Aaseth and Norseth 1986). Copper is not associated with an elevated incidence of cancer in humans or animals exposed by way of inhalation, oral, dermal, or intramuscular injection routes. A slightly increased incidence of reticulum cell sarcoma was noted in mice 18 months after a single subcutaneous injection of copper 8-hydroxyquinoline, but this needs to be verified (ATSDR 1990).

Sensitivity of cancerous cells to copper may reflect cell DNA content. Two closely related rat hepatoma cell lines differed in sensitivity to copper toxicity by a factor of four; DNA content in each cell line decreased with increasing copper concentrations, but at different rates. Severity of toxicity was associated with increasing accumulations of copper in the cell nucleus and with decreasing DNA (Toussaint and Nederbragt 1993).

Mutagenicity

Grasshoppers (*Oxya velox*) injected intra-abdominally with relatively high concentrations of soluble copper showed a 1.6% frequency of chromosomal anomalies in meiotic cells of testes 24 h after injection (Bhunya and Behura 1986); however, no control data were presented. Copper-induced DNA strand breaks in rats and chromosomal aberrations and sperm abnormalities in mice suggest that copper is a potential human mutagen (ATSDR 1990). Copper salts affect chromosomes in vitro in the presence of hydrogen peroxide and ascorbic acid and can also increase the frequency of non-complementary nucleotides in the synthesized DNA double helix (Aaseth and Norseth 1986). Sheep, age 1.5 years, given about 10.7 mg Cu/kg BW daily—in addition to other metals—until they died (65 to 84 days later) show a significant increase in sister chromatid exchanges in bone marrow (Bires et al. 1993); however, the specific role of copper on survival and mutagenicity is unclear and requires verification.

Teratogenicity

Grossly elevated concentrations of dissolved copper produce teratogenicity in fish embryos. A significant number of malformed fish larvae came from eggs treated with 500 µg Cu/L (Birge and Black 1979). In studies with laboratory animals and elevated concentrations of copper salts, copper penetrates the placental barrier into the fetus; intramuscular injection of 4 mg Cu/kg BW early in pregnancy adversely affects fetal central nervous system development (Aaseth and Norseth 1986). In humans, no definitive data are available on whether copper can cause birth defects; however, incubation of human spermatozoa with metallic copper results in loss of sperm motility (Aaseth and Norseth 1986).

Concentrations in Field Collections

General

Copper concentrations in air, soil, water, sediments, and other abiotic materials are elevated as a result of human activities, especially near copper smelters and mines, urban areas, municipal and industrial wastewater outfalls, marinas containing copper-based antifouling paints, and agricultural soils receiving prolonged applications of copper-based fungicides (Table 2). Maximum copper concentrations in selected abiotic materials are 5 µg/m^3 in air, 5 µg/L in groundwater, 12 µg/L in rainwater, 300 mg/kg DW in black shales, 1,200 mg/kg DW in poultry litter, 6,500 mg/kg DW in marine sediments, 7,000 mg/kg DW in soils, and 7,700 mg/kg DW in sewage sludge (Table 2).

Table 2. Copper concentrations in selected abiotic materials.

Table 2.

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
Air, µg/m^3		
Near copper smelters	1-2; Max. 5.0	1, 2
Nonurban locations	0.16-0.21; Max. 1.2	3
Remote locations	Usually <0.001; sometimes 0.001-0.003; Max. 0.012	4
South Pole	0.00004	5
Urban locations	0.15-0.18; Max. 1.6	4
United States	0.01-0.67	5
U.S. cities	Usually 0.09-0.81; sometimes 0.81-2.4; infrequently >2.4	2, 6
Uncontaminated	0.001-0.2	1, 7
Coal, µg/kg dry weight (DW)	17,000	7

Table 2.

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
Drinking water, µg/L		
Conducted via copper pipes	Max. 1,000	1
Private houses		
White Plains, New York	540	6
Bridgeport, Connecticut	185	6
Vermont		
Private houses	75-1,400	6
Hospital	17-730	6
United States	134; Max. 8,350	1, 2
Glaciers, µg/kg fresh weight (FW)	0.2	7
Groundwater, µg/L		
New Jersey	About 5.0	1
Lakes and rivers, µg/L		
Canada	1-8	1
Contaminated vs. noncontaminated	50-100 vs. 1-7	6
Lake Asosca, Nicaragua, 1991-92	Usually <2.0; mean 3.1; Max. 13.1	8
Ligurian Sea drainage	<0.3-1.75 (equivalent to 3.5-7.1 tons annually)	22
New Jersey	3.0	1
Sweden; near brassworks vs. reference site	9.4 vs. 1.0	21
United States	5.3 (0.83-105.0); usually <2.0-4.2	1, 5, 7
Manure, µg/kg DW		
Cattle	5,000	1
Mine tailings, mg/kg DW		
Butte Lake, Canada, 1982	7,100	9
Municipal water supplies, µg/L	8.3 (0.6-250.0)	6
Oil, µg/kg FW		
Crude	140	7
Shale	70,000	7
Pond water, µg/L		

Table 2.

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
Massachusetts	(<10-105)	1
Poultry litter, mg/kg DW	1,196	10
Precipitation, µg/L		
Soluble vs. total	6.0 vs. 12.3	4
Rocks, µg/kg DW		
Crustal and sedimentary	24,000-45,000	6, 7
Sandstones	10,000-40,000	11
Shales	30,000-150,000	11
Marine black shales	20,000-300,000	11
Seawater, µg/L		
Central Texas coast	Max. 50.0	12
Chesapeake Bay, Maryland;	11.7 (ND-80.0)	13
1985-86; dissolved		
In water flowing through		
copper pipes	45.0	6
Mediterranean, northwestern coast	Max. 22.4	12
North Sea	0.2-2.6	14
Oceanic		
Dissolved	0.15	7
Total	0.06-6.7	5, 12, 13
Surface waters		
Atlantic Ocean	0.06-0.21	1
East Arctic Ocean	0.13	1
Taiwan, coastal		
Total	10.2	15
Particulate	2.49	15
Dissolved	7.75	15
Labile	2.19	15
Inorganic labile	2.15	15
Free labile	0.04	15

Table 2.

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
Nonlabile	5.56	15
Polar nonlabile	3.81	15
Nonpolar nonlabile	1.75	15
Taiwan, near copper recycling facility		
Total	0.8-737.0	15
Dissolved	3.5-36.5	15
Particulates	0.2-723.0	15
United Kingdom estuaries		
Contaminated	3-176	14
Noncontaminated	2-3	14
Sediments, mg/kg DW		
England and Wales, streams	7-70	17
Lake Asosca, Nicaragua; 1991-92	(36.6-73.7)	8
Long Island Sound, New York;		
1984-85	190	18
Southwest England		
Carnon River (water 1,080 µg/L)	1,650: Max. 6,500	14
Fowey (water 7-21 µg/L)	50; Max. 370	14
Red River (water 17-35 µg/L)	590	14
Sweden; freshwater lakes; 1988		
3-5 km from smelter	707-2,531	19
50-80 km from smelter	37-54	19
United Kingdom estuaries,		
contaminated vs. noncontaminated	>2,000 vs. 10	14
Sediment interstitial waters, µg/L		
Butte Lake, Canada; 1982	Max. 14.8	9
Clean vs. copper-contaminated	<10 vs. 100	14
sediments		
Sewage sludge, mg/kg DW		
Missouri	390 (45-5,200)	16

Table 2.

Material, units of concentration, and other variables	Concentration[a]	Reference[b]
Primary sludge	21 (3-77)	1
United States, 23 cities	991 (126-7,729)	1
Soils, mg/kg DW		
Global	(2-250)	1, 5
Italy	51	20
Near copper production facility	7,000	1
To 100 cm depth		
Total	20	7
Organic fraction	350	7
Under oak trees	3.5	6
Under maple trees	6.0	6
United States	19 (1-70)	11, 16

[a]Concentrations are shown as means, range (in parentheses), maximum (Max.), or nondetectable (ND).

[b]1, ATSDR 1990; 2, USEPA 1980; 3, Nriagu 1979a; 4, Nriagu 1979d; 5, Aaseth and Norseth 1986; 6, Schroeder et al. 1966; 7, Nriagu 1979c; 8, Cruz et al. 1994; 9, Pedersen 1983; 10, van der Watt et al. 1994; 11, NAS 1977; 12, Neff and Anderson 1977; 13, Hall et al. 1988; 14, Bryan and Langston 1992; 15, Hung et al. 1990; 16, Beyer 1990; 17, Thornton 1979; 18, Turgeon and O'Connor 1991; 19, Johnson et al. 1992; 20, Arduini et al. 1995; 21, Hogstrand et al. 1991; 22, Migon 1993.

Copper concentrations in field collections of plants and animals are usually elevated in areas treated with copper-containing herbicides, near smelters, and from heavily urbanized and industrialized areas (Stokes 1979; Eisler 1984; Winger et al. 1984; Read and Martin 1993; Swiergosz et al. 1993; Fishelson et al. 1994; Storm et al. 1994). The amount and distribution of copper in animal tissues varies with tissue, organism age, sex, and amount of copper in the diet (Cuill et al. 1970; NAS 1977; USEPA 1980; Fishelson et al. 1994). Additional and more detailed information on copper concentrations in field collections of plants and animals is found in Jenkins (1980) and Eisler (1979, 1981).

In terrestrial vegetation, copper is usually less than 35 mg/kg DW except near smelters, where it may approach 700 mg/kg DW, and in copper-accumulator plants that may normally contain as much as 13,700 mg/kg DW (Table 3). In aquatic vegetation, copper is elevated in metals-contaminated water bodies, reaching concentrations as high as 1,350 mg/kg DW in eelgrass (*Zostera* spp.) from contaminated bays vs. 36 mg/kg DW in conspecifics from reference sites (Table 3).

Table 3. Copper concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in field collections of representative plants and animals.

Table 3. **Taxonomic group, organism, and other variables**	**Concentration[a] in (mg/kg)**	**Reference[b]**
Terrestrial Plants		
Red maple, *Acer rubrum*; leaf; Ontario, Canada; distance from smelter		
1.6 km	37 DW	1
2.6 km	26 DW	1
10.4 km	19 DW	1
28.9 km	16 DW	1
Copper plant mint, *Aeolanthus biformifolius*; Zaire		
Leaf	2,150-2,600 DW	1
Flower stem	2,150-3,500 DW	1
Corm	2,600-13,700 DW	1
Whole	10,000-13,700 DW	1
Agricultural crops, various	3-36 DW	2
Hair grass, *Deschampia flexuosa*; Ontario, Canada; distance from smelter		
1.7 km	726 DW	1
2.1 km	121 DW	1
7.4 km	103 DW	1
52.7 km	13 DW	1
Ferns, seven species; leaves	0.51 (0.22-0.98) FW	1
Fungi		
Seven species, whole	2.4 (1.5-3.0) FW	3
Various species		
Cap	Max. 131.7 DW	1
Spore	Max. 165.0 DW	1
Stalk	Max. 14.2 DW	1
Whole	Max. 95.9 DW	1
Grasses, various species	5 DW	2
Moss, *Hypnum cupressiforme* Wales; distance downwind from smelter		
Up to 3 km	All dead	1
8 km	62-68 DW	1
25 km	18-19 DW	1
Control site	11 DW	1
Sweden; near industries	Max. 265-580 DW	1
Legumes, various	15 DW	2
Lichens, various species		
Arctic	5 DW	4
Near copper smelter; Sudbury, Ontario	(15-20) DW	4
Tomato, *Lycopersicon esculentum*; United States		
Fruit	14 (8-34) DW	1
Leaf	(3-12) DW	1
Terrestrial plants, various species; seeds	1.1 (0.6-2.9) FW	3
Poppy, *Papaver orientale*; pods	14.3 FW	3

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Lichen, *Parimelia baltimorensis*; Washington, D.C.; various years		
1938	17 DW	1
1958	22 DW	1
1970	32 DW	1
Norway spruce, *Picea abies*		
Connecticut		
Leaf	6.0 DW	1
Twig	15.0 DW	1
England		
Bark	5.0 DW	1
Wood	0.6 DW	1
Sweden		
Bark	25.0 DW	1
Needle	(4.4-8.1) DW	1
Root	(8-21) DW	1
Twig	(42-76) DW	1
Wood	2.0 DW	1
Trees, various species; leaves	1.8 (0.6-5.2) FW	3
Tundra plants; whole; Spitsbergen, Norway; 1987		
Lichens, 14 species	1.8-36.7 DW	5
Mosses, four species	3.4-33.0 DW	5
Vascular plants, five species	3.9-10.0 DW	5
Elm, *Ulmus americana*; wood	7.9 FW	3
Corn *Zea mays*		
Grain		
East Asia	1.6 FW	1
Lower Dahomey	(1.0-2.9) DW	1
United States	8 (4-17) DW	1
From soils with Cu additions of 360 kg Cu/ha		
Grain	1.7-2.8 DW	6
Leaves	7.8-12.5 DW	6
Aquatic plants		
Algae and macrophytes; 11 species; Brazil; November 1989; whole	2.4-6.9 DW	14
Alga, *Ascophyllum nodosum*		
England; polluted bay vs. reference site	68 (46-96) DW vs. 12 (6-18) DW	1
Norway; polluted fjord vs. reference site	(45-240) DW vs. 5.5 (4-8) DW	1
Freshwater macrophytes; various species	2.5-256.0 DW	15
Water milfoil, *Myriophyllum* spp.	10.0-41.3 DW	1
Brown alga, *Pelvetia canaliculata*; whole		
Norway	55 DW	1
Scotland	5-16 DW	1
Pondweed, *Potamogeton* spp.; whole; Pennsylvania	5.0-102.9 DW	1
Eelgrass, *Zostera* spp.		
Denmark; 1979-80; metals-contaminated site vs. reference site		
Leaves	9-13 DW vs. 5-6 DW	16
Roots	27.4 DW vs. 6-7 DW	1
Portugal and Spain; contaminated bay	1,350 DW vs. (9-36) DW	1

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
vs. reference site		
Porifera		
Sponges; three species; whole	13-34 DW	1
Coelenterates		
Jellyfish, *Cyanea capillata*; whole		
New England	8.2 DW	1
Sweden	68.0 DW	1
Octacorals; Venezuela; whole; five species	0.9-3.1 DW	17
Terrestrial invertebrates		
Honeybee, *Apis mellifera*; Czechoslovakia; industrial locations vs. reference site; 1986-87		
Foraging workers	32-37 DW vs. 20-24 DW	7
Honey	1.1-1.7 DW vs. 0.6 DW	7
Pollen	6.1-8.2 DW vs. 5.4 DW	7
Landsnail, *Arianta arbustorum*; urban areas vs. reference site; Innsbruck, Austria; 1987; soft parts	188 (30-408) DW vs. 84 (46-104) DW	8
Bumblebee; four species of *Bombus*; queens; whole; Sweden, April 1991	18-23 (11-38) DW	9
Pine moth, *Bupalus piniarius*; pupae; whole; Finland, 1987; industrialized area vs. reference site	Max. 137 DW vs. 53 DW	10
Earthworm, *Lumbricus rubellus*; Cardiff, Wales; 1984; contaminated soils (2,740 mg Cu/kg DW soil) vs. reference site (26 mg Cu/kg DW soil)		
Anterior alimentary canal	85.4 DW vs. 18.2 DW	11
Posterior alimentary canal	64.4 DW vs. 21.1 DW	11
Remainder	23.2 DW vs. 10.1 DW	11
17-year cicadas, *Magicicada* spp.;Maryland; 1987; whole	(33.2-60.3) DW	12
Pine noctuid, *Panolis flammea*; pupae; whole; Finland, 1987; industrialized area vs. reference site	Max. 89 DW vs. 20 DW	10
Cuckoo bumblebee, *Psithyrus bohemicus*; queens; Sweden; April, 1991; whole	19 (12-29) DW	9
Spiders, whole; from old-field subjected to 11 years of nutrient enrichment (3,410 g Cu/ha yearly) vs. reference site (2-3 g Cu/ha yearly)		
Garden orb weaver, *Argiope aurantia*	110 DW vs. 80 DW	13
Wolf spiders, Lycosidae	130 DW vs. 85 DW	13
Aquatic mollusks		
Antarctic scallop, *Adamussium colbecki*; Ross Sea; 1987-88 vs. 1990		
Digestive gland	12.6 vs. 3.5 FW	18, 19

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Gills	6.5 DW vs. 1.4 FW	18, 19
Gonad	4.7 DW vs. ND	18
Kidney	4.0 DW vs. ND	18
Mantle	3.5 DW vs. ND	18
Muscle	1.6 DW vs. ND	18
Freshwater mussel, *Amblema* sp.; Texas		
Digestive gland	9.5 FW	1
Foot	2.9 DW	1
Gill	6.1 DW	1
Mantle	3.6 DW	1
Blood clam, *Anadara granosa*; soft parts; Malaysia	0.7-0.8 FW; 6.3 (4.5-8.0) DW	20, 21
Freshwater mussel, *Anodonta grandis*; soft parts; Manitoba, Canada; 1986	45.3 (5-80) DW	22
Lake mussel, *Anodonta piscinalis*; gills		
No glochidia	5.4 DW	23
With glochidia	8.0 DW	23
Ocean quahog, *Arctica islandica*		
Soft parts		
Block Island Sound	10.0 DW	24
Chesapeake Bay	5.4 DW	24
Georges Bank	3.5-10.3 DW	24
New York Bight	11.3 DW	24
Western Baltic Sea, 1992-93		
Adductor muscle	1.8-2.2 DW	24
Digestive gland	13.5 DW	24
Foot	3.1 DW	24
Gills	6.7 DW	24
Kidney	40.1 DW	24
Mantle	5.0 DW	24
Soft parts	14.3-15.3 DW	24
Whelk, *Buccinum undatum*; soft parts		
Irish Sea	180 DW	1
Scotland	78 DW	1
Channeled whelk, *Busycon canaliculatum*		
Digestive gland	(32-1,135) FW	1
Muscle	(12-21) FW	1
Cephalopods; liver	150 FW	3
Scallop, *Chlamys operculis*		
Kidney	240.0 FW	1
Shell	2.1 FW	1
Soft parts	1.7 FW	1
Pacific oyster, *Crassostrea gigas*		
Shell	(1.6-2.9) DW	1
Hong Kong, 1989; various locations		
Gill	840 DW	25
Mantle	509 DW	25
Muscle	750 DW	25
Soft parts	344-422 DW; max. 1,071 DW	25
Visceral mass	383 DW	25
Arcachon Bay, France, soft parts		
1979-82	48.3-63.8 DW	26

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
1983-87	67.7-116.2 DW	26
1988-91	101.8-135.0 DW	26
Soft parts		
England	(340-6,480) DW	1
South Africa	33.0 DW	1
Tasmania	(9.4-84.4) DW	1
United States	(7.8-38.0) FW	1
Taiwan		
Soft parts; 1989; seawater had 5.0-23.6 µg Cu/L from discharges of copper recycling facility	4,401 DW; green in color	27
Soft parts		
From copper-contaminated environment	2,225 DW	28
As above; after 6 days in clean seawater	746 DW	28
As above; after 32 days in clean seawater	344 DW	28
American oyster, *Crassostrea virginica*		
Florida, soft parts		
From a canal lined with chromated-copper arsenate wood vs. reference site	150-200 FW vs. 10 FW; elevated concentrations were associated with greenish color and higher frequency of histopathology of digestive gland diverticula	29
Reference site oysters transplanted into above canal		
After 3 months	130 FW	29
After 4 months	220 FW; no increase in frequency of digestive gland lesions	29
North Carolina, soft parts		
Marina sites	36.7 FW	30
Open water sites	7.1 FW	30
At 12 ‰ salinity	6.0 FW	31
At 33 ‰ salinity	2.0 FW	31
Soft parts		
Alabama	20 (4-78) FW	1
Chesapeake Bay	(5-240) FW	1
Eastern USA	91 (7-517) FW	1
Georgia	(48-261) DW	1
Gulf of Mexico states	16 (6-27) FW	1
Maryland (green oysters)	Max. 1,120 DW	1
NW Atlantic	46 (11-110) DW	1
Rhode Island	121 (92-140) FW	1
Texas	161 DW	1
Virginia; 1972-73		
At 7.5 ‰ salinity	29 FW	31
At 9.5 ‰ salinity	16 FW	31
At 12 ‰ salinity	12 FW	31
At 13.5 ‰ salinity	3 FW	31
Zebra mussel, *Dreissena polymorpha*; soft parts; caged for 15-60 days; water contained 0.8-1.4 µg Cu/L and particulates had 0.3-3.2 µg Cu/L	12.6-17.7 DW	32
Freshwater mussels; two species; soft	7.8-16.2 DW	33

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
parts; St. Lawrence River; 1989-90; sediment copper ranged from 4 to 148 mg/kg DW		
Octopus, *Eledone cirrhosa*; English Channel;		
October 1987		
Branchial hearts	335 DW	34
Genital tract	60-66 DW	34
Gill	268 DW	34
Kidney	594 DW	34
Mantle	102 DW	34
Muscle	17 DW	34
Whole	122 DW	34
Mud snail, *Ilyanassa obsoleta*; soft parts; North Carolina		
Marina sites	402.2 FW	30
Open water sites	219.5 FW	30
Baltic clam, *Macoma balthica*; soft parts; The Netherlands; 1990-92		
Acid-soluble fraction	4.1 (2.7-6.7) DW	35
Total copper	13.8-22.6 DW	35
Lagoon mussel, *Mytella strigata*; soft parts; Baja California, Mexico; 1989-91	Max. 3.9 DW	36
Common mussel, *Mytilus edulis*		
Shell		
California	(<5.8-8.6) DW	1
England	9.6 DW	1
Japan	(1.2-2.8) DW	1
New Zealand	3.0 DW	1
Soft parts		
California	(5.0-11.2) DW	1
Canada, Halifax	13.7-154.3 DW	39
England	(7-11) DW	1
Long Island Sound, New York		
1983	1.0-2.3 FW	38
1986-87	15 DW	37
Norway	(3.0-130.0) DW	1
Portugal and Spain	(6.5-14.0) DW	1
Mussel, *Mytilus smarangdium*; soft parts; copper-contaminated environment vs. 6 days in clean seawater	20.2 DW vs. 1.8 DW	28
Mussels; *Mytilus* spp.; soft parts; United States;		
1970's vs. 1980's		
Bodega Bay, California	6.9 DW vs. 7.7 DW	40
Narragansett Bay, Rhode Island	11.0 DW vs. 14.0 DW	40
Octopus, *Octopus vulgaris*; hepatopancreas	4,880 DW	1
Squid, *Ommastrephes bartrami*; liver	195 (17-696) DW	1
Clam, *Paphia undulata*; soft parts;Malaysia; 1993	0.9-1.1 FW	20
Scallop, *Pecten jacobeus*; Adriatic Sea; June 1988		
Digestive gland	16.6 DW	18

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Gills	6.3 DW	18
Gonad	10.3 DW	18
Kidney	17.5 DW	18
Mantle	3.3 DW	18
Muscle	1.1 DW	18
Green-lipped mussel, *Perna viridis*; Hong Kong; soft parts; March 1986	Max. 35.1 DW	41
Tropical rock oyster, *Saccostrea cucullata*; soft parts		
Australia, 1983-84; near sewage discharge vs. reference site	285 DW vs. 34 DW	42
Hong Kong, March 1986	Max. 556 DW	41
Sydney rock oyster, *Saccostrea commercialis*; soft parts; Georges River, Australia; 1970's vs. 1980's	20-46 FW vs. 14-93 FW	43
Cuttlefish, *Sepia officinalis*; English Channel; October 1987		
Branchial hearts	256 DW	34
Digestive gland	313-317 DW	34
Genital tract	55-56 DW	34
Gill	183 DW	34
Kidney	185 DW	34
Mantle	141 DW	34
Muscle	9 DW	34
Whole	59 DW	34
Freshwater clam, *Sphaerium* sp.; soft parts; Illinois	10.1 DW	1
Squid, *Symplectoteuthis oualaniensis*; liver	1,720 DW	1
Freshwater mussel, *Unio* sp.; soft parts	11.9-19.3 DW	32
Aquatic arthropods		
Amphipods, various species; whole; Antarctica; 1989	31.3 (30.7-32.0) DW	44
Crayfish, *Astacus astacus*; raw vs. cooked		
Hepatopancreas	52.0 FW vs. 31.0 FW	45
Muscle	5.7 FW vs. 11.0 FW	45
Mayfly, *Baetis thermicus*; whole; larvae; Japan; metal-contaminated river (28.6 µg Cu/L) vs. reference site	73.5 FW vs. 4.0 FW; Cu localized in midgut epithelial cells	46
Crustaceans; 17 species; whole; Antarctic Ocean; 1985-88		
Two species	5.5-7.7 DW	47
Three species	37-42 DW	47
Six species	53-68 DW	47
Four species	81-107 DW	47
Two species	123-149 DW	47
Benthic crab, *Dorippe granulata*; Hong Kong (contaminated harbor)		
Exoskeleton	7.7 DW	48
Gills	123.9 DW	48
Hemolymph	53.2 FW	48
Midgut gland	114.9 DW	48
Muscle	36.6 DW	48

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Euphausiids; Antarctic and Atlantic Oceans; 1985-86; whole		
Euphausia superba	55 (30-86) DW	49
Meganyctiphanes norvegica	58 (40-83) DW	49
Lobster, *Homarus vulgaris*; England		
Blood	32 FW	1
Exoskeleton	3 FW	1
Gill	26 FW	1
Liver	335 FW	1
Muscle	4 FW	1
Ovaries	50 FW	1
Stomach fluid	10 FW	1
Testes	1 FW	1
Urine	2 FW	1
Whole	17 FW	1
Insects; immature benthic species; whole; from copper-contaminated river up to 60 km downstream from outfall (779 mg Cu/kg DW sediments) vs. reference site (18 mg Cu/kg DW sediments)		
Plecoptera	84 DW vs. 16-32 DW	50
Trichoptera	204 DW vs. 11-18 DW	50
Mayflies, four species; whole; nymphs	11-17 DW	1
Beach hopper (amphipod), *Orchestia gammarellus*; whole; North Sea; 1989-90; reference site vs. contaminated site	Usually <70 DW vs. >145 DW (Max. 340 DW)	51
Crayfish, *Pacifasticus leniusculus*; raw vs. cooked		
Hepatopancreas	44 FW vs. 17 FW	45
Muscle	5 FW vs. 8 FW	45
Shrimp, *Pandalus jordani*; muscle	14.3-18.2 DW	1
Brown shrimp, *Penaeus aztecus*; Texas		
Exoskeleton	32 DW	1
Muscle	18-29 DW	1
Whole	34 DW	1
Viscera	173 (65-260) DW	1
Oceanic amphipods, *Themisto* spp; whole; Antarctic and Atlantic Oceans; 1985-86	28-31 (13-79) DW	49
Aquatic annelids		
Polychaete, *Lycastis ouanaryensis*; whole; India; 1984-85; contaminated site vs. reference site	32-95 DW vs. 4-27 DW	52
Tubificid worm, *Tubifex tubifex*; whole; Illinois	23 (10-42) DW	1
Echinoderms		
Sea star (Asteroidea), *Pisaster brevispinus*; California		
Gonad	(2-10) DW	1
Hepatic caecum	(18-38) DW	1
Stomach	(5-40) DW	1
Tunicates		

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Sea squirt, *Ciona intestinalis*		
California		
Tunic	55 DW	1
Viscera	73 DW	1
Sweden, whole	13 DW	1
Elasmobranchs and fishes		
Rockbass, *Ambloplites rupestris*; Ontario, Canada		
Gill	2.1 FW	1
Kidney	3.0 FW	1
Liver	4.9 FW	1
Muscle	1.7 FW	1
Jolthead porgy, *Calamus bajonado*; Puerto Rico		
Eye	1.3 FW; 6.7 DW	1
Gills	1.2 FW; 3.5 DW	1
Intestine	2.4 FW; 10.0 DW	1
Muscle	0.4 FW; 1.5 DW	1
Scales	4.9 FW; 6.9 DW	1
Vertebra	8.3 FW; 14.0 DW	1
Oceanic whitetip shark, *Carcharhinus longimanus*; Puerto Rico		
Liver	1.3 FW; 2.2 DW	1
Muscle	0.5 FW; 2.4 DW	1
Skin	8.6 FW; 21.0 DW	1
Vertebra	3.5 FW; 11.0 DW	1
White sucker, *Catostomus commersoni*; northern Ontario; September 1986; copper-contaminated site (water 9.7 µg Cu/L, sediments 232 mg/kg DW) vs. reference site (2.1 µg/L water, 10 mg/kg DW sediments)		
Feces	208 DW vs. 49 DW	53
Gill	15 DW vs. 6 DW	53
Kidney	26 DW vs. 14 DW	53
Liver	83 DW vs. 50 DW	53
Stomach Contents	155 DW vs. 7 DW	53
Blackfin icefish, *Chaenocephalus aceratus*; Antarctica; 1989		
Liver	4.5 FW	44
Muscle	1.5 DW	44
African sharp-tooth catfish, *Clarias gariepinus*; South Africa; 1988-89; metals-contaminated lake (sediments 216 mg Cu/kg DW)		
Muscle, body fat, vertebra, gonads	9-15 DW	54
Intestine, spleen, liver, kidney, heart, gills	26-46 DW	54
Brain	100 DW	54
Lake whitefish, *Coregonus clupeaformis*; liver, Lake Superior vs. Lake Michigan	2.4 FW vs. 8.5 FW	1
Bloater, *Coregonus hoyi*; liver;		

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Lake Superior vs. Lake Michigan	2.4 FW vs. 7.4 FW	1
Spotted seatrout, *Cynoscion nebulosus*; whole; South Carolina; 1990-93	0.03-2.9 FW (0.0-19.0) FW	55
Adriatic anchovy, *Engraulis encrasicolus*		
Liver	3.9 FW	1
Muscle	0.7 FW	1
Whole	1.1 FW	1
Northern pike, *Esox lucius*; Ontario		
Gill	1.9 FW	1
Kidney	2.6 FW	1
Liver	10.9 FW	1
Freshwater fishes; Lake Tanganyika, Burundi; two commercially important species, *Lates* sp., *Stolothrissa* sp.)		
Gonads	2.0 DW	56
Heart	2.9 DW	56
Intestine	3.2 DW	56
Liver	11.9 DW	56
Muscle	1.7 DW	56
Whole	3.2 DW	56
Freshwater fishes; Tennessee; muscle	0.1-0.9 FW; Max. 2.2 FW	58
Freshwater fishes; USA, nationwide; whole; 8 species		
1984	0.65 FW; Max. 23.1 FW	57
1980-81	0.65 FW; Max. 24.1 FW	57
1978-79	0.82 FW; Max. 38.7 FW	57
Mummichog, *Fundulus heteroclitus*; whole		
Body length 40-51 mm	59 AW	132
Body length 54-121 mm	45-49 AW	132
Atlantic cod, *Gadus morhua*; Norway		
Gill	(4-19) DW	1
Liver	(8-18) DW	1
Muscle	(1-3) DW	1
Brown bullhead, *Ictalurus nebulosus*; Ontario, Canada		
Gill	1.8 FW	1
Kidney	2.5 FW	1
Liver	30.3 FW	1
Muscle	1.3 FW	1
Dab, *Limanda limanda*; liver; German Bight; March 1990; males vs. females	4.3-10.4 FW vs. 5.5-16.0 FW	130
Black marlin, *Makaira indica*; Australia		
Liver	4.6 (0.5-22.0) FW	1
Muscle	0.4 (0.3-1.2) FW	1
Blue marlin, *Makaira nigricans*; muscle		
Japan	0.4 (0.1-0.7) FW	1
Puerto Rico	1.3 (0.4-2.6) FW; 2.7 (1.5-10.0) DW	1
Red mullet (Mullidae), *Mullus barbatus*; gills; Coutou, France	17.6-48.1 DW	59
Hump rock cod (Notothenidae), *Notothenia gibberifrons*; Antarctica;	0.85 DW	44

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
1989; muscle		
Kelp bass, *Paralabrax clathratus*; California; Los Angeles site near effluent discharge of steam utility plant vs. Catalina Island (reference site)		
Eyeball	8.0 DW vs. 4.0 DW	1
Gonad	6.0 DW vs. 5.0 DW	1
Heart	1.5 DW vs. 12.0 DW	1
Liver	5.0 DW vs. 6.0 DW	1
Muscle	5.0 DW vs. 2.0 DW	1
Southern flounder, *Paralichthys lethostigma*; South Carolina; 1990-93; whole	1.1-1.9 (0.0-22.2) FW	55
Yellow perch, *Perca flavescens*; Michigan; 1993; Torch Lake (34 µg Cu/L) vs. reference site (10 µg Cu/L)		
Ovaries	5.0 DW vs. 2.1 DW	60
Testes	3.5 DW vs. 1.3 DW	60
Southern mouth brooder, *Pseudocrenilabrus philander*; South Africa; whole fish; mine-polluted impoundment	9 (4-26) DW	61
Winter flounder, *Pleuronectes americanus*		
New York		
Muscle	(0.5-1.1) FW	1
Liver	(2.7-13.8) FW	1
Texas		
Muscle	1.0 (0.6-1.5) DW	1
Skin	1.7 (1.2-2.1) DW	1
Atlantic guitarfish, *Rhinobatos lentiginosus*		
Liver	6.6 DW	1
Muscle	2.2 DW	1
Stomach	6.2 DW	1
Red drum, *Sciaenops ocellatus*; South Carolina; 1990-93; whole	0.4-9.2 (0.0-52.9) FW	55
Spanish mackerel, *Scomberomorus maculatus*		
Liver	3.3 DW	1
Muscle	2.3 DW	1
Painted comber, *Serranus cabrilla*; gills; Coutou, France	5.3-27.2 DW	59
Sharks, 10 species; British and Atlantic waters; 1984-88		
Gills	0.05-2.2 FW	62
Gonads	0.1-4.9 FW	62
Heart	0.03 FW	62
Jaws	1.7-3.3 FW	62
Kidney	0.02-4.0 FW	62
Liver	0.2-7.8 FW	62
Muscle	0.2-2.4 FW	62
Pancreas	0.7 FW	62
Skin	0.6-12.1 FW	62

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Spleen	0.03-2.5 FW	62
Vertebra	0.5-5.9 FW	62
Spiny dogfish, *Squalus acanthias*		
Liver	4.5 DW	1
Muscle	2.3 DW	1
Spleen	16.0 DW	1
Bluefin tuna, *Thunnus thynnus*; Spain		
Heart	4.2 FW; 18.1 DW	1
Intestine	1.4 FW; 5.8 DW	1
Kidney	8.6 FW; 27.8 DW	1
Liver	74.0 FW; 245.0 DW	1
Ovary	(1.4-2.3) FW; (5.4-11.0) DW	1
Spleen	1.2 FW; 4.4 DW	1
Red hake, *Urophycis chuss*		
Liver	(3.2-6.0) FW	1
Muscle	(0.5-0.7) FW	1
Swordfish, *Xiphias gladius*; muscle	(0.3-1.4) FW	1
Amphibians and reptiles		
Frogs; Maryland, 1990-91; tadpoles		
Northern cricket frog, *Acris crepitans*;whole	9.8-15.7 DW	131
Gray treefrog, *Hyla versicolor*; whole	7.4-12.6 DW	131
Green frog, *Rana clamitans*		
Gut vs. remainder	21.5 DW vs. 6.7 DW	131
Frogs and toads; Yugoslavia; liver; near mercury mines		
European toad, *Bufo bufo*	56.2-81.4 FW	1
Toad, *Bombina variegata*	(5.0-5.6) FW	1
European frog, *Rana temporaria*	318.9 FW	1
Giant toad, *Bufo marinus*; liver		
Australia	Max. 1,640 DW	63
Dominican Republic		
Black livers	1,248-2,091 DW	63
Yellow livers	367-469 DW	63
American crocodile, *Crocodylus acutus*; egg; Florida	(0.9-15.0) FW	1
Birds		
Western grebe, *Aechmophorus occidentalis*;		
Puget Sound, Washington; 1985-86; sediments had 52 mg Cu/kg DW		
Diet (fish muscle)	0.3-0.5 FW	64
Liver	12.7-17.6 DW	64
Mallard, *Anas platyrhynchos*; Canada; 1975; feathers; near smelter vs. reference site	23 DW vs. 7-14 DW	65
Black duck, *Anas rubripes*		
Canada; 1975; feathers; near smelter vs. reference site	53 DW vs. 10 DW	65
Ducks, *Anas* spp.; Poland; 1988-91		
Kidney	9.9 (3.5-30.0) FW	66
Liver	58.0 (11.0-200.0) FW	66
Muscle	4.5 (2.1-10) FW	66
Geese, *Anser* spp.; Poland; 1988-91		

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Liver	80 (29-160) FW	66
Muscle	4.0 (1.6-8.8) FW	66
Antarctica; February-March 1989		
Blue eyed cormorant, *Phalacrocorax atriceps*; muscle	10 DW	67
Southern giant petrel, *Macronectes giganteous*; muscle	7.2 DW	67
Adelie penguin, *Pygoscelis adeliae*		
Liver	11.9 (11.0-12.6) DW	67
Muscle	7.9 (6.5-8.5) DW	67
Chinstrap penguin, *Pygoscelis antarctica*		
Feces	37.6 (35.1-49) DW	67
Liver	12.6 (12-13) DW	67
Muscle	9.7 (9.5-10.1) DW	67
Gentoo penguin, *Pygoscelis papua*		
Liver	26.5 (24.0-27.6) DW	67
Muscle	8.2 (7.7-8.9) DW	67
Redhead, *Aythya americana*; Louisiana and Texas; 1987-88; liver	7.3 (3.9-11.5) DW	68
Canvasback, *Aythya valisineria*; Louisiana; 1987-88; liver; females	Usually 76-187 DW	69
Ruffed grouse, *Bonasa umbellus*; liver	5.2 FW	3
Lesser kestrel, *Falco naumanni*; nonviable eggs; Spain; 1988-91	3.1 (0.2-7.1) FW	3
Bald eagle, *Haliaeetus leucocephalus*; eggs		
Florida	(0.7-1.2) FW; (4.8-8.0) DW	1
Maine	(0.3-0.6) FW; (2.0-5.0) DW	1
Wisconsin	(0.5-1.2) FW; (3.0-9.0) DW	1
Willow ptarmigan, *Lagopus lagopus*; Norway; winter 1986-87; kidney; adults vs. juveniles	2.8-4.9 FW (Max. 8.0 FW) vs. 1.9-3.6 FW (Max. 5.5 FW)	71
Lesser black-backed gull, *Larus fuscus*		
Egg	1.0 FW	1
Kidney	14.0 DW	1
Liver	17.0 DW	1
Muscle	14.0 DW	1
Marine birds, New Zealand; 1975-83		
Albatrosses, eight species; adults vs. juveniles		
Feather	44.0 FW vs. 18.4-32.3 FW	72
Liver	5.0-8.6 FW vs. 12.2-225.3 FW	72
Gulls, *Larus* spp.; adults vs. juveniles		
Feather	13.1-20.0 FW vs. 25.3-60.5 FW	72
Liver	5.0-6.6 FW vs. 23.8-35.0 FW	72
Penguins, three species; liver; adults vs. juveniles	4.3-13.2 FW vs. 8.5-18.5 FW	72
Petrels, 19 species; adults vs. juveniles		
Feather	14-40 FW vs. 20-79 FW	72
Liver	4-45 FW vs. 8-75 FW	72
Shearwaters, three species of *Puffinus*; liver; adults vs. juveniles	6.4-7.2 FW vs. 4.6-446.3 FW	72
Surf scoter, *Melanitta perspicillata*; San Francisco Bay; 1985; liver; January vs.	37.8 (29.3-47.0) DW vs. 50.1 (41.3-58.3) DW	73

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
March		
Turkey, *Meleagris gallopavo*; Poland; 1988-91		
Kidney	3.0 (2.3-5.2) FW	66
Liver	4.7 (3.1-13.0) FW	66
Muscle	0.3 (0.2-0.4) FW	66
Brown pelican, *Pelecanus occidentalis*		
Egg		
Florida	(0.9-1.1) FW	1
South Carolina	(0.7-1.3) FW	1
Liver; Florida, Georgia, South Carolina	(4.3-9.0) FW	1
Flamingo, *Phoenicopterus ruber roseus*; France; 1988		
Blood serum, nestlings	0.25 (0.13-0.51) FW	74
Feather, adults	Max. 7.43 DW	74
Seabirds, 19 species; pelagic; North Pacific Ocean; 1982-87		
Kidney	4.7 FW	75
Liver	5.9 FW; Max. 7.7 FW	75
Muscle	5.1 FW	75
Shorebirds; Chile; November 1981-March 1982; near abandoned copper mine; liver vs. stomach contents		
Sanderling, *Calidris alba*	(9.2-11.5) FW vs. no data	76
Oyster catcher, *Haematopus ostralegus*	8.0 (6.8-8.6) FW vs. (24.4-27.2) FW	76
Kelp gull, *Larus dominicanus*	(3.8-6.3) FW vs. (0.8-3.4) FW	76
Grey gull, *Larus modestus*	6.2 (4-7.4) FW vs. (30-46.7) FW	76
Franklin's gull; *Larus pipixcan*	(4.7-5.5) FW vs. no data	76
Whimbrel, *Numenius phaeopus*	(3.9-17.8) FW vs. (6.1-86.4) FW	76
Eider, *Somateria mollissima*; Norway		
Egg	4.0 DW	1
Kidney	43.0 DW	1
Liver	367.0 DW	1
Muscle	13.0 DW	1
Tree swallow, *Tachycineta bicolor*; nestlings; acidified (pH 4.8) vs. reference (pH 6.7) lakes; Ontario, Canada; 1986-89		
Kidney	12.8 DW vs. 10.4 DW	77
Liver	42.6 DW (elevated metallothionein) vs. 17.3 DW	77
Redshank, *Tringa totanus*; liver; feeding on sandworms (*Nereis diversicolor*) containing 500-1,000 mg Cu/kg DW	30 DW	78
Marine mammals		
Gray whale, *Eschrichtius robustus*; stranded along North American west coast; 1988-91		
Brain	2.4 FW	79
Kidney	2.4 (0.5-4.9) FW	79
Liver	9.2 (0.6-25.0) FW	79
Stomach contents	21.0 (3.0-66.0) FW	79

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Pilot whale, *Globicephala melaena*; stranded on Cape Cod, Massachusetts, 1986-90		
Adults		
Brain	9.1 (5.7-12.3) DW	80
Kidney	14.7 (7.4-21.0) DW	80
Liver	15.5 (9.9-20.3) DW	80
Ovary	5.5 (2.8-8.4) DW	80
Fetuses		
Brain	5.1 (4.4-6.2) DW	80
Kidney	20.0 (8.1-28.1) DW	80
Gray seal, *Halichoerus grypus*; British Isles and vicinity; 1988-89		
Blubber	<0.1 FW	81
Kidney	(3.2-27.0) FW	81
Liver	(4.0-26.0) FW	81, 82
Muscle	2.5 FW	81
Leopard seal, *Hydrurga leptonyx*; Antarctic; 1989		
Kidney	32.6 (22.5-43.8) DW	83
Liver	105.0 (98.0-116.0) DW	83
Muscle	4.0 (2.5-8.4) DW	83
Stomach contents	14.4 (13.3-16.4) DW	83
Pygmy sperm whale, *Kogia breviceps*; Argentina; found dead		
Heart	6.9 FW	84
Kidney	7.4 FW	84
Liver	10.3 FW	84
Other tissues	<2.3 FW	84
Weddell seal, *Leptonychotes weddelli*; Antarctic; 1989		
Kidney	22.8 (21.7-24.5) DW	83
Liver	57.4 (28-87) DW	83
Muscle	2.8 (2.1-3.1) DW	83
Crabeater seal, *Lobodon carcinophagus*; Antarctic 1989		
Kidney	25.6 (18.9-39.5) DW	83
Liver	71.1 (42-105) DW	83
Muscle	3.3 (2.7-4.3) DW	83
Harbour seal, *Phoca vitulina*; British Isles; 1988-89; liver	7-21 FW	82
Common harbour porpoise, *Phocoena phocoena*		
England; 1988-89; liver	6-160 FW	82
Greenland; 1988-89		
Kidney	5.5 (3.7-8.0) FW	85
Liver	12.0 (5-50) FW	85
Muscle	2.0 (1.1-5.4) FW	85
Skin	1.0 (0.6-1.9) FW	85
Whales; unidentified; 1989; found dead		
Blubber	0.2-1.7 FW	81
Liver	6.6-8.7 FW	81
Muscle	3.0 FW	81

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
La Plata river dolphin, *Pontoporia blainvillei*; Argentina; found dead		
Kidney	14 FW	84
Liver	16 FW	84
Other tissues	<2.8 FW	84
Striped dolphin, *Stenella coeruleoalba*; Wales; 1989; found dead		
Blubber	0.3-0.7 FW	81
Muscle	2.1 FW	81
Manatee, *Trichechus manatus*; Florida; 1977-81; liver	175.0 (4.4-1,200.0) DW	86
Dolphin, *Tursiops gephyreus*; Argentina; found dead		
Blubber	4.0 FW	84
Kidney	29.5 FW	84
Liver	77.7 FW	84
Melon	2.7 FW	84
Muscle	6.3 FW	84
Stomach contents	1.2 FW	84
Bottlenose dolphin, *Tursiops truncatus*		
England; 1988-89; liver	4-12 FW	82
Wales; 1989		
Blubber	0.9-1.1 FW	81
Muscle	2.5 FW	81
Polar bear, *Ursus maritimus*		
Canada, Northwest Territories; 1982-84; liver	81-146 DW	87
Svalbard (Arctic Ocean region); 1978-89; adults vs. juveniles		
Kidney	8.3 FW vs. 6.2 FW	88
Liver	42 FW vs. 33 FW	88
Welsh coast and Irish Sea; adults of 17 species of marine mammals; found dead; 1989-91; liver	Usually between 3.2 and 30.0 FW	89
Terrestrial mammals		
Impala, *Aepyceros melampus*; Kruger National Park, South Africa; 1989		
Kidney	(3-141) FW	90
Liver	(3-444) FW	90
Moose, *Alces alces*		
Alaska		
Hair	(5.2-11.7) DW	1
Hoof	(3.2-5.3) DW	1
Estonia; 1980-82		
Kidney	5.1 FW	91
Liver	3.1 FW	91
Poland; 1977-87; muscle	(0.9-2.6) FW	91
Sweden; 1979-80		
Kidney	(2.2-7.4) FW	91
Liver	(3.2-96.0) FW	91

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Arctic fox, *Alopex lagopus*; Norway; 1984-86; liver	6.0 (2.4-26.0) FW	92
Wood mouse, *Apodemus sylvaticus*		
Kidney	(3.7-6.0) FW	1
Liver	(2.6-18.1) FW	1
Testes	(12.2-18.7) FW	1
Whole	(2.8-5.5) FW	1
Bison, *Bison bison*; Canada; 1986		
Kidney	6.7 (5.5-8.0) FW	91
Liver	35 (13-52) FW	91
European bison, *Bison bonasus*; Poland; 1987		
Kidney	4.4 FW	91
Liver	3.4 FW	91
Muscle	2.0 FW	91
Cattle, *Bos* spp.		
Poland; 1987-91		
Kidney	5.6 FW	93
Liver	29.0 FW	93
Muscle	1.2 FW	93
South Africa; 1989; found dead near copper smelter; surface soil had 103 mg Cu/kg DW (14 at reference site)		
Kidney	36 (6-83) FW; 108 DW	90
Liver	359 (161-600) FW; 1,078 DW	90
Various locations; liver	38.2-156.1 DW	94
Water buffalo, *Bubalus* sp.; Kruger National Park, South Africa; 1989; liver	Usually 18-80 FW; (6-144) FW	90
Bactrian camel, *Camelus bactrianus*; China; 1992		
Normal		
Blood	0.86 FW	95
Hair	6.4 DW	95
Camels with sway disease (severe copper deficiency)		
Nonpregnant females		
Blood	0.36 FW	95
Hair	4.3 DW	95
Pregnant camels vs. post-partum		
Blood	0.17 FW vs. 0.26 FW	95
Hair	3.0 DW vs. 3.3 DW	95
Dog, *Canis familiaris*		
Brain	3.9 FW; 19 DW	96
Kidney	6.9 FW; 26 DW	96
Liver	82 FW; 336 DW	96
Muscle	1.1 FW; 3.7 DW	96
Serum	0.7 FW	96
Whole body	2.3 FW	96
Coyote, *Canis latrans*; kidney	5.2 FW	97
Goat, *Capra hircus*; mother vs. newborn		
Hair	8.9 DW vs. 8.3 DW	1
Kidney	9.8 DW vs. 19.0 DW	1

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Liver	11.3 DW vs. 63.3 DW	1
Roe deer, *Capreolus capreolus*; Poland; 1987-91		
Kidney	7.8 FW	91
Liver	28.0 FW	91
Muscle	4.5 FW	91
European red deer, *Cervus elaphus*		
The Netherlands; 1989-92		
Kidney	54-86 DW	98
Liver	14-18 DW	98
Poland; 1986-91		
Kidney	5.4 FW	91
Kidney	9.4 DW	99
Liver	12.0 FW	91
Muscle	6.3 FW	91
Muscle	19.0 DW	99
Bank vole, *Clethrionomys glareolus*		
Poland; 1990; whole, less stomach and gastrointestinal tract	5.7-9.5 DW	100
Poland; 1985; various sites		
Bone	18.2-22.7 DW	101
Fur	12.0-14.5 DW	101
Kidney	43.4-73.8 DW	101
Liver	27.6-31.2 DW	101
Remainder	12.5-28.8 DW	101
Horse, *Equus caballus*; liver	10.3-51.5 DW	94
North American porcupine, *Erethizon dorsatum*		
Heart	8.4 FW	97
Lung	4.7 FW	97
Human, *Homo sapiens*		
Healthy adults vs. adults with Wilson's Disease		
Bone	2.9 FW vs. 31.0 FW	58
Brain	5.4 FW vs. 54.9 FW	58
Cornea	3.8 FW vs. 35.1 FW	58
Kidney	2.8 FW vs. 36.2 FW	58
Liver	7.8 FW vs. 99.2 FW	58
Normal adults		
Aorta	82-280 AW	97
Blood	1.0 FW	102
Brain	310-540 AW	97
Hair	31 DW	102
Heart	310-420 AW	97
Kidney	220-880 AW	97
Liver	480-2,000 AW; 10 FW	58, 97
Lung	140-470 AW	97
Pancreas	96-310 AW	97
Serum	1.64 FW	102
Spleen	93-470 AW	97
Whole body	1.4 (1.0-1.7) FW	58, 102
Fetus (33 weeks)	22.0 FW	103

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Full term (still birth)	37.9 FW	103
Newborn, whole	4.0 FW	102
Diet, adults		
Beverages	0.44 FW	97
Condiments	6.8 FW	97
Dairy products	1.8 FW	97
Most fruits	0.82 FW	97
Coconut seed	3.3 FW	97
Most grains and cereals	2.0 FW	97
Grapenuts®	15.0 FW	97
Meats	3.9 (0.95-11.0) FW	97
Beef liver	11.0 FW	97
Nuts	14.8 FW	97
Most oils and fats	4.6 FW	97
Lecithins	21.0 FW	97
Most seafoods	1.5 (0.5-3.4) FW	97
Oysters	137.1 FW	97
Most vegetables	1.2 FW	97
Peas, split, green, dry	12.3 FW	97
Woodchuck, *Marmota monax*; liver	9.4 FW	97
Mice, *Mus* spp.		
Fat	2.4 FW	97
Kidney	3.8 FW	97
Liver	2.0 FW	97
Lung	3.9 FW	97
Deer, *Odocoileus* spp.		
Brain	0.3-2.4 FW	97
Hooves	0.6 FW	97
Kidney	5.8-8.4 FW	97
White-tailed deer, *Odocoileus virginianus*; Texas; 1979-80; uranium mining district vs. reference site		
Antlers	16.7 (0.5-71.0) FW vs. 18.0 (0.6-94.0) FW	104
Liver	0.5-94.0 FW vs <1.0->70.0 FW	104
Muskrat, *Ondatra zibethicus*; Virginia; 1986-88; contaminated site (many chemicals; 68 mg Cu/kg DW sediment) vs. reference site (26 mg Cu/kg DW sediment); kidney	12.9 DW vs. 11.1 DW	105
Rabbit, *Oryctolagus* sp.; Poland; 1990; industrialized area vs. reference site		
Heart	5.9 FW vs. 3.0 FW	106
Kidney	6.6 FW vs. 2.6 FW	106
Liver	5.8 FW vs. 3.1 FW	106
Muscle	2.4 FW vs. 1.2 FW	106
Muskox, *Ovibus moschatus*; Canadian Arctic; 1985-90		
Kidney	11 DW	107
Liver	67 DW	107
Domestic sheep, *Ovis aries*		
Copper-poisoned vs. normal sheep		

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Blood	1.74-9.1 FW vs. 0.6-1.6 FW	108
Kidney	60 FW vs. 5 FW	109
Liver	432 FW vs. 12 FW	109
Muscle	2.5 FW vs. 2.1 FW	109
Spleen	19 FW vs. 5 FW	109
England; in paddock near heavily traveled highway for 150 days vs. reference site		
Blood	0.98 FW vs. 0.97 FW	110
Wool, tip	28.6 DW vs. 12.4 DW	110
Poland; 1988-91		
Kidney	5.7 (3.1-13.0) FW	66
Liver	41 (7-98) FW	66
Muscle	0.9 (0.8-1.3) FW	66
Raccoon, *Procyon lotor*; fat	1.2 FW	97
Caribou, *Rangifer tarandus*; Canadian Arctic; 1985-90		
Kidney	29 DW	107
Liver	68 DW	107
Rat, *Rattus* spp.		
Mature and aged		
Brain	6.6 FW	97
Heart	1.0 FW	97
Kidney	0.9 FW	97
Liver	0.7 FW	97
Lung	0.9 FW	97
Spleen	0.3 FW	97
Tumors		
Hepatic	2.5 FW	94
Ovarian	5.9 FW	97
Mammarian	1.3 FW	97
Young, whole	0.52 FW	97
Gray squirrel, *Sciurus carolinensis*; liver	4.8 FW	97
Shrews, *Sorex* spp.; England; 3 km from lead-zinc smelter vs. 23 km		
Carcass		
Immature	21.2 DW vs. 11.9 DW	111
Mature	21.7 DW vs. 13.1 DW	111
Kidney		
Immature	19.2 DW vs. 6.5 DW	111
Mature	13.6 DW vs. 8.8 DW	111
Liver		
Immature	32.5 DW vs. 14.8 DW	111
Mature	23.3 DW vs. 22.9 DW	111
Rock squirrel, *Spermophilus variegatus*		
Bone	(4.0-7.8) DW	1
Liver	(12.1-24.1) DW	1
Wild boar, *Sus scrofa*		
Germany; 1988; near metal foundry vs. reference site; liver	20.0 (10.9-49.6) FW vs. 15.9 (5.7-26.7) FW	112
The Netherlands; 1989-92; kidney vs. liver	17-24 DW vs. 4-20 DW	
Poland, 1986-91		

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Kidney	1.7 FW; 17.2-24.5 DW	91, 99
Liver	1.8 FW	91
Muscle	1.6 FW; 6.4-7.4 DW	91, 99
Swine, *Sus* sp.; Poland; 1987-91		
Kidney	8.4 (2.1-44.0) FW	113
Liver	8.5 (1.1-41.0) FW	113
Muscle	1.1 (0.1-14.0) FW	113
Red fox *Vulpes vulpes*; liver	41.8 FW	97
Integrated studies		
Canada; northern Ontario; August 1988; Lake		
Manitouwadge (contaminated) vs. Lake Wowun (reference site)		
Sediments	93 DW vs. 3 DW	114
Water (soluble copper)	0.015 FW vs. 0.002 FW	114
Invertebrates	89 DW vs. 57 DW	114
White sucker, *Catostomus commersoni*		
Bone	4 DW vs. 3 DW	114
Digestive tract	107 DW vs. 16 DW	114
Gill	9 DW vs. 3 DW	114
Kidney	31 DW vs. 10 DW	114
Liver	98 DW vs. 46 DW	114
Muscle	5 DW vs. 3 DW	114
Ovary	13 DW vs. 8 DW	114
Testes	10 DW vs. 2 DW	114
Canada; Sudbury, Ontario; 1970		
Soils; distance from smelter		
0.8-1.9 km	940-2,070 DW	115
7.4-13.5 km	940-1,620 DW	115
49.8 km	20-30 DW	115
Red maple, *Acer rubrum*; foliage; distance from smelter		
1.6 km	37 DW	115
6.5-18 km	19-28 DW	115
Wavy hairgrass, *Deschampia flexuosa*; distance from smelter		
1.6 km	726 DW	115
7.4 km	103 DW	115
49.8 km	13 DW	115
Lowbush blueberry, *Vaccinium angustifolium*; foliage; distance from smelter		
1.6 km	75 DW	115
4.6 km	35 DW	115
6.5-31 km	14-22 DW	115
India; river near Madras; receives industrial wastes		
Sediments	760-930 DW	116
Water	0.01-0.04 FW	116
Alga, *Enteromorpha intestinalis*; whole	12.3 FW	116
Oyster, *Crassostrea madrasensis*; soft parts	4.2 FW	116
Crustaceans, whole	Max. 18.4 FW	116

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Fishes, muscle	Max. 0.09 FW	116
Israel; Acre Valley; 1988-91		
Mollusks; soft parts		
Bivalves	9.4-13.3 DW	117
Gastropods	31.0-48.0 DW	117
African sharp-tooth catfish, *Clarias gariepinus*; liver	Max. 92.0 DW	117
Italy; Goro Bay; 1991-92		
Sediments	42-54 DW	118
Seawater	0.0005-0.0022 FW	118
Mussel, *Mytilus galloprovincialis*; soft parts; purged for 48 h in aerated synthetic seawater vs. not purged	6.9 DW vs. 13.1 DW	118
New Zealand; pasture soil contaminated by runoff from an adjacent timber treatment plant; 1993; copper-contaminated soils (70-1,233mg Cu/kg DW soil) vs. reference site (25 mg Cu/kg DW soil)	In less-contaminated soils, plant-feeding nematodes were predominant. With increasing copper loadings, bacterial-feeding and predatory nematodes dominated; at highest loadings, microbial biomass declined	119
New Zealand; pasture contaminated by runoff from chromated copper arsenate timber preservation facility; 1991; control surface soils contained an average of 19 mg Cu/kg DW, low contamination 109 mg/kg, medium contamination 425 mg/kg, and high contamination 835 mg/kg DW soil		
Vegetation	Herbage yield decreased with increasing copper loadings; after35 days roots had 10.5 mg Cu/kg DW in controls, 14.6 in low group, in medium group and 23.9 in high group 18.4	120
Earthworms, *Lumbricus rubellus*, *Aporrectodea rosea*	Earthworms absent from plats with medium and high contamination. Surface casts of *L. rubellus* had 17.5 mg/kg DW in low contamination soils vs. 7.0 in controls for *A. rosea* these values were 13.3 vs. 7.0	120
Nematodes	Most abundant in low-contamination soils; proportion of predatory nematodes in population increased with increasing copper contamination	120
Soil microflora	Reduced with increasing contamination	120
Norway; small lakes; 1991; near highway vs. reference site		
Freshwater mussel, *Anodonta piscinalis*; soft parts	3.5 FW vs. 3.1 FW	121
Perch, *Perca fluviatilis*		
Liver	1.6 FW vs. 1.5 FW	121
Muscle	0.16 FW vs. 0.19 FW	121
South Africa; metal-polluted wetland; 1989		
Sediments	67.4 (44.3-93.3) DW	122
Sago pondweed, *Potamogeton pectinatus*; whole	29.0 DW	122

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Red-knobbed coot, *Fulica cristata*; feeding on *Potamogeton pectinatus*		
Egg contents	8.5 DW	122
Egg shell	5.5 DW	122
Gonads	32.6 (10.8-59.9) DW	122
Internal organs	24.5 (0.4-125.1) DW	122
Stomach contents	37.0 (11.3-90.1) DW	122
Wales; 1989; coastal area		
Sediments	8.0 DW	123
Anemones, whole	0.6 FW	123
Soft corals, whole	1.0 FW	123
Mussels, soft parts	1.2 FW	123
Crab, hepatopancreas	58.0 FW	123
Lugworms, whole	3.9 FW	123
Tunicates, whole	2.6 FW	123
Fishes, four species; liver	1.6-4.4 FW	123
United States; Florida; 1979; national wildlife refuge; treated with copper-containing herbicides vs. nontreated areas		
Water	Max. 0.56 FW after 1 h to 0.04 FW after 24 h vs. 0.027 FW	124
Detritus	Max. 20.1 DW after 7 days vs. 12-13 DW	124
Aquatic plants	Max. 151.3 DW after 14 h vs. 9-10 DW	124
Apple snail, *Pomacea paludosa*; soft parts		
Adults	82.3 DW after 7 days vs. 17-21 DW	124
Immatures	80.3 DW after 7 days vs. 11-22 DW	124
United States; Kansas: 1990; near landfill; upstream vs. downstream site		
Sediments	8.2-17.9 DW vs. 12.4-14.6 DW	125
Water	0.01-0.018 vs. 0.007-0.019 FW	125
Crayfish, *Orconectes nais*; whole	60.3-61.3 DW vs. 56.2-77.7 DW	125
Orangespotted sunfish, *Lepomis humilis*; whole	1.5-7.3 DW vs. 1.4-2.5 DW	125
United States; Maryland and Pennsylvania; 1985; at disposal facilities for dredged materials; low soil copper site (15 mg/kg DW)		
vs. high soil copper site (150 mg/kg DW)		
Common reed, *Phragmites australis*; whole	2.8 DW vs. 4.7 DW	126
Ladybug, *Coccinella septempunctata*; whole	14 DW vs. 17 DW	126
Earthworms, *Eisenia foetida*; whole	21 DW vs. 57 DW	126
House mouse, *Mus musculus*; whole less skin and tail	13 DW vs. 18 DW	126
United States; Montana; 1990; wetland conta minated by mining wastes (arsenic, cadmium, copper, lead, zinc)		
Soil	532.0 DW	127
Water	0.078 FW	127
Vegetation		
Aboveground	7.2-24.2 DW	127

Table 3. Taxonomic group, organism, and other variables	Concentration[a] in (mg/kg)	Reference[b]
Belowground	75.0-274.0 DW	127
Meadow vole, *Microtus pennsylvanicus*		
Carcass	2.8 FW	127
Kidney	5.1 FW	127
Liver	4.2 FW	127
Testes	1.9 FW	127
Deer mice, *Peromyscus maniculatus*		
Carcass	3.4 FW	127
Kidney	5.7 FW	127
Liver	5.7 FW	127
Testes	1.5 FW	127
United States; Ohio; 1987; old-field community; treated with sewage sludge for 10 years beginning in 1978; treated plots vs. reference site		
Sludge	320-381 DW vs. not applicable	128
Soil	Sludge loading equivalent to 15-37 DW vs. no data	128
Plants, stems		
Japanese brome, *Bromus japonicum*	5.9 DW vs. 6.0 DW	128
Bluegrass, *Poa* spp.	7.4 DW vs. 6.3 DW	128
Raspberry, *Rubus* sp.	4.7 DW vs. 3.4 DW	128
Foxtail, *Setaria* sp.	6.3 DW vs. 2.9 DW	128
Earthworms, *Lumbricus rubellus*	17-23 DW vs. no data	128
Meadow vole, *Microtus pennsylvanicus*		
Kidney	3.3 DW vs. 3.0 DW	128
Liver	3.1 DW vs. 3.5 DW	128
United States; Pennsylvania; Palmerton zinc smelter; 1986 (6 years after smelter was closed); near smelter vs. distant sites		
Soil	190 DW vs. <30 DW	129
Litter	552 DW vs. <70 DW	129
Green frog, *Rana clamitans*; tadpoles; whole	0.8 FW vs. 0.3 FW	129
Eastern red-backed salamander, *Plethodon cinereus*; whole less gastrointestinal tract	2.2 FW vs. 1.7 FW	129
White-tailed deer, *Odocoileus virginianus*		
Bone	11 DW vs. 16 DW	129
Kidney	29 DW vs. 33 DW	129
Liver	122 DW vs. 149 DW	129
Eastern cottontail rabbit, *Sylvilagus floridanus*		
Bone	6.7 DW vs. 6.7 DW	129
Kidney	21.5 DW vs. 17.8 DW	129
Liver	19.2 DW vs. 14.8 DW	129
Muscle	11.9 DW vs. 9.6 DW	129

[a]Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND)

[b]1, Jenkins 1980; 2, NAS 1977; 3, Schroeder et al. 1966; 4, Hutchinson 1979; 5, Jozwik 1990; 6, Reed et al. 1993; 7, Veleminsky et al. 1990; 8, Berger and Dallinger 1993; 9, Lindquist 1993; 10, Heliovaara and Vaisanen 1990; 11, Morgan and Morgan 1990; 12, Clark 1992; 13, Larsen et al. 1994; 14, Karez et al. 1994; 15, Stokes 1979; 16, Brix and Lyngby 1982; 17, Jaffe et al. 1992; 18, Mauri et al. 1990; 19, Viarengo et al. 1993; 20, Mat

1994; 21, Mat et al. 1994; 22, Pip 1990; 23, Balogh and Mastala 1994; 24, Swaileh and Adelung 1994; 25, Cheung and Wong 1992; 26, Claisse and Alzieu 1993; 27, Han and Hung 1990; 28, Han et al. 1993; 29, Weis et al. 1993a; 30, Byers 1993; 31, Huggett et al. 1975; 32, Camusso et al. 1994; 33, Metcalfe-Smith 1994; 34, Miramand and Bentley 1992; 35, Bordin et al. 1994; 36, Paez-Osuna et al. 1994; 37, Turgeon and O'Connor 1991; 38, Greig and Sennefelder 1985; 39, Ward 1990; 40, Lauenstein et al. 1990; 41, Chu et al. 1990; 42, Talbot et al. 1985; 43, Brown and McPherson 1992; 44, Szefer et al. 1993; 45, Jorhem et al. 1994; 46, Sumi et al. 1991; 47, Petri and Zauke 1993; 48, Depledge et al. 1993; 49, Rainbow 1989; 50, Cain et al. 1992; 51, Moore et al. 1991; 52, Athalye and Gokhole 1991; 53, Munkittrick et al. 1991; 54, Bezuidenhout et al. 1990; 55, Mathews 1994; 56, Sindayigaya et al. 1994; 57, Schmitt and Brumbaugh 1990; 58, ATSDR 1990; 59, Romeo et al. 1994; 60, Ellenberger et al. 1994; 61, de Wet et al. 1994; 62, Vas 1991; 63, Goldfischer et al. 1970; 64, Henny et al. 1990; 65, Ranta et al. 1978; 66, Falandysz et al. 1994; 67, Szefer et al. 1993; 68, Michot et al. 1994; 69, Custer and Hohman 1994; 70, Negro et al. 1993; 71, Wren et al. 1994; 72, Lock et al. 1992; 73, Ohlendorf et al. 1991; 74, Amiard-Triquet et al. 1991, 75, Honda et al. 1990; 76, Vermeer and Castilla 1991; 77, St. Louis et al. 1993; 78, Bryan and Langston 1992; 79, Varanasi et al. 1994; 80, Meador et al. 1993; 81, Morris et al. 1989; 82, Law et al. 1991; 83, Szefer et al. 1994; 84, Marcovecchio et al. 1990; 85, Paludan-Muller et al. 1993; 86, O'Shea et al. 1984; 87, Braune et al. 1991; 88, Norheim et al. 1992; 89, Law et al. 1992; 90, Gummow et al. 1991; 91, Falandysz 1994; 92, Prestrud et al. 1994; 93, Falandysz 1993a; 94, Cuill et al. 1970; 95, Zong-Ping et al. 1994; 96, Goresky et al. 1968; 97, Schroeder et al. 1966; 98, Wolkers et al. 1994; 99, Swiergosz et al. 1993; 100, Zakrzewska et al. 1993; 101, Sawicka-Kapusta et al. 1990; 102, USEPA 1980; 103, Bakka and Webb 1981; 104, King et al. 1984; 105, Halbrook et al. 1993; 106, Krelowska-Kulas et al. 1994; 107, Gamberg and Scheuhammer 1994; 108, MacPherson and Hemingway 1969; 109, Todd 1969; 110, Ward and Savage 1994; 111, Read and Martin 1993; 112, Launer et al. 1991; 113, Falandysz 1993b; 114, Miller et al. 1992; 115, Hutchinson 1979; 116, Govindarajan and Rao 1992; 117, Fishelson et al. 1994; 118, Fagioli et al. 1994; 119, Bardgett et al. 1994; 120, Yeates et al. 1994; 121, Baekken 1994; 122, van Eeden and Schoonbee 1993; 123, Morris et al. 1989; 124, Winger et al. 1984; 125, Morrissey and Edds 1994; 126, Beyer et al. 1990; 127, Pascoe et al. 1994; 128, Levine et al. 1989; 129, Storm et al. 1994; 130, Hylland et al. 1992; 131, Sparling and Lowe 1996; 132, Eisler and LaRoche 1972.

Copper concentrations in terrestrial invertebrates from industrialized areas range from 137 to 408 mg/kg DW. Soil invertebrates are not likely to accumulate copper but are important in recycling copper through terrestrial food webs. Aquatic invertebrates seldom contain as much as 95 mg Cu/kg DW, regardless of collection locale; exceptions include whole amphipods and lobster hepatopancreas (335-340 mg/kg DW) from copper-contaminated sites and many species of mollusks that normally contain 1,100-6,500 mg Cu/kg DW (Table 3).

Maximum concentrations of copper in elasmobranchs and teleosts from all collection sites range from 7-15 mg/kg DW in eyeballs, intestines, muscle, scales, vertebrae, heart, and gonads and from 16-48 mg/kg DW in gills, kidneys, skin, and spleens and reach 53 mg/kg DW in whole animals, 155 mg/kg DW in stomach contents, 208 mg/kg DW in feces, and 245 mg/kg DW in livers (Table 3).

Data on copper concentrations in field collections of amphibians and reptiles are scarce. Crocodile eggs contain as much as 60 mg Cu/kg DW; however, some toads (*Bufo* spp.) may contain as much as 2,100 mg Cu/kg DW in livers without apparent adverse effects (Table 3; Goldfischer et al. 1970).

Birds from contaminated sites may contain as much as 9-28 mg Cu/kg DW in eggs, muscle, and stomach contents; 43-53 mg/kg DW in kidneys, feces, and feathers; and 367 mg/kg DW in livers (Table 3).

Marine mammals usually contain less than 44 mg Cu/kg DW in all tissues except livers. Copper in livers seldom exceeds 116 mg/kg DW except in polar bears (146 mg/kg DW), and manatees, *Trichechus manatus*, (1,200 mg/kg DW) from a copper-contaminated site (Table 3). Maximum copper concentrations in terrestrial mammals from all collection sites are usually less than 29 mg/kg DW in all tissues except kidneys (108 mg/kg DW) and livers (1,078 mg/kg DW; Table 3).

Abiotic Materials

Copper concentrations in abiotic materials are comparatively elevated near copper smelters and urban areas (Table 2). Copper concentrations are also elevated in drinking water from copper pipes, in poultry and livestock manures, mine tailings, fossil fuels, shales (Table 2), sewage sludge, and in wastes from plating

industries, foundries, and coking plants (ATSDR 1990). Drinking waters from certain locales contain elevated concentrations of copper added intentionally to control algal growth; drinking water may account for 10-20% of the daily intake of copper in humans (USEPA 1980).

Copper is found in the rocks and minerals of the earth's crust, occurring usually as sulfides and oxides, and sometimes as metallic copper (USEPA 1980). The mean concentration of copper in the upper lithosphere ranges from 70-100 mg/kg, ranking 14th of the trace elements in this compartment (Schroeder et al. 1966). Copper in the environmental crust averages 50 mg/kg, but is higher (140 mg/kg) in ferromagnesium minerals (NAS 1977). Soil contamination by copper occurs around all known smelter locations; contamination may persist for decades, and plants and animals are often unable to survive the harsh chemical environments created (Hutchinson 1979). Italian soils have higher copper concentrations (51 mg/kg DW) than those of other European countries, probably as a result of the widespread and prolonged application of copper-based fungicides in Italian orchards and vineyards (Arduini et al. 1995).

Copper concentrations in lake sediments within a radius of 80 km from a smelter in northern Sweden are positively correlated with proximity to the smelter (Johnson et al. 1992). In some cases, lake sediments are sinks for copper, with little release to the overlying lake water. For example, copper-bearing mine tailings in Butte Lake, British Columbia, do not undergo oxidative diagenesis because of a rapid rate of accumulation and short exposure time to dissolved oxygen in bottom waters (Pedersen 1983). In Michigan, lakes with elevated concentrations of copper (34 µg/L) have low densities of fish populations (Ellenberger et al. 1994). In the Elizabeth River estuary of southern Chesapeake Bay, anthropogenic copper and other chelatable metals are present at concentrations sufficient to adversely affect growth and survival of the copepod *Acartia tonsa* (Sunda et al. 1990). In Norway, freshwater fish are present only when copper is less than 60 µg/L and some humic acids are present (Hodson et al. 1979). Successful reproduction of the spotted salamander (*Ambystoma maculatum*) occurs at low water concentrations of copper (<10 µg/L), lead, and aluminum, and high concentrations of silicon. Failed reproduction occurs at low water concentrations of silicon, and elevated concentrations of copper (>25 µg/L), lead, and aluminum (Blem and Blem 1991).

In marine ecosystems, the high copper levels measured in heavily contaminated coastal areas sometimes approach the incipient lethal concentrations for some organisms (Neff and Anderson 1977). Elevated copper concentrations in marine and estuarine environments may result from atmospheric deposition, industrial and municipal wastes, urban runoff, rivers, and shoreline erosion. Chesapeake Bay, for example, receives more than 1,800 kg of copper daily from these sources (Hall et al. 1988). Copper concentrations in abiotic marine materials are generally higher near shore than off shore. Copper is elevated in sediments of many marinas, probably from the copper antifouling bottom paints used on boats housed in these marinas (Hall et al. 1988). In New Zealand, copper concentrations in contaminated inshore sediments frequently exceed 100 mg Cu/kg DW vs. 14 mg Cu/kg DW at noncontaminated sites (Roper and Hickey 1994). The fine particle fraction of sediments collected near bulkheads made of chromated copper arsenate (CCA)-treated wood contain elevated concentrations of copper, chromium, and arsenic; metal concentrations decreased with increasing distance from the bulkhead. Sediments, for example, decreased from 11 mg Cu/kg DW in the vicinity of treated bulkheads to less than 2 mg/kg DW at more distant sites (Weis and Weis 1994).

Terrestrial Plants and Invertebrates

In general, copper concentrations in terrestrial vegetation seldom exceed 35 mg/kg DW, except near point sources of copper contamination and in certain copper-tolerant species (Table 3). The highest copper concentration recorded in nonaccumulator plants is 726 mg/kg DW in hair grass (*Deschampsia flexuosa*) near a smelter (Table 3). Several species of terrestrial plants accumulate spectacular concentrations of copper. Mint plants (*Aeolanthus* spp., *Elsholtzia* spp.) growing in copper-rich soils contain unusually high concentrations and are used as economic indicators of copper deposits in the former Soviet Union and the People's Republic of China (Jenkins 1980). The copper plant mint (*Aeolanthus biformifolius*), for example, normally contains as much as 13,700 mg Cu/kg DW whole plant (Table 3). Copper-tolerant species of mosses, lichens, fungi, and higher plants occur in Greenland, Canada, the former Soviet Union, Africa, and elsewhere. In Zambia and Rhodesia, the copper-tolerant *Becium homblei* is found only in soils containing more than 1,000 mg Cu/kg and is believed responsible for the discovery of copper deposits in those nations (Hutchinson 1979). Some species of copper-indicator plants in Zambia tolerate as much as 70,000 mg Cu/kg in the soil and accumulate as much as 3,000 mg Cu/kg in leaves (Hutchinson 1979).

Copper is not accumulated from soils by most crop plants, suggesting a soil-plant barrier for copper (Levine et al. 1989). Thus, corn (*Zea mays*) did not accumulate copper from soils treated with 365 kg of copper per surface hectare (as copper-rich pig manure or copper sulfate) over a 13-year period; corn yield is not affected under these conditions (Reed et al. 1993).

Copper burdens in terrestrial invertebrates are highest in organisms collected near industrial locations and urban areas or from copper-contaminated soils. The highest copper concentration recorded among terrestrial invertebrates is 408 mg Cu/kg DW soft parts in gastropods from urban areas (Table 3). Copper concentrations in pine moths (*Bupalus piniaria*) and pine noctuids (*Panolis flammea*) from industrialized areas range from 89-137 mg/kg DW, but are lower than dietary concentrations and suggest negligible accumulation (Heliovaara and Vaisanen 1990). Accumulations of as much as 60 mg Cu/kg DW in 17-year cicadas (*Magicicada* spp.) pose no apparent dietary threat to insectivorous birds (Clark 1992).

Earthworms from soils heavily contaminated with copper (2,740 mg/kg DW soil) can regulate copper more efficiently than cadmium and lead. However, copper is more toxic to earthworms than lead or zinc in the soil due, in part, to the inability of most soft tissues to synthesize copper-binding ligands when challenged with copper (Morgan and Morgan 1990).

In woodland ecosystems, copper concentrations in the litter horizon are rarely exceeded by those in soil animals—which play a key role in copper cycling (Wieser 1979). Meiofaunal feces comprise an efficient distributing system through which copper and other nutrients are cycled through the food web of woodland ecosystems. During a 12-month cycle the total copper bound in litter progresses through a cycle of chemical binding states. It may be released from a strongly chelated organic complex as the litter is attacked by the digestive juices of animals or it may be discharged in soluble form with the feces and become complexed again by the activity of microorganisms in these feces. When feces are ingested by coprophagous animals, such as isopods, the copper may become trapped in proteins or membrane-bound vesicles (Wieser 1979).

Aquatic Organisms

Copper is essential for the successful growth and development of many species of aquatic organisms, but its rate and extent of accumulation and retention are modified by numerous biological and abiotic variables. Abiotic variables known to modify copper concentrations in tissues of aquatic biota include water temperature, pH, salinity, and depth; the presence of other inorganics, organics, and chelators; the chemical species of copper; and proximity to anthropogenic point sources of copper. Biological variables affecting copper accumulations in marine organisms include the organism's age, size, and developmental stage; physiological or genetic adaptation to high copper substrates; inherent species differences; and tissue specificity, such as the thorax of barnacles, gill and osphradium of gastropods, and livers of teleosts (Eisler 1979). Among marine organisms, the highest accumulations are generally found in molluskan tissues and soft parts, especially those of cephalopods and oysters. In order of decreasing copper accumulations, mollusks are followed by crustaceans, macrophytes, annelids, tunicates, algae, echinoderms, and coelenterates. Lowest concentrations of copper were consistently found among the vertebrates—elasmobranchs, fishes, mammals—and strongly indicates a discrimination against copper among the highest marine trophic levels examined (Eisler 1979, 1981). Aquatic mollusks and arthropods that possess hemocyanin—a copper-containing respiratory pigment—have elevated tissue and plasma copper concentrations when compared to the ambient medium (Neff and Anderson 1977). Unlike many species of invertebrates, no vertebrate animal has a copper pigment as the main metallic constituent of blood (Schroeder et al. 1966). Marine organisms without hemocyanin have lower tissue concentrations of copper than those possessing this respiratory pigment (Neff and Anderson 1977).

Diet is the most important route of copper accumulation in aquatic animals, and food choice influences body loadings of copper. For example, whole body copper concentrations in aquatic insects from copper-contaminated rivers are highest in detritovores (as high as 102 mg/kg DW), followed by predators (54 mg/kg DW) and omnivores (43 mg/kg DW; Cain et al. 1992). Little or no biomagnification of copper is evident in freshwater food chains (Stokes 1979).

Copper concentrations in freshwater macrophytes near mining areas are elevated (as much as 256 mg/kg DW) compared to conspecifics collected from more remote sites (Stokes 1979). Bioconcentration factors (ratio

of milligrams of copper per kilogram fresh weight organism to milligrams of copper per liter of ambient water) for copper by various species of freshwater algae range from 770-83,000. In general, copper accumulations in algae are higher at pH 8 than at pH 5; under conditions of low oxygen and reduced illumination; at low ambient concentrations of calcium, cobalt, zinc, magnesium, manganese, and organic chelators; and at high ambient concentrations of fluoride (Stokes 1979). Benthic communities in the vicinity of bulkheads made of chromated copper arsenate-treated wood had elevated concentrations of these elements, reduced species richness and diversity, and reduced numbers of total organisms when compared to reference sites (Weis and Weis 1994). American oysters (*Crassostrea virginica*) from a canal lined with chromated copper arsenate-treated wood had 150 mg Cu/kg FW soft parts vs. 20 mg Cu/kg FW in oysters from a more distant site (Weis and Weis 1993).

Copper concentrations in cephalopod mollusks are, in general, higher than those in bivalve mollusks; in cephalopods, 50 to 80% of the copper is localized in the digestive gland (Miramand and Bentley 1992). Copper concentrations in tissues of clams *(Macoma balthica*) in San Francisco Bay are associated with seasonal variations in tissue weight, concentrations of copper in the sediments, and anthropogenic inputs from nearby sources (Cain and Luoma 1990). In cockles (*Cerastoderma edule*), copper concentrations in tissues decrease with increasing age, decrease in summer when compared to other seasons, and increase with increasing sediment copper concentrations (Savari et al. 1991). In the cockle (*Anadara trapezium*), tissue copper concentrations are positively related to dissolved copper concentrations in the water column and independent of sediment copper concentrations (Scanes 1993). Small freshwater clams (*Anodonta grandis*) have higher copper concentrations in soft tissues than large clams because small clams take up copper at a greater rate and excrete it more slowly than large clams (Pip 1990); a similar case is made for oysters and other bivalve mollusks (Weis et al. 1993a). Zebra mussels (*Dreissena polymorpha*) regulate body copper concentrations at water copper levels of 13 µg Cu/L and lower (Camusso et al. 1994). Proximity to point sources, such as sewage discharge plants, is associated with elevated copper burdens in common mussels, *Mytilus edulis* (Ward 1990). Copper concentrations increased in mussels (*Mytilus* spp.) analyzed in the coastal mussel watch program between the late 1970's and the late 1980's. This may be due to increased availability of copper from anthropogenic sources; however, concentrations of other metals (silver, nickel, cadmium, lead, zinc) in mussels analyzed during this period showed a decrease (Lauenstein et al. 1990).

Pacific oysters near a copper recycling facility in Taiwan have elevated concentrations of copper (as high as 4,400 mg/kg DW soft parts), a characteristic green color, and low survival after exposure to waste effluents for 3 months (Hung et al. 1990). Diet is the major pathway by which greenish-colored Pacific oysters accumulate copper; initial daily accumulation rates are as high as 214 mg Cu/kg DW soft parts (Han and Hung 1990). Elimination of 50% of the copper from green Pacific oysters with elevated copper loadings takes only 11.6 days vs. 25.1 days in reference oysters (Han et al. 1993). Elevated concentrations of copper in Pacific oysters (135 mg/kg DW soft parts) near a marina in Arcachon Bay, France, are attributed to the ban on tributyltin antifouling paints in 1982 and the subsequent growing use of copper-based antifouling paints (Claisse and Alzieu 1993). Copper concentrations in soft tissues of the American oyster are higher in oysters from low salinity waters than those from more saline waters; accumulations are not related to sediment copper concentrations in the immediate environment (Huggett et al. 1975). In Maryland, copper concentrations in tissues of the American oyster are seasonally highest in July and lowest in October and higher in low salinity waters than in high salinity waters (Roesijadi 1994). In Australia, copper concentrations in oyster soft parts from the Georges River, New South Wales, rose from 20 mg/kg FW to 46 mg/kg FW in the 1970's to as high as 93 mg/kg FW in 1987, possibly as a result of urban and industrial discharges; this concentration exceeds the recommended limit of 70 mg Cu/kg FW in shellfish edible tissues for protection of human health in Australia (Brown and McPherson 1992).

In amphipod (*Orchestia gammarellus*) crustaceans, copper concentrations vary seasonally due to variable copper loadings, are higher in organisms from contaminated sites than reference sites, and higher in females with juveniles in the brood pouch than females without juveniles (Moore et al. 1991). The existence of copper-rich granules is common to all invertebrate phyla; these granules are usually found in the digestive gland or its evolutionary equivalent, and their formation is related to high concentrations of copper in the immediate environment (Weeks 1992). The tolerance of talitrid amphipods to high concentrations of ambient copper is attributable, in part, to the formation of intracellular granules within the cells of the ventral caeca (Weeks 1992). In the shore crab (*Carcinus mediterraneus*), tissue copper concentrations are lower in winter than in summer and correlate positively with total protein and hemolymph copper contents (Devescovi and Lucu 1995). Elevated copper burdens in hemolymph of crabs probably reflects the incorporation of copper atoms in the structure of

hemocyanin, the major hemolymph protein (Depledge et al. 1993). Marine decapod crustaceans regulate tissue copper concentrations within the range of 25 to 35 mg/kg DW (Neff and Anderson 1977).

In *Limnodrilus* sp., an oligochaete worm, copper bioavailability from surficial freshwater sediments is associated with the amount of copper present in the manganese oxide fraction of the sediment. The redox potential and pH in the gut of *Limnodrilus* allows the dissolution of the manganese oxide coating, making copper and other metals available for uptake (Diks and Allen 1983).

Copper concentrations in freshwater fishes collected nationwide in the United States have not changed significantly since 1978 (Schmitt and Brumbaugh 1990). In 1984, samples with the highest copper concentrations were Mozambique tilapia *(Tilapia mossambica*) from Hawaii and white perch (*Morone americana*) from the Susquehanna River in Maryland. These locations have historically yielded fish with relatively high concentrations of copper; in Hawaii, this may develop from copper-containing pesticides (Schmitt and Brumbaugh 1990). Copper concentrations in fishes are usually higher in liver than other tissues, higher in fish from copper-contaminated lakes than reference lakes, and higher in small fish than large fish of the same species (Cuill et al. 1970; Eisler 1984; ATSDR 1990; de Wet et al. 1994; Table 3). Residue data on copper in fish that are dead on collection are probably worthless for purposes of risk assessment owing to copper accumulation after death (Eisler and Gardner 1973). Among sharks collected in British waters, copper concentrations in all tissues are highest from inshore demersal species and lowest from offshore pelagic species, with males having higher copper concentrations in liver than females (Vas 1991).

Copper concentrations in tissues of marine vertebrates tend to decrease with increasing age of the organism (Law et al. 1992). Concentrations of copper in marine and coastal vertebrates—including elasmobranchs, teleosts, and pinniped mammals—are related to the age of the animal. Regardless of species or tissues, except brain, concentrations decrease with increasing age of the organism; brain copper concentrations in marine mammals increase with organism age (Eisler 1984). Decreases in tissue copper content are also associated with spawning migrations of salmonids when entering freshwater from the sea and with reproductive cycles of cod and other gadoids (Eisler 1984). In the copper-contaminated Miramichi River, Canada, populations of Atlantic salmon (*Salmo salar*) are reduced in numbers due to poor survival and reproduction (Sprague et al. 1965). Copper-containing mine wastes entering the Northwest Miramichi River cause many adult Atlantic salmon on their normal upstream spawning migration to return prematurely downstream; about 62% do not reascend. Downstream returns of salmon rose from 1 to 3% before pollution to 10 to 22% during four years of pollution. During some periods, dissolved copper and zinc concentrations exceed the lethal levels for immature salmon and the avoidance concentrations for subadults (Sprague et al. 1965; Saunders and Sprague 1967).

In polar bears, concentrations of copper in liver are 3-5 times higher than their seal diet (Braune et al. 1991). Copper concentrations in liver and kidney of polar bears are lower in juveniles than adults (Norheim et al. 1992), which is contrary to a reverse trend noted in most species of vertebrates. Neonatal marine mammals, for example, have higher concentrations of copper in liver than those found in the mother (Law et al. 1992). The use of copper herbicides in Florida to control aquatic plants may be hazardous to the endangered manatee. Copper concentrations in livers of these aquatic herbivores from areas of high copper herbicide use are as high as 1,200 mg/kg DW. The maximum copper concentrations in livers of copper-challenged manatees are higher than any copper concentration measured in any species of free-ranging mammalian wildlife and are comparable to copper concentrations in livers of some species of domestic animals poisoned by copper (O'Shea et al. 1984).

Amphibians and Reptiles

Eggs of the Jefferson salamander (*Ambystoma jeffersonianum*) from a series of ponds that contain 1-25 µg Cu/L have—at the higher copper concentrations—a reduction in hatching success and an increase in embryonic mortality (Horne and Dunson 1995).

For reasons unknown, livers of some adult giant toads (*Bufo marinus*) normally contain grossly elevated concentrations of copper (>2,000 mg/kg DW). The toads' livers are undamaged by this level of copper, and this lack of effect is in sharp contrast to human patients with Wilson's disease (2,000 mg Cu/kg DW liver) wherein hepatocyte degeneration, necrosis, and ultimately cirrhosis result (Goldfischer et al. 1970). In toad livers, the

copper is sequestered in lysosomes, which seems to protect the cell from the toxic effects of copper. In contrast, copper in livers of humans with Wilson's disease is diffusely distributed in the cytoplasm of hepatocytes and is associated with severe and often fatal pathological changes (Goldfischer et al. 1970).

Birds

Season of collection and organism age affect copper concentrations in avian tissues. In livers of surf scoters (*Melanitta perspicillata*) from San Francisco Bay, copper concentrations are higher in March than in January; in livers of canvasbacks (*Aythya valisineria*) from Louisiana, concentrations are lower in November than later months; and in primary flight feathers of mallards (*Anas platyrhynchos*) and black ducks *(Anas rubripes*) from the vicinity of a smelter in Sudbury, Ontario, copper concentrations are highest in autumn (Ranta et al. 1978). Copper concentrations in tissues of coastal seabirds tend to decrease with increasing age (Eisler 1984). In New Zealand, younger marine birds have higher concentrations of copper in livers than adults (Lock et al. 1992). But juveniles and adults of common murres (*Uria aalge*) from Scotland have similar concentrations of copper in kidneys, livers, and muscle (Stewart et al. 1994).

In general, birds retain a very small portion of copper and other metals ingested (Bryan and Langston 1992). It is therefore noteworthy that livers of some canvasbacks collected in Louisiana (Custer and Hohman 1994) and livers of some mute swans (*Cygnus olor*) from England (Bryan and Langston 1992) both contain more than 2,000 mg Cu/kg DW. In the case of mute swans, several thousands of milligrams of copper per kilogram dry weight occur in the blackened livers; blackening is attributed to ingestion of flakes of copper-based antifouling paints (Bryan and Langston 1992). Tree swallows (*Tachycineta bicolor*) nesting near acidified aquatic ecosystems accumulate sufficient copper from the diet to induce elevated hepatic metallothionein concentrations (St. Louis et al. 1993). However, there is no evidence of copper biomagnification in the sediment food chain of sediment-pondweed-red-knobbed coot (*Fulica cristata*; van Eeden and Schoonbee 1993).

Mammals

Impalas (*Aepyceros melampus*) found dead in Kruger National Park, South Africa, had elevated concentrations of copper in livers (maximum 444 mg/kg FW) and kidneys (maximum 141 mg/kg FW); authors assert that copper poisoning is the most likely cause of death (Gummow et al. 1991), but this needs verification. Copper concentrations in bones, kidneys, and livers of white-tailed deer (*Odocoileus virginianus*) near a copper smelter and from distant sites are about the same; however, deer near the smelter have significantly elevated concentrations of cadmium in kidneys and livers, lead in bone, and zinc in kidneys (Storm et al. 1994).

Only a small portion (0.037%) of copper mining wastes discharged into riparian wetlands is bioavailable to resident rodents, as judged by measurements of copper in carcasses of mice and voles (Pascoe et al. 1994). Populations of brown-backed voles (*Clethrionomys rufocanus*) and other microtine rodents (*Microtus* spp., *Lemmus*) are low or absent in the vicinity of Russian copper-nickel smelters (Kataev et al. 1994). The reasons for this decline are unknown but may be due to a decrease in the abundance of important food plants (lichens, mosses, seed plants), and—as shown in preference studies—to an avoidance of plants from the contaminated area (Kataev et al. 1994). Bank voles (*Clethrionomys glareolus*) from areas of Poland subjected to various degrees of industrial contamination have copper concentrations in tissues comparable to those in animals from polluted sites in North America and the United Kingdom (Sawicka-Kapusta et al. 1990). Compared to animals from a reference site, muskrats (*Ondatra zibethicus*) from a site contaminated by copper and other chemicals have higher concentrations of copper in kidneys, and have smaller spleens, larger adrenals, less fat, and lower body weight (Halbrook et al. 1993).

In Poland near copper foundries, livers from cattle (*Bos* sp.) have higher copper concentrations (35-140 mg/kg FW) than cattle from agricultural regions (7-32 mg/kg FW); however, kidney copper concentrations are comparable for both regions (Falandysz 1993a). Cattle found dead in South Africa near a copper smelter have elevated levels of copper in liver (600 mg/kg FW; 1,078 mg/kg DW); airborne copper from the smelter is considered the most likely cause of death (Gummow et al. 1991). Sheep held for 150 days in a paddock near a heavily-traveled highway have significantly elevated copper concentrations in wool; these differences are not as pronounced in hair from horses (*Equus caballus*) and alpacas (*Lama pacos*) held under similar conditions (Ward and Savage 1994).

Interspecies differences in copper contents are considerable. Serum from domestic dogs (*Canis familiaris*) lacks the strong copper binding site available on the serum albumin molecule of humans and rats. Accordingly, copper concentrations in livers from dogs (82 mg/kg FW; 336 mg/kg DW) are normally about 12 times higher than those of human livers and 19 times higher than those of rat livers (Goresky et al. 1968).

Human foods that are particularly rich in copper (20-400 mg Cu/kg) include oysters, crustaceans, beef and lamb livers, nuts, dried legumes, dried vine and stone fruits, and cocoa (USEPA 1980). In humans, copper is present in every tissue analyzed (Schroeder et al. 1966). A 70-kg human male usually contains 70-120 mg of copper (USEPA 1980). The brain cortex usually contains 18% of the total copper, liver 15%, muscle 33%, and the remainder in other tissues—especially the iris and choroid of the eye. Brain gray matter (cortex) has significantly more copper than white matter (cerebellum); copper tends to increase with increasing age in both cortex and cerebellum. In newborns, liver and spleen contain about 50% of the total body burden of copper (USEPA 1980). Liver copper concentrations were usually elevated in people from areas with soft water (Schroeder et al. 1966). Elevated copper concentrations in human livers are also associated with hepatic disease, tuberculosis, hypertension, pneumonia, senile dementia, rheumatic heart disease, and certain types of cancer (Schroeder et al. 1966).

Copper Deficiency Effects

General

Adverse effects of copper deficiency are documentable in terrestrial plants and invertebrates, poultry, small laboratory animals, livestock—especially ruminants—and humans. Data are scarce or missing on copper deficiency effects in aquatic plants and animals and in avian and mammalian wildlife. Copper deficiency in sheep—the most sensitive ruminant mammal—is associated with depressed growth, bone disorders, depigmentation of hair or wool, abnormal wool growth, fetal death and resorption, depressed estrous, heart failure, cardiovascular defects, gastrointestinal disturbances, swayback, pathologic lesions, and degeneration of the motor tracts of the spinal cord (NAS 1977).

Terrestrial Plants and Invertebrates

Copper is an essential micronutrient of all higher plants studied, being a cofactor for the enzymes polyphenol oxidase, monophenol oxidase, laccase, and ascorbic acid oxidase (Schroeder et al. 1966). In copper-deficient soils, copper is strongly held on inorganic and organic exchange sites and in complexes with organic matter (Thornton 1979), causing reduced availability of copper to vegetation in these soils. Copper deficiency in terrestrial plants is usually associated with reduced growth, abnormally dark coloration in rootlets, and chlorotic leaves (Gupta 1979). In agricultural crops, copper deficiency occurs at less than 1.6 mg dissolved Cu/kg DW soil (Thornton 1979), and in sensitive plants at less than 2 to less than 5 mg total Cu/kg DW leaves (Gupta 1979). In fruit trees, copper deficiency is characterized by death of apical buds, formation of multiple buds, and yellowing (chlorosis) of the leaf margins (NAS 1977). Copper deficiency in alfalfa (*Medicago sativa*) and clover (*Trifolium* spp.) is associated with a faded green leaf color, growth inhibition, and withering (Gupta 1979). In grasses, copper deficiency is characterized by chlorosis, stunting, and necrosis and in cereals by pale color, reduced growth, and a reduction in the number of pollen grains (Gupta 1979).

Increased yields of various crops occur when copper salts are added to fertilizers at 300 to 800 mg Cu/m^3 (NAS 1977). In corn (*Zea mays*) and other vegetables, younger plants are more sensitive to copper deficiency than mature plants; in all cases, copper-deficient vegetables show chlorosis, reduced growth and reproduction, and low survival (Gupta 1979).

No evidence of copper deficiency exists in terrestrial species of invertebrates examined; however, relatively low concentrations of copper stimulated growth and reproduction. Reproduction in mites (*Platynothrus peltifer*) increases when fed diets containing 28 mg Cu/kg DW (vs. 13 mg/kg in controls) for 3 months (Denneman and van Straalen 1991). And juvenile earthworms (*Eisenia andrei*) show increased growth at 18 mg Cu/kg DW soil after 12 weeks (van Gestel et al. 1991).

Aquatic Organisms

No documented report of fatal copper deficiency is available for any species of aquatic organism. And no correlation is evident in aquatic biota for the presumed nutritional copper requirements of a species and its sensitivity to dissolved copper (Neff and Anderson 1977). Extremely low copper concentrations (5.5 and 6.7 mg/kg DW) in whole bodies of 2 of 17 species of crustaceans from the Antarctic Ocean support the hypothesis that certain Antarctic species may show copper deficiencies or reduced metal requirements (Petri and Zauke 1993).

Birds and Mammals

Copper deficiency is not a major public health concern in the United States (Percival 1995). Copper deficiency is rarely observed in humans except in cases of severely malnourished children or those with Menkes' disease—an X-linked recessively inherited disorder. This disease is a severe congenital copper deficiency marked by slow growth, progressive cerebral degeneration, convulsions, temperature instability, bone alterations, and peculiar steel-like hair (ATSDR 1990; Yoshimura et al. 1995). Treatment of Menkes' disease is now restricted to parenteral administration of copper salts, although complete prevention of neurodegradation is difficult to obtain (Yoshimura et al. 1995). Copper deficiency is sometimes reported in humans after intestinal resection surgery (reduced absorptive surface), in people who consume high levels of zinc (zinc induces intestinal metallothionein that blocks copper transport), in infants who consume a diet based on cow milk (cow milk is a poor source of copper), and in genetic cases (Percival 1995). Moderate copper deficiency also exists in burn and trauma patients, two groups at high risk for sepsis (DiSilvestro et al. 1995).

An inherited abnormal copper metabolism has been established in certain strains of mice, rats, and dogs (Sugawara and Sugawara 1994). Feeding a copper-deficient diet to these animals may prevent acute hepatitis. In rats with abnormal copper metabolism and hereditary hepatitis, the feeding of a copper-deficient diet (0.5 mg Cu/kg ration for 35 days) prevents copper accumulation (94-139 mg Cu/kg DW liver) and dysfunction. But feeding a normal diet of 30 mg Cu/kg DW ration to these rats produces liver copper concentrations of 375 mg/kg DW (Sugawara and Sugawara 1994). Administered copper protects copper-deficient strains of mice against neurodegradation, and protects ponies against selenium poisoning when pretreated with 20 or 40 mg Cu/kg BW (Stowe 1980).

Chickens (*Gallus domesticus*) given diets deficient in copper (less than 2.7 mg kg ration) have anemia, poor growth, low survival, and a high frequency of cardiovascular and skeletal lesions (Carlton and Henderson 1963, 1964a, 1964b). It is emphasized, however, that copper deficiency does not usually arise from eating a copper-poor diet because copper is found ubiquitously in foods (Percival 1995). Chickens, turkeys (*Meleagris gallopavo*), cattle, and pigs deficient in copper are prone to die suddenly (Gallagher 1979). Sudden death in some copper-deficient species is sometimes associated with rupture of a major blood vessel or rupture of the heart (Carlton and Henderson 1964b; NAS 1977; ATSDR 1990; Saari et al. 1994). Male weanling rats given a copper-deficient diet of 0.13 mg Cu/kg ration (vs. copper-normal diet of 5.7 mg Cu/kg ration) for 7 weeks show high mortality (24%) from cardiac rupture; ruptured hearts had elevated concentrations of sodium, potassium, and calcium, and depressed magnesium (Saari et al. 1994). Copper deficiency in weanling rats is confirmed by low activities of ceruloplasmin in serum and by superoxide dismutase in liver and serum (DiSilvestro et al. 1995). Skeletal deformities and leg fractures occur in copper-deficient chickens, dogs, pigs, sheep, cattle, and children because of decreased tensile strength of bones (Carlton and Henderson 1964a; NAS 1977; Gallagher 1979). In lambs from copper-deficient ewes, locomotor disturbances of gait or posture occur because of lesions of excessive myelination of the central nervous system (Gallagher 1979).

Copper deficiency in humans and other mammals is characterized by slow growth, hair loss, anemia, weight loss, emaciation, edema, altered ratios of dietary copper to molybdenum and other metals, impaired immune response, decreased cytochrome oxidase activity, central nervous system histopathology, decreased phospholipid synthesis, fetal absorption, and eventually death (NAS 1977; Gallagher 1979; Kirchgessner et al. 1979; USEPA 1980; ATSDR 1990; Percival 1995).

In laboratory white rats, signs of copper deficiency include reductions in tissue copper concentrations; reduced activities of cytochrome oxidase, superoxide dismutase, succinoxidase, and ceruloplasmin; increased activity of 7-ethoxyresorufin *O* deethylase (EROD) in small intestines; anemia associated with low hematocrit and hemoglobin; increased acute inflammatory response; increased sensitivity to endotoxins; central nervous

system lesions; and reduced phospholipid synthesis (Gallagher 1979; Johnson and Smith 1994; Schuschke et al. 1994; DiSilvestro et al. 1995). Copper-deficient rats also have prolonged sleeping times and significant reductions in activities of aniline hydroxylase and hexobarbital oxidase in liver (Moffitt and Murphy 1973). Earliest signs of copper deficiency in rats include low concentrations of copper in livers (1.4-<3.0 mg/kg DW vs. 12.6-15.0 mg/kg DW in controls); profound reductions in activities of cytochrome oxidase and succinoxidase; and reductions in hematocrit, hemoglobin, ceruloplasmin, and phospholipid synthesis (Gallagher 1979; Johnson and Smith 1994). Severe copper deficiency in rats results in anemia characteristic of defective hemoglobin synthesis resulting from abnormal use of iron by mitochondria in heme synthesis (Johnson and Smith 1994). Copper-deficient rats are extraordinarily sensitive to endotoxins and die after receiving normally sublethal doses of various endotoxins (DiSilvestro et al. 1995). Copper deficiency-induced lesions in the central nervous system are produced experimentally in rats and guinea pigs and are a characteristic feature of Menkes' disease (Gallagher 1979).

Sway disease of Bactrian camels (*Camelus bactrianus*)—characterized by anemia, emaciation, falling, fractures, and death—is caused by copper deficiency associated with high molybdenum content in soils and forage; deficiency effects are aggravated during reproduction (Zong-Ping et al. 1994).

Sheep fed copper-deficient diets of less than 2.5 mg Cu/kg DW ration (vs. a normal diet of 11.0 mg Cu/kg DW) produce a high frequency of swaybacked lambs. Swaybacks have lower concentrations of copper in liver than nonswaybacked lambs from copper-deficient ewes; both groups have lower concentrations of copper in livers than normal lambs (Lewis et al. 1967; Buckley and Tait 1981).

Copper deficiency effects are reported in mink (*Mustela vison*) and domestic swine. Copper deficiency in mink, as judged by reduced survival, occurs by feeding rations containing the equivalent of 3.5 mg Cu/kg BW daily for a period of 50 weeks (ATSDR 1990). Swine, which seem to have higher copper requirements than mink, given low copper diets equivalent to 15 to 36 mg Cu/kg BW daily for 7 days have decreased hemoglobin, hematocrit, and growth rate (ATSDR 1990).

Dietary copper deficiency increases the acute inflammatory response in rats and other small laboratory animals (Schuschke et al. 1994). The release of inflammatory mediators, such as histamine and serotonin, from mast cells increases the vascular permeability of postcapillary venules and results in edema. In copper-deficient rats, release of histamine from mast cells positively correlates with frequency of the acute inflammatory response. Copper-deficient rats (0.6 mg Cu/kg DW ration for 4 weeks) have more mast cells in muscle than copper-adequate controls given diets containing 6.3 mg Cu/kg DW ration; however, histamine content of mast cells is not affected (Schuschke et al. 1994). An early clinical sign of copper deficiency is a reduction in the number of circulating neutrophils; the mechanism for copper-deficient neutropenia (leukopenia in which the decrease in white blood cells is chiefly neutrophils) is unknown (Percival 1995). Proposed mechanisms to account for neutropenia from copper deficiency include (1) early destruction of bone marrow progenitor cells; (2) impaired synthesis of neutrophils from progenitor cells; (3) a decrease in the rate of cellular maturation in the bone marrow; (4) impaired secretion of neutrophils from the bone marrow; and (5) rapid clearance of circulating copper-deficient neutrophils (Percival 1995).

Lethal and Sublethal Effects

General

Copper is toxic to sensitive species of terrestrial vegetation at greater than 40 µg/L nutrient solution (seedlings of pines, *Pinus* spp.), at greater than 10 mg/kg DW leaves (cucumber, *Cucumis sativus*), and greater than 60 mg extractable Cu/kg DW soil (sweet orange, *Citrus sinensis*; Table 4). Among sensitive species of terrestrial invertebrates, adverse effects on survival, growth, or reproduction occur at 2 µg Cu/cm^2 on paper discs (earthworms), greater than 50 mg Cu/kg diet (larvae of gypsy moth, *Lymantria dispar*), and 53 to 70 mg Cu/kg DW soil (earthworms and soil nematodes; Table 4).

Table 4. Effects of copper on representative terrestrial plants and invertebrates.

Table 4. Organism, copper concentration or dose, and other variables	Effects	Reference[a]
Plants		
Agricultural crops from soils containing dissolved copper		
0.0-1.6 mg/kg soil	Copper deficiency in susceptible crops	1
1.7-2.4 mg/kg soil	Slight deficiency	1
2.5-4.0 mg/kg soil	Deficiency unlikely	1
>4.0 mg/kg soil	Soil well supplied with copper	1
Sweet orange, *Citrus sinensis*; 4-year old trees; M3 extractable soil copper >60 mg/kg DW (from treated plots containing about 120 kg Cu/ha)	Growth adversely affected; positive correlation between copper concentrations in feeder roots (4 to 450 mg Cu/kg DW) and M3 extractable soil copper	17
Cucumber, *Cucumis sativus*; leaves		
<2 mg/kg dry weight (DW)	Deficient	2
2-10 mg/kg DW	Sufficient	2
>10 mg/kg DW	Toxic	2
Soybean, *Glycine max*; leaves		
<4 mg/kg DW	Deficient	2
10-30 mg/kg DW	Sufficient	2
>50 mg/kg DW	Toxic	2
Pasture grasses; aboveground portions		
<5 mg/kg DW	Deficient	2
5-12 mg/kg DW	Sufficient	2
>12 mg/kg DW	Toxic	2
Seedlings of stone pine, *Pinus pinea* and maritime pine, *Pinus pinaster*; exposed to nutrient solutions containing 0.4 (controls) 4, 40, or 200 µg Cu/L for as long as 4 weeks		
4 µg/L	Slight to no enhancement of root elongation	16
40 µg/L	Taproot elongation reduced but partial growth recovery in 7 days; cell membrane damage evident after 10 days	16
200 µg/L	Root growth completely inhibited within 3 days in both species	
Faba bean, *Vicia faba*; cultured hydroponically with nutrient solutions containing 100 mg Cu/L for 24 days; shoots analyzed before (day 4) and after (day 24) 20-day infestation by the black bean aphid, *Aphis fabae*. Controls were raised in copper-free nutrient solutions	Aphid infestation caused a significant reduction in copper content of shoots from 51 mg/kg DW to 17 mg/kg; copper in control was 25 mg/kg DW prior to aphid infestation and 14 mg/kg after 20-day infestation	3
Invertebrates		
Soil nematode, *Caenorhabditis elegans*		
70 mg/kg DW sandy soil for 24 h	LC50	4
105 mg/L for 24 h; no soil	LC50	4

Table 4. Organism, copper concentration or dose, and other variables	Effects	Reference[a]
1,061 mg/kg loam substrate for 24 h	LC50	4
2,476 mg/L for 24 h; loam substrate	LC50	4
Soil ciliate, *Colpoda steini*		
250 µg/L for 24 h	Growth reduced 50%	5
Fruitfly, *Drosophila melanogaster*		
In culture medium containing 80 µg cm^2 for 4 weeks	Survival reduced 35%; copper elevated in cytoplasm, malpighian tubule epithelial cells, and other tissues	6
Earthworms, three species; 40-238 mg/kg soil; exposure duration unknown	No effect on growth, survival, or reproduction	7
Earthworm, *Eisenia andrei*; juveniles; exposure for 12 weeks		
18 mg/kg DW soil	Growth stimulated	8
56 mg/kg DW soil	No effect on growth or reproduction	8
100 mg/kg DW soil	<50% effective in reducing growth; inhibited sexual development	8
Earthworm, *Eisenia fetida*		
32 mg/kg DW soil for 56 days	No effect on cocoon production	9
53.3 (32.5-186.0) mg/kg DW soil for 56 days	Cocoon production reduced 50%	9
210 mg/kg DW soil for 56 days	No deaths	9
555 (460-678) mg/kg DW soil for 56 days	50% dead	9
683 (570-812) mg/kg DW soil for 14 days	50% dead	9
Earthworm, *Eisenia fetida andrei*		
Adults held in soil containing as much as 300 mg/kg DW for 3 weeks; resultant cocoons incubated in uncontaminated soil for 5 weeks to assess hatchability soil for 5 weeks to assess hatchability	No adverse effects on cocoon production or hatchability in soil containing 60-120 mg/kg DW; adult growth retarded during exposure at 300 mg/kg DW	10
Earthworm, *Lumbricus rubellus*		
100-150 mg/kg DW soil	Decreased cocoon production	11
150-300 mg/kg DW soil	Decrease in litter breakdown activity	11
>300 mg/kg DW soil	Reduced growth and increased mortality	11
1,000 mg/kg DW soil for 6 weeks	Lethal to 50%	11
Earthworm, *Lumbricus terrestris*		
Exposed for five days to filter paper disc containing 0.5, 1, 2, 4, or 8 µg Cu/cm^2	At 4 µg/cm^2 and higher, mortality was >90%; 20% were dead at 2 µg/cm^2 and none were dead at lower concentrations. Whole worms contained, in mg Cu/kg DW, 5.9 in controls, 28.5 in the 0.5 group, and 73.1 in the 1.0 group. At sublethal concentrations, worms had decreased lysozyme activity in coelomic fluid and coelomocytes	12
Gypsy moth, *Lymantria dispar*		
Larvae were fed diets containing 10, 50, 250, or 1,250 mg/kg ration from first instar to pupation; effects measured on development rate,	No adverse effects at 10 mg/kg diet. Significant adverse effects at 50 mg/kg and higher on development and reproductive success and at 250 mg/kg and higher on growth	13

Table 4. **Organism, copper concentration or dose, and other variables**	**Effects**	**Reference[a]**
growth, survival, and reproductive success		
Oribatid mite, *Platynothrus peltifer*		
Fed diets with 13 (control), 28, 64, 168, 598, or 1,498 mg Cu/kg DW diet for 3 months	No deaths at any dose. Reproduction increased at 28 mg/kg but decreased steadily with increasing dose. The no-observable-effect-concentration (NOEC) for reproduction was 168 mg/kg diet; the NOEC for growth was 598 mg/kg. Copper concentrations in whole mites increased significantly at dietary loadings >168 mg/kg	7
84 mg/kg DW soil	NOEC on growth, survival, or reproduction	7
Soil faunal communities		
Forest soil treated to contain 100, 200, 400, or 600 mg Cu/kg DW; nematodes and macroarthropods enumerated after 7 days	Sensitive species of nematodes and mites were reduced in number at 100 mg/kg soil; total nematode and arthropod numbers declined at 200 mg/kg and higher	14
Termites, subterranean; Karachi, Pakistan; termite-infested area (*Microtermes* spp., *Heterotermes* spp., *Coptotermes* spp., *Odontotermes* spp.)		
Fir (*Abies pindrow*) wooden stakes coated with 5% copper sulfate in gelatin solution vs. uncoated stakes	Copper-treated stakes prevented termite attack in soil up to 4 years vs. severe termite damage within 6 months in control stakes	15

[a]1, Thornton 1979; 2, Gupta 1979; 3, Crawford et al. 1990; 4, Donkin and Dusenbery 1993; 5, Forge et al. 1993; 6, Marchal-Segault et al. 1991; 7, Denneman and van Straalen 1991; 8, van Gestel et al. 1991; 9, Spurgeon et al. 1994; 10, van Gestel et al. 1989; 11, Ma 1984; 12, Goven et al. 1994; 13, Gintenreiter et al. 1993; 14, Parmelee et al. 1993; 15, Roomi et al. 1990; 16, Arduini et al. 1995; 17, Alva et al. 1995.

Sensitive species of representative freshwater plants and animals die within 96 h at waterborne copper concentrations of 5.0 to 9.8 µg/L (Hodson et al. 1979; Table 5). The most sensitive freshwater species have LC50(96 h) values between 0.23 and 0.91 µg Cu/L and include daphnids (*Daphnia* spp.), amphipods (*Gammarus pseudolimnaeus*), snails (*Physa* spp.), and chinook salmon (*Oncorhynchus tshawytscha*; USEPA 1980; Table 5). In general, mortality of tested aquatic species is greatest under conditions of low water hardness (as measured by $CaCO_3$), starvation, elevated water temperatures, and among early developmental stages (Hodson et al. 1979; Table 5). Toxicity testing of copper-contaminated sediments to amphipods (*Hyalella azteca*) and daphnids (*Daphnia magna*) using techniques of enzyme inhibition and growth rate show that these variables are more sensitive in accurately predicting copper sensitivity than LC50 (48 h) values (Kubitz et al. 1995) and should be considered when assessing risk of contaminated sediments to freshwater systems. The most sensitive saltwater species to copper have LC50 (96 h) values from 28 to 39 µg/L and include summer flounders (*Paralichthys dentatus*), copepods (*Acartia tonsa*), and softshell clams (*Mya arenaria*; USEPA 1980; Eisler 1995; Table 5). Adverse sublethal effects of copper on representative species of estuarine algae, mollusks, and arthropods frequently occur at 1 to 10 µg/L (Bryan and Langston 1992; Table 5).

Table 5. Effects of copper on representative aquatic plants and animals.

Table 5. Taxonomic group, organism, copper concentration, and other variables	**Effects**	**Reference[a]**
Plants		
Algae; mixed culture; 5 µg/L	Photosynthesis reduced	1
Aquatic weeds, fresh water		
170 µg/L for 99 days, continuous exposure	Eliminated or controlled most submerged species; adverse effects first noted at day34. Weeds contained 360 to 4,280 mg/kg dry weight (DW)	2
250-1,000 µg/L for 99 days, continuous exposure	Unsuccessful in controlling emergent aquatic weeds; successful in eliminating filamentous algae and most submerged species	2
Marine alga, *Chlamydomonas bullosa*; 49.9 µg/L for 96 h	Growth reduced 50%	3
Green alga (fresh water), *Chlamydomonas reinhardtii*		
18 µg/L for 24 h	Reduction in number of cells bearing flagella	4
21 µg/L for 7 days	Growth normal	5
32 µg/L for 7 days	Growth reduced 50%	5
60 µg/L for 10 min inhibited for 24 h	Flagella shed; flagellar refabrication	4
79 µg/L for 72 h	Growth inhibited 50%	5
Freshwater alga, *Chlorella* spp.		
1.0 µg/L	Growth reduced	1
6.3 µg/L	Photosynthesis inhibited	1
Marine alga, *Dunaliella salina*		
0.031 µg/L for 8 months	Minor adverse effects on lipid metabolism	6
380 µg/L for 96 h	Growth reduced 50%; negligible effects on cellular ultrastructure	3,6
Marine alga, *Dunaliella tertiolecta*		
8,000 µg/L for 48 h	Growth normal	7
12,000-16,000 µg/L for 48 h	Adverse effects on photosynthesis, cell division rates, and pigment metabolism	7
Euglena, *Euglena gracilis*; 10,000 µg/L for 5 days	Adverse sublethal effects, including altered free cysteine metabolism	8
Freshwater diatom, *Nitzschia palea*; 5 µg/L	Complete inhibition of growth	1
Alga, *Ochromonas danica*		
10,000 µg/L for as long as 9 days	Growth normal	11
Aquatic moss, *Rhynchostegium riparioides*; 4.5 (controls), 9, 21, or 50 µg/L for 27 days followed by 14 days in clean media	Copper accumulation plateaued after 18 days. Maximum concentrations reached in mg/kg DW, were 900 (9 µg/L group), 2,000 (20 µg/L group), and 3,500 (50 µg/L group). At end of depuration mosses had lost about 50% of accumulated copper	12

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Freshwater alga, *Scenedesmus acutiformis*; 100 µg/L for 20 min at pH 4.8, 5.8, or 6.8 (pH 5.8) to 4,000 (pH 6.8)	Copper concentrations, in mg/kg DW, increased from 400 (pH 4.8) to 750	10
Freshwater alga, *Scenedesmus subspicatus*		
56 µg/L for 72 h	Growth normal	5
120 µg/L for 72 h	Growth reduced 50%	5
Marine alga, *Scrippsiella faeroense*; 5 µg/L for 5 days	Growth inhibited 50%	1
Marine alga, *Thalassiosira pseudonana*; 5 µg/L for 72 h	Growth inhibited 50%	1
Protists		
Freshwater protozoan ciliate, *Tetrahymena pyriformis*		
3,818 µg/L for 96 h	Growth normal	5
8,000 µg/L for 48 h	Growth inhibited 50%	5
Cnidarians		
Sea anemone, *Anemonia viridis*; 50 or 200 µg/L for 5 days	Immediate tentacle retraction; copious production of mucus; progressive visible bleaching and loss of zooxanthellae	13
Hydroid, *Campanularia flexuosa*		
1.4 µg/L for 11 days	Enzyme disruption	1
10-13 µg/L for 11 days	Growth rate reduced	1
Ctenophore, *Pleurobrachia pileus*; 33 µg/L for 24 h	Fatal to 50%	1
Rotifers		
Freshwater rotifer, *Brachionus calyciflorus*		
2.5-5.0 µg/L	MATC[b]	14
14 µg/L for 5 h	Swimming behavior impaired 50%	14
25 µg/L for 5 h	All immobilized	14
26 µg/L for 24 h	Fatal to 50%	14, 15
34 µg/L for 5 h	Feeding rate reduced 50%	15
43 µg/L for 24 h	Feeding rate reduced 50%	16
80 µg/L for 24 h	No deaths when molar ratio of fulvic acid to copper was 1:1	17
Nematodes		
Free-living nematode, *Caenorhabditis elegans*		
260 µg/L for 96 h	LC50	18
22,000 µg/L for 24 h	LC50	18
Mollusks		
Freshwater unionid mussel, *Anodonta cygnea*		
2.1 (95% confidence interval [= CI] of 0.01-7.2) µg/L for 72 h	Reduction by 50% in valve closure of glochidia; ability to infect fish reduced	19
5.3 µg/L for 48 h	Valve closure rate reduced 50%	19
Freshwater mussel, *Anodonta grandis*		
17 µg/L for 24 h	Valve closure normal	20
33 µg/L for 24 h	Valve closure rate reduced 50%	20
44 µg/L for 24 h	Fatal to 50%	20
Bay scallop, *Argopecten irradians*		
5.0 µg/L for 119 days	All dead	1

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
5.8 µg/L for 42 days	Growth rate reduced 50%	1
Freshwater snail, *Biomphalaria glabrata*; 60 µg/L for 60 h	Lethal; epithelial cell histopathology	21
Freshwater snail, *Bulinus globosus*; 707 µg/L for 24 h	LC50	22
Channeled whelk, *Busycon canaliculatum*		
100 µg/L for 54 days	Copper concentrations, in mg/kg FW, were 43 (vs. 35 in controls) in gills and25 (vs. 16) in osphradium	23
500 µg/L for 16 days	All dead	23
Snail, *Campeloma decisum*		
>30 µg/L for 24 h	Motility inhibited	24
1,700 µg/L for 96 h	LC50	24
Asiatic clam, *Corbicula fluminea*		
5.5 µg/L for 30 days	Growth normal; soft tissues contained 80 mg/kg DW (vs. 40-60 in controls)	25
8.4-26.7 µg/L for 30 days	Some deaths; growth reduction in juveniles and adults; soft parts had205-278 mg/kg DW	25
19.2 µg/L for 30 days	LC50	25
Pacific oyster, *Crassostrea gigas*		
Adults		
10 µg/L for 14 days	LC20	27
100 µg/L	No deaths in 96 h; 30% dead in 14 days	27
560 µg/L for 96 h	LC50	27
Embryos, exposed for 48 h		
5 µg/L in controls	94-98% normal development vs. 97-99%	28
6.5 µg/L	8-25% abnormal (retarded shell size, reduced growth, erratic swimming behavior)	28
10 µg/L	26-79% abnormal	28
18 µg/L	No embryos developed normally	28
American oyster, *Crassostrea virginica*; adults with soft parts containing 837 mg/kg DW were held in flowing seawater of 1-2 µg Cu/L for 56 weeks	No significant depuration; soft parts contained 746-1,526 mg/kg DW during exposure	26
Clam, *Donax incarnatus*		
4.0 µg/L for 4 h	Increased oxygen consumption and increased ammonia excretion	29
26.1 µg/L for 96 h	LC50	29
Zebra mussel, *Dreissena polymorpha* 4.5, 9, 21, or 50 µg/L for 27 days followed by 14 days in clean media	No deaths. Filtration rate reduced in 50 µg/L group during exposure but not afterwards. Maximum concentrations, in mg/kg DW soft parts, were about 30 (9 µg/L), 70 (21 µg/L), and 100 (50 µg/L); about 18% of the accumulated copper was lost during depuration	12
13 µg/L for 9 weeks	No effect on survival or filtration rate	30
>28 µg/L for 48 h	Copper accumulation	31
41-43 µg/L for 48 h to as long as 9 weeks	Filtration rate reduced 50%	30, 31
90 µg/L for 9 weeks	28% dead; 78% reduction in filtration rate	30
Black abalone, *Haliotis cracherodii*; 50	LC50	1

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
µg/L for 96 h		
Red abalone, *Haliotis rufescens*; 86 µg/L for 96 h	LC50	1
Freshwater mussel, *Lamellidens marginalis*		
250 µg/L for 96 h	Moribund; complete dissolution of crystalline style in 9.8 h; style reforms in 2.5 h on transfer to uncontaminated media and this may be useful as indicator of copper stress	32
250, 500, 750, or 1,000 µg/L for 30 days	No deaths. Initial dose-dependent increase in respiratory rate and decrease in growth rate; similar to controls by day 30	33
5,000 µg/L for 96 h	LC50	32, 33
Baltic clam, *Macoma balthica*; 40 µg/L for 48 h	Copper in soft parts was 23.5 mg/kg DW vs. 20.0 in controls	34
Clam, *Macoma liliana*; juveniles held in sediments containing <1 (controls), 5, 10, 15, 25, 30, 50, 70, or 140 mg/kg DW.	Maximal avoidance was in sediments containing 25 mg/kg and higher (interstitial water had 113 µg/L). Ability to bury in sediments was inhibited in sediments	35
Effects on avoidance in 96 h, burial rate in 90 min, and survival in 10 days were measured	Containing 15 mg/kg and higher (pore water of 120 µg/L). Reduced survival at 30 mg/kg DW sediment and higher	
Quahaug clam, *Mercenaria mercenaria*		
25 µg/L for 77 days	53% dead	1
640-6,400 µg/L	Dose-dependent increase in cytotoxicity by isolated brown cells	36
Scallop, *Mizuhopecten yessoensis*; 25 µg/L for 21 days	Hepatopancreas had 513 mg/kg DW (vs. <50 in controls); accumulations accompanied by a significant increase in hydroperoxide and malondialdehyde contents in microsomal membranes and alterations in lipid peroxidation rates	37
Softshell clam, *Mya arenaria*		
35 µg/L for 168 h	LC50 at 22º C	38, 160
39 µg/L for 96 h	LC50	1
86 µg/L for 504 h	LC50 at 17.5º C	38, 160
3,000 µg/L for 336 h	No deaths at 4º C	38, 160
Common mussel, *Mytilus edulis* 0, 1, 3.2, 10, 32, or 100 µg/L for 7 days;mantle tissue analyzed for heat shock protein 60	Adverse effects on growth in the 32 and 100 µg/L groups; dose-dependent protein increase at 3.2 µg/L and higher	39
Mussels age 2.5 months continuously exposed to 0, 1, 5, or 10 µg/L for 21 months. Growth, histopathology, and residues in soft parts measured after 12, 18, and 21 months	Growth adversely affected in the 10 µg/L group; histopathology evident in the 5 and 10 µg/L groups. After 21 months, concentrations in soft parts, in mg/kg FW, were 5.5 in controls and the 1.0 µg/L group, 19.2 in the 5 µg/L group, and 62 in the highest exposure group	40
1, 3.2, 10, 32, or 100 µg/L for 7 days	No effect on protein activity in gill and mantle at 32 µg/L and lower; increased accumulations at 100 µg/L. At 32 µg/L and higher growth was	41

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
	reduced. At 100 µg/L survival decreased and copper concentrations increased from 24 to 89 mg/kg DW in gill and from 14 to 54 mg/kg DW in mantle	
2 µg/L for 30 days	Spawning frequency reduced 50%	42
5-6 µg/L for 10 days	Growth reduced 50%	42
50 µg/L for 6 days, then transferred to clean seawater	Lysosomal destabilization in all age groups; ability to recover declined with increasing age	43
430 µg/L for 120 h	Cardiac activity reduced 50% within4 h and reduction persisted for 120 h	44
Dipped for 5 sec in $CuSO_4$ solutions containing 5, 10, 25, or 50 g/L and stored in air for 6, 24, or 48 h	Fatal at 5 to 10 g/L if kept out of water for24 h; fatal at 10-20 g/L if stored only a few hours. Oysters (*C. virginica*) survived this treatment	45
Mussel, *Mytilus galloprovincialis*		
15 µg/L for 5 days	Stimulates the synthesis of thionein-like copper-binding proteins in gill, mantle, and digestive gland	46
40 µg/L for 6 days	Gills contained 22.3 mg/kg FW (vs. 2.4 in controls); digestive gland had 6.8 mg/kg FW (3.0). Exposed mussels show stimulated lipid peroxidation rates in tissues	47
80 µg/L for 2 h	Induces the synthesis of copper-binding proteins similar to that of metallothioneins in gills and mantle	46
Common Limpet, *Patella vulgata*; 10 µg/L for 6 h	Pedal mucus production reduced 40%	48
Brown mussel, *Perna indica*		
2-6 µg/L for 4 h	Increased oxygen consumption	29
21.8 µg/L for 96 h	LC50	29
Green mussel, *Perna viridis*		
25 µg/L for 2 weeks	Reduction in filtration rate, growth, and oxygen to nitrogen ratio; histopathology of digestive cells and tissues. Residues, in mg/kg FW, were 38.2 in digestive gland vs. 2.6 in controls and 24.7 in total soft parts vs. 1.3 in controls	49
86 µg/L for 96 h	LC50	49
Snail, *Physa integra*		
15 µg/L for 6 weeks	No adverse effects on growth, survival, or feeding	24
39 µg/L for 96 h	LC50	1, 24
Apple snail, *Pomacea paludosa*; 24-57µg/L for 96 h	LC50	50
Cuttlefish, *Sepia officinalis*; eggs; 4 (control), 50, 100, or 200 µg/L for 8 weeks	Dose-dependent decrease in hatching time and survival; no external malformations	51
Freshwater snail, *Thiara tuberculata*		
450 µg/L for 20 days	Progressive decline over time in oxygen consumption	52
2,180 µg/L for 72 h	LC50; survivors had decreased oxygen consumption	52
Giant clam, *Tridacna derasa*; embryos age 1 h; exposed at 27º C		

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
0.1 µg/L for 72 h	LC50	53
1.0 µg/L for 72 h	LC65	53
10.0 µg/L for 72 h	LC91	53
Clam, *Villorita cyprinoides*		
450 µg/L for 120 h	No deaths	54
1,000, 3,000, or 5,000 µg/L for 120 h	No deaths. Hemolymph protein levels reduced at 1,000 and 3,000 µg/L, but not in 5,000 µg/L	54, 161
Freshwater mussel, *Villosa iris*		
24 µg/L for 24 h	Valve closure normal	55
27-29 µg/L for 24 h	50% reduction in valve closure	55
83 µg/L for 24 h	LC50	55
Crustaceans		
Copepod, *Acartia clausi*; 52 µg/L for 96 h	LC50	1
Copepod, *Acartia tonsa*; 31 µg/L for 96 h	LC50	1
Amphipod, *Allorchestes compressa*		
3.7 µg/L for 4 weeks	Extrapolated concentration causing detectable decreases in survival and biomass	9
10 µg/L for 4 weeks	Lowest concentration tested causing adverse effects on growth and survival; bioconcentration factor (BCF) of 51,500	9
500 µg/L for 96 h	LC50	9
Cladoceran, *Bosmina longirostris*		
1.4 µg/L for 48 h; starved	50% immobilized	56
3.7 µg/L for 48 h; fed	50% immobilized	56
16 µg/L for 15 days	Growth rate reduced	158
18 µg/L for 15 days	Survival reduced	158
Lesser blue crab, *Callinectes similis*		
50 µg/L for 118 days	No effect on survival or molting during exposure	57
250 µg/L; juveniles	LC50 (30 days); LC100 (68 days)	57
500 µg/L	50% of megalops dead in 3.7 days; 50% of juveniles dead in 7.7 days; all juveniles dead in 49 days	57
Crayfish, *Cambarus bartoni*; copper-tolerant strain exposed to 19 (controls), 125, 250, or 500 µg/L for 4 weeks; concentrations in controls (mg/kg DW) vs. all experimental groups (mg/kg DW)		
Exoskeleton	54 DW vs. 78-116 DW	58
Gills	368 DW vs. 571-1,167 DW	58
Hepatopancreas	1,778 DW vs. 1,494-2,346 DW	58
Muscle	88 DW vs. 99-129 DW	58
Viscera	92 DW vs. 158-276 DW	58
Shore crab, *Carcinus maenas*		
500 µg/L for 5-18 days	Gill histopathology; some recovery after exposure	59
500 µg/L for 28 days Controls (fed) vs. exposed (fed); values in mg/kg DW		
Carapace	5 DW vs. 51 DW	60
Midgut gland	26 DW vs. 474 DW	60
Controls (starved) vs. exposed (starved); values in mg/kg DW		
Carapace	4 DW vs. 72 DW	60

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Midgut gland	298 DW vs. 583 DW	60
2,000 µg/L for 5 days	Some deaths; severe gill cellular hyperplasia	59
Daphnid, *Ceriodaphnia dubia*		
9.5 µg/L for 48 h	LC50 at pH 6.0-6.5	61
28 µg/L for 48 h	LC50 at pH 7.0-7.5	61
200 µg/L for 48 h	LC50 at pH 8.0-8.5	61
Cladoceran, *Chydorus sphaericus*		
3.3 µg/L for 48 h; starved	50% immobilized	56
7.6 µg/L for 48 h; fed	50% immobilized	56
Amphipod, *Corophium volutator*; exposed to <0.1, 50, or 100 µg/L for 14 days in seawater under conditions of normoxia, moderate hypoxia (29% oxygen saturation), and hypoxia (19% oxygen saturation)	Exposure to increasing levels of copper resulted in a significant increase in total body copper concentrations (from 76 to 174 mg/kg DW), and a lowering of egg production; mortality was higher at low oxygen saturations and high copper concentrations (max. 35% dead at 100 µg/L and 19% saturation)	62
Brown shrimp, *Crangon crangon*; 330 µg/L for 96 h	LC50	1
Daphnids, *Daphnia ambigua*, *D. parvula*, *D. pulex*; 49 µg/L for lifetime exposure	Reduced productivity	1
Daphnid, *Daphnia carinata*; 28 µg/L for 96 h	LC50	63
Daphnid, *Daphnia magna*		
5.9 µg/L for 21 days	Growth reduced 10%; bioconcentration factor (BCF) of 4,900; maximum whole body concentration of 43 mg/kg DW	64
10 µg/L for 96 h	LC50 at 45 mg $CaCO_3$/L	1
10 µg/L, life cycle	Inhibited reproduction	1
11.4-16.3 µg/L	MATC[b] at 51 mg $CaCO_3$/L	1
16.1 µg/L for 21 days	Growth reduced 50%	64
20-43 µg/L	MATC[b] at 104 mg $CaCO_3$/L	1
26-59 µg/L for 48 h; fed	LC50; no weight loss among survivors	65
28-58 µg/L for 48 h; starved	LC50; survivors had significant weight loss	65
59 µg/L for 26 h	Feeding rate reduced 50%	16
69 (37-110) µg/L for 21 days	LC50	64
200 µg/L for 96 h	LC50 at 226 mg $CaCO_3$/L	1
Daphnid, *Daphnia pulex*		
0.003-0.3 µg/L for 21 days	Increased reproduction	66
3 µg/L for 21 days	Impaired reproduction	66
5 µg/L for 70 days	Decreased survival beginning at day 58; no effect on reproduction	67
20-37 µg/L for 48 h	LC50	66, 67, 68
20 µg/L for 6 h daily for 70 days	Decreased survival and brood size	67
30 µg/L for 15 days	No significant effect on growth or survival	158
Daphnid, *Daphnia pulicaria*		
7.2-11.4 µg/L for 96 h	LC50 at 44-48 mg $CaCO_3$/L	1
17.8-27.3 µg/L for 96 h	LC50 at 95-245 mg $CaCO_3$/L	1
Amphipod, *Gammarus pseudolimnaeus*		
<4.6 µg/L for 15 weeks (two generations)	No adverse effects	24

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
4.6-8 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
6.2-12.9 µg/L for 5 weeks	Decreased survival	24
20 µg/L for 96 h	LC50	24
Amphipod, *Gammarus pulex*		
Immersed in solutions containing 2.6 (controls), 11, 14.6, 18.2 or 23.1 µg/L for 100 days	Population density doubled in the controls and the 11 µg/L group. Rate of increase was adversely affected at 14.6 and 18.2µg/L; the high-dose group lost population. Low-dose groups were composed mainly of juveniles; at 14.6 µg/L and higher, the number of juveniles decreased; and at 18.2µg/L and higher, number of adults decreased	69
33 µg/L for 240 h	LC50	69
Mysid shrimp, *Holmesimysis costata*; 17 µg/L for 96 h	LC50	70
American lobster, *Homarus americanus*		
48 µg/L for 96 h	Larval LC50	1
100 µg/L for 96 h	Adult LC50	1
Amphipod, *Hyalella azteca*		
1.3 (control), 5.6, 10, 18, 32, 56, or 100 µg/L for 10 weeks beginning at age 1 week	Survival reduced at 32 µg/L and higher; no significant copper accumulations over controls in all groups	71
1.3 (control), 5.6, 10, 18, 32, 56, 100, or 180 µg/L for 4 weeks; adults	Copper residues, in mg/kg DW, were 98 in controls; 122-150 for the 5.6-32 µg/L groups, and >196 for the high dose groups	71
17 µg/L for 96 h	LC50 at pH 6.0-6.5, adults	61
31 (28-35) µg/L for 10 days	LC50, juveniles	73
34 µg/L for 96 h	LC50; age 6-8 days	72
52 µg/L for 96 h	LC50; age 20-24 days	72
87 µg/L for 96 h	LC50 at pH 8.0-8.5	61
Freshwater prawn, *Macrobrachium rosenbergii*; 12 µg/L for 96 h	LC50	74
Freshwater prawn, *Macrobrachium rude*; 18-65 µg/L for 96 h	LC50-LC84	63, 75
Macroinvertebrate communities; 11.3 µg/L for 10 days	Abundance was reduced by 75% in laboratory studies vs. 44% in field experimental streams; number of taxa was reduced 56% in the laboratory vs. 10% in field streams	76
Peneid Shrimp, *Metapenaeus ensis*		
160 µg/L for 48 h	LC50 for larvae	77
250 µg/L for 2 h	Feeding inhibited >50%	77
4,760 µg/L for 48 h	LC50 for postlarvae	77
Cladoceran, *Moina irrasa*		
1.4 µg/L for 24 h	LC50 at pH 5.0, 30º C	78
2.8 µg/L for 24 h	LC50 at pH 6.5, 30º C	78
3.3 µg/L for 96 h	LC50 at pH 5.0, 20º C	78
5.5 µg/L for 48 h	LC50 at pH 5.0, 25º C	78
6.5 µg/L for 96 h	LC50 at pH 6.5, 20º C	78
7.5 µg/L for 96 h	LC50 at pH 8.0, 20º C	78
11.8 µg/L for 48 h	LC50 at pH 8.0, 25º C	78
19.7 µg/L for 24 h	LC50 at pH 8.0, 20º C	78

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Mysid shrimp, *Mysidopsis bahia*; 38-77 µg/L	MATC[b]	1
Norway lobster, *Nephrops norvegicus*		
10 µg/L for 30 days; 4.9 cm in length	Copper concentrations were elevated in most tissues, especially ovary (to 393 from115 mg/kg DW), but not hepatopancreas or external eggs	79
100 µg/L for 14 days	LC100	79
Crab, *Paragrapsus quadridentatus*		
110-250 µg/L for 96 h	LC16-LC84 for larvae	80
170 µg/L for 96 h	LC50 for larvae	80
Freshwater shrimp, *Paratya australiensis*		
15 µg/L, continuous exposure	Mean molt period of 23 days (range20-27 days) vs. 25 days (18-36 days) for controls	81
40 µg/L for 96 h	LC50	81
Amphipod *Parhallella natalensis*; 72 µg/L for 48 h	LC50	82
Crayfish, *Procambarus clarkii*		
120 µg/L for 20 days	LC50 for larvae	83
1,300 µg/L for 20 days	LC50 for adults; increased copper concentrations at >480 µg/L in gills but not other tissues	83
3,700 µg/L for 20 days	LC50 for embryos	83
Copepod, *Pseudodiaptomus coronatus*; 138 µg/L for 96 h	LC50	1
Barnacle, *Semibalanus balanoides*; 20-90 µg/L for 100 days	Dose-dependent increase in copper loadings in bodies and egg masses	84
Copepod, *Tigriopus japonicus*; 487µg/L for 96 h	LC50	1
Copepod, *Tisbe furcata*; 37-57 µg/L	MATC[b]	85
Aquatic insects		
Midge, *Chironomus ninevah*; 0, 20, 100, 150 or 200 µg/L for 21 days (eggs through fourth stage larvae)	Statistically significant, dose-dependent decrease in gene activity of salivary gland chromosomes at 20 µg/L and higher	86
Midge, *Chironomus* sp.; 30 µg/L for 96 h	LC50 at 50 mg $CaCO_3$/L	1
Midge, *Tanytarsus dissimilis*; 16.3 µg/L for 10 days	LC50	1
Various species; 25 µg/L for 10 days in outdoor experimental streams	Mayflies were the most sensitive group with 67-100% reduction in numbers; chironomids had 80% reduction, and caddisflies were reduced by 16-30%	87
Annelids		
Ragworm, *Hediste diversicolor*		
5, 10, or 20 µg/L at four salinities and three temperatures; 1-day-old larvae	20 µg/L caused high mortality at all thermosaline regimens tested; some adverse effects noted at lower concentrations	88
247-513 µg/L for 96 h; no sediments in assay containers	LC50's at various thermosaline regimens	89
3,200-4,100 µg/L for 96 h; sediments present in assay containers	LC50's at various thermosaline regimens	89

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Oligochaete, *Lumbriculus variegatus*		
130 µg/L for 96 h	LC50 at pH 6.0-6.5	61
500 µg/L for 96 h	LC50 at pH 8.0-8.5	61
Marine worm, *Nereis diversicolor*; 500 µg/L at three salinities and three temperatures	Mortality was greatest at 5‰ salinity (50% dead in 44 h vs. 66-82 h at higher salinities), and at 20º C (50% dead in 32 h vs. 88-106 h at lower temperatures)	90
Echinoderms		
Echinoid, *Echinometra mathaei*; 20 µg/L for 4 days	Skeletal development of larvae suppressed	1
Sea urchin, *Paracentrotus lividus*; 10-20 µg/L for 4 days	Pluteal growth retarded	1
Sea urchin, *Strongylocentrotus nudus*; adults held in seawater containing 25 µg/L for 30 days; resultant embryos reared in uncontaminated seawater for 30 days	Food consumption of adults decreased after day 16; accelerated development of pluteal stages; all developmental stages had increased activities of acid phosphatase	91
Fish		
Topsmelt, *Atherinops affinis*		
53 µg/L for 15 min; sperm	No effect on fertilization in 48 h	92
100 µg/L for 7 days; larvae, age 5-20 days	No effect	93
109 µg/L for 15 min; sperm	Egg fertilization reduced 50% in 48 h	92
123 µg/L for 96 h; larvae	No deaths	92
137 µg/L for 7 days; larvae, age 7-20 days	LC50	93
146 µg/L for 48 h; embryos	50% abnormal development	92
180 µg/L for 7 days; larvae, age 1-3 days	No deaths	93
238 µg/L for 96 h; larvae	LC50	92
365 µg/L for 7 days; larvae, age 0-5 days	LC50	93
Zebrafish, *Brachydanio rerio*		
0.05 µg/L for 16 days; eggs and larvae	Delayed hatch	94
0.25 µg/L for 16 days; eggs and larvae	No deaths	94
1.0 µg/L for 16 days; eggs	<50% hatched	94
1.0 µg/L; adults	No avoidance but inhibition of attraction response to L-alanine	95
50-150 µg/L for 7 days; adults	No adverse effects on survival or behavior; dose-dependent decrease in kidney leucocyte numbers and phagocytic response	96
Goldfish, *Carassius auratus*		
36 µg/L for 96 h	LC50 at 20 mg $CaCO_3$/L	1
300 µg/L for 96 h	LC50 at 52 mg $CaCO_3$/L	1
368 µg/L for 96 h	LC50 at 272 mg $CaCO_3$/L	97
White sucker, *Catostomus commersoni*; 12.9-33.8 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
Murrel, *Channa punctatus*; 50 or 100 µg/L for 7 days	Liver pathology	98
Catfish, *Clarias* sp.		
27, 55, or 110 µg/L for 8 weeks; whole fish analyzed for total copper at end of exposure	Copper concentrations, in mg/kg DW, were 15.7 for the low-dose group, 21.8 for the 55 µg/L group, and 31.2 for the high-dose group vs. 6.9	99

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
	DW in controls	
425 µg/L for 96 h	LC50; nonresistant strain	99
4,301 µg/L for 96 h	LC50; copper-resistant strain	100
African sharp-tooth catfish, *Clarias gariepinus*; Olifants River (water of 32-55 µg/L), South Africa		
767-991 µg/L for 96 h	10-20% dead	101
1,240-1,380 µg/L for 96 h; adults and juveniles	LC50 at 21-28º C	101
Pacific herring, *Clupea harengus pallasi*; 33 µg/L for 6 days; embryos	LC50	1
Common carp, *Cyprinus carpio*; 100 µg/L for 43 days	Skin histopathology	102
Northern pike, *Esox lucius*; 34.9-104.4 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
Freshwater fishes; eight species; embryos and larvae; 31.7-43.5 µg/L for 30-60 days	Reduced survival	103
Mummichog, *Fundulus heteroclitus*		
1,000 µg/L for 96 h	Renal and lateral line canal lesions	104
1,700-8,000 µg/L for 96 h	LC30-LC50	104, 105
Indian catfish, *Heteropneustes fossilis*		
250 µg/L; 5 h daily for 30 days	Time-dependent increase in adverse effects on blood chemistry, liver effects on blood chemistry, liver metabolism, and respiration	106
5,000 µg/L for 48-96 h	After 48 h, decreased hematocrit, erythrocyte number, and hemoglobin; after 96 h, increased liver glycogen	107, 108
10,500-25,500 µg/L for 72-96 h	LC50	107, 108
Brown bullhead, *Ictalurus nebulosus*		
4, 8, 16, 32, 64, or 104 µg/L for as long as 600 days; blood chemistry analyzed periodically	Some deaths at 104 µg/L; no deaths at lower doses; no adverse biochemical effects at 16 µg/L and lower	109
4 to 512 µg/L for as long as 20 months	Increases in liver and gill copper concentrations in survivors at 275 µg/L and higher; equilibrium reached within30 days. Copper levels in blood were the same as in controls	110
170 to 190 µg/L for 96 h; juveniles	LC50	110
Channel catfish, *Ictalurus punctatus*; fingerlings exposed for 96 h at 16 mg $CaCO_3$/L		
51-65 µg/L	LC50; chelated copper	111
54-55 µg/L	LC50; nonchelated copper	111
Exposed for 96 h at 239 mg $CaCO_3$/L		
925-1,041 µg/L	LC50; nonchelated copper	111
1,603-1,878 µg/L	LC50; chelated copper	111
Spot, *Leiostomus xanthurus*; 280 (240-330) µg/L for 96 h; adults	LC50	112
Green sunfish, *Lepomis cyanellus*; 937 (686-	LC50	97

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
1,281) µg/L for 96 h		
Bluegill, *Lepomis macrochirus*		
21-40 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1, 114
31 µg/L	Consumed 27% fewer prey than controls	113
40-162 µg/L for 90 days; larvae	Reduced survival	114
40-162 µg/L for 24 months; adults	At 162 µg/L, survival was reduced, growth retarded, and spawning inhibited. Maximum copper concentrations, in mg/kg FW, in treated fish (vs. controls) were 13 in gills (3), 480 in liver (7), and44 in kidneys (22)	114
236-620 µg/L for 96 h; adults	LC50	97, 115
261 µg/L for 7 days, then subjected to a drop in dissolved oxygen over 60 min from 7.8 to 1.3 mg/L and then allowed to recover in copper-free aerated water	No deaths during copper exposure. During hypoxia; 2 of 77 died; survivors had hyperglycemia, lower plasma sodium, lower liver ATP, and higher plasma potassium than did nonexposed controls. Authors concluded that previous copper exposure causes some hypoxia responses to be accentuated in an additive manner	115
1,100 µg/L for 96 h; larvae	LC50	114
4,300 µg/L for 48 h	LC50	116
Atlantic silverside, *Menidia menidia*; 136 µg/L for 96 h; larvae	LC50	1
Tidewater silverside, *Menidia peninsulae*; 140 (110-180) µg/L for 96 h; larvae	LC50	112
Striped bass, *Morone saxatilis*		
50-100 µg/L for 96 h; larvae	LC50 at 68 mg $CaCO_3$/L	1
150 µg/L for 96 h; fingerlings	LC50 at 68 mg $CaCO_3$/L	1
2,680 µg/L for 96 h; fingerlings; 5‰ salinity	LC50	117
7,880-8,080 µg/L for 96 h; fingerlings; 10-15‰ salinity	LC50	117
Cutthroat trout, *Oncorhynchus clarki*		
37 µg/L for 96 h	LC50 at 18 mg $CaCO_3$/L	1
232 µg/L for 96 h	LC50 at 204 mg $CaCO_3$/L	1
Coho salmon, *Oncorhynchus kisutch*		
0, 15, 60, or 90 µg/L for 170 h; yearlings	No deaths; distress noted at 60 and 90 µg/L. Dose-dependent elevation in serum cortisol. When challenged with seawater, copper-exposed salmon had lowered survival and dose-dependent depression in serum chloride levels	118
5-30 µg/L for as long as 172 days; yearlings	Altered downstream migration patterns, lowered gill ATPase activity, and reduced survival. When subjected to >20 µg/L, appetite was depressed for several weeks to months	119
15.1-31.9 µg/L for 96 h; juveniles	LC50	120
18.2 µg/L for 31 days then challenged with seawater	Reduced survival during adaptation to seawater	121
24.6 µg/L for 31 days; fingerlings	Reduced survival; survivors unable to adapt to seawater	121

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
26 µg/L for 96 h; alevins	LC50 at 25 mg $CaCO_3$/L	1
46 µg/L for 96 h; adults	LC50 at 20 mg $CaCO_3$/L	1
60 µg/L for 96 h; smolts	LC50 at 95 mg $CaCO_3$/L	1
60-74 µg/L for 96 h; yearlings	LC50 at 95 mg $CaCO_3$/L	1, 119
70 or 140 µg/L for 14 weeks; fingerlings	Loss of appetite and reduced growth Copper concentrations, in mg/kg DW, at end of study for the controls, the 70 µg/L group, and the 140 µg/L group were 2.9, 5.6, and 9.8 in gills, and 5.7, 6.1, and 7.5 in kidneys	122
70 or 140 µg/L for 14 weeks; liver cytosol samples from fingerlings	Copper concentrations in the low molecular weight fractions of the 70µg/L group were higher than controls after 6 weeks and increased rapidly; those of the 140 µg/L group increased in the first 2-4 weeks then leveled off. Increasing levels of metallothioneins were detected in low molecular weight fractions of copper-exposed salmon. In the high molecular weight fractions, copper concentrations in both groups increased after 8-10 weeks	123
140 or 210 µg/L for 78 h; yearlings	Median survival times were 60 h for the low-dose group and 48 h for the high dose group; survivors had elevated serum cortisol. Livers were normal but kidney and gill histopathology was evident in both groups	118
220-280 µg/L for 168 h; fingerlings	LC50	122
310 µg/L for 168 h; prior exposure to 70 µg/L for 16 weeks; fingerlings	LC50	122
550 µg/L for 168 h; prior exposure to 140 µg/L for 16 weeks; fingerlings	LC50	122
Rainbow trout, *Oncorhynchus mykiss*		
0.1 µg/L for 1 h	Avoidance by fry	1
7.0 µg/L for 200 h; smolts	LC10	1
8.0 µg/L for 2 h	Depressed olfactory bulbar electrical responses to the standard stimulant L-serine	124
9.0 µg/L for 200 h; swimup stage	LC10	1
11.4-31.7 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
13.8 µg/L for 96 h; juveniles	LC50	120
19.0 µg/L for 200 h; alevins	LC10	1
20-30 µg/L for 96 h	LC50 at 30-32 mg $CaCO_3$/L	1
21.5 µg/L for 30 days; juveniles	No adverse effects; no altered susceptibility to *Aeromonas hydrophila* infections	125
22 µg/L for 37 to 41 weeks; two groups: age 14 days postfertilization and posthatch. Controls were held in water containing 4 µg/L	Survival of embryo group reduced 30%. Alterations in cell architecture in both treated groups were noted as early as week 8 posthatch. Both groups had irreversible histopathology of the olfactory organ after 7 months; no histopathology in controls. After 8 months,	126, 127

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
	controls preferred their own rearing water but both copper-exposed groups showed no preference; some recovery 2 to 10 weeks after removal from copper	
36 µg/L for 96 h; alevins	LC50	120
50 µg/L for 24 h; adults	No deaths; some degeneration of sensory receptors	128
50 µg/L for 21 days; juveniles	Rapid and sustained elevation of plasma cortisol levels; altered plasma cholesterol and sodium levels	129
55 µg/L for 28 days; juveniles	Initial inhibition of sodium uptake and whole body sodium content that were normal by day 28. Abnormal liver enzyme activity. Liver copper increased from 23 mg/kg FW at start to 113 mg/kg FW at day 28	164, 165
70 µg/L	Avoidance by juveniles	166
70-514 µg/L for 96 h	LC50 at 194-370 mg $CaCO_3$/L	1
75 µg/L for 24 h	LC50; survivors had complete degeneration of olfactory receptors	128
90 (50-150) µg/L; embryo through posthatch	LC50 at 28 days	162
130-140 µg/L for 24 h	LC50 at pH 6.5-7.5	130
308 µg/L for 24 h in freshwater vs. 400 µg/L for 24 h in 35‰ seawater	All dead in freshwater vs. no deaths in seawater and no major changes in plasma Na^+, Cl^-, K^+, or Ca^{2+}	131
500 or 1,000 µg/L for 2 or 24 h; fingerlings	Gill histopathology in low-dose, low exposure group; damage more severe with increasing dose and exposure	131
500 µg/L for 9 days; weight 400 g; under conditions of normal and low oxygen	No signs of respiratory dysfunction; no difference in dissolved copper uptake due to dissolved oxygen levels	133
1,200 µg/L for 6 h	LC50	130
4,560 µg/L	Juveniles attracted	166
Fed diet containing 13 or 684 mg/kg ration for 42 days and simultaneously exposed to waterborne-copper concentrations of 5, 32, 55, or 106 µg/L (low-copper diet) or 13, 38, 62, or 127 µg/L (high-copper diet)	No adverse effects on growth, survival, or food conversion efficiency. Elevated dietary copper increased copper concentrations in liver, kidney, gill, and digesta; increasing waterborne-copper concentrations produced increasing copper concentrations in liver and kidney. For fish in the high-copper diet, the diet provided 99% of the liver copper in the 38 µg/L group, 85% in the 62 µg/L group, and 73% in the 127 µg/L group	134
Fed diets containing 25.8 mg/kg DW ration (vs. 15.8 mg/kg DW in controls) for 28 days; equivalent to 69.2 mg/kg fish (130 g) daily	Fish readily ate copper-contaminated food. Elevated copper levels in gill, liver, and muscle. Some food regurgitation on days 20-28	135

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Juveniles fed diet containing 200 mg/kg DW for 32 days followed by normal (15.8 mg/kg DW) diet for 12 days	No deaths. After 32 days whole fish contained 1.5 mg/kg FW vs 1.2 at start; copper concentrations were elevated in gill, gut, blood, skin, and mucus, but not in muscle, liver, or kidney. Copper concentrations in gill and kidney tissues were elevated 12 days after exposure, but other tissues were normal	136
Chinook salmon, *Oncorhynchus tshawytscha*		
10-38 µg/L for 96 h	LC50 in soft water	1
19 µg/L for 200 h; swimup stage	LC50	1
20 µg/L for 200 h; alevins	LC50	1
26 µg/L for 200 h; smolts	LC50	1
30 µg/L for 200 h; parr	LC50	1
54-60 µg/L for 96 h; fry	LC50	138
78-145 for 24 h; fry	LC50	138
85-130 µg/L for 96 h	LC50 in hardwater	1
Green snakehead, *Ophiocephalus punctatus*; weight 15-18 g		
5,000-7,500 µg/L for 24 h	Sublethal. Disrupted kidney and liver alkaline phosphatase and acid phosphatase activity	139
70,000 µg/L for 48 h	LC50	139
Nile tilapia, *Oreochromis niloticus* 50, 100, or 200 µg/L for 8 weeks	At end of exposure, whole fish contained 34.7 and 36.1 mg/kg DW in the two lowest-dose groups and 81.0 mg/kg DW in the high-dose group (vs. 17.4 mg/kg DW in controls)	140
964 µg/L for 96 h	LC50	140
Summer flounder, *Paralichthys dentatus*; embryos; 28 µg/L for 96 h	LC50	1
Flounder, *Paralichthys* spp.; juveniles		
6.4 µg/L for 14 days	Interference with calcium metabolism	157
448 µg/L for 14 days	LC50	157
Fathead minnow, *Pimephales promelas* 2 µg/L for 96 h; larvae	LC50 at pH 5.6 and dissolved organic carbon (DOC) of 0.2 mg/L	
10.6-18.4 µg/L	MATC[b] at 30 mg $CaCO_3$/L	
14.5-33.0 µg/L	MATC[b] at 200 mg $CaCO_3$/L	142
15 µg/L for 96 h	LC50 at pH 6.0-6.5	142
23 µg/L for 96 h	LC50 at 20 mg $CaCO_3$/L	143
44 µg/L for 96 h	LC50 at pH 7.0-7.5	1
182 µg/L for 96 h	LC50 at pH 6.9 and dissolved organic carbon of 15.6 mg/L	143
>200 µg/L for 96 h	LC50 at pH 8.0-8.5	143
210 µg/L for 96 h	LC50 at 100 mg $CaCO_3$/L	163
390 µg/L for 96 h	LC50 at 250 mg $CaCO_3$/L	163
430-470 µg/L for 96 h	LC50 in hard water; continuous flow and static assays	142
European flounder, *Platichthys flesus*		

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
Seawater-adapted; exposure for 42 days; experimentals (170 µg/L) vs. controls (3 µg/L); values in mg/kg DW tissue		
Gill	7.7 vs. 2.7	167
Kidney	13.1 vs. 4.1	167
Liver	640.2 vs. 15.6	167
Muscle	7.7 vs. 2.7	167
Freshwater-adapted; exposure for 37 days; experimentals (15 µg/L) vs. controls (5 µg/L); values in mg/kg DW tissue		
Gill	16.2 vs. 6.5	167
Kidney	28.7 vs. 14.3	167
Liver	295.6 vs. 157.8	167
Muscle	4.9 vs. 1.8	167
Guppy, *Poecilia reticulata*		
36 µg/L for 96 h	LC50 at 20 mg $CaCO_3$/L	1
112-138 µg/L for 96 h	LC50 at 67-82 mg $CaCO_3$/L	1
75-84 µg/L for 96 h	LC50 in soft water; continuous flow and static assays	142
Winter flounder, *Pleuronectes americanus*		
129 µg/L for 96 h; embryos	LC50	1
180 µg/L for 29.1 days; adults	Gill histopathology	144
560-3,200 µg/L for 29.2 days; adults	Copper-induced histopathology of kidney, liver, and gill; reduced food intake	144
Mangrove rivulus, *Rivulus marmoratus*; 1,400 µg/L for 96 h	LC50	145
Air-breathing catfish, *Saccobranchus fossilis*; 56, 100, or 320 µg/L for 28 days	Dose-dependent decrease in red and white blood cell numbers, hemoglobin, and hematocrit; histopathology in gill, skin, spleen, and kidney	146
Atlantic salmon, *Salmo salar*		
2.4 µg/L	Avoidance threshold in laboratory	147
12.8-621.0 µg/L	Dose-dependent inhibition of olfactory response; toxic effect mainly on transduction mechanisms of the olfactory receptor cells	148
16.9-20.6 µg/L	Avoidance threshold in field	147
32-125 µg/L for 96 h	LC50 at 8-20 mg $CaCO_3$/L	1, 147
Brown trout, *Salmo trutta*;		
22.0-43.2 µg/L	MATC[b] at 45 mg $CaCO_3$/L	1
103-148 (91-165) µg/L	LC50 at 48 h, juveniles	159
Brook trout, *Salvelinus fontinalis*		
2.7 (control), 4.5, 6.1, or 9.4 µg/L for two generations	No adverse effects on growth, survival, or reproduction; no elevated copper concentrations in gill, liver, kidney, muscle, or eggs	152
3.4, 5.7, 9.5, 17.4, or 32.5 µg/L for 337 days	No significant changes in blood chemistry except for measurable decrease in plasma glutamic oxalacetic transaminase activity at 17.4 and 32.5 µg/L	149

Table 5. Taxonomic group, organism, copper concentration, and other variables	Effects	Reference[a]
6-15 µg/L for 2-24 h; yearlings	Increased cough frequency, increased locomotor activity, and decreased feeding response	150
9.5-17.4 µg/L	MATC[b] at 45 mg $CaCO_3$/L and pH 7.5	151
23, 39, or 68 µg/L for 6 or 21 days	At 39 and 68 µg/L, adverse effects on blood chemistry; decreases in plasma chloride and osmolarity	149
100 µg/L for 96 h; age 14 months	LC50	151
Lake trout, *Salvelinus namaycush*; 22.0-42.3 µg/L	MATC[b] at 45 mg $CaCO_3$/L	92
Red drum, *Sciaenops ocellatus*		
250 µg/L for 96 h; juveniles	No deaths	153
520 µg/L for 96 h; juveniles	LC50 at 25º C and 8‰ salinity	153
Pearl dace, *Semotilus margarita*; 1,000-279,000 µg/L for as long as 7 h then transferred to clean water for 48 h	Decreasing survival and coordination with increasing concentration or duration of exposure after exposure to 1,000 µg/L for 6 h, 9,000 µg/L for 1 h, 74,000 µg/L for 0.33 h, or 279,000 µg/L for 0.25 h	154
Walleye, *Stizostedion vitreum*; 13-21 µg/L	MATC[b] at 35 mg $CaCO_3$/L	1
Florida pompano, *Trachinotus carolinus*; 360-510 µg/L for 96 h	LC50	1
Arctic grayling, *Thymallus arcticus*		
2.65 µg/L for 96 h; swimup fry	LC50	120
9.6 µg/L for 96 h; fry	LC50	120
23-131 µg/L for 96 h; alevins	LC50	120
Amphibians		
Marbled salamander, *Ambystoma opacum*; 50 µg/L for 96 h; embryos	97% survival 4 days posthatch	155
American toad, *Bufo americanus*; tadpoles		
10 µg/L	Avoidance	166
930 µg/L	Attraction	166
Fowler's toad, *Bufo fowleri*; 2,696 µg/L for 7 days; embryos	LC50	155
Two-lined salamander, *Eurycea bislineata*; 1,120 µg/L for 48 h; juveniles	LC50	156
Narrow-mouthed toad, *Gastrophryne carolinensis*		
10 µg/L for 4 days; embryos	34% dead 4 days after hatching	155
40 (30-50) µg/L; embryos through posthatch	LC50 (7 days)	162
50 µg/L for 72 h; embryos	LC50	155
Southern gray treefrog, *Hyla chrysoscelis*		
10 µg/L for 96h; embryos	39% dead 4 days after hatching	155
40 µg/L for 7 days; embryos	LC50	155
60 µg/L for 72 h; embryos	LC50	155
Northern leopard frog, *Rana pipiens*		
10 µg/L for 96h; embryos	34% dead 4 days after hatching	155
50 µg/L for 8 days; embryos	LC50	155

[a]1, USEPA 1980; 2, Bartley 1967; 3, Visviki and Rachlin 1994a; 4, Winner and Owen 1991; 5, Schafer et al. 1994; 6, Visviki and Rachlen 1994b; 7, Abalde et al. 1995; 8, Coppellotti 1989; 9, Ahsanullah and Williams 1991;

10, Stokes 1979; 11, Piccinni and Copellotti 1982; 12, Mersch et al. 1993; 13, Harland and Nganro 1990;14, Janssen et al. 1994; 15, Ferrando et al. 1993; 16, Ferrando and Andreu 1993; 17, Porta and Ronco 1993; 18, Williams and Dusenbery 1990; 19, Huebner and Pynnonen 1992; 20, Jacobson et al. 1993; 21, Cheng 1979; 22, Ebele et al. 1990; 23, Betzer and Yevich 1975; 24, Arthur and Leonard 1970; 25, Belanger et al. 1990; 26, Zaroogian 1979; 27, Okazaki 1976; 28, Coglianse and Martin 1981; 29, Mathew and Menon 1993; 30, Kraak et al. 1992; 31, Kraak et al. 1994; 32, Hameed and Raj 1989; 33, Raj and Hameed 1991; 34, Bordin et al. 1994; 35, Roper and Hickey 1994; 36, Zaroogian et al. 1992; 37, Chelomin and Belcheva 1992; 38, Eisler 1977; 39, Sanders et al. 1991; 40, Calabrese et al. 1984; 41, Sanders et al. 1994; 42, Stromgren and Nielsen 1991; 43, Hole et al. 1993; 44, Gainey and Kenyon 1990; 45, MacKenzie 1961; 46, Viarengo et al. 1981; 47, Viarengo et al. 1990; 48, Davies 1992; 49, Krishnakumar et al. 1990; 50, Winger et al. 1984; 51, Paulij et al. 1990; 52, Mule and Lomte 1994; 53, Soria-Dengg and Ochavillo 1990; 54, Suresh and Mohandas 1993; 55, Jacobson et al. 1993; 56, Koivisto et al. 1992; 57, Neff and Anderson 1977; 58, Zia and Alikhan 1989; 59, Nonnotte et al. 1993; 60, Scott-Fordsmand and Depledge 1993; 61, Schubauer-Berigan et al. 1993; 62, Ericksson and Weeks 1994; 63, Mukhopadhyay et al. 1994; 64, Enserink et al. 1991; 65, Lazorchak and Waller 1993; 66, Roux et al. 1993; 67, Ingersoll and Winner 1982; 68, Dobbs et al. 1994; 69, Maund et al. 1992; 70, Martin et al. 1989; 71, Borgmann et al. 1993; 72, Collyard et al. 1994; 73, West et al. 1993; 74, Natarajan et al. 1992; 75, Vijayaraman and Geraldine 1992; 76, Clements et al. 1990; 77, Wong et al. 1993; 78, Zou and Bu 1994; 79, Canli and Furness 1993; 80, Ahsanullah and Arnott 1978; 81, Daly et al. 1992; 82, Bhat and Vamsee 1993; 83, Rice and Harrison 1983; 84, Powell and White 1990; 85, Bechmann 1994; 86, Aziz et al. 1991; 87, Clements et al. 1992; 88, Ozoh and Jones 1990; 89, Ozoh 1992a; 90, Fernandez and Jones 1990; 91, Durkina and Evtushenko 1991; 92, Anderson et al. 1991; 93, McNulty et al. 1994; 94, Dave and Xiu 1991; 95, Steele et al. 1990; 96, Rougier et al. 1994; 97, Johnson and Finley 1980; 98, Khangarot 1992; 99, Daramola and Oladimeji 1989; 100, Ebele et al. 1990; 101, van der Merwe et al. 1993; 102, Iger et al. 1994; 103, McKim et al. 1978; 104, Eisler and Gardner 1973; 105, Lin and Dunson 1993; 106, Singh and Reddy 1990; 107, Banerjee and Homechaudhuri 1990; 108, Srivastava 1982; 109, Christensen et al. 1972; 110, Brungs et al. 1973; 111, Straus and Tucker 1993; 112, Mayer 1987; 113, Sandheinrich and Atchison 1989; 114, Benoit 1975; 115, Heath 1991; 116, Dobbs et al. 1994; 117, Reardon and Harrell 1990; 118, Schreck and Lorz 1978; 119, Lorz and McPherson 1977; 120, Buhl and Hamilton 1990; 121, Stevens 1977; 122, Buckley et al. 1982; 123, McCarter et al. 1982; 124, Hara et al. 1977; 125, Snarski 1992; 126, Saucier et al. 1991a; 127, Saucier et al. 1991b; 128, Klima and Applehans 1990; 129, Munoz et al. 1991; 130, Shaw and Brown 1974; 131, Wilson and Taylor 1993; 132, Kirk and Lewis 1993; 133, Pilgaard et al. 1994; 134, Miller et al. 1993; 135, Handy 1993; 136, Handy 1992; 137, Carbonell and Tarazona 1994; 138, Hamilton and Buhl 1990; 139, Srivastava and Pandey 1982; 140, Daramola and Oladimeji 1989; 141, Welsh et al. 1993; 142, Mount and Stephan 1969; 143, Schubauer-Berigan et al. 1993; 144, Baker 1969; 145, Lin and Dunson 1993; 146, Khangarot and Tripathi 1991; 147, Sprague et al. 1965; 148, Winberg et al. 1992; 149, McKim et al. 1970; 150, Drummond et al. 1973; 151, McKim and Benoit 1971; 152, McKim and Benoit 1974; 153, Peppard et al. 1991; 154, Tsai 1979; 155, Birge and Black 1979; 156, Dobbs et al. 1994; 157, Dodoo et al. 1992; 158, Koivisto and Ketola 1995; 159, Marr et al. 1995; 160, Eisler 1995; 161, Suresh et al. 1993; 162, Birge 1978; 163, Benson and Birge 1985; 164, Lauren and McDonald 1987a; 165, Lauren and McDonald 1987b; 166, Birge et al. 1993; 167, Stagg and Shuttleworth 1982.

[b]MATC = Maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

No data are available on copper toxicity to avian wildlife. Experiments with domestic poultry show that copper accumulates in livers of mallard ducklings at dietary concentrations as low as 15 mg/kg DW ration; that gizzard histopathology and a reduction in weight gain of chicks (*Gallus* sp.) occur at 250 to 350 mg Cu/kg DW ration; and that growth of turkey poults is improved at 60 mg Cu/kg DW ration and inhibited at 120 mg/kg DW ration, with signs of gizzard histopathology at 500 mg/kg DW ration (Wood and Worden 1973; Poupoulis and Jensen 1976; NAS 1977; Kashani et al. 1986; Table 6).

Table 6. Effects of copper on selected birds

Table 6. Organism, copper dose, and other variables	Effects	Reference[a]
Mallard, *Anas platyrhynchos*		
Fed diets containing 15 or 135 mg/kg ration for 18 days; ducklings	Livers from low-dose group had 30 mg/kg dry weight (DW) at day 4 and 107 mg/kg at day 18; values for the high-dose group were 45 mg/kg at day 4, 74 mg/kg at day 7, and 254 mg/kg DW at day 18	1
For 15 days adults were given a choice of distilled water or water with 30, 60, or 100 mg/L	Ducks consumed significantly more water treated at 100 mg/L than distilled water; no preference was evident at lower doses	2
Ducks, *Anas* spp.		
Ducklings fed diets containing 15 or 50 mg/kg ration for 51 days	Livers from control ducklings had 9.3 mg/kg DW. Livers from both treated groups had about 17 mg/kg DW at day 9, 37 mg/kg at day 30, and 47 mg/kg DW at day 51	1
Ducklings fed diet containing 200 mg/kg DW ration for 58 days	Copper concentrations in livers increased from 23 mg/kg DW at day 23 to 141 mg/kg DW at day 44; at day 58 it had declined to 80 mg/kg DW	1
Domestic chicken, *Gallus* spp.		
Chicks age 1-day fed copper-deficient diet of 0.7 mg/kg ration or copper-adequate diet of 8.0 mg/kg ration for 4-6 weeks	Chicks fed copper-deficient diet had >50% mortality and high frequency of cardiovascular and skeletal lesions. Chicks on copper-adequate diet had negligible mortality, no histopathology, and normal growth	3, 4
Chicks fed diet containing 1.5 mg/kg ration for 60 days	95% dead of copper deficiency	5
Chicks fed diet containing 2.7 mg/kg ration for 60 days	Normal growth but high frequency of vascular rupture	5
Chicks fed diet containing 8.7 mg/kg feed for 60 days	Good survival and growth	5
Day-old chicks fed diets containing 10 (control), 100, 200, or 350 mg/kg ration for 25 days	Reduced weight gain in the 350 mg/kg group; other groups same as controls	6
Chicks fed diets containing 15 or 50 mg/kg ration for 51 days	Livers from controls had 5.9 mg/kg DW; treated groups were similar to controls, with copper concentrations in livers between 4.3 and 8.5 mg/kg DW	1
Adults were fed diets equivalent to 28 mg/kg body weight (BW) daily for the first week, 42 mg/kg BW daily for week 2, and 100 mg/kg BW daily until anemia, toxicosis, or death occurred	After 2 to 6 weeks, chickens were weak, anorectic, and lethargic; 35% were anemic	6
Chicks fed diet containing 200 mg/kg DW for 58 days	Maximum copper concentration in liver was 17.2 mg/kg DW at day 20; by day 58 it had dropped to 7.2 mg/kg DW	1

Table 6. Organism, copper dose, and other variables	Effects	Reference[a]
Chicks fed diets supplemented with 250, 500, or 1,000 mg/kg ration for 4 weeks	No gizzard erosion in controls; chicks fed the 250 mg/kg diet grew better than other treated groups but some had gizzard erosion. Chicks fed the 500 and 1,000 mg/kg diets had decreased growth decreased feed efficiency, and a high frequency of gizzard erosion. Severity of gizzard erosion was significantly reduced in the 500 mg/kg group (but not the 1,000 mg/kg group) by adding 0.35% cholic acid	7
Laying hens fed diets supplemented with 250, 500, 1,000, or 2,000 mg/kg ration for 48 days	Controls and the 250 mg/kg group had lower concentrations of copper in liver than those fed diets containing 500 mg/kg and higher. Copper concentration in the2,000 mg/kg group increased from 3 mg/kg DW at day 3 to 1,790 mg/kg DW at day48 (vs. 11.3 mg/kg DW in controls)	8
Turkey, *Meleagris gallopavo*		
Day-old poults fed diets containing 0, 60, 120, or 240 mg/kg ration and adequate levels of methionine for 24 weeks	Diets containing 60 mg/kg improved body weight at age 8 weeks; the 120 and 240 mg/kg diets inhibited growth for the first8 weeks but not during the next 16 weeks	9
Week-old poults fed a purified corn starch, isolated soy protein diet supplemented with 50 to 800 mg/kg ration for 3 weeks	Dose-dependent increase in mortality and decrease in growth	10
Week-old poults fed corn-soybean meal supplemented with 100 to 800 mg/kg ration	No adverse effects on survival; growth reduced only at 800 mg/kg diet	10
Day-old poults fed diet containing 500 mg/kg ration for 24 weeks	Reduced growth and increased gizzard histopathology	9

[a]1, Wood and Worden 1973; 2, Rowe and Prince 1983; 3, Carlton and Henderson 1963; 4, Carlton and Henderson 1964a; 5, Carlton and Henderson 1964b; 6, National Academy of Sciences 1977; 7, Poupoulis and Jensen 1976; 8, Stevenson and Jackson 1978; 9, Kashani et al. 1986; 10, Supplee 1964.

Copper is lethal to mammals through a variety of routes (Table 7). Single oral doses of 6-637 mg Cu/kg BW are fatal to humans. A single oral dose of 200 mg/kg BW is usually fatal to cattle. Dietary copper is lethal when eaten for extended periods at more than 80 mg Cu/kg ration in sheep (equivalent to 5.1-10.7 mg Cu/kg BW daily), more than 238 mg/kg ration in pigs, and more than 4,000 mg/kg ration in rats (equivalent to more than 133 mg Cu/kg BW daily; Table 7). Adverse sublethal effects of copper to sensitive mammals occur in human infants at drinking water concentrations more than 3 mg Cu/L; in cattle at dietary levels greater than 20 mg Cu/kg BW by way of intraperitoneal injection and more than 4.2 mg Cu/kg BW via drinking water; in sheep given daily oral doses of 7.5 to 15.0 mg Cu/kg BW or fed diets containing more than 37.3 mg Cu/kg ration; in rats at greater than 100 mg Cu/kg ration (equivalent to greater than 7.9 mg Cu/kg BW daily), greater than 400 mg Cu/L drinking water, or greater than 2.0 to 2.5 mg Cu/kg BW daily via injection; and in pigs at more than 14.5 mg Cu/kg BW daily via diet. Elevated copper concentrations (328 mg Cu/kg DW) occur in livers of surviving cattle fed diets containing 8.2 mg Cu/kg ration; of sheep (1,109 mg/kg DW liver) fed diets containing 37.3 mg Cu/kg ration; and of rats (710 mg/kg FW liver) given intraperitoneal injections of 3.75 mg Cu/kg BW daily for 18 weeks (Table 7).

Table 7. Effects of copper on selected mammals

Table 7. Organism, copper dose, and other variables	**Effects**	**Reference[a]**
Cattle, *Bos* spp.		
Fed diet containing 8.2 mg/kg ration for 333 days	Copper concentration in liver increased from 111 to 328 mg/kg dry weight (DW)	1
Fed diets containing 20 to 125 mg/kg ration for extended period	Intoxication	2
Single dose; 200 mg/kg body weight (BW)	Lethal	2
Horses, *Equus* sp.		
Horses given a single oral dose of 20 or 40 mg/kg BW were challenged 24 h later with oral doses of 2, 4, 6, or 8 mg selenium/kg BW	All horses given 20 or 40 mg/kg BW were unaffected by selenium, regardless of dosage; without copper pretreatment, signs of severe Se toxicosis—including lethargy, colic, and death—developed in horses given 6 or 8 mg Se/kg BW	3
Fed diet containing 800 mg/kg ration for 6 months	No adverse effects	4
Humans, *Homo sapiens*		
3 mg/L drinking water for 9 months	Liver damage in infants	5
30 mg/L drinking water; single exposure; total intake unknown	Vomiting, diarrhea, stomach cramps	5
6 to 637 mg/kg BW; single exposure (attempted suicides)	13 of 53 patients died; death attributed to shock and hepatic or renal complications	5
Children who died from Wilson's disease vs. normal children		
Brain	2,090 mg/kg ash weight (AW), equivalent to 31 mg/kg fresh weight (FW) or 129 mg/kg DW vs. 290 mg/kg AW	6
Heart	6,800 mg/kg AW, equivalent to 75 mg/kg FW or 298 mg/kg DW vs. 340 mg/kg AW	6
Kidney	27,160 mg/kg AW, equivalent to 299 mg/kg FW or 1,245 mg/kg DW vs. 250 mg/kg AW	6
Liver	74,570 mg/kg AW, equivalent to 820 mg/kg FW or 2,217 mg/kg DW vs. 1,300 mg/kg AW	6
Pancreas	1,200 mg/kg AW vs. 160 mg/kg AW	6
Spleen	1,930 mg/kg AW vs. 100 mg/kg AW	6
Mice, *Mus* spp.		
Strain genetically deficient in copper (Menkes disease) given subcutaneous injections of 50 µg copper chloride ($CuCl_2$) on postnatal days 7 and 10. Before therapy, liver copper concentration was 3.1 mg/kg FW (vs. 30.1 mg/kg FW in normal mice)	Seven months postinjection there was some reduction in neurodegeneration; copper was distributed normally in liver; in intestine, copper accumulated in histiocytes	7
120 µg/m^3 air for 1-2 weeks	Alveoli thickening	5
<3.3 mg/kg BW; single intraperitoneal (ip) injection	No effect on oxygen consumption or body temperature	8
3.3-8.0 mg/kg BW; single ip injection	Dose-dependent reduction in oxygen consumption and	8

Table 7. Organism, copper dose, and other variables	Effects	Reference[a]
	body temperature	
4.02 mg/kg BW; single ip injection	50% dead	8
Drinking water equivalent of 4.2 mg/kg BW daily for 850 days	Decreased growth and survival	5
Drinking water equivalent of 42.5 mg/kg BW daily as copper glutamate; lifetime exposure	Maximal lifespan reduced from 986 days to 874 days	5
640 mg/L drinking water for 850 days	Decreased survival	5
Mink, *Mustela vison*		
Dietary equivalent of 3.5 mg/kg BW daily for 50 weeks	Decreased survival (deficiency)	5
Dietary equivalent of 13.5 mg/kg BW daily for 50 weeks	Some deaths; no adverse effect on reproduction of survivors	5
Rabbit, *Oryctolagus* sp.		
600 µg/m^3 air for 4 to 6 weeks	No adverse systemic or immunological effects	5
Domestic sheep, *Ovis aries*		
Ewes were fed a copper-deficient diet of 1.3 to 2.5 mg/kg DW ration. At mating, livers contained 20 to 106 mg/kg DW; after lambing, livers contained 3 to 12.3 mg/kg DW	22 of 54 (41%) lambs from ewes fed a copper-deficient diet developed swayback; these lambs had liver concentrations of 5.9 (1.5-11.0) mg/kg DW vs. 6.9 (2.5-14) mg/kg DW in non-swaybacked lambs	11
Ewes from vicinity of copper production plant receiving daily dietary intake of 465 mg/ewe (10.7 mg/kg BW daily) vs. control ewes with average daily dietary intake of 29 mg/ewe (0.67 mg/kg BW daily)	All ewes near copper facility were dead by day 89 vs. none dead in controls. At day 35, ewes near copper production plant had 11.8 mg/kg DW in wool vs. <7 mg/kg DW in controls	9
Merino sheep, 6 to 9 months old; given 5.1 mg/kg BW 5 times weekly for 28 weeks through the mouth as copper sulfate. Heliotrope and nonheliotrope diets	Some deaths. Yellow discoloration of sclera of eye; passing of red-colored urine. Copper concentrations, in mg/kg DW, from sheep fed nonheliotrope diets were 1,394 in liver (824 in controls) and 132 in kidney (20 in controls). Sheep on heliotrope diet had 2,783 mg/kg DW in liver and 321 mg Cu/kg DW in kidney	10
Oral administration of 7.5 mg/kg BW daily for 83 days, as copper sulfate	Severe morphological changes in liver, kidney, and brain; tissue damage continued after cessation of copper and was sufficiently severe to lead to repeated hemolytic crises. Maximum copper concentrations at day 83 were 3,289 mg/kg DW in liver (138 in controls), and 683 in kidney (15 in controls)	12
Lambs fed diets containing 9.1 (control) or 37.3 mg/kg ration for 11 weeks	Normal growth and survival. At slaughter, liver copper concentrations, in mg/kg DW, were 372 in controls and 1,109 in the treated group; plasma aspartate aminotrans- ferase was elevated in the high-dose group	13
Lambs fed diets containing 11 (control), 18, or 25 mg/kg ration for 10 weeks	Survival and growth normal in all groups. Liver concentrations, in mg/kg DW,were239 (11 mg/kg group), 454 (18 mg/kg group), and 721 (25 mg/kg group)	13

Table 7. Organism, copper dose, and other variables	Effects	Reference[a]
Rams, age 4.5 to 5.5 years; daily intake of15 mg/kg BW for 50 days	Increased concentrations of copper in ejaculates (16 mg/kg DW vs. 2 in controls) and liver (1,435 mg/kg DW vs. 63). Sperm motility in test rams was significantly decreased, abnormalities were increased, and testes copper was elevated (96-101 mg/kg DW vs. 60-69 in controls)	14
Equivalent of 20 mg/kg BW daily for 9 weeks	Hemolysis	15
Lambs fed diet containing 80 mg/kg DW ration for 6 weeks	Postmortem examination of 17 lambs that died suddenly showed brain histopathology, particularly in white matter of midbrain, pons, and cerebellum. Severe liver cirrhosis and necrosis of kidney tubules. Liver copper elevated at 3,225 to 4,325 mg/kg DW	16
Laboratory white rat, *Rattus* sp.		
Dietary route		
Male weanlings fed copper-deficient (0.13 mg/kg ration) or copper-adequate (5.7 mg/kg ration) diets for 49 days	24% of the copper-deficient rats died of cardiac rupture; ruptured hearts had lower magnesium and higher sodium, phosphorus, and calcium. Copper-adequate rats had 21.7 mg/kg DW liver vs. 2.2 in copper-deficient rats in which hearts had ruptured	17
Low copper diet of 1 mg/kg DW ration vs. 5 mg/kg diet for 12 weeks	Dose-dependent increase in copper concentrations in kidney, liver, and plasma. Low Cu status increases retention of cadmium in liver	18
100 mg/kg diet for 20 weeks	Increased blood pressure	5
250 mg/kg diet for 3 months	No deaths	5
500 mg/kg diet for 3 months	Kidney damage	5
1,000 mg/kg diet for 3 months	Stomach and liver damage	5
2,000 mg/kg diet for 1 to 3 weeks	Liver and kidney damage	5
4,000 mg/kg diet (133 mg/kg BW daily) for 1 week	Increased mortality	5
6,000 mg/kg diet (300 mg/kg BW daily) for2 weeks	Weanlings died from extensive centrilobular necrosis	5
Equivalent to 7.9 mg/kg BW daily for 90 days	Increased serum glutamic oxaloacetic transaminase enzyme activity	5
Equivalent to 10 mg/kg BW daily for20 weeks	Increased blood pressure; increased hemoglobin	5
Equivalent to 40 mg/kg BW daily for30 days	Anemia, increased liver enzyme activity, increased cholesterol and urea	5
Equivalent to 130 mg/kg BW daily for18 weeks	Decreased body growth; decreased testes weight	5
Equivalent to 144 mg/kg BW daily for4 weeks	Decrease in rate of body weight gain	5
Drinking water route		
0.25, 2, or 16 mg/L for 109 to 119 days	Serum copper rose from 44 µg/L (controls) to 106 µg/L (0.25 mg/L group) to 848 (2 mg/L) to 943 µg/L (16 mg/L group); dose-dependent decrease in serum cholesterol, triglycerides, and phospholipids	19
50 or 150 mg/L for 15 to 30 days	No adverse effect on liver microsomal activity	20
398 to 450 mg/L for 15 to 30 days	Reduction in liver aniline hydroxylase activity; liver	5, 20

Table 7. Organism, copper dose, and other variables	Effects	Reference[a]
	histopathology	
Inhalation route Copper sulfate spray containing 330 g/L for daily exposures of 1 h for as long as 10 days	Concentrations of copper in liver, in mg/kg FW, were 32 after 6 hr, 84 after 5 days, and 285 after 10 days	27
Injection route 0.26 mg/rat daily as copper sulfate for 60 days; subcutaneous (sc) injection	Treated rats had 1,000 mg/kg FW liver (vs. 4.7 in controls); lowered hemoglobin, hematocrit, and red cell counts; mean survival time of 67 days; hepatic and renal histopathology	15
0.625, 1.25, 2.5, or 3.75 mg/kg BW daily for 18 weeks; intraperitoneal injection	Dose-time-dependent increase in copper concentrations in liver, spleen, and lung; little accumulation in muscle and skin. Reduced growth at 2.5 and 3.75 mg/kg BW daily; reduced survival at 3.75 mg/kg BW. Maximum copper concentrations recorded, in mg/kg FW (vs. saline controls,) were 710 in liver (<5), 212 in kidney (<10), 7 in lung (<1.5), 27 in spleen (<2.0), 6 in bone (<2.0), and 2.2 in testes (<1.6)	21
Adult males given 2 mg/kg BW daily as copper acetate for 14 days; intraperitoneal injection	Increased serum ceruloplasmin and white blood cell number	22
Other routes Isolated cells from adrenal and testes held in media containing 0.065, 0.65, or 6.5 in media containing 0.065, 0.65, or 6.5 mg/kg for 2 h	No effect at lowest doses. High dose caused decreased survival of cells from both organs and reduced testosterone production	23
Rodents, various species 3-7 mg/kg BW; single ip or sc injection	50% dead	15
Common shrew, *Sorex araneus* Newly weaned shrews fed diets equivalent to 2.13 mg/shrew daily for 12 weeks; uncontaminated diets contained 25.1 mg/kg DW ration	No effect on growth, survival, or tissue copper burdens; kidney and liver copper concentrations increased in response to cadmium dosing	24, 25
Domestic pig, *Sus* spp. Dietary equivalent of 14.6 mg/kg BW daily for 54 days	Decreased hemoglobin and hematocrit; decreased growth rate	5
Dietary equivalent of 36 mg/kg BW daily for 7 weeks	Decreased hemoglobin, altered serum enzyme activity	5
Fed diets containing <150 mg/kg ration for 9 months	No copper accumulations over controls in liver (16-48 mg/kg DW) or kidney(20-49 mg/kg DW); growth promoting effects	26
Fed diets supplemented with 238-250 mg/kg ration, as copper sulfate, from age 3 weeks for 9 months	High mortality, usually between age 14 and 20 weeks. Dead pigs had 1,300 mg/kg DW in liver and 95 mg/kg in liver; survivors had as much as 2,100 mg/kg DW liver, 670 mg/kg DW kidney, and 3.3 mg/L serum	26
Fed diets containing 700 mg/kg ration for several months	High mortality; survivors had anemia, gastric ulcers, liver pathology, and100-170 mg/kg FW in liver	15

[a]1, Miltmore et al. 1978; 2, Gummow et al. 1991; 3, Stowe 1980; 4, Bremner 1979; 5, ATSDR 1990; 6,

Schroeder et al. 1966; 7, Yoshimura et al. 1995; 8, Gordon et al. 1990; 9, Bires and Vrzgula 1990; 10, Howell et al. 1991; 11, Lewis et al. 1967; 12, Gopinath and Howell 1975; 13, Buckley and Tait 1981; 14, Gamcik et al. 1990; 15, Aaseth and Norseth 1986; 16, Doherty et al. 1969; 17, Saari et al. 1994; 18, Panemangelore 1993; 19, Petering et al. 1977; 20, Moffitt and Murphy 1973; 21, Lal and Sourkes 1971; 22, Jehan and Motlag 1994; 23, Ng and Liu 1990; 24, Dodds-Smith et al. 1992a; 25, Dodds-Smith et al. 1992b; 26, Higgins 1981; 27, Romeu-Moreno et al. 1994.

Terrestrial Plants and Invertebrates

Copper is toxic to sensitive plants when plant nutrient solutions contain greater than 40-200 µg Cu/L, when leaves have greater than 10 to 12 mg Cu/kg DW, and when extractable copper in soils is greater than 60 mg/kg DW soil (Table 4). Excess copper inhibits root elongation and branching and reduces the ability of the plant to explore the soil for water and nutrients (Arduini et al. 1995). Root damage occurs in pine seedlings (*Pinus* spp.) after exposure for 10 days to nutrient solutions that contain 40 µg Cu/L. A lower concentration of 4 µg Cu/L has no adverse effects on root growth and morphology, while a higher concentration of 400 µg Cu/L completely inhibits root growth within 3 days (Arduini et al. 1995). Poultry litter is a useful agricultural byproduct with high nitrogen and phosphorus content and is frequently added to agricultural soils. Poultry litter from northern Georgia containing 1,196 mg Cu/kg DW and applied at a final rate of 5-15 mg Cu/kg soil to fields of Sudex (*Sorghum bicolor* x *S. sudanense*) did not affect copper levels of treated Sudex or produce any evidence of toxicity (van der Watt et al. 1994). But most terrestrial vegetation in the United States, Sweden, Wales, and other locales is usually adversely affected by emissions from copper mines, brass foundries, and copper smelters (Hutchinson 1979). Damage to vegetation persists for at least 50 years after closure of a copper smelter because of copper, arsenic, and lead in the soil. Particularly sensitive to copper in the soils are white pine (*Pinus strobus*) and red maple (*Acer rubrum*); less sensitive are Douglas fir (*Pseudotsuga menziesii*) and lodgepole pine (*Pinus contorta*; Hutchinson 1979).

Earthworms (*Eisenia fetida*) held in soils containing 53 mg Cu/kg DW show a 50% reduction in cocoon production in 56 days; 32 mg Cu/kg soil had no effect on cocoon production (Spurgeon et al. 1994). The LC50 (56 days) value for earthworms is 555 mg Cu/kg DW soil; no deaths occur at 210 mg/kg soil during this period. Copper is more toxic to *Eisenia fetida* than are salts of cadmium, zinc, or lead (Spurgeon et al. 1994). Copper adversely affects the earthworm *Lumbricus rubellus* (Ma 1984). Concentrations of 150 mg Cu/kg surface soil from an accidental spill of copper sulfate in grasslands reduced earthworm populations by about 50%; surface soil concentrations of 260 mg Cu/kg kill almost 100% of the *Lumbricus*. Copper is most toxic to *Lumbricus* at low soil pH (4.8-7.1) and at low temperatures (Ma 1984).

Tests show that the presence of soil reduces the toxicity of copper to the soil-dwelling nematode *Caenorhabditis elegans*; copper toxicity to nematodes increases with increasing densities of bacteria and increasing concentrations of sodium chloride or potassium chloride (Donkin and Dusenbery 1993). Terrestrial isopods efficiently assimilate and store copper as detoxified granules in the hepatopancreas; this activity is in contrast to many species of marine crustaceans that are unable to assimilate, detoxify, or otherwise regulate copper (Weeks and Rainbow 1993).

Aquatic Organisms

Plants

Photosynthesis and growth in sensitive species of freshwater algae are inhibited by copper concentrations of 1-6 µg/L (NAS 1977; Table 5). For sensitive species of estuarine phytoplankton, copper is lethal at 50 µg/L and most toxic under conditions of decreasing salinity, pH, and concentrations of chelators (Erickson et al. 1970). Sensitivity to copper varies widely among species of estuarine algae (Erickson et al. 1970; Table 5); some species, for example, grow normally at concentrations as high as 10 mg Cu/L during exposure for 9 days (Piccinni and Copellotti 1982). In mesocosm studies, 50 µg Cu/L caused a reduction of about 80% in total zooplankton and total algal biovolumes; the algal assemblage that persisted was dominated by diatoms (Havens 1994). Copper-resistant strains of *Euglena gracilis* challenged with high sublethal concentrations of copper for 5 days had an altered cysteine metabolism (Coppellotti 1989).

Some species of aquatic plants absorb or adsorb dissolved copper at extremely high rates (Table 5). Bioconcentration factors for copper and freshwater alga (*Chlorella* sp.) range from 203-2,000 after exposure for 14 to 30 h (USEPA 1980). Seagrass (*Heterozostera tasmanica*) in seawater containing 42 µg Cu/L for several

weeks contain 2,700 mg Cu/kg DW; seagrasses in media containing 0.3 µg Cu/L contain 2.5 mg Cu/kg DW; and intermediate values are reported for 10 µg Cu/L (306 to 564 mg/kg DW) and 20 µg/L (1,280 mg/kg DW; Ahsanullah and Williams 1991). Some freshwater aquatic macrophytes accumulate as much as 54,500 mg Cu/kg DW, as was the case for *Lemna* sp. during exposure to 1,000 µg Cu/L; a lower dose regimen of 35 µg Cu/L results in 256 mg Cu/kg DW *Lemna* (Stokes 1979).

Cnidarians

Sea anemones (*Anemonia viridis*) in seawater solutions containing 50 or 200 µg Cu/L regulate copper by expelling zooxanthellae which are shown to accumulate copper (Harland and Nganro 1990).

Mollusks

Initial effects of copper on mussels (*Mytilus* spp.) include valve closure, a reduction in filtration rates, and cardiac inhibition; these responses all serve to slow the uptake of copper through a reduction in mussel contact with the ambient environment and a reduction in blood flow within the organism (Gainey and Kenyon 1990). Copper impairs the structure and function of cellular membranes in mussels by stimulating the peroxidation of membrane lipids; end products of lipid peroxidation contribute to the formation of lipofuscins (Viarengo et al. 1990). Copper-induced lysosomal lipofuscin accumulations, together with metallothioneins, control copper residues at the cellular levels and are responsible for the short half-time persistence (6 to 8 days) of copper in the digestive gland of mussels (Viarengo et al. 1990). Concentrations of heat shock protein (hsp60) in mantle tissues of mussels exposed to copper increased in a dose-dependent manner; hsp60 may have potential as a biomarker of copper insult (Sanders et al. 1991). Copper-stressed common mussels (*Mytilus edulis*) die more quickly under conditions of anoxia, high temperatures, and low salinities (Weber et al. 1992). Concentrations of copper that cause a decrease in yields of normal larvae in populations of *Mytilus edulis* from unpolluted or mildly contaminated sites did not affect embryonic development of mussels from polluted sites; cross breeding of mussels from these sites suggests that copper tolerance in mussels is mostly maternally determined (Hoare et al. 1995a). Embryos of common mussels are more sensitive to copper than veliger larvae or postlarval spat stages (Hoare et al. 1995b). A copper-induced decrease in glochidial viability is a possible explanation for the disappearance of freshwater unionid mussels from acid- and metals-contaminated waters (Huebner and Pynnonen 1992). Hole et al. (1993) state that mussels of all ages are equally susceptible to copper and that their capacity to recover declines with increasing age; however, this phenomenon needs verification.

Bioconcentration factors for marine bivalves (ratio of milligrams of copper per kilogram fresh weight soft parts to milligrams of copper per liter of medium) vary from 85 to 28,200. Bioconcentration factors for copper are highest for American oysters after exposure for 140 days (20,700-28,200), and lowest for bay scallops (*Argopecten irradians*) after exposure for 112 days (3,310) and for softshell clams after exposure for 35 days (3,300; USEPA 1980). Copper is more toxic to embryos of the tropical giant clam (*Tridacna derasa*) than to embryos of bivalves from temperate regions (Soria-Dengg and Ochavillo 1990), possibly because many tropical species of shellfish live near their upper lethal thermal limits and are unable to withstand additional environmental stressors. Juveniles of Asiatic clams (*Corbicula fluminea*) are more sensitive than adults to ionic copper (Belanger et al. 1990).

On exposure to lethal concentrations of copper the channeled whelk (*Busycon canaliculatum*), a marine gastropod, accumulates the metal in gill and osphradium. These tissues show progressive histopathology including swelling of the gill filaments, amoebocytic infiltration of the connective tissue, and necrosis and sloughing of the mucosa (Betzer and Yevich 1975). Copper-resistant strains of freshwater gastropods are found in media containing elevated concentrations of 35 µg Cu/L (Ebele et al. 1990), suggesting physiological or genetic adaptation. Fine suspensions of copper and kaolinite mixtures are more toxic to freshwater gastropods than copper alone; toxicity is greater at pH 8 than at pH 7 (Al-Sabri et al. 1993). The authors conclude that copper is strongly adsorbed by kaolinite in alkaline media and that the acidic pH of the snail gut enhances release of ionic copper. In freshwater gastropods, ionic copper causes hypersynthesis of lysosomal enzymes and acid and alkaline phosphatases; immature gastropods are more sensitive than adults (Winger et al. 1984).

Arthropods

Life-cycle exposures of four daphnid species to graded concentrations of copper show reductions in survival at more than 40 µg/L and reductions in growth and reproduction at 40 to 60 µg/L; heavier and larger species are the most resistant to copper (Winner and Farrell 1976; Table 5). Starvation increases the sensitivity of most species of freshwater cladocerans to copper (Koivisto et al. 1992); however, there is no difference in LC50 (48

h) values between fed and starved *Daphnia magna* (Lazorchak and Waller 1993). Bioavailability and toxicity of copper to *D. magna* and other tested arthropods are usually higher under conditions of increasing acidification, ionic copper, alkalinity, and temperature, or of decreasing dissolved organic carbon (Meador 1991; Taylor et al. 1994; Zou and Bu 1994). Mixtures of copper and other metals produce additive or more-than-additive effects in *D. magna* than would be expected on the basis of individual components (Enserink et al. 1991). The concept that chronic exposures to pulses of the LC50 concentrations of copper or cadmium causes no damage to freshwater organisms—provided that the average daily concentration never exceeds the no-observable-effect concentration—was tested in daphnids. The concept was true for cadmium but not copper, and the use of pulsed exposures for establishing water quality criteria to protect aquatic life needs to be reexamined (Ingersoll and Winner 1982).

Copper uptake by aquatic arthropods occurs usually by way of the gut after eating or from the gills and other permeable surfaces in contact with the ambient medium (Weeks and Rainbow 1993). Copper accumulations by crustaceans are greatest at elevated (summer) temperatures and during molting (Powell and White 1990). A relatively high bioconcentration factor of 2,000 is documented for copper and freshwater stoneflies (*Pteronarcys californica*; USEPA 1980), but the reasons for this phenomenon are unknown. The high tolerance to copper and other metals of mayfly larvae (*Baetis thermcius*), and high copper accumulations, is attributed, in part, to the selective induction of metal binding proteins in the gut (Sumi et al. 1991; Table 3). Marine amphipods readily accumulate dissolved copper from seawater in a dose-dependent manner (Weeks and Rainbow 1991). But some species of talitrad amphipods are unable to meet their copper requirements from seawater alone and depend on dietary sources of copper (Weeks and Rainbow 1993). Mesocosm studies with freshwater zooplankton assemblages show that increasing copper concentrations in the range 0 to 50 µg/L causes a reduction in total zooplankton and changes in diversity; within 4 days, copepods became dominant at the expense of cladocerans (Havens 1994).

Soldier crabs (*Mictyris longicarpus*) accumulate copper mostly from sediments rather than the water column (Weimin et al. 1994). The fine particles of sediment trapped as food contain bioavailable fractions of copper and other metals, and these significantly correlate with metal concentrations in the body of the crab. However, copper accumulation from sediments by soldier crabs occurred only at an artificially high concentration (1,900 mg Cu/kg DW sediment), which also had toxic effects. Soldier crabs seem unable to regulate copper within their bodies (Weimin et al. 1994).

In shore crabs (*Carcinus maenas*), several days of exposure to sublethal concentrations of waterborne copper cause extensive damage to gill epithelium; at lethal concentrations, tissue hypoxia is probably the major effect of copper (Nonnotte et al. 1993). Starved shore crabs show a reduction in carapace copper concentrations and heavier midgut glands; starvation in combination with copper exposure (500 µg/L) results in an increase in copper in the carapace and a decrease in carapace calcium (Scott-Fordsmand and Depledge 1993). Shore crabs in seawater with high (10 mg/L) levels of waterborne copper show reductions in hemolymph sodium, gill sodium-potassium-ATPase activity, activities of various midgut gland enzymes (hexokinase, phosphofructokinase, pyruvate kinase), and hemolymph electrolytes (Hansen et al. 1992a, 1992b).

In the rusty crayfish (*Orconectes rusticus*), toxicity of copper at high concentrations is due to the coagulatory action on cellular proteins and to interference with respiratory processes; at low concentrations, copper causes degenerative changes in certain tissues and interferes with glutathione equilibrium (Hubschman 1967). Larvae of the red crayfish (*Procambarus clarkii*) exposed to copper as embryos are less sensitive than those exposed after hatching, suggesting acclimatization (Rice and Harrison 1983).

Annelids

Aquatic oligochaetes (*Lumbriculus variegatus*) do not accumulate significant amounts of copper when compared to controls after exposure for 30 days in sediments containing as much as 90.1 mg Cu/kg DW or in water containing as much as 2.3 µg Cu/L (Ankley et al. 1994). Larvae of the sandworm (*Nereis diversicolor*) are more resistant to copper with increasing organism age and with increasing temperature and salinity of the medium (Ozoh and Jones 1990). In adult sandworms, whole body loadings of copper usually increase with increasing temperature in the range of 12-22º C and with decreasing salinity in the range 0.7-3.1% (Ozoh 1992b); however, copper-temperature-salinity interactions are significant and complex in this species (Ozoh 1994).

Fishes

Adverse sublethal effects of copper on behavior, growth, migration, and metabolism occur in representative species of fishes at nominal water concentrations between 4 and 10 µg/L. In sensitive species of teleosts, copper adversely affects reproduction and survival from 10-20 µg Cu/L (Hodson et al. 1979; Table 5). Copper exerts a wide range of physiological effects in fishes, including increased metallothionein synthesis in hepatocytes, altered blood chemistry, and histopathology of gills and skin (Iger et al. 1994). At environmentally realistic concentrations, free copper adversely affects resistance of fishes to bacterial diseases; disrupts migration (that is, fishes avoid copper-contaminated spawning grounds); alters locomotion through hyperactivity; impairs respiration; disrupts osmoregulation through inhibition of gill Na^+-K^+-activated ATPase; is associated with tissue structure and pathology of kidneys, liver, gills, and other hematopoietic tissues; impacts mechanoreceptors of lateral line canals; impairs functions of olfactory organs and brain; and is associated with changes in blood chemistry, enzyme activities, and corticosteroid metabolism (Hodson et al. 1979). Copper-induced cellular changes or lesions occur in kidneys, lateral line, and livers of several species of marine fishes (Gardner and LaRoche 1973).

Copper-induced mortality in teleosts is reduced in waters with high concentrations of organic sequestering agents and in genetically resistant species (Hodson et al. 1979). At pH values less than 4.9 (that is, at pH values associated with increased aluminum solubility and toxicity), copper may contribute to the demise of acid-sensitive fishes (Hickie et al. 1993). Copper affects plasma Na^+ and gill phospholipid activity; these effects are modified by water temperature and hardness (Hansen et al. 1993). In red drum, copper toxicity is higher at comparatively elevated temperatures and reduced salinities (Peppard et al. 1991). Copper is acutely toxic to freshwater teleosts in soft water at concentrations between 10 and 20 µg/L (NAS 1977). In rainbow trout, copper toxicity is markedly lower at high salinities (Wilson and Taylor 1993). Comparatively elevated temperatures and copper loadings in the medium cause locomotor disorientation of tested species (Kleerekoper 1973). Copper may affect reproductive success of fish through disruption of hatch coordination with food availability or through adverse effects on larval fishes (Ellenberger et al. 1994). Chronic exposure of representative species of teleosts to low concentrations (5 to 40 µg/L) of copper in water containing low concentrations of organic materials adversely affects survival, growth, and spawning; this range is 66 to 120 µg Cu/L when test waters contain enriched loadings of organic materials (Hodson et al. 1979).

Larval and early juvenile stages of eight species of freshwater fishes are more sensitive to copper than embryos (McKim et al. 1978) or adults (Hodson et al. 1979). But larvae of topsmelt (*Atherinops affinis*) are increasingly sensitive to copper with increasing age. Topsmelt sensitivity is associated with increasing respiratory surface area and increasing cutaneous and branchial uptake of copper (McNulty et al. 1994).

Sublethal exposure of fishes to copper suppresses resistance to viral and bacterial pathogens (Rougier et al. 1994) and, in the case of the air-breathing catfish (*Saccobranchus fossilis*), affects humoral and cell-mediated immunity, the skin, and respiratory surfaces (Khangarot and Tripathi 1991). Rainbow trout exposed to 50 µg Cu/L for 24 h—a sublethal concentration—show degeneration of olfactory receptors that may cause difficulties in olfactory-mediated behaviors such as migration (Klima and Applehans 1990). The primary site of sublethal copper toxicity in rainbow trout is the ion transport system of the gills (Hansen et al. 1993). In European sea bass (*Dicentrarchus labrax*), copper compromises the defense system of red blood cells against active forms of oxygen, leading to increased membrane lipid peroxidation (Roche and Boge 1993).

Dietary copper is more important than waterborne copper in reducing survival and growth of larvae of rainbow trout (Woodward et al. 1994). Simultaneous exposure of rainbow trout to dietary and waterborne copper results in significant copper assimilation. Diet is the main source of tissue copper; however, the contribution of waterborne copper to tissue burdens increases as water concentrations rise (Miller et al. 1993).

Rate and extent of copper accumulations in fish tissues are extremely variable between species and are further modified by abiotic and biological variables. Copper accumulations in fish gills increase with increasing concentrations of free copper in solution, increasing dissolved organic carbon (DOC), and decreasing pH and alkalinity (Playle et al. 1993a, 1993b). Starved Mozambique tilapia accumulate significantly more copper from the medium in 96 h than did tilapia fed a diet containing 5.9 mg Cu/kg DW ration (Pelgrom et al. 1994). The bioconcentration factor for whole larvae of the fathead minnow was 290 after exposure for 30 h, but only 0.1 in muscle of bluegills after 660 h (USEPA 1980). Prior exposure of brown bullheads (*Ictalurus nebulosus*) to

sublethal copper concentrations for 20 days before exposure to lethal copper concentrations produces higher copper concentrations in tissues of dead bullheads than in those not previously exposed; however, the use of tissue residues is not an acceptable autopsy procedure for copper (Brungs et al. 1973). Rising copper concentrations in blood plasma of catfish (*Heteropneustes fossilis*) seem to reflect copper stress, although the catfish appear outwardly normal. Plasma copper concentrations of catfish increase from 290 µg Cu/L in controls at start to 380 µg Cu/L in survivors at 72 h (50% dead); a plasma copper concentration of 1,060 µg Cu/L at 6 h is associated with 50% mortality (Banerjee and Homechaudhuri 1990). In rainbow trout, copper is rapidly eliminated from plasma; the half-time persistence is 7 min for the short-lived component and 196 min for the long-lived component (Carbonell and Tarazona 1994).

Attraction to waters containing low (11 to 17 µg/L) concentrations of copper occurs in several species of freshwater teleosts, including goldfish (*Carassius auratus*) and green sunfish (*Lepomis cyanellus*); however, other species, including white suckers (*Catostomus commersonii*), avoid these waters (Kleerekoper 1973). In avoidance/attraction tests, juvenile rainbow trout avoided waters containing 70 µg Cu/L but were significantly attracted to water containing 4,560 µg Cu/L; a similar pattern was observed in tadpoles of the American toad, *Bufo americanus* (Birge et al. 1993). Copper concentrations in the range of 18 to 28 µg/L interfere with bluegill growth and prey choice (Sandheinrich and Atchison 1989). Copper interferes with the ability of fish to respond positively to L-alanine, an important constituent of prey odors; concentrations as low as 1 µg Cu/L inhibit this attraction response in some species (Steele et al. 1990).

Increased tolerance to copper was observed in fathead minnows after prolonged exposure to sublethal concentrations, but tolerance was not sustained on removal to clean water. Copper tolerance in fathead minnows is attributed to increased production of metallothioneins (Benson and Birge 1985). Copper tolerance in rainbow trout seems dependent on changes in sodium transport and permeability (Lauren and McDonald 1987a).

Integrated Studies

Bioconcentration and biomagnification of copper occurs in the food chain of diatom (*Skeletonema costatum*) to clam (*Donax cuneatus*) to white prawn (*Penaeus indicus*). All species accumulate copper from the medium, and clams and shrimp from the diet. Maximum concentrations after exposure to 200 µg Cu/L and diets for 10 days, in mg Cu/kg FW, are 2.8 in whole diatoms, 13.6 in clam soft parts, and 33.9 in whole shrimp (Rao and Govindarajan 1992). In the marine food chain of phytoplankton to clam *(Tellina tenuis*) to juvenile plaice (*Pleuronectes platessa*), copper accumulates in a concentration-dependent manner in viscera of plaice. All organisms held in 10, 30, or 100 µg Cu/L solutions for 100 days had reduced growth. Copper concentrations, in mg Cu/kg DW at day 100, in soft parts of clams *(T. tenuis)* were 270 in the 10 µg/L group, 470 in the 30 µg/L group, and 1,100 in the 100 µg/L group vs. less than 50 in the controls; for plaice viscera, these values were 30 in controls, 71 in the 10 µg/L group, 147 in the 30 µg/L group, and 467 mg/kg DW in the 100 µg/L group (Saward et al. 1975). Accumulations in Pacific oysters held in copper-loaded sediments are similar to those of oysters contaminated through ingestion of diatoms (*Haslea ostrearia*). However, accumulations are highest in Pacific oysters when exposed through the medium (Ettajani et al. 1992); in that study, a concentration of 30 µg Cu/L medium for 21 days results in copper concentrations of 137 mg/kg DW in diatoms and 1,320 mg/kg DW in oyster soft parts. Oysters fed contaminated diatoms in the study had 419 mg Cu/kg DW soft parts. Oysters held in sediments containing 108 mg Cu/kg DW—a level reached after exposure for 21 days to 300 µg Cu/L—had 401 mg Cu/kg DW (Ettajani et al. 1992). Copper-induced changes in population density and community metabolism occur in an aquatic mesocosm of algae, protozoans, rotifers, oligochaetes, and bacteria; death of rotifers, algae, and oligochaetes occurs at concentrations as low as 700 µg Cu/L. Adverse effects occur at 300 to 700 µg Cu/L but are negated by increasing concentrations of dissolved organic matter (Sugiura et al. 1982).

Transfer of copper from wood treated with chromated copper arsenate (CCA) occurs in estuarine algae (*Ulva* sp., *Enteromorpha* sp.), American oysters, mud snails (*Nassarius obsoletus*), and fiddler crabs (*Uca* spp.; Weis and Weis 1992). Algae, barnacles, and mussels from CCA-treated lumber show elevated concentrations of copper when compared to reference sites. The epibiotic estuarine community that forms on CCA-treated wood has lower species richness, diversity, and biomass when compared to untreated lumber (Weis et al. 1993b). Copper is trophically transferred from CCA-exposed American oysters to predatory gastropods (*Thais* sp.), resulting in reduced gastropod feeding and growth (Weis and Weis 1993).

Birds

No data are available on the toxicity of copper to avian wildlife. All studies with birds and copper use domestic chickens, ducks, or turkeys (Table 6). Copper, however, may indirectly affect avian wildlife by curtailing certain prey species. Winger et al. (1984), for example, show that apple snails (*Pomacea paludosa*) are not only extremely susceptible to copper (LC50 of 24 to 57 µg/L in 96 h; immatures most sensitive), but are the primary food of the snail kite (*Rostrhamus sociabilis*), an endangered species. The decline of the apple snail in southern Florida coincided with the use of copper-diquat to control hydrilla aquatic weeds (*Hydrilla verticillata*), with serious implications for the snail kite (Winger et al. 1984).

In the domestic chicken, adverse effects of copper occur in chicks fed diets containing 350 mg Cu/kg ration for 25 days (reduced weight gain) and in adults given a dietary equivalent of more than 28 mg Cu/kg BW (Table 6). Chicks fed diets of 500 mg Cu/kg ration show damage to the gizzard lining; damage effects are attributed to the shedding of gizzard glandular cells into the keratin-like koilin layer, disrupting koilin production (Bremner 1979). Copper-induced gizzard histopathology in growing chicks is not reversed by zinc or vitamins B_{12} or E (Poupoulis and Jensen 1976). Supplementing chick diets with copper did not prove markedly advantageous (Poupoulis and Jensen 1976), provided that normal rations had about 4 mg Cu/kg and adequate iron (Carlton and Henderson 1964b). Unlike mammals, chicks fed copper-supplemented diets do not have elevated copper concentrations in liver or signs of liver damage (Bremner 1979). Broiler hens housed on slats made of lumber pressure-treated with chromated copper arsenate showed severe foot-pad dermatitis and excessive mortality after 17 weeks; however, arsenic and cresylic acid—not copper—may be the responsible agents (Sander et al. 1994).

Ducklings (*Anas* spp.), unlike chicks, accumulate copper in livers when fed diets supplemented with high loadings of copper (Wood and Worden 1973). Domesticated mallards show a dose-time dependent increase in copper liver concentrations, with a maximum concentration of 254 mg Cu/kg DW liver (Table 6). Mallards seem to prefer drinking water containing 100 mg Cu/L over distilled water (Table 6); however, these birds were molting and this may have influenced their response because trace mineral requirements rise during molting (Rowe and Prince 1983).

In turkeys, natural diets with as much as 800 mg Cu/kg ration have no adverse effects on growth or survival. But purified diets are toxic to turkeys in three weeks, and purified diets that contain as little as 50 mg Cu/kg ration produce adverse effects (Waibel et al. 1964). Turkeys fed purified diets with supplemented copper show a dose-dependent increase in mortality and decrease in growth; these effects are attributed to a copper-accelerated dietary deterioration (Supplee 1964). Turkey growth and survival are acceptable when fed purified diets supplemented with as much as 800 mg Cu/kg ration provided that effective levels of added antioxidant (0.02% ethoxyquin) and stabilized sources of vitamins A and D are present (Supplee 1964).

Mammals

Wilson’s disease is the only naturally occurring neuropathological condition in humans and other mammals in which copper poisoning is implicated. People with Wilson’s disease have severe pathological changes in the brain, especially in the basal ganglia, and in the liver; pathology is associated with excess copper in tissues (Doherty et al. 1969). Copper concentrations in tissues from children that die from Wilson’s disease are as much as 2,217 mg/kg DW in liver and 1,245 mg/kg DW in kidney (Table 7). Long-term exposure of humans to copper dust irritates the nose, eyes, and mouth and causes headaches, dizziness, nausea, and diarrhea (USEPA 1980; ATSDR 1990). Drinking water that contains higher than normal concentrations of copper may cause vomiting, diarrhea, stomach cramps, nausea, and greenish or bluish stools and saliva. Intentionally high intakes of copper may result in liver and kidney damage, and sometimes death, especially in children. The seriousness of the effects of copper is expected to increase with increasing dose and duration of exposure (USEPA 1980; ATSDR 1990). Human tissues exposed directly to copper or copper salts will suffer adverse effects because of copper absorption. This is the case for copper bracelets on sweaty skin, for certain intrauterine devices, and for copper dental fillings (USEPA 1980). In monkeys, copper used as dental fillings in deciduous teeth causes more severe pulp damage than did other materials studied (USEPA 1980).

Mammals and birds are 100-1,000 times more resistant to copper than other animals (Schroeder et al. 1966). But excessive dietary intakes of copper by 20- to 50-fold over normal levels may have serious effects in mammals. Depending on the species, growth and food intake may be reduced, anemia may develop, and liver,

kidney, brain, and muscle may degenerate, often resulting in death (Bremner 1979; ATSDR 1990). Copper poisoning in mammals may result from consumption of plants treated with copper-containing pesticides, from the veterinary use of copper sulfate to control helminthiasis and infectious pododermatitis in cattle and sheep, and from the ingestion of contaminated soils and vegetation near copper mining and refining operations (NAS 1977). Emissions from copper mines and smelters are often associated with deaths of horses, cows, and sheep; pasture lands, in some cases, are fit for grazing only after heavy rains (Hutchinson 1979).

Ruminant mammals are significantly more sensitive to copper than nonruminant mammals and poultry (Schroeder et al. 1966; NAS 1977). Signs of copper poisoning in ruminants include vomiting, excessive salivation, abdominal pain, diarrhea with greenish-tinted feces, pathology of internal organs, elevated copper concentrations in liver, altered enzyme activities in liver and serum, and collapse and death within 24 to 48 h (NAS 1977). Young calves may develop copper toxicosis at relatively low copper intakes, especially when receiving milk-based diets; goats, however, seem resistant to copper toxicosis (Bremner 1979). Among ruminants, domestic sheep are particularly susceptible to copper insult from grazing on pastures treated with copper-containing fungicides and molluskicides or from inadvertently consuming diets specially formulated for pigs and which contain large amounts of copper as a swine growth stimulant (Todd 1969; Bremner 1979).

Chronic copper poisoning in domestic sheep is first characterized by a period of passive accumulation of copper in the tissues. This period varies from a few weeks to more than a year. During this time the animal appears outwardly normal although the liver may contain more than 1,000 mg Cu/kg DW and plasma activities of aspartate transaminase, sorbitol dehydrogenase, lactic dehydrogenase, and arginase increase, indicating that liver damage has occurred. During the last few weeks of the passive phase, and prior to the so-called toxic phase, liver histopathology of parenchymal cells and copper-containing Kupffer cells occurs. The toxic phase, which is an acute illness and referred to as the hemolytic crisis, usually results in death 2-4 days later. During this phase sheep refuse to eat but have an excessive thirst. The eyes are usually sunken. The venous blood is chocolate colored. The liver is jaundiced. The kidneys are completely gorged with hemoglobin breakdown products and the medulla and cortex are black. The spleen is enlarged, with the parenchyma a deep brown to black color. The onset of these signs in sheep is associated with liberation of copper from the liver and a massive increase in blood copper concentrations. The increased blood copper concentrations lead to an increase in blood methemoglobin and a sudden fall in the erythrocyte glutathione level immediately followed by massive hemolysis and kidney damage, leading to uremia and death. At the time of crisis, elevated serum creatine phosphokinase activity suggests that muscle cell membranes are affected, and elevated serum glutamic oxaloacetate transaminase (SGOT) and lactic dehydrogenase activities indicate progressive liver necrosis (Doherty et al. 1969; Todd 1969; Thompson and Todd 1974; Bremner 1979). It is emphasized that (1) blood copper status and liver function in sheep experimentally poisoned with copper sulfate are linked to elevated SGOT activities 1 to 6 weeks in advance of obvious external signs (MacPherson and Hemingway 1969); (2) copper chloride is 2 to 4 times more toxic to sheep than copper sulfate is (NAS 1977); and (3) the use of copper-enriched feeding stuffs increases the risk of chronic copper poisoning in sheep fed purified rations (Froslie et al. 1983). Also, sheep that accumulate higher than normal amounts of copper in the liver (i.e., 1,900 mg Cu/kg DW) are more severely affected by lupinosis (acute liver atrophy due to poisoning by ingestion of plants of *Lupinus* spp.) than sheep with normal (40 mg/kg DW) concentrations of copper in the liver (Gardiner 1967).

Copper toxicosis in lambs of domestic sheep occurs at dietary concentrations between 8 and 60 mg Cu/kg ration. The wide range of dietary concentrations is a function of copper availability. Availability, in turn, is influenced by dietary composition, genetic influence, age, breed, sex, physiological state, and interactions with other dietary constituents including iron, zinc, and molybdenum (Bremner 1979). Chronic copper poisoning in lambs occurs at dietary levels as low as 27 mg Cu/kg DW ration (Buckley and Tait 1981). During the passive phase, lambs—like adults—have normal plasma copper concentrations and seem outwardly unaffected. Unlike adults, copper accumulates in livers of lambs during a shorter period (several weeks to months vs. months to years). Signs of hemolytic crisis and death within a few days are similar for both adults and lambs. Elevated plasma aspartate aminotransferase (AAT) activity in lambs—up to 10 times higher than controls—occurs 4 to 8 weeks before the hemolytic crisis (Buckley and Tait 1981) and strongly indicates a need for more research on the usefulness of AAT and other enzymes as early indicators of copper stress. A recommended treatment for lambs diagnosed with chronic copper poisoning is 20 mL of a mixture containing 100 mg of ammonium molybdate and 1 g of sodium sulfate administered orally 5 days weekly (Doherty et al. 1969).

In domestic pigs, copper toxicosis results from eating diets containing 250 mg Cu/kg ration and is characterized by anemia, jaundice, elevated levels of Cu in serum and liver, and elevated serum AAT activity (USEPA 1980). Shortly before death, copper-poisoned pigs had white noses, poor balance, stomach histopathology, orange cirrhotic livers, anorexia, and anemia (Higgins 1981).

In rodents, copper administered by single intraperitoneal or subcutaneous injection is lethal at 3 to 7 mg Cu/kg BW (Table 7). Mice died when their drinking water had 640 mg Cu/L (Table 7). In rats, copper accumulation in kidneys and lungs is similar regardless of route of administration (Romeu-Moreno et al. 1994). Concentrations of copper in serum of rats (*Rattus* sp.) reflect dietary copper; concentrations in liver and kidney are directly related to serum Cu and ceruloplasmin (Petering et al. 1977). As serum Cu concentrations rise in rats, levels fall for serum cholesterol, triglycerides, and phospholipids (Petering et al. 1977).

Proposed Criteria and Recommendations

Proposed copper criteria for the protection of agricultural crops, aquatic life, terrestrial invertebrates, poultry, laboratory white rats, livestock, and human health are summarized in Table 8.

Table 8. Proposed copper criteria for the protection of natural resources and human health.

Table 8. Resource, criteria, and other variables	Effective copper concentration	Reference[a]
Agricultural Crops		
Irrigation water	<1.0 mg/L	1
Leaves		
Severe deficiency	<4 mg/kg dry weight (DW)	2
Deficient	<5 mg/kg DW	1, 3
Mild to moderate deficiency	4 to 5 mg/kg DW	1, 3
Deficiency rare	>6 mg/kg DW	2
Sewage sludge		
Europe, acidic soils	50 to 140 kg/ha	4
United States		
All agricultural lands	<1,000 mg/kg DW	5
Florida	<100 mg/kg DW	4
Illinois	<280 kg/ha	4
Maryland, Massachusetts	140 to 280 kg/ha[b]	4
Minnesota, Missouri	140 to 560 kg/ha[c]	4
New York		
Agricultural soils	<125 kg/ha	4
Forests	<280 kg/ha	4
Wisconsin, acidic soils	50 to 140 kg/ha	4
Soils		
Deficient	<10 mg/kg DW	6
Safe	<280 kg/ha[d]	7
M-3 extractable soil copper	<60 mg/kg DW	8
Canada		
Agricultural lands	<100 mg/kg DW	4
Acidic soils, Alberta	<200 mg/kg DW	4
Industrial and other lands	<300 mg/kg DW	4
Former Soviet Union, maximum allowable concentration	3 mg/kg DW when extracted with ammonium acetate buffer	4
The Netherlands		
Normal	50 mg/kg DW	4
Moderately contaminated	100 mg/kg DW	4
Requires remediation	>500 mg/kg DW	4
United States, New Jersey	<170 mg/kg DW	4

Table 8. Resource, criteria, and other variables	Effective copper concentration	Reference[a]
Aquatic life, fresh water		
Sediments		
Great Lakes		
Nonpolluted	<25 mg/kg DW	4
Moderately polluted	25 to 50 mg/kg DW	4
Heavily polluted	>50 mg/kg DW	4
Reduced abundance of benthos	480 to 1,093 mg/kg DW	9
Toxic to benthos	>9,000 mg/kg DW	9
Tissue concentrations; rainbow trout, *Oncorhynchus mykiss*; ratio of zinc to copper in gill or operclula		
Normal	Ratio >1.5	10
Probably copper-poisoned	Ratio 0.5 to 1.5	10
Acute copper poisoning	Ratio <0.5	10
Water		
Safe. No adverse effects on rainbow trout exposed from fertilization through 4 days after hatching		
In soft or medium water	2 to 5 µg/L	11
In hard water	5 to 8 µg/L	11
Death or teratogenicity in eggs of sensitive species of fishes and amphibians	5 to 10 µg/L	11
United States		
Safe; total recoverable copper; 24h average	<5.6 µg/L	12
Maximum allowable concentration at 50 mg $CaCO_3$/L	12 µg/L	12
Maximum allowable concentration at 100 mg $CaCO_3$/L	22 µg/L	12
Maximum allowable concentration at 200 mg $CaCO_3$/L	43 µg/L	12
Inhibits fish growth and ability of fish to discriminate prey	18 to 28 µg/L	13
The Netherlands; total recoverable copper; maximum allowable concentration	<50 µg/L	14
Aquatic life, marine		
Seawater		
Safe. Total recoverable copper, 24 h average	<4.0 µg/L; not to exceed 23 µg/L at any time	12
Safe. Maximum concentration	<5.0 µg/L	15
Sediments		
Avoidance by clams	>5 mg/kg DW	16
Clam burrowing ability inhibited (water concentrations of 113 to 120 µg Cu/L)	>15 mg/kg DW	16
Not polluted	<40 mg/kg DW	15
Moderately polluted	40 to 60 mg/kg DW	15
Very polluted	>60 mg/kg DW	15
Reduced species diversity; sensitive species absent	>200 mg/kg DW	17

Table 8. Resource, criteria, and other variables	Effective copper concentration	Reference[a]
Toxic to juvenile bivalve mollusks	>2,000 mg/kg DW	17
Terrestrial invertebrates		
Earthworms, whole; disrupted lysozyme activity in coelomic fluid and coelomocytes	>28.5 mg/kg DW	18
Isopod, *Porcellio scaber*; whole		
Deficiency	Unknown	19
Uncontaminated	<250 mg/kg DW	19
Low contamination	250 to 400 mg/kg DW	19
Medium contamination	400 to 600 mg/kg DW	19
High contamination	600 to 1,000 mg/kg DW	19
Very high contamination	>1,000 mg/kg DW	19
Poultry, diets		
Deficient	<8.7 mg/kg DW ration; some deaths at 0.7 to 1.5 mg/kg DW ration; high frequency of vascular rupture at 2.7 mg/kg DW ration	3, 20, 33
Safe	<200 mg/kg DW feed	17
Recommended for growing chickens	>4 mg/kg DW diet plus adequate iron	20
Laboratory white rat, *Rattus* sp.		
Minimal	3 to 6 mg/kg FW diet; 0.15-0.3 mg/kg body weight (BW) daily	5
Adequate	10 mg/kg DW diet	21
Livestock		
All species except sheep; diet		
Deficient	<5 mg/kg DW	2
Minimal	>5 to <15 mg/kg DW	1
Adequate	20 to 30 mg/kg DW	2
Cattle, *Bos* sp.; liver, copper-poisoned	>150 mg/kg FW; >450 mg/kg DW	22
Sheep, *Ovis aries*		
Toxic	20 to 30 mg/kg DW diet	2
Pig, *Sus* sp.		
Diet		
Safe	3 to 5 mg/kg DW	5
United Kingdom, maximum	200 mg/kg DW[e]	23
Tissue concentrations		
Fatal anemia with jaundice and stomach ulcerations; kidney vs. liver	95 to 800 mg/kg DW vs. 1,300 to 2,600 mg/kg DW	23
Human health		
Air		
Montana	<0.26 µg/m^3 for 8 h; <1.57 µg/m^3 for 24 h	5
Massachusetts	<0.54 µg/m^3 for 24 h	5
Connecticut, North Dakota	<2 µg/m^3 for 8 h	5
Florida	<4 µg/m^3 for 8 h	5
Nevada	<5 µg/m^3 for 8 h	5
Virginia	<16 µg/m^3 for 24 h	5
New York	<20 µg/m^3 for 1 year	5
United States; workplace; 8 h daily		
Fumes	<0.1 to <0.2 mg/m^3	5

Table 8. Resource, criteria, and other variables	Effective copper concentration	Reference[a]
Dusts and mists	<1.0 mg/m^3	5
Total	<1.0 mg/m^3	12
Daily intake, all sources		
Deficiency in children	<0.1 µg/kg BW	12
Infants, normal	14 to 80 µg/kg BW; 0.5 to 1.0 mg	12, 24, 25
Children, normal	40 to 100 µg/kg BW; 1 to 2 mg	12, 24, 25
Teenagers and adults, normal	28 to 40 µg/kg BW; 2 to 4 mg	5, 12, 24, 25
Adults, safe and adequate	2 to 3 mg	5
Adults, toxic	15 mg in single dose	12
Diet		
Australia		
Seafood	<30 mg/kg FW	30
Shellfish; soft parts	<70 mg/kg FW; <266 mg/kg DW	27, 28
Fish muscle	<15 mg/kg FW	31
Malaysia; bivalve mollusks; soft parts	<30 mg/kg FW	29
Spain, total diet	<20 mg/kg DW	32
Drinking water		
United States, safe	<1.0 mg/L (exceeded by about 1% of all samples)	12
Kansas, Rhode Island	<1.0 mg/L	5
Minnesota	<1.3 mg/L	5
Proposed, United States	<1.3 mg/L	5
Satisfactory smell and taste	<1.0 to 1.3 mg/L	5, 12
Associated with diarrhea, abdominal cramps, and nausea	>1.3 mg/L	26
Health advisory for children and adults	Not to exceed 1.3 mg/L for more than 1 day	5
Adverse taste	>1.5 mg/L	12
Fish and shellfish collection locales; marine	<4 µg/L	27
Tissues; human		
Blood; deficient vs. adequate	<0.8 mg/L vs. 1.03 mg/L	12
Serum; normal vs. toxic	1.64 mg/L vs. 2.86 mg/L	12

[a]1,NAS 1977; 2, Gupta 1979; 3, Carlton and Henderson 1963; 4, Beyer 1990; 5, ATSDR 1990; 6, King et al. 1984; 7, Reed et al. 1993; 8, Alva et al. 1995; 9, Mackenthun and Cooley 1952; 10, Carbonell and Tarazona 1993; 11, Birge and Black 1979; 12, USEPA 1980; 13, Sandheinrich and Atchison 1989; 14, Enserink et al. 1991; 15, Fagioli et al. 1994; 16, Roper and Hickey 1994; 17, Bryan and Langston 1992; 18, Goven et al. 1994; 19, Hopkin et al. 1993; 20; Carlton and Henderson 1964b; 21, Dodds-Smith et al. 1992a; 22, Gummow et al. 1991; 23, Higgins 1981; 24, Aaseth and Norseth 1986; 25, Schroeder et al. 1966; 26, Knobeloch et al. 1994; 27, Talbot et al. 1985; 28, Brown and McPherson 1992; 29, Mat 1994; 30, Greig and Sennefelder 1985; 31, Mathews 1994; 32, Daramola and Oladimeji 1989; 33, Carlton and Henderson 1964a.

[b]Soil cation exchange capacity less than 5 meq/100 g for 140 kg/ha and more than 5 meq/100 g for 280 kg/ha.

[c]Soil cation exchange capacity ranges from less than 5 to more than 15 meq/100 g.

[d]Higher levels of 365 kg Cu/ha had no effect on corn yield or copper content in corn.

[e]Diet should also contain 150 mg Zn/kg and 200 mg Fe/kg to further reduce the chances of copper toxicity to pigs.

Copper is essential to normal plant growth, and copper deficiency is known in various agricultural crops such as vegetables and grains (Gupta 1979). Crops seem to be protected against copper deficiency when growing soils contain greater than 10 mg Cu/kg DW and leaves greater than 6 mg Cu/kg DW (Table 8). With

some exceptions, agricultural crops are protected against copper toxicosis when irrigation waters contain less than 1.0 mg Cu/L and soils less than 170 mg Cu/kg DW (Table 8). But adverse effects occur on root development of seedling pines at irrigation water concentrations as low as 200 µg Cu/L (Arduini et al. 1995) and on growth of citrus trees when extractable copper in the soil exceeds 60 mg/kg DW (Alva et al. 1995). States allow application of sewage sludge to agricultural soils if total copper in the sludge does not exceed 1,000 mg/kg DW (100 mg/kg DW in Florida), or if the application rate for sludge does not exceed 280 kg sewage sludge per surface acre (50 kg/ha in Wisconsin; Table 8). The practice by some localities of applying raw sewage sludge to crop soils on the basis of kg sludge/surface acre ratio should be discouraged unless the sludge is periodically analyzed for copper and other contaminants.

Proposed criteria to protect most species of freshwater aquatic life from copper toxicity or deficiency include maximum water concentrations over a 24-h period of 12 µg Cu/L in soft water and 43 µg/L in hard water, sediment concentrations less than 480 mg Cu/kg DW, and, in rainbow trout, a zinc/copper ratio in gill or opercle greater than 1.5 (Table 8). However, the proposed maximum water concentration range of 12-43 µg Cu/L exceeds the 5-10 µg/L range that is lethal or teratogenic to sensitive species of fishes and amphibians (Birge and Black 1979) and overlaps the 18-28 µg/L range that inhibits growth and ability to discriminate prey for other species (Sandheinrich and Atchison 1989). Some scientists state that laboratory studies tend to overestimate the adverse effects of copper on freshwater abundance and diversity and suggest more research on field mesocosms receiving water directly from the system under investigation (Clements et al. 1990). In marine ecosystems, copper concentrations should not exceed 23 µg Cu/L at any time, and sediments should contain less than 200 mg Cu/kg DW (Table 8). But adverse sublethal effects of copper to representative species of estuarine algae, mollusks, and arthropods frequently occur at less than 10 µg Cu/L (Bryan and Langston 1992). Also, extrapolation of laboratory data on copper and marine benthos to actual field conditions is difficult because of changing environmental conditions such as thermosaline regimes and the nature of the sediment substrate (Ozoh 1992c).

Among sensitive species of terrestrial invertebrates, earthworms show disrupted enzyme activities at whole body concentrations as low as 28.5 mg Cu/kg DW (Table 8). Soil copper concentrations between 53 and 100 mg/kg DW kill soil nematodes and soil faunal communities (Parmelee et al. 1993; Donkin and Dusenbery 1993) and cause a reduction in cocoon production of earthworms (Ma 1984; Spurgeon et al. 1994). Diets that contain between 50 and 63 mg Cu/kg ration inhibit development and reproduction in gypsy moths and oribatid mites (Denneman and van Straalen 1991; Gintenreiter et al. 1993). The wood louse (*Porcellio scaber*), an isopod, is proposed as a bioindicator of copper contamination in terrestrial ecosystems because whole body concentrations seem to reflect copper loadings in the isopod's immediate environment (Hopkin et al. 1993; Table 8). More research is recommended on isopods and other sentinel organisms.

Quantitative data are missing on copper effects on avian and mammalian wildlife, and this represents a high priority research need. Some data are available for copper and poultry and livestock, but extrapolation of these results to wildlife species is contraindicated in view of the wide range in sensitivities to copper between species. Domestic chickens show good growth and survival when their diets contain adequate iron and more than 4 and less than 200 mg Cu/kg ration (Carlton and Henderson 1964b). In sheep—and some other mammals—prior knowledge of copper stress would allow adequate time for treatment (i.e., prophylactic dosing with ammonium molybdate plus sodium sulfate or intravenous injection of chelating agents) to prevent sudden death during copper-induced hemolytic crisis (MacPherson and Hemingway 1969). In sheep, for example, elevated SGOT activity is an early indicator of copper poisoning and is measurable 1 to 6 weeks before the hemolytic crisis stage (MacPherson and Hemingway 1969). Providing prophylactic licks containing zinc sulfate and sulfur to African cattle, buffaloes, and impalas seems to be successful in protecting against the lethal effects of excess airborne copper in the grazing area (Gummow et al. 1991).

The proposed domestic drinking water criterion of less than 1.0 mg Cu/L for the protection of human health is not based on copper toxicosis but on the unpleasant taste which develops with higher levels of copper in drinking water (USEPA 1980). Increased copper levels (>1.3 mg Cu/L) in household water supplies caused by corrosion of copper plumbing materials may adversely affect infants and young children among residents of newly constructed or renovated homes (Knobeloch et al. 1994). Human groups at greatest risk to copper toxicosis now include young children subjected to unusually high concentrations of copper in soft or treated water held in copper pipes or vessels, medical patients with Wilson's disease, medical patients treated with copper-contaminated fluids in dialysis or parenteral administration, people with a glucose-6-phosphate

dehydrogenase (G-6-PD) deficiency (about 13% of the Afro-American male population has a G-6-PD deficiency) who drink water containing greater than 1.0 mg Cu/L, and occupationally exposed workers (USEPA 1980).

Other copper research areas that seem to merit additional effort include (1) establishment of specific biomarkers for copper toxicity (ATSDR 1990); (2) development of a national system to verify incidents of deficiency and excess of copper and interrelated trace elements in species of concern (NAS 1977); (3) clarification of copper interactions with molybdenum, sulfate, iron, and zinc in plant and animal metabolisms (NAS 1977; Eisler 1989, 1993); (4) the role of copper in carcinogenesis, mutagenesis, and teratogenesis (NAS 1977; ATSDR 1990) because preliminary evidence suggests that exposure to grossly elevated concentrations of copper produces teratogenicity in fish (Birge and Black 1979) and mammals (Aaseth and Norseth 1986), carcinogenicity in rodents (USEPA 1980; ATSDR 1990; Toussaint and Nederbragt 1993), and mutagenicity in rodents (ATSDR 1990), sheep (Bires et al. 1993), and grasshoppers (Bhunya and Behura 1986); (5) mechanisms by which copper deficiency results in neutropenia, with emphasis on the process of cellular differentiation and the viability of neutrophils in blood and marrow (Percival 1995); (6) copper status effects on resistance to endotoxin-induced injuries because burn and trauma patients show moderate copper deficiency and high risk to sepsis, and copper deficient rats are sensitive to endotoxins causing sepsis (DiSilvestro et al. 1995); (7) the role of aquatic organisms in copper cycling in aquatic ecosystems (Stokes 1979); (8) mechanisms of copper tolerance or acclimatization to high doses of copper (ATSDR 1990); (9) the relation between copper toxicosis, copper absorption rates, and copper retention (Stokes 1979; ATSDR 1990); (10) effects on reproduction, neurotoxicity, and immune response (ATSDR 1990); (11) biochemistry and physiology of copper proteins (NAS 1977); (12) measurement of flux rates of ionic copper from metallic copper (ATSDR 1990); and (13) determination of safe levels of copper in livestock and poultry feeds (NAS 1977), and in diets of avian and mammalian wildlife.

Conclusions

Copper discharges to the global biosphere are due primarily to human activities, especially from the mining, smelting, and refining of copper and from the treatment and recycling of municipal and industrial wastes. Some copper compounds, especially copper sulfate, also contribute to environmental copper burdens because they are widely and intensively used in confined geographic areas to control nuisance species of aquatic plants and invertebrates, diseases of terrestrial crop plants, and ectoparasites of fish and livestock.

Copper concentrations in field collections of abiotic materials and living organisms are usually elevated in the vicinity of human activities and intensive copper use. Maximum copper concentrations recorded in selected abiotic materials are 5 $\mu g/m^3$ in air, 5 µg/L in groundwater, 12 µg/L in rainwater, 1,200 mg/kg DW in poultry litter, 7,000 mg/kg DW in soils, and 7,700 mg/kg DW in sewage sludge. In terrestrial vegetation, copper is usually less than 35 mg/kg DW except near smelters where it may approach 700 mg/kg DW and in certain copper-accumulator plants that may normally contain as much as 13,700 mg/kg DW. Aquatic vegetation from copper-contaminated sites contain as much as 1,350 mg Cu/kg DW vs. 36 mg/kg DW in conspecifics from reference sites. Terrestrial invertebrates from industrialized areas may contain from 137 to 408 mg Cu/kg DW whole organism. Aquatic invertebrates seldom contain as much as 95 mg Cu/kg DW, regardless of collection locale; exceptions include whole amphipods and lobster hepatopancreas (335-340 mg/kg DW) from copper-contaminated sites and many species of mollusks that normally contain 1,100-6,500 mg Cu/kg DW. Data are scarce on copper concentrations in field populations of amphibians and reptiles: crocodile eggs may contain as much as 60 mg Cu/kg DW and livers of some toads may contain as much as 2,100 mg Cu/kg DW without apparent adverse effects. Maximum copper concentrations in tissues of fishes, elasmobranchs, birds, and marine mammals from all collection sites are low when compared to more primitive organisms and never exceed 53 mg Cu/kg DW except liver (146-367 mg/kg DW); an exception is liver from endangered manatees (1,200 mg/kg DW) collected at a site treated with a copper-containing herbicide. Maximum copper concentrations in all tissues of terrestrial mammals, regardless of collection locale, are low and seldom exceed 29 mg/kg DW except kidneys (108 mg/kg DW) and livers (1,078 mg/kg DW) from animals near a copper refinery.

Copper deficiency is not a major public health concern in the United States, although skeletal deformities and leg fractures may occur in some copper-deficient children. Copper deficiency effects occur, however, in various species of terrestrial plants (reduced growth, necrosis, reduction in number of pollen grains, death), chickens (poor growth, high frequency of cardiovascular and skeletal lesions, low survival), turkeys (sudden

death), rats (defective hemoglobin synthesis, lesions of the central nervous system, low survival, altered blood and liver enzyme activities), guinea pigs (lesions of the central nervous system), dogs (leg fractures), sheep and other ruminant mammals (sudden death, skeletal deformities), pigs (poor growth, decreased hemoglobin and erythrocytes, skeletal deformities), mink (reduced survival), and camels (anemia, emaciation, falling, fractures, death). Data are scarce or missing on copper deficiency effects in aquatic flora and fauna and in avian and terrestrial mammalian wildlife; additional studies of copper deficiency in these groups are merited. In sensitive terrestrial agricultural crops, copper deficiency occurs at less than 1.6 mg dissolved Cu/kg DW soil and less than 5 mg total Cu/kg DW leaves. For domestic chickens, copper deficiency occurs when chickens are fed diets containing less than 2.7 mg Cu/kg ration. Male weanling rats show deficiency effects when fed diets containing 0.13 mg Cu/kg ration vs. a copper-normal diet of 5.7 mg Cu/kg ration; earliest signs of copper deficiency in rats include low concentrations of copper in livers (less than 3.0 mg/kg DW vs. 12.6-15.0 mg/kg DW in controls), reductions in activities of cytochrome oxidase and succinoxidase, and prolonged sleeping times. Ewes of Bactrian camels fed copper-deficient diets of less than 2.5 mg Cu/kg DW ration (vs. normal diet of about 11.0 mg Cu/kg DW) produce a high frequency of swaybacked lambs. Copper deficiency in mink is produced at daily intake rates equivalent to 3.5 mg Cu/kg BW for 50 weeks. Swine require high intakes of copper to avoid deficiency; daily intakes of less than 36 mg Cu/kg BW are associated with reductions in growth rate, hemoglobin, and hematocrit.

Copper and its compounds are not carcinogenic, mutagenic, or teratogenic at environmentally realistic concentrations. But under controlled conditions of grossly elevated exposures some studies suggest that copper is a potential carcinogen in rodents; mutagen in rodents, sheep, and grasshoppers; and teratogen in fish and small laboratory animals. More research is needed in this area.

Bioavailability and toxicity of copper to aquatic organisms depends on the total concentration of copper and its speciation. Both availability and toxicity are significantly reduced by increased loadings of suspended solids and natural organic chelators and increased water hardness. Toxicity to aquatic life is related primarily to the dissolved cupric ion (Cu^{+2}) and possibly to some hydroxyl complexes. Cupric copper (Cu^{+2}) is the most readily available and toxic inorganic species of copper in fresh water, seawater, and sediment interstitial waters. Cupric ion accounts for about 1% of the total dissolved copper in seawater and less than 1% in fresh water. In fresh water, cupric copper and some copper hydroxyl species are correlated with high toxicity to aquatic life, although carbonato species are much less toxic than other copper complexes. More research seems needed on the adsorption characteristics of most cupric ion complexes. In solution, copper interacts with numerous inorganic and organic compounds resulting in altered bioavailability and toxicity. Acknowledgment of these interactions is essential to the understanding of copper toxicokinetics. In aquatic invertebrates, copper disrupts gill epithelium at high concentrations and in fishes it interferes with osmoregulation; death is caused by tissue hypoxia associated with disrupted ATP synthesis. Copper detoxifying mechanisms in fishes include the induction of metallothioneins, allowing copper retention for weeks or months after absorption without toxicity. In higher vertebrates, excess copper is cytotoxic and alters protein configuration and lipid peroxidation rates. Mechanisms implicated in copper poisoning of mammals include free radical production, alteration in activities of several enzymes, and inhibited metallothionein synthesis. In mammals, copper is normally excreted via the bile in association with glutathione or unidentified high molecular weight proteins.

Excess copper is toxic to representative species of plants and animals. Significant adverse effects in terrestrial plants occur at concentrations as low as 40 µg Cu/L of nutrient solution, more than 10 mg Cu/kg DW in leaves, and greater than 60 mg extractable Cu/kg DW of soil. Sensitive species of terrestrial invertebrates show a reduction in growth, survival, or reproduction at more than 50 mg Cu/kg diet or 53-70 mg Cu/kg DW of soil. Many species of freshwater plants and animals die within 96 h at waterborne copper concentrations of 5.0-9.8 µg Cu/L, and sensitive species of freshwater mollusks, crustaceans, and fishes die at 0.23-0.91 µg Cu/L within 96 h. The most sensitive tested species of marine mollusks, crustaceans, and fishes have an LC50 (96 h) range from 28-39 µg Cu/L; significant sublethal effects to representative species of estuarine algae, mollusks, and arthropods frequently occur at 1-10 µg Cu/L. Mammals and birds are at least 100 times more resistant to copper than other organisms, but ruminant mammals are significantly more sensitive to copper than nonruminant animals and poultry. Excessive dietary intakes of copper by 20- to 50-fold over normal levels may, however, have serious adverse effects on birds and mammals. No data are available on copper toxicity to avian wildlife. Studies with poultry demonstrate that copper accumulates in livers at dietary concentrations as low as 15 mg Cu/kg DW ration, inhibits growth at 120 mg Cu/kg DW ration, and causes gizzard histopathology at 250

mg Cu/kg DW ration. Copper is lethal to representative species of mammals through a variety of routes: single oral doses of 6 to 637 mg Cu/kg BW in humans and 200 mg/kg BW in cattle or diets with more than 80 mg Cu/kg ration (about 5.1 to 10.7 mg Cu/kg BW daily) fed to sheep or more than 238 mg/kg ration (more than 133 mg/kg BW daily) fed to rats. Adverse sublethal effects of copper to sensitive mammals occur in human infants at drinking water concentrations greater than 3 mg/L, in cattle at more than 4.2 mg/kg BW by way of drinking water or more than 20 mg/kg BW via diet, in sheep given daily oral doses of 7.5 to 15.0 mg/kg BW or fed diets containing more than 37.3 mg/kg ration, in rats given more than 7.9 mg/kg BW daily by way of diet (equivalent to more than 100 mg/kg DW ration), and in pigs at more than 14.5 mg/kg BW daily via diet.

Numerous and disparate copper criteria are proposed for protecting the health of agricultural crops, aquatic life, terrestrial invertebrates, poultry, laboratory white rats, and humans (Table 8); however, no copper criteria are now available for protection of avian and mammalian wildlife, and this needs to be rectified. Several of the proposed criteria do not adequately protect sensitive species of plants and animals and need to be reexamined. Other research areas that merit additional effort include biomarkers of early copper stress; copper interactions with interrelated trace elements in cases of deficiency and excess; copper status effects on disease resistance, cancer, mutagenicity, and birth defects; mechanisms of copper tolerance or acclimatization; and chemical speciation of copper, including measurement of flux rates of ionic copper from metallic copper.

Acknowledgments

I thank L. J. Garrett and P. W. Manning for library services; W. J. Birge, C. Hogstrand, O. H. Pattee, D. W. Sparling, and J. S. Weis for scientific and technical reviews of the manuscript; D. S. McGrath and B. A. Vairin for editorial services; and S. M. Lauritzen for layout.

Literature Cited

Aaseth, J., and T. Norseth. 1986. Copper. Pages 233-254 *in* L. Friberg, G.F. Nordberg, and V.B. Vouk, editors. Handbook on the toxicology of metals. Second edition. Volume II: specific metals. Elsevier, New York.

Abalde, J., A. Cid, S. Reisiz, E. Torres, and C. Herrero. 1995. Response of the marine macroalga *Dunaliella tertiolecta* (Chlorophycea) to copper toxicity in short time experiments. Bulletin of Environmental Contamination and Toxicology 54:317-324.

Absil, M.C.P., L.S.A. Gerringa, and B. T. Wolterbeek. 1993. The relation between salinity and copper complexing capacity of natural estuarine waters and the uptake of dissolved ^{64}Cu by *Macoma balthica*. Chemical Speciation and Bioavailability 5:119-128.

Agency for Toxic Substances and Disease Registry (ATSDR). 1990. Toxicological profile for copper. U.S. Public Health Service, Atlanta, Georgia, TP-90-08. 143 pp.

Ahsanullah, M., and G. H. Arnott. 1978. Acute toxicity of copper, cadmium, and zinc to larvae of the crab *Paragrapsus quadridentatus* (H. Milne Edwards), and implications for water quality criteria. Australian Journal of Marine and Freshwater Research 29:1-8.

Ahsanullah, M., and A. R. Williams. 1991. Sublethal effects and bioaccumulation of cadmium, chromium, copper and zinc in the marine amphipod *Allorchestes compressa*. Marine Biology 108:59-65.

Al-Sabri, I. Y. N., J. D. Smith, and J. D. Thomas. 1993. Copper molluscicides for controls of schistosomiasis. 3. Absorption by clay suspensions. Environmental Science & Technology 27:299-303.

Alva, A. K., J. H. Graham, and C. A. Anderson. 1995. Soil pH and copper effects on young “Hamlin” orange trees. Soil Science Society of America Journal 59:481-487.

Amiard-Triquet, A., D. Pain, and H. T. Delves. 1991. Exposure to trace elements of flamingos living in a biosphere reserve, the Camargue (France). Environmental Pollution 69:193-201.

Anderson, B. S., D. P. Middaugh, J. W. Hunt, and S. L. Turpen. 1991. Copper toxicity to sperm, embryos and larvae of topsmelt *Atherinops affinis* with notes on induced spawning. Marine Environmental Research 31:17-35.

Ankley, G. T., E. N. Leonard, and V. R. Mattson. 1994. Prediction of bioaccumulation of metals from contaminated sediments by the oligochaete, *Lumbriculus variegatus*. Water Research 28:1071-1076.

Ankley, G. T., V. R. Mattson, E. N. Leonard, C. W. West, and J. L. Bennett. 1993. Predicting the acute toxicity of copper in freshwater sediments: evaluation of the role of acid-volatile sulfide. Environmental Toxicology and Chemistry 12:315-320.

Arduini, I., D. L. Godbold, and A. Onnis. 1995. Influence of copper on root growth and morphology of *Pinus pinea* L. and *Pinus pinaster* Ait. seedlings. Tree Physiology 15:411-415.

Arthur, J. W., and E. N. Leonard. 1970. Effects of copper on *Gammarus pseudolimnaeus*, *Physa integra*, and *Campeloma decisum* in soft water. Journal of the Fisheries Research Board of Canada 27:1277-1283.

Arzul, G., and J. F. Maguer. 1990. Influence of pig farming on the copper content of estuarine sediments in Brittany, France. Marine Pollution Bulletin 21:431-434.

Athalye, R. P., and K. S. Gokhole. 1991. Heavy metals in the polychaete *Lycastis ouanaryensis* from Thane Creek, India. Marine Pollution Bulletin 22:233-236.

Aziz, J. B., N. M. Akrawi, and G. A. Nassori. 1991. The effect of chronic toxicity of copper on the activity of Balbiani rings and nucleolar organizing region in the salivary gland chromosomes of *Chironomus ninevah* larvae. Environmental Pollution 69:125-130.

Baekken, T. 1994. Effects of highway pollutants on a small Norwegian lake. Science of the Total Environment 146/147:131-139.

Baker, J. T. P. 1969. Histological and electron microscopical observations on copper poisoning in the winter flounder (*Pseudopleuronectes americanus*). Journal of the Fisheries Research Board of Canada 26:2785-2793.

Bakka, A., and M. Webb. 1981. Metabolism of zinc and copper in the neonate: changes in the concentrations and contents of thionein-bound Zn and Cu with age in the livers of the newborn of various mammalian species. Biochemical Pharmacology 30:721-725.

Balogh, K. V., and Z. Mastala. 1994. The influence of size and glochidia bearing upon the heavy metal accumulation in gills of *Anodonta piscinalis* (Nilss.). Chemosphere 28:1539-1550.

Banerjee, S., and S. Homechaudhuri. 1990. Hematological monitoring of a bio-indicator fish, *Heteropneustes fossilis*, on exposure to copper toxicity. Israeli Journal of Aquaculture Bamigdeh 42:46-51.

Bardgett, R. D., T. W. Speir, D. J. Ross, G. W. Yeates, and H. A. Kettles. 1994. Impact of pasture contamination by copper, chromium, and arsenic timber preservative on soil microbial properties and nematodes. Biology and Fertility of Soils 18:71-79.

Bartley, T. R. 1967. Progress report on evaluation of copper for aquatic weed control and herbicide residues on irrigation systems. U.S. Bureau of Reclamation Report No. WC-32. 58 pp.

Bechmann, R. K. 1994. Use of life tables and LC50 tests to evaluate chronic and acute toxicity effects of copper on the marine copepod *Tisbe furcata* (Baird). Environmental Toxicology and Chemistry 13:1509-1517.

Belanger, S. E., J. L. Farris, D. S. Cherry, and J. Cairns, Jr. 1990. Validation of *Corbicula fluminea* growth reductions induced by copper in artificial streams and river systems. Canadian Journal of Fisheries and Aquatic Sciences 47:904-914.

Benoit, D. A. 1975. Chronic effects of copper on survival, growth, and reproduction of the bluegill (*Lepomis macrochirus*). Transactions of the American Fisheries Society 104:353-358.

Benson, W. H., and W. J. Birge. 1985. Heavy metal tolerance and metallothionein induction in fathead minnows: results from field and laboratory investigations. Environmental Toxicology and Chemistry 4:209-217.

Berger, B., and R. Dallinger. 1993. Terrestrial snails as quantitative indicators of environmental metal pollution. Environmental Monitoring and Assessment 25:65-84.

Betzer, S. B., and P. P. Yevich. 1975. Copper toxicity in *Busycon canaliculatum* L. Biological Bulletin 148:16-25.

Beyer, W. N. 1990. Evaluating soil contamination. U.S. Fish and Wildlife Service Biological Report 90(2). 25 pp.

Beyer, W. N., G. Miller, and J. W. Simmers. 1990. Trace elements in soil and biota in confined disposal facilities for dredged material. Environmental Pollution 65:19-32.

Bezuidenhout, L. M., H. J. Schoonbee, and L. P. D. de Wet. 1990. Heavy metal content in organs of the African sharptooth catfish, *Clarias gariepinus* (Burchell), from a Transvaal lake affected by mine and industrial effluents. Part 1. Zinc and copper. Water SA (Pretoria) 16:125-129.

Bhat, U. G., and K. Vamsee. 1993. Toxicity of heavy metals Cu, Cd and Hg to the gammarid amphipod *Parhalella natalensis*. Science of the Total Environment, Supplement 1993, Part 2:887-897.

Bhunya, S. P., and T. Behura. 1986. Evaluation of clastogenicity of three pesticides in the grasshopper test system. Journal of the Zoological Society of India 38:73-82.

Bires, J., J. Dianovsky, P. Bartko, and Z. Juhasova. 1993. Changes in the selected biochemical indicators and on a genetic apparatus of sheep in the course of application of copper from industrial emission source. Ekologia (Bratislava) 12:153-162.

Bires, J., and L. Vrzgula. 1990. Wool as an indicator of sheep exposure to Cu, Fe, Zn, Mo, As, Pb, Cd, and Se from the industrial emission source. Ekologia CSSR 9:419-428.

Birge, W. J. 1978. Aquatic toxicology of trace elements of coal and fly ash. Pages 219-240 *in* J. H. Thorp and J. W. Gibbons, editors. Energy and environmental stress in aquatic systems. U. S. Department of Energy, Symposium Series 48, CONF-771114.

Birge, W. J., and J. A. Black. 1979. Effects of copper on embryonic and juvenile stages of aquatic animals. Pages 373-399 *in* J. O. Nriagu, editor. Copper in the environment. Part 2: health effects. John Wiley, New York.

Birge, W. J., R. D. Hoyt, J. A. Black, M. D. Kercher, and W. A. Robison. 1993. Effects of chemical stresses on behavior of larval and juvenile fishes and amphibians. Pages 55-65 *in* L. A. Fuiman, editor. Water quality and the early life stages of fishes. American Fisheries Society Symposium 14, Bethesda, Maryland.

Blem, C. R., and L. B. Blem. 1991. Cation concentrations and acidity in breeding ponds of the spotted salamander, *Ambystoma maculatum* (Shaw) (Amphibia: Ambystomatidae), in Virginia. North Carolina State Museum of Natural History 17:67-76.

Blust, R., A. Fontaine, and W. Decleir. 1991. Effect of hydrogen ions and inorganic complexing on the uptake of copper by the brine shrimp *Artemia franciscana*. Marine Ecology Progress Series 76:273-282.

Bordin, G., J. McCourt, and A. Rodriguez. 1994. Trace metals in the marine bivalve *Macoma balthica* in the Westerschelde estuary, the Netherlands. Part 2: intracellular partitioning of copper, cadmium, zinc and iron—variations of the cytoplasmic metal concentrations in natural and in vitro contaminated clams. Science of the Total Environment 151:113-124.

Borgmann, U., W. P. Norwood, and C. Clarke. 1993. Accumulation, regulation and toxicity of copper, zinc, lead and mercury in *Hyalella azteca*. Hydrobiologia 259:79-89.

Boyle, E. A. 1979. Copper in natural waters. Pages 77-88 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Braune, B. M., R. J. Norstrom, M. P. Wong, B. T. Collins, and J. Lee. 1991. Geographical distribution of metals in livers of polar bears from the Northwest Territories, Canada. Science of the Total Environment 100:283-299.

Bremner, I. 1979. Copper toxicity studies using domestic and laboratory animals. Pages 285-306 *in* J. O. Nriagu, editor. Copper in the environment. Part 2: health effects. John Wiley, New York.

Brix, H., and J. E. Lyngby. 1982. The distribution of cadmium, copper, lead, and zinc in eelgrass (*Zostera marina* L.). Science of the Total Environment 24:51-63.

Brown, K. R., and R. G. McPherson. 1992. Concentrations of copper, zinc and lead in the Sydney rock oyster, *Saccostrea commercialis* (Iredale and Roughley) from the Georges River, New South Wales. Science of the Total Environment 126:27-33.

Brungs, W. A., E. N. Leonard, and J. M. McKim. 1973. Acute and long-term accumulation of copper by the brown bullhead, *Ictalurus nebulosus*. Journal of the Fisheries Research Board of Canada 30:583-586.

Bryan, G. W., and W. J. Langston. 1992. Bioavailability, accumulation and effects of heavy metals in sediments with special reference to United Kingdom estuaries: a review. Environmental Pollution 76:89-131.

Buckley, J. T., M. Roch, J. A. McCarter, C. A. Rendell, and A. T. Mathieson. 1982. Chronic exposure of coho salmon to sublethal concentrations of copper. I. Effect on growth, on accumulation and distribution of copper, and on copper tolerance. Comparative Biochemistry and Physiology 72C:15-19.

Buckley, W. T., and R. M. Tait. 1981. Chronic copper toxicity in lambs: a survey of blood constituent responses. Canadian Journal of Animal Science 61:613-624.

Buhl, K. J., and S. J. Hamilton. 1990. Comparative toxicity of inorganic contaminants released by placer mining to early life stages of salmonids. Ecotoxicology and Environmental Safety 20:325-342.

Byers, J. E. 1993. Variations in the bioaccumulation of zinc, copper, and lead in *Crassostrea virginica* and *Ilyanassa obsoleta* in marinas and open water environments. Journal of the Elisha Mitchell Scientific Society 109:163-170.

Cain, D. J., and S. N. Luoma. 1990. Influence of seasonal growth, age, and environmental exposure on Cu and Ag in a bivalve indicator, *Macoma balthica*, in San Francisco Bay. Marine Ecology Progress Series 60:45-55.

Cain, D. J., S. N. Luoma, J. L. Carter, and S. V. Fend. 1992. Aquatic insects as bioindicators of trace element contamination in cobble-bottom rivers and streams. Canadian Journal of Fisheries and Aquatic Sciences 49:2141-2154.

Calabrese, A., J. R. MacInnes, D. A. Nelson, R. A. Greig, and P. P. Yevich. 1984. Effects of long-term exposure to silver or copper on growth, bioaccumulation and histopathology in the blue mussel *Mytilus edulis*. Marine Environmental Research 11:253-274.

Calabrese, E. J., J. A. Garreffi, and E. J. Stanek. 1992. The effects of joint exposures to environmental oxidants on methemoglobin formation: copper/nitrate and copper/chlorite. Journal of Environmental Science and Health 27A:629-642.

Camusso, M., R. Balestrini, F. Muriano, and M. Mariani. 1994. Use of freshwater mussel *Dreissena polymorpha* to assess trace metal pollution in the lower River Po (Italy). Chemosphere 29:729-745.

Canli, M., and R. W. Furness. 1993. Toxicity of heavy metals dissolved in sea water and influences of sex and size on metal accumulation and tissue distribution in the Norway lobster *Nephrops norvegicus*. Marine Environmental Research 36:217-236.

Carbonell, G., and J. V. Tarazona. 1993. A proposed method to diagnose acute copper poisoning in cultured rainbow trout (*Oncorhynchus mykiss*). Science of the Total Environment, Supplement 1993, Part 2:1329-1334.

Carbonell, G., and J. V. Tarazona. 1994. Toxicokinetics of copper in rainbow trout (*Oncorhynchus mykiss*). Aquatic Toxicology 29:213-221.

Carlton, W. W., and W. Henderson. 1963. Cardiovascular lesions in experimental copper deficiency in chickens. Journal of Nutrition 81:200-208.

Carlton, W. W., and W. Henderson. 1964a. Skeletal lesions in experimental copper deficiency in chickens. Avian Diseases 8:48-55.

Carlton, W. W., and W. Henderson. 1964b. Studies on the copper requirement of growing chickens. Avian Diseases 8:227-234.

Casas, A. M., and E. A. Crecelius. 1994. Relationship between acid volatile sulfide and toxicity of zinc, lead and copper in marine sediments. Environmental Toxicology and Chemistry 13:529-536.

Chancellor, R. J., A. V. Coombs, and H. S. Foster. 1960. Control of aquatic weeds by copper sulphate. Pages 80-84 *in* Proceedings of the 4th British Weed Control Conference, Brighton, U. K., 4-6 November 1958. Society of Chemical Industry, London.

Chelomin, V. P., and N. N. Belcheva. 1992. The effect of heavy metals on processes of lipid peroxidation in microsomal membranes from the hepatopancreas of the bivalve mollusc *Mizuhopecten yessoensis*. Comparative Biochemistry and Physiology 103C:419-422.

Cheng, T. C. 1979. Use of copper as a molluscicide. Pages 401-432 *in* J. O. Nriagu, editor. Copper in the environment. Part 2: health effects. John Wiley, New York.

Cheung, Y. H., and M. H. Wong. 1992. Trace metal contents of the Pacific oyster (*Crassostrea gigas*) purchased from markets in Hong Kong. Environmental Management 16:753-761.

Chu, K. H., W. M. Cheung, and S. K. Lau. 1990. Trace metals in bivalves and sediments from Tolo Harbour, Hong Kong. Environment International 16:31-36.

Christensen, G. M., J. M. McKim, W. A. Brungs, and E. P. Hunt. 1972. Changes in the blood of the brown bullhead (*Ictalurus nebulosus* (Leseuer)) following short and long term exposure to copper (II). Toxicology and Applied Pharmacology 23:417-427.

Claisse, D., and C. Alzieu. 1993. Copper contamination as a result of antifouling paint regulations? Marine Pollution Bulletin 26:395-397.

Clark, D. R., Jr. 1992. Organochlorines and heavy metals in 17-year cicadas pose no apparent dietary threat to birds. Environmental Monitoring and Assessment 20:47-54.

Clements, W. H., D. S. Cherry, and J. Cairns, Jr. 1990. Macroinvertebrate community responses to copper in laboratory and field experimental streams. Archives of Environmental Contamination and Toxicology 19:361-365.

Clements, W. H., D. S. Cherry, and J. H. V. Hassel. 1992. Assessment of the impact of heavy metals on benthic communities at the Clinch River (Virginia): evaluation of an index of community sensitivity. Canadian Journal of Fisheries and Aquatic Sciences 49:1686-1694.

Coglianse, M. P., and M. Martin. 1981. Individual and interactive effects of environmental stress on the embryonic development of the Pacific oyster, *Crassostrea gigas*. I. The toxicity of copper and silver. Marine Environmental Research 5:13-27.

Collyard, S. A., G. T. Ankley, R. A. Hoke, and T. Goldenstein. 1994. Influence of age on the relative sensitivity of *Hyalella azteca* to diazinon, alkylphenol ethoxylates, copper, cadmium, and zinc. Archives of Environmental Contamination and Toxicology 26:110-113.

Coppellotti, O. 1989. Glutathione, cysteine and acid-soluble thiol levels in *Euglena gracilis* cells exposed to copper and cadmium. Comparative Biochemistry and Physiology 94C:35-40.

Crawford, L. A., I. D. Hodkinson, and N. W. Lepp. 1990. The effects of feeding by the black bean aphid *Aphis fabae* Scap. (Homoptera: Aphididae) on copper and cadmium accumulation in broad bean (*Vicia faba* L.). Environmental Geochemistry and Health 12:245-251.

Cruz, A. C., I. S. Fomsgaard, and J. Lacayo. 1994. Lead, arsenic, cadmium and copper in Lake Asosca, Nicaragua. Science of the Total Environment 155:229-236.

Cuill, T. O., A. F. Hamilton, and D. A. Egan. 1970. Copper distribution in the liver. Irish Veterinary Journal 24(2):21-25.

Custer, T. W., and W. L. Hohman. 1994. Trace elements in canvasbacks (*Aythya valisineria*) wintering in Louisiana, USA, 1987-1988. Environmental Pollution 84:253-259.

Daly, H. R., I. C. Campbell, and B. T. Hart. 1990a. Copper toxicity to *Paratya australiensis*: I. Influence of nitrilotriacetic acid and glycine. Environmental Toxicology and Chemistry 9:997-1006.

Daly, H. R., I. C. Campbell, and B. T. Hart. 1990b. Copper toxicity to *Paratya australiensis*: II. Influence of bicarbonate and ionic strength. Environmental Toxicology and Chemistry 9:1007-1011.

Daly, H. R., B. T. Hart, and I. C. Campbell. 1992. Copper toxicity to *Paratya australiensis*: IV. Relationship with ecdysis. Environmental Toxicology and Chemistry 11:881-883.

Daly, H. R., M. J. Jones, B. T. Hart, and I. C. Campbell. 1990c. Copper toxicity to *Paratya australiensis*: III. Influence of dissolved organic matter. Environmental Toxicology and Chemistry 9:1013-1018.

Daramola, J. A., and A. A. Oladimeji. 1989. Accumulation of copper in *Clarias anguillaris* L. and *Oreochromis niloticus* L. Water, Air, and Soil Pollution 48:457-461.

Dave, G., and R. Xiu. 1991. Toxicity of mercury, copper, nickel, lead, and cobalt to embryos and larvae of zebrafish, *Brachydanio rerio*. Archives of Environmental Contamination and Toxicology 21:126-134.

Davies, M. S. 1992. Heavy metals in seawater: effects on limpet pedal mucus production. Water Research 26:1691-1693.

Denneman, C. A. J., and N. M. van Straalen. 1991. The toxicity of lead and copper in reproduction tests using the oribatid mite *Platynothrus peltifer*. Pedobiologia 35:305-311.

Depledge, M. H., T. L. Forbes, and V. E. Forkes. 1993. Evaluation of cadmium, copper, zinc, and iron concentrations and tissue distributions in the benthic crab, *Dorippe granulata* (De Haan, 1841) from Tolo Harbour, Hong Kong. Environmental Pollution 81:15-19.

Deubert, K. H., and I. E. Demoranville. 1970. Copper sulfate in flooded cranberry bogs. Pesticides Monitoring Journal 4:11-13.

Devescovi, M., and C. Lucu. 1995. Seasonal changes of the copper level in shore crabs *Carcinus mediterraneus*. Marine Ecology Progress Series 120:169-174.

de Wet, L. M., H. J. Schoonbee, L. P. D. de Wet, and A. J. B. Wild. 1994. Bioaccumulation of metals by the southern mouthbrooder, *Pseudocrenilabras philander* (Weber 1897) from a mine-polluted impoundment. Water SA (Pretoria) 20:119-126.

Diks, D. M., and H. E. Allen. 1983. Correlation of copper distribution in a freshwater-sediment system to bioavailability. Bulletin of Environmental Contamination and Toxicology 30:37-43.

DiSilvestro, R. A., F. L. Yang, J. E. Jenkins, and Z. Liao. 1995. Physiological responses to endotoxin in copper deficient rats. Nutrition Research 15:221-229.

Dobbs, M. G., J. L. Farris, R. J. Reash, D. S. Cherry, and J. Cairns, Jr. 1994. Evaluation of the resident-species procedure for developing site-specific water quality criteria for copper in Blaine Creek, Kentucky. Environmental Toxicology and Chemistry 13:963-971.

Dodds-Smith, M. E., M. S. Johnson, and D. J. Thompson. 1992a. Trace metal accumulation by the shrew *Sorex araneus*. I. Total body burden, growth, and mortality. Ecotoxicology and Environmental Safety 24:102-117.

Dodds-Smith, M. E., M. S. Johnson, and D. J. Thompson. 1992b. Trace metal accumulation by the shrew *Sorex araneus*. II. Tissue distribution in kidney and liver. Ecotoxicology and Environmental Safety 24:118-130.

Dodoo, D. K., D. W. Engel, and W. G. Sunda. 1992. Effect of cupric ion activity on calcium accumulation in juvenile flounder (*Paralichthys* spp.). Marine Environmental Research 33:101-109.

Doherty, P. C., R. M. Barlow, and K. W. Angus. 1969. Spongy changes in the brains of sheep poisoned by excess dietary copper. Research in Veterinary Science 10:303-304.

Donkin, S. G., and D. B. Dusenbery. 1993. A soil toxicity test using the nematode *Caenorhabditis elegans* and an effective method of recovery. Archives of Environmental Contamination and Toxicology 25:145-151.

Drummond, R. A., W. A. Spoor, and G. F. Olson. 1973. Some short-term indicators of sublethal effects of copper on brook trout, *Salvelinus fontinalis*. Journal of the Fisheries Research Board of Canada 30:698-701.

Durkina, V. B., and Z. S. Evtushenko. 1991. Changes in activity of certain enzymes in sea urchin embryos and larvae after exposure of adult organisms to heavy metals. Marine Ecology Progress Series 72:111-115.

Ebele, S., A. A. Oladimeji, and J. A. Daramola. 1990. Molluscicidal and piscicidal properties of copper (II) tetraoxosulfate (VI) on *Bulinus globosus* (Morelet) and *Clarias anguillaris* (L). Aquatic Toxicology 17:231-238.

Eisler, R. 1973. Annotated bibliography on biological effects of metals in aquatic environments (No. 1-567). U.S. Environmental Protection Agency Report R3-73-007. 287 pp.

Eisler, R. 1977. Acute toxicities of selected heavy metals to the softshell clam, *Mya arenaria*. Bulletin of Environmental Contamination and Toxicology 17:137-145.

Eisler, R. 1979. Copper accumulations in coastal and marine biota. Pages 383-449 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. Biological Trace Element Research 6:165-180.

Eisler, R. 1989. Molybdenum hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.19). 61 pp.

Eisler, R. 1993. Zinc hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 10. 106 pp.

Eisler, R. 1995. Electroplating wastes in marine environments: a case history at Quonset Point, Rhode Island. Pages 539-548 *in* D. J. Hoffman, B. A. Rattner, G. A. Burton, and J. Cairns, Jr., editors. Handbook of ecotoxicology. Lewis Publishers, Boca Raton, Florida.

Eisler, R., and G. R. Gardner. 1973. Acute toxicology to an estuarine teleost of mixtures of cadmium, copper and zinc salts. Journal of Fish Biology 5:131-142.

Eisler, R., and G. LaRoche. 1972. Elemental composition of the estuarine teleost *Fundulus heteroclitus* (L.). Journal of Experimental Marine Biology and Ecology 9:9-42.

Eisler, R., D. J. O'Neill, Jr., and G. W. Thompson. 1978. Third annotated bibliography on biological effects of metals in aquatic environments (No. 1293-2246). U. S. Environmental Protection Agency Report 600/3-78-005. 486 pp.

Eisler, R., R. M. Rossoll, and G. A. Gaboury. 1979. Fourth annotated bibliography on biological effects of metals in aquatic environments (No. 2247-3132). U.S. Environmental Protection Agency Report 600/3-79-084. 591 pp.

Eisler, R., and M. Wapner. 1975. Second annotated bibliography on biological effects of metals in aquatic environments (No. 568-1292). U.S. Environmental Protection Agency Report 600/3-75-008. 399 pp.

Ellenberger, S. A., P. C. Baumann, and T. W. May. 1994. Evaluation of effects caused by high copper concentrations in Torch Lake, Michigan, on reproduction of yellow perch. Journal of Great Lakes Research 20:531-536.

Elsenhans, B., W. Forth, and E. Richter. 1991. Increased copper concentrations in rat tissues after acute intoxication with 2, 3, 7, 8-tetrachlorodibenzo-*p*-dioxin. Archives of Toxicology 65:429-432.

Enserink, E. L., J. L. Maas-Diepeveen, and C. J. Van Leeuwen. 1991. Combined effects of metals; an ecotoxicological evaluation. Water Research 25:679-687.

Erickson, S. J., N. Lackie, and T. E. Maloney. 1970. A screening technique for estimating copper toxicity to estuarine phytoplankton. Journal of the Water Pollution Control Federation 42(8), Part 2: R270-R278.

Ericksson, S. P., and J. M. Weeks. 1994. Effects of copper and hypoxia on two populations of the benthic amphipod. *Corophium volutator* (Pallas). Aquatic Toxicology 29:73-81.

Ettajani, H., C. Amiard-Triquet, and J. C. Amiard. 1992. Etude experimentale du transfert de deux elements traces (Ag, Cu) dans une chaine trophique marine: eau — particules (sediment natural, microalgue) — mollusques filtreurs (*Crassostrea gigas* Thunberg). Water, Air, and Soil Pollution 65:215-236.

Fagioli, F., C. Locatelli, and S. Landi. 1994. Heavy metals in the Goro Bay: sea water, sediments and mussels. Annali di Chimica 84:129-140.

Falandysz, J. 1993a. Some toxic and essential trace metals in cattle from the northern part of Poland. Science of the Total Environment 136:177-191.

Falandysz, J. 1993b. Some toxic and essential trace metals in swine from northern Poland. Science of the Total Environment 136:193-204.

Falandysz, J. 1994. Some toxic and trace metals in big game hunted in the northern part of Poland in 1987-1991. Science of the Total Environment 141:59-73.

Falandysz, J., W. Kotecka, and K. Kannan. 1994. Mercury, lead, cadmium, manganese, copper, iron and zinc concentrations in poultry, rabbit and sheep from the northern part of Poland. Science of the Total Environment 141:51-57.

Fernandez, T. V., and N. V. Jones. 1990. Studies on the toxicity of zinc and copper applied singly and jointly to *Nereis diversicolor* at different salinities and temperatures. Tropical Ecology 31:47-55.

Ferrando, M. D., and E. Andreu. 1993. Feeding behavior as an index of copper stress in *Daphnia magna* and *Brachionus calyciflorus*. Comparative Biochemistry and Physiology 106C:327-331.

Ferrando, M. D., C. R. Janssen, E. Andreu, and G. Persoone. 1993. Ecotoxicological studies with the freshwater rotifer *Brachionus calyciflorus*. III. The effects of chemicals on the feeding behavior. Ecotoxicology and Environmental Safety 26:1-9.

Fishelson, L., A. Yawetz, A. S. Perry, Z. Zuk-Rimon, R. Manelis, and A. Dotan. 1994. The Environmental Health Profile (EHP) for the Acre Valley (Israel): xenobiotics in animals and physiological evidence of stress. Science of the Total Environment 144:33-45.

Flora, S. J. S. 1991. Influence of simultaneous supplementation of zinc and copper during chelation of lead in rats. Human & Experimental Toxicology 10:331-336.

Forge, T. A., M. L. Berrow, J. J. Darbyshire, and A. Warren. 1993. Protozoan bioassays of soil amended with sewage sludge and heavy metals, using the common soil ciliate *Colpoda steinii*. Biology and Fertility of Soils 16:282-286.

Froslie, A., G. Norheim, and N. E. Soli. 1983. Levels of copper, molybdenum, zinc and sulphur in concentrates and mineral feeding stuffs in relation to chronic copper poisoning in sheep in Norway. Acta Agriculturae Scandinavica 33:261-267.

Gainey, L. F., Jr., and J. R. Kenyon. 1990. The effects of reserpine on copper induced cardiac inhibition in *Mytilus edulis*. Comparative Biochemistry and Physiology 95C:177-179.

Gallagher, C. H. 1979. Biochemical and pathological effects of copper deficiency. Pages 57-82 *in* J. O. Nriagu, editor. Copper in the environment. Part 2: health effects. John Wiley, New York.

Gamberg, M., and A. M. Scheuhammer. 1994. Cadmium in caribou and muskoxen from the Canadian Yukon and Northwest Territories. Science of the Total Environment 143:221-234.

Gamcik, P., J. Bires, L. Vrzgula, and P. Mesaros. 1990. Effect of experimental intoxication with copper from industrial emission on reproductive ability in rams. Reproduction in Domestic Animals 25:235-241.

Gardiner, M. R. 1967. The role of copper in the pathogenesis of subacute and chronic lupinosis of sheep. Australian Veterinary Journal 43:243-248.

Gardner, G. R., and G. LaRoche. 1973. Copper induced lesions in estuarine teleosts. Journal of the Fisheries Research Board of Canada 30:363-368.

Gintenreiter, S., J. Ortel, and H. J. Nopp. 1993. Effects of different dietary levels of cadmium, lead, copper, and zinc on the vitality of the forest pest insect *Lymantria dispar* L. (Lymantriidae, Lepid). Archives of Environmental Contamination and Toxicology 25:62-66.

Goldfischer, S., B. Schiller, and I. Sternlieb. 1970. Copper in hepatocyte lysosomes of the toad, *Bufo marinus* L. Nature 228:172-173.

Gopinath, C., and J. M. Howell. 1975. Experimental chronic copper toxicity in sheep. Changes that follow the cessation of dosing at the onset of haemolysis. Research in Veterinary Science 19:35-43.

Gordon, C. J., L. Fogelson, and J. W. Highfill. 1990. Hypothermia and hypometabolism: sensitive indices of whole-body toxicity following exposure to metallic salts in the mouse. Journal of Toxicology and Environmental Health 29:185-200.

Goresky, C. A., T. H. Holmes, and A. Sass-Korstak. 1968. The initial uptake of copper by the liver in the dog. Canadian Journal of Physiology and Pharmacology 46:771-784.

Goven, A. J., S. C. Chen, L. C. Fitzpatrick, and B. J. Venables. 1994. Lysozyme activity in earthworm (*Lumbricus terrestris*) coelomic fluid and coelomocytes: enzyme assay for immunotoxicity of xenobiotics. Environmental Toxicology and Chemistry 13:607-613.

Govindarajan, S., and V. N. R. Rao. 1992. Accumulation of trace metals in the marine biota and their biological transport. Acta Botanica Indica 20:1-5.

Greig, R. A., and G. Sennefelder. 1985. Metals and PCB concentrations in mussels from Long Island Sound. Bulletin of Environmental Contamination and Toxicology 35:331-334.

Gummow, B., C. J. Botha, A. T. Basson, and S. A. Bastianello. 1991. Copper toxicity in ruminants: air pollution as a possible cause. Onderstepoort Journal of Veterinary Research 58:33-40.

Gupta, U.C. 1979. Copper in agricultural crops. Pages 255-288 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Halbrook, R. S., R. L. Kirkpatrick, P. F. Scanlon, M. R. Vaughan, and H. P. Veit. 1993. Muskrat populations in Virginia's Elizabeth River: physiological condition and accumulation of environmental contaminants. Archives of Environmental Contamination and Toxicology 25:438-445.

Hall, W. S., S. J. Bushong, L. W. Hall, Jr., M. S. Lenkevich, and A. E. Pinkney. 1988. Monitoring dissolved copper concentrations in Chesapeake Bay, U.S.A. Environmental Monitoring and Assessment 11:33-42.

Hameed, P. S., and A. I. M. Raj. 1989. Effect of copper cadmium and mercury on crystalline style of the freshwater mussel *Lamellidens marginalis* (Lamarck). Indian Journal of Environmental Health 31:131-136.

Hamilton, S. J., and K. J. Buhl. 1990. Safety assessment of selected inorganic elements to fry of chinook salmon (*Oncorhynchus tshawytscha*). Ecotoxicology and Environmental Safety 20:307-324.

Han, B. C., and T. C. Hung. 1990. Green oysters caused by copper pollution on the Taiwan Coast. Environmental Pollution 65:347-362.

Han, B. C., W. L. Jeng, Y. N. Tsai, and M. S. Jeng. 1993. Depuration of copper and zinc by green oysters and blue mussels of Taiwan. Environmental Pollution 82:93-97.

Handy, R. D. 1992. The assessment of episodic metal pollution. II. The effects of cadmium and copper enriched diets on tissue contaminant analysis in rainbow trout (*Oncorhynchus mykiss*). Archives of Environmental Contamination and Toxicology 22:82-87.

Handy, R. D. 1993. The effect of acute exposure to dietary Cd and Cu on organ toxicant concentrations in rainbow trout, *Oncorhynchus mykiss*. Aquatic Toxicology 27:1-14.

Hansen, H. J. M., A. G. Olsen, and P. Rosenkilde. 1993. The effect of Cu^{2+} on osmoregulation in rainbow trout (*Oncorhynchus mykiss*) assayed by changes in plasma salinity and gill lipid metabolism. Science of the Total Environment, Supplement 1993, Part 2:899-905.

Hansen, J. I., T. Mustafa, and M. Depledge. 1992a. Mechanisms of copper toxicity in the shore crab, *Carcinus maenas*. I. Effects on Na, K-ATPase activity, haemolymph electrolyte concentrations and tissue water contents. Marine Biology 114:253-257.

Hansen, J. I., T. Mustafa, and M. Depledge. 1992b. Mechanisms of copper toxicity in the shore crab, *Carcinus maenas*. II. Effects on key metabolic enzymes, metabolites and energy charge potential. Marine Biology 114:259-264.

Hara, T. J., Y. M. C. Law, and S. Macdonald. 1977. Effects of mercury and copper on the olfactory response in rainbow trout, *Salmo gairdneri*. Journal of the Fisheries Research Board of Canada 33:1568-1573.

Harland, A. D., and N. R. Nganro. 1990. Copper uptake by the sea anemone *Anemonia viridis* and the role of zooxanthellae in metal regulation. Marine Biology 104:297-301.

Hasler, A. D. 1949. Antibiotic aspects of copper treatment of lakes. Transactions of the Wisconsin Academy of Sciences, Arts and Letters 39:97-103.

Havens, K. E. 1994. An experimental comparison of the effects of two chemical stressors on a freshwater zooplankton assemblage. Environmental Pollution 84:245-251.

Heath, A. G. 1991. Effect of water-borne copper on physiological responses of bluegill (*Lepomis macrochirus*) to acute hypoxic stress and subsequent recovery. Comparative Biochemistry and Physiology 100C:559-564.

Heliovaara, K., and R. Vaisanen. 1990. Heavy-metal contents in pupae of *Bupalus piniarius* (Lepidoptera: Geometridae) and *Panolis flammea* (Lepidoptera: Noctuidae) near an industrial source. Environmental Entomology 19:481-485.

Henny, C. J., L. J. Blus, and R. A. Grove. 1990. Western grebe, *Aechmophorus occidentalis*, wintering biology and contaminant accumulation in Commencement Bay, Puget Sound, Washington. Canadian Field-Naturalist 104:460-472.

Hickie, B. E., N. J. Hutchinson, D. G. Dixon, and P. V. Hodson. 1993. Toxicity of trace metal mixtures to alevin rainbow trout (*Oncorhynchus mykiss*) and larval fathead minnow (*Pimephales promelas*) in soft, acidic water. Canadian Journal of Fisheries and Aquatic Sciences 50:1348-1355.

Higgins, R. J. 1981. Chronic copper poisoning in growing pigs. Veterinary Record 109(7):134-135.

Hoare, K., A. R. Beaumont, and J. Davenport. 1995a. Variation among populations in the resistance of *Mytilus edulis* embryos to copper: adaptation to pollution? Marine Ecology Progress Series 120:155-161.

Hoare, K., J. Davenport, and A. R. Beaumont. 1995b. Effects of exposure and previous exposure to copper on growth of veliger larvae and survivorship of *Mytilus edulis* juveniles. Marine Ecology Progress Series 120:163-168.

Hodson, P. V., U. Borgmann, and H. Shear. 1979. Toxicity of copper to aquatic biota. Pages 307-372 *in* J. O. Nriagu, editor. Copper in the environment. Part 2: health effects. John Wiley, New York.

Hogstrand, C. 1991. Regulation of metallothionein in teleost fish during exposure. Ph.D. dissertation. University of Goteborg, Goteborg, Sweden. 176 pp.

Hogstrand, C., G. Lithner, and C. Haux. 1991. The importance of metallothionein for the accumulation of copper, zinc and cadmium in environmentally exposed perch, *Perca fluviatilis*. Pharmacology & Toxicology 69:492-501.

Hole, L. M., M. N. Moore, and D. Bellamy. 1993. Age-related cellular reactions to copper in the marine mussel *Mytilus edulis*. Marine Ecology Progress Series 94:175-179.

Holwerda, D. A. 1991. Cadmium kinetics in freshwater clams. V. Cadmium-copper interaction in metal accumulation by *Anodonta cygnea* and characterization of the metal-binding protein. Archives of Environmental Contamination and Toxicology 21:432-437.

Honda, K., J. E. Marcovecchio, S. Kan, R. Tatsukawa, and H. Ogi. 1990. Metal concentrations in pelagic seabirds from the north Pacific Ocean. Archives of Environmental Contamination and Toxicology 19:704-711.

Hopkin, S. P., D. T. Jones, and D. Dietrich. 1993. The isopod *Porcellio scaber* as a monitor of the bioavailability of metals in terrestrial ecosystems: towards a global “woodlouse watch” scheme. Science of the Total Environment, Supplement 1993, Part 1:357-365.

Horne, M. T., and W. A. Dunson. 1995. Toxicity of metals and low pH to embryos and larvae of the Jefferson salamander, *Ambystoma jeffersonianum*. Archives of Environmental Contamination and Toxicology 29:110-114.

Howell, J. M., H. S. Deol, P. R. Dorling, and J. B. Thomas. 1991. Experimental copper and heliotrope intoxication in sheep: morphological changes. Journal of Comparative Pathology 105:49-74.

Hubschman, J. H. 1967. Effects of copper on the crayfish *Orconectes rusticus* (Girard). II. Mode of toxic action. Crustaceana 12:141-150.

Huebner, J. D., and K. S. Pynnonen. 1992. Viability of glochidia of two species of *Anodonta* exposed to low pH and selected metals. Canadian Journal of Zoology 70:2348-2355.

Huggett, R. J., F. A. Cross, and M. E. Bender. 1975. Distribution of copper and zinc in oysters and sediments from three coastal-plain estuaries. Pages 224-238 *in* Proceedings of a symposium on mineral cycling in southeastern ecosystems, Augusta, Georgia, 1974. U.S. Energy Research and Development Administration, ERDA Symposium Series, CONF-740513.

Hung, T. C., A. Chuang, S. J. Wu, and C. C. H. Tsai. 1990. Relationships among the species and forms of copper and biomass along the Erhjin Chi coastal water. Acta Oceanographic Taiwanica 25:65-76.

Hutchinson, T. C. 1979. Copper contamination of ecosystems caused by smelter activities. Pages 451-502 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Hylland, K., C. Haux, and C. Hogstrand. 1992. Hepatic metallothionein and heavy metals in dab *Limanda limanda* from the German Bight. Marine Ecology Progress Series 91:89-96.

Iger, Y., R. A. C. Lock, H. A. Jenner, and S. E. W. Bonga. 1994. Cellular responses in the skin of carp (*Cyprinus carpio*) exposed to copper. Aquatic Toxicology 29:49-64.

Ingersoll, C. G., and R. W. Winner. 1982. Effect on *Daphnia pulex* (De Geer) of daily pulse exposures to copper or cadmium. Environmental Toxicology and Chemistry 1:321-327.

Jacobson, P. J., J. L. Farris, D. S. Cherry, and R. J. Neves. 1993. Juvenile freshwater mussel (Bivalvia: Unionidae) responses to acute toxicity testing with copper. Environmental Toxicology and Chemistry 12:879-883.

Jaffe, R., C. A. Fernandez, and J. Alvarado. 1992. Trace metal analyses in octocorals by microwave acid digestion and graphite furnace atomic-absorption spectrometry. Talanta 39:113-117.

Janssen, C. R., M. D. Ferrando, and G. Persoone. 1994. Ecotoxicological studies with the freshwater rotifer *Brachionus calyciflorus*. IV. Rotifer behavior as a sensitive and rapid sublethal test criterion. Ecotoxicology and Environmental Safety 28:244-255.

Jehan, Z. S., and D. B. Motlag. 1994. Biochemical changes in the blood and liver of metal-treated rats. Medical Science Research 22:499-501.

Jenkins, D. W. 1980. Biological monitoring of toxic trace metals. Volume 2: Toxic trace metals in plants and animals of the world. Part II. U.S. Environmental Protection Agency Report 600/3-80-091. p. 504-982.

Johnson, R. K., L. Ericksson, and T. Wiederholm. 1992. Ordination of profundal zoobenthos along a trace metal pollution gradient in northern Sweden. Water, Air, and Soil Pollution 65:339-351.

Johnson, W. T., and T. B. Smith. 1994. Copper deficiency increases cytochrome P450-dependent 7-ethoxyresorufin-O-deethylase activity in rat small intestine. Proceedings of the Society for Experimental Biology and Medicine 207:302-308.

Johnson, W. A., and M. T. Finley. 1980. Handbook of acute toxicity of chemicals to fish and aquatic invertebrates. U.S. Fish and Wildlife Service Resource Publication 137. 98 pp.

Jorhem, L., J. Engman, B. Sundstrom, and A. M. Thim. 1994. Trace elements in crayfish: regional differences and changes induced by cooking. Archives of Environmental Contamination and Toxicology 26:137-142.

Jozwik, Z. 1990. Heavy metals in tundra plants of Bellsund area, Spitsbergen. Polish Polar Research 11:401-409.

Karez, C. S., V. F. Magalhaes, and W. C. Pfeiffer. 1994. Trace metal accumulation by algae in Sepetiba Bay, Brazil. Environmental Pollution 83:351-356.

Kashani, A. B., H. Samie, R. J. Emerick, and C. W. Carlson. 1986. Effect of copper with three levels of sulfur containing amino acids in diets for turkeys. Poultry Science 65:1754-1759.

Kataev, G. D., J. Suomela, and P. Palokangas. 1994. Densities of microtine rodents along a pollution gradient from a copper-nickel smelter. Oecologia 97:491-498.

Khangarot, B. S. 1992. Copper-induced hepatic ultrastructural alterations in the snake-headed fish, *Channa punctatus*. Ecotoxicology and Environmental Safety 23:282-293.

Khangarot, B. S., and D. M. Tripathi. 1991. Changes in humoral and cell-mediated immune responses and in skin and respiratory surfaces of catfish, *Saccobranchus fossilis*, following copper exposure. Ecotoxicology and Environmental Safety 22:291-308.

King, K. A., J. Leleuxs, and B. M. Mulhern. 1984. Molybdenum and copper levels in white-tailed deer near uranium mines in Texas. Journal of Wildlife Management 48:267-270.

Kirchgessner, M., F. J. Schwarz, E. Grassmann, and H. Steinhart. 1979. Interactions of copper with other trace elements. Pages 433-472 *in* J. O. Nriagu, editor. Copper in the environment. Part 2: health effects. John Wiley, New York.

Kirk, R. S., and J. W. Lewis. 1993. An evaluation of pollutant induced changes in the gills of rainbow trout using scanning electron microscopy. Environmental Technology 14:577-585.

Kleerekoper, H. 1973. Effects of copper on the locomotor orientation of fish. U.S. Environmental Protection Agency Report R3-73-045. 97 pp.

Klima, K. E., and F. M. Applehans. 1990. Copper exposure and the degeneration of olfactory receptors in rainbow trout (*Oncorhynchus mykiss*). Chemical Speciation and Bioavailability 2:149-154.

Knobeloch, L., M. Ziarik, J. Howard, B. Theis, D. Farmer, H. Anderson, and M. Proctor. 1994. Gastrointestinal upsets associated with ingestion of copper-contaminated water. Environmental Health Perspectives 102:958-961.

Koivisto, S., and M. Ketola. 1995. Effects of copper on life-history traits of *Daphnia pulex* and *Bosmina longirostris*. Aquatic Toxicology 32:255-269.

Koivisto, S., M. Ketola, and M. Walls. 1992. Comparison of five cladoceran species in short- and long-term copper exposure. Hydrobiologia 248:125-136.

Kraak, M. H. S., D. Lavy, W. H. M. Peeters, and C. Davids. 1992. Chronic ecotoxicity of copper and cadmium to the zebra mussel *Dreissena polymorpha*. Archives of Environmental Contamination and Toxicology 23:363-369.

Kraak, M. H. S., M. Toussaint, D. Lavy, and C. Davids. 1994. Short-term effects of metals on the filtration rate of the zebra mussel *Dreissena polymorpha*. Environmental Pollution 84:139-143.

Krelowska-Kulas, M., W. Kudelka, Z. Stalinski, and J. Bieniek. 1994. Content of metals in rabbit tissues. Die Nahrung 38:393-396.

Krishnakumar, P. K., P. K. Asokan, and V. K. Pillai. 1990. Physiological and cellular responses to copper and mercury in the green mussel *Perna viridis* (Linnaeus). Aquatic Toxicology 18:163-174.

Kubitz, J. A., E. C. Lewek, J. M. Besser, J. B. Drake III, and J. P. Giesy. 1995. Effects of copper-contaminated sediments on *Hyalella azteca*, *Daphnia magna*, and *Ceriodaphnia dubia*: survival, growth, and enzyme inhibition. Archives of Environmental Contamination and Toxicology 29:97-103.

Lal, S., and T. L. Sourkes. 1971. Deposition of copper in rat tissues—the effect of dose and duration of administration of copper sulfate. Toxicology and Applied Pharmacology 20:269-283.

Langlois, C. J., and E. J. Calabrese. 1992. The interactive effect of chlorine, copper and nitrite on methaemoglobin formation in red blood cells of Dorset sheep. Human & Experimental Toxicology 11:223-228.

Larsen, K. J., S. R. Brewer, and D. H. Taylor. 1994. Differential accumulation of heavy metals by web spiders and ground spiders in an old-field. Environmental Toxicology and Chemistry 13:503-508.

Lauenstein, G. G., A. Robertson, and T. P. O'Connor. 1990. Comparison of trace metal data in mussels and oysters from a mussel watch programme of the 1970s with those from a 1980s programme. Marine Pollution Bulletin 21:440-447.

Launer, V. P., E. Kasten, K. Graeser, and T. Hahnewald. 1991. Schwermet alluntersuchungen bei Schwarzwild aus dem immissionsbelasteten Gebiet "Tharandter Wald", Kreis Freital. Wissenschaftlichen Gesellschoft fur Veterinarmedizin in der Deutschen Demokratischen Republik 46(19):683-687.

Lauren, D. J., and D. G. McDonald. 1987a. Acclimation to copper by rainbow trout, *Salmo gairdneri*: physiology. Canadian Journal of Fisheries and Aquatic Sciences 44:99-104.

Lauren, D. J., and D. G. McDonald. 1987b. Acclimation to copper by rainbow trout, *Salmo gairdneri*: biochemistry. Canadian Journal of Fisheries and Aquatic Sciences 44:105-111.

Law, R. J., C. F. Fileman, A. D. Hopkins, J. R. Baker, J. Harwood, D. B. Jackson, S. Kennedy, A. R. Martin, and R. J. Morris. 1991. Concentrations of trace metals in the livers of marine mammals (seals, porpoises and dolphins) from waters around the British Isles. Marine Pollution Bulletin 22:183-191.

Law, R. J., B. R. Jones, J. R. Baker, S. Kennedy, R. Milne, and R. J. Morris. 1992. Trace metals in the livers of marine mammals from the Welsh coast and the Irish Sea. Marine Pollution Bulletin 24:296-304.

Lazorchak, J. M., and W. T. Waller. 1993. The relationship of total copper 48h LC50s to *Daphnia magna* dry weight. Environmental Toxicology and Chemistry 12:903-911.

Leckie, J. O., and J. A. Davis. 1979. Aqueous environmental chemistry of copper. Pages 89-121 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Levine, M. B., A. T. Hall, G. W. Barrett, and D. H. Taylor. 1989. Heavy metal concentrations during ten years of sludge treatment to an old-field community. Journal of Environmental Quality 18:411-418.

Lewis, A. G., P. H. Whitfield, and A. Ramnarine. 1972. Some particulate and soluble agents affecting the relationship between metal toxicity and organism survival in the calanoid copepod *Euchaeta japonica*. Marine Biology 17:215-221.

Lewis, G., S. Terlecki, and R. Allcroft. 1967. The occurrence of swayback in the lambs of ewes fed a semi-purified diet of low copper content. Veterinary Record 81:415-416.

Lin, H. C., and W. A. Dunson. 1993. The effect of salinity on the acute toxicity of cadmium to the tropical, estuarine, hermaphroditic fish, *Rivulus marmoratus*: a comparison of Cd, Cu, and Zn tolerance with *Fundulus heteroclitus*. Archives of Environmental Contamination and Toxicology 25:41-47.

Lindquist, L. 1993. Individual and interspecific variation in metal concentrations in five species of bumblebees (Hymenoptera: Apidae). Environmental Entomology 22:1355-1357.

Liu, X. Y., T. Y. Jin, G. F. Nordberg, S. Ranner, M. Sjostrom, and Y. Zhou. 1992. A multivariate study of protective effects of Zn and Cu against nephrotoxicity induced by cadmium metallothionein in rats. Toxicology and Applied Pharmacology 114:239-245.

Lock, J. W., D. R. Thompson, R. W. Furness, and J. A. Bartle. 1992. Metal concentrations in seabirds of the New Zealand region. Environmental Pollution 75:289-300.

Lorz, H. W., and B. P. McPherson. 1977. Effects of copper and zinc on smoltification of coho salmon. U.S. Environmental Protection Agency Report 600/3-77-032. 84 pp.

Ma, W. C. 1984. Sublethal toxic effects of copper on growth, reproduction and litter breakdown activity in the earthworm *Lumbricus rubellus*, with observations on the influence of temperature, and soil pH. Environmental Pollution 33A:207-219.

Mackenthun, K. N., and H. L. Cooley. 1952. The biological effect of copper sulphate treatment on lake ecology. Transactions of the Wisconsin Academy of Sciences, Arts and Letters 41:177-187.

MacKenzie, C. L., Jr. 1961. A practical chemical method for killing mussels and other oyster competitors. Commercial Fisheries Review 23(3):15-19.

MacPherson, A., and R. G. Hemingway. 1969. The relative merit of various blood analyses and liver function tests in giving an early diagnosis of chronic copper poisoning in sheep. British Veterinary Journal 125:213-221.

Marchal-Segault, D., C. Briancon, S. Halpern, P. Fragu, and G. Lauge. 1991. Secondary ion mass spectrometry analysis of the copper distribution in *Drosophila melanogaster* chronically intoxicated with Bordeaux mixture. Biology of the Cell 70:129-132.

Marcovecchio, J. E., V. J. Moreno, R. O. Bastida, M. S. Gerpe, and D. H. Rodriguez. 1990. Tissue distribution of heavy metals in small cetaceans from the southwestern Atlantic Ocean. Marine Pollution Bulletin 21:299-304.

Marr, J. C. A., H. L. Bergman, J. Lipton, and C. Hogstrand. 1995. Differences in relative sensitivity of naive and metals-acclimated brown and rainbow trout exposed to metals representative of the Clark Fork River, Montana. Canadian Journal of Fisheries and Aquatic Sciences 52:2016-2030.

Martin, M., J. W. Hunt, B. S. Anderson, S. L. Turpen, and F. H. Palmer. 1989. Experimental evaluation of the mysid *Holmesimysis costata* as a test organism for effluent toxicity testing. Environmental Toxicology and Chemistry 8:1003-1012.

Mat, I. 1994. Arsenic and trace metals in commercially important bivalves, *Anadara granosa* and *Paphia undulata*. Bulletin of Environmental Contamination and Toxicology 52:833-839.

Mat, I., M. J. Maah, and A. Johari. 1994. Trace metals in sediments and potential availability to *Anadara granosa*. Archives of Environmental Contamination and Toxicology 27:54-59.

Mathew, P., and N. R. Menon. 1993. Heavy metal stress induced variations in O:N ratio in two tropical bivalves *Perna indica* (Kuriakose and Nair) and *Donax incarnatus* Gmelin. Indian Journal of Experimental Biology 31:694-698.

Mathews, T. D. 1994. Contaminants in recreationally important estuarine finfish from South Carolina. Bulletin of Environmental Contamination and Toxicology 53:412-419.

Maund, S. J., E. J. Taylor, and D. Pascoe. 1992. Population responses of the freshwater amphipod crustacean *Gammarus pulex* (L.) to copper. Freshwater Biology 28:29-36.

Mauri, M., E. Orlando, M. Nigro, and F. Regoli. 1990. Heavy metals in the Antarctic scallop *Adamussium colbecki*. Marine Ecology Progress Series 67:27-33.

Mayer, F. L., Jr. 1987. Acute toxicity handbook of chemicals to estuarine organisms. U.S. Environmental Protection Agency Report 600/8-87/017. 274 pp.

McCarter, J. A., A. T. Mathieson, M. Roch, R. W. Olafson, and J. T. Buckley. 1982. Chronic exposure of coho salmon to sublethal concentrations of copper-II. Distribution of copper between high- and low-molecular weight proteins in liver cytosol and the possible role of metallothionein in detoxication. Comparative Biochemistry and Physiology 72C:21-26.

McKim, J. M., and D. A. Benoit. 1971. Effects of long-term exposures to copper on survival, growth, and reproduction of brook trout (*Salvelinus fontinalis*). Journal of the Fisheries Research Board of Canada 28:655-662.

McKim, J. M., and D. A. Benoit. 1974. Duration of toxicity tests for establishing “no effect” concentrations for copper with brook trout (*Salvelinus fontinalis*). Journal of the Fisheries Research Board of Canada 31:449-452.

McKim, J. M., G. M. Christensen, and E. P. Hunt. 1970. Changes in the blood of brook trout (*Salvelinus fontinalis*) after short-term and long-term exposure to copper. Journal of the Fisheries Research Board of Canada 27:1883-1889.

McKim, J. M., J. G. Eaton, and G. W. Holcombe. 1978. Metal toxicity to embryos and larvae of eight species of freshwater fish—II: copper. Bulletin of Environmental Contamination and Toxicology 19:608-616.

McNulty, H. R., B. S. Anderson, J. W. Hunt, S. L. Turpen, and M. M. Singer. 1994. Age-specific toxicity of copper to larval topsmelt *Atherinops affinis*. Environmental Toxicology and Chemistry 13:487-492.

Meador, J. P. 1991. The interaction of pH, dissolved organic carbon, and total copper in the determination of ionic copper and toxicity. Aquatic Toxicology 19:13-32.

Meador, J. P., U. Varanasi, P. A. Robisch, and S. L. Chan. 1993. Toxic metals in pilot whales (*Globicephala melaena*) from strandings in 1986 and 1990 on Cape Cod, Massachusetts. Canadian Journal of Fisheries and Aquatic Sciences 50:2698-2706.

Mersch, J., E. Morhain, and C. Mouvet. 1993. Laboratory accumulation and depuration of copper and cadmium in the freshwater mussel *Dreissena polymorpha* and the aquatic moss *Rhynchostegium riparioides*. Chemosphere 27:1475-1485.

Metcalfe-Smith, J. L. 1994. Influence of species and sex on metal residues in freshwater mussels (Family Unionidae) from the St. Lawrence River, with implications for biomonitoring programs. Environmental Toxicology and Chemistry 13:1433-1443.

Michot, T. C., T. W. Custer, A. J. Nault, and C. A. Mitchell. 1994. Environmental contaminants in redheads wintering in coastal Louisiana and Texas. Archives of Environmental Contamination and Toxicology 26:425-434.

Migon, C. 1993. Riverine and atmospheric inputs of heavy metals to the Ligurian Sea. Science of the Total Environment 138:289-299.

Miller, P. A., R. P. Lanno, M. E. McMaster, and D. G. Dixon. 1993. Relative contributions of dietary and waterborne copper to tissue copper burdens and waterborne-copper tolerance in rainbow trout (*Oncorhynchus mykiss*). Canadian Journal of Fisheries and Aquatic Sciences 50:1683-1689.

Miller, P. A., K. R. Munkittrick, and D. G. Dixon. 1992. Relationship between concentrations of copper and zinc in water, sediment, benthic invertebrates, and tissues of white sucker (*Catostomus commersoni*) at metal-contaminated sites. Canadian Journal of Fisheries and Aquatic Sciences 49:978-984.

Miltimore, J. E., C. M. Kalnin, and J. B. Clapp. 1978. Copper storage in the livers of cattle supplemented with injected copper and with copper sulfate and chelated copper. Canadian Journal of Animal Science 58:525-529.

Miramand, P., and D. Bentley. 1992. Concentration and distribution of heavy metals of two cephalopods, *Eledone cirrhosa* and *Sepia officinalis*, from the French coast of the English Channel. Marine Biology 114:407-414.

Moffitt, A. E., Jr., and S. D. Murphy. 1973. Effect of excess and deficient copper intake on rat liver microsomal enzyme activity. Biochemical Pharmacology 22:1463-1476.

Moore, P. G., P. S. Rainbow, and E. Hayes. 1991. The beach-hopper *Orchestia gammarellus* (Crustacea: Amphipoda) as a biomonitor for copper and zinc: North Sea trials. Science of the Total Environment 106:221-238.

Morgan, J. E., and A. J. Morgan. 1990. The distribution of cadmium, copper, lead, zinc and calcium in the tissues of the earthworm *Lumbricus rubellus* sampled from one uncontaminated and four polluted soils. Oecologia 84:559-566.

Morris, R. J., R. J. Law, C. R. Allchin, C. A. Kelly, and C. F. Fileman. 1989. Metals and organochlorines in dolphins and porpoises of Cardigan Bay, West Wales. Marine Pollution Bulletin 20:512-523.

Morrissey, J. R., and D. R. Edds. 1994. Metal pollution associated with a landfill: concentrations in water, sediment, crayfish, and fish. Transactions of The Kansas Academy of Science 97:18-25.

Mount, D. L., and C. E. Stephen. 1969. Chronic toxicity of copper to the fathead minnow (*Pimephales promelas*) in soft water. Journal of the Fisheries Research Board of Canada 26:2449-2457.

Mukhopadhyay, M. P., B. B. Ghosh, and M. M. Bagchi. 1994. Toxicity of heavy metals to fish, prawn and fish food organisms of Hooghly estuarine system. Geobios 21:13-17.

Mule, M. B., and V. S. Lomte. 1994. Effect of heavy metals ($CuSO_4$ and $HgCl_2$) on the oxygen consumption of the freshwater snail, *Thiara tuberculata*. Journal of Environmental Biology 15:263-268.

Munkittrick, K. R., P. A. Miller, D. R. Barton, and D. G. Dixon. 1991. Altered performance of white sucker populations in the Manitouwadge chain of lakes is associated with changes in benthic macroinvertebrate communities as a result of copper and zinc contamination. Ecotoxicology and Environmental Safety 21:318-326.

Munoz, M. J., M. Carballo, and J. V. Tarazona. 1991. The effect of sublethal levels of copper and cyanide on some biochemical parameters of rainbow trout along subacute exposition. Comparative Biochemistry and Physiology 100C:577-582.

Mwangi, S. M., and M. A. Alikhan. 1993. Cadmium and nickel uptake by tissues of *Cambarus bartoni* (Astacidae, Decapoda, Crustacea): effects on copper and zinc stores. Water Research 27:921-927.

Natarajan, E., R. S. Biradar, and J. P. George. 1992. Acute toxicity of pesticides to giant freshwater prawn *Macrobrachium rosenbergii* (De Man). Journal of Aquaculture in the Tropics 7:183-188.

National Academy of Sciences (NAS). 1977. Copper. Committee on Medical and Biologic Effects of Environmental Pollutants, National Research Council, National Academy of Sciences, Washington, D.C. 115 pp.

Neff, J. M., and J. W. Anderson. 1977. The effects of copper (II) on molting and growth of juvenile lesser blue crabs *Callinectes similis*. Pages 155-165 *in* C. S. Giam, editor. Pollutant effects on marine organisms. D.C. Heath and Company, Lexington, Massachusetts.

Negro, J. J., J. A. Donazar, F. Hiraldo, L. M. Hernandez, and M. A. Fernandez. 1993. Organochlorine and heavy metal contamination in non-viable eggs and its relation to breeding success in a Spanish population of lesser kestrels (*Falco naumanni*). Environmental Pollution 82:201-205.

Ng, T. B., and W. K. Liu. 1990. Toxic effect of heavy metals on cells isolated from the rat adrenal and testis. In Vitro Cellular & Developmental Biology: Journal of the Tissue Culture Association 26:24-28.

Nonnotte, L., F. Boitel, and J. P. Truchot. 1993. Waterborne copper causes gill damage and hemolymph hypoxia in the shore crab *Carcinus maenas*. Canadian Journal of Zoology 71:1569-1576.

Norheim, G., J. U. Skaare, and O. Wiig. 1992. Some heavy metals, essential elements, and chlorinated hydrocarbons in polar bear (*Ursus maritimus*) at Svalbard. Environmental Pollution 77:51-57.

Nriagu, J. O., editor. 1979a. Copper in the environment. Part 1: ecological cycling. John Wiley, New York. 522 pp.

Nriagu, J. O., editor. 1979b. Copper in the environment. Part 2: health effects. John Wiley, New York. 489 pp.

Nriagu, J. O. 1979c. The global copper cycle. Pages 1-17 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Nriagu, J. O. 1979d. Copper in the atmosphere and precipitation. Pages 45-75 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Ohlendorf, H. M., K. C. Marois, R. W. Lowe, T. E. Harvey, and P. R. Kelly. 1991. Trace elements and organochlorines in surf scoters from San Francisco Bay, 1985. Environmental Monitoring and Assessment 18:105-122.

Okazaki, R. K. 1976. Copper toxicity in the Pacific oyster *Crassostrea gigas*. Bulletin of Environmental Contamination and Toxicology 16:658-664.

O'Shea, T. J., J. F. Moore, and H. I. Kochman. 1984. Contaminant concentrations in manatees in Florida. Journal of Wildlife Management 48:741-748.

Ozoh, P. T. E. 1992a. The effects of salinity, temperature and sediment on the toxicity of copper to juvenile *Hediste* (*Nereis*) *diversicolor* (O. F. Muller). Environmental Monitoring and Assessment 21:1-10.

Ozoh, P. T. E. 1992b. The effect of temperature and salinity on copper body-burden and copper toxicity to *Hediste* (*Nereis*) *diversicolor*. Environmental Monitoring and Assessment 21:11-17.

Ozoh, P. T. E., 1992c. The importance of adult *Hediste* (*Nereis*) *diversicolor* in managing heavy metal pollution in shores and estuaries. Environmental Monitoring and Assessment 21:165-171.

Ozoh, P. T. E. 1994. The effect of salinity, temperature and time on the accumulation and depuration of copper in ragworm, *Hediste* (*Nereis*) *diversicolor* (O. F. Muller). Environmental Monitoring and Assessment 29:155-164.

Ozoh, P. T. E., and N. V. Jones. 1990. The effects of salinity and temperature on the toxicity of copper to 1-day and 7-day-old larvae of *Hediste* (*Nereis*) *diversicolor* (O. F. Muller). Ecotoxicology and Environmental Safety 19:24-32.

Paez-Osuna, F., J. I. Osuna-Lopez, G. Izaguirse-Fiero, and H. M. Zazueta-Padilla. 1994. Trace metals in mussels from the Ensenada del Pallon Lagoon, Mexico. Marine Pollution Bulletin 28:124-126.

Paludan-Muller, P., C. T. Agger, R. Deitze, and C. C. Kinze. 1993. Mercury, cadmium, zinc, copper and selenium in harbour porpoise (*Phocoena phocoena*) from west Greenland. Polar Biology 13:311-320.

Panemangalore, M. 1993. Interaction among zinc, copper, and cadmium in rats: effects of low zinc and copper diets and oral cadmium exposure. Journal of Trace Elements in Experimental Medicine 6:125-139.

Parmelee, R. W., R. S. Wentsel, C. T. Phillips, M. Simini, and R. T. Checkai. 1993. Soil microcosm for testing the effects of chemical pollutants on soil fauna communities and trophic structure. Environmental Toxicology and Chemistry 12:1477-1486.

Parrott, J. L., and J. B. Sprague. 1993. Patterns in toxicity of sublethal mixtures of metals and organic chemicals determined by Microtox^{R} and by DNA, RNA, and protein content of fathead minnows (*Pimephales promelas*). Canadian Journal of Fisheries and Aquatic Sciences 50:2245-2253.

Pascoe, G. A., R. J. Blanchet, and G. Linder. 1994. Bioavailability of metals and arsenic to small mammals at a mining waste-contaminated wetland. Archives of Environmental Contamination and Toxicology 27:44-50.

Paulij, W. P., W. Zurberg, J. M. Denuce, and E. J. van Hannen. 1990. The effect of copper on the embryonic development and hatching of *Sepia officinalis* L. Archives of Environmental Contamination and Toxicology 19:797-801.

Pedersen, T. F. 1983. Dissolved heavy metals in a lacustrine mine tailings deposit—Butte Lake, British Columbia. Marine Pollution Bulletin 14:249-254.

Pelgrom, S. M. G. J., L. P. M. Lamers, J. A. M. Garritsen, B. M. Pels, R. A. C. Lock, P. H. M. Balm, and S. E. W. Bonga. 1994. Interactions between copper and cadmium during single and combined exposure in juvenile tilapia *Oreochromis mossambicus*: influence of feeding condition on whole body metal accumulation and the effect of the metals on tissue water and ion content. Aquatic Toxicology 30:117-135.

Peppard, E. M., W. R. Walters, J. W. Avault, Jr., and W. G. Perry, Jr. 1991. Toxicity of chelated copper to juvenile red drum *Sciaenops ocellatus*. Journal of the World Aquaculture Society 22:101-108.

Percival, S. S. 1995. Neutropenia caused by copper deficiency: possible mechanisms of action. Nutrition Reviews 53(3):59-66.

Petering, H. G., L. Murphy, and E. O'Flaherty. 1977. Influence of dietary copper and zinc on rat lipid metabolism. Agricultural and Food Chemistry 25:1105-1109.

Petri, G., and G. P. Zauke. 1993. Trace metals in crustaceans in the Antarctic Ocean. Ambio 22:529-536.

Piccinni, E., and O. Coppellotti. 1982. Response to heavy metals in organisms-II. Effects of physiological metals on *Ochromonas danica*. Comparative Biochemistry and Physiology 71C:135-140.

Pilgaard, L., H. Malte, and F. B. Jensen. 1994. Physiological effects and tissue accumulation of copper in freshwater rainbow trout (*Oncorhynchus mykiss*) under normoxic and hypoxic conditions. Aquatic Toxicology 29:197-212.

Pip, E. 1990. Copper, lead and cadmium concentrations in a sample of Lake Winnipeg *Anodonta grandis*. The Nautilus 103:140-142.

Playle, R. C., D. G. Dixon, and K. Burnison. 1993a. Copper and cadmium binding to fish gills: modification by dissolved organic carbon and synthetic ligands. Canadian Journal of Fisheries and Aquatic Sciences 50:2667-2677.

Playle, R. C., D. G. Dixon, and K. Burnison. 1993b. Copper and cadmium binding to fish gills: estimates of metal-gill stability constants and modelling of metal accumulation. Canadian Journal of Fisheries and Aquatic Sciences 50:2678-2687.

Playle, R. C., R. W. Gensemer, and D. G. Nelson. 1992. Copper accumulation on gills of fathead minnows: influence of water hardness, complexation and pH of the gill micro-environment. Environmental Toxicology and Chemistry 11:381-391.

Porta, A. A., and A. E. Ronco. 1993. Cu (II) toxicity to the rotifer *Brachionus calyciflorus*, as affected by fulvic acids of freshwater origin. Environmental Pollution 82:263-267.

Poupoulis, C., and L. S. Jensen. 1976. Effects of high dietary copper on gizzard integrity of the chick. Poultry Science 55:113-121.

Powell, M. L., and K. N. White. 1990. Heavy metal accumulation by barnacles and its implications for their use as biological monitors. Marine Environmental Research 30:91-118.

Prestrud, P., G. Norheim, T. Sivertsen, and H. L. Daae. 1994. Levels of toxic and essential elements in arctic fox in Svalbard. Polar Biology 14:155-159.

Rainbow, P. S. 1989. Copper, cadmium and zinc concentrations in oceanic amphipod and euphausiid crustaceans, as a source of heavy metals to pelagic seabirds. Marine Biology 103:513-518.

Raj, A. I. M., and P. S. Hameed. 1991. Effect of copper, cadmium and mercury on metabolism of the freshwater mussel *Lamellidens marginalis* (Lamarck). Journal of Environmental Biology 12:131-135.

Ranta, W. B., G. D. Tomassini, and E. Nieboer. 1978. Elevation of copper and nickel levels in primaries from black and mallard ducks collected in the Sudbury district, Ontario. Canadian Journal of Zoology 56:581-586.

Rao, V. N. R., and S. Govindarajan. 1992. Transfer of copper and zinc through a marine food chain. Acta Botanica Indica 20:71-75.

Read, H. J., and M. H. Martin. 1993. The effect of heavy metals on populations of small mammals from woodlands in Avon (England) with particular emphasis on metal concentrations in *Sorex araneus* L. and *Sorex minutus* L. Chemosphere 27:2197-2211.

Reardon, L. S., and R. M. Harrell. 1990. Acute toxicity of formalin and copper sulfate to striped bass fingerlings held in varying salinities. Aquaculture 87:255-270.

Reed, S. T., M. G. Allen, D. C. Martens, and J. R. McKenna. 1993. Copper fractions extracted by Mehlich-3 from soils amended with either $CuSO_4$ or copper rich pig manure. Communications in Soil Science and Plant Analysis 24:827-839.

Reid, S. S., and D. G. McDonald. 1991. Metal binding activity of the gills of rainbow trout (*Oncorhynchus mykiss*). Canadian Journal of Fisheries and Aquatic Sciences 48:1061-1068.

Rice, D. W., Jr., and F. L. Harrison. 1983. The sensitivity of adult, embryonic, and larval crayfish *Procambarus clarkii* to copper. U.S. Nuclear Regulatory Commission (NRC), Report NUREG/CR-3133 UCRL-53048. 19 pp. NRC, Washington, D.C.

Roche, H., and G. Boge. 1993. Effects of Cu, Zn and Cr salts on antioxidant enzyme activities *in vitro* of red blood cells of a marine fish *Dicentrarchus labrax*. Toxicology In Vitro 7:623-629.

Roesijadi, G. 1994. Behavior of metallothionein-bound metals in a natural population of an estuarine mollusc. Marine Environmental Research 38:147-168.

Romeo, M., A. Mathieu, M. Gnassia-Barelli, A. Romana, and M. Lafaurie. 1994. Heavy metal content and biotransformation enzymes in two fish species from the NW Mediterranean. Marine Ecology Progress Series 107:15-22.

Romeu-Moreno, A., A. Aguilar, L. Arola, and A. Mas. 1994. Respiratory toxicity of copper. Environmental Health Perspectives 102 (Supplement 3):339-340.

Roncero, V., E. Duran, F. Soler, J. Masot, and L. Gomez. 1992. Morphometric, structural, and ultrastructural studies of tench (*Tinca tinca* L.) hepatocytes after copper sulfate administration. Environmental Research 57:45-58.

Roomi, M. W., A. H. Shah, M. Anwarullah, and M. Hussain. 1990. Studies on the control of subterranean termites by inorganic pesticides. Anzeiger fur Schadlingskunde, Pflanzenschutz, Umweltschutz 63:50-52.

Roper, D. S., and C. W. Hickey. 1994. Behavioural responses of the marine bivalve *Macoma liliana* exposed to copper- and chlordane-dosed sediments. Marine Biology 118:673-680.

Rose, E. T. 1954. Blue-green algae control at Storm Lake. Proceedings of the Iowa Academy of Science 61:604-614.

Rougier, F., D. Troutaud, A. Ndoye, and P. Deschaux. 1994. Non-specific immune response of zebrafish, *Brachydanio rerio* (Hamilton-Buchanan) following copper and zinc exposure. Fish and Shellfish Immunology 4:115-127.

Roux, D. J., P. L. Kempster, E. Truter, and L. van der Merwe. 1993. Effect of cadmium and copper on survival and reproduction of *Daphnia pulex*. Water SA (Pretoria) 19:269-274.

Rowe, B. L., and H. H. Prince. 1983. Behavioral response of mallards to contaminated drinking water. Bulletin of Environmental Contamination and Toxicology 30:505-510.

Saari, J. T., D. A. Schuschke, and D. M. Ackermann. 1994. Trace elements in humans and copper-deficient rats experiencing cardiac ventricular rupture. Journal of Trace Elements in Experimental Medicine 7:59-67.

St. Louis, V. L., L. Breebaart, J. C. Barlow, and J. F. Klaverkamp. 1993. Metal accumulation and metallothionein concentrations in tree swallow nestlings near acidified lakes. Environmental Toxicology and Chemistry 12:1203-1207.

Sander, J. E., J. L. Wilson, P. B. Bush, and G. N. Rowland. 1994. Severe pododermatitis in broiler breeder hens housed on pressure-treated slats. Avian Diseases 38:172-176.

Sanders, B. M., L. S. Martin, S. R. Howe, W. G. Nelson, E. S. Hegre, and D. K. Phelps. 1994. Tissue-specific differences in accumulation of stress proteins in *Mytilus edulis* exposed to a range of copper concentrations. Toxicology and Applied Pharmacology 125:206-213.

Sanders, B. M., L. S. Martin, W. G. Nelson, D. K. Phelps, and W. Welch. 1991. Relationships between accumulation of a 60 kDa stress protein and a scope-for-growth in *Mytilus edulis* exposed to a range of copper concentrations. Marine Environmental Research 31:81-97.

Sandheinrich, M. B., and G. J. Atchison. 1989. Sublethal copper effects on bluegill, *Lepomis macrochirus*, foraging behavior. Canadian Journal of Fisheries and Aquatic Sciences 46:1977-1985.

Saucier, D., L. Astic, and P. Rioux. 1991a. The effects of early chronic exposure to sublethal copper on the olfactory discrimination of rainbow trout, *Oncorhynchus mykiss*. Environmental Biology of Fishes 30:345-351.

Saucier, D., L. Astic, P. Rioux, and F. Godinot. 1991b. Histopathological changes in the olfactory organ of rainbow trout (*Oncorhynchus mykiss*) induced by early chronic exposure to a sublethal copper concentration. Canadian Journal of Zoology 69:2239-2245.

Saunders, R. L., and J. B. Sprague. 1967. Effects of copper-zinc mining pollution on a spawning migration of Atlantic salmon. Water Research 1:419-432.

Savari, A., A. P. M. Lockwood, and M. Sheader. 1991. Effects of season and size (age) on heavy metal concentrations of the common cockle (*Cerastoderma edule* (L.)) from Southampton water. Journal of Molluscan Studies 57:45-57.

Saward, D., A. Stirling, and G. Topping. 1975. Experimental studies on the effects of copper on a marine food chain. Marine Biology 29:351-361.

Sawicka-Kapusta, K., R. Swiergosz, and M. Zakrzewska. 1990. Bank voles as monitors of environmental contamination by heavy metals. A remote wilderness area in Poland imperilled. Environmental Pollution 67:315-324.

Sayer, M. D. J., J. P. Reader, and R. Morris. 1991. Embryonic and larval development of brown trout, *Salmo trutta* L.: exposure to trace metal mixtures in soft water. Journal of Fish Biology 38:773-787.

Scanes, P. 1993. Trace metal uptake in cockles *Anadara trapezium* from Lake Macquarie, New South Wales. Marine Ecology Progress Series 102:135-142.

Schafer, H., H. Hettler, U. Fritsche, G. Pitzen, G. Roderer, and A. Wenzel. 1994. Biotests using unicellular algae and ciliates for predicting long-term effects of toxicants. Ecotoxicology and Environmental Safety 27:64-81.

Schmitt, C. J., and W. G. Brumbaugh. 1990. National Contaminant Biomonitoring Program. Concentrations of arsenic, cadmium, copper, lead, mercury, selenium, and zinc in U.S. freshwater fish, 1976-1984. Archives of Environmental Contamination and Toxicology 19:731-747.

Schreck, C. B., and H. W. Lorz. 1978. Stress response of coho salmon (*Oncorhynchus kisutch*) elicited by cadmium and copper and potential use of cortisol as an indicator of stress. Journal of the Fisheries Research Board of Canada 35:1124-1129.

Schroeder, H. A., A. P. Nason, I. H. Tipton, and J. J. Balassa. 1966. Essential trace metals in man: copper. Journal of Chronic Diseases 19:1007-1034.

Schubauer-Berigan, M. K., J. R. Dierkes, P. H. Monson, and G. T. Ankley. 1993. pH-dependent toxicity of Cd, Cu, Ni, Pb, and Zn to *Ceriodaphnia dubia*, *Pimephales promelas*, *Hyalella azteca* and *Lumbricus variegatus*. Environmental Toxicology and Chemistry 12:1261-1266.

Schuschke, D. A., J. T. Saari, C. A. West, and F. N. Miller. 1994. Dietary copper deficiency increases the mast cell population of the rat. Proceedings of the Society for Experimental Biology and Medicine 207:274-277.

Scott-Fordsmand, J. J., and M. H. Depledge. 1993. The influence of starvation and copper exposure on the composition of the dorsal carapace and distribution of trace metals in the shore crab *Carcinus maenas* (L.). Comparative Biochemistry and Physiology 106C:537-543.

Shaw, T. L., and V. M. Brown. 1974. The toxicity of some forms of copper to rainbow trout. Water Research 8:377-382.

Sindayigaya, E., R. V. Cauwenbergh, H. Robberecht, and H. Deelstra. 1994. Copper, zinc, manganese, iron, lead, cadmium, mercury and arsenic in fish from Lake Tanganyika, Burundi. Science of the Total Environment 144:103-115.

Singh, H. S., and T. V. Reddy. 1990. Effect of copper sulfate on hematology, blood chemistry, and hepato-somatic index of an Indian catfish, *Heteropneustes fossilis* (Bloch), and its recovery. Ecotoxicology and Environmental Safety 20:30-35.

Snarski, V. M. 1992. The response of rainbow trout *Salmo gairdneri* to *Aeromonas hydrophila* after sublethal exposures to PCB and copper. Environmental Pollution 28A:219-232.

Soria-Dengg, S., and D. Ochavillo. 1990. Comparative toxicities of trace metals on embryos of the giant clam, *Tridacna derasa*. Asian Marine Biology 7:161-166.

Sparling, D. W., and T. P. Lowe. 1996. Metal concentrations of tadpoles in experimental ponds. Environmental Pollution 91:149-159.

Sprague, J. B., P. F. Elson, and R. L. Saunders. 1965. Sublethal copper-zinc pollution in a salmon river—a field and laboratory study. International Journal of Air and Water Pollution 9:531-543.

Spurgeon, D. J., S. P. Hopkin, and D. T. Jones. 1994. Effects of cadmium, copper, lead and zinc on growth, reproduction and survival of the earthworm *Eisenia fetida* (Savigny): assessing the environmental impact of point-source metal contamination in terrestrial ecosystems. Environmental Pollution 84:123-130.

Srivastava, D. K. 1982. Comparative effects of copper, cadmium and mercury on tissue glycogen of the catfish, *Heteropneustes fossilis* (Bloch). Toxicology Letters 11:134-139.

Srivastava, D. K., and K. C. Pandey. 1982. Effect of copper on tissue acid and alkaline phosphatases in the green snakehead, *Ophiocephalus punctatus* (Bloch). Toxicology Letters 11:237-241.

Stacey, N. H., and C. D. Klaassen. 1981. Copper toxicity in isolated rat hepatocytes. Toxicology and Applied Pharmacology 58:211-220.

Stagg, R. M., and T. J. Shuttleworth. 1982. The accumulation of copper in *Platichthys flesus* L. and its effects on plasma electrolyte concentrations. Journal of Fish Biology 20:491-500.

Steele, C. W., D. W. Owens, and A. D. Scarfe. 1990. Attraction of zebrafish, *Brachydanio rerio*, to alanine and its suppression by copper. Journal of Fish Biology 36:341-352.

Stevens, D. G. 1977. Survival and immune response of coho salmon exposed to copper. U.S. Environmental Protection Agency Report 600/3-77-031. 44 pp.

Stevenson, M. H., and N. Jackson. 1978. The accumulation of copper in the liver of the domestic laying hen. Proceedings of the Nutrition Society 38:29A.

Stewart, F. M., D. R. Thompson, R. W. Furness, and N. Harrison. 1994. Seasonal variation in heavy metal levels in tissues of common guillemots, *Uria aalge* from northwest Scotland. Archives of Environmental Contamination and Toxicology 27:168-175.

Stokes, P. M. 1979. Copper accumulations in freshwater biota. Pages 357-381 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Storm, G. L., G. J. Fosmire, and E. D. Bellis. 1994. Persistence of metals in soil and selected vertebrates in the vicinity of the Palmerton zinc smelters. Journal of Environmental Quality 23:508-514.

Stowe, H. D. 1980. Effects of copper pretreatment upon the toxicity of selenium in ponies. American Journal of Veterinary Research 41:1925-1928.

Straus, D. L., and C. S. Tucker. 1993. Acute toxicity of copper sulfate and chelated copper to channel catfish *Ictalurus punctatus*. Journal of the World Aquaculture Society 24:390-395.

Stromgren, T., and M. V. Nielsen. 1991. Spawning frequency, growth and mortality of *Mytilus edulis* larvae, exposed to copper and diesel oil. Aquatic Toxicology 21:171-180.

Sugawara, N., D. Li, M. Katakura, and C. Sugawara. 1994. Biliary excretion of copper in Fischer rats treated with copper salt and in Long-Evans Cinnamon (LEC) rats with an inherently abnormal copper metabolism. Biological Trace Element Research 46:125-134.

Sugawara, N., and C. Sugawara. 1994. A copper deficient diet prevents copper accumulation and dysfunction in Long-Evans Cinnamon (LEC) rats with an abnormal copper metabolism and hereditary hepatitis. Archives of Toxicology 69:137-140.

Sugiura, K., M. Goto, and Y. Kurihara. 1982. Effect of Cu^{2+} stress on an aquatic microcosm: a holistic study. Environmental Research 27:307-315.

Sumi, Y., H. R. Fukuoka, T. Murakami, T. Suzuki, S. Hatakeyama, and K.T. Suzuki. 1991. Histochemical localization of copper, iron and zinc in the larvae of the mayfly *Baetis thermicus* inhabiting a river polluted with heavy metals. Zoological Science (Japan) 8:287-293.

Sunda, W. G., P. A. Tester, and S. A. Huntsman. 1990. Toxicity of trace metals to *Acartia tonsa* in the Elizabeth River and southern Chesapeake Bay. Estuarine, Coastal and Shelf Science 30:207-221.

Supplee, W. C. 1964. Observations on the effect of copper additions to purified turkey diets. Poultry Science 43:1599-1600.

Suresh, K., and A. Mohandas. 1993. Haemolymph protein levels in copper-stressed bivalves. Science of the Total Environment, Supplement 1993, Part 1: 631-639.

Suresh, P. G., M. K. Reju, and A. Mohandas. 1993. Haemolymph phosphatase activity levels in two fresh-water gastropods exposed to copper. Science of the Total Environment, Supplement 1993, Part 2:1265-1277.

Suzuki, K. T., H. Sunaga, S. Hatakeyama, Y. Sumi, and T. Suzuki. 1989. Differential binding of cadmium and copper to the same protein in a heavy metal tolerant species of mayfly (*Baetis thermicus*) larvae. Comparative Biochemistry and Physiology 94C:99-103.

Swaileh, K. M., and D. Adelung. 1994. Levels of trace metals and effect of body size on metal content and concentration in *Arctica islandica* L. (Mollusca: Bivalvia) from Kiel Bay, western Baltic. Marine Pollution Bulletin 28:500-505.

Swiergosz, R., K. Perzanowski, U. Makosz, and L. Bilek. 1993. The incidence of heavy metals and other toxic elements in big game tissues. Science of the Total Environment, Supplement 1993, Part 1:225-231.

Szefer, P., J. Pempkowiak, B. Skwarzec, R. Bojanowski, and E. Holm. 1993. Concentration of selected metals in penguins and other representative fauna of the Antarctica. Science of the Total Environment 138:281-288.

Szefer, P., K. Szefer, J. Pempkowiak, B. Skwarzec, and R. Bojanowski. 1994. Distribution and coassociations of selected metals in seals of the Antarctic. Environmental Pollution 83:341-349.

Talbot, V., S. Creagh, and R. Schulz. 1985. The derivation of threshold mean concentrations of copper and zinc in seawater, to protect the edible tropical rock oyster, *Saccostrea cucullata*, from exceeding the health (food) standards. Department of Conservation and Environment Perth, Western Australia, Bulletin 12. 25 pp.

Taylor, E. J., E. M. Rees, and D. Pascoe. 1994. Mortality and drift-related response of the freshwater amphipod *Gammarus pulex* (L.) exposed to natural sediments, acidification and copper. Aquatic Toxicology 29:83-101.

Thompson, R. H., and J. R. Todd. 1974. Muscle damage in chronic copper poisoning of sheep. Research in Veterinary Science 16:97-99.

Thornton, I. 1979. Copper in soils and sediment. Pages 171-216 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Todd, J. R. 1969. Chronic copper toxicity of ruminants. Proceedings of the Nutrition Society 28:189-198.

Toussaint, M. J. M., and H. Nederbragt. 1993. Copper and zinc toxicity in two rat hepatoma cell lines varying in differentiation. Comparative Biochemistry and Physiology 104C:253-262.

Truchot, J. P., and F. Boitel. 1992. In vitro and in vivo effects of copper on hemocyanin-O_2 binding in the shore crab, *Carcinus maenas*. Comparative Biochemistry and Physiology 103C:339-343.

Tsai, C. F. 1979. Survival, overturning and lethal exposure times for the pearl dace, *Semotilus margaritus* (Cope), exposed to copper solution. Comparative Biochemistry and Physiology 64C:1-6.

Turgeon, D. D., and T. P. O'Connor. 1991. Long Island Sound: distributions, trends, and effects of chemical contamination. Estuaries 14:279-289.

U.S. Environmental Protection Agency (USEPA). 1980. Ambient water quality criteria for copper. U.S. Environmental Protection Agency Report 440/5-80-036. 162 pp.

van der Merwe, M., J. H. J. van Vuren, and H. H. du Preez. 1993. Lethal copper concentration levels for *Clarias gariepinus* (Burchell 1822)—a preliminary study. Koedoe 36:77-86.

van der Watt, H. V. H., M. E. Summer, and M. L. Cabrera. 1994. Bioavailability of copper, manganese, and zinc in poultry litter. Journal of Environmental Quality 23:43-49.

van Eeden, P. H., and H. J. Schoonbee. 1993. Metal concentrations in sediments and some organisms from a polluted wetland. South African Journal of Wildlife Research 23:12-16.

van Gestel, C. A. M., W. A. van Dis, E. M. van Breeman, and P. M. Sparenburg. 1989. Development of a standardized reproduction toxicity test with the earthworm species *Eisenia fetida andrei* using copper, pentachlorophenol, and 2, 4-dichloroaniline. Ecotoxicology and Environmental Safety 18:305-312.

van Gestel, C. A. M., W. A. van Dis, E. M. Dirven-van Breeman, P. M. Sparenburg, and R. Baerselman. 1991. Influence of cadmium, copper, and pentachlorophenol on growth and sexual development of *Eisenia andrei* (Oligochaeta:Annelida). Biology and Fertility of Soils 12:117-121.

Varanasi, U., J. E. Stein, K. L. Tilbury, J. P. Mador, C. A. Sloan, R. C. Clark, and S. L. Chan. 1994. Chemical contaminants in gray whales (*Eschrichtius robustus*) stranded along the west coast of North America. Science of the Total Environment 145:29-53.

Vas, P. 1991. Trace metal levels in sharks from British and Atlantic waters. Marine Pollution Bulletin 22:67-72.

Veleminsky, M., P. Laznicka, and P. Stary. 1990. Honeybees (*Apis mellifera*) as environmental monitors of heavy metals in Czechoslovakia. Acta Entomologica Bohemoslovaca 87:37-44.

Vermeer, K., and J. C. Castilla. 1991. High cadmium residues observed during a pilot study in shorebirds and their prey downstream from the El Salvador copper mine, Chile. Bulletin of Environmental Contamination and Toxicology 46:242-248.

Viarengo, A., L. Canesi, A. Mazzucotelli, and E. Ponzano. 1993. Cu, Zn and Cd content in different tissues of the Antarctic scallop *Adamussium colbecki*: role of metallothionein in heavy metal homeostasis and detoxication. Marine Ecology Progress Series 95:163-168.

Viarengo, A., L. Canesi, M. Pertica, G. Poli, M.N. Moore, and M. Orunesu. 1990. Heavy metal effects on lipid peroxidation in the tissues of *Mytilus galloprovincialis* Lam. Comparative Biochemistry and Physiology 97C:37-42.

Viarengo, A., M. Pertica, G. Mancinelli, S. Palermo, G. Zanicchi, and M. Orunesu. 1981. Synthesis of Cu-binding proteins in different tissues of mussels exposed to the metal. Marine Pollution Bulletin 12:347-350.

Vijayaraman, K., and P. Geraldine. 1992. Toxicity of cadmium, copper, chromium and zinc to *Macrobrachium rude*. Geobios 19:77-80.

Visviki, L., and J. W. Rachlin. 1994a. Acute and chronic exposure of *Dunaliella salina* and *Chlamydomonas bullosa* to copper and cadmium: effects on growth. Archives of Environmental Contamination and Toxicology 26:149-153.

Visviki, I., and J. W. Rachlin. 1994b. Acute and chronic exposure of *Dunaliella salina* and *Chlamydomonas bullosa* to copper and cadmium: effects on ultrastructure. Archives of Environmental Contamination and Toxicology 26:154-162.

Waibel, P. E., D. C. Snetsinger, R. A. Ball, and J. H. Sautter. 1964. Variation in tolerance of turkeys to dietary copper. Poultry Science 43:504-506.

Ward, N. I., and J. M. Savage. 1994. Elemental status of grazing animals located adjacent to the London Orbital (M25) motorway. Science of the Total Environment 146/147:185-189.

Ward, R. E. 1990. Metal concentrations and digestive gland lysosomal stability in mussels from Halifax inlet, Canada. Marine Pollution Bulletin 21:237-240.

Weber, R. E., A. de Zwaan, and A. Bang. 1992. Interactive effects of ambient copper and anoxic, temperature and salinity stress on survival and hemolymph and muscle tissue osmotic effectors in *Mytilus edulis*. Journal of Experimental Marine Biology and Ecology 159:135-156.

Weeks, J. M. 1992. Copper-rich granules in the ventral caeca of talitrid amphipods (crustacea: amphipoda: talitridae). Ophelia 36:119-133.

Weeks, J. M., and P. S. Rainbow. 1991. The uptake and accumulation of zinc and copper from solution by two species of talitrid amphipods (Crustacea). Journal of the Marine Biological Association of the United Kingdom 71:811-826.

Weeks, J. M., and P. S. Rainbow. 1993. The relative importance of food and seawater as sources of copper and zinc to talitrid amphipods (crustacea; amphipoda; talitridae). Journal of Applied Ecology 30:722-735.

Weimin, Y., G. E. Batley, and M. Ahsanullah. 1994. Metal bioavailability to the soldier crab *Mictyris longicarpus*. Science of the Total Environment 141:27-44.

Weis, J. S., and P. Weis. 1992. Transfer of contaminants from CCA-treated lumber to aquatic biota. Journal of Experimental Marine Biology and Ecology 161:189-199.

Weis, J. S., and P. Weis. 1993. Trophic transfer of contaminants from organisms living by chromated-copper-arsenate (CCA)-treated wood to their predators. Journal of Experimental Marine Biology and Ecology 168:25-34.

Weis, J. S., and P. Weis. 1994. Effects of contaminants from chromated copper arsenate-treated lumber on benthos. Archives of Environmental Contamination and Toxicology 26:103-109.

Weis, P., J. S. Weis, and J. Couch. 1993a. Histopathology and bioaccumulation in oysters *Crassostrea virginica* living on wood preserved with chromated copper arsenate. Diseases of Aquatic Organisms 17:41-46.

Weis, P., J. S. Weis, and E. Lores. 1993b. Uptake of metals from chromated-copper-arsenate (CCA)-treated lumber by epibiota. Marine Pollution Bulletin 26:428-430.

Welsh, P. G., J. F. Skidmore, D. J. Spry, D. G. Dixon, P. V. Hodson, N. J. Hutchinson, and B. E. Hickie. 1993. Effect of pH and dissolved organic carbon on the toxicity of copper to larval fathead minnow (*Pimephales promelas*) in natural lake waters of low alkalinity. Canadian Journal of Fisheries and Aquatic Sciences 50:1356-1362.

West, C. W., V. R. Mattson, E. N. Leonard, G. L. Phipps, and G. T. Ankley. 1993. Comparison of the relative sensitivity of three benthic invertebrates to copper-contaminated sediments from the Keweenaw waterway. Hydrobiologia 262:57-63.

Wieser, W. 1979. The flow of copper through a terrestrial food web. Pages 325-355 *in* J. O. Nriagu, editor. Copper in the environment. Part 1: ecological cycling. John Wiley, New York.

Williams, P. L., and D. B. Dusenbery. 1990. Aquatic toxicity testing using the nematode, *Caenorhabditis elegans*. Environmental Toxicology and Chemistry 9:1285-1290.

Wilson, R. W., and E. W. Taylor. 1993. Differential responses to copper in rainbow trout (*Oncorhynchus mykiss*) acclimated to sea water and brackish water. Journal of Comparative Physiology 163B:239-246.

Winberg, S., R. Bjerselius, E. Baatrup, and K. J. Doving. 1992. The effect of Cu(II) on the electro-olfactogram (EOG) of the Atlantic salmon (*Salmo salar* L.) in artificial freshwater of varying inorganic carbon concentrations. Ecotoxicology and Environmental Safety 24:167-178.

Winger, P. V., M. J. Imlay, W. E. McMillan, T. W. Martin, J. Takekawa, and W. W. Johnson. 1984. Field and laboratory evaluation of the influence of copper-diquat on apple snails in southern Florida. Environmental Toxicology and Chemistry 3:409-424.

Winner, R. W., and M. P. Farrell. 1976. Acute and chronic toxicity of copper to four species of *Daphnia*. Journal of the Fisheries Research Board of Canada 33:1685-1691.

Winner, R. W., and H. A. Owen. 1991. Toxicity of copper to *Chlamydomonas reinhardtii* (Chlorophyceae) and *Ceriodaphnia dubia* (Crustacea) in relation to changes in water chemistry of a freshwater pond. Aquatic Toxicology 21:157-170.

Winner, R. W., H. A. Owen, and M. V. Moore. 1990. Seasonal variability on the sensitivity of freshwater lentic communities to a chronic copper stress. Aquatic Toxicology 17:75-92.

Wolkers, H., T. Wensing, and G. W. T. A. G. Bruinderink. 1994. Heavy metal contamination in organs of red deer (*Cervus elaphus*) and wild boar (*Sus scrofa*) and the effect on some trace elements. Science of the Total Environment 144:191-199.

Wong, C. K., K. H. Chu, K. W. Tang, T. W. Tam, and L. J. Wong. 1993. Effects of chromium, copper and nickel on survival and feeding behavior of *Metapenaeus ensis* larvae and postlarvae (Decapoda:Penaeidae). Marine Environmental Research 36:63-78.

Wood, E. C., and A. N. Worden. 1973. The influence of dietary copper concentration on hepatic copper in the duckling and the chick. Journal of the Science of Food and Agriculture 24:167-174.

Woodward, D. F., W. G. Brumbaugh, A. J. Deloney, E. E. Little, and C. E. Smith. 1994. Effects on rainbow trout fry of a metals-contaminated diet of benthic invertebrates from the Clark Fork River, Montana. Transactions of the American Fisheries Society 123:51-62.

Wren, C. D., T. Nygard, and E. Steinnes. 1994. Willow ptarmigan (*Lagopus lagopus*) as a biomonitor of environmental metal levels in Norway. Environmental Pollution 85:291-295.

Yeates, G. W., V. A. Orchard, T. W. Speir, J. L. Hunt, and M. C. C. Hermans. 1994. Impact of pasture contamination by copper, chromium, arsenic timber preservative on soil biological activity. Biology and Fertility of Soils 18:200-208.

Yoshimura, N., K. Kida, S. Usutani, and M. Nishimura. 1995. Histochemical localization of copper in various organs of brindled mice after copper therapy. Pathology International 45:10-18.

Yu, S., R. B. Beems, J. A. Joles, G. A. Kaysen, and A. C. Beynen. 1995. Iron and copper metabolism in analbuminaemic rats fed a high-iron diet. Comparative Biochemistry and Physiology 110A:131-138.

Yu, S., C. E. West, and A. C. Beynen. 1994. Increasing intakes of iron reduce status, absorption and biliary excretion of copper in rats. British Journal of Nutrition 71:887-895.

Zakrzewska, M., K. Sawicka-Kapusta, A. Perdenia, and A. Wosik. 1993. Heavy metals in bank voles from Polish national parks. Science of the Total Environment, Supplement 1993, Part 1:167-172.

Zaroogian, G. E. 1979. Studies on the depuration of cadmium and copper by the American oyster *Crassostrea virginica*. Bulletin of Environmental Contamination and Toxicology 23:117-122.

Zaroogian, G., S. Anderson, and R. A. Voyer. 1992. Individual and combined cytotoxic effects of cadmium, copper, and nickel on brown cells of *Mercenaria mercenaria*. Ecotoxicology and Environmental Safety 24:328-337.

Zia, S., and M. A. Alikhan. 1989. A laboratory study of the copper and nickel uptake and regulation in a copper-tolerant decapod, *Cambarus bartoni* (Fabricus) (Decapoda, Crustaceana). Archives Internationales de Physiologie et de Biochimie 97:211-219.

Zong-Ping, L., M. Zhuo, and Z. You-Jia. 1994. Studies on the relationship between sway disease of bactrian camels and copper status in Gansu province. Veterinary Research Communications 18:251-260.

Zou, E., and S. Bu. 1994. Acute toxicity of copper, cadmium, and zinc to the water flea, *Moina irrasa* (Cladocera). Bulletin of Environmental Contamination and Toxicology 52:742-748.

Biological Science Report USGS/BRD/BSR-1998-0001
April 1998

Contaminant Hazard Reviews
Report No. 34

NICKEL HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Geological Survey
Laurel, MD 20708

TABLE OF CONTENTS

TABLES

NICKEL HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by
Ronald Eisler
Patuxent Wildlife Research Center
U.S. Geological Survey
Laurel, MD 20708-4017

Abstract

Abstract. This account is a selective review and synthesis of the technical literature on nickel and nickel salts in the environment and their effects on terrestrial plants and invertebrates, aquatic plants and animals, avian and mammalian wildlife, and other natural resources. The subtopics include nickel sources and uses; physical, chemical, and metabolic properties of nickel; nickel concentrations in field collections of abiotic materials and living organisms; nickel deficiency effects; lethal and sublethal effects, including effects on survival, growth, reproduction, metabolism, mutagenicity, teratogenicity, and carcinogenicity; currently proposed nickel criteria for the protection of human health and sensitive natural resources; and recommendations for additional research.

Key words: Nickel, nickel compounds, toxicity, deficiency, cancer, residues, criteria, fishes, invertebrates, amphibians, birds, wildlife, livestock.

Introduction

In Europe, nickel (Ni) is listed on European Commission List II (Dangerous Substances Directive) and regulated through the Council of European Communities because of its toxicity, persistence, and affinity for bioaccumulation (Bubb and Lester 1996). In Canada, nickel and its compounds are included in the Priority Substances List under the Canadian Environmental Protection Act (Hughes et al. 1994). The World Health Organization (WHO) classifies nickel compounds in Group 1 (human carcinogens) and metallic nickel in group 2B (possible human carcinogen; U. S. Public Health Service [USPHS] 1993). The U.S. Environmental Protection Agency (USEPA) classifies nickel refinery dust and nickel subsulfide as Group A human carcinogens (USPHS 1993) and nickel oxides and nickel halides as Class W compounds, that is, compounds having moderate retention in the lungs and a clearance rate from the lungs of several weeks (USEPA 1980). Nickel and its compounds are regulated by USEPA's Clean Water Effluent Guideline for many industrial point sources, including the processing of iron, steel, nonferrous metals, and batteries; timber products processing; electroplating; metal finishing; ore and mineral mining; paving and roofing; paint and ink formulating; porcelain enameling; and industries that use, process, or manufacture chemicals, gum and wood, or carbon black (USPHS 1993).

Nickel is ubiquitous in the biosphere. Nickel introduced into the environment from natural or human sources is circulated through the system by chemical and physical processes and through biological transport mechanisms of living organisms (National Academy of Sciences [NAS] 1975; Sevin 1980; WHO 1991). Nickel is essential for the normal growth of many species of microorganisms and plants and several species of vertebrates, including chickens, cows, goats, pigs, rats, and sheep (NAS 1975; USEPA 1980; WHO 1991; USPHS 1993).

Human activities that contribute to nickel loadings in aquatic and terrestrial ecosystems include mining, smelting, refining, alloy processing, scrap metal reprocessing, fossil fuel combustion, and waste incineration (NAS 1975; WHO 1991; Chau and Kulikovsky-Cordeiro 1995). Nickel mining and smelting in the Sudbury, Ontario, region of Canada is associated with denudation of terrestrial vegetation and subsequent soil erosion (Adamo et al. 1996) and gradual ecological changes, including a decrease in the number and diversity of species and a reduction in community biomass of crustacean zooplankton (WHO 1991). At nickel-contaminated sites, plants accumulate nickel and growth is retarded in some species at high nickel concentrations (WHO 1991). But nickel accumulation rates in terrestrial and avian wildlife near nickel refineries are highly variable; Chau and Kulikovsky-Cordeiro (1995) claim similar variability for plants, soils, and interstitial sediment waters.

The chemical and physical forms of nickel and its salts strongly influence bioavailability and toxicity (WHO 1991). In general, nickel compounds have low hazard when administered orally (NAS 1975; USEPA 1980). In humans and other mammals, however, nickel-inhalable dust, nickel subsulfide, nickel oxide, and especially nickel carbonyl induce acute pneumonitis, central nervous system disorders, skin disorders such as dermatitis, and cancer of the lungs and nasal cavity (Graham et al. 1975; NAS 1975; USPHS 1977; Sevin 1980; Smialowicz et al. 1984; WHO 1991; Benson et al. 1995; Table 1). Nickel carbonyl is acutely lethal to humans and animals within 3-13 days of exposure; recovery is prolonged in survivors (Sevin 1980). An excess number of deaths from lung cancer and nasal cancer occurs in nickel refinery workers, usually from exposure to airborne nickel compounds (USPHS 1977). At one nickel refinery, workers had a fivefold increase in lung cancer and a 150-fold increase in nasal sinus cancer when compared to the general population (Lin and Chou 1990). Pregnant female workers at a Russian nickel hydrometallurgy refining plant, when compared to a reference group, showed a marked increase in frequency of spontaneous and threatening abortions and in structural malformations of the heart and musculoskeletal system in live-born infants with nickel-exposed mothers (Chashschin et al. 1994). Nickel is also a common cause of chronic dermatitis in humans as a result of industrial and other exposures, including the use of nickel-containing jewelry, coins, utensils, and various prostheses (NAS 1975; Chashschin et al. 1994). Additional information on ecological and toxicological aspects of nickel in the environment is presented in reviews and annotated bibliographies by Sunderman (1970), Eisler (1973), Eisler and Wapner (1975), NAS (1975), USEPA (1975, 1980, 1985, 1986), International Agency for Research on Cancer (IARC; 1976), Nielsen (1977), USPHS (1977, 1993), Eisler et al. (1978b, 1979), Norseth and Piscator (1979), Brown and Sunderman (1980), Nriagu (1980a), Sevin (1980), National Research Council of Canada (NRCC; 1981), Norseth (1986), Kasprzak (1987), Sigel and Sigel (1988), WHO (1991), Hausinger (1993), Outridge and Scheuhammer (1993), and Chau and Kulikovsky-Cordeiro (1995).

Table 1. Nickel chronology.

Table 1. Date	Event	Reference[a]
220 BCE	Nickel alloys made by the Chinese	1
1500's	Toxicity observed in miners of nickel	2
1751	Nickel isolated and identified. The name nickel was derived from "Old Nick," a gremlin to whom miners ascribed their problems	3
early 1800's	Purified nickel obtained	1
1826	Nickel toxicity in rabbits and dogs demonstrated experimentally. High doses of nickel sulfate given by stomach gavage caused gastritis, convulsions, and death; sublethal doses produced emaciation and conjunctivitis	1, 2, 4
1840's	Commercial nickel electroplating initiated	1
1850's	Commercial exploitation of nickel begins after development of technology to remove copper and other impurities	3
1850-1900	Nickel used therapeutically in human medicine to relieve rheumatism (nickel sulfate) and epilepsy (nickel bromide)	2, 5
1880's	Excess nickel found lethal to animals under controlled conditions	2
1889	Skin dermatitis in humans caused by chemicals used in nickel plating	5
1890	Extraordinary toxicity of nickel carbonyl ($Ni(CO)_4$) established	1
1893	Excess nickel found lethal to plants	2
1912	Nickel dermatitis documented	1
1915-1960	Nickel applied as fungicide found to enhance plant growth and increase yield	2

Table 1. Date	Event	Reference[a]
1926	Nickel dust caused skin dermatitis, especially in hot, industrial environments	5
1932	Increased frequency of lung and nasal cancers reported among English nickel refinery workers exposed to high concentrations of nickel carbonyl	1, 5, 6
1939-1958	Certain forms of nickel found to be carcinogenic to humans	2
1943	Certain forms of nickel found to be carcinogenic to animals	2
1965-1967	Nickel found beneficial to plants	2
1970's	Nickel deficiency leads to adverse effects in microorganisms and plants	2
1980's	Nickel found to be constituent of various essential plant enzymes	2

[a]1, Nriagu 1980b; 2, Hausinger 1993; 3, Sevin 1980; 4, Nielsen 1977; 5, U.S. Public Health Service 1977; 6, Benson et al. 1995.

This report summarizes available ecological and toxicological data on nickel, with emphasis on fishery and wildlife resources. It is part of a continuing series of brief reviews on chemical contaminants and natural resources that are prepared in response to informational requests from environmental specialists of the U.S. Fish and Wildlife Service.

Sources and Uses

General

About 250,000 people in the United States are exposed annually to inorganic nickel in the workplace. This group includes workers in the mining, refining, smelting, electroplating, and petroleum industries and workers involved in the manufacture of stainless steel, nickel alloys, jewelry, paint, spark plugs, catalysts, ceramics, disinfectants, varnish, magnets, batteries, ink, dyes, and vacuum tubes (USPHS 1977). Non-occupational exposure to nickel and its compounds occurs mainly by ingestion of foods and liquids and by contact with nickel-containing products, especially jewelry and coins (Sunderman et al. 1984; WHO 1991). Food processing adds to nickel already present in the diet through leaching from nickel-containing alloys in food-processing equipment made from stainless steel, milling of flour, use of nickel catalysts to hydrogenate fats and oils, and use of nickel-containing fungicides in growing crops (NAS 1975; USEPA 1980). Nickel contamination of the environment occurs locally from emissions of metal mining, smelting, and refining operations; from combustion of fossil fuels; from industrial activities, such as nickel plating and alloy manufacturing; from land disposal of sludges, solids, and slags; and from disposal as effluents (Cain and Pafford 1981; Chau and Kulikovsky-Cordeiro 1995). In Canada in 1988, the mining industry released a total of 11,664 tons of nickel into the air (9.4%), water (0.5%), and on land as sludges or solids (15.4%) and slags (74.7%). The global nickel cycle is unknown, but recent estimates suggest that 26,300 to 28,100 tons are introduced each year into the atmosphere from natural sources and 47,200 to 99,800 tons from human activities; airborne nickel is annually deposited on land at 50,800 tons and in the ocean at 21,800 tons (Chau and Kulikovsky-Cordeiro 1995).

Sources

More than 90% of the world's nickel is obtained from pentlandite ($(FeNi)_9S_8$), a nickel-sulfitic mineral mined underground in Canada and the former Soviet Union (Sevin 1980; IARC 1976; WHO 1991). One of the largest sulfitic nickel deposits is in Sudbury, Ontario (USPHS 1993). Nickeliferous sulfide deposits are also found in Manitoba, South Africa, the former Soviet Union, Finland, western Australia, and Minnesota (Norseth and Piscator 1979; USPHS 1993). Most of the rest of the nickel obtained is from nickel minerals such as laterite, a nickel oxide ore mined by open pit techniques in Australia, Cuba, Indonesia, New Caledonia, and the former Soviet Union (Sevin 1980). Lateritic ores are less well defined than sulfitic ores, although the nickel content (1-3%) of both ores is similar (USPHS 1993). Important deposits of laterite are located in New Caledonia, Indonesia, Guatemala, the Dominican Republic, the Philippines, Brazil, and especially Cuba, which holds 35%

of the known reserves (USPHS 1993). Nickel-rich nodules are found on the ocean floor, and nickel is also present in fossil fuels (Sevin 1980).

Total world mine production of nickel is projected to increase steadily from 7,500 metric tons in 1900 to 2 million tons by 2000 (Table 2). In 1980, nickel mine production in the United States was 14,500 tons, or about 1.8% of the world total (Kasprzak 1987). In 1986, primary nickel production ceased in the United States; secondary nickel production from scrap became a major source of nickel for industrial applications (USPHS 1993). In 1988, the United States imported 186,000 tons of primary nickel; Canada supplied 58% of the total and Norway 14% (USPHS 1993). In 1990, Canada produced 196,606 metric tons of nickel. About 63% of the total production was exported, mostly (56%) to the United States (Chau and Kulikovsky-Cordeiro 1995).

Table 2. World mine production of nickel (National Academy of Sciences 1975; International Agency for Research on Cancer 1976; Duke 1980; Kasprzak 1987; World Health Organization 1991).

Year	Metric tons
1900	7,500
1925	42,700
1950	141,000
1970	694,100
1975	753,000[a]
1980	784,100
1985	821,000[b]
2000 (projected)	>2,000,000

[a]About 32% from Canada, 18% from New Caledonia, 17% from the former Soviet Union, 10% from Australia, 5% from Cuba, 4% from the Dominican Republic, 3% from the Republic of South Africa, 2% each from Greece, Indonesia, and the United States, and 5% from other countries.

[b]Mostly from Canada, the former Soviet Union, Australia, and Cuba, in that order. The United States produced 6,900 tons in 1985.

Natural sources of airborne nickel include soil dust, sea salt, volcanoes, forest fires, and vegetation exudates and account for about 16% of the atmospheric nickel burden (Kasprzak 1987; WHO 1991; Chau and Kulikovsky-Cordeiro 1995). Human sources of atmospheric nickel—which account for about 84% of all atmospheric nickel—include emissions from nickel ore mining, smelting, and refining activities; combustion of fossil fuels for heating, power, and motor vehicles; incineration of sewage sludges; nickel chemical manufacturing; electroplating; nickel-cadmium battery manufacturing; asbestos mining and milling; and cement manufacturing (NAS 1975; IARC 1976; USEPA 1986; Kasprzak 1987; WHO 1991; USPHS 1993). In Canada in 1975, human activities resulted in the release of about 3,000 tons of nickel into the atmosphere, mostly from metallurgical operations (NRCC 1981). Between 1973 and 1981, atmospheric emissions of nickel from stacks of four smelters in the Sudbury Basin, Canada, averaged a total of 495 tons annually (WHO 1991). Industrial nickel dust emissions from a single Canadian stack 381 meters high averaged 228 tons annually (range 53-342) between 1973 and 1981; this stack accounted for 396 tons annually (range 53-896) between 1982 and 1989 (Chau and Kulikovsky-Cordeiro 1995). Three other emission stacks of Canadian nickel producers emitted an average of 226, 228, and 396 tons of nickel, respectively, each year between 1973 and 1989. Industrial emissions of nickel to the Canadian atmosphere in 1982 were estimated at 846 tons, mostly from nickel production in Ontario (48% of total) and Quebec (14%) and from industrial fuel combustion (17%). Nickel released into the air in Canada from smelting processes is likely in the form of nickel subsulfide (52%), nickel sulfate (20%), and nickel oxide (6%). Fuel combustion is also a major contributor of airborne nickel in Canada, mostly from combustion of petroleum (Chau and Kulikovsky-Cordeiro 1995). In the United States, yearly atmospheric emissions from coal and oil combustion are estimated at 2,611 metric tons (WHO 1991).

Chemical and physical degradation of rocks and soils, atmospheric deposition of nickel-containing particulates, and discharges of industrial and municipal wastes release nickel into ambient waters (USEPA 1986; WHO 1991). Nickel enters natural waterways from waste water because it is poorly removed by treatment processes (Cain and Pafford 1981). The main anthropogenic sources of nickel in water are primary nickel production, metallurgical processes, combustion and incineration of fossil fuels, and chemical and catalyst

production (USEPA 1986). The primary human sources of nickel to soils are emissions from smelting and refining operations and disposal of sewage sludge or application of sludge as a fertilizer. Secondary sources include automobile emissions and emissions from electric power utilities (USEPA 1986). Weathering and erosion of geological materials release nickel into soils (Chau and Kulikovsky-Cordeiro 1995), and acid rain may leach nickel from plants into soils as well (WHO 1991).

Uses

Most metallic nickel produced is used to manufacture stainless steel and other nickel alloys with high corrosion and temperature resistance (Norseth and Piscator 1979; Norseth 1980; WHO 1991). These alloys are used in ship building, jet turbines and heat elements, cryogenic installations, magnets, coins, welding rods, electrodes, kitchenware, electronics, and surgical implants; other nickel compounds are used in electroplating, battery production, inks, varnishes, pigments, catalysts, and ceramics (IARC 1976; Nriagu 1980b; Sevin 1980; Sunderman et al. 1984; USEPA 1986; Kasprzak 1987; USPHS 1993). Some nickel compounds are preferred for use in nickel electroplating (nickel sulfate, nickel ammonium sulfate, nickel chloride, nickel fluoborate, nickel sulfamate), refining (nickel carbonyl), nickel-cadmium batteries (nickel hydroxide, nickel fluoride, nickel nitrate), manufacture of stainless steel and alloy steels (nickel oxide), electronic components (nickel carbonate), mordant in textile industry (nickel acetate), catalysts and laboratory reagents (nickel acetate, nickel hydroxide, nickel nitrate, nickel carbonate, nickel monosulfide, nickelocene), and some—such as nickel subsulfide—are unwanted toxic byproducts (IARC 1976).

In 1973, global consumption of nickel was 660,000 tons and that of the United States 235,000 tons (Sevin 1980). End uses of nickel in the United States in 1973 were transportation (21%), chemicals (15%), electrical goods (13%), fabricated metal products (10%), petroleum (9%), construction (9%), machinery (7%), and household appliances (7%; IARC 1976); a similar pattern was evident for 1985 (Table 3). In 1988, 40% of all nickel intermediate products consumed was in the production of steel; 21% was in alloys, 17% in electroplating, and 12% in super alloys (USPHS 1993). The pattern for 1985 was similar (Table 3). In Canada, nickel is the fourth most important mineral commodity behind copper, zinc, and gold. In 1990, Canada produced 197,000 tons of nickel worth 2.02 billion dollars and was the second largest global producer of that metal (Chau and Kulikovsky-Cordeiro 1995). Most of the nickel used in the United States is imported from Canada, and secondarily from Australia and New Caledonia (USPHS 1977).

Table 3. Nickel consumption in the United States by intermediate product and end-use industry in 1985[a] (Kasprzak 1987; World Health Organization 1991).

Index	Consumption (% of total)
Intermediate product	
Stainless and alloy steels	42
Nonferrous alloys	36
Electroplating	18
Other	4
Total	100
End-use industry	
Transportation	23
Chemicals	15
Electrical equipment	12
Construction	10
Fabricated metal products	9
Petroleum	8
Household appliances	8
Machinery	8
Other	7
Total	100

[a] Nickel consumption in the United States, exclusive of scrap, was 160,000 tons.

Various nickel salts—including the sulfate, chloride, and bromide—were used in human medicine during the mid- to late-1800's to treat headache, diarrhea, and epilepsy and as an antiseptic. Therapeutic use of nickel compounds was abandoned in the early 1900's after animal studies demonstrated acute and chronic toxicity of these salts (NAS 1975; Nriagu 1980b). Some nickel salts have been incorporated into fungicides to combat plant pathogens, although their use has not been approved by regulatory agencies (NAS 1975).

Chemical and Biological Properties

General

Nickel normally occurs in the 0 and +2 oxidation states, although other oxidation states are reported (NAS 1975; Nriagu 1980b; Higgins 1995). In natural waters Ni^{2+} is the dominant chemical species in the form of $(Ni(H_2O)_6)^{2+}$ (WHO 1991; Chau and Kulikovsky-Cordeiro 1995). In alkaline soils, the major components of the soil solution are Ni^{2+} and $Ni(OH)^{+}$; in acidic soils, the main solution species are Ni^{2+}, $NiSO_4$, and $NiHPO_4$ (USPHS 1993). Most atmospheric nickel is suspended onto particulate matter (NRCC 1981).

Nickel interacts with numerous inorganic and organic compounds (Schroeder et al. 1974; Nielsen 1980a; USEPA 1980, 1985; USPHS 1993). Some of these interactions are additive or synergistic in producing adverse effects, and some are antagonistic.

Toxic and carcinogenic effects of nickel compounds are associated with nickel-mediated oxidative damage to DNA and proteins and to inhibition of cellular antioxidant defenses (Rodriguez et al. 1996). Most authorities agree that albumin is the main transport protein for nickel in humans and animals and that nickel is also found in nickeloplasmin—a nickel-containing alpha-macroglobulin—and in an ultrafilterable serum fraction similar to a nickel-histidine complex (Norseth and Piscator 1979; Sarkar 1980; Sevin 1980; USEPA 1980; Norseth 1986; Sigel and Sigel 1988; WHO 1991; USPHS 1993). Normal routes of nickel intake for humans and animals are ingestion, inhalation, and absorption through the skin (Mushak 1980; USEPA 1975, 1980, 1986; Sigel and Sigel 1988; WHO 1991; USPHS 1993). Nickel absorption is governed by the quantities inhaled or ingested and by the chemical and physical forms of the nickel. Following oral intake by mammals, nickel was found mainly in the kidneys after short-term or long-term exposure to various soluble nickel compounds; significant levels of nickel were also found in the liver, heart, lung, and fat. Nickel also crosses the placental barrier, as indicated by increases in the levels of nickel in the fetuses of exposed mothers (USPHS 1993). Inhaled nickel carbonyl results in comparatively elevated nickel concentrations in lung, brain, kidney, liver, and adrenals (USEPA 1980). Parenteral administration of nickel salts usually results in high levels in kidneys and elevated concentrations in endocrine glands, liver, and lung (USEPA 1980, 1986; WHO 1991). Nickel concentrations in whole blood, plasma, serum, and urine provide good indices of nickel exposure (Sigel and Sigel 1988).

Physical and Chemical Properties

Nickel was first isolated in 1751, and a relatively pure metal was prepared in 1804. In nature, nickel is found primarily as oxide and sulfide ores (USPHS 1977). Nickel has high electrical and thermal conductivities and is resistant to corrosion at environmental temperatures between -20 C and +30 C (Chau and Kulikovsky-Cordeiro 1995). Nickel, also known as carbonyl nickel powder or C.I. No. 77775, has a CAS number of 7440-02-0. Metallic nickel is a hard, lustrous, silvery white metal with a specific gravity of 8.9, a melting point of about 1,455 C, and a boiling point of about 2,732 C. It is insoluble in water and ammonium hydroxide, soluble in dilute nitric acid or aqua regia, and slightly soluble in hydrochloric and sulfuric acid. Nickel has an atomic weight of 58.71. Nickel is a composite of five stable isotopes: Ni-58 (68.3%), -60 (26.1%), -61 (1.1%), -62 (3.6%), and -64 (0.9%). Seven unstable isotopes have been identified: ^{56}Ni (half-life of 6 days), ^{57}Ni (36 h), ^{59}Ni (80,000 years), ^{63}Ni (92 years), ^{65}Ni (2.5 h), ^{66}Ni (55 h), and ^{67}Ni (50 sec). Radionickel-59 (^{59}Ni) and ^{63}Ni are available commercially. In addition to the 0 and +2 oxidation states, nickel can also exist as -1, +1, +3, and +4 (NAS 1975; IARC 1976; Kasprzak 1987; Nriagu 1980b; WHO 1991; Hausinger 1993; USPHS 1993; Foulds 1995; Higgins 1995).

Nickel enters surface waters from three natural sources: as particulate matter in rainwater, through the dissolution of primary bedrock materials, and from secondary soil phases. In aquatic systems, nickel occurs as soluble salts adsorbed onto or associated with clay particles, organic matter, and other substances. The divalent ion is the dominant form in natural waters at pH values between 5 and 9, occurring as the octahedral,

hexahydrate ion $(Ni(H_2O)_6)^{2+}$. Nickel chloride hexahydrate and nickel sulfate hexahydrate are extremely soluble in water at 2,400-2,500 g/L. Less soluble nickel compounds in water include nickel nitrate (45 g/L), nickel hydroxide (0.13 g/L), and nickel carbonate (0.09 g/L). Nickel forms strong, soluble complexes with OH-, SO_4^{2-}, and HCO_3^-; however, these species are minor compared with hydrated Ni^{2+} in surface water and groundwater. The fate of nickel in fresh water and marine water is affected by the pH, pE, ionic strength, type and concentration of ligands, and the availability of solid surfaces for adsorption. Under anaerobic conditions, typical of deep groundwater, precipitation of nickel sulfide keeps nickel concentrations low (IARC 1976; USEPA 1980; WHO 1991; USPHS 1993; Chau and Kulikovsky-Cordeiro 1995).

In alkaline soils, the major components of the soil solution are Ni^{2+} and $Ni(OH)^+$; in acidic soils the main solution species are Ni^{2+}, $NiSO_4$, and $NiHPO_4$ (USPHS 1993). Atmospheric nickel exists mostly in the form of fine respirable particles less than 2 μm in diameter (NRCC 1981), usually suspended onto particulate matter (USEPA 1986).

Nickel carbonyl ($Ni(CO)_4$) is a volatile, colorless liquid readily formed when nickel reacts with carbon monoxide; it boils at 43 C and decomposes at more than 50 C; this compound is unstable in air and is usually not measurable after 30 min (NRCC 1981; Norseth 1986; USPHS 1993). The intact molecule is absorbed by the lung (USEPA 1980) and is insoluble in water but soluble in most organic solvents (WHO 1991).

Analytical methods for detection of nickel in biological materials and water include various spectrometric, photometric, chromatographic, polarographic, and voltametric procedures (Sunderman et al. 1984; WHO 1991). Detection limits for the most sensitive procedures—depending on sample pretreatment and extraction and enrichment procedures—were 0.7-1.0 ng/L in liquids, 0.01-0.2 $\mu g/m^3$ in air, 1-100 ng/kg in most biological materials, and 12 μg/kg in hair (WHO 1991; Chau and Kulikovsky-Cordeiro 1995).

Metabolism

In mammalian blood, absorbed nickel is present as free hydrated Ni^{2+} ions, as small complexes, as protein complexes, and as nickel bound to blood cells. The partition of nickel among these four components varies according to the metal-binding properties of serum albumin, which is highly variable between species (NAS 1975; USEPA 1980, 1986; Kasprzak 1987). A proposed transport model involves the removal of nickel from albumin to histidine via a ternary complex composed of albumin, nickel, and L-histidine. The low molecular weight L-histidine nickel complex can then cross biological membranes (Sunderman et al. 1984; Kasprzak 1987; USPHS 1993). Once inside the mammalian cell, nickel accumulates in the nucleus and nucleolus (Sunderman et al. 1984), disrupting DNA metabolism and causing cross links and strand breaks (Kasprzak 1987; USPHS 1993; Hartwig et al. 1994). The observed redox properties of the nickel-histidine complex are crucial for maximizing the toxicity and carcinogenicity of nickel (Datta et al. 1992, 1994).

The acute toxicity and carcinogenicity of Ni_3S_2 and Ni_3S_2-derived soluble nickel (Ni^{2+}) in mice depend, in part, on the antioxidant capacity of target organs, which varies among different strains (Rodriguez et al. 1996). Experimental evidence now support the conclusion that the nickel-dependent formation of an activated oxygen species—including superoxide ion, hydrogen peroxide, and hydroxy radical—is a primary molecular event in acute nickel toxicity and carcinogenicity (WHO 1991; Hausinger 1993; Tkeshelashvili et al. 1993; Novelli et al. 1995; Stohs and Bagchi 1995; Rodriguez et al. 1996). For example, the superoxide radical (O_2^-) is an important intermediate in the toxicity of insoluble nickel compounds such as NiO and NiS (Novelli et al. 1995). One of the keys to the mechanism of nickel-mediated damage is the enhancement of cellular redox processing by nickel. Accumulated nickel in tissues elicits the production of reactive oxygen species, such as the superoxide radical, as the result of phagocytosis of particulate nickel compounds and through the interaction of nickel ions with protein ligands, which promote the activation of the Ni^{2+}/Ni^{3+} redox couple. Thus, NiS and NiO can elicit the formation of O_2^- (Novelli et al. 1995).

The most serious type of nickel toxicity is that caused by the inhalation of nickel carbonyl (Nielsen 1977). The half-time persistence of nickel carbonyl in air is about 30 min (Sevin 1980). Nickel carbonyl can pass across

cell membranes without metabolic alteration because of its solubility in lipids, and this ability of nickel carbonyl to penetrate intracellularly may be responsible for its extreme toxicity (NAS 1975). In tissues, nickel carbonyl decomposes to liberate carbon monoxide and Ni^0, the latter being oxidized to Ni^{2+} by intracellular oxidation systems. The nickel portion is excreted with urine and the carbon monoxide is bound to hemoglobin and eventually excreted through the lungs (USEPA 1980; Kasprzak 1987). Nickel carbonyl inhibits DNA-dependent RNA synthesis activity, probably by binding to chromatin or DNA and thereby preventing the action of RNA polymerase, causing suppression of messenger-RNA-dependent induction of enzyme synthesis (Sunderman 1968; NAS 1975; USEPA 1980). The lung is the target organ in nickel carbonyl poisoning (USEPA 1980). Acute human exposures result in pathological pulmonary lesions, hemorrhage, edema, deranged alveolar cells, degeneration of bronchial epithelium, and pulmonary fibrosis. The response of pulmonary tissue to nickel carbonyl is rapid: interstitial edema may develop within 1 h of exposure and cause death within 5 days. Animals surviving acute exposures show lung histopathology (USEPA 1980).

Gastrointestinal intake of nickel by humans is high compared to some other trace metals because of contributions of nickel from utensils and food processing machinery; average human dietary values range from 300 to 500 μg daily, with absorption from the gastrointestinal tract of 1-10% (USEPA 1980, 1986; Sigel and Sigel 1988). In humans, nearly 40 times more nickel was absorbed from the gastrointestinal tract when nickel sulfate was given in the drinking water (27%) than when it was given in the diet (0.7%). Uptake was more rapid in starved individuals (WHO 1991; USPHS 1993). Dogs and rats given nickel, nickel sulfate hexahydrate, or nickel chloride in the diet or by gavage rapidly absorbed 1-10% of the nickel from the gastrointestinal tract, while unabsorbed nickel was excreted in the feces (USPHS 1993).

During occupational exposure, respiratory absorption of soluble and insoluble nickel compounds is the major route of entry, with gastrointestinal absorption secondary (WHO 1991). Inhalation exposure studies of nickel in humans and test animals show that nickel localizes in the lungs, with much lower levels in liver and kidneys (USPHS 1993). About half the inhaled nickel is deposited on bronchial mucosa and swept upward in mucous to be swallowed; about 25% of the inhaled nickel is deposited in the pulmonary parenchyma (NAS 1975). The relative amount of inhaled nickel absorbed from the pulmonary tract is dependent on the chemical and physical properties of the nickel compound (USEPA 1986). Pulmonary absorption into the blood is greatest for nickel carbonyl vapor; about half the inhaled amount is absorbed (USEPA 1980). Nickel in particulate matter is absorbed from the pulmonary tract to a lesser degree than nickel carbonyl; however, smaller particles are absorbed more readily than larger particles (USEPA 1980). Large nickel particles (>2 μm in diameter) are deposited in the upper respiratory tract; smaller particles tend to enter the lower respiratory tract. In humans, 35% of the inhaled nickel is absorbed into the blood from the respiratory tract; the remainder is either swallowed or expectorated. Soluble nickel compounds were more readily absorbed from the respiratory tract than insoluble compounds (USPHS 1993). In rodents, the half-time persistence of nickel particles was a function of particle diameter: 7.7 months for particles 0.6 μm in diameter, 11.5 months for particles 1.2 μm in diameter, and 21 months for particles 4.0 μm in diameter (USPHS 1993). In rodents, a higher percentage of insoluble nickel compounds was retained in the lungs for a longer time than soluble nickel compounds, and the lung burden of nickel decreased with increasing particle size. Nickel retention was 6-10 times greater in rodents exposed to insoluble nickel subsulfide compared to soluble nickel sulfate. Lung burdens of nickel generally increased with increasing duration of exposure and increasing concentrations of various nickel compounds in the air (USPHS 1993). Animals exposed to nickel carbonyl by inhalation exhale some of the respiratory burden in 2-4 h. The remainder is slowly degraded to divalent nickel, which is oxidized, and carbon monoxide, which initially binds to hemoglobin, with nickel eventually undergoing urinary excretion (NAS 1975; Norseth and Piscator 1979; USEPA 1980; Norseth 1986).

Dermal absorption of nickel occurs in animals and humans and is related to nickel-induced hypersensitivity and skin disorders (Samitz and Katz 1976; USEPA 1986). Absorption of nickel sulfate from the skin is reported for guinea pigs, rabbits, rats, and humans (Norseth and Piscator 1979). Nickel ions in contact with the skin surface diffuse through the epidermis and combine with proteins; the body reacts to this conjugated protein (Samitz and Katz 1976; Nielsen 1977). Nickel penetration of the skin is enhanced by sweat, blood and other body fluids, and detergents (Nielsen 1977; USEPA 1980). Absorption is related to the solubility of the compound, following the general relation of nickel carbonyl, soluble nickel compounds, and insoluble nickel compounds, in that order; nickel carbonyl is the most rapidly and completely absorbed nickel compound in mammals (WHO 1991). Anionic species differ markedly in skin penetration: nickelous ions from a chloride

solution pass through skin about 50 times faster than do nickelous ions from a sulfate solution (USPHS 1993). Radionickel-57 (^{57}Ni) accumulates in keratinous areas and hair sacs of the shaved skin of guinea pigs and rabbits following dermal exposure. After 4 h, ^{57}Ni was found in the stratum corneum and stratum spinosum; after 24 h, ^{57}Ni was detected in blood and kidneys, with minor amounts in liver (USPHS 1993). As much as 77% of nickel sulfate applied to the occluded skin surface of rabbits and guinea pigs was absorbed within 24 h; sensitivity to nickel did not seem to affect absorption rate (USPHS 1993). In humans, some protection against nickel may be given by introducing a physical barrier between the skin and the metal, including fingernail polish, a polyurethane coating, dexamethasone, or disodium EDTA (Nielsen 1977).

Nickel retention in the body of mammals is low. The half-time residence of soluble forms of nickel is several days, with little evidence for tissue accumulation except in the lung (USEPA 1980, 1986). Radionickel-63 (^{63}Ni) injected into rats and rabbits cleared rapidly; most (75%) of the injected dose was excreted within 24-72 h (USEPA 1980). Nickel clears at different rates from various tissues. In mammals, clearance was fastest from serum, followed by kidney, muscle, stomach, and uterus; relatively slow clearance was evident in skin, brain, and especially lung (Kasprzak 1987). The half-time persistence in human lung for insoluble forms of nickel is 330 days (Sevin 1980).

The excretory routes for nickel in mammals depend on the chemical forms of nickel and the mode of nickel intake. Most (>90%) of the nickel that is ingested in food remains unabsorbed within the gastrointestinal tract and is excreted in the feces (NAS 1975; Sevin 1980; USEPA 1986; Kasprzak 1987; Hausinger 1993; USPHS 1993). Urinary excretion is the primary route of clearance for nickel absorbed through the gastrointestinal tract (USEPA 1976, 1986; USPHS 1993). In humans, nickel excretion in feces usually ranges between 300 and 500 μg daily, or about the same as the daily dietary intake; urinary levels are between 2 and 4 μg/L (USEPA 1980, 1986). Dogs fed nickel sulfate in the diet for as long as 2 years excreted most of the nickel in feces and 1-3% in the urine (USPHS 1993). Biliary excretion occurs in rats, calves, and rabbits, but the role of bile in human metabolism of nickel is not clear (USEPA 1980). Absorbed nickel is excreted in the urine regardless of the route of exposure. The excretory route of inhaled nickel depends on the solubility of the nickel compound. Inhalation studies show that rats excrete 70% of the nickel in soluble nickel compounds through the urine within 3 days and 97% in 21 days. Less soluble nickel compounds (nickel oxide, nickel subsulfide) are excreted in urine (50%) and feces (50%); 90% of the initial dose of nickel subsulfide was excreted within 35 days, and 60% of the nickel oxide—which is less soluble and not as rapidly absorbed as nickel subsulfide—was excreted in 90 days (USPHS 1993). The half-time persistence of inhaled nickel oxide is 3 weeks in hamsters (Sevin 1980). In addition to feces, urine, and bile, other body secretions—including sweat, tears, milk, and mucociliary fluids—are potential routes of excretion (WHO 1991). Sweat may constitute a major route of nickel excretion in tropical climates. Nickel concentrations in sweat of healthy humans sauna bathing for brief periods were 52 μg/L in males and 131 μg/L in females (USEPA 1980). Hair deposition of nickel also appears to be an excretory mechanism (as much as 4 mg Ni/kg dry weight [DW] hair in humans), but the relative magnitude of this route, compared to urinary excretion, is unclear (USEPA 1980, 1986). In the case of nickel compounds administered by way of injection, tests with small laboratory animals show that nickel is cleared rapidly from the plasma and excreted mainly in the urine (Norseth and Piscator 1979; USEPA 1980). About 78% of an injected dose of nickel salts was excreted in the urine during the first 3 days after injection in rats and during the first day in rabbits (Norseth 1986). Exhalation via the lungs is the primary route of excretion during the first hours following injection of nickel carbonyl into rats, and afterwards via the urine (Norseth and Piscator 1979).

In microorganisms, nickel binds mainly to the phosphate groups of the cell wall. From this site, an active transport mechanism designed for magnesium transports the nickel (Kasprzak 1987). In microorganisms and higher plants, magnesium is the usual competitor for nickel in the biological ion-exchange reactions. In lichens, fungi, algae, and mosses, the active binding sites are the carboxylic and hydroxycarboxylic groups fixed on the cell walls. Nickel in hyperaccumulating genera of terrestrial plants is complexed with polycarboxylic acids and pectins, although phosphate groups may also participate (Kasprzak 1987). In terrestrial plants, nickel is absorbed through the roots (USEPA 1975).

Interactions

In minerals, nickel competes with iron, cobalt, and magnesium because of similarities in their ionic radius and electronegativity (NRCC 1981). At the cellular level, nickel interferes with enzymatic functions of calcium,

iron, magnesium, manganese, and zinc (Kasprzak 1987). Binding of nickel to DNA is inhibited by salts of calcium, copper, magnesium, manganese, and zinc (WHO 1991). In toads (*Bufo arenarum*), ionic nickel interferes with voltage-sensitive ionic potassium channels in short muscle fibers (Bertran and Kotsias 1997). Among animals, plants, and microorganisms, nickel interacts with at least 13 essential elements: calcium, chromium, cobalt, copper, iodine, iron, magnesium, manganese, molybdenum, phosphorus, potassium, sodium, and zinc (Nielsen 1980a). Nickel interacts noncompetitively with all 13 elements and also interacts competitively with calcium, cobalt, copper, iron, and zinc. Quantification of these relationships would help clarify nickel-essential mineral interactions and the circumstances under which these interactions might lead to states of deficiency or toxicity (Nielsen 1980a). Mixtures of metals (arsenic, cadmium, copper, chromium, mercury, lead, zinc) containing nickel salts are more toxic to daphnids and fishes than are predicted on the basis of individual components (Enserink et al. 1991). Additive joint action of chemicals, including nickel, should be considered in the development of ecotoxicologically relevant water quality criteria (Enserink et al. 1991).

Nickel may be a factor in asbestos carcinogenicity. The presence of chromium and manganese in asbestos fibers may enhance the carcinogenicity of nickel (USEPA 1980), but this relationship needs to be verified. Barium-nickel mixtures inhibit calcium uptake in rats, resulting in reduced growth (WHO 1991). Pretreatment of animals with cadmium enhanced the toxicity of nickel to the kidneys and liver (USPHS 1993). Simultaneous exposure to nickel and cadmium—an industrial situation common in nickel and cadmium battery production—caused a significant increase in beta-2-macroglobulin excretion (Sunderman et al. 1984). Nickel or cadmium alone did not affect calcium kinetics of smooth muscle from bovine mesenteric arteries. However, mixtures of cadmium and nickel at greater than 100 nM inhibited the calcium function and may explain the vascular tension induced by nickel and other cations (Stockand et al. 1993). Smooth muscle of the ventral aorta of the spiny dogfish (*Squalus acanthias*) contracted significantly on exposure to cadmium or nickel but not to other divalent cations. Atropine inhibited vasoconstriction of shark muscle induced by cadmium, but not that induced by nickel (Evans and Walton 1990). Nickel toxicity in soybeans (*Glycine max*) was inhibited by calcium, which limited the binding of nickel to DNA (WHO 1991). Chromium-nickel mixtures were more-than-additive in toxicity to guppies (*Poecilia reticulata*) in 96-h tests (Khangarot and Ray 1990). Rabbits (*Oryctolagus* sp.) exposed by inhalation to both nickel and trivalent chromium had more severe respiratory effects than did rabbits exposed to nickel alone (USPHS 1993). In natural waters, the geochemical behavior of nickel is similar to that of cobalt (USEPA 1980). It is therefore not surprising that nickel-cobalt mixtures in drinking water of rats were additive in toxicity (WHO 1991) and that there is a high correlation between nickel and cobalt concentrations in terrestrial plants (Memon et al. 1980).

Copper-nickel mixtures have a beneficial effect on growth of terrestrial plants but are more-than-additive in toxic action to aquatic plants (NRCC 1981; WHO 1991). Nickel interacts with iron in rat nutrition and metabolism, but the interaction depends on the form and level of the dietary iron (Nielsen 1980b; USEPA 1985). Weanling rats fed diets containing nickel chloride and ferric sulfate had altered hematocrit, hemoglobin level, and alkaline phosphatase activity which did not occur when a mixture of ferric and ferrous sulfates were fed (Nielsen 1980b). In iron-deficient rats, nickel enhanced the absorption of iron administered as ferric sulfate (USPHS 1993), and nickel acted as a biological cofactor in facilitating gastrointestinal absorption of ferric ion when iron was given as ferric sulfate (USPHS 1993). Mice given a lead-nickel mixture in drinking water (57 mg Ni/L-200 mg Pb/L) for 12 days had increased urinary excretion of delta aminolevulinic acid and increased delta aminolevulinic dehydratase activity in erythrocytes when compared to groups given lead alone or nickel alone (Tomokuni and Ichiba 1990).

Magnesium competes with nickel in isolated cell studies (WHO 1991). Treatment with magnesium reduces nickel toxicity, presumably through inhibition of nickel binding to DNA (USPHS 1993; Hartwig et al. 1994). Manganese also inhibits the binding of nickel to DNA (WHO 1991), and manganese administration reduces the accumulation of nickel in some organs (Murthy and Chandra 1979). Manganese dust inhibits nickel subsulfide-induced carcinogenesis in rats following simultaneous intramuscular injection of the two compounds (USPHS 1993). Also, nickel-manganese mixtures are less-than-additive in producing cytotoxicity of alveolar macrophages in rats (WHO 1991). Nickel compounds enhance the cytotoxicity and genotoxicity of ultraviolet radiation, x-rays, and cytostatic agents such as *cis*-platinum, *trans*-platinum, and mitomycin C (Hartwig et al. 1994). Nickel is less-than-additive in toxicity to aquatic algae in combination with zinc (WHO 1991). Treatment with zinc lessens nickel toxicity, presumably by competing with nickel in binding to DNA and proteins (USEPA 1985; WHO 1991; USPHS 1993; Hartwig et al. 1994). Zinc binding sites of DNA-binding proteins, known as “finger loop domains,” are likely molecular targets for metal toxicity. Ionic nickel has a similar ionic radius to

Zn^{2+} and substitution is possible. Such substitution may disrupt nickel-induced gene expression by interfering with site-specific free radical reactions, which can result in DNA cleavage, formation of DNA protein cross links, and disturbance of mitosis (WHO 1991).

Nickel also interacts with chelating agents, phosphatases, viruses, vitamins, and polycyclic aromatic hydrocarbons (PAHs). Chelating agents mitigate the toxicity of nickel by stimulating nickel excretion (USPHS 1993). Chelators reduced the toxicity of nickel to aquatic plants, presumably by lowering nickel bioavailability (WHO 1991). Lipophilic chelating agents, such as triethylenetetramine and Cyclam (1,4,8,11-tetraazacyclotetradecane), are more effective in reducing toxicity than hydrophilic chelating agents such as EDTA, cyclohexanediamine tetraacetic acid, diethylenetriamine pentaacetic acid, and hydroxyethylenediamine triacetic acid. The greater efficacy of the lipophilic agents may be due to their ability to bind to nickel both intracellularly and extracellularly, while the hydrophilic agents can only bond extracellularly (USPHS 1993). Nickel irreversibly activates calcineurin, a multifunctional intracellular phosphatase normally activated by calcium and calmodulin (Kasprzak 1987). With nickel present, Newcastle Disease virus suppresses mouse L-cell interferon synthesis, suggesting virus-nickel synergism (USEPA 1980). Nickel interacts with vitamin C (USEPA 1985) and has a synergistic effect on the carcinogenicities of various PAHs (USEPA 1980). Rats given intratracheal doses of nickel oxide and 20-methylcholanthrene develop squamous cell carcinomas more rapidly than with 20-methylcholanthrene alone. Simultaneous exposure of rats to benzopyrene and nickel subsulfide reduced the latency period of sarcomas by 30% and induced lung histopathology at a higher frequency than either agent alone. Also, tissue retention of PAH carcinogens is prolonged with nickel exposure (USEPA 1980).

Carcinogenicity, Mutagenicity, Teratogenicity

General

Some forms of nickel are carcinogenic to humans and animals (IARC 1976; Smialowicz et al. 1984; USEPA 1986; WHO 1991; Hausinger 1993; USPHS 1993; Hartwig et al. 1994). Carcinogenicity of nickel compounds varies significantly with the chemical form of nickel, route of exposure, animal model used (including intraspecies strain differences), dose, and duration of exposure (USEPA 1980). In tests with small laboratory mammals, inducement of carcinomas of the types found in humans has only been accomplished following exposures by the respiratory route (Sunderman 1968). Inhalation studies with nickel subsulfide and nickel oxide show evidence of carcinogenicity in mammals and humans; however, the evidence based on oral or cutaneous exposure to these and other nickel compounds is either negative or inconclusive (NAS 1975; IARC 1976; Norseth 1980; USEPA 1980, 1986; WHO 1991; USPHS 1993). Nickel carbonyl and metallic nickel are carcinogenic in experimental animals, but data regarding their carcinogenicity in humans are inconclusive (USEPA 1975; Norseth 1980; USPHS 1993).

Certain nickel compounds are weakly mutagenic in a variety of test systems, but much of the evidence is inconclusive or negative (USPHS 1977, 1993; USEPA 1986; Kasprzak 1987; WHO 1991; Outridge and Scheuhammer 1993). Mutagenicity—as measured by an increased frequency of sister chromatid exchange, chromosome aberrations, cell transformations, spindle disturbances, and dominant lethal effects—is induced by various nickel compounds at high concentrations in isolated cells of selected mammals, including humans; however, these effects have not been observed in vivo (Sunderman 1981; USEPA 1986; WHO 1991; USPHS 1993). Nickel mutagenesis is thought to occur through inhibition of DNA synthesis and excision repair, resulting in an increased frequency of cross links and strand breaks (USEPA 1986; WHO 1991; USPHS 1993). DNA strand breaks occur in rat cells exposed to 5-40 mg Ni/kg medium as nickel carbonate; similar effects occur in hamster cells at 10-2,000 mg Ni/kg medium as nickel chloride and nickel subsulfide and in human cells with nickel sulfate (WHO 1991). The ability of a particular nickel compound to cause mutations is considered proportional to its cellular uptake; however, data on nickel bioavailability to cells is scarce (Niebuhr et al. 1980; USPHS 1993).

No teratogenic effects of nickel compounds occur in mammals by way of inhalation or ingestion except from nickel carbonyl (USEPA 1986; Outridge and Scheuhammer 1993). However, injection of low nickel doses results in consistent fetal malformations, particularly when nickel is administered during the organogenic stage of gestation of mammals or during the early development of domestic chick embryos (Outridge and Scheuhammer 1993). Injected doses causing teratogenic effects in rodents were as low as 1.0-1.2 mg Ni/kg body weight (BW), although more malformations resulted at higher dosages (2.3-4.0 mg/kg BW), which also increased fetal mortality and toxicity in the dam (Mas et al. 1985; Outridge and Scheuhammer 1993). Possible

causes of nickel-induced malformations include direct toxicity from high transplacental nickel levels, reduced availability of alpha-fetoprotein to fetuses, or an increase in maternal glucose levels, which induces hyperglycemia in fetuses (Mas et al. 1985; Outridge and Scheuhammer 1993).

Carcinogenicity

Epidemiological studies conducted some decades ago in England, Canada, Japan, Norway, Germany, Russia, New Caledonia, and West Virginia indicated that humans working in the nickel processing and refining industries—or living within 1 km of processing or refining sites—had a significantly increased risk of developing fatal cancers of the nose, lungs, larynx, and kidneys, and a higher incidence of deaths from nonmalignant respiratory disease (Sunderman 1968, 1981; NAS 1975; IARC 1976; USPHS 1977, 1993; Norseth and Piscator 1979; Norseth 1980; Sevin 1980; USEPA 1980; Kasprzak 1987; WHO 1991). Nasal cancers in nickel refinery workers were similar to those of the general population; however, lung cancers of nickel refinery workers had a higher frequency of squamous cell carcinomas (USPHS 1993). Smoking of tobacco contributed to the development of lung cancers in the nickel-exposed workers. Smoking about 15 cigarettes daily for 1 year adds about 1,930 μg of nickel, as nickel carbonyl, to the human lung; this amount is equivalent to a carcinogenic dose of nickel for rats (Sunderman 1970, 1981). Symptoms of cancer in humans may occur 5 to 35 years after exposure (Furst and Radding 1980; Kasprzak 1987; USPHS 1993). The incidence of human lung and nasal cancers in occupationally exposed workers are related to nickel concentration and duration of exposure (USEPA 1986). Nickel compounds implicated as carcinogens include insoluble dusts of nickel subsulfide (Ni_3S_2) and nickel oxides (NiO, Ni_2O_3), the vapor of nickel carbonyl ($Ni(CO)_4$), and soluble aerosols of nickel sulfate ($NiSO_4$), nickel nitrate ($NiNO_3$), and nickel chloride ($NiCl_2$; USPHS 1977; USEPA 1980). Soluble nickel compounds, though toxic, have relatively low carcinogenic activities (Ho and Furst 1973). In general, carcinogenicity of nickel compounds is inversely related to its solubility in water, the least soluble being the most active carcinogen (Sunderman 1968; Furst and Radding 1980; USEPA 1980; USPHS 1993). The highest risk to humans of lung and nasal cancers comes from exposure to respirable particles of metallic nickel, nickel sulfides, nickel oxide, and the vapors of nickel carbonyl (NAS 1975; USPHS 1977; Norseth and Piscator 1979; Norseth 1980; Sunderman 1981; Sunderman et al. 1984; USEPA 1986; Kasprzak 1987; WHO 1991; USPHS 1993). Cancers were most frequent when workers were exposed to soluble nickel compounds at concentrations greater than 1.0 mg Ni/m^3 air and to exposure to less soluble compounds at greater than 10.0 mg Ni/m^3 air (USPHS 1993). Nickel subsulfide appears to be the nickel compound most carcinogenic to humans, as judged by animal studies and epidemiological evidence (Furst and Radding 1980; Outridge and Scheuhammer 1993). The death rate of nickel workers from cancer has declined significantly since the mid-1920's because of improved safety and awareness (USPHS 1977, 1993).

The underlying biochemical mechanisms governing the carcinogenicity of various nickel compounds are imperfectly understood. There is general agreement that intra-cellular nickel accumulates in the nucleus, especially the nucleolar fraction (NAS 1975; USEPA 1980). Intracellular binding of nickel to nuclear proteins and nuclear RNA and DNA may cause strand breakage and other chromosomal aberrations, diminished RNA synthesis and mitotic activity, and gene expression (USEPA 1980; Kasprzak 1987). A key mechanism of the transformation of tumorous cells involves DNA damage resulting from mutation (Sigel and Sigel 1988) caused by hydroxy radical or other oxidizing species (Datta et al. 1994). Alterations in cytokine (also known as tumor necrosis factor) production is associated with fibrotic lung injury in rats. Inhaled nickel oxide is known to increase cytokine production in rats (Morimoto et al. 1995).

Nickel entering the digestive tract of mammals is likely to be noncarcinogenic. Chronic ingestion studies of various nickel compounds that lasted as long as 2 years using several species of mammals show no evidence of carcinogenesis (Outridge and Scheuhammer 1993). Inhalation is the dosing route most relevant to human occupational exposure (Sunderman et al. 1984) and probably an important route for wildlife exposure in the case of nickel powder, nickel carbonyl, and nickel subsulfide (IARC 1976).

Inhalation of airborne nickel powder at 15 mg Ni/m^3 air causes an increased frequency of lung anaplastic carcinomas and nasal cancers in rodents and guinea pigs, especially when the particles are less than 4 μm in diameter (USPHS 1977; USEPA 1980). Rats exposed to airborne dusts of metallic nickel at 70 mg Ni/m^3 air for 5 h daily, 5 days weekly over 6 months had a 40% frequency of lung cancers; the latent period for tumor development was 17 months (Sunderman 1981). A similar case is made for nickel sulfide and nickel oxide

(Sunderman 1981). In Canada, however, metallic nickel is considered “unclassifiable with respect to carcinogenicity” due to the limitations of identified studies (Hughes et al. 1994). Inhaled nickel carbonyl is carcinogenic to the lungs of rats, a species generally considered to be peculiarly resistant to pulmonary cancer (Sunderman and Donnelly 1965; NAS 1975; IARC 1976; USEPA 1980; WHO 1991). Pulmonary cancers developed in rats 24-27 months after initial exposure to nickel carbonyl, and growth and survival of rats during chronic exposure were markedly reduced (Sunderman and Donnelly 1965). Rats exposed to air containing 250 μg nickel carbonyl/L for only 30 min had a 4% incidence of lung cancer in 2-year survivors versus 0% in controls; rats exposed to 30-60 μg/L air for 30 min, three times weekly for 1 year had a 21% incidence of lung cancer in 2-year survivors (Sunderman 1970; NAS 1975). Inhaled nickel oxides do not seem to be tumorogenic to hamsters at concentrations of 1.2 mg Ni/m^3 air during exposure for 12 months (Outridge and Scheuhammer 1993). Hamsters did not develop lung tumors during lifespan inhalation exposure to nickel oxide; however, inhaled nickel oxide enhanced nasal carcinogenesis produced by diethylnitrosamine (USPHS 1977). Inhalation of nickel subsulfide produced malignant lung tumors and nasal cancers in rats in a dose-dependent manner (Ottolenghi et al. 1974; IARC 1976; USPHS 1977, 1993; WHO 1991; Benson et al. 1995; Rodriguez et al. 1996). Rats develop benign and malignant lung tumors (14% frequency vs. 0% in controls) after exposure for 78 weeks (6 h daily, 5 days weekly) to air containing 1.0 mg Ni/m^3 (as nickel subsulfide; particles <1.5 μm in diameter) and during a subsequent 30-week observation period (IARC 1976; USPHS 1977; USEPA 1980; NRCC 1981).

Local sarcomas may develop in humans and domestic animals at sites of nickel implants and prostheses made of nickel. Latency of the implant sarcomas varies from 1 to 30 years in humans (mean, 10 years) and from 1 to 11 years in dogs (mean, 5 years). No cases of malignant tumors are reported at sites of dental nickel prostheses (Kasprzak 1987).

Injection site tumors are induced by many nickel compounds that do not cause cancer in animals by other routes of exposure (USPHS 1977). In fact, most of the published literature on nickel carcinogenesis concerns injected or implanted metallic nickel or nickel compounds. However, these data seem to be of limited value in determining carcinogenic exposure levels for avian and terrestrial wildlife (Outridge and Scheuhammer 1993). The applicability of these studies to a recommendation for human workplace exposure is also questionable (USPHS 1977). Nevertheless, injection or implantation site sarcomas have been induced by many nickel compounds after one or repeated injections or implantations in rats, mice, hamsters, guinea pigs, rabbits, and cats (NAS 1975; IARC 1976; USPHS 1977, 1993; Norseth and Piscator 1979; USEPA 1980; NRCC 1981; Sunderman 1981; WHO 1991). Nickel compounds known to produce sarcomas or malignant tumors by these routes of administration (implantation, intratracheal, intramuscular, intraperitoneal, subcutaneous, intrarenal, intravenous, intratesticular, intraocular, intraosseus, intrapleural, intracerebral, intrahepatic, intraarticular, intrasubmaxillary, intraadipose, intramedullary) include nickel subsulfide, nickel carbonyl, nickel powder or dust, nickel oxide, nickel hydroxide, nickel acetate, nickel fluoride, nickelocene, nickel sulfate, nickel selenide, nickel carbonate, nickel chromate, nickel arsenide, nickel telluride, nickel antimonide, nickel-iron matte, nickel ammonium sulfate, and nickel monosulfide.

Some parenteral routes of administration were less effective than others in producing an increase in the frequency of benign or malignant tumors, including intravenous, submaxillary, and intrahepatic injection routes (Sunderman 1981). Some nickel compounds are more effective at inducing tumors than others, for example, nickel sulfate and nickel acetate induce tumors in the peritoneal cavity of rats after repeated intraperitoneal injections but nickel chloride does not (WHO 1991). Likewise, some species are more sensitive to tumor inducement by injection than others; rats, for example, are more sensitive than hamsters (USPHS 1977). Most nickel compounds administered by way of injection usually produce responses at the site of injection; however, nickel acetate injected intraperitoneally produced pulmonary carcinomas in mice (USEPA 1980). Some carcinogenic nickel compounds produce tumors only when a threshold dose is exceeded (IARC 1976; USPHS 1993), and some strains of animals are more sensitive than others. In one study, three strains of male mice (*Mus* sp.) were given a single intramuscular injection of 0.5, 2.5, 5.0, or 10.0 mg nickel subsulfide per mouse—equivalent to 19, 95, 190, or 380 mg Ni_3S_2/kg BW—and observed for 78 weeks for tumor development (Rodriguez et al. 1996). Nickel subsulfide is a water-insoluble compound suspected to damage cells through oxidative mechanisms. The highest dose injected was lethal (53-93% dead) within 7 days. The final incidence of sarcomas in the 5 mg/mouse groups ranged between 40 and 97%, with decreased survival and growth noted in all test groups. In the most sensitive strain tested, there was a dose-dependent increase in tumor frequency, with a significant increase in tumors at the lowest dose tested (Rodriguez et al. 1996).

Carcinogenic properties of nickel are modified by interactions with other chemicals (NAS 1975; USEPA 1985; WHO 1991). Nickel-cadmium battery workers exposed to high levels of both nickel and cadmium have an increased risk of lung cancer when compared to exposure from cadmium alone (WHO 1991). Some nickel compounds interact synergistically with known carcinogens (WHO 1991). Nickel chloride enhances the renal carcinogenicity of N-ethyl-N-hydroxyethyl nitrosamine in rats. Metallic nickel powder enhances lung carcinogenicity of 20-methylcholanthrene when both are administered intratracheally to rats. Nickel subsulfide in combination with benzo(a)pyrene shortens the latency time to local tumor development and produces a disproportionately higher frequency of malignant tumors. Nickel sulfate enhanced dinitrosopiperazine carcinogenicity in rats (WHO 1991). And nickel potentiated the specific effects of cobalt in rabbits by enhancing the formation of lung nodules (Johansson et al. 1991). Some chemicals inhibit nickel-induced carcinogenicity. Carcinogenicity induced by nickel subsulfide is reduced by manganese dust (Sunderman 1981; Sunderman et al. 1984; WHO 1991). Manganese protects male guinea pigs against tumorogenesis induced by nickel subsulfide, possibly due to the stimulating effect of manganese on macrophage response and by displacing nickel from the injection site (Murthy and Chandra 1979). Sodium diethyldithiocarbamate reduced tumor incidence in rats implanted with nickel subsulfide (WHO 1991). And magnesium acetate and calcium acetate inhibit lung adenoma formation in mice treated intraperitoneally with nickel acetate (WHO 1991). Nickel interactions with other suspected carcinogens, such as chromium, merit additional research (Norseth 1980). Nickel and other trace metals in asbestos fibers are responsible, in part, for the pulmonary carcinogenicity found in asbestos workers (Sunderman 1968). Nickel-sulfur mineral complexes may also have carcinogenic potential; a similar case is made for the corresponding arsenides, selenides, and tellurides (USEPA 1980).

Mutagenicity

Nickel salts gave no evidence of mutagenesis in tests with viruses (USPHS 1977), and bacterial mutagenesis tests of nickel compounds have consistently yielded negative or inconclusive results (USPHS 1977; Sunderman 1981; Sunderman et al. 1984; WHO 1991). However, nickel chloride and nickel sulfate were judged to be mutagenic or weakly mutagenic in certain bacterial eukaryotic test systems (USEPA 1985). Nickel subsulfide was positively mutagenic to the protozoan *Paramecium* sp. at 0.5 mg Ni/L (WHO 1991). Ionic Ni^{2+} was mutagenic to *Escherichia coli*; mutagenesis was enhanced by the addition of both hydrogen peroxide and tripeptide glycyl-L-histidine, suggesting that short-lived oxygen free radicals are generated (Tkeshelashvili et al. 1993). Nickel chloride hexahydrate induced respiratory deficiency in yeast cells, but this may be a cytotoxic effect rather than a gene mutation (USPHS 1977; WHO 1991).

Nickel is weakly mutagenic to plants (USPHS 1977) and insects (WHO 1991). Abnormal cell divisions occur in roots of the broad bean (*Vicia faba*) during exposure to various inorganic nickel salts at nickel concentrations of 0.1-1,000 mg/L (USPHS 1977). All nickel salts tested produced more abnormal cell divisions than did controls. In beans, nickel nitrate was the most effective inorganic nickel compound tested in producing deformed cells, abnormal arrangement of chromatin, extra micronuclei, and evidence of cell nucleus disturbances; however, nickel salts showed only weak mutagenic action on rootlets of peas, *Pisum* sp. (USPHS 1977). Nickel sulfate induced chromosomal abnormalities in root tip cells of onions, *Allium* sp. (Donghua and Wusheng 1997) and caused sex-linked recessive mutations in the fruit fly (*Drosophila melanogaster*) at 200-400 mg Ni/L culture medium (WHO 1991).

Human cells exposed to various nickel compounds have an increased frequency of chromosomal aberrations, although sister chromatid exchange frequency is unaffected. Cells from nickel refinery workers exposed to nickel monosulfide (0.2 mg Ni/m^3) or nickel subsulfide (0.5 mg Ni/m^3) showed a significant increase in the incidence of chromosomal aberrations (Boysen et al. 1980; WHO 1991; USPHS 1993). No correlation was evident between nickel exposure level and the frequency of aberrations (USPHS 1993).

In Chinese hamster ovary cells, nickel chloride increased the frequency of chromosomal aberrations and sister chromatid exchanges. Cells with aberrations increased from 8% at about 6 μg Ni/L to 21% at about 6 mg Ni/L in a dose-dependent manner (Howard et al. 1991). There is a large difference in the mutagenic potential of soluble and insoluble nickel compounds that seems to reflect the carcinogenic potential of these nickel forms (Lee et al. 1993). For example, insoluble particles less than 5 μm in diameter of crystalline nickel subsulfide—a carcinogen—produced a strong, dose-dependent mutagenic response in Chinese hamster ovary cells up to 80 times higher than in untreated cells; however, soluble nickel sulfate produced no significant increase in mutational response over background in Chinese hamster ovary cells (Lee et al. 1993). A similar response is

reported for Syrian hamster embryo cells (USPHS 1993). Interactions of carcinogens and soluble nickel salts need to be considered. Benzo(a)pyrene, for example, showed a comutagenic effect with nickel sulfate in hamster embryo cells (USEPA 1985).

In rats, nickel carbonyl is reported to cause dominant lethal mutations (WHO 1991), but this needs verification. Nickel sulfate, when given subcutaneously at 2.4 mg Ni/kg BW daily for 120 days causes infertility; testicular tissues are adversely affected after the first injection (USEPA 1980). Nickel salts given intraperitoneally to rats at 6 mg Ni/kg BW daily for 14 days did not produce significant chromosomal changes in bone marrow or spermatogonial cells (Mathur et al. 1978).

In mice, nickel chloride produces a dose-dependent increase in abnormal lymphoma cells (WHO 1991). Mice given high concentrations of nickel in drinking water, equivalent to 23 mg Ni/kg BW daily and higher, have an increased incidence of micronuclei in bone marrow (USPHS 1993). However, mice injected once with 50 mg Ni/kg BW as nickel chloride show no evidence of mutagenicity (USPHS 1977).

Teratogenicity

Nickel carbonyl at high doses is a potent animal teratogen (Sunderman et al. 1984). Inhalation exposure to nickel carbonyl caused fetal death and decreased weight gain in rats and hamsters (WHO 1991) and eye malformations in rats (Sevin 1980; Sunderman et al. 1980). Studies on hamsters, rats, mice, birds, frogs, and other species suggest that some individuals are susceptible to reproductive and teratogenic effects when given high doses of nickel by various routes of administration (USPHS 1977; Sunderman et al. 1980; USEPA 1986; WHO 1991; Hausinger 1993). Intravenous injection of nickel sulfate to hamsters at 2-25 mg/kg BW on day 8 of gestation produces developmental abnormalities (USPHS 1977; Norseth and Piscator 1979). Teratogenic malformations—including poor bone ossification, hydronephrosis, and hemorrhaging—occur in rats when nickel is administered during organogenesis, and these malformations are maximal at dose levels toxic for the dam (Mas et al. 1985). A dose of 4 mg/kg BW given intraperitoneally on day 12 or 19 of pregnancy is teratogenic in rats (Mas et al. 1985). Rats exposed continuously for three generations to drinking water containing 5 mg Ni/L produce smaller litters, higher offspring mortality, and fewer males (NAS 1975; USPHS 1977). An increase in the number of runts suggests that transplacental toxicity occurs (USPHS 1977; Norseth and Piscator 1979).

Divalent nickel is a potent teratogen for the South African clawed frog (*Xenopus laevis*). Frog embryos actively absorb Ni^{2+} from the medium and develop ocular, skeletal, craniofacial, cardiac, and intestinal malformations (Sunderman et al. 1990; Hopfer et al. 1991; Hausinger 1993; Luo et al. 1993; Hauptman et al. 1993; Plowman et al. 1994). A Ni^{2+}-binding serpin, *pNiXa*, is abundant in clawed frog oocytes and embryos; binding of Ni^{2+} to *pNiXa* may cause embryotoxicity by enhancing oxidative reactions that produce tissue injury and genotoxicity (Beck et al. 1992; Haspel et al. 1993; Sunderman et al. 1996). Another Ni^{2+}-binding protein, *pNiXc*, isolated from mature oocytes of the clawed frog, was identified as a monomer of fructose-1,6-biphosphate aldolase A and raises the possibility that aldolase A is a target enzyme for nickel toxicity (Antonijczuk et al. 1995).

Nickel is embryolethal and teratogenic to white leghorn strains of the domestic chicken (*Gallus* sp.), possibly due to the mitosis-inhibiting activity of nickel compounds (Gilani and Marano 1980). Fertilized chicken eggs injected with 0.02-0.7 mg Ni/egg as nickel chloride on days 1-4 of incubation show a dose-dependent response. All dose levels of nickel tested were teratogenic to chickens. Malformations include poorly developed or missing brain and eyes, everted viscera, short and twisted neck and limbs, hemorrhaging, and a reduction in body size. Toxicity and teratogenicity are highest in embryos injected on day 2 (Gilani and Marano 1980). Mallard (*Anas platyrhynchos*) ducklings from fertile eggs treated at age 72 h with 0.7 μg Ni as nickel mesotetraphenylporphine show a marked decrease in survival. Among survivors, there is a significant increase in the frequency of developmental abnormalities, a reduction in bill size, and a reduction in weight (Hoffman 1979).

Changes in employment practices in North America and Europe have increased the proportion of women among workers in nickel mines and refineries and in nickel-plating industries; this increase has heightened concern regarding possible fetal toxicity associated with exposures of pregnant women to nickel during gestation (Sunderman et al. 1978). One preliminary report (Chashschin et al. 1994) strongly suggests that exposure to nickel of Russian female hydrometallurgy workers causes significantly increased risks for abortion, total defects, cardiovascular defects, and defects of the musculoskeletal system.

Nonteratogenic reproductive effects of nickel include increased resorption of embryos and fetuses, reduced litter size, testicular damage, altered rates of development and growth, and decreased fertility. Nickel compounds can penetrate the mammalian placental barrier and affect the fetus (USEPA 1980; Sunderman et al. 1984; Mas et al. 1985). Intravenous administration of nickel acetate (0.7-10.0 mg Ni/kg BW) to pregnant hamsters on day 8 of gestation resulted in dose-dependent increases in the number of resorbed embryos (USEPA 1980). Rats injected intramuscularly with nickel chloride on day 8 of gestation with 12 or 16 mg Ni/kg BW produced significantly fewer live fetuses than did controls (USPHS 1977). Three generations of rats given nickel in their diets at 250-1,000 mg Ni/kg ration had increased fetal mortality in the first generation and reduced body weights in all generations at 1,000 mg/kg (USPHS 1977). Litter sizes were reduced in pregnant rats fed nickel in various forms at 1,000 mg Ni/kg ration (USEPA 1980). Rodents exposed to nickel during gestation show a decline in the frequency of implantation of fertilized eggs, enhanced resorption of fertilized eggs and fetuses, an increased frequency of stillbirths, and growth abnormalities in live-born young (Hausinger 1993). Exposure of eggs and sperm of rainbow trout to 1.0 mg Ni/L as nickel sulfate for 30 min did not affect fertilization or hatchability; however, most exposed zygotes hatched earlier than the controls (NAS 1975). Nickel salts produced testicular damage in rats and mice given oral, subcutaneous, or intratesticular doses of 10-25 mg Ni/kg BW; nickel-treated male rats were unable to impregnate females (USPHS 1977). Nickel sulfate at 25 mg Ni/kg BW daily for 120 days via the esophagus selectively damaged the testes of rats (inhibition of spermatogenesis) and resulted in a reduced procreative capacity (USPHS 1977); males were permanently infertile after 120 days on this regimen (NAS 1975).

Concentrations in Field Collections

General

Nickel is ubiquitous in the biosphere and is the 24th most abundant element in the earth's crust with a mean concentration of 75 mg/kg (Sevin 1980; Chau and Kulikovsky-Cordeiro 1995). Nickel enters the environment from natural and human sources and is distributed throughout all compartments by means of chemical and physical processes and biological transport by living organisms. Nickel is found in air, soil, water, food, and household objects; ingestion or inhalation of nickel is common, as is dermal exposure (USPHS 1977). In general, nickel concentrations in plants, animals, and abiotic materials are elevated in the vicinity of nickel smelters and refineries, nickel-cadmium battery plants, sewage outfalls, and coal ash disposal basins (NAS 1975; Kasprzak 1987; WHO 1991; USPHS 1993; Chau and Kulikovsky-Cordeiro 1995). A global inventory estimate of nickel shows that living organisms contain about 14 million metric tons of nickel, mostly (98.8%) in terrestrial plants (Table 4). But plants and animals account for only 0.00000031% of the total nickel inventory estimate of 4,500 trillion metric tons, the vast majority of the nickel being present in the lithosphere and other abiotic materials (Table 4).

Table 4. Inventory of nickel in various global environmental compartments (modified from Nriagu 1980b).

Compartment	Mean concentration (mg/kg)	Nickel in compartment (metric tons)
Lithosphere, down to 45 km	75	4,300,000,000,000,000
Sedimentary rocks	48	120,000,000,000,000
Soils, to 100 cm	16	5,300,000,000,000
Oil shale deposits	30	1,400,000,000,000
Dissolved oceanic	0.0006	840,000,000
Nickel ore reserves	>2,000	160,000,000
Coal deposits	15	150,000,000
Terrestrial litter	15	33,000,000
Terrestrial plants	6	14,000,000
Suspended oceanic particulates	95	6,600,000
Crude oil	10	2,300,000
Terrestrial animals	2.5	50,000
Swamps and marshes	7	42,000
Lakes and rivers, total	0.001	34,000
Consumers/reducers (biological)	3.5	11,000
Atmosphere	0.3	1,500
Oceanic plants	2.5	500
Lakes and rivers, plankton	4	230

Table 5. Nickel concentrations in selected abiotic materials.

Table 5. Material and units of concentration	Concentration[a]	Reference[b]
Air, ng/m^3		
Asbestos textile plants, 1961-65	8.8	1
Canada, 1987-90		
Arctic	0.38; Max. 0.68	2
Copper Cliff, Ontario	Max. 6,100	2
Hamilton, Ontario	7; Max. 77	2
Quebec City	5; Max. 15	2
Toronto	3; Max. 11	2
Near nickel alloy plants	Max. 1,200	3
Occupational exposure		
Miners	6-40	24
Mill area	Max. 2,800,000	24
Matte separation area	170,000-15,300,000	24
Converter furnace area	Max. 200,000	24
Particulate materials, United States		
Remote areas	0.0-6.0	4
Rural areas	0.6-78	4
Urban areas	1-328	4
Urban areas, North America		
Canada, 1971		
Sudbury, Ontario	Max. 2,101	5
Toronto	Usually <59	5
United States		
1970-74; various locations	9-15	5
1982; 111 cities	8 (1-86)	4, 7
217 locations; summer vs. winter	17 (Max. 39) vs. 25 (Max. 112)	3, 4, 8, 9
All locales	Usually <20; Max. 328	10
Chicago, 1968-71	18	4
Detroit		
1971-82	21-51 (6-130)	10
1982-92	7-14 (4-32)	10
Houston, 1968-71	15	4
New York, 1968-71	42	4
Texas, 1978-82	1; Max. 49	4
Washington, D.C., 1968-71	23	4
Various locations		
Canadian Arctic	0.1-0.5	4
Continental	1-3	11
Europe	Usually <20; Max. 1,400	10
Marine	<0.1-1	11
Nonurban areas	6 (2-11)	3, 6, 8, 9
Remote areas	<0.1-3	11
Drinking water, μg/L		
Canada		
Ontario except Sudbury	0.2-7	2
Sudbury		
Prior to 1972	200 (141-264)	5
1972-92	26-300	2
Current	Max. 72	4
Europe	1-11	4
United States		
All locations	Usually <10; sometimes 10-20;	4, 8, 9
rarely 75; Max. 200		

Table 5. Material and units of concentration	Concentration[a]	Reference[b]
969 locations, 1964-70	4.8; <1% had >20; Max. 75	3, 4, 6, 12
Ten largest cities	Usually <5.6	6
Hartford, Connecticut	1	4, 5
Philadelphia	13	6
Fossil fuels, mg/kg		
Coal		
Canadian	15 dry weight (DW)	11
Flyash; particle diameter 1.1-2.1 μm vs. >11.3 μm	1,600 DW vs. 460 DW	5
Crude oil		
Western Canadian	0.1-76 fresh weight (FW)	11
Various	10 FW; Max. 20 FW	5, 8
Groundwater, μg/L		
Contaminated with nickel compounds from a nickel-plating factory	Max. 2,500	4
Guelph, Ontario	2.5	2
Newfoundland	<0.2	2
New Jersey, 1977-79	3; Max. 600	4
United States; 1982; upper Mississippi River Basin vs. Ohio River Basin	3 vs. 4,430	7
Meteorites, mg/kg, selected	50,000-500,000	5
Rain, μg/L		
Bermuda	0.2	4
Delaware	0.8	4
Massachusetts	0.8 (0.5-1.5)	4
Ontario, Canada; 1982	0.5-0.6	4
Prince Edward Island, Canada	<0.5; Max. 30	2
Sweden	0.2-0.5	4
Rivers and lakes (freshwater), µg/L		
Lake Huron, 1980	0.5; Max. 3.8	4
Lake Ontario, 1980 vs. 82	4 vs. 6 (<1-17)	4
Most locations	Usually <10; 4.8 (4-71)	4, 5, 12
Near Sudbury, Ontario	131 (8-2,700)	2, 14
Near Sudbury refinery	Max. 183,000	13
New York State, Adirondacks region; summer, 1975		
Six lakes	0.4-1.1	16
Lake Champlain (contaminated)	12-15	16
River basins, United States; 1975; dissolved	0.5-0.6; Max. 56.0	4, 13
Smoking Hills, Northwest Territories of combustion of bituminous shales)	6,300 (from atmospheric releases	2
United Kingdom		
River Ivel (receives municipal wastes) vs. River Yare (reference)	28 (11-84) vs. 3.7 (1.3-11.5)	15
United States; 1982; Great Basin of southern Nevada vs. Ohio River basin	Max. <5 vs. Max. >600	7
Rocks, mg/kg		
Acid	5-20	2
Mafic	130-160	2
Sandstone, limestone	5-20	2
Shales	50-70	2
Ultramific	1,400-2,000	2
Seawater, μg/L		
Dissolved		

Table 5. Material and units of concentration	Concentration[a]	Reference[b]
Atlantic Ocean; offshore; surface vs. 400 m	0.10 vs. 0.16	4
Eastern Arctic Ocean; surface vs. 2,000 m	0.13 vs. 0.22	4
Most locations	0.1-0.7	4, 5, 9, 11
Dissolved plus particulate		
Caribbean Sea	2.1	12
Indian Ocean	5.4	12
Northwest Atlantic	3.1-3.5	12
Southwest Atlantic	4.8-19.2	12
Nearshore vs. open ocean	1.8 vs. 1.2	12
Estuaries, Greece		
Euripos Straits; 1980 vs. 1993		
Dissolved	2.5 vs. 1.8	18
Particulate	0.6 vs. 1.4	18
Louros estuary; summer, 1986		
Dissolved; surface vs. 5 m	0.5-7.4 vs. 3.1-9.2	17
Particulate; surface vs. 5 m	Max. 1 vs. Max. 36	17
Sediments, mg/kg DW		
Canada, lake sediments		
Uncontaminated vs. contaminated	<20 vs. >4,000 (Max. 100,000)	2, 14
Precambrian Shield lakes	20-30	14
34% of all samples	<16	2
About 65% of all samples	16-74	2
0.1% of all samples	>75	2
50% of all samples	27	2
15% of all samples	>31	2
Sudbury, Ontario		
About 180 km from Sudbury smelters	<31	4
Within 10 km of smelters	2,500-4,490	4, 12, 13
Europe		
Ems estuary	21-42	12
Louros estuary, Greece; summer 1986	113-242	17
Europos Straits, Greece; 1980 vs. 1993	59 vs. 64	18
Former West Germany	100-210	12
Rhine-Meuse estuary	19-59	12
United States		
Alaska, off northern coast	25-31	4
Casco Bay, Maine	18	4
Eastern Long Island	8	4
Great Lakes	0.1-500	12
Lake St. Clair	14 (9-31)	4
New England	4-58	4
New York; Adirondacks region; six lakes vs. Lake Champlain	0.1-3 vs. 3-5	16
Penobscot Bay, Maine	8-35	4
Rocky Mountain lakes		
four lakes	(10-18)	4
five lakes	(6-38)	4
Washington; Puget Sound; near sewage treatment plant outfall	35-50	19
Sewage liquids, µg/L		
New York City, 1974		
Industrial	100 (70-240)	13
Municipal	50 (10-150)	13

Table 5. Material and units of concentration	Concentration[a]	Reference[b]
Sewage recipients; harbor waters vs. adjacent marine waters	15 vs. 4	13
Wastewater treatment plants	200	11
Sewage sludge, mg/kg DW		
Missouri; 74 publicly owned treatment works (POTW)	33 (10-13,000)	20
United States; 50 POTW	134	20
United States	Max. 53,000	7
Snow, µg/kg DW		
Montreal, Canada	2-300	4
Snow particulates	100-500	4
Soils, mg/kg DW		
Cultivated soils		
Canada	5-50; Max. 950	2, 4, 14
England and Wales	26 (4-80)	4
Farm soils, all locales	Usually 4-80 (<5-1,000)	4, 9, 11, 20
Farm soils, United States; mean vs. too acidic to support plant growth	30 vs. <3	5
Forest soils; nine northeastern states vs. Idaho	11 vs. 12-23	4
Contaminated soils		
Near metal refineries	Max. 24,000 DW	14
Near nickel smelter	80-5,100; Max. 9,372	4, 14
Near nickel smelter, top 5 cm		
Mineral soils; 3 km from smelter vs. 11-18 km distant	500-1,500 vs. 16	21
Organic soils; 1 km from smelter vs. reference site	600-6,455 vs. 29	21
Near Sudbury smelter vs. site 10 km distant	580 (80-2,149) vs. 210 (23-475)	22
Roadside soils, Germany; near road vs. site 5 m from road	32 vs. 8	23
Earth's crust		
Mean	60-90	14
Glacial till	>1,000	4
Podzol soil	5,000	4
United States	13 (<5-700)	4
Wastewaters, µg/L		
Canada; 1988-90; from nickel mining, smelting, and refinery operations	16-27,200	2

[a]Concentrations are shown as means, range (in parentheses), and maximum (Max.).

[b]1, Sunderman 1968; 2, Chau and Kulikovsky-Cordeiro 1995; 3, Sevin 1980; 4, U.S. Public Health Service (USPHS) 1993; 5, National Academy of Sciences 1975; 6, U.S. Environmental Protection Agency (USEPA) 1980; 7, USEPA 1986; 8, Norseth 1986; 9, Norseth and Piscator 1979; 10, Pirrone et al. 1996; 11, World Health Organization 1991; 12, Snodgrass 1980; 13, Kasprzak 1987; 14, National Research Council of Canada 1981; 15, Bubb and Lester 1996; 16, Williams et al. 1977; 17, Scoullos et al. 1996; 18, Dassenakis et al. 1996; 19, Schell and Nevissi 1977; 20, Beyer 1990; 21, Frank et al. 1982; 22, Adamo et al. 1996; 23, Munch 1993; 24, USPHS 1977.

Abiotic Materials

Nickel concentrations are elevated in air, water, soil, sediment, and other abiotic materials in the vicinity of nickel mining, smelting, and refining activities; in coal flyash; in sewage sludge; and in wastewater outfalls (Table 5). Maximum concentrations of nickel found in abiotic materials were 15,300 ng/L in air under conditions of extreme occupational exposure, 19.2 µg/L in seawater, 30 µg/L in rain, 240 µg/L in sewage liquids, 300 µg/L

in drinking water near a nickel refinery, 500 μg/kg in snow, 183,000 μg/L in fresh water near a nickel refinery, 4,430 μg/L in groundwater, 27,200 μg/L in waste water from nickel refineries, 1,600 mg/kg in coal flyash, 2,000 mg/kg in ultramific rocks, 24,000 mg/kg in soils near metal refineries, 53,000 mg/kg in sewage sludge, more than 100,000 mg/kg in lake sediments near a nickel refinery, and 500,000 mg/kg in some meteorites (Table 5).

Nickel in the atmosphere is mainly in the form of particulate aerosols (WHO 1991) resulting from human activities (Sevin 1980). Air concentrations of nickel are elevated near urbanized and industrialized sites and near industries that process or use nickel (USPHS 1993; Chau and Kulikovsky-Cordeiro 1995; Pirrone et al. 1996; Table 5). The greatest contributor to atmospheric nickel loadings is combustion of fossil fuels in which nickel appears mainly as nickel sulfate, nickel oxide, and complex metal oxides containing nickel (USEPA 1986). Nickel concentrations in the atmosphere of the United States are highest in winter and lowest in summer, demonstrating the significance of oil and coal combustion sources (USPHS 1993; Pirrone et al. 1996). Nickel in the atmosphere is removed through rainfall and dry deposition, locating into soils and sediments; atmospheric removal usually occurs in several days. When nickel is attached to small particles, however, removal can take more than a month (USPHS 1993). Cigarette smoke contributes significantly to human intake of nickel by inhalation; heavy smokers can accumulate as much as 15 μg of nickel daily from this source (USEPA 1980).

Most unpolluted Canadian rivers and lakes sampled between 1981 and 1992 contained 0.1-10 μg Ni/L; however, natural waters near industrial sites may contain 50-2,000 μg Ni/L (Chau and Kulikovsky-Cordeiro 1995). Nickel concentrations in snow from Montreal, Canada, are high compared with ambient air (Table 5); nickel burdens in Montreal snow are positively correlated with those of vanadium, strongly suggesting that combustion of fuel oil is a major source of nickel (USPHS 1993). In drinking water, nickel levels may be elevated due to the corrosion of nickel-containing alloys used in the water distribution system and from nickel-plated faucets (USPHS 1993). Nickel concentrations in uncontaminated surface waters are usually lower with increasing salinity or phosphorus loadings (USPHS 1993). Nickel tends to accumulate in the oceans and leaves the ocean as seaspray aerosols which release nickel-containing particles into the atmosphere (USEPA 1986).

Sediment nickel concentrations are grossly elevated near the nickel-copper smelter at Sudbury, Ontario, and downstream from steel manufacturing plants. Sediments from nickel-contaminated sites have between 20 and 5,000 mg Ni/kg DW; these values are at least 100 times lower at comparable uncontaminated sites (Chau and Kulikovsky-Cordeiro 1995). A decrease in the pH of water caused by acid rain may release some of the nickel in sediments to the water column (NRCC 1981). Transfer of nickel from water column to sediments is greatest when sediment particle size is comparatively small and when sediments contain high concentrations of clays or organics (Bubb and Lester 1996).

In soils, nickel exists in several forms, including inorganic crystalline minerals or precipitates, as free ion or chelated metal complexes in soil solution, and in various formulations with inorganic cationic surfaces (USEPA 1986). Soil nickel is preferentially adsorbed onto iron and manganese oxides (USPHS 1993; Chau and Kulikovsky-Cordeiro 1995); however, near Sudbury, Ontario, soil nickel is mostly associated with inorganic sulfides (Adamo et al. 1996). The average residence time of nickel in soils is estimated at 3,500 years, as judged by nickel concentrations in soils and estimates of the loss of nickel from continents (Nriagu 1980b). Natural levels of soil nickel are augmented by contamination from anthropogenic activities including atmospheric fallout near nickel-emitting industries, automobile traffic, and treatment of agricultural lands with nickel-containing phosphate fertilizers or municipal sewage sludge (USEPA 1980; Munch 1993). Soils with less than 3 mg Ni/kg DW are usually too acidic to support normal plant growth (NAS 1975). Nickel availability to plants grown in sludge-amended soils is correlated with soil-solution nickel (USPHS 1993). Sewage-derived fertilizers from industrial areas may contain 1,000 mg Ni/kg DW or more (NRCC 1981). In sewage sludge, a large percentage of the nickel exists in a form that is easily released from the solid matrix (USPHS 1993). Water solubility of nickel in soils and its bioavailability to plants are affected by soil pH, with decreases in pH below 6.5 generally mobilizing nickel (USPHS 1993; Chau and Kulikovsky-Cordeiro 1995).

Terrestrial Plants and Invertebrates

Nickel is found in all terrestrial plants, usually at concentrations of less than 10 mg/kg DW (NRCC 1981; Kasprzak 1987). The majority of terrestrial plants are nickel-intolerant species and are restricted to soils of relatively low nickel content; some plants without specific nickel tolerance can accumulate anomalous levels of nickel, but at a cost of reduced metabolism (Rencz and Shilts 1980). Plants grown on nickel-rich soils can accumulate high concentrations of nickel (Sigel and Sigel 1988). Crops grown in soils amended with sewage

sludge may contain as much as 1,150 mg Ni/kg DW (USEPA 1986). Vegetation near point sources of nickel, such as nickel refineries, have elevated nickel concentrations that decline with increasing distance from the source (WHO 1991; Table 6). Fruits and vegetables grown near nickel smelters contain 3-10 times more nickel in edible portions than those grown in uncontaminated areas (NRCC 1981). Trees, ferns, and grasses near nickel smelters had elevated concentrations of nickel, as much as 174 mg/kg DW in trees and ferns and 902 mg/kg DW in wavy hairgrass (*Deschampsia flexuosa*; Table 6). Nickel concentrations in lichens and other vegetation were elevated when grown on nickeliferous rocks, serpentine soils, near nickel smelters (Jenkins 1980b), near urban and industrial centers (Richardson et al. 1980), and near roadsides treated with superphosphate fertilizers (NAS 1975).

Table 6. Nickel concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in field collections of representative plants and animals.

Table 6. Taxonomic group, organism, and other variables	**Concentration (mg/kg)[a]**	**Reference[b]**
Terrestrial Plants		
Red maple, *Acer rubrum*; leaf; various distances from nickel smelter		
2 km	98 DW	1
20 km	57 DW	1
40 km	14 DW	1
Onion, *Allium cepa*; spring vs. fall		
Leaf	9.4 DW vs. 3.8 DW	1
Root	18.4 DW vs. 10.9 DW	1
Celery, *Apium graveolans*; spring vs. fall		
Leaf	36 DW vs. 5 DW	1
Root	32 DW vs. 3 DW	1
Paper birch, *Betula papyrifera*; leaf; various distances from nickel smelter; June vs. August		
1.0 km	158 DW vs. 148 DW	1
4.6 km	82 DW vs. 111 DW	1
12.0 km	66 DW vs. 64 DW	1
Coffee, *Coffea arabacia*; green beans	0.1-0.3 FW	1
Sweet fern, *Comptonia peregrina*; leaf; various distances from nickel smelter; August		
1.0 km	174 DW	1
6.5 km	46 DW	1
31.0 km	15 DW	1
Lichen, *Compylium polyanum*; whole; from serpentine soils	420 DW	1
Wavy hairgrass, *Deschampsia flexuosa*; leaf; various distances from nickel smelter		
1.7 km	902 DW	1
2.1 km	242 DW	1
7.4 km	160 DW	1
20.4 km	43 DW	1
52.7 km	37 DW	1
Tall fescue, *Festuca* sp.; shoot; Maryland; various distances from highway		
8 m	(3.8-5.0) DW	1
16 m	(2.5-3.8) DW	1
32 m	(1.3-2.8) DW	1
Forest species; Nagoya University, Japan; leaves		
57 species	2-8 DW	2

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
3 species	10-16 DW	2
Grasses, various species; near roadside vs. >30 m from roadside	3.8 DW vs. 1.3 DW	3
Hypnum moss, *Hypnum cupressiforme*; whole; United Kingdom; downwind of nickel industrial complex <3 km	All dead; no residues measured	1
8 km	193 DW	1
25 km	420 DW	1
Lettuce, *Lactuca sativa*; spring vs. fall		
Leaf	28 DW vs. 3 DW	1
Root	15 DW vs. 4 DW	1
Lichens		
Industrial sites; 13 species	2-52 DW	4
Near nickel smelters; three species	220-846 DW	4
Rural sites		
Mineralized substrates; 19 species	1-115 DW	4
Nonmineralized substrates; 13 species	1-10 DW	4
Urban sites; two species	33-183 DW	4
Macrophytes, four species; 1.6 km from smelter (soil had 2,679 mg Ni/kg DW)	109-902 DW	5
Mosses, 4 species; isolated areas	0.2-5.0 DW	4
Nickel hyperaccumulator plants		
Allysum spp.; various locations		
Flowers	Max. 5,400 DW	1
Fruits	Max. 5,800 DW	1
Leaves	2,590-9,330 DW; Max. 20,400 DW	1, 6
Roots	Max. 3,100 DW	1
Seeds	Max. 6,100 DW	1
Stems	Max. 13,500 DW	1
Geissosis prainosa; New Caledonia; leaves	6,720 DW	6
Homalium spp; New Caledonia; nine species; leaves		
Three species	3,730-9,580 DW	6
Three species	446-662 DW	6
Three species	15-75 DW	6
Hybanthus spp.; New Caledonia; two species; leaves	6,820-14,900 DW	6
Pearsonia metallifera; Rhodesia; leaves	10,600 DW	6
Planchonella oxyedra; southeast Asia; leaves	1,600 (50-19,600) DW	1
Psychotria douarrei; New Caledonia; leaf	13,400 DW; Max, 47,000 DW	1, 6
Sebertia acuminata; New Caledonia		
Latex	112,000 FW; 167-257,000 DW	1, 6
Leaves	10,200-11,700 DW	1, 6
Rice, *Oryza sativa*; Japan; polished vs. unpolished grain	0.50-0.65 FW vs. 1.8 FW	1
Moss, *Pleurozium schreberi*		
Near nickel smelter	Max. 195 DW	4
Rural sites	1-34 DW	4
Urban sites	Max. 100 DW	4
Red oak, *Quercus rubra*; leaf; 1.6 km vs. 10.6 km from nickel smelter	(79-108) DW vs. (12-57) DW	1
Spinach, *Spinacia oleracea*; leaf		
Alabama	2.3 DW	1

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
New Jersey	2.2 DW	1
World, 44 varieties	4.2 DW	1
United States	0.35 FW	1
Lichen, *Umbilicaria* sp.; whole; 16 km vs. 90 km from nickel smelter	220 DW vs. 37 DW	1
Terrestrial vegetation		
Hyperaccumulator plants	>1,000 DW	5
Most species	0.05-5.0 DW (>50 DW is toxic)	5
Vegetables		
Grown on soils containing 558 mg Ni/kg DW through sewage sludge application		
Beans and peas	42-65 DW	5
Green vegetables, cabbage, onions	11-65 DW	5
Root vegetables	8-27 DW	5
Grown on nickel-contaminated soils (>1,500 mg Ni/kg DW surface soils) vs. reference site		
Heads and tops	15-400 DW vs. Max. 5.0 DW	8
Roots	24-280 DW vs. Max. 5.0 DW	8
Near nickel smelter vs. reference site; edible portions		
Cabbage, *Brassica oleracea capitata*	4.7 DW vs. 1.2 DW	7
Lettuce, *Lactuca sativa*	11.0 DW vs. 3.5 DW	7
Corn, *Zea mays*	2.8 DW vs. 1.1 DW	7
Wheat, *Triticum aestivum*; from sludge-amended soil (19.4 mg Ni/kg DW soil) vs. nonsludge-amended soil	0.98 DW vs. 0.40 DW	9
Lowbush blueberry, *Vaccinium angustifolium*; leaf; various distances from nickel smelter		
1.7 km	92 DW	1
7.4 km	45 DW	1
52.7 km	14 DW	1
Corn, *Zea mays*		
Grain vs. root	(0.1-5.0) DW vs. 28.0 DW	1
Grown on soil containing 745 mg Ni/kg DW		
Kernels	2.3-4.3 DW	5
Leaves	6.7-10.7 DW	5
Stems	4.3-5.5 DW	5
Aquatic Plants		
Algae and macrophytes: nickel-contaminated areas vs. reference sites	About 150 DW vs. usually <15 DW	5
Brown alga, *Ascophyllum nodosum*		
Norway	(1-22) DW	1
Nova Scotia	0.6 DW	1
Former Soviet Union	0.4 DW	1
Scotland	0.9 FW; (1.5-6.3) DW	1
Alga, *Cymodocea* sp.; Puerto Rico	2.1 (1.5-2.6) FW; 24 (19-29) DW	1
Bladder wrack, *Fucus vesiculosus*		
England	(1.2-29.6) DW	1
Greenland	(0.6-2.3) DW	1
Norway	(2-7) DW	1

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Nova Scotia	2 DW	1
Scotland	1.4 FW; 4.9 DW	1
Duckweed, *Lemna minor*; from ponds (27 µg Ni/L) in southern Ontario, Canada	5.4-35.1 DW	5
Marine algae and macrophytes		
England, 14 species	2.7-10.3 DW	10
India, 27 species	3.5-39.1 DW	10
Japan, 60 species	0.2-31.0 DW	10
Texas, Harbour Island, 14 species	0.2-2.6 DW	10
Pond lily, *Nuphar* sp.; Ontario, Canada; nickel-contaminated areas		
Leaf	8-62 FW	1
Peduncle	3-9 FW	1
Petiole	5-35 FW	1
Root	5-14 FW	1
Laver, *Porphyra umbilicalis*; whole	0.2-9.7 DW	1
Sargassum, *Sargassum* spp.; Gulf of Mexico; whole	0.9-15.6 DW	10
Smooth cordgrass, *Spartina alterniflora*; leaves	5.3 DW	1
Terrestrial Invertebrates		
Earthworm, *Allolabophophora* sp.; whole; Maryland	12.9-37.5 DW	1
Beach flies, two species; whole; California	Max. 7.0 DW	1
Gypsy moth, *Porthetria dispar*; near ore smelter at Sudbury, Ontario, Canada vs. reference site		
Adult males; whole	8.8 DW vs. 2.9 DW	11
Larvae		
Feces	28 DW (reflects nickel content	11
of leaf diet) vs. <2 DW		
Whole	20.4 DW vs. 0.4-7.2 DW	11
Pupae	1.5 DW vs. 1.6 DW	11
Termites, *Odontotermes transvaalensis*, *Trinervitermes dispar*; whole		
Queen	20 DW	1
Soldier	100 DW	1
Worker	5,000 DW	1
Aquatic Invertebrates		
Protozoans, marine		
Foraminiferan tests	15.4-23.0 DW	10
Radiolarians, whole	3.7 DW	10
Sponge, *Halichondria* sp.; whole; Sweden	22.0 DW	1
Corals; open ocean species vs. shallow coastal zone species	<2.0-23.0 DW vs. Max. 3.0 DW	10
Mollusks		
Duck mussel, *Anodonta anatina*; Thames River, England; soft parts; near sewage outfall	Max. 46.0 DW	12
Ocean quahog, *Arctica islandica*; soft parts		
Long Island, New York; 1974-75; offshore	1.1-7.0 FW	13
New England; offshore; February vs. March	5-29 DW vs. 4-18 DW	10
Waved whelk, *Buccinum undatum*; soft parts; near sludge dump site vs. reference site	8.5 DW vs. 0.6 DW	1

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Scallop, *Chlamys opercularis*		
Digestive gland	4.3 DW	10
Kidneys	78.2 DW	10
Shell	(0.2-7.6) DW	10
Other tissues	0.2-1.6 DW	10
Pacific oyster, *Crassostrea gigas*; soft parts		
South Africa	Max. 2.0 DW	1
United Kingdom	(1-10) DW	1
United States	Max. 0.2 FW	1
World	0.1-1.6 DW	10
Eastern oyster, *Crassostrea virginica*; shell vs. soft parts	<1.0 DW vs. (0.9-5.4) DW; 0.19 (0.08-1.8) FW	1, 10
Common Atlantic slippersnail, *Crepidula fornicata*; United Kingdom; shell vs. soft parts	1.6 DW vs. 127.0 FW; 850.0 DW	1, 10
Red abalone, *Haliotis rufescens*; California		
Digestive gland	(3-11) DW	1, 10
Foot	(0.2-1.6) DW	1, 10
Gills	(69-112) DW	1, 10
Mantle	(19-57) DW	1, 10
Abalone, *Haliotis tuberculata*; soft parts; England	13.6-15.9 DW	14
Marine mollusks; 21 species; soft parts	Max. 3.4 FW	10
Northern quahog, *Mercenaria mercenaria*; soft parts		
United Kingdom	2.2 FW; (6.5-19.2) DW	1
United States	1.2 (0.1-2.4) FW	1
Common mussel, *Mytilus edulis*; soft parts		
France	0.5 FW; 2.4 DW	1
The Netherlands, 1985-90	0.33-0.52 FW	15
Norway	(6-43) DW	1
United Kingdom	0.4 FW; Max. 53.0 FW; 3.7 (5-12) DW	1
United States	(11-14) DW	1
Mud snail, *Nassarius* sp.; soft parts; Los Angeles, California	36 DW	1
Common limpet, *Patella vulgata*; soft parts		
Israel; near sewage discharge vs. control site	12 DW vs. 5-9 DW	1
Norway	(4-11) DW	1
United Kingdom	7.3 (2.5-24.0) DW	1
Pen shell, *Pinna nobilis*; contaminated area		
Byssus gland	200 DW	10
Gonads	74 DW	10
Nervous system	18 DW	10
Soft parts	21 DW	10
Stomach plus intestines and hepatopancreas	170 DW	10
Sea scallop, *Placopecten magellanicus*		
Long Island, New York; 1974-75; soft parts	(<0.5-3.3) FW	13
North Atlantic coast, 42 stations		
Gonads	0.2-2.5 FW	16
Muscle	<0.3-0.7 FW	16
Viscera	0.3-1.6 FW	16
Vicinity ocean disposal sites; soft parts	4.4 DW	17
Clam, *Scrobicularia plana*		

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Contaminated estuary, soft parts	Max. 11.9 DW	18
United Kingdom; digestive gland		
Camel estuary	10.6 DW	10
Gannel estuary	43.1 DW	10
Tamar estuary	(6.6-25.0) DW	10
Arthropods		
Amphipods; whole; Antarctica	2.2 DW	19
Green crab, *Carcinus maenas*; all tissues	6.2-12.3 FW	1
Sand shrimp, *Crangon allmanni*;	15 DW vs. 92 DW	1
Scotland; soft parts; reference site vs. waste dump site		
Seaskaters (oceanic insects), *Halobates* spp.,	6-18 DW	20
Rheumobates sp.; whole; from mangrove swamps		
American lobster, *Homarus americanus*; serum	0.012 (0.008-0.020) FW	3, 21
Marine crustaceans		
Muscle, 10 species	0.2-0.9 FW	10
Whole, various species	6.5-9.8 FW	10
Aesop shrimp, *Pandalus montagui*;	25 DW vs. 70 DW	1
soft parts; Scotland; reference site vs. waste dump site		
Caribbean spiny lobster, *Panulirus argus*; soft parts;		
Puerto Rico		
Anasco Bay	1.3 (1-2) FW; 4.5 (8-9) DW	1
West coast	4.6 (1.4-5.0) FW; 36 (22-60) DW	1
Brown shrimp, *Penaeus aztecus*; Texas		
Exoskeleton	6.2 DW; Max. 17.9 DW	1
Muscle	1.4 DW; Max. 1.9 DW	1
Viscera	5.7 DW; Max. 5.8 DW	1
Zooplankton; New York Bight vs. Long Island Sound	1.7-4.6 DW vs. 0.9-4.5 DW	22
Annelids, marine		
Sandworm, *Nereis diversicolor*; whole;	2.1-5.2 DW	10
British Columbia; various locations		
Polychaete worms, three species;	(3.8-18.7) DW	1
whole; California		
Echinoderms		
Starfish, *Asterias rubens*		
Gonad	2.4 DW	10
Pyloric caeca	4.1 DW	10
Other tissues	0.7-1.5 DW	10
Rock boring sea urchin, *Echinometra lucunter*; Puerto Rico; skeleton vs. whole	51 (42-78) DW vs. 37 DW	1
Sea urchin, *Tripneustes esculentus*; Puerto Rico		
Ovary	1.4 FW	1
Skeleton	35 (18-54) DW	1
Testes	22 FW	1
Tunicate, *Halocynthia roretzi*; whole	0.1 FW	10
Fishes and Elasmobranchs		
Rock bass, *Ambloplites rupestris*; near smelter; Sudbury, Ontario, Canada		
Gills	31.7 FW	1
Kidneys	17.3 FW	1

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Livers	17.0 FW	1
Muscle	12.5 FW	1
Whitetip shark, *Carcharhinus longimanus*		
Liver	0.05 FW; 0.1 DW	1
Skin	1.9 FW; 7.3 DW	1
Vertebrae	1.6 FW; 4.9 DW	1
White sucker, *Catostomus commersoni*; muscle; near smelter vs. reference site	13.2 FW vs. 0.1 FW	1
Blackfin icefish, *Chaenocephalus aceratus*; Antarctica; muscle vs. liver	0.2 DW vs. 0.3 (0.2-0.5) DW	19
Lake whitefish, *Coregonus clupeaformis*; muscle; northern Quebec; 1989-90	<0.01 FW	23
Lumpfish, *Cyclopterus lumpus*; United Kingdom; all tissues	3.2-5.2 FW	1
Northern pike, *Esox lucius*; muscle		
Canada		
Ontario; near smelter	13.3 FW	1
Northern Quebec, 1989-91	<0.05-0.05 FW	23
Illinois vs. New York	0.15 (0.08-0.19) FW vs. (0.2-3.8) FW	1
Muskellunge, *Esox masquinongy*; muscle; New York	0.2-1.3 FW	1
Chain pickerel, *Esox niger*; muscle; New York	0.1-0.25 FW	1
Pickerel, *Esox* sp.; near smelter; Sudbury, Ontario		
Gills	16.0 FW	1
Kidneys	51.6 FW	1
Livers	14.4 FW	1
Muscle	13.8 FW	1
Skipjack tuna, *Euthynnus pelamis*; muscle		
Peru	2.0 FW; 5.0 DW	1
Puerto Rico	0.5 FW; 2.2 DW	1
Fishes, 10 species; muscle; Bay of Bengal, India	0.7-6.1 DW	24
Atlantic cod, *Gadus morhua*; all tissues	1.6-4.6 FW	1
Brown bullhead, *Ameiurus nebulosus*; near smelter;		
Canada		
Gills	11.1 FW	1
Kidneys	11.8 FW	1
Livers	10.7 FW	1
Muscle	9.5 FW	1
Yellowtail flounder, *Pleuronectes ferruginea*; New York Bight; liver vs. muscle	0.2-1.1 FW vs. <0.2-0.4 FW	1
Marine fishes		
Liver; five species; New York Bight; 1971-73	<0.2-1.7 FW	25
Most species; all tissues	Usually <0.3 FW; rarely >3.0 FW in uncontaminated areas; Max. 16.0 DW	10
Muscle		
New Zealand, nine species	0.02-0.07 FW	1
United Kingdom, eight species	2.1-3.5 DW	1
Atlantic croaker, *Micropogonias*	2.7 DW vs. 3.8 DW	1

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
undulatus; Texas; muscle vs. skin		
Smallmouth bass, *Micropterus dolomieu*; muscle; New York vs. Illinois	(0.16-1.2) FW vs. 0.13 (0.08-0.19) FW	1
Largemouth bass, *Micropterus salmoides*; muscle; New York vs. Illinois	(0.18-1.9) FW vs. 0.11 (0.05-0.23) FW	1
Dover sole, *Microstomus pacificus*; California; muscle vs. liver	0.2 (0.1-0.3) FW vs. 1.4-2.6 FW	1
Hump rock cod, *Notothenia gibberfrons*; muscle; Antarctica	0.22 DW	19
Rainbow trout, *Oncorhynchus mykiss*		
Kidney, liver	Usually <1.5 FW	5
Muscle	Usually <0.5 FW	5
Kelp bass, *Paralabrax clathratus*; California		
Gonad	1.5-2.2 DW	1
Liver	3.9-7.6 DW	1
Muscle	5.0-6.4 DW	1
Skin	9.0-10.2 DW	1
Winter flounder, *Pleuronectes americanus*		
New York Bight; muscle vs. skin	<0.3-0.5 FW vs. <0.3-1.0 FW	1
Texas; muscle vs. skin	3.3 (0.6-7.4) DW vs. 4.4 (2.9-7.4) DW	1
Lake trout, *Salvelinus namaycush*; whole less head and viscera; New York		
Ages 1-4 years	Max. 0.009 FW	1
Ages 5-8 years	Max. 0.022 FW	1
Ages 9-12 years	Max. 0.022 FW	1
Sharks, 10 species; British and Atlantic waters; 1984-88; inshore species vs. offshore species		
Gills	0.3-1.8 FW vs. 1.7-1.9 FW	26
Gonads	<0.02-8.3 FW vs. 1.7 FW	26
Heart	No data vs. 2.8 FW	26
Jaws	5.7 FW vs. 0.3 FW	26
Kidneys	0.07-1.2 FW vs. 1.6 FW	26
Liver	<0.02-0.8 FW vs. 1.9-3.2 FW	26
Muscle	<0.02-1.8 FW vs. 1.4-2.6 FW	26
Pancreas	0.9 FW vs. No data	26
Skin	<0.02-3.4 FW vs. 1.0-2.0 FW	26
Spleen	<0.02-0.8 FW vs. 1.3 FW	26
Vertebrae	0.5-2.4 FW vs. 0.2-10.8 FW	26
South Carolina; gamefish; 1990-93; whole		
Spotted seatrout, *Cynoscion nebulosus*	Max. 12.6 FW	27
Southern flounder, *Paralichthys lethostigma*	Max. 8.2 FW	27
Red drum, *Sciaenops ocellatus*	Max. 2.9 FW	27
Scup, *Stenotomus chrysops*; Texas		
Muscle	1.0 (0.5-2.0) DW	1
Skin	4.9 (2.8-7.4) DW	1
Viscera	3.5 DW	1
Amphibians		
Maryland; 1991; tadpoles		
Northern cricket frog, *Acris crepitans*; whole	2.4-10.0 DW	28
Gray treefrog, *Hyla versicolor*; whole	2.0-7.1 DW	28

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Green frog, *Rana clamitans*; body vs. gut coil	4.7 DW vs. 16.4 DW	28
Birds		
Wood duck, *Aix sponsa*; ducklings; liver; Ontario, Canada; polluted area	0.2 FW	29
Mallard, *Anas platyrhynchos*		
Canada; nickel-contaminated areas vs. reference site		
Liver	0.1-1.4 FW vs. 0.2 FW	29
Muscle (breast)	0.1-0.8 FW vs. 0.6 FW	29
New Jersey; Raritan Bay; contaminated environment; liver vs. salt gland	0.1-2.5 FW vs. 9.7 FW	30, 31
Primary flight feathers; 1975; various distances from nickel smelter		
20-30 km	2.0-12.5 DW; Max. 36.7 DW	32
50-60 km	0.2-3.8 DW	32
85 km	0.2-1.5 DW	32
95-140 km	0.0-4.3 DW	32
Reference site	0.0-0.4 DW	32
Black duck, *Anas rubripes*		
Canada; ducklings; nickel-contaminated vs. reference site		
Kidney	0.3 FW vs. 0.3 FW	29
Liver	0.6 FW vs. 0.4 FW	29
Canada; primary feathers; contaminated vs. noncontaminated areas	2.5-3.7 DW vs. 0.2-1.5 DW	32
Raritan Bay, New Jersey; liver vs. salt gland	0.2-2.7 FW vs. 15.2 FW	30, 31
Gadwall, *Anas strepera*; Canada; muscle; contaminated area	0.3 FW	29
Antarctica; February-March 1989		
Gentoo penguin, *Pygoscelis papua*; muscle vs. liver	<0.03 DW vs. 0.09 DW	19
Adelie penguin, *Pygoscelis adeliae*; muscle vs. liver	<0.03 DW vs. 0.06 DW	19
Chinstrap penguin, *Pygoscelis antarctica*		
Feces	3.5 (3.2-3.7) DW	19
Liver	0.07 DW	19
Muscle	<0.03 DW	19
Blue-eyed cormorant, *Phalocrocorax atriceps*; muscle	0.29 DW	19
South giant petrel, *Macronectes giganteus*; muscle	0.06 DW	19
Redhead, *Aythya americana*; Texas and Louisiana; liver; winter 1987-88	<4.0 DW	33
Ring-necked duck, *Aythya collaris*; ducklings; contaminated vs. reference location		
Kidney	0.3 FW vs. 0.1 FW	29
Liver	0.5 FW vs. 0.2 FW	29
Greater scaup, *Aythya marila*; contaminated areas		
Ontario; muscle	0.2 FW	29
New Jersey; liver vs. salt gland	0.3-3.6 FW vs. 2.7 FW	30, 31
Canvasback, *Aythya valisineria*; Louisiana; winter 1987-88; liver	Usually <1.0 DW; Max. 2.0 DW	34

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Ruffed grouse, *Bonasa umbellus*		
Canada; nickel-contaminated vs. reference areas		
May		
Feathers, primaries	7.3 DW vs. 2.9 DW	35
Dung	19.4 DW vs. <0.5 DW	35
Kidney	2.8 DW vs. 1.7 DW	35
Liver	1.0 DW vs. 0.9 DW	35
Muscle	1.4 DW vs. <0.5 DW	35
September		
Feathers, primaries	4.8 DW vs. 0.8 DW	35
Dung	47.7 DW vs. <0.5 DW	35
Kidney	2.1 DW vs. <0.5 DW	35
Liver	3.5 DW vs. 0.7 DW	35
Muscle	0.2 DW vs. 0.2 DW	35
New England		
Kidney	5.0 DW	1
Liver	1.1-2.4 DW	1
Common goldeneye, *Bucephala clangula*; ducklings; Canada; contaminated vs. reference areas		
Kidney	0.3 FW vs. 0.1 FW	29
Liver	0.5 FW vs. 0.8 FW	29
Turkey vulture, *Cathartes aura*; California; kidney vs. liver	<0.1-0.4 FW vs. <0.1 FW	36
Common raven, *Corvus corax*; California; kidney vs. liver	<0.1-0.12 FW vs. <0.1 FW	36
American coot, *Fulica americana*; Ontario; muscle	1.5 FW	37
Domestic chicken, *Gallus* sp.; serum; United States	0.0036 (0.0033-0.0053) FW	3, 21
Common loon, *Gavia immer*; Ontario; muscle	1.1 FW	37
California condor, *Gymnogyps californianus*; feathers	0.5-2.0 DW	36
Willow ptarmigan, *Lagopus lagopus*; near nickel smelter; 1990-93; Norway; kidney	Max. 2.3 DW	38
Herring gull, *Larus argentatus*; Ontario; muscle	1.0 (0.6-1.3) FW	37
Lesser black-backed gull, *Larus fuscus*; Norway		
Kidney	5.0 DW	1
Liver	2.0 DW	1
Muscle	5.0 DW	1
Hooded merganser, *Lophodytes cucullatus*; ducklings; nickel-contaminated vs. reference areas		
Kidney	1.2 FW vs. 1.0 FW	29
Liver	0.07 FW vs. 0.14 FW	29
Turkey, *Meleagris gallopavo*; liver vs. muscle	0.002 FW vs. 0.015 FW	39
Black-crowned night-heron, *Nycticorax nycticorax*; liver; northeastern United States; nickel-contaminated vs.reference areas	<0.1-9.2 DW vs. <0.1 DW	40
Owl (species unidentified); Germany; polluted area vs. reference site; tail feathers		
Lower feather	2.0 FW vs. 1.6 FW	41
Upper feather	14.3 FW vs. 2.0 FW	41
Osprey, *Pandion haliaetus*; liver	<0.2-0.3 FW	42
Brown pelican, *Pelecanus occidentalis*		

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Egg	Max. 0.072 FW	1
Liver	Max. 0.078 FW	1
Common eider, *Somateria mollissima*; Norway		
Egg, liver	1.0 DW	1
Muscle, kidney	2.0 DW	1
Common tern, *Sterna hirundo*		
Rhode Island; 1981; immatures; liver vs. diet	Max. 1.0 DW vs. 0.8-2.1 DW	43
Hamilton Harbor, Ontario vs. Long Island Sound, New York		
Bone	Max. 19 DW vs. Max. 36 DW	44
Kidney	Max. 9 DW vs. Max. 26 DW	44
Liver	<5 DW vs. < 5 DW	44
Muscle	<2 DW vs. <2 DW	44
Tree swallow, *Tachycineta bicolor*; Hackensack River, New Jersey (contaminated area)		
Brain, prefledgling	27.6 FW	45
Eggshell	31.4 FW	45
Embryo, whole	1.6 FW	45
Feather	4.3 FW	45
Gizzard	9.4 FW	45
Liver	23.8 FW	45
Muscle	7.6 FW	45
American robin, *Turdus migratorius*; New England; kidney vs. liver	1.7 FW vs. 0.9 FW	1
Terrestrial Mammals		
Cow, *Bos* sp.		
Blood, whole	0.011 FW	39
Blood, plasma	0.0017-0.0044 FW	39
Bone	0.58 FW	1
Feces	0.75 FW	1
Kidney	0.01-0.66 FW	1
Liver	0.13 FW	39
Muscle	Not detectable	1
Pancreas	0.14 FW	39
Goat, *Capra hircus*; serum; England	0.0035 (0.0027-0.0044) FW	21
Common beaver, *Castor canadensis*		
Ontario, Canada; 1986-87; adults; near nickel smelter vs. reference site		
Kidney	2.6 DW vs. 1.5 DW	46
Liver	1.5 DW vs. 1.1 DW	46
Ontario; uncontaminated site		
Intestine	0.4 FW	47
Kidney	0.4 FW	47
Liver	0.5 FW	47
Muscle	0.9 (0.6-1.3) FW	48
Least shrew, *Cryptotis parva*; Virginia; whole body; polluted areas vs. reference sites	1.3-1.6 DW vs. 0.8 DW	49
Horse, *Equus caballus*; serum; United States	0.002 (0.0013-0.0025) FW	21
Human, *Homo sapiens*		
Adrenal gland	0.13 (0.05-0.34) DW	50
Average daily intake, in mg Ni/kg body weight (BW) daily; Canada		

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
General population; age >12 years vs. age <12 years		
Air	Max. 0.000007 vs. Max. 0.000009	51
Water	Max. 0.00016 vs. Max. 0.00077	51
Food	0.0044-0.0057 vs. Max. 0.022	51
Soil	Max. 0.000018 vs. Max. 0.00025	51
Tobacco smoking	Max. 0.00015 vs. no data	51
Canadians living near nickel point sources; age >12 years vs. age <12 years		
Air	Max. 0.000008 vs. Max. 0.000009	51
Water	Max. 0.0025 vs. Max. 0.012	51
Food	Max. 0.0057 vs. Max. 0.022	51
Soil	Max. 0.00013 vs. Max 0.0019	51
Blood, plasma		
Workers from nickel refinery	0.0064-0.0119 FW	52
Occupationally exposed workers vs. same workers after 2-week vacation	0.0102-0.0111 FW vs. 0.0053 FW	3
Normal	0.0016-0.0020 FW	3
Blood, whole; normal	0.003-0.007 FW	52, 53
Blood, serum		
Near nickel mine	0.0046 FW	52
Normal	0.0026 (0.0011-0.0046) FW	3, 21, 52, 53, 54
Diet		
Condiments		
Most	<1.0 FW	3
Baking powder	13.4 FW	54
Nutmeg	1.2 FW	54
Pepper, black	3.9 FW	54
Fish and seafoods		
Most	<0.3 FW	3, 55
Salmon, muscle	1.7 FW	3, 39
Oysters, soft parts	1.5 FW	3, 39
Shrimp, muscle	0.03 FW	39
Swordfish	0.02 FW	39
Fruits and vegetables	Usually 0.02-0.65 FW; Max. 2.6 FW	3, 55
Grains and grain products	Usually 0.2-1.3 FW; Max. 2.7-6.4 FW	3, 39, 55
Liquids		
Beer, wine, soft drinks	0.01-0.2 FW	3, 39
Cocoa	5.0 FW	54
Coffee	1.0 FW	39
Drinking water	0.0048 (0.001-0.2)FW	39
Tea, orange pekoe	7.6 FW	54
Meats		
Beef, pork	0.06-0.4 FW	39
Chicken	0.14-0.24 FW	39
Feces, normal	3.3 (2.1-4.4) FW; 14.2 (10.8-18.7) DW	54
Hair		
Near refineries	3.6 (1.1-32.0) DW	3

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Rural areas	2.1 (1.6-17.0) DW	3
Urban areas	2.4 (1.2-20.0) DW	3
Heart, normal	0.0061 FW; 0.023 DW	54
Kidney, normal	1.82 DW	3
Liver, normal	1.85 DW	3
Lung		
Bituminous coal miners vs. controls	2.5 DW vs. 0.6 DW	56
Normal	0.17 (0.07-0.37) DW	50
Perspiration; males vs. females	0.052 (0.007-0.182) FW vs.	53, 54
0.131 (0.039-0.270) FW		
Spleen, normal	1.72 DW	3
Thyroid, normal	0.14 (0.04-0.24) DW	50
Urine		
Normal	0.001-0.005 FW	3, 52, 53
Nickel battery workers	0.0117 FW	3
Nickel plate workers	0.0275 FW	3
Nickel refinery workers	0.222 FW	3
(atmospheric nickel =489 $\mu g/m^3$)		
Near nickel refinery	0.045-0.129 FW	52
Snowshoe hare, *Lepus americanus*;	0.2 FW	57
whole; Wisconsin		
River otter, *Lutra canadensis*; Ontario, Canada; reference areas vs. nickel-contaminated areas		
Kidney	0.7 FW vs. 0.44 FW	47, 58
Liver	0.4-0.5 FW vs. 0.5 FW	47, 58
Muscle	0.9 (0.6-1.0) FW vs. no data	47, 48
Mammals; serum; healthy adults		
Normal levels for horses, humans,	0.0020-0.0027 (0.0009-0.0046) FW	3
cattle, dogs, and rats		
Normal levels for goats, cats,	0.0035-0.0053 (0.0015-0.0083) FW	3
guinea pigs, hamsters, and swine		
Normal for rabbits	0.0093 (0.0065-0.0140) FW	3
Meadow vole, *Microtus pennsylvanicus*; whole		
Virginia; contaminated area vs. reference site	Max. 2.5 DW vs. Max. 1.8 DW	49
Wisconsin; near undeveloped ore deposits	Max. 2.6 FW	57
House mouse, *Mus musculus*		
Kidney	0.46-0.52 FW	1, 39
Liver	(0.02-0.62) FW	1, 39
Lung	(0.32-0.61) FW	1, 39
Mink, *Mustela vison*		
Illinois; 1984-89; trapped		
Kidney	1.1 (0.4-6.6) FW	59
Liver	0.9 (0.3-2.6) FW	59
Muscle	0.7 (0.3-1.5) FW	59
Ontario, Canada; nickel-contaminated area vs. reference area		
Kidney	0.6 FW vs. 0.6 FW (same)	58
Liver	0.7 FW vs. 0.7 FW (same)	58
Norway; 1990-91; near nickel processing plants vs. reference site		
Moose, *Alces alces*		
Kidney	0.19 FW vs. 0.12 FW	60

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Liver	0.02 FW vs. <0.01 FW	60
Domestic sheep, *Ovis aries*		
Kidney	0.03 FW vs. 0.03 FW (same)	60
Liver	0.01 FW vs. 0.01 FW (same)	60
Caribou, *Rangifer tarandus*		
Kidney	0.28 FW vs. 0.13 FW	60
Liver	0.09 FW vs. 0.02 FW	60
Mule deer, *Odocoileus hemionus*; Montana; kidney and liver	Max. 3 DW	61
White-tailed deer, *Odocoileus virginianus*; kidney vs. liver	0.0-2.9 FW vs. 0.0-2.5 FW	1
Rabbit, *Oryctolagus* sp.; serum; New Zealand	0.0093 (0.0065-0.0140) FW	21
White-footed mouse, *Peromyscus leucopus*; Virginia; whole; contaminated area vs. reference site	Max. 1.5 DW vs. Max. 3.1 DW	49
Raccoon, *Procyon lotor*; Ontario, Canada		
Kidney	0.7 FW	47
Muscle	1.0 (0.9-1.3) FW	48
Laboratory white rat, *Rattus* sp.		
Fur	0.16 FW	62
Kidney	0.32 FW	62
Muscle	0.17 FW	62
Shrews; southern Finland		
Common shrew, *Sorex araneus*; nickel-contaminated vs. reference site		
Liver	Max. 7.2 DW vs. <0.1 DW	63
Kidney	Max. 23.0 DW vs. Max. 37.5 DW	63
Long-tailed shrew, *Sorex minutus*; kidney vs. liver	Max. 0.7 DW vs. 3.4 DW; Max. 68.1 DW	63
Gray squirrel, *Sciurus carolinensis*; New England		
Heart	3.7 FW	1
Kidney	3.2 FW	1
Liver	1.5 FW	1
Masked shrew, *Sorex cinereus*; whole; nickel-contaminated area vs. reference site	Max. 0.9 FW vs. Max. 4.2 DW	63
Swine, *Sus* sp.		
Heart	Max. 0.43 FW	39
Kidney	Max. 3.4 FW	1
Muscle	Max. 0.02 FW	1
Serum	(0.0035-0.0083) FW	21, 39
Mole, *Talpa europaea*; rural areas; Finland; liver	0.13 DW; Max. 0.25 DW	63
Red squirrel, *Tamasciurus hudsonicus*		
New England; liver and kidney	<0.2 FW	1
Canada; fur; polluted area vs. reference site		
Spring (premoult)	3-9 DW vs. 2.2 DW	64
Fall (postmoult)	1-3 DW vs. 0.6 DW	64
Marine Mammals		
British Isles; eight species; 1988-89; livers limit of 0.5 FW	All values below detection	65
Wales coast and Irish Sea; eight species; 1989-91; livers	Usually <0.5 FW; Max. 2.1 FW	66
Vaquita (porpoise), *Phocoena sinus*; Baja California,		

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Mexico		
Heart	0.7 FW	67
Kidney	0.5 FW	67
Liver	<0.4 FW	67
Sperm whale, *Physeter macrocephalus*; North Sea; 1994-95; found stranded; livers	0.39 FW; Max. 2.1 FW	68
Sweden, three species (harbor seal, *Phoca vitulina*; gray seal, *Halichoerus grypus*; ringed seal, *Phoca hispida*); livers and kidneys	Usually <0.0006 FW; maximum concentrations were 0.17 FW in livers and 0.08 FW in kidneys	69
Integrated Studies		
Arctic; Spitsbergen, Svalbard; July-August 1988		
Surface water	0.0015 FW	70
Glacier ice	0.00725 FW	70
Algae, *Zygnema* sp.	3.25 DW	70
Lichen, *Cetraria nivalis*	1.6 DW	70
Mosses, *Tamenthypnum* sp., *Rhacomitrium* sp.	2.4-6.4 DW	70
Vascular plant, *Cassiope* sp.	4.1 DW	70
Herring gull, *Larus argentatus*; feathers	1.9-9.9 DW	70
Reindeer, *Rangifer tarandus*; fur	4.8 DW	70
Canada; Wanapitei River (near nickel smelter) vs. Pickerel River (reference site); Ontario; 1974		
Water	0.042 FW vs. 0.002 FW	71
Sediments	224 FW vs. 13 FW	71
Pondweed, *Potamogeton* sp.		
Leaves	480 FW vs. 39 FW	71
Stems	255 FW vs. 7 FW	71
Periphyton, whole	826 FW vs. 43 FW	71
Zooplankton, whole	27 FW vs. 7 FW	71
Crayfish, whole	39 FW vs. 9 FW	71
Clams, soft parts	11 FW vs. 4 FW	71
Fishes, six species		
Gills	11.1-31.7 FW vs. no data	71
Kidneys	11.8-51.6 FW vs. no data	71
Livers	10.7-17.0 FW vs. no data	71
Muscles	9.5-13.8 FW vs. no data	71
Florida; near sewage outfall; exposure for 120 days		
Turtle grass, *Thalassia testudinum*; leaves	45 DW	72
Mangrove, *Rhizophora mangle*; roots	10 DW	72
Sea urchin, *Lytechinus variegatus* (consumes *Thalassia*); whole	30 DW	72
Sea cucumber, *Holothuria mexicana*; whole	40 DW	72
Florida; stormwater ponds in Orlando vs. reference sites; 1991-92		
Sediments	2.4 FW vs. 0.07 FW	73
Fishes, whole		
Redear sunfish, *Lepomis microlophus*	5.3 FW vs. 0.6 FW	73
Bluegill, *Lepomis macrochirus*	0.2 FW vs. 0.08 FW	73
Largemouth bass, *Micropterus salmoides*	2.5 FW vs. 1.2 FW	73
French-Spanish border; Bidason estuary; four sites; April 1993		

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Sediments	35 (22-44) DW	74
Clam, *Scrobicularia plana*; soft parts	4.1 (2.9-5.7) DW	74
Sandworm, *Nereis diversicolor*; whole	5.4 (3.2-8.5) DW	74
Israel, Mediterranean coast; 1974		
Water	0.0028-0.0036 FW	75
Sediments	4.8 DW	75
Algae	5.2-5.8 DW	75
Fishes, 10 species; whole	0.1-10.8 DW	75
Lake Erie; near coal ash disposal basin; 1983-84		
Sediment	Max. 26.4 DW (vs. 19.8	76
DW in reference site)		
Coal ash	65.0 DW	76
Oligochaetes	Max. 32.5 DW	76
Chronomids	<9.1 DW	76
Fishes, whole		
Brown bullhead, *Ameiurus nebulosus*;	<9.1 DW vs. Max. 26.6 DW	76
adults vs. yearlings		
Yellow perch, *Perca flavescens*; white bass,	<9.1 DW	76
Morone chrysops		
Lebanon; near Ras Beirut		
Seawater	Max. 0.027 FW	77
Mollusks, three species; soft parts	27.4-40.1 DW	77
Mississippi River delta and northwestern Gulf of Mexico		
Sargassum weed, *Sargassum* spp. plus mixed	0.9-15.6 DW	78
phytoplankton; whole		
Zooplankton	<0.5-8.2 DW	78
New York; Hudson river; near nickel-cadmium battery plant; 1972		
Water; insoluble vs. soluble	0.043 FW vs. 0.068 FW	79
Sediments	Max. 7,000 DW	79
Cordgrass, *Spartina* sp.; roots	Max. 500 DW	79
New Guinea; Upper Fly River; September 1974		
Water	<0.001-0.005 FW	80
Sediments	24-38 DW	80
Gastropod, *Melanoides* sp.; soft parts	8-18 DW	80
Prawn, *Macrobrachium* sp.; whole	5-17 DW	80
Fishes, various species; liver and muscle	3-93 DW	80
Texas; outer continental shelf		
Sargassum weed, *Sargassum* spp.	5.2 DW	81
Squid, muscle	2.5 DW	81
Zooplankton, whole	4.6 DW	81
Shrimp, two species; whole	1.4-1.6 DW	81
Fish, various species; muscle	0.6-4.9 DW	81
Turkey; Tigris River (contaminated by wastes from smelter)		
Water	0.5-0.8 FW	82
Sediments with living organisms	41-305 DW	82
Sediments with no living organisms	403 DW	82
Fish, *Cyprinion macrostomus*		
Liver	105-502 FW	82
Muscle	8-95 FW	82
Fish, *Garra rufa*		

Table 6. Taxonomic group, organism, and other variables	Concentration (mg/kg)[a]	Reference[b]
Liver	Max. 380 FW	82
Muscle	Max. 43 FW	82

[a]Concentrations are shown as means, range (in parentheses), and maximum (Max.).

[b]1, Jenkins 1980b; 2, Memon et al. 1980; 3, U.S. Environmental Protection Agency 1980; 4, Richardson et al. 1980; 5, World Health Organization 1991; 6, Lee et al. 1978; 7, Anke et al. 1980a; 8, Frank et al. 1982; 9, Stoewsend et al. 1984; 10, Eisler 1981; 11, Bagatto and Shorthouse 1996; 12, Manly and George 1977; 13, Palmer and Rand 1977; 14, Bryan et al. 1977; 15, Stronkhorst 1992; 16, Greig et al. 1978; 17, Pesch et al. 1977; 18, Bryan and Hummerstone 1978; 19, Szefer et al. 1993; 20, Cheng et al. 1976; 21, Mushak 1980; 22, Greig et al. 1977; 23, Langlois and Langis 1995; 24, Sharif et al. 1993; 25, Greig and Wenzloff 1977; 26, Vas 1991; 27, Mathews 1994; 28, Sparling and Lowe 1996; 29, Outridge and Scheuhammer 1993; 30, Burger and Gochfeld 1985; 31, Gochfeld and Burger 1987; 32, Ranta et al. 1978; 33, Michot et al. 1994; 34, Custer and Hohman 1994; 35, Rose and Parker 1983; 36, Wiemeyer et al. 1986; 37, Wren et al. 1988; 38, Kalas et al. 1995; 39, Kasprzak 1987; 40, Custer and Mulhern 1983; 41, Ahmed and Stoeppler 1994; 42, Wiemeyer et al. 1987; 43, Custer et al. 1986; 44, Connors et al. 1975; 45, Kraus 1989; 46, Hillis and Parker 1993; 47, Wren 1984; 48, Wren et al. 1983; 49, Scanlon 1987; 50, Hausinger 1993; 51, Hughes et al. 1994; 52, Norseth 1986; 53, National Research Council of Canada 1981; 54, National Academy of Sciences 1975; 55, Norseth and Piscator 1979; 56, Sevin 1980; 57, Smith and Rongstad 1981; 58, Wren et al. 1988; 59, Halbrook et al. 1996; 60, Sivertsen et al. 1995; 61, Munshower and Neuman 1979; 62, Kirchgessner and Schnegg 1980; 63, Pankakoski et al. 1994; 64, Lepage and Parker 1988; 65, Law et al. 1991; 66, Law et al. 1992; 67, Villa et al. 1993; 68, Law et al. 1996; 69, Frank et al. 1992; 70, Drbal et al. 1992; 71, Hutchinson et al. 1975; 72, Montgomery et al. 1978; 73, Campbell 1994; 74, Saiz-Salinas et al. 1996; 75, Roth and Hornung 1977; 76, Hatcher et al. 1992; 77, Shiber and Shatila 1978; 78, Trefry and Presley 1976; 79, Kniep et al. 1974; 80, Boyden et al. 1978; 81, Horowitz and Presley 1977; 82, Gumgum et al. 1994.

Terrestrial vegetation within 3.5 km of one of the Sudbury, Ontario, smelters had as much as 140 mg Ni/kg DW; concentrations decreased with distance from the smelter, reaching a mean concentration of about 12 mg Ni/kg DW at a distance of 60 km (Chau and Kulikovsky-Cordeiro 1995). Some vegetation near a Sudbury smelter—including lawn grasses, timothy (*Phleum pratense*), and oats (*Avena sativa*)—showed signs of nickel toxicosis; concentrations in these species ranged between 80 and 150 mg Ni/kg DW. Vegetables—beets (*Beta vulgaris*), radishes (*Raphanus* spp.), cabbages (*Brassica oleracea capitata*), and celery (*Apium graveolans*)—grown in soils about 1 km from a nickel refinery had 40-290 mg Ni/kg DW in their top portions. All of these vegetables had reduced yield, stunted growth, and chlorosis and necrosis, which were attributed to the high levels of nickel in local soils (Chau and Kulikovsky-Cordeiro 1995).

Mosses and lichens accumulate nickel readily and at least nine species are used to monitor environmental gradients of nickel (Jenkins 1980a). Maximum concentrations of nickel found in whole lichens and mosses from nickel-contaminated areas range between 420 and 900 mg/kg DW versus 12 mg/kg DW from reference sites (Jenkins 1980a). Nickel concentrations in herbarium mosses worldwide have increased dramatically during this century. In one case, nickel concentrations in *Brachythecium salebrosum* from Montreal, Canada, rose from 6 mg/kg DW in 1905 to 105 mg/kg DW in 1971 (Richardson et al. 1980).

Nickel-tolerant or accumulator species of plants are likely to be found only on nickel-rich soils (Rencz and Shilts 1980). Hyperaccumulator species usually grow on relatively infertile, nickel-rich serpentine soils and contain more than 10,000 mg Ni/kg DW (Jenkins 1980b; NRCC 1981; WHO 1991; Table 6). Leaves from some genera of nickel hyperaccumulator plants, including *Alyssum*, *Homalium*, and *Hybanthus*, growing on soils derived from volcanic rocks, which are rich in nickel, accumulate nickel to concentrations of 120,000 mg/kg DW (Kasprzak 1987; Table 6). Nickel is bound as a citrate complex in hyperaccumulator plants from New Caledonia; however, nickel accumulator plants from other locations do not contain unusually high levels of citrate, and nickel is not present as a citrate complex but as a carboxylic acid complex (Lee et al. 1978).

Terrestrial plants take up nickel from soil primarily via the roots (NRCC 1981; WHO 1991). The nickel uptake rate from soil is dependent on soil type, pH, humidity, organic content, and concentration of extractable

nickel (NAS 1975; WHO 1991). For example, at soil pH less than 6.5 nickel uptake is enhanced due to breakdown of iron and manganese oxides that form stable complexes with nickel (Rencz and Shilts 1980). The exact chemical forms of nickel that are most readily accumulated from soil and water are unknown; however, there is growing evidence that complexes of nickel with organic acids are the most favored (Kasprzak 1987). In addition to their uptake from the soils, plants consumed by humans may receive several milligrams of nickel per kilogram through leaching of nickel-containing alloys in food-processing equipment, milling of flour, and catalytic hydrogenation of fats and oils by use of nickel catalysts (USEPA 1986). Nickel reportedly disrupts nitrogen cycling and this could have serious ecological consequences for forests near nickel smelters (WHO 1991), although adverse effects of nitrogen disruption by nickel need to be verified.

Data are limited on nickel concentrations in terrestrial invertebrates. Earthworms from uncontaminated soils may contain as much as 38 mg Ni/kg DW and workers of certain termite species may normally contain as much as 5,000 mg Ni/kg DW (Table 6). Larvae of the gypsy moth (*Porthetria dispar*) near a nickel smelter had 20.4 mg Ni/kg DW; concentrations in pupae and adults were lower because these stages have higher nickel elimination rates than larvae (Bagatto et al. 1996).

Aquatic Organisms

Nickel concentrations are comparatively elevated in aquatic plants and animals in the vicinity of nickel smelters, nickel-cadmium battery plants, electroplating plants, sewage outfalls, coal ash disposal basins, and heavily populated areas (Kniep et al. 1974; Eisler et al. 1978a; Montgomery et al. 1978; Jenkins 1980a; Eisler 1981; Kasprzak 1987; Chau and Kulikovsky-Cordeiro 1995; Table 6). For example, at Sudbury, Ontario, mean nickel concentrations, in mg/kg DW, were 22 for larvae of aquatic insects, 25 for zooplankton, and 290 for aquatic weeds; maximum concentrations reported were 921 mg/kg DW in gut of crayfish (*Cambarus bartoni*) and 52 mg/kg fresh weight (FW) in various fish tissues (Chau and Kulikovsky-Cordeiro 1995; Table 6). For all aquatic species collected, nickel concentrations were highly variable between and within species; this variability is attributable, in part, to differential tissue uptake and retention of nickel, depth of collection, age of organism, and metal-tolerant strains (Bryan et al. 1977; Bryan and Hummerstone 1978; Jenkins 1980a; Eisler 1981; Chau and Kulikovsky-Cordeiro 1995; Table 6).

The bioaccumulation of nickel under field conditions varies greatly among groups. Bioconcentration factors (BCF, which equals the milligrams of nickel per kilogram fresh weight of the sample divided by the milligrams of nickel per liter in the medium) for aquatic macrophytes range from 6 in pristine areas to 690 near a nickel smelter; for crustaceans these values are 10-39; for mollusks, 2-191; and for fishes, 2-52 (Sigel and Sigel 1988). Bioconcentration factors of 1,700 have been reported for marine plankton, 800 and 40 for soft parts and shell, respectively, of some marine mollusks, and 500 for brown algae, suggesting that some food chain biomagnification may occur (NAS 1975).

Concentrations of nickel in roots of *Spartina* sp. from the vicinity of a discharge from a nickel-cadmium battery plant on the Hudson River, New York, ranged between 30 and 500 mg/kg DW and reflected sediment nickel concentrations in the range of 100-7,000 mg Ni/kg DW (Kniep et al. 1974). The detritus produced from dead algae and macrophytes is the major food source for fungi and bacteria, and in this way nickel can again enter the food chain (NRCC 1981; Chau and Kulikovsky-Cordeiro 1995). Nickel concentrations in tissues of sharks from British and Atlantic water range between 0.02 and 11.5 mg/kg FW; concentrations were highest in fish-eating, mid-water species such as the blue shark (*Prionace glauca*) and tope shark (*Galeorhinus galeus*; Vas 1991). Concentrations of nickel in livers of tautogs *(Tautoga onitis*) from New Jersey significantly decreased with increasing body length in both males and females; however, this trend was not observed in bluefish (*Pomatomus saltatrix*) or tilefish (*Lopholatilus chamaeleonticeps*; Mears and Eisler 1977).

Amphibians

In Maryland, USA, nickel concentrations in tadpoles of gray treefrogs (*Hyla versicolor*) and northern cricket frogs (*Acris crepitans*) increased with increasing soil nickel concentrations, with maximum nickel concentrations recorded of 7.1 mg/kg DW in gray treefrogs and 10.0 mg/kg DW in northern cricket frogs (Sparling and Lowe 1996). In study sites 9-66 km from Sudbury, Ontario, populations of treefrogs (*Hyla crucifer*) and American toads (*Bufo americanus*) declined. Population abundance of adult treefrogs declined with increasing atmospheric deposition of nickel, and abundance of toad tadpoles declined as nickel concentrations in pond

water rose from 3.3 μg Ni/L at more distant sites to 19.5 μg Ni/L at sites near Sudbury (Glooschenko et al. 1992).

Birds

Nickel concentrations in the organs of most avian wildlife species in unpolluted ecosystems range from about 0.1 to 2.0 mg/kg DW and occasionally reach 5.0 mg/kg DW (Eisler 1981; Outridge and Scheuhammer 1993). In nickel-contaminated areas, nickel concentrations were elevated in feathers, eggs, and internal tissues of birds when compared to conspecifics collected at reference sites (Darolova et al. 1989; Outridge and Scheuhammer 1993; Table 6). In contaminated ecosystems, mean nickel concentrations between 31 and 36 mg/kg DW occur in primary feathers of mallards (*Anas platyrhynchos*) collected 20-30 km from a nickel smelter, bone of the common tern (*Sterna hirundo*) from Hamilton Harbor, Ontario, and eggshell of the tree swallow (*Tachycineta bicolor*) from the Hackensack River, New Jersey (Table 6).

Waterfowl feeding in areas subjected to extensive nickel pollution—such as smelters and nickel-cadmium battery plants—are at special risk because waterfowl food plants in those areas contain 500-690 mg Ni/kg DW (Eastin and O'Shea 1981). Dietary items of the ruffed grouse (*Bonasa umbellus*) near Sudbury, Ontario, had 32-95 mg Ni/kg DW, whereas nickel concentrations in grouse body tissues usually contain less than 10% of the dietary level. Nickel concentrations in aspen (*Populus tremula*) from the crop of ruffed grouse near Sudbury ranged from 62 mg/kg DW in May to 136 mg/kg DW in September (Chau and Kulikovsky-Cordeiro 1995), which shows the role of season in dietary nickel composition.

Mammals

Mammalian wildlife from uncontaminated habitats usually contain less than 0.1 to about 5 mg Ni/kg DW in tissues; in nickel-contaminated areas, these same species have 0.5 to about 10 mg Ni/kg DW in tissues (Outridge and Scheuhammer 1993; Chau and Kulikovsky-Cordeiro 1995), with a maximum of 37 mg/kg DW in kidneys of the common shrew (*Sorex araneus*; Table 6). Nickel accumulations in wildlife vary greatly between species. For example, tissues of mice have higher concentrations of nickel than rats and other rodents while beavers and minks have higher nickel concentrations in their liver than birds in similar sites near Sudbury (Chau and Kulikovsky-Cordeiro 1995).

The highest concentrations in wildlife tissues from nickel-contaminated locales are associated with tissues exposed to the external environment, such as fur and skin; nickel concentrations in internal organs are usually similar, regardless of degree of contamination (Outridge and Scheuhammer 1993; Table 6). However, nickel concentrations in bone, reproductive organs, and kidneys in certain herbivorous species of wildlife and livestock are elevated when compared to other internal tissues, especially in the vicinity of nickel smelters and other nickel point sources (Outridge and Scheuhammer 1993; Kalas et al. 1995). Trophic position in the food chain, sex, and reproductive state do not seem to significantly influence the nickel body burdens of mammals (Outridge and Scheuhammer 1993), but age is an important variable and nickel generally increases in various organs with increasing age of terrestrial and marine mammals. Fetuses of a variety of wildlife and domestic species contain concentrations of nickel significantly lower than those in their mothers or in juveniles, suggesting that placental transfer of nickel is restricted. Nickel concentrations in aquatic macrophytes and lower plants in the vicinity of nickel smelters may approach or exceed dietary levels known to cause adverse effects in young animals. Sensitive species of wildlife ingesting this vegetation for extended periods could experience nickel-related toxicity or risk alterations in community structure as nickel-sensitive taxa are eliminated or their abundance is reduced (Outridge and Scheuhammer 1993).

Elevated nickel concentrations in Norwegian wildlife are linked to emissions from Russian nickel smelters (Kalas et al. 1995). In Norway, nickel concentrations were elevated in livers and kidneys of moose (*Alces alces*) and reindeer (*Rangifer tarandus*) because of atmospheric transport of wastes from nickel-processing plants of nearby Russian towns (Sivertsen et al. 1995). In Russia between 1974 and 1992, three species of voles (*Clethrionomys glareolus*, *Clethrionomys rutilus*, *Lemmus lemmus*) were eliminated from the immediate vicinity of a copper-nickel smelter that discharged 2,700 metric tons of nickel annually to the atmosphere, and these species were scarce at a moderately contaminated area 28 km south of the smelter (Kataev et al. 1994). Declines were associated with a decrease of important food plants: lichens for *C. glareolus* and *C. rutilus*, mosses for *L. lemmus*, and seed plants for other species of *Clethrionomys*. Close to the smelter, direct toxic effects of accumulated nickel and other metals also may have reduced population densities (Kataev et al. 1994).

Nickel concentrations are also elevated in rodents, shrews, soil, vegetation, and earthworms in the vicinity of roads with high automobile density (Pankakoski et al 1993). In ruminant mammals, tissue nickel concentrations were higher in winter (WHO 1991), presumably because of increased combustion of fossil fuels.

Nickel is normally present in human tissues, and under conditions of high exposure, these levels may increase significantly (WHO 1991). Nickel enters the human body through the diet, through inhalation, by absorption through the skin, and in medications (NAS 1975). The diet accounts for about 97% of the total intake and drinking water about 2.5% (Kasprzak 1987). Foods rich in nickel include tea (7.6 mg/kg DW), cereals (6.5 mg/kg DW), vegetables (2.6 mg/kg DW), and fish (1.7 mg/kg DW) (IARC 1976; Table 6). The daily dietary intake of nickel by humans in the United States ranges between 0.15 and 0.6 mg, almost all of which is excreted in the feces (NAS 1975; Norseth and Piscator 1979; USEPA 1980; NRCC 1981; Sunderman et al. 1984). Minor amounts are also excreted in sweat, urine, and hair (Kasprzak 1987). Residents of the Sudbury, Ontario, area who consume homegrown garden products ingest an average of 1.85 mg of nickel daily, of which 0.6 mg comes from the drinking water (NRCC 1981). Inhalation intake of nickel for residents of New York City is estimated at 2.4 μg daily; for Chicago, a maximum value of 13.8 μg daily is recorded; and 14.8 μg are inhaled daily by smokers of 40 cigarettes (NAS 1975; WHO 1991). Canadians in urban areas inhale 0.06-0.6 μg Ni daily; near nickel smelters this may increase to 15 μg daily (NRCC 1981). In Connecticut, serum nickel levels in newborns were normal (3 μg/L) and similar to those of their mothers (Norseth and Piscator 1979). Nickel concentrations in human serum, however, are modified by disease and stress. Concentrations are usually elevated after strokes, pregnancy, and extensive burns and are depressed in cases of cirrhosis, hypoalbuminemia, extremes of heat, and uremia (Mushak 1980; USEPA 1980, 1986).

About 727,000 workers were potentially exposed to nickel metal, nickel alloys, or nickel compounds during the period 1980-83 (USPHS 1993). Worker exposure differs from that of the general population in that the major route of exposure for nickel workers is inhalation and for the general population it is dermal contact (Sevin 1980). Nickel workers with lung cancer had elevated concentrations of 1.97 mg/kg DW in their lungs when compared to the general population (0.03-0.15 mg/kg DW; USPHS 1977). Plasma concentrations of nickel quickly reflect current exposure history to nickel (USEPA 1980). Mean nickel concentrations in plasma of humans occupationally exposed to nickel have declined by about 50% since 1976, suggesting decreased exposure due to improved safety (Boysen et al.1980).

Integrated Studies

Beaver ponds downstream from an abandoned copper-nickel ore roast yard near Sudbury, Ontario, were devoid of fish and had reduced macroinvertebrate taxon richness and diversity when compared to upstream ponds. Nickel water concentrations, in μg Ni/L, were 57 in upstream ponds, 82 in downstream ponds, and 1,800 at the station directly on the roast pit (Rutherford and Mellow 1994). Beavers (*Castor canadensis*) near nickel smelters had elevated nickel concentrations in livers and kidneys when compared to conspecifics from a reference site; accumulations were attributed to food chain contamination (Hillis and Parker 1993).

Hutchinson et al. (1975) found nickel contamination in the Sudbury, Ontario, region to be the result of aerial transport and terrestrial drainage from mining and smelting activities. Nickel concentrations in soils were elevated as far as 52 km from the source. Erosion of soils following the death of vegetation was widespread and affected an area of more than 820 km^2. Soils increased in acidity, increasing the solubility of nickel. In aquatic ecosystems, nickel was accumulated from the water column by periphyton, rooted aquatic macrophytes, zooplankton, crayfish, clams, and fishes. However, there was no evidence of food chain biomagnification of nickel in the Sudbury ecosystem (Hutchinson et al. 1975). For example, in the nickel-contaminated Wanapitei River, bioconcentration factors during summer 1974 were highest for whole periphyton (19,667), followed by whole pondweeds (11,429), sediments (5,333), whole crayfish (929), whole zooplankton (643), muscle of carnivorous fishes (329), soft tissues of clams (262), and muscle of omnivorous fishes (226) (Hutchinson et al. 1975). Higher BCF values are recorded for acid- and metal-tolerant flora (Outridge and Scheuhammer 1993).

There is little convincing evidence for the biomagnification of nickel in the food chain. Most authorities agree that nickel concentrations do not increase with ascending trophic levels of food chains and that predatory animals do not have higher concentrations (Jenkins 1980a; WHO 1991; Outridge and Scheuhammer 1993; Chau and Kulikovsky-Cordeiro 1995). The potential for biomagnification exists because algae and macrophytes have comparatively elevated concentrations of nickel; however, animals seem to be able to regulate the nickel

content of their tissues by controlled uptake and increased excretion (Jenkins 1980a; Outridge and Scheuhammer 1993).

Nickel Deficiency Effects

General

Nickel is reportedly an essential micronutrient for maintaining health in certain species of plants, invertebrates, birds, and mammals, including humans (NAS 1975; Spears et al. 1979; Sunderman et al. 1984; Norseth 1986; USEPA 1986; Sigel and Sigel 1988; Hausinger 1993; USPHS 1993; Stangl and Kirchgessner 1996, 1997). However, nickel essentiality for humans has not yet been proven (Norseth and Piscator 1979; USPHS 1993), and the evidence for marine tunicates and land snails is inconclusive (Hausinger 1993). To prevent nickel deficiency in rats and chickens, diets should contain at least 50 μg Ni/kg ration; cows and goats require more than 100 μg Ni/kg ration, perhaps reflecting the increased use of nickel by rumen bacteria (USPHS 1993). In humans, nickel deficiency is not a public health concern because daily oral intake normally exceeds 170 μg of nickel (USPHS 1993).

Nickel is considered essential to animals because it is present in the fetus or newborn, is homeostatically regulated, the metabolic pool of nickel is specifically influenced by hormonal substances or pathologic processes, certain metalloproteins contain nickel, and because nickel deficiency has been induced experimentally in certain species of birds and animals (NAS 1975; USPHS 1977; Kirchgessner and Schnegg 1980). In general, the nickel deficiency syndrome can be cured or prevented by trace amounts of nickel (NAS 1975). However, nickel administration may not be successful in reversing all abnormalities produced by nickel deprivation (USPHS 1977).

Nickel deficiency effects from dietary deprivation of nickel are now documented in at least 17 animal species, including chickens, cows, goats, pigs, rats, and sheep (USPHS 1977, 1993; Norseth and Piscator 1979; USEPA 1985; Norseth 1986; WHO 1991). According to Kirchgessner and Schnegg (1980), nickel deficiency can be induced only by very low nickel concentrations in the diet—not by its bioavailability. Signs of nickel deficiency include delayed gestation periods and fewer offspring; decreased growth and sometimes dwarfism; anemia; skin eruptions; brittle hair; reduced oxygen consumption; decreased levels of serum proteins; enhanced urinary nitrogen excretion; reduced tissue iron and zinc concentrations; reduced hemoglobin and hematocrit values; abnormal liver morphology and lipid metabolism; reduced liver glucose, lipids, glycogen, and triglycerides; and reduced activity of several enzymes, including dehydrogenases, transaminases, and alpha-amylases (USEPA 1980, 1985, 1986; WHO 1991; USPHS 1993; Stangl and Kirchgessner 1996).

Bacteria and Plants

Nickel is essential for the active synthesis of urease in plant cells and of various hydrogenases in bacteria (Thauer et al. 1980; USEPA 1986; WHO 1991; Hausinger 1993). In several species of higher plants, including jack beans (*Canavalia* sp.), soybeans (*Glycine max*), rice (*Oryza sativa*), and tobacco (*Nicotiana tabacum*), nickel is required for effective urea metabolism and urease synthesis (Kasprzak 1987; Sigel and Sigel 1988). Some terrestrial plants, such as *Alyssum* spp., accumulate nickel and require it for growth (Thauer et al. 1980). In bacteria, nickel is required for the growth of *Oscillatoria* sp. and *Alcaligenes* sp., for the synthesis of carbon monoxide dehydrogenase in *Clostridium posterianum*, and as a component of coenzyme F_{430} in *Methanobacterium* spp. (Babich and Stotzky 1982a; Kasprzak 1987). Nickel deficiency in bacteria may adversely affect reproductive processes, such as endospore formation, and cause a decrease in nickel-containing intracellular pigments in strains of *Bacillus cereus* (Thauer et al. 1980); however, both of these observations require verification.

Birds

All studies demonstrating nickel deficiency in birds were conducted on a single species, specifically, chicks of the domestic chicken, *Gallus* sp. The relevance of these results to avian wildlife species is unknown. Chicks grew normally when fed nickel-deficient diets (2-15 μg Ni/kg ration) for 3-4 weeks. But these chicks had liver histopathology, decreased concentrations of yellow lipochrome pigments in liver, low hematocrit, skin dermatitis, leg thickening, altered lengths of leg bones, and decreased plasma cholesterol (Nielsen et al. 1975a; Hausinger 1993). Adverse effects of nickel-deficient diets (<20 μg Ni/kg ration) were reversed by the addition of nickel to the diet (Ling and Leach 1979). Chicks fed diets containing 25-2,500 μg Ni/kg ration for 3-4 weeks grew

normally and all organs appeared normal (Nielsen et al. 1975a). Nickel-deficient chicks (40-80 µg Ni/kg ration), when compared to controls (3-5 mg Ni/kg ration), had swollen hock joints, reduced length-to-width ratios of tibias, scaly dermatitis of the legs, orange-yellow discoloration of the legs, fat-depleted livers, altered liver metabolism, and elevated concentrations of nickel in liver, spleen, and aorta (Sunderman et al. 1972; NAS 1975; USEPA 1980; USEPA 1985). Chicks fed nickel-deficient diets of 44 µg Ni/kg ration for 30 days had markedly lower nickel concentrations in serum and livers than did controls fed diets containing 3.4 mg Ni/kg ration; nickel-deficient chicks had 1.6 µg Ni/L in serum versus 4.2 in controls and 64 µg Ni/kg DW liver versus 82 in controls (Sunderman et al. 1972). Livers of nickel-deficient chicks had an altered gross appearance, reduced oxidative ability, and decreased lipid phosphorus concentrations (Nielsen et al. 1975a). Nickel deficiency in chicks may be associated with thyroid hormone imbalance (Nielsen et al. 1975a), but this needs verification.

Mammals

In humans, there is no evidence of a nickel deficiency syndrome (USEPA 1985) or proof that nickel is essential (Norseth and Piscator 1979; Norseth 1986).

Cows (*Bos* sp.) fed nickel-deficient diets containing less than 100 µg Ni/kg ration had reduced growth and survival (Hausinger 1993). Nickel deficiency in cows was exacerbated when diets were also low in protein, but effects were lessened when diets were supplemented with 5 mg Ni/kg ration (Spears et al. 1979). Lambs from domestic sheep (*Ovis aries*) fed a low nickel diet (30 µg Ni/kg ration) for 97 days had lower growth, higher mortality, and altered blood and tissue chemistry when compared to controls fed a diet containing 5 mg Ni/kg ration (Spears et al. 1979). Lambs given diets containing 65 µg Ni/kg DW ration had disrupted metabolism (USEPA 1980).

Adults and offspring of breeding goats (*Capra hircus*) and swine (*Sus* sp.) fed nickel-deficient diets (<100 µg Ni/kg ration) or control diets (10 mg Ni/kg ration) for 6 years had normal conception and abortion rates. However, nickel-deficient goats and pigs had delayed pregnancies, reduced litter sizes, lower birth rates, lower weight gains during suckling, and significant increases in mortality during the suckling period; mortality was 41% higher than controls in kids and 51% higher than controls in piglets (Anke et al. 1978). Nickel-deficient adult goats had lower nickel concentrations in kidneys, liver, and other tissues than did controls, specifically, 0.2-0.6 mg Ni/kg DW tissue versus 0.6-1.2 mg Ni/kg DW in controls (Anke et al. 1980a). Kids of nickel-deficient ewes (100 µg Ni/kg DW ration for 6 years vs. control diet of 300 µg Ni/kg ration) had inhibited growth starting at age 8 weeks and reduced survival (Anke et al. 1980b). During lactation, hemoglobin concentrations and hematocrits of nickel-deficient goats were significantly lower than control values (Anke et al. 1980b). Nickel-deficient pigs had rough coats, decreased growth, and impaired reproduction (USEPA 1980; Hausinger 1993).

Signs of nickel deficiency in the laboratory white rat (*Rattus* sp.) include retarded growth, anemia, a reduction in hematocrit and hemoglobin values, decreased enzyme activities (malate dehydrogenase, glucose-6-phosphate dehydrogenase, alpha amylase), a reduction in liver total lipids and phospholipids, and altered tissue concentrations of fatty acids, iron, copper, and zinc (Nielsen et al. 1975b; Norseth and Piscator 1979; Nielsen 1980b; Norseth 1986; Hausinger 1993; Stangl and Kirchgessner 1996, 1997). Nickel concentrations in fur, kidneys, and muscle of rats fed nickel-deficient diets (15 µg Ni/kg DW ration) were about 66% lower than those of controls given 20 mg Ni/kg ration (Kirchgessner and Schnegg 1980). Signs of nickel deficiency in rats were usually reversed by supplementing the diet with nickel (Ling and Leach 1979) at more than 50 µg Ni/kg ration (USEPA 1985). Rats fed nickel-deficient diets (<5 µg Ni/kg ration) for three generations produced offspring that were anemic and grew poorly in the first two generations and that had impaired reproduction in all generations (USEPA 1980; Sevin 1980). In another three-generation study, rats fed nickel-deficient diets containing 2-15 µg Ni/kg ration had increased perinatal mortality, unthrifty appearance of young rats, decreased physical activity, decreased liver cholesterol, and liver histopathology compared to controls fed diets containing 3 mg Ni/kg ration (Nielsen et al. 1975b).

Lethal and Sublethal Effects

General

Nickel toxicity reduces photosynthesis, growth, and nitrogenase activity of algae; fermentative activity of a mixed rumen microbiota; growth rate of marine bacteria; metabolism of soil bacteria; and mycelial growth, spore germination, and sporulation of fungi (Babich and Stotzky 1982a). Adverse effects of excess nickel have also been observed with yeasts, higher plants, protozoans, mollusks, crustaceans, insects, annelids, echinoderms,

fishes, amphibians, birds, and mammals (USEPA 1975). As discussed later, sensitive species of aquatic organisms are adversely affected at nominal concentrations of 11-113 μg Ni^{2+}/L.

In birds, mortality occurred in young individuals of sensitive species when rations contained more than 500 mg Ni/kg (Outridge and Scheuhammer 1993). Nickel accumulated in avian tissues at dietary loadings as low as 0.7-12.5 mg Ni/kg ration (Cain and Pafford 1981; Eastin and O'Shea 1981; Stoewsand et al. 1984); however, nickel intoxication in some species tested was not always reflected by elevated tissue nickel concentrations (Outridge and Scheuhammer 1993).

In mammals, the toxicity of nickel is a function of the chemical form of nickel, dose, and route of exposure. Exposure to nickel by inhalation, injection, or cutaneous contact is more significant than oral exposure. Toxic effects of nickel to humans and laboratory mammals are documented for respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, dermal, ocular, immunological, developmental, neurological, and reproductive systems (NAS 1975; Nielsen 1977; USEPA 1980, 1986; WHO 1991; USPHS 1993).

Terrestrial Plants and Invertebrates

In general, the effects of long-term, low-level exposure to nickel are shown in growth inhibition with no other visible signs (WHO 1991). However, many species of plants growing on soils contaminated with excess nickel show stunted and discolored roots and tops, wilting, chlorosis, necrosis, twisted stalks, thickening of leaf tissues, and failure of leaves to fold to form compact heads (NAS 1975; Frank et al. 1982; WHO 1991; Barman and Bhargava 1997; Donghua and Wusheng 1997). In solution culture, 1 mg of soluble nickel/L is toxic to sensitive plants (NRCC 1981; Outridge and Scheuhammer 1993). Accumulations of 50 mg Ni/kg DW plant and higher are toxic to most plants (NAS 1975; NRCC 1981; WHO 1991). Depending on soil conditions and chemical form, nickel in soil is toxic when concentrations exceed 500 mg Ni/kg DW soil with more than 25 mg Ni/L extractable in a 2.5% acetic acid solution (NRCC 1981). Accumulation and toxic effects occur in vegetables grown on soils treated with sewage sludge and in vegetation close to nickel-emitting sources (WHO 1991). Nickel was shown experimentally to decrease growth of soybeans (*Glycine max*) when administered as particulate nickel through the atmosphere or in the rooting medium (Ormrod et al. 1986). Crop plants are the most sensitive group of terrestrial vegetation tested against nickel. Adverse effects on chlorophyll metabolism and growth occur at soil water concentrations as low as 1 mg Ni/L (Outridge and Scheuhammer 1993). Radishes, beets, cabbages, celery, and lettuce planted in organic soils contaminated by aerial fallout from a nearby nickel smelter and containing between 1,570 and 6,550 mg Ni/kg DW soil had decreasing yields with increasing soil nickel concentrations (Frank et al. 1982). No radishes or cabbages were suitable for marketing. Celery, lettuce, and beets were reduced from a normal yield on soil with 1,300 mg Ni/kg to zero on soils with 4,800 mg/kg. Dried cabbage heads and celery tops had as much as 400 mg Ni/kg (Frank et al. 1982). Decreased yields of alfalfa (*Medicago sativa*) occur when plant nickel content exceeds 44 mg/kg DW (NAS 1975). Decreased yield of oats (*Avena sativa*) was associated with nickel concentrations more than 60 mg/kg DW grain, more than 28 mg/kg DW oat straw, or more than 500 mg Ni/kg DW soil (NAS 1975). Signs of nickel toxicity in oats decrease in severity with increasing magnesium concentrations in culture solution during exposure for 35 days (Proctor and McGowan 1976).

Temperature, pH, chlorophyll, and various metals all modify the toxicity of nickel to fungi (Babich and Stotzky 1982b). A reduction in the toxicity of nickel to the mycelial growth rates of five species of filamentous fungi occurs when pH increases from acidic to alkaline (*Achyla* sp., *Saprolegnia* sp.); at elevated concentrations of magnesium, zinc, or lead (*Achyla* sp.); at chlorophyll or humic acid contents equivalent to 1% (*Saprolegnia* sp., *Cunninghamella blakesleeana*, *Aspergillus clavatus*); and at increased temperatures of 33 C versus 23 C (*Aspergillus flavus*; Babich and Stotzky 1982b). Growth of sensitive species of filamentous fungi is inhibited at 10 mg Ni/L and abnormal mycelia occurs at 50 mg/L (Babich and Stotzky 1982a). Histidine may govern nickel accumulation in the approximately 400 known species of nickel-hyperaccumulating plants. Nickel hyperaccumulator plants, including 48 of 170 species of *Alyssum* spp., contain as much as 3% of the dry leaf biomass as nickel (Kramer et al. 1996). Exposing hyperaccumulator species of *Alyssum* to nickel elicits a large and proportional increase in the levels of free histidine, which is shown to be coordinated with nickel in vitro. Supplying histidine to a nonaccumulating species greatly increases both nickel tolerance and capacity for nickel transport to the shoot, indicating that enhanced production of the amino acid histidine is responsible for the nickel hyperaccumulation phenotype in *Alyssum* (Kramer et al. 1996).

Data on nickel toxicity to terrestrial invertebrates are scarce. A soil concentration of 757 mg/kg DW soil is lethal to 50% of earthworms (*Eisenia foetida*) in 14 days, and higher concentrations of 1,200-12,000 mg/kg DW soil for shorter periods produces reduced growth and survival in the same species (WHO 1991). Earthworms are less sensitive to nickel if the medium is rich in microorganisms and organic matter, thus making the nickel less bioavailable (WHO 1991).

Aquatic Organisms

Signs of nickel poisoning in fishes include surfacing, rapid mouth and opercular movements and, prior to death, convulsions and loss of equilibrium (Khangarot and Ray 1990). Destruction of the gill lamellae by ionic nickel decreases the ventilation rate and may cause blood hypoxia and death (Ellgaard et al. 1995). Other signs of nickel poisoning in fishes include decreased concentrations of glycogen in muscle and liver with simultaneous increases in levels of lactic acid and glucose in blood (Ghazaly 1992), depressed hydrogen peroxide production in tissues and a reduction in superoxide dismutase (Bowser et al. 1994), and contractions of vascular smooth muscle—signs similar to those associated with hypertension in mammals (Evans et al. 1990). Ionic nickel is lethal to sensitive species of aquatic organisms at 11-113 µg/L. Deaths occur among embryos of rainbow trout at 11-90 µg/L, daphnids at 13 µg/L, embryos of channel catfish at more than 38 µg/L, embryos of the narrow-mouthed toad at 50 µg/L, and embryos of largemouth bass at 113 µg/L (Table 7). Species intermediately resistant to nickel died at 150-410 µg Ni/L, including mysid shrimp at 150 µg/L, freshwater snails at 237 µg/L, clam embryos at 310 µg/L, and embryos of salamanders at 410 µg/L (Table 7). Aquatic bacteria and yeasts are comparatively tolerant to nickel. Sensitive species of freshwater eubacteria and actinomycetes show reduced growth at 5 mg Ni/L; for marine eubacteria, growth inhibition begins at 10-20 mg/L (Babich and Stotzky 1982a). Sensitive species of yeasts show growth inhibition at 1.0 mg Ni/L (*Torulopsis glabrata*); resistant species of yeasts (*Rhodotorula* sp., *Cryptococcus terrens*) show a reduction in growth at 5-20 mg Ni/L (Babich and Stotzky 1982a; WHO 1991).

Table 7. Nickel effects on selected aquatic plants and animals.

Table 7. Taxonomic group, organism, dose, and other variables	**Effect**	**Reference[a]**
Algae and macrophytes		
Alga, *Anabaena inequalis*		
125 µg/L	Growth inhibited	1
10.0 mg/L	Photosynthesis inhibited	1
20.0 mg/L	Nitrogenase activity inhibited	1
Blue-green alga, *Anacystis nidulans*		
160 µg/L	Growth of wild strains inhibited 50%	2
1.3 mg/L	Growth of nickel-tolerant strain inhibited 50%	2
10.0 mg/L	Decreased growth in 14 days	3
50.0 mg/L	No growth in 14 days	3
Freshwater algae, four species		
100-700 µg/L	Reduced growth at 50 mg $CaCO_3$/L	4
Green algae, four species		
100 µg/L	Growth inhibition at 20 C	1
Giant kelp, *Macrocystis pyrifera*		
2.0 mg/L	Photosynthesis inhibited 50%	4
Diatom, *Navicula pelliculosa*		
100 µg/L	Growth inhibited 50% in 14 days	1
Alga, *Phaeodactylum tricornutum*		
1.0 mg/L	Reduced growth	4
Alga, *Scenedesmus acutiformis*; from lake containing 2.5 mg Ni/L		
1.9 mg/L	Growth reduced 47%	1

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
3.0 mg/L	Growth reduced 82%	1
Marine diatom, *Thalassiosira rotula*		
30 μg/L	Growth inhibited	5
300 μg/L	Toxic threshold	5
Rotifers		
Rotifer, *Philodena acuticornis*		
2.9-7.4 mg/L	LC50 (96 h) at 25 mg $CaCO_3$/L	4
Mollusks		
Eastern oyster, *Crassostrea virginica*		
100 μg/L, embryos	None dead in 48 h	6
1.18 mg/L embryos	LC50 (48 h)	6
3.0 mg/L, embryos	All dead in 48 h	6
12.0 mg/L, larvae	LC50 (12 days); normal	7
growth in survivors		
Freshwater snail, *Juga plicifera*		
124 μg/L	No adverse effects in 96 h	1
237 μg/L	LC50 (96 h)	1
Freshwater mussel, *Lamellidens marginalis*		
Exposed for 15 days to 22 mg Ni/L; tissue concentrations, in mg/kg fresh weight (FW), experimental vs. controls		
Foot	218 vs. 122	8
Gills	570 vs. 153	8
Hepatopancreas	327 vs. 160	8
Mantle	277 vs. 145	8
Muscle	186 vs. 130	8
110 mg/L	LC50 (96 h)	8
Northern quahog, *Mercenaria mercenaria*		
100 μg/L, embryos	No deaths in 48 h	6
310 μg/L, embryos	LC50 (48 h)	6
600 μg/L, embryos	All dead in 48 h	6
5.7 mg/L, larvae	LC50 (8-10 days); survivors had reduced growth	7
Softshell clam, *Mya arenaria*; adults		
10.0-50.0 mg/L	No deaths in 168 h	9, 11
112.0 mg/L	LC50 (168 h)	9
200.0 mg/L	All dead in 168 h	9
320.0 mg/L	LC50 (96 h)	9
Common mussel, *Mytilus edulis*		
Exposed to 0, 13, 25, 30, 56 or 107 μg Ni/L for 4 weeks	No accumulations in soft parts at 30 μg/L and lower. After 4 weeks, the 56 μg/L group had 32 mg Ni/kg dry weight (DW) soft parts, and the 107 μg/L group had 41 mg Ni/kg DW soft parts vs. 12 mg/kg DW in controls	10
Exposed to 0, 20.0, 40.0, or 80.0 mg/L for 96 h	No deaths in any group. No byssal thread secretion in 40 and 80 mg/L groups. Nickel concentrations, in mg/kg DW soft parts, were 12 in controls, 400-420 in intermediate dose groups, and 820 in the high	10

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
	dose group	
Mud snail, *Nassarius obsoletus*; adults		
10.0 mg/L	No deaths in 168 h	9
25.0 mg/L	All dead in 168 h	9
72.0 mg/L	LC50 (96 h)	9
Arthropods		
Aquatic insects, five species		
4.0-33.5 mg/L	LC50 (96 h) at 42-50 mg $CaCO_3$/L	4
Caddisfly, *Clistoronia magnifica*		
295-734 µg/L	MATC[b] at 50 mg $CaCO_3$/L	4
Copepods, four species		
600-9,700 µg/L	LC50 (96 h)	4
Copepod, *Cyclops abyssorum prealpinus*		
15.0 (8.0-26.0) mg/L	LC50 (48 h)	12
Daphnid, *Ceriodaphnia dubia*		
13 µg/L	LC50 (48 h) at pH 8.0-8.5	13
>200 µg/L	LC50 (48 h) at pH 6.0-6.5	13
Daphnid, *Daphnia hyalina*		
1.9 (1.5-2.5) mg/L	LC50 (48 h)	12
Daphnid, *Daphnia magna*		
10.2-21.4 µg/L	MATC[b] at 51 mg $CaCO_3$/L	4
30-95 µg/L	Reproduction impaired in 21 days	4
100 µg/L	Growth inhibited in 9 days	4
101-150 µg/L	MATC[b] at 105 mg $CaCO_3$/L	4
220-570 µg/L	MATC[b] at 205 mg $CaCO_3$/L	4
360 (330-400) µg/L	LC50 (21 days)	14
500 µg/L	LC50 (9 days) at 60 mg $CaCO_3$/L	4
510 µg/L	LC50 (96 h) at 45 mg $CaCO_3$/L	4
540 µg/L	Population biomass reduced	14
10% in 21 days		
950 (670-1,300) µg/L	Population biomass reduced	14
50% in 21 days		
2.34 mg/L	LC50 (96 h) at 100 mg $CaCO_3$/L	4
4.96 mg/L	LC50 (96 h) at 206 mg $CaCO_3$/L	4
Daphnid, *Daphnia pulicaria*		
1.8-2.2 mg/L	LC50 (48 h) at 44-48 mg $CaCO_3$/L	4
2.4-3.8 mg/L	LC50 (48 h) at 194-244 mg $CaCO_3$/L	4
Copepod, *Eudiaptomus padanus*		
3.6 (2.8-4.6) mg/L	LC50 (48 h)	12
Amphipod, *Gammarus* sp.		
13.0 mg/L	LC50 (96 h)	4
Amphipod, *Hyalella azteca*		
890 µg/L	LC50 (96 h) at pH 8.0-8.5	13
2.0 mg/L	LC50 (96 h) at pH 6.0-6.5	13
Mysid shrimp, *Mysidopsis bahia*		
61-141 µg/L	MATC[b]	4
Mysid shrimp, *Mysidopsis bigelowi*		
510-640 µg/L	LC50 (96 h)	4
Mysid shrimp, *Mysidopsis formosa*		

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
150 μg/L	LC50 (96 h)	4
Copepod, *Nitocra spinipes*		
6.0 mg/L	LC50 (96 h)	15
Hermit crab, *Pagurus longicarpus*		
10.0 mg/L	No deaths in 168 h	9
47.0 mg/L	LC50 (96 h)	9
50.0 mg/L	All dead in 168 h	9
Annelids		
Oligochaete, *Lumbriculus variegatus*		
26.0 mg/L	LC50 (96 h) at pH 8.0-8.5	13
100.0 mg/L	LC50 (96 h) at pH 6.0-6.5	13
Sandworm, *Nereis diversicolor*; adults		
10.0 mg/L	No deaths in 168 h	9
25.0 mg/L	LC50 (96-168 h)	9
50.0 mg/L	All dead in 168 h	9
Polychaete annelids, three species		
17.0-49.0 mg/L	LC50 (96 h)	4
Oligochaete, *Tubifex tubifex*		
80-61,400 μg/L; various water hardnesses	LC50 (48 h) range; most sensitive in soft waters; survivors had increased respiration rate	16, 17
Echinoderms		
Sea urchin, *Arbacia punctulata*; embryos		
17.0 mg/L	More than 50% dead in 42 h	4
Starfish, *Asterias forbesi*; adults		
5.0 mg/L	No deaths in 168 h	9
13.0 mg/L	LC50 (168 h)	9
50.0 mg/L	All dead in 168 h	9
150.0 mg/L	LC50 (96 h)	9
Sea urchin, *Lytechinus pictus*; embryos; exposed continuously from fertilization through hatching to 5.8, 58, 580, 5,800, 58,000, or 580,000 μg Ni/L, as nickel chloride		
5.8 μg/L group	Normal growth and development	18
58 and 580 μg/L groups	Normal development through gastrulation, but larvae developed abnormally (no dorsoventral symmetry)	4, 18
58.0 mg/L and higher	Normal cleavage, but gastrulation unsuccessful	18
Sea urchin, *Strongylocentrotus purpuratus*		
Sperm held in 0.6, 5.9, 59, 590, or 5,900 μg Ni/L for 50 min	0.6 and 5.9 μg/L had no effect on sperm motility; 59 μg/L had initial depressing effect followed by increased motility; 590 μg/L had initial depressing effect in motility with recovery; 5,900 μg/L caused significant depression in sperm motility	19
Sea urchins, various species; embryos		
180 μg/L	No adverse effects on development	20
370-1,470 μg/L	Embryonic development inhibited	20
Fishes		

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
Rock bass, *Ambloplites rupestris*		
2.48 mg/L	LC50 (96 h) at 26 mg $CaCO_3$/L	4
Climbing perch, *Anabas testudineus*		
146.0 mg/L for 30 days	No deaths; significant depletion of glycogen and total proteins in liver and gonads	21
American eel, *Anguilla rostrata*		
13.0 mg/L	LC50 (96 h)	4
Zebradanio, *Brachydanio rerio*; exposed from 2 h after fertilization through hatching and larval stages until day 16; 11 different doses as nickel sulfate hexahydrate		
40 µg/L	No effect on hatching time	22
>40 µg/L	Delayed hatching time	22
80 µg/L	No effect on larval survival	22
1,024 µg/L	No effect on embryonic survival	22
Goldfish, *Carassius auratus*		
500 µg/L for 2 weeks	Some accumulation in scales and otoliths, but not statistically significant	23
25 mg/L in 96 h	Swimming activity reduced 31%	24
75 mg/L	LC25 (96 h)	24
100 mg/L	LC88 (96 h)	24
Giant gourami, *Colisa fasciata*; adults		
64 mg/L as nickel sulfate (equivalent to 0.8 x LC50 [96 h] value); gonads examined after 96 h	Testicular degeneration (spermatogonial activity reduced, germ cells in testicular lobules degenerating, congested blood vessels); ovaries histologically different, oocytes resorbed	25
Common carp, *Cyprinus carpio*		
750 µg/L, larvae	LC50 (257 h) at 128 mg $CaCO_3$/L	4
1.0 mg/L for 16 days (in mixture containing 1.0 mg/L each of Cd, Cr, and Pb salts); adults	Maximum nickel concentrations, in mg/kg DW, were 77 in liver, 49 in gill, 39 in brain, and 19 in muscle; other metals tested showed time-dependent increases in tissues	26
1.3-40.0 mg/L	LC50 (96 h)	4, 27
8.0 mg/L for 15 days, adults	No deaths; disrupted protein metabolism in gills and kidneys	8
8.0 mg/L for 15 days (sublethal exposure); nickel concentrations (in mg/kg FW) in tissues of experimentals at end of exposure vs. controls		
Brain	41 vs. 25	29
Gill	103 vs. 31	29
Kidney	80 vs. 50	29
Liver	97 vs. 32	29
Muscle	58 vs. 30	29
10.4-10.6 mg/L	LC50 (96 h) at 55 mg $CaCO_3$/L	4
Carp, *Cyprinus carpio communis*		
Fingerlings; exposed to 2.5, 5, 7.5, or 10 mg Ni/L for 30 days	No deaths; protein content significantly decreased over time	30

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
	in dose-dependent pattern in brain, intestine, and muscle	
Orange chromide, *Etroplus maculatus*		
Exposed to 10, 30, 60, 80, or 100 mg Ni/L for 96 h at 3 salinities (2.5, 5, and 15 ppt)	At 2.5 ppt salinity, whole body nickel concentrations increased from 19 to 232 mg/kg DW in a dose-dependent manner (vs. control of 12.5 mg/kg DW); for 15 ppt salinity, nickel increased from 20 to 113 mg/kg DW; in combination with copper salts, nickel uptake increased at intermediate salinities	31
Fishes; most species; adults		
4-14 mg/L	LC50 (96 h), soft water	1
24-44 mg/L	LC50 (96 h), hard water	1
Banded killifish, *Fundulus diaphanus*		
46.1 mg/L	LC50 (96 h) at 53 mg $CaCO_3$/L	4
Mummichog, *Fundulus heteroclitus*		
50 mg/L	No deaths in 168 h	9
150 mg/L	LC50 (96 h)	9
250 mg/L	All dead in 168 h	9
Channel catfish, *Ictalurus punctatus*; from fertilization through day 4 posthatch		
38 (18-68) µg/L	LC10	28
710 (490-1,010) µg/L	LC50	28
Spot, *Leiostomus xanthurus*		
70 mg/L	LC50 (96 h), adults	1
Pumpkinseed, *Lepomis gibbosus*		
5.2 mg/L	LC50 (96 h) at 20 mg $CaCO_3$/L	4
8.0 mg/L	LC50 (96 h) at 55 mg $CaCO_3$/L	4
Bluegill, *Lepomis macrochirus*		
5.4 mg/L	LC50 (96 h) at 20 mg $CaCO_3$/L	4
39.6 mg/L	LC50 (96 h) at 360 mg $CaCO_3$/L	4
Atlantic silverside, *Menidia menidia*		
8.0 mg/L	LC50 (96 h)	4
Tidewater silverside, *Menidia peninsulae*; larvae		
38.0 mg/L	LC50 (96 h)	1
Largemouth bass, *Micropterus salmoides*		
113 (61-185) µg/L; exposed from fertilization through day 4 after hatching	LC10	28
2.02 mg/L, embryos	LC50 (8 days) at 93-105 mg $CaCO_3$/L	4
2.06 (1.48-2.84) mg/L; exposed from fertilization through day 4 after hatching	LC50	28
White perch, *Morone americana*		
13.6 mg/L	LC50 (96 h) at 55 mg $CaCO_3$/L	4
Striped bass, *Morone saxatilis*		
6.2 mg/L	LC50 (96 h) at 54 mg $CaCO_3$/L	4
Coho salmon, *Oncorhynchus kisutch*		
16.7 mg/L	LC50 (96 h), alevins	32
18.0 mg/L	LC50 (96 h), juveniles	32
Rainbow trout, *Oncorhynchus mykiss*		

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
11 µg/L; embryos exposed from fertilization through day 4 after hatching	LC10	28
23.9 µg/L	Avoidance by adults	33
<35 µg/L; chronic exposure; newly fertilized eggs	No adverse effects	33
50 µg/L; embryos exposed from fertilization through day 4 after hatching	LC50 (28 days) at 93-105 mg $CaCO_3$/L	4, 28
60 µg/L; fertilization through day 4 after hatching	LC50 at 125 mg $CaCO_3$/L	1
90 µg/L; fertilization through day 4 after hatching	LC50 at 174 mg $CaCO_3$/L	1
134 µg/L; chronic exposure of eyed eggs and larvae	No adverse effects	33
230-535 µg/L	MATC[b] at 50 mg $CaCO_3$/L	4
1.0 mg/L, as hexahydrate nickel chloride; exposure for 6 months plus 3-month postexposure observation period in uncontaminated media; juveniles	All fish appeared outwardly normal at all times; after 6 months of exposure, nickel concentrations—in mg/kg FW—were 4.0 in kidneys, 2.9 in liver, and 0.8 in muscle. Nickel concentrations following the 3-month postexposure period (controls) in mg/kg FW, were 2.5 (1.5) in kidneys, 1.8 (1.5) in liver, and 0.6 (0.5) in muscle	34
7.8-10.9 mg/L	LC50 (96 h), juveniles	32, 33
25.1 mg/L	LC50 (96 h), alevins	32
31.7 mg/L	LC50 (96 h); adults; hard water	35
35.7 mg/L, adults	LC50 (48 h) at 42 mg $CaCO_3$/L	4
Fed diet containing 61 mg Ni/kg DW ration (and other metals found in activated sewage sludge) for 10 weeks	Whole body nickel concentration increased from 0.33 mg/kg DW to 0.63 mg/kg DW	36
Isolated R1 liver cells exposed to culture media containing 84 mg Ni/L	50% inhibition of neutral red dye uptake	35
Isolated liver cells in 116 mg Ni/L	Cytotoxic	35
Tilapia, *Oreochromis niloticus*		
1.5 or 3.0 mg/L for 10 days	Significant depletion in liver and muscle glycogen; significant increase in plasma glucose; differences more pronounced at higher dose	37
Fathead minnow, *Pimephales promelas*		
109-433 µg/L	MATC[b] at 44 mg $CaCO_3$/L	4
380-730 µg/L	MATC[b] at 210 mg $CaCO_3$/L	4, 38
730-1,600 µg/L; lifetime exposure	No adverse effects on growth or survival; reproduction inhibited	38
3.1 mg/L	LC50 (96 h) at pH 8.0-8.5	13
>4.0 mg/L	LC50 (96 h) at pH 6.0-6.5	13
4.6-9.8 mg/L	LC50 (96 h) at 20 mg $CaCO_3$/L	4

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
25.0-32.2 mg/L	LC50 (96 h) at 210 mg $CaCO_3$/L	4
42.0-44.5 mg/L	LC50 (96 h) at 360 mg $CaCO_3$/L	4
Guppy, *Poecilia reticulata*		
31.0 mg/L	LC50 (10 days)	39
36.0 mg/L	LC50 (96 h)	39
Brook trout, *Salvelinus fontinalis*		
54.4 mg/L	LC50 (48 h) at 42 mg $CaCO_3$/L	4
Lake trout, *Salvelinus namaycush*		
16.7 mg/L	LC50 (48 h) at 42 mg $CaCO_3$/L	4
Spiny dogfish, *Squalus acanthias*		
6.0-11.0 mg/L	Nickel causes in vitro contraction of vascular smooth muscle of ventral aorta	40
Nile tilapia, *Tilapia nilotica*		
1.0 mg/L for 16 days	Maximum nickel concentrations, in mg/kg DW, were 49 in liver, 42 in brain, 37 in gill, and 14 in muscle	26
Exposed to 19, 32 or 51 mg/L for up to 96 h	Dose- and time-dependent increase in blood glucose and lactic acid concentrations; liver glycogen decreased at all nickel levels and muscle glycogen decreased at the two higher levels; high nickel concentrations were associated with elevated erythrocyte number, hemoglobin, and hematocrit. Nickel accumulated in blood, liver, muscle, and especially in kidney	41
65 mg/L	LC50 (96 h)	41
Arctic grayling, *Thymallus arcticus*		
8.2 (5.6-12.0) mg/L	LC50 (96 h), alevins	32
8.7 (6.7-11.4) mg/L	LC50 (96 h), juveniles	32
Amphibians		
Marbled salamander, *Ambystoma opacum*		
410 µg/L as nickel chloride; fertilization through day 4 after hatching	LC50	28
420 µg/L, embryos	LC50 (8 days) at 93-105 mg $CaCO_3$/L	4
Fowler's toad, *Bufo fowleri*		
11.03 mg/L as nickel chloride; fertilization through day 4 after hatching	LC50	28
Egyptian toad, *Bufo regularis*		
Females given single subcutaneous injection of nickel sulphate at 3-160 mg Ni/kg BW		
73 mg/kg BW	Calculated LD50 (96 h)	42
120 mg/kg BW	Calculated LD50 (24 h)	42
Concentrations of nickel in selected tissues of nickel-exposed survivors (all groups) vs. controls at 96 h		
Whole blood	320 µg/FW (Max. 1,420 µg/L	42
at 24 h) vs. 40 µg/L		
Kidney	1.82 mg/kg FW (Max. 3.6 mg/kg	42

Table 7. Taxonomic group, organism, dose, and other variables	Effect	Reference[a]
FW at 24 h) vs. 0.11 mg/kg FW		
Liver	0.54 mg/kg FW (Max. 2.02 mg/kg	42
FW at 48 h) vs. 0.3 mg/kg FW		
Serum	0.3 mg/L vs. 0.05 mg/L	42
Skin	0.6 mg/kg FW (Max. 1.56 mg/kg	42
FW at 24 h) vs. 0.01 mg/kg FW		
Urine	2.12 mg/L (Max. 70.0 mg/L at	42
24 h) vs. not detectable		
Narrow-mouthed toad, *Gastrophryne carolinensis*		
50 µg/L as nickel chloride; fertilization through day 4 after hatching	LC50	28
50 µg/L; embryos	LC50 (7 days) at 195 mg $CaCO_3$/L	4

[a] 1, World Health Organization 1991; 2, Whitton and Shehata 1982; 3, Lee and Lustigman 1996; 4, U.S. Environmental Protection Agency (EPA) 1980; 5, Dongmann and Nurnberg 1982; 6, Calabrese and Nelson 1974; 7, Calabrese et al. 1977; 8, Sreedevi et al. 1992a; 9, Eisler and Hennekey 1977; 10, Friedrich and Felice 1976; 11, Eisler 1977b; 12, Baudouin and Scoppa 1974; 13, Schubauer-Berigan et al. 1993; 14, Enserink et al. 1991; 15, Bengtsson 1978; 16, Brkovic-Povic and Popovic 1977a; 17, Brkovic-Popovic and Popovic 1977b; 18, Timourian and Watchmaker 1972; 19, Timourian and Watchmaker 1977; 20, Kobayashi and Fujinaga 1976; 21, Jha and Jha 1995; 22, Dave and Xiu 1991; 23, Mugiya et al. 1991; 24, Ellgaard et al. 1995; 25, Nath and Kumar 1990; 26, Canli and Kargin 1995; 27, Alam and Maughan 1992; 28, Birge and Black 1980; 29, Sreedevi et al. 1992b; 30, Thatheyus et al. 1992; 31, Patterson and Fernandez 1995; 32, Buhl and Hamilton 1991; 33, Nebeker et al. 1985; 34, Calamari et al 1982; 35, Segner et al. 1994; 36, Singh and Ferms 1978; 37, Alkahem 1995; 38, Pickering 1974; 39, Khangarot and Ray 1990; 40, Evans et al. 1990; 41, Ghazaly 1992; 42; Daabees et al. 1991.

[b] MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair is highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value is lowest concentration tested producing a measurable effect.

The biocidal properties of nickel are modified by many variables. For example, nickel is most lethal to freshwater crustaceans and fishes at pH 8.3 and least lethal at pH 6.3 (Schubauer-Berigan et al. 1993); less toxic to algae when copper is reduced or absent (NRCC 1981) and chelating agents, such as EDTA, are present (Lee and Lustigman 1996); most lethal to echinoderm embryos prior to gastrulation (Timourian and Watchmaker 1972); and more toxic to estuarine amphipods and clams under conditions of decreased salinity in the 0.5-3.5% range and increased temperature in the 5-15 C range (WHO 1991).

Representative nickel-sensitive aquatic species show sublethal effects at 11.7-125 µg Ni/L. These effects include altered immunoregulatory mechanisms in tissues of the rainbow trout at 11.7 µg/L (Bowser et al. 1994), inhibited reproduction of daphnids at 30 µg/L, growth inhibition of freshwater and marine algae at 30-125 µg/L, reduced growth of rainbow trout at 35 µg/L, accumulation from the medium by mussels at 56 µg/L, and abnormal development of sea urchin embryos at 58 µg/L (NRCC 1981; WHO 1991; Outridge and Scheuhammer 1993; Table 7).

Bioconcentration factors (BCF) for nickel vary among organisms under laboratory conditions. For freshwater species, typical BCF values for nickel are about 10 for algae, 61 for fathead minnows, and 100 for cladocerans; for marine mussels and oysters, typical BCF values range between 299 and 414 (USEPA 1980). The alga *Thalassiosira rotula* can accumulate as much as 90 mg Ni/kg DW (Dongmann and Nurnberg 1982). Other species of aquatic plants can extract nickel from water and concentrate it to as much as 10,000 mg/kg DW (NRCC 1981). The alga *Anacystis nidulans* can develop tolerance to nickel and other metals under laboratory conditions (Whitton and Shehata 1982), and this may account for high BCF values in this species. Nickel at 50 µg/L was accumulated from seawater by softshell clams (*Mya arenaria*) more rapidly during summer at water temperatures of 16-22 C than during winter temperatures of 0-10 C; no accumulations occurred at 10 µg Ni/L in winter, but clams accumulated twice as much nickel over controls in summer (Eisler 1977a). Embryos of sea urchins actively accumulate nickel from seawater at all dose levels tested (Timourian and Watchmaker 1972).

Bioconcentration factors for rainbow trout after exposure for 6 months to 1.0 mg Ni/L were 0.8 for muscle, 2.9 for liver, and 4.0 for kidneys (Calamari et al. 1982). Fish can accumulate nickel from food and water. Levels up to 13 mg Ni/kg DW occurred in northern pike (*Esox lucius*) and pickerel (*Esox* sp.) from a contaminated river (NRCC 1981). Common carp (*Cyprinus carpio*) and tilapia (*Tilapia nilotica*) exposed for 16 days to 1.0 mg Ni/L had elevated concentrations in livers of 49-77 mg Ni/kg DW (Canli and Kargin 1995). Goldfish (*Carassius auratus*) that died during immersion in solutions containing more than 35 mg Ni/L showed elevated concentrations in tissues; however, most of the nickel was washed off with water, and it is not clear if accumulation occurred after death (Kariya et al. 1968). Nickel accumulates in fish tissues and causes alterations in gill structure, including hypertrophy of respiratory and mucus cells, separation of the epithelial layer from the pillar cell system, cauterization and sloughing, and necrosis of the epithelium (Nath and Kumar 1989). Although aquatic organisms can accumulate nickel from their surroundings, there is little evidence of significant biomagnification of nickel levels along food chains (NRCC 1981; Sigel and Sigel 1988; WHO 1991).

Birds

In mallards (*Anas platyrhynchos*), nickel accumulates in tissues when diets contain as little as 12.5 mg Ni/kg DW ration (Table 8). Metabolic upset and altered bone densities occur in mallards fed diets containing 800 mg Ni/kg ration for 90 days (Cain and Pafford 1981; Eastin and O'Shea 1981). Inhibited growth and reduced survival occur in mallards at dietary loadings of 1,200 mg Ni/kg ration (Table 8). Dietary nickel concentrations of 0.074 mg Ni/kg ration have no adverse effects on Coturnix quail (*Coturnix risoria*). However, Japanese quail (*Coturnix japonica*) fed diets containing 0.71 mg Ni/kg ration have significantly elevated nickel concentrations in liver compared to controls fed diets containing 0.48 mg Ni/kg (Table 8). Increased concentrations of nickel in the diets of domestic chickens (*Gallus* sp.) were associated with decreased growth and survival and increased nickel concentrations in bone and kidney (Ling and Leach 1979). Dietary loadings of 500 mg Ni/kg ration and higher were associated with reduced growth and high mortality in some strains of chickens, but not others (Table 8). No developmental abnormalities occurred in chicks from survivors challenged by nickel during embryogenesis (USPHS 1977). Chick embryos receiving a single injected dose of 3.6 mg Ni/kg embryo, however, experienced 50% mortality within 18 days (Ridgway and Karnofsky 1952). Chicks are more resistant than embryos to injected nickel. Chicks injected with 10 mg Ni/kg BW survived but had disrupted glucose metabolism; effects were exacerbated by starvation (Nielsen 1977).

Table 8. Nickel effects on birds.

Variables		
Mallard, *Anas platyrhynchos*		
Breeding adults 20-months old fed diets containing 0, 12.5, 50, 200, or 800 mg Ni/kg ration for 90 days. All birds killed at day 90 and examined		
All groups	No effect on egg production, hatchability, or survival of ducklings; adults had normal blood chemistry and no organ histopathology; nickel accumulated in kidneys at all doses and in feathers, blood, and livers of birds fed high doses	1, 9
50 mg/kg group	Feathers contained 5.2 mg Ni/kg dry weight (DW) vs. 0.9 mg/kg DW in controls	1
800 mg/kg group	Abnormal black, tarry feces in test birds. Mean nickel concentrations, in mg/kg fresh weight (controls), were 1.9 (0.09) in kidneys, 0.52 (0.12) in livers, and 0.14 (0.005) in blood. Newly grown feathers had 68 (range 8-558) mg Ni/kg DW vs. 0.9 (0.5-1.6) mg/kg DW in controls	1
Ducklings age 1 day fed diets containing 0, 200, 800, or 1,200 mg Ni/kg fresh weight (FW) ration, as nickel sulfate, for 90 days		
800 mg/kg group and lower	No effect on growth or survival	2
800 mg/kg group	Lower bone density in females at day 60	2
1,200 mg/kg group	Tremors and paresis beginning at day 14; 71% dead by day 60. Survivors weighed less at day 28 than did birds fed other diets. Lower bone density evident at day 30. Livers and kidneys of survivors had <1.0 mg Ni/kg FW; dead birds had as much as 22.7 mg Ni/kg FW liver and 74.4 mg Ni/kg FW kidney	2
Japanese quail, *Coturnix japonica*		
For 2 generations quail ate diets containing wheat (*Triticum aestivum*) grown on sludge-amended soils (980 µg Ni/kg DW wheat) or control wheat (400 µg Ni/kg DW). Total diets contained 710 µg Ni/kg DW (sludge-grown wheat) or 480 µg Ni/kg DW (controls)	Nickel concentrations in livers of birds fed sludge-grown wheat were significantly elevated in males (210 µg Ni/kg DW vs. 130 in controls) and females (120 vs. 80 µg Ni/kg DW); mixed function oxidase activities were elevated in livers of both sexes when compared to controls	3
Coturnix quail, *Coturnix risoria*		
Fed diets containing 74 µg Ni/kg ration for 4 generations	No observed adverse effects	4
Domestic chicken, *Gallus* sp.		
Chicks given single intraperitoneal injection of 10 mg Ni (as nickel chloride)/kg body weight (BW)	Initial increase in plasma glucose after 15 min followed by hypoglycemia 60-120 min after injection. Starved chicks remained hyperglycemic during 120 min postinjection observation period	5
Day-old Plymouth Rock males fed semi-purified diets for 3 weeks		
300 mg Ni/kg diet	Reduced growth rate; elevated kidney nickel concentration of 4.2 mg/kg FW vs. 0.13 in controls	6, 9

[a]1, Eastin and O'Shea 1981; 2, Cain and Pafford 1981; 3, Stoewsand et al. 1984; 4, National Academy of Sciences 1975; 5, Nielsen 1977; 6, Ling and Leach 1979; 7, Weber and Reid 1968; 8, Ridgway and Karnofsky 1952; 9, Outridge and Scheuhammer 1993.

Mammals

Outridge and Scheuhammer (1993), in their excellent review of nickel hazards, draw six major conclusions regarding nickel toxicity to mammals. (1) Lifetime exposure of resistant species of mammals to diets containing 2,500 mg Ni/kg DW or to drinking water containing 10,000 mg Ni/L are not lethal. (2) Lethal nickel doses in mammals are usually derived from studies with laboratory animals injected with nickel and its compounds, not from realistic exposure regimens. (3) Inhaled nickel is at least 100 times more toxic than ingested nickel because it is more readily absorbed from the lungs than from the gastrointestinal tract, and death is more often the result of respiratory failure than of nervous system effects. For example, oral ingestion of 0.05 mg Ni/kg BW and inhalation at 0.005 mg Ni/m^3 are equally effective threshold doses in rats (USPHS 1977). (4) Large differences in sensitivity to nickel exist between closely related taxonomic species, such as rats and mice. (5) Threshold effects on lung function or morphology in several species of laboratory mammals occur at airborne nickel concentrations of 0.1-0.2 mg/m^3, depending on nickel compound and duration of exposure. (6) Juveniles were usually more sensitive to nickel than were adults.

Nickel salts administered by intravenous or subcutaneous injection are comparatively toxic. For all routes of parenteral administration, the LD50 (lethal dose to 50% of the sample) range for injected nickel salts is 6 mg Ni/kg BW for dogs given nickel oxide intravenously to 600 mg Ni/kg BW for mice given nickel disodium EDTA intraperitoneally (Nielsen 1977).

Several trends were evident among sensitive species of mammals tested against nickel through administration routes other than injection (Table 9). (1) Nickel carbonyl is lethal to mice, rats, and cats at 0.067-0.24 mg Ni/L. (2) Inhalation of nickel compounds other than nickel carbonyl causes significant effects in humans, rats, mice, rabbits, and dogs, with respiratory effects being most common. (3) Nickel-contaminated drinking water has adverse effects on rat reproduction and may neurologically affect the eyes of humans, although this needs to be verified. (4) Diets containing nickel carbonate, nickel chloride, or nickel sulfate cause reduced growth, disruptions of food intake and thyroid function, and emphysema and pneumonia in calves, dogs, mice, or rats. (5) Dermal application of nickel sulfate hexahydrate causes skin and testicular damage. (6) Single oral doses of 136-410 mg Ni/kg BW as nickel acetate are lethal to mice.

Table 9. Nickel effects on selected mammals.

Table. 9. Organism, route of exposure, dose, and other variables	**Effect**	**Reference[a]**
Cow, *Bos* sp.		
Diet		
63 mg Ni/kg ration for 8 weeks as nickel carbonate; male calves	Normal growth and food consumption	1, 2
250 mg Ni/kg ration for 42 days; lactating cows	Negligible transfer of nickel from diet to milk	3
250 mg Ni/kg DW ration for 8 weeks as nickel carbonate; male calves; equivalent to daily intake of 1,218 mg nickel	No accumulations in tissues; slight (13%) reduction in food intake and growth rate (11%)	1, 2
1,000 mg Ni/kg dry weight (DW) ration for 8 weeks as nickel carbonate; male calves; equivalent to daily intake of 1,410 mg nickel	Abnormal rumen fluid composition; nickel accumulations in tissues; marked reduction in food intake and growth rate. During a 6-week post exposure recovery period, growth rate was same as in controls	1,2
1,750 mg Ni/kg ration; adult females	No detectable nickel in milk	2
In vitro culture; isolated brain cells exposed for 20 h to graded concentrations of nickel chloride up to 116 mg Ni/L	Time- and dose-dependent effects on kinetics of brain microtubule polymerization; effects reversed on removal of Ni^{2+} from culture media	4
Domestic dog, *Canis familiaris*		
Diet		
0, 100, 1,000, or 2,500 mg Ni/kg ration for 2 years as nickel sulfate hexahydrate	No significant adverse effects at 1,000 mg Ni/kg ration and lower. At 2,500 mg Ni/kg, adverse effects observed on growth and blood chemistry; livers and kidneys enlarged; lung lesions; hyperplasia of bone marrow	5
Equivalent to 25 or 63 mg Ni/kg BW daily, as nickel sulfate, for 2 years	No serious adverse effects at low dose; high dose group had emphysema, pneumonia, low hematocrit, increased liver and kidney weight, and a 40% decrease in body weight gain	6
Inhalation		
2.7 mg Ni/L, as nickel carbonyl ($Ni(CO)_4$), for 75 min	LC80 (1-5 days postexposure)	8
5 to 6 mg Ni powder/m^3, 10 min daily for 6 months; observed for additional 19 months following treatment	No change in weight or general condition. At 3 months after treatment, leucocyte and primary neutrophil counts were low, and nickel was elevated in liver and kidneys. At 12 months, blood flow was reduced in small vessels of lungs. At 19 months, survivors had increased pulse and respiration rates	7
Intravenous injection, single dose		
6 to 7 mg Ni/kg BW, as nickel oxide	Lethal	2
10 to 20 mg Ni/kg BW as colloidal nickel	Death preceded by gastroenteritis,	2,9

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
	tremors, and paralysis	
10 to 20 mg Ni/kg BW as nickel chloride Oral	Some deaths	2, 9
12 mg/kg BW daily for 200 days	Tolerated without ill effects	10
1,000-3,000 mg Ni/kg BW as powdered nickel	Tolerated	9
Subcutaneous injection; single dose of 500 mg Ni/kg BW as nickel sulfate hexahydrate	Some deaths	2
Domestic goat, *Capra* hircus; pulmonary macrophages cultured in vitro for 20 h with media containing 14.5-58.0 mg Ni/kg as nickel chloride	Concentration-dependent decrease in viability of alveolar macrophages; highest dose had survival of <50%. Death associated with release of superoxide anions	11
Guinea pig, *Cavia* sp.		
Drinking water; 2.5 mg Ni/L for 4 months were between 3.4 and 4.6 mg Ni/kg DW hair	No accumulations in hair; all values	12
Inhalation; 15 mg Ni/m^3 as elemental nickel; lifetime exposure	Excess blood, swelling, hemorrhage, and increased frequency of lesions in the pharyngeal area	7
Intravenous injection; 62 mg Ni/kg BW as nickel sulfate; single injection	LD50	2
Subcutaneous injection; males given 0.0001, 0.001 or 1.0 mg Ni/kg BW daily as nickel chloride for 15 days were mated with fertile females	No effect on female gestation period, number of litters or offspring, weight of offspring, or offspring development	7
Hamster, *Cricetus* sp.		
Gavage; 5 mg of nickel oxide	After 24 h, no increase in nickel content of lungs, liver, kidney or carcass	7
Inhalation		
Exposed to nickel oxide aerosols at concentrations of 2-160 µg/L (2 to 160 mg/m^3) and particle size of 1 to 2.5 µm	45 days after exposure about 50% of the original dose remained in lungs with no significant accumulations in other tissues	10
15 mg Ni/m^3 as elemental nickel; lifetime exposure	No significant effect on survival or health	7
39 mg Ni/m^3 as nickel oxide for 3 weeks	Inflammation and congestion of lungs; emphysema	7
48.4 mg Ni/m^3 as nickel oxide for 61 days	No deaths	6
Domestic cat, *Felis domesticus*		
Inhalation; nickel carbonyl		
0.19 mg/L for 30 min	LC50 (0.2 h-6 days after exposure)	8
3.0 mg/L for 75 min	LC50 (1-5 days after exposure)	8
Oral; 12-25 mg/Ni kg BW daily for as long as 200 days as elemental and inorganic nickel salts	Tolerated, with no apparent ill effects	2, 9, 10
Human, *Homo sapiens*		
Dermal; <59 µg Ni/L; nickel-sensitive persons	No contact allergic reaction	14
Dialysis; 23 patients; nickel leached into dialysate from a nickel-plated stainless	At plasma nickel concentrations of about 3 mg/L, patients had adverse	8

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
steel water heater tank	effects including headaches, nausea, vomiting, and weakness; recovery occurred 3 to 13 h after cessation of dialysis	
Drinking water		
Equivalent to 0.012 or 0.05 mg Ni/L as nickel sulfate	Neurological effect on eyes at high dose; no adverse effects at low dose	6
250 mg Ni/L in contaminated drinking water	Stomach ache, increased red blood cell number, increased protein in urine	6
32 workers in an electroplating plant drank water accidentally contaminated with nickel sulfate and nickel chloride at 1,630 mg Ni/L;estimated intake of 0.5-2.5 g, equivalent to 8.3-41.6 mg/kg BW	Symptoms included nausea, vomiting, abdominal discomfort, diarrhea, giddiness, lassitude, headache, cough, and shortness of breath, and persisted for at least 2 h and sometimes 2 days. Serum nickel concentrations on day 1 after exposure were 286 (13-1,340) µg/L vs. 50 µg/L in nonaffected workers; for urine these concentrations were 5.8 (0.2-37.0) mg/L vs. 4.0 µg/L	8
Inhalation		
>0.04 mg Ni/m^3 air, usually as nickel oxide or metallic nickel	Chronic bronchitis, emphysema, reduced lung capacity, and increased incidence of deaths from respiratory disease among workers occupationally exposed	6
30 mg Ni/L air as nickel carbonyl for 30 min	Lethal	13
Chronic exposure		
Nickel aerosols, occupational exposure	Lung cancer, nasal sinusitis, chronic rhinitis	10
Nickel particulates	Chronic respiratory infections	10
Oral		
Low nickel diet fed to patients with chronic nickel dermatitis	Significant improvement in 6 weeks; adverse effects when placed on normal diet	10
Accidental ingestion of nickel sulfate crystals (15-20 grams) by 2.5 year-old female child	Death in 4 h of heart failure; blood had 7.5 mg Ni/kg, urine 50 mg/L, and liver 25 mg Ni/kg FW	6,8
Monkeys, various species; different forms of nickel in diet; as much as 1,000 mg Ni/kg ration for 24 weeks	No adverse effects on growth, behavior, or blood chemistry	10,13
Domestic mouse, *Mus* spp.		
Diet		
Young mice fed diets containing 0, 1,100 or 1,600 mg Ni/kg ration as the acetate salt for 4 weeks	Food consumption and growth reduced in the male 1,600 mg/kg group and the female 1,100 and 1,600 mg/kg groups. All nickel groups had significant decreases in liver cytochrome oxidase and isocitric dehydrogenase activities; in heart and kidney homegenates, malic dehydrogenase activity decreased in the high nickel groups	15, 16
Equivalent to >1.4 mg Ni/kg BW daily for 2 years as nickel chloride or nickel sulfate	Decreased liver weight	6

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
Equivalent to 108 mg Ni/kg BW daily for 180 days as nickel sulfate Drinking water	Renal tubular damage at the corticomedullary junction	6
Equivalent to >23 mg Ni/kg BW for 6-30 h as nickel chloride, nickel sulfate, or nickel nitrate	Abnormal sperm in mature males	6
150 mg/L as nickel sulfate for 6 months	No deaths	6
160 mg/L as nickel chloride in drinking water of pregnant females from gestation day 2 to day 7	Increased incidence of spontaneous abortions	6
Inhalation		
Nickel carbonyl		
0.01 mg/L for 120 min	All dead	8
0.067 mg/L for 30 min	LC50 (0.2 h-6 days after exposure)	8, 9
Nickel oxide		
>3.9 mg/m^3 for as long as 13 weeks	Adverse respiratory effects including chronic inflammation, fibrosis, macrophage hyperplasia, interstitial infiltrates, and increased lung weight	6
23.6 mg/m^3 for 16 days	No deaths	6
Nickel subsulfide		
>0.11 mg/m^3 for 16-91 days	Adverse respiratory effects	6
7.3 mg/m^3 for 16 days	All dead	6
Nickel sulfate		
>0.1 mg/m^3 for 16-91 days	Adverse respiratory effects	6
1.6 mg/m^3 for 16 days	All dead	6
Single intramuscular injection of 18.3 mg Ni/kg BW as nickel chloride	Involution of thymus and suppression of cellular and humoral activity and transient immunosuppressive effects within 2 days of injection with responses returning to normal within a few days	17
Single intraperitoneal injection		
Nickel acetate		
11 mg/kg BW	Adverse effects	21
32 mg/kg BW	LD50 (48 h)	7
39-50 mg/kg BW; adult males; age 9-15 weeks	LD50 (5 days postinjection)	20
48-54 mg/kg BW; adult females; age 9-15 weeks	LD50 (5 days postinjection)	20
89-97 mg/kg BW; juveniles; age 3 weeks	LD50 (5 days postinjection)	20
Nickel chloride		
Pregnant females given 1.2, 2.0, 3.0, 3.5, 4.6, 5.7, or 6.9 mg Ni/kg BW between days 7 and 11 of gestation	Dose-related increase in fetal deaths and malformations	8
3.1 mg Ni/kg BW	Normal spleen lymphocyte function	18
Pregnant mice given 4.6 mg Ni/kg BW on day 16 of gestation and killed 2 to 48 h after injection	Maximum nickel concentrations in tissues (in mg/kg FW) were reached in blood (19.8) and placentas (3.9) 2 h following injection; those in liver (4.9), spleen (1.3), and kidneys (56.2) were	19

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
	reached 4 h after injection; and maximum concentration in fetal tissues (1.1) was reached after 8 h. Authors estimate that all nickel is excreted in 42 to 84 h	
9.3-12.3 mg Ni/kg BW	Immunosuppression in spleen lymphocyte function	18
26 mg Ni/kg BW	LD50 (48 h)	7
Nickel chloride hexahydrate; 48 mg Ni/kg BW	LD50 (48 h)	7
Nickelocene; 27 mg Ni/kg BW	Adverse sublethal effects	21
Nickel oxide; >744 mg/kg BW	LD50 (72 h)	7
Nickel perchlorate heptahydrate; 100 mg Ni/kg BW	LD50 (12 h)	7
Nickel sulfate; 21-38 mg Ni/kg BW	LD50 (10-30 days)	7
Oral, single dose		
Nickel acetate; 136-410 mg Ni/kg BW	LD50 (72-120 h)	7, 21
Nickelocene; 186 mg/kg BW	LD50	21
Rabbit, *Oryctolagus* sp.		
Inhalation		
Metallic nickel dust		
>0.2 mg/m^3 for about 8 months	Alterations in alveolar macrophages; impaired cellular function	6
1.0 mg/m^3 for 3 or 6 months, 5 days weekly, 6 h daily; lungs examined	At both 3 and 6 months, there was a twofold to threefold increase in volume density of alveolar Type II cells; after 6 months, lungs had foci of pneumonia, suggesting a higher susceptibility to pulmonary infections due to a decrease in function of alveolar macrophages	22
Nickel carbonyl; 1.4 mg/L for 50 min	Alveolar cell degeneration within 5 days; LC80 (120 h)	8, 10
Nickel chloride; >0.2 mg/m^3 for about 8 months	Alterations in alveolar macrophages	6
Single intravenous injection; nickel chloride		
10 mg/kg BW	Transient hyperglycemia 1-4 h after injection	7
15 mg/kg BW	Pronounced hyperglycemia 1-4 h after injection, returning to normal after 24 h	7
15-20 mg/kg BW	Pancreas histopathology	7
Single subcutaneous injection; various nickel salts; 1,300 mg Ni/kg BW	Lethal	9
Laboratory white rat, *Rattus* sp.		
Dermal; nickel sulfate hexahydrate; dose equivalent to 40, 60, or 100 mg Ni/kg BW daily for 30 days (rats licked skin so exposure route may be oral in part)	No adverse effects in 40 mg/kg BW group. High dose groups had skin damage (atrophy, acanthosis, hyperkeratinization) and testicular damage abnormal seminiferous tubules, tubular lumens filled with degenerated sperm)	6,8,10
Diet		
Weanlings fed rations containing 0, 100, 500, or 1,000 mg Ni/kg, as nickel	At high doses (500, and 1,000 mg/kg), rats had depressed growth, low	38

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
acetate, for 6 weeks	hematocrit and hemoglobin, and low tissue cytochrome oxidase and alkaline phosphatase activities; the 1,000 mg/kg group (vs. controls) had elevated nickel concentrations—in mg Ni/kg DW—of 2.1 (0.9) in heart, 40.7 (5.0) in kidney, 4.0 (0.7) in liver, and 7.2 (1.6) in testes	
0, 100, 1,000, or 2,500 mg Ni/kg ration, as nickel sulfate hexahydrate, for 2 years	No histopathology in any group; at 1,000 and 2,500 mg Ni/kg ration, rats had depressed growth, lower liver weights, and increased heart weights	5
0, 250, 500, or 1,000 mg Ni/kg ration, as nickel sulfate hexahydrate, for 3 generations; equivalent to 0.7, 12.5, 25, or 50 mg Ni/kg BW daily; reproductive study	Higher incidence of stillborns and fetal mortalities noted only in the first generation at all nickel dietary levels; weanling body weight was lower at 1,000 mg Ni/kg ration in all generations	5,6,21
0.08 mg Ni/kg ration for 55 days	No adverse effects	2
250 mg Ni/kg ration for 16 months	Normal growth	16
1,000 mg Ni/kg ration (as nickel carbonate or nickel catalysts) for 8 weeks	Normal growth	10
1,000 mg Ni/kg ration for 13 days; juveniles	Altered blood chemistry, diminished food intake, and reduced growth within a few days	39
Dietary equivalent of 1, 25, or 100 mg/kg BW daily for 4 months; nickel chloride	Thyroid function affected; decreased iodine uptake at 1 mg/kg BW, increased at 25 mg/kg BW, and decreased at 100 mg/kg BW	7
Dietary equivalent of >1.4 mg Ni/kg BW daily for 2 years; nickel chloride or nickel sulfate	Decreased liver weight	6
Drinking water		
5 mg/L; lifetime exposure	No effect on growth or survival	35, 36
5 mg/L for 3 generations; diets contained 0.31 mg Ni/kg FW ration	Significant increase in mortality of young rats in all generations; significant increase in runts in first and third generations; litter size decreased with each generation; total number of rats reduced; few males were born in the third generation	35
225 mg/L for 4 months as nickel chloride	Depressed growth rate; lower serum triglyceride and cholesterol concentrations	13,40
Inhalation		
Nickel carbonyl ($Ni(CO)_4$)		
0.1 mg/L for 20 min	Some deaths after exposure	8
0.24 mg/L for 30 min	LC50 (0.2 h-6 days)	2, 8, 9
0.24-1.0 mg/L for 30 min	Lung histopathology within 10 days	10
0.9 mg/L for 30 min	LC80 (2 h-several months)	8
100 mg/L for 15 min	About 26% of the inhaled nickel was excreted in urine within 4 days; absorption estimated at 50%	10
160 mg/m^3 on days 7-8 of gestation or 300 mg/m^3 on day 7	Increased fetal mortality; reduced body weight in live pups; 16% incidence of fetal malformations	8

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
	(anophthalmia, microphthalmia, cystic lungs, hydronephrosis)	
Nickel chloride ($NiCl_2$); 0.05-5.0 mg/m^3	Significant decrease in iodine uptake	10
for 2 to 4 weeks	by thyroid	
Nickel dust; 15 mg/m^3; lifetime exposure	Increased frequency of adenoidal lesions and chronic sinus inflammation and ulceration	7
Nickel oxide (NiO)		
0.06 mg/m^3; lifetime exposure	Survival time decreased from 125 weeks in controls to 88 weeks; body weight loss after 13 months; alveolar proteinosis and marked lung enlargement	6
0.2 mg/m^3 for 1 year	Pneumonia and bronchial epithelial metaplasia	6
0.5 mg/m^3 for 1 month	Bronchial gland hyperplasia 20 months after exposure	6
1.6 mg/m^3 on gestation days 1-21	Decrease in fetal body weight	6
>3.9 mg/m^3 for as long as 13 weeks	Adverse respiratory effects	6
11.7 mg/m^3, 8 h daily, 5 days weekly, for 4 weeks	Significant increase in tumor necrosis factor for alveolar macrophages	24
23.6 mg/^{3} for 16 days	No deaths	6
Nickel subsulfide (Ni_3S_2)		
Equivalent to 0, 0.4, or 1.8 mg Ni/m^3; 6 h daily for as long as 22 days	The high dose group had reduced survival, nose and lung histopathology, and disrupted enzyme activity levels; survivors were lethargic and grew poorly. At day 22, nickel concentrations in lungs, in mg/kg FW, were<1.8 in controls, 12 in the low dose group and 34.0 in the high dose group	26
Equivalent to 0.11, 0.44, or 1.8 mg Ni m/^{3} for as long as 13 weeks; exposures were 6 h daily and 5 days weekly	Dose-dependent increase in pulmonary lesions; atrophy of the nasal olfactory epithelium at 0.44 mg/m^3 and higher	26
Equivalent to 0.73 mg/m^3 for 78 weeks plus 30 weeks of postexposure observation; exposure for 6 h daily and 5 days weekly	Pulmonary tumor growth (14% incidence in lung tumors vs. 1% in controls) and increased mortality (95% dead vs. 69% in controls)	6,25
7.3 mg/m^3 for 16 days	LC20	6
Nickel sulfate ($NiSO_4$)		
50 µg/rat	Half-time persistence in lung of 32 h; lung inflammatory responses disrupted lung enzyme activity	29
>0.1 mg/m^3 for as long as 13 weeks	Adverse respiratory effects	6
0.635 mg/m^3 for 16 days, 6 h daily	Induced lesions of olfactory epithelium but no measurable changes in olfactory	31

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
	function	
1.6 mg/m^3 for 16 days	No deaths	6
Single intramuscular injection, unless noted otherwise		
Metallic nickel; 110 mg/kg BW	Lowest toxic dose	2
Nickel acetate		
Males and females given 2.32 mg Ni/kg BW daily for 4 days	Males had inhibited testosterone levels and reduced growth, while females had increased uterine weights	7
420 mg/kg BW	Lowest toxic dose	2
Nickel chloride		
Females given 1.5-2.0 mg/kg BW daily on days 6-10 of gestation	Significant intrauterine mortality, but body weight of live pups was normal	8
Females given 2.0 mg/kg BW twice daily	No congenital abnormalities on days 6-10 of gestation	34
12 mg/kg BW to pregnant and nonpregnant females; tissues analyzed 24 h following injection	Relative tissue concentrations were kidney >serum > adrenal = lung = ovary > spleen = heart = liver > muscle. Nickel concentration in pituitary gland was significantly higher in pregnant rats	34
16 mg Ni/kg BW on day 8 of gestation	Reduction in number of live pups and diminished body weight of fetus on day 20 of gestation and of weanlings 4 to 8 weeks after birth; no developmental abnormalities	34
23-98 mg/kg BW	LD50 (7 days)	7,21,23,80
Nickel oxide		
7 mg Ni/kg BW	Significantly increased levels of serum alkaline phosphatase, amylase, aspartate transaminase, and lipoperoxide. Daily injections of copper-zinc superoxide dismutase prevented these changes	28
180 mg/kg BW	Toxic	2
Nickel subsulfide		
80 mg Ni/kg BW on day 6 of gestation	Reduction in mean number of live pups	34
90 mg/kg BW	Lowest toxic dose	2
Nickel sulfate; 12-16 mg/kg BW on day 8 of gestation	Reduction in mean number of live pups; reduced body weight in fetuses on day 20 of gestation and in pups 4-8 weeks after birth	8
Nickel sulfide; 7 mg/kg BW	Disrupted serum enzyme activity	28
Single intraperitoneal injection, unless indicated otherwise		
Nickel acetate		
8 mg/kg BW	Toxic	21
24 (19-28) mg/kg BW	LD50 (48 h)	7, 8
Nickel carbonyl; 13 mg/kg BW	LD50	8
Nickel chloride		
4 mg/kg BW	Tissue concentrations at 24 h	33

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
	(and at 15 min) after injection, in mg/kg FW, were 2.7 (16.1) in kidney, 0.3 (4.7) in liver, 1.2 (5.9) in blood, and 0.9 (1.4) in placenta	
6.0 (5.5-6.5) mg/kg BW	LD50 (7 days) for females pregnant 19 days	33
6.3 (5.6-7.1) mg/kg BW	LD50 (7 days) for females pregnant 12 days	33
8.0 mg/kg BW	Rapid transient increase in serum glucose and decrease in serum insulin	40
9.3 (8.5-10.2) mg/kg BW	LD50 (7 days) for virgin females	33
11-19 mg/kg BW	LD50 (7 days)	2, 7, 8
Nickelocene; 16-59 mg/kg BW	LD50, usually within 14 days	8, 21
Nickel oxide; >690 mg/kg BW	LD50 (3 days)	7
Nickel sulfate; 3 or 6 mg/kg BW daily for 7 or 14 days; killed 48 h after last injection	Highest nickel concentrations were in myocardium (5.7 mg/kg FW vs. 2.2 in controls) and spleen (2.1 vs. 0.6), followed by kidney, bone, and other tissues	37
Single intrarenal injection of nickel subsulfide equivalent to 39 mg/kg BW	Pronounced erythrocytosis; increased hematocrit and reticulocyte count	30
Intratracheal injection		
Nickel chloride; 1.0 mg/kg BW; examined 6 and 72 h after injection	At 6 h, tissue nickel concentrations were elevated in kidneys, lungs, adrenals, liver, pancreas, spleen, heart, and testes, in that order; by 72 h, 90% of the nickel was excreted, mostly (75%) in the urine	7
Nickel oxide; >110 mg/kg BW	LD50 (72 h)	7
Single intravenous injection of nickel carbonyl		
11 mg/kg BW; day 7 of gestation	High incidence of fetal deaths and malformations; reduced body weight in live pups	8
22 mg/kg BW	LD50, usually within 14 days	8
65 mg/kg BW	Massive lung histopathology within 6 days	10
Single oral exposure, unless indicated otherwise		
Nickel acetate		
116-120 mg/kg BW	Toxic	21
304-410 mg/kg BW	LD50 (7 days)	7, 8
Nickel chloride		
0.35 mg/kg BW daily for 28 days	Hyperglycemia, decreased body weight, reduced food and water intake	6
8.6 mg/kg BW daily for 91 days	LD25; decreased body weight in survivors	6
116 mg/kg BW	Toxic	6, 21
285 mg/kg BW	LD50, usually within 14 days	7
Nickel fluoborate ($Ni(BF_4)_2$); 500 mg/kg BW	Lethal	2
Nickel hexahydrate; 8.5 mg/kg BW daily for 91 days	Death preceded by lethargy, ataxia, irregular breathing, hypothermia, salivation, squinting, and loose stools	6

Table. 9. Organism, route of exposure, dose, and other variables	Effect	Reference[a]
Nickel nitrate ($Ni(NO_3)_2$); 1,620 mg/kg BW	LD50, usually within 14 days	2
Nickelocene		
154 mg/kg BW	Toxic	21
471-525 mg/kg BW	LD50, usually within 14 days	8
Nickel sulfate		
25 mg/kg BW daily for 120 days	Infertility	8
66 mg/kg BW	LD50, usually within 14 days	6
Single subcutaneous injection		
Nickel carbonyl; 21 mg/kg BW	LD50 within several days	8
Nickel chloride		
10 or 20 mg/kg BW; young males; observed for 7 days	Increased prolactin levels that persisted for 4 days;increased insulin levels on days 1 and 2	8
11.9 mg/kg BW	5% dead	27
59.5 mg/kg BW given 16 h prior to sacrifice	Significant increase in hepatic glutathione S-transferase activity	32

[a] 1, O'Dell et al. 1970; 2, National Academy of Sciences 1975; 3, Stevens 1991; 4, Lin and Chou 1990; 5, Ambrose et al. 1976; 6, U.S. Public Health Service (USPHS) 1993; 7, USPHS 1977; 8, World Health Organization 1991; 9, Sunderman 1970; 10, U.S. Environmental Protection Agency (USEPA) 1980; 11, Waseem et al. 1993; 12, Scheiner et al. 1976; 13, Nielsen 1977; 14, USEPA 1975; 15, Weber and Reid 1969; 16, Ling and Leach 1979; 17, Smialowicz et al. 1984; 18, Graham et al. 1975; 19, Lu et al. 1981; 20, Hogan 1985; 21, USEPA 1985; 22, Hohansson et al. 1981; 23, Sunderman et al. 1983; 24, Morimoto et al. 1995; 25, Ottolenghi et al. 1974; 26, Benson et al. 1995; 27, Iscan et al. 1992; 28, Novelli et al. 1995; 29, Hirano et al. 1994; 30, Oskarsson et al. 1981; 31, Evans et al. 1995; 32, Iscan et al. 1993; 33, Mas et al. 1985; 34, Sunderman et al. 1978; 35, Schroeder and Mitchener 1971; 36, Schroeder et al. 1974; 37, Mathur et al. 1978; 38, Whanger 1973; 39, Schnegg and Kirchgessner 1976; 40, Clary 1975; 41, Ho and Furst 1973.

Nickel carbonyl ($Ni(CO)_4$) is the only nickel compound known to cause severe acute effects, such as pulmonary damage and death; acute toxic effects of other nickel compounds to mammals are a minor risk (Norseth and Piscator 1979; Sevin 1980; WHO 1991). In fatal cases, death occurs 3-13 days after exposure; recovery from nickel carbonyl poisoning usually occurs within 70 days after exposure, but sometimes may take up to 6 months (Sunderman 1970; Sevin 1980; WHO 1991). Nickel carbonyl is a volatile, colorless liquid formed when finely divided nickel or its compounds come into contact with carbon monoxide. It is unstable under atmospheric conditions, and if inhaled, nickel is deposited in a highly active form on the respiratory mucosa on contact. Nickel carbonyl is widely used commercially as a catalyst but is one of the most toxic gases encountered in industrial operations (Sunderman 1970; Norseth and Piscator 1979; USEPA 1980, 1986). Exposure to air containing more than 50 mg $Ni(CO)_4/m^3$ for 0.5-2.0 h may be fatal to humans (WHO 1991). Intraperitoneal injection of nickel carbonyl was the most toxic route of administration; for all routes of administration, LD50 values to various tested mammals ranged between 13 and 65 mg/kg BW (WHO 1991; Table 9). Nickel carbonyl toxicity is due, in part, to its volatility and lipophilicity (Sigel and Sigel 1988). Signs of nickel carbonyl poisoning—which strongly resemble those of viral pneumonia—include headache, vertigo, nausea, vomiting, insomnia, and irritability followed by an asymptomatic interval and then the onset of insidious, persistent signs that include chest pains, dry coughing, cyanosis, sweating, visual and gastrointestinal disturbances, severe weakness, paralysis of the hind limbs, and convulsions; the lungs are the primary target organs in all animals tested, although the liver, kidneys, adrenal glands, spleen, and brain are also affected (Sunderman 1970; Nielsen 1977; Mushak 1980; USEPA 1980, 1986; Norseth 1986; WHO 1991).

Adverse effects in mammals by inhalation of nickel compounds other than nickel carbonyl occur with aerosols of both soluble and insoluble nickel compounds (USEPA 1980). Inhalation of nickel by humans and other mammals produces respiratory, hepatic, renal, dermal, immune system, and body weight effects (WHO 1991; USPHS 1993). Respiratory effects of nickel include asthma, nasal septal perforations, chronic rhinitis and

sinusitis, and increased risk for chronic respiratory tract infections (USPHS 1977; USEPA 1986; WHO 1991); immunological, genotoxic, and carcinogenic effects were also observed (USPHS 1993). Lung reactions in the form of asthma were attributed to sensitization by nickel (Norseth and Piscator 1979). Insoluble forms of inhaled nickel are more persistent in lungs than are soluble forms, as judged by 90-day studies with nickel chloride (soluble) and nickel oxide (insoluble) given to rodents by intratracheal administration (English et al. 1981). Severity of respiratory toxicity was higher with increasing solubility of the nickel compound tested and not with increasing burden of nickel on the lung; insoluble nickel oxide had the lowest toxicity but the highest lung burden. Nickel sulfate was more toxic than nickel subsulfide, which was more toxic than nickel oxide (USPHS 1993).

Local effects noted in guinea pigs, rats, mice, and hamsters caused by inhalation of metallic nickel powder (15 mg/m^3), nickel subsulfide (0.97 mg/m^3), or nickel oxide (53 mg/m^3) include nasal sinus inflammations, ulcers, lung irritation, nickel accumulations in lungs, emphysema, and increased viral respiratory infections (Norseth 1986; WHO 1991). Rats inhaling nickel subsulfide at 2.5 mg/m^3 for 22 days had nasal and lung histopathology within 4 days and disrupted enzyme activities and elevated nickel accumulations within 7 days (Benson et al. 1995). Repeated inhalation of nickel subsulfide by rats for 3 months resulted in chronic inflammation in the lung and atrophy of the olfactory epithelium (Benson et al. 1995). Rats exposed via inhalation of nickel sulfate hexahydrate of 635 μg Ni/m^3 for 6 h daily over 16 days had no outward signs of toxicity; however, internal examination revealed lesions on the olfactory epithelium (Evans et al. 1995). Rats and mice died following inhalation exposure for 16 days to equal doses of nickel sulfate or nickel subsulfide, but not nickel oxide (USPHS 1993). Rats showed epithelial hyperplasia after inhalation exposure to aerosols of nickel chloride or nickel oxide and pulmonary fibrosis after inhalation exposure to nickel subsulfide; a similar syndrome was reported in rabbits after high level inhalation exposure to nickel-graphite dust (WHO 1991). Dogs exposed to nickel powder for 6 months by way of inhalation developed lung pneumosclerosis causing cardiac insufficiency (USPHS 1977). Rats exposed to airborne nickel dusts (100 μg Ni/m^3, 12 h daily for 2 months) had respiratory irritation (NRCC 1981). Single exposures of mice to 250 μg Ni/m^3 for 2 h depressed the humoral immune response (NRCC 1981). Rats exposed to 1,000 μg Ni dust/m^3 (5 days/week for 3-6 months) had high accumulations of nickel in the lungs and kidneys and interstitial fibrosis (NRCC 1981).

Nickel and nickel salts are comparatively nontoxic when taken orally because of homeostatic mechanisms that control nickel metabolism and limited intestinal absorption (Nielsen 1977). In cattle, young calves fed nickel carbonate at concentrations as high as 1,000 mg Ni/kg ration for 8 weeks had nephritic kidneys, with degree of severity increasing with dietary nickel level. However, dietary nickel did not affect growth or food consumption of calves or cause histopathology of the rumen, abomasum, duodenum, liver, or testes (O'Dell et al. 1970). Human and animal data indicate that death is unlikely from oral nickel exposure except when exposed accidentally to high levels (USPHS 1993). Oral exposure studies for humans were limited to acute intoxication and include death (due to cardiac arrest) and the effects of gastrointestinal (nausea, cramps, diarrhea, vomiting), hematological (increase in reticulocytes), hepatic (increase in serum bilirubin), renal (albuminuria), and neurological damage. A child that accidentally ingested 20.36 grams of Ni/kg BW as crystals of nickel sulfate died from heart failure (USPHS 1993). Oral LD50 doses of nickel chloride to rats produced depression of the nervous system, edema of the mucous membranes of the mouth and nose, diffusions from the oral cavity, lacrimation, bleeding from the nose, and diarrhea (USPHS 1977). Prior to death, rats were lethargic, ataxic, and with irregular breathing and cool body temperatures (USPHS 1993).

Nickel is a reproductive toxicant in animals. Specific effects of nickel on reproduction include degenerative changes in the testes, epididymis, and spermatozoa of rats; adverse effects on embryo viability of rats and hamsters; and delayed embryonic development of rodents (Smialowicz et al. 1984; USEPA 1986; USPHS 1993). Nickel salts given by injection cause intrauterine mortality and decreased weight gain in rats and mice (WHO 1991). Inhibited testosterone and reduced growth occur in male rats given 2.32 mg Ni/kg BW as nickel acetate via intramuscular injection. Females given the same treatment had increased uterine weights (USPHS 1977). Nickel given in drinking water of rats for three generations at concentrations which do not interfere with growth or survival (i.e., 5 mg/L) were intolerable for normal reproduction (Schroeder and Mitchener 1971). All generations of rats given nickel in drinking water had increased proportions of runts and increased neonatal mortality when compared to controls. In the third generation of nickel-treated rats, there were reductions in litter size and a reduction in the proportion of males (Schroeder and Mitchener 1971). Excess nickel also inhibits

prolactin secretion in rats. Because prolactin influences milk production, the observation that suckling pups from nickel-exposed dams were most severely affected lends support to the concept that nickel plays a role in lactation at the pituitary level (Nielsen et al. 1975b).

The most commonly observed toxic reaction to nickel and nickel compounds in the general human population is nickel dermatitis and skin sensitivity arising from dermal contact with metals containing nickel (Sunderman 1970; NAS 1975; Norseth and Piscator 1979; USEPA 1980, 1986; WHO 1991; USPHS 1993). Studies on occupational dermatitis—which is the most prevalent occupational disease—show that 8% of the cases are due to nickel (Sunderman et al. 1984). Nickel dermatitis in occupational exposure begins as an itching or burning in the web of the fingers, spreading to the fingers, the wrists, and the forearms; the eruption is similar to atopic dermatitis (NAS 1975; USEPA 1980, 1986). Once an individual is dermally sensitized to nickel, even minimal contact (i.e., 0.007-0.04 mg Ni/kg BW daily) by any route of exposure may elicit a reaction (USEPA 1980; WHO 1991; USPHS 1993; Hughes et al. 1994). Nickel, in fact, is the most common allergin tested in North America; about 1-5% of human males and 7-14% of females are contact sensitized to nickel (NAS 1975; Nielsen 1977; Sevin 1980; USEPA 1980, 1986; Sunderman et al. 1984; USPHS 1993; Ikarashi et al. 1996). Nickel contact hypersensitivity has been documented worldwide, with 10% of the female population and 1% of the male population affected. Of these, 40-50% have vesicular hand eczema that, in some cases, can be severe and lead to loss of working ability (WHO 1991). Nickel contact dermatitis is decreasing in occupational exposure, but increasing elsewhere due to increasing contact with nickel alloys in jewelry, coins, zippers, tools, pots and pans, stainless steel, detergents, prostheses, and certain hair dressings (NAS 1975; Nielsen 1977; USEPA 1980; Sunderman et al. 1984; WHO 1991; USPHS 1993). Nickel is a major allergen for women, and between 1970 and 1980 there was a two- to threefold increase in the number of cases (Sunderman et al. 1984). In recent years, the incidence of nickel allergy has increased disproportionately in young females due to an increased frequency of ear piercing by this group to accommodate nickel-plated jewelry (Ikarashi et al. 1996).

Although contact allergy to nickel is common in humans, experimental sensitization in animals is only successful under special conditions (WHO 1991). Dermal studies with nickel salts and small laboratory mammals show that primary nickel sensitization typically takes place beneath nickel-containing metal objects that are in contact with the skin for hours and exposed to friction and sweating; nickel is released from nickel-containing objects by the action of blood, sweat, or saliva; ionic nickel diffuses through the skin at sweat-duct and hair-follicle openings, with a special affinity for keratin; and that nickel subsequently binds to proteins, including animo and carboxyl groups of keratin and serum albumin (NAS 1975; USEPA 1980; USPHS 1993). Rats, guinea pigs, and rabbits absorbed and subsequently distributed 55-77% of nickel applied dermally (USPHS 1977, 1993). Dermal effects in animals after dermal exposure to nickel include distortion of the dermis and epidermis, hyperkeratinization, atrophy of the dermis, and biochemical changes (USPHS 1993; Ikarashi et al. 1996). For example, in rats treated dermally with more than 40 mg Ni/kg BW daily as nickel hexahydrate for 30 days, distortion of the epidermis and dermis occurred by day 15 and hyperkeratinization, vacuolization, hydropic degeneration of the basal layer, and atrophy of the epidermis occurred by day 30 (USPHS 1993). Skin irritation and death from nickel salts is reported in rabbits when nickel was applied dermally to abraded skin; no negative effects occurred in rabbits when the same dose was applied to intact skin (USPHS 1977). As was the case for humans, allergic reactions occur in laboratory animals after oral nickel challenge in sensitized individuals (USPHS 1993).

Nickel affects endocrine and enzymatic processes. Nickel-induced endocrine effects include inhibition of insulin production in pancreas, prolactin in hypothalamus, amylase excretion in parotid gland, and iodine uptake in thyroid (Mushak 1980; USEPA 1980, 1986; USPHS 1977; WHO 1991). Inhibition of enzyme activity by nickel is reported for RNA polymerase, ATPase, dialkyl fluorophosphate, and aspartase (NAS 1975). Inhibition of ATPase is associated with neurological abnormalities, such as tremors, convulsions, and coma; altered hormone release or action; and internal rearrangement of calcium ions in muscle that might cause paralysis and abnormal heart rhythm (Nielsen 1977). Nickel increases the duration of the action potential of excitable membranes of nerve and muscle tissues; this effect is competitive with and imitative of those of calcium (NAS 1975). Nickel hexahydrate at 14.8 mg Ni/kg BW disrupts hepatic monooxygenases; mice were more sensitive to this disruption than rats or guinea pigs (Iscan et al. 1992). Nickel is also reported to activate various enzymes, including bovine pancreatic ribonuclease, pancreatic deoxyribonuclease, carboxypeptidase, arginase, phosphoglucomutase (Sevin 1980), and calcineurin—a calmodulin-dependent phosphoprotein phosphatase (USEPA 1986). Nickel affects the activity of heme oxygenase, thereby affecting the absorption of hemoglobin iron. Nickel, like many other metals and metalloids, induces heme oxygenase activity in tissues of mice,

hamsters, and guinea pigs in a dose-related manner (Sunderman et al. 1983).

Systemic effects of nickel exposure include hyperglycemia, increased levels of plasma glucagon, damage to the pancreatic islet cells, decreased body weight, reduced food and water intake, and hypothermia (NAS 1975; USEPA 1980; USPHS 1993). Acute administration of nickel salts caused prompt hyperglucagonemia and subsequent hyperinsulinemia in rats, rabbits, and guinea pigs (WHO 1991). Nickel chloride given orally to young male rabbits at 500 µg daily for 5 months produced a decrease in liver glycogen and an increase in muscle glycogen, with prolonged hyperglycemia (NAS 1975). Nickel increased glucose metabolism in rats injected intratracheally with 0.5 mg ionic nickel. This phenomenon probably reflected the influence of nickel on the production or secretion of insulin through decreased production of pituitary hormone secretions—specifically, prolactin—which control insulin concentrations (USPHS 1977). Nickel significantly affects the activity of hepatic glutathione S-transferases (GST); these compounds play important roles in the detoxification of electrophilic xenobiotics, such as nickel, epoxides, and diolepoxides (Iscan et al. 1993), and readily eliminate the cytotoxic products of lipid peroxidation, particularly the organic peroxides (Coban et al. 1996). The influence of nickel chloride on hepatic GST activity levels depends on the animal species tested, being depressed in mice, unchanged in rats, and increased in guinea pigs (Iscan et al. 1992). In humans, nickel toxicity is not related to GST depletion or increased lipid peroxidases in vitro, whereas in rat kidney, nickel toxicity may be due to GST depletion and stimulation of lipid peroxidases (Coban et al. 1996).

Nickel affects the immune, cardiac, and excretory systems. Nickel adversely affects the immune system by reducing host resistance to bacterial and viral infections, suppressing phagocytic activity of macrophages, reducing the number of T-lymphocytes (thereby suppressing the natural kill cell activity), and increasing susceptibility to allergic dermatitis (WHO 1991; USPHS 1993). In mice, nickel chloride suppresses the activity of natural killer cells within 24 h of a single intramuscular injection (USEPA 1986). Nickel-induced cardiovascular effects include vasoconstriction, inhibition of contraction by myocardial muscle, and a reduction in coronary vascular flow (USEPA 1986; WHO 1991; USPHS 1993). Nickel salts are demonstrably cardiotoxic in dogs (Sigel and Sigel 1988). Cats injected intravenously with $NiCl_2$ had altered heart rhythms, conductivity, and calcium metabolism (Nielsen 1977). Nickel is a nephrotoxin with greatest adverse effect on the glomerular epithelium of the kidney. Kidneys from mammals exposed to nickel showed renal tubular damage, protein loss, and weight changes (USPHS 1993).

Nickel accumulations in tissues and organs of mammals vary significantly with species, route of administration, sex, and general health. No significant accumulations of nickel were observed in liver or kidney of Holstein calves fed diets containing 1,000 mg Ni/kg ration for 21 weeks (Stevens 1992). In lactating dairy cows, no transfer of soluble nickel was observed from diet to tissues (Stevens 1992). In rats, guinea pigs, rabbits, sheep, dogs, and other species of mammals, nickel tends to accumulate in kidneys and other tissues after nickel exposure (as quoted in Eastin and O'Shea 1981). Nickel-poisoned rats had elevated accumulations primarily in myocardium (5.7 mg/kg FW vs. 2.2 in controls) and spleen (2.1 mg/kg FW vs. 0.6), followed by kidney, bone, and other tissues (Mathur et al. 1978). In rats, nickel accumulated mainly in lung and secondarily in heart tissues after intratracheal administration of nickel chloride; nickel was retained for at least 40 days after dosing (Novelli and Rodrigues 1991). In rodents, nickel accumulates in endocrine tissues, including the pituitary, adrenals, and pancreas (Mushak 1980; USEPA 1980). High nickel concentrations in the pituitary gland of rodents were associated with inhibition of insulin release and decreased prolactin secretion (Clary 1975). Rat weanlings fed diets containing 500 mg Ni/kg ration as nickel acetate show elevated nickel accumulations in plasma, erythrocytes, heart, liver, testes, and especially kidneys; high accumulations were associated with reductions in growth, hematocrit, hemoglobin, cytochrome oxidase, and alkaline phosphatase (Whanger 1973; Nielsen 1977). Male guinea pigs accumulated higher concentrations of nickel in hair than did females after exposure for 4 months to drinking water containing 2.5 mg Ni/L (Scheiner et al. 1976). Invading microorganisms can change the distribution of ^{63}Ni in mice infected with coxsackie B3 virus. Infected mice had high accumulations of ^{63}Ni in the pancreas and the wall of the ventricular myocardium. Healthy mice had almost no ^{63}Ni accumulations in these tissues, but residues were elevated in blood, kidney, and lung (Ilback et al. 1992).

Excretion of ingested nickel by rats, regardless of amount ingested, usually occurs through the feces within 48 h (Ho and Furst 1973). Most nickel administered to rats through a variety of routes, and irrespective of chemical form, is usually excreted within a few days; however, excretion is slower for nickel powder and from lungs (USPHS 1977). Nickel caused a twofold increase in urinary corticoid excretion in guinea pigs (USPHS

1977), increased urinary excretion of protein in rats (USPHS 1977), and increased urinary excretion of B-2-macroglobulin in nickel refinery workers (USPHS 1993). Nickelemia was associated with increased urinary B-2-macroglobulin levels, and 5 of 11 workers with urinary nickel concentrations more than 100 µg/L had increased urinary B-2-macroglobulin (>240 µg/L; USPHS 1993).

Proposed Criteria and Recommendations

While nickel may be carcinogenic, perhaps in all forms, there is little or no detectable risk in most sectors of the nickel industry at current exposure levels, including in some processes that had previously been associated with very high lung and nasal cancer risks (WHO 1991). More research is in progress to clarify the hazards of nickel to humans, including chronic inhalation carcinogenicity studies of nickel subsulfide, nickel oxide, and nickel sulfate hexahydrate in rats and mice (USPHS 1993). Nevertheless, additional research on nickel-induced cancer has been proposed, including research on (1) route of administration (USPHS 1993); (2) oxidative state of nickel (Kasprzak 1987); (3) effect of nickel on nucleic acid synthesis (Sunderman 1981); (4) interaction effects with asbestos (USEPA 1980), zinc and magnesium (Furst and Radding 1980), tobacco smoke (NRCC 1981), and agents thought to inhibit nickel carcinogenesis, such as manganese, copper, and aluminum (Furst and Radding 1980); (5) role of diet in nickel carcinogenesis (Furst and Radding 1980) and specificity and mechanism of uptake of nickel ion from the gastrointestinal tract (Hausinger 1993); and (6) nickel immunosuppressive mechanisms, especially effects of nickel on natural killer cell activity and the relation between suppression of these cells and the known carcinogenesis of nickel compounds (Smialowicz et al. 1984). Large-scale studies are needed to establish the upper limits of cancer risk from nickel (WHO 1991).

Humans have been shown to develop sensitivity to nickel (USPHS 1993). The use of nickel in products that may release the metal when in contact with the skin should be regulated (WHO 1991). Among various subgroups of the U.S. population who may be at special risk for adverse effects of nickel are those who have nickel hypersensitivity and suffer chronic flare-ups of skin disorders with frank exposure (USEPA 1986). The role of oral nickel exposure in dermatic responses by sensitive individuals suggests that nickel-limited diets resulted in marked improvement of hand eczema and that nickel added to the diets appeared to aggravate the allergic response (USEPA 1986). More research is needed on the role of nickel in contact dermatitis, including the role of oral nickel exposure, and the pathogenesis and therapy of nickel dermatitis (NAS 1975; Sunderman et al. 1984; USEPA 1986). Additional dermal exposure studies are needed to determine if testicular effects result from both oral and dermal exposure to nickel (USPHS 1993).

Animal experimental models of nickel-induced skin sensitivity are few and have been conducted only under very specialized conditions (USEPA 1986). Studies examining the mechanism of nickel contact sensitization and its extent in wildlife are needed (USPHS 1993). The importance of the surface properties and crystalline structure of nickel compounds in relation to their reactivity and protein-binding activities is well documented. It is therefore necessary to identify clearly the nickel compounds to which exposure occurs (Sunderman et al. 1984). Acute and chronic dermal and inhalation studies using all nickel compounds would determine if certain compounds are more effective in eliciting allergic dermatitis (USPHS 1993).

To protect terrestrial vegetation against decreased growth and other toxic effects, nickel residues in leaves should contain less than 44 to less than 50 mg/kg DW, soils should contain less than 50 to less than 250 mg Ni/kg DW, and sewage sludge applied to agricultural soils should be limited to 30-140 kg Ni/surface ha at the low end and 50-560 kg/ha at the high end (Table 10). Research is needed on the direct effects on vegetation of nickel from airborne deposition, the effects of soil acidification on mobility and toxicity of nickel in soil, differences in nickel metabolism between tolerant and nickel-sensitive plants (NRCC 1981), and on the interactions of nickel and organic acids in nickel-accumulating plants and in the surrounding soils (Lee et al. 1978).

To protect freshwater plants and animals against nickel, a proposed range of less than 25 to 96 µg total recoverable Ni/L is recommended by various authorities (Table 10). This range will protect most species of freshwater biota; however, certain species have reduced survival within this range, including embryos of rainbow trout (*Oncorhynchus mykiss*) at 11 µg/L (Birge and Black 1980), daphnids (*Ceriodaphnia dubia*) at 13 µg/L (Schubauer-Berrigan et al. 1993), and embryos of the narrow-mouthed toad (*Gastrophryne carolinensis*) at 50 µg/L (Birge and Black 1980; USEPA 1980). Mixtures of metals are additive or more-than-additive in toxicity and, in some cases, will exceed the recommended water quality criteria based on the individual metals. Such additive effects were demonstrated for daphnids and rainbow trout using water quality criteria developed in the

Netherlands for mixtures of nickel salts and those of arsenic, cadmium, chromium, copper, lead, mercury, or zinc (Enserink et al. 1991). To protect marine life, the 24-h average for total recoverable Ni/L should not exceed 7.1 μg/L, and the maximum concentration should not exceed 140 μg/L at any time (Table 10). The maximum concentration level for marine life protection needs to be reexamined because 30 μg Ni/L adversely affects growth of marine diatoms (Dongmann and Nurnberg 1982), 56 μg/L results in nickel accumulations in mussels (Friedrich and Filice 1976), 58 μg/L causes abnormal sea urchin development (Timourian and Watchmaker 1972), and 59 μg/L has adverse effects on motility of sperm of sea urchins (Timourian and Watchmaker 1977). In aquatic systems, research is needed to determine the mechanisms of nickel toxicity to biota, the transport of nickel, the interaction of nickel with other inorganic and organic chemicals, and the mobility of nickel in sediments under various environmental conditions (NRCC 1981).

Table 10. Proposed nickel criteria for protection of natural resources and human health.

Table 10. Resource, criterion, and other variables	**Effective nickel concentration**	**Reference a**
Aquatic life, freshwater		
Sediments		
Great Lakes		
Safe	Less than 20 mg/kg dry weight (DW)	1
Moderately polluted	20-50 mg/kg DW	1
Heavily polluted	More than 50 mg/kg DW	1
Wisconsin; for disposal in water	Less than 100 mg/kg DW	1
Water		
Canada; safe level	Less than 25 µg/L	2
Rainbow trout, *Oncorhynchus mykiss*; safe level	Less than 29 µg/L	3
Toxic effects expected	30-50 µg/L	4
Ontario, Canada; from sediment disposal in water; final water concentration	Less than 50 µg/L	1
The Netherlands; safe level	Less than 50 µg/L	5
United States; water hardness of 50 mg $CaCO_3$/L	24-h average not to exceed 56 µg total recoverable Ni/L; maximum concentration not to exceed 1,100 µg/L at any time	6
Sweden; safe level	Less than 80 µg/L	7
United States; water hardness of 100 mg $CaCO_3$/L	24-h average not to exceed 96 µg total recoverable Ni/L; maximum concentration not to exceed 1,800 µg/L at any time	6
United States; water hardness of 200 mg $CaCO_3$/L	24-h average not to exceed 160 µg total recoverable Ni/L; maximum concentration not to exceed 3,100 µg/L at any time	6
Aquatic life, marine		
Water	24-h average not to exceed 7.1 µg total recoverable Ni/L; maximum concentration not to exceed 140 µg/L at any time	6
Birds		
Diet		
Domestic chicken, *Gallus* sp.; to prevent nickel deficiency in chicks	More than 50 µg/kg ration	8,9,10
Mallard, *Anas platyrhynchos*		
Ducklings; no adverse effects	Less than 200 mg/kg ration	4
Adults; no adverse effects	Less than 800 mg/kg ration	4
Adults; adverse effects	More than 800 mg kg fresh weight (FW) ration	11
Tissue concentrations		
Adverse effects expected; most species		
Kidney	More than 10 mg/kg DW	4

Table 10. Resource, criterion, and other variables Aquatic life, freshwater	Effective nickel concentration	Reference a
Liver	More than 3 mg/kg DW	4
Internal organs, most species		
Normal	Less than 3 mg/kg DW	4
Nickel-contaminated environments	As much as 30 mg/kg DW	4
Mallard; liver or kidney; significant exposure to dietary nickel that may be harmful	More than 1.0 mg/kg FW	11
Crops and other terrestrial vegetation		
Plant residues		
Alfalfa, *Medicago sativa*		
Normal	0.3-3.2 mg/kg DW	12
Decreased growth	44.0 mg/kg DW	12
Terrestrial vegetation		
Hyperaccumulator plants	More than 1,000 mg/kg DW	13
Most species		
Normal	0.05-5.0 mg/kg DW	13
Toxic	More than 50 mg/kg DW	13
Sewage sludge; maximum addition to agricultural soils		
Europe	30-75 kg/ha	1
South Africa	200 mg/kg DW	24
United States; soils with low exchange capacity vs. soils with high exchange capacity		
Maryland	140 kg/ha vs. 280 kg/ha	1
Massachusetts	56 kg/ha vs. 112 kg/ha	1
Minnesota and Vermont	56 kg/ha vs. 112-224 kg/ha	1
Missouri	140 kg/ha vs. 280-560 kg/ha	1
New York, all soils	34-50 kg/ha	1
Oregon	50 kg/ha vs. 100-200 kg/ha	1
Wisconsin	50-100 kg/ha vs. 150-200 kg/ha	1
Soils; suitability for crop production		
Canada; Alberta; acidic soils; acceptable	Less than 250 mg/kg DW	1
The Netherlands		
Background	50 mg/kg DW	1
Moderate contamination	100 mg/kg DW	1
Unacceptable and requires cleanup	More than 500 mg/kg DW	1
Russia; maximum acceptable concentration; extractable by ammonium acetate buffer at pH 4.6	4.0 mg/kg	1
South Africa, no phytotoxicity or elevated nickel concentrations in crops	38 mg/kg DW	24
United States; New Jersey; acceptable	Less than 100 mg/kg DW	1
Mammals, except humans		
Air		
Laboratory white rat, *Rattus* sp.		
Adverse effects; nickel sulfate	More than 0.1 mg/m^3	9
No adverse effects		
Nickel refinery dust	Equivalent to less than 0.84 mg/kg BW daily	9
Nickel subsulfide	Equivalent to less than 1.7 mg/kg BW daily	9
Nickel sulfate	Less than 0.1 mg/m^3	9
Rodents, *Mus* spp., *Rattus* spp.		

Table 10. Resource, criterion, and other variables Aquatic life, freshwater	Effective nickel concentration	Reference a
Adverse effects; nickel oxide, nickel sulfate	More than 0.02 mg/m^3	14
No adverse effects; nickel chloride, nickel subsulfide	Less than 0.1 mg/m^3	4
Diet		
To prevent deficiency		
Rats, *Rattus* spp.	More than 50 µg/kg ration	9, 10, 15
Ruminants (*Bos* spp.), swine (*Sus* spp.)	More than 100 µg/kg DW ration[b]	9, 10
No observable adverse effects during chronic exposure		
Cattle, *Bos* spp.	Less than 0.5 mg/kg DW ration	10
Dogs (*Canis* sp.), rats (*Rattus* spp.), monkeys (*Macaca* spp.)	Less than 1.0 mg/kg ration	4
Rat	Equivalent to 16.7 µg/kg BW daily[c]	9
Various species	Less than 100 mg/kg ration, equivalent to 0.8 to less than 40.0 mg/kg BW daily	4
Adverse effects expected		
Cattle		
Adults	More than 50 mg/kg ration	16
Calves	More than 5 mg/kg ration, equivalent to more than 0.16 mg/kg BW daily	4,16
Dogs	Equivalent to more than 1.3 mg/kg BW daily	14
Mammals, most species	More than 500 to 2,500 mg/kg diet, equivalent to 10-50 mg Ni/kg BW daily	4
Drinking water		
Adverse effects observed		
Rat	5 mg/L, equivalent to 0.35 mg/kg BW daily	4
Most species	200-225 mg/L	4
Tissue residues		
Evidence of significant nickel exposure		
Kidney	More than 10 mg/kg DW	4
Liver	More than 3 mg/kg DW	4
Human health		
Air		
Cancer risk		
Increased risk; soluble nickel compounds	More than 1 to 2 mg/m^3	13
No increased risk; metallic nickel	Less than 0.5 mg/m^3	13
Industrial plant; United States; nickel carbonyl		
Safe	Daily average less than 1.0 µg/L; single air sample less than 40 µg/L	17
Discontinue operations	More than 1 to 5 µg/L daily average; single air sample more than 200 to 2,000 µg/L	17
Shut down plant	Daily average more than 5 µg/L; single air sample more than 2,000 µg/L	17
Outside industrial plant; nickel carbonyl		
Acceptable	Less than 0.3 µg/L monthly average	17
Shut down plant	More than 1.0 µg/L monthly average	17

Table 10. Resource, criterion, and other variables Aquatic life, freshwater	Effective nickel concentration	Reference a
Safe		
Canada		
Soluble nickel compounds	Less than 0.1 mg/m^3	18
Sparingly soluble nickel compounds	Less than 1.0 mg/m^3	18
Nickel carbonyl	Less than 0.12 mg/m^3 (equivalent to less than 0.35 mg $Ni(CO)_4/m^3$)	18
Former Soviet Union		
Nickel metal, nickel monoxide and sulfide dust, soluble nickel compound	Less than 0.5 mg/m^3	19
Nickel carbonyl	Less than 0.005 mg/m^3	19
Germany; nickel carbonyl	Less than 0.7 mg/m^3	19
Sweden; nickel metal	Less than 0.01 mg/m^3	19
United States		
Nickel carbonyl	Less than 0.007 mg/m^3	19
Nickel metal and relatively insoluble nickel compounds; 8 h daily, 40 h weekly	Less than 1.0 mg/m^3	6, 9, 19
Inorganic nickel in workplace (elemental and all nickel compounds except organonickel compounds with a covalent C-Ni bind, such as nickel carbonyl); 10-h work shift, 40-h workweek, over a working lifetime	Less than 0.015 mg/m^3	20
Water soluble nickel compounds; 8 h daily, 40 h weekly	Less than 0.1 mg/m^3	9 ,19
Oral, via diet and drinking water		
Safe chronic exposure via diet or drinking water; soluble nickel compounds	Less than 0.002 mg/kg BW daily	9
Diet; Australia; marine fish muscle; acceptable concentration	Less than 1.0 mg/kg FW	21
Drinking water		
Acceptable daily intake for 70-kg person (with a safety factor of 1,000)	0.031mg daily (equivalent to 0.443µg/kg BW daily)	6
Concentrations developed for noncarcinogenic effects		
Daily intake, lifetime exposure, 70-kg adult (safety factor of 100)	Less than 350 µg/L	15
Daily intake, 10-day health advisory for 10-kg child (with safety factor of 100)	Less than 1.0 mg/L	15
Daily intake, 10-day health advisory for 70-kg adult with safety factor of 100)	Less than 3.5 mg/L	15
Water containing edible fishery products		
From ingestion through water and nickel-contaminated fishery products	Less than 13.4 µg total recoverable Ni/L	6
From consumption of fish and shellfish products alone	Less than 101.1 µg/L	6
Tissue residues		
Plasma; total nickel; nickel workers; considered elevated	More than 11.9 µg/L	22
Serum; total nickel		

Table 10. Resource, criterion, and other variables Aquatic life, freshwater	Effective nickel concentration	Reference a
Normal	Less than 2.6 µg/L, excretion of 2.6 µg daily	22
Elevated (near nickel mine)	More than 4.6 µg/L, excretion of 7.9 µg daily	22
Urine; nickel carbonyl		
Mild exposure	Less than <0.1 mg/L during the first 8 h after exposure	22,23
Significant exposure	More than 0.1 mg/L during the first 8 h after exposure	23
Urine; total nickel; nickel workers; considered elevated	More than 129 µg/L	22

a 1, Beyer 1990; 2, Rutherford and Mellow 1994; 3, Nebeker et al. 1985; 4, Outridge and Scheuhammer 1993; 5, Enserink et al. 1991; 6, USEPA 1980; 7, Sreedevi et al. 1992a; 8, Nielsen et al. 1975a; 9, USPHS 1993; 10, Hausinger 1993; 11, Cain and Pafford 1981; 12, Jenkins 1980b; 13, WHO 1991; 14, Hughes et al. 1994; 15, USEPA 1985; 16, Stevens 1991; 17, NAS 1975; 18, NRCC 1981; 19, Sevin 1980; 20, USPHS 1977; 21, Sharif et al. 1993; 22, Norseth and Piscator 1979; 23, Norseth 1986; 24, Steyn et al. 1996.

b Elevated requirement may reflect increased use by rumen bacteria.

c Based on no observable adverse effects during chronic exposure to diets containing 100 mg Ni (as soluble salts) per kg ration (=5 mg Ni/kg BW daily) divided by uncertainty factor of 300.

To protect birds, diets should contain at least 50 μg Ni/kg ration to prevent nickel deficiency but less than 200 mg Ni/kg ration in the case of young birds and less than 800 mg/kg ration in the case of adults to prevent adverse effects on growth and survival (Table 10). Nickel residues in avian kidneys in excess of 10 mg/kg DW or in liver in excess of 3 mg/kg DW are sometimes associated with adverse effects (Outridge and Scheuhammer 1993); however, nickel accumulates in kidneys of mallards (*Anas platyrhynchos*) at dietary concentrations as low as 12.5 mg Ni/kg ration (Eastin and O'Shea 1981). In general, tissue concentrations of nickel were not reliable indicators of potential toxicity in mammals and birds because adverse effects, including death, frequently occurred in the absence of elevated tissue nickel concentrations (Outridge and Scheuhammer 1993). For monitoring birds, analysis of kidneys, bone, and feathers is most likely to reveal elevated exposure to environmental nickel contamination; nickel concentrations in liver and spleen often do not reflect elevated exposure (Outridge and Scheuhammer 1993).

To protect humans and other mammals, proposed air quality criteria range from 0.01 to less than 1.0 mg/m^3 for metallic nickel and slightly soluble nickel compounds, 0.015-0.5 mg/m^3 for water-soluble nickel compounds, and 0.005-0.7 mg/m^3 for nickel carbonyl (Table 10). Inhalation of nickel subsulfide concentrations (0.11-1.8 mg Ni/m^3) near the current threshold limit value of 1 mg Ni/m^3 can produce detrimental changes in the respiratory tract of rats after only a few days of exposure (Benson et al. 1995). Additional animal studies are recommended to identify minimally effective inhalation exposure levels for the various nickel compounds (USPHS 1993). Continued monitoring of nickel refining, nickel-cadmium battery manufacture, and nickel powder metallurgy installations is recommended because ambient air levels of bioavailable nickel at these installations in excess of 1 mg/m^3 can sometimes still be found (NAS 1975; Sevin 1980; Sunderman et al. 1984; Chau and Kulikovsky-Cordeiro 1995).

Most species of mammals had normal growth and survival during chronic exposure to diets equivalent to 0.8-40 mg Ni/kg BW daily (Outridge and Scheuhammer 1993). Reduced growth and survival sometimes occurred when sensitive species of wildlife were fed diets containing 500-2,500 mg Ni/kg ration, equivalent to 10-50 mg Ni/kg BW daily (Outridge and Scheuhammer 1993). Proposed criteria for nickel by way of the diet or drinking water range from 2 μg total Ni/kg BW daily (USPHS 1993) to 443 μg total Ni/kg BW daily (USEPA 1980) for soluble nickel compounds, less than 1.0 mg Ni/kg FW diet, and less than 350 μg Ni/L drinking water (Table 10). Further research is needed to clarify the role of nickel in mammalian nutrition, including dietary requirements of nickel and identification of the chemical forms of nickel present in foods and their bioavailability

(NAS 1975; Sunderman et al. 1984; Hausinger 1993). Studies are needed on the absorption and cellular uptake, transport, and metabolism of well-characterized nickel species following different routes and types of administration (NAS 1975; WHO 1991; Hausinger 1993) and on the transfer of dietary nickel to tissues of lactating dams and juveniles (Stevens 1992). Because young female laboratory mice were more susceptible to dietary nickel than were adults, it is possible that no-observable-adverse-effect-levels (NOAELs) derived from adult animals may be inappropriately high for neonates and juveniles (Outridge and Scheuhammer 1993). Studies that compare the toxicokinetics of humans and animals concurrently could be helpful in determining which species of animal is the most appropriate model for assessing the effects of nickel in human health (USPHS 1993). Animal studies designed to examine neurological effects after inhalation or oral exposure are needed to determine, in part, if human exposure to nickel will cause permanent neurological damage (USPHS 1993).

Nickel affects reproduction of selected mammals. Drinking water containing 5 mg Ni/L—equivalent to 0.2-0.4 mg Ni/kg BW daily—had adverse effects on rat reproduction and iron metabolism (Outridge and Scheuhammer 1993). Dogs given the equivalent of 1.3 mg Ni/kg BW daily had decreased litter survival (Hughes et al. 1994). Nickel is known to cross the placental barrier and reach the fetus in mammals and humans. More information is needed on the effects of in utero nickel exposure in pregnant women (USEPA 1986; Chashschin et al. 1994). Such information may be obtained using appropriate animal models (USPHS 1977). Multigenerational inhalation studies are recommended to determine if developmental effects result from both inhalation and oral exposure (USPHS 1993).

Biomarkers of nickel exposure and effects include nickel concentrations in feces and urine and changes in serum antibodies and serum proteins (USPHS 1993). Levels of carnosine, a dipeptide, seem to reflect the extent of nickel-induced damage to olfactory mucosa of rats, although the rodent olfactory system is more resilient than is the human (Evans et al. 1995). Studies on the availability of trace levels of nickel in food and water and in air would be helpful to relate levels of nickel found in the hair, nails, blood, and urine to levels of nickel in internal organs (USPHS 1993). Nickel concentrations in human tissues now considered elevated include 4.6 μg/L in serum, 11.9 μg/L in plasma, and 100-129 μg/L in urine (Table 10). Treatment of mammals suffering from nickel poisoning is usually through administration of various classes of chelating agents, including dithiocarb (sodium diethyl-dithiocarbamate—the drug of choice in the management of nickel carbonyl poisoning), EDTA salts, BAL (2,3-dimercaptopropanol), and penicillamine (Norseth and Piscator 1979; Norseth 1986). In all cases, the agents accelerate urinary excretion of absorbed nickel before extensive tissue injury occurs (USEPA 1980).

The nomenclature of nickel compounds should be further standardized (WHO 1991). Analytical methods must be developed and standardized in order to facilitate speciation of nickel compounds in atmospheric emissions, biological materials, and in other environmental samples (NAS 1975; WHO 1991). Studies are needed to elucidate the biogeochemical nickel cycle on a global scale and determine its potential for long-range transport (WHO 1991).

Conclusions

Nickel is found in air, soil, water, food, and household objects; ingestion or inhalation of nickel is common, as is dermal exposure. Recent estimates suggest that as much as 28,100 tons of nickel are introduced into the atmosphere each year from natural sources and as much as 99,800 tons from human activities. In the atmosphere, nickel is mostly suspended onto particulate matter. In natural waters the dominant chemical species is Ni^{2+} in the form of $(Ni(H_2O)_6)^{2+}$. In alkaline soils the major components of the soil solution are Ni^{2+} and $Ni(OH)^{+}$; in acidic soils the main solution species are Ni^{2+}, $NiSO_4$, and $NiHPO_4$.

Nickel is an essential micronutrient for maintaining health in certain species of plants and animals. Nickel deficiency effects from dietary deprivation of nickel have been induced experimentally in many species of birds and mammals. To prevent nickel deficiency in rats and chickens, diets should contain at least 50 μg Ni/kg ration, while cows and goats require more than 100 μg Ni/kg rations, perhaps reflecting the increased use by rumen bacteria. Nickel deficiency is not a public health concern for humans because daily oral intake is sufficient to prevent deficiency effects.

Nickel contamination from anthropogenic activities occurs locally from emissions of metal mining, smelting, and refining operations; combustion of fossil fuels; nickel plating and alloy manufacturing; land disposal of sludges, solids, and slags; and disposal as effluents. Nickel concentrations in living organisms and abiotic materials tend to be elevated in the vicinity of nickel smelters and refineries, nickel-cadmium battery plants, sewage outfalls, and coal ash disposal basins.

Adverse effects of excess nickel are documented for bacteria, algae, yeasts, higher plants, protozoans, mollusks, crustaceans, insects, annelids, echinoderms, fishes, amphibians, birds, and mammals. To protect terrestrial vegetation against decreased growth and other toxic effects, nickel concentrations in leaves should contain less than 50 mg Ni/kg DW (and in some cases less than 44 mg Ni/kg DW), growing soils should contain less than 250 mg Ni/kg DW (and in some cases <50 mg Ni/kg DW), and sewage sludge applied to agricultural soils should be limited to 30-140 kg Ni/surface ha at the low end and 50-560 kg/surface ha at the high end. To protect freshwater plants and animals against nickel, a proposed range of less than 25 to 96 μg total recoverable Ni/L is recommended by various authorities; however, certain species have reduced survival within this range. To protect marine organisms, the 24-h average for total recoverable nickel per liter should not exceed 7.1 μg/L and the maximum concentration should not exceed 140 μg/L at any time; however, certain marine organisms show adverse effects to as little as 30 μg Ni/L.

To protect young birds against adverse effects of excess nickel on growth and survival, diets should contain less than 200 mg Ni/kg ration, and diets of older birds should contain less than 800 mg Ni/kg ration. Nickel concentrations in avian tissues in excess of 10 mg/kg DW kidney or 3 mg/kg DW liver are sometimes associated with adverse effects.

Toxic effects of nickel to humans and laboratory mammals are documented for respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, dermal, ocular, immunological, developmental, neurological, and reproductive systems. Nickel toxicity in mammals is governed by the chemical form of nickel, dose, and route of exposure. Mammalian exposure to nickel by inhalation or cutaneous contact was more significant than oral exposure. To protect humans and other mammals against respiratory effects, proposed air quality criteria are 0.01 to less than 1.0 mg/m^3 for metallic nickel and sparingly soluble nickel compounds and 0.005-0.7 mg/m^3 for nickel carbonyl. Most species of mammals tested had normal growth and survival during chronic exposure to dietary nickel (equivalent to 0.8-40 mg Ni/kg BW daily) and reduced growth and survival when fed diets containing 500-2,500 mg Ni/kg ration (equivalent to 10-50 mg Ni/kg BW daily). Proposed nickel criteria for sensitive species by way of the diet or drinking water now range from 2 to less than 443 μg total Ni/kg BW daily for soluble nickel compounds, less than 1.0 mg Ni/kg FW diet, and less than 350 μg Ni/L in drinking water. Nickel concentrations in human tissues now considered elevated include 4.6 μg/L serum, 11.9 μg/L plasma, and 100-129 μg/L urine; comparable data for mammalian wildlife are lacking.

Some forms of nickel are carcinogenic to humans and animals, but only when exposure is by the respiratory route. Toxic and carcinogenic effects of nickel compounds are associated with nickel-mediated oxidative damage to DNA and proteins and to inhibition of cellular antioxidant defenses. Some nickel compounds are weakly mutagenic in a variety of test systems, but much of the evidence is inconclusive or negative. In mammals, no teratogenic effects of nickel compounds occur by way of inhalation or ingestion, except from nickel carbonyl. Inhaled nickel carbonyl results in comparatively elevated nickel concentrations in lung, brain, kidney, liver, and adrenals and is the most hazardous form of nickel.

Overall, nickel is not an immediate threat to the health of plants, animals, and humans at environmentally encountered levels, except in the case of nickel carbonyl, and progress has been made toward minimizing or eliminating occupational nickel exposure.

Acknowledgments

I thank L. J. Garrett and P. W. Manning for library services; W. N. Beyer, D. J. Hoffman, A. M. Scheuhammer, and F. W. Sunderman, Jr. for scientific and technical input; D. S. McGrath and B. A. Vairin for editorial services; and S. M. Lauritzen for layout.

Cited Literature

Adamo, P., S. Dudka, M. J. Wilson, and W. J. McHardy. 1996. Chemical and mineralogical forms of Cu and Ni in contaminated soils from the Sudbury mining and smelting region, Canada. Environmental Pollution 91:11-19.

Ahmed, R., and M. Stoeppler. 1994. Levels of heavy metals in owl's feathers and atmospheric pollution. Pakistan Journal of Scientific and Industrial Research 37:179-182.

Alam, M. K., and O. E. Maughan. 1992. The effect of malathion, diazinon, and various concentrations of zinc, copper, nickel, lead, iron, and mercury on fish. Biological Trace Element Research 34:225-236.

Alkahem, H. F. 1995. Effects of nickel on carbohydrate metabolism of *Oreochromis niloticus*. Dirasat Series B Pure and Applied Sciences 22B:83-88.

Ambrose, A. M., P. S. Larson, J. F. Borzelleca, and G. R. Hennigar, Jr. 1976. Long term toxicologic assessment of nickel in rats and dogs. Journal of Food Science and Technology 13:181-187.

Anke, M., B. Groppel, E. Riedel, and H. J. Schneider. 1980a. Plant and animal tissues as indicators of exposure to nickel. Pages 65-68 *in* S. S. Brown and F. W. Sunderman, Jr., editors. Nickel toxicology. Academic Press, New York.

Anke, M., M. Grun, and H. Kronemann. 1980b. Distribution of nickel in nickel-deficient goats and their offspring. Pages 69-72 *in* S. S. Brown and F. W. Sunderman, Jr., editors. Nickel toxicology. Academic Press, New York.

Anke, M., M. Partschefeld, M. Grun, and B. Groppel. 1978. Nickel--ein essentielles Spurenelement. 3. Der Einfluss des nickelmangels auf die Fortpflanzungs leistung weiblicher Tiere. Archiv fur Tierernahrung 28:83-90.

Antonijczuk, K., O. S. Kroftova, A. H. Varghese, A. Antonijczuk, D. C. Henjum, G. Korza, J. Ozols, and W. F. Sunderman, Jr. 1995. The 40kDa $^{63}Ni^{2+}$-binding protein (pNiXc) on Western blots of *Xenopus laevis* oocytes and embryos is the monomer of fructose-1,6-bisphosphate aldolase A. Biochimica et Biophysica Acta 1247:81-89.

Babich, H., and G. Stotzky. 1982a. Nickel toxicity to microbes: effect of pH and implications for acid rain. Environmental Research 29:335-350.

Babich, H., and G. Stotzky. 1982b. Nickel toxicity to fungi: influence of environmental factors. Ecotoxicology and Environmental Safety 6:577-589.

Bagatto, G., and J. D. Shorthouse. 1996. Accumulation of Cu and Ni in successive stages of *Lymantria dispar* L. (Lymantriidae, Lepidoptera) near ore smelters at Sudbury, Ontario, Canada. Environmental Pollution 92:7-12.

Barman, S. C., and S. K. Bhargava. 1997. Accumulation of heavy metals in soil and plants in industrially polluted fields. Pages 289-314 *in* P. N. Cheremisinoff, editor. Ecological issues and environmental impact assessment. Gulf Publishing Company, Houston, Texas.

Baudouin, M. F., and P. Scoppa. 1974. Acute toxicity of various metals to freshwater zooplankton. Bulletin of Environmental Contamination and Toxicology 12:745-751.

Beck, B. L., D. C. Henjum, K. Antonijczuk, O. Zaharia, G. Korza, J. Ozols, S. M. Hopfer, A. M. Barber, and F. W. Sunderman, Jr. 1992. *pNiXa*, a Ni^{2+}-binding protein in *Xenopus* oocytes and embryos, shows identity to *Ep45*, an estrogen-regulated hepatic serpin. Research Communications in Chemical Pathology and Pharmacology 77:3-16.

Bengtsson, B. E. 1978. Use of a harpacticoid copepod in toxicity tests. Marine Pollution Bulletin 9:238-241.

Benson, J. M., Y. S. Cheng, A. F. Eidson, F. H. Hahn, R. H. Henderson, and J. A. Pickrell. 1995. Pulmonary toxicity of nickel subsulfide in F344/N rats exposed for 1-22 days. Toxicology 103:9-22.

Bertran, G. C., and B. A. Kotsias. 1997. Blockade of the inward rectifier potassium currents by zinc and nickel ions in voltage-clamped toad muscles. Life Sciences 60:119-125.

Beyer, W. N. 1990. Evaluating soil contamination. U.S. Fish and Wildlife Service Biological Report 90(2). 25 pp.

Birge, W. J., and J. A. Black. 1980. Aquatic toxicology of nickel. Pages 349-366 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Bowser, D. H., K. Frenkel, and J. T. Zelikoff. 1994. Effects of *in vitro* nickel exposure on the macrophage-mediated immune functions of rainbow trout (*Oncorhynchus mykiss*). Bulletin of Environmental Contamination and Toxicology 52:367-373.

Boyden, C. R., B. E. Brown, K. P. Lamb, R. F. Drucker, and S. J. Tuft. 1978. Trace elements in the Upper Fly River, Papua, New Guinea. Freshwater Biology 8:189-205.

Boysen, M., H. Waksvik, L. A. Solberg, A. Reith, and A. C. Hogetveit. 1980. Pages 35-38 *in* S. S. Brown and F. W. Sunderman, Jr. editors. Nickel toxicology. Academic Press, New York.

Brkovic-Popovic, I., and M. Popovic. 1977a. Effects of heavy metals on survival and respiration rate of tubificid worms: part I--effects on survival. Environmental Pollution 13:65-72.

Brkovic-Popovic, I., and M. Popovic. 1977b. Effects of heavy metals on survival and respiration rate of tubificid worms: part II--effects on respiration. Environmental Pollution 13:93-98.

Brown, S. S., and F. W. Sunderman, Jr. (editors). 1980. Nickel toxicology. Academic Press, New York. 193 pp.

Bryan, G. W., and L. G. Hummerstone. 1978. Heavy metals in the burrowing bivalve *Scrobicularia plana* from contaminated and uncontaminated estuaries. Journal of the Marine Biological Association of the United Kingdom 58:401-419.

Bryan, G. W., G. W. Potts, and G. R. Forster. 1977. Heavy metals in the gastropod mollusc *Haliotis tuberculata* (L.). Journal of the Marine Biological Association of the United Kingdom 57:379-390.

Bubb, J. M., and J. N. Lester. 1996. Factors controlling the accumulation of metals within fluvial systems. Environmental Monitoring and Assessment 41:87-105.

Buhl, K. J., and S. J. Hamilton. 1991. Relative sensitivity of early life stages of Arctic grayling, coho salmon, and rainbow trout to nine inorganics. Ecotoxicology and Environmental Safety 22:184-197.

Burger, J., and M. Gochfeld. 1985. Comparisons of nine heavy metals in salt gland and liver of greater scaup (*Aythya marila*), black duck (*Anas rubripes*) and mallard (*A. platyrhynchos*). Comparative Biochemistry and Physiology 81C:287-292.

Cain, B. W., and E. A. Pafford. 1981. Effects of dietary nickel on survival and growth of mallard ducklings. Archives of Environmental Contamination and Toxicology 10:737-745.

Calabrese, A., J. R. MacInnes, D. A. Nelson, and J. E. Miller. 1977. Survival and growth of bivalve larvae under heavy-metal stress. Marine Biology 41:179-184.

Calabrese, A., and D. A. Nelson. 1974. Inhibition of embryonic development of the hard clam, *Mercenaria mercenaria*, by heavy metals. Bulletin of Environmental Contamination and Toxicology 11:92-97.

Calamari, D., G. F. Gaggino, and G. Pacchetti. 1982. Toxicokinetics of low levels of Cd, Cr, Ni and their mixture in long-term treatment on *Salmo gairdneri* Rich. Chemosphere 11:59-70.

Campbell, K. R. 1994. Concentrations of heavy metals associated with urban runoff in fish living in stormwater treatment ponds. Archives of Environmental Contamination and Toxicology 27:352-356.

Canli, M., and F. Kargin. 1995. A comparative study on heavy metal (Cd, Cr, Pb and Ni) accumulation in the tissue of the carp *Cyprinus carpio* and the Nile fish *Tilapia nilotica*. Turkish Journal of Zoology 19:165-171.

Chashschin, V. P., G. P. Artunina, and T. Norseth. 1994. Congenital defects, abortion and other health effects in nickel refinery workers. The Science of the Total Environment 148:287-291.

Chau, Y. K., and O. T. R. Kulikovsky-Cordeiro. 1995. Occurrence of nickel in the Canadian environment. Environmental Reviews 3:95-120.

Cheng, L., G. V. Alexander, and P. J. Franco. 1976. Cadmium and other heavy metals in seaskaters (Gerridae: *Halobates*, *Rheumobates*). Water, Air and Soil Pollution 6:33-38.

Clary, J. J. 1975. Nickel chloride-induced metabolic changes in the rat and guinea pig. Toxicology and Applied Pharmacology 31:55-65.

Coban, T., Y. Beduk, and M. Iscan. 1996. *In vitro* effects of cadmium and nickel on glutathione, lipid peroxidation and glutathione *S*-transferase in human kidney. Toxicology in Vitro 10:241-245.

Connors, P. G., V. C. Anderlini, R. W. Risebrough, M. Gilbertson, and H. Hays. 1975. Investigations of heavy metals in common tern populations. Canadian Field-Naturalist 89:157-162

Custer, T. W., and W. L. Hohman. 1994. Trace elements in canvasbacks (*Aythya valisineria*) wintering in Louisiana, USA, 1987-1988. Environmental Pollution 84:253-259.

Custer, T. W., J. C. Franson, J. F. Moore, and J. E. Myers. 1986. Reproductive success and heavy metal contamination in Rhode Island common terns. Environmental Pollution 41A:23-52.

Custer, T. W., and B. L. Mulhern. 1983. Heavy metal residues in prefledgling black-crowned night-herons from three Atlantic coast colonies. Bulletin of Environmental Contamination and Toxicology 30:178-185.

Daabees, A. Y., N. A. El Domiaty, A. M. Hilmy, A. M. Awadallah, and E. M. A. Taleb. 1991. Mortality, distribution and excretion of cobalt and nickel administered subcutaneously to toads. Journal of the Medical Research Institute (Egypt) 12:185-201.

Darolova, A, E. Reichrtova, and J. Pavelka. 1989. Bioaccumulation of metals from nickel works waste in the gull (*Larus ridibundus* L., 1766). Biologia Bratislava 44:567-573.

Dassenakis, M. I., M. A. Kloukiniotou, and A. S. Pavlidou. 1996. The influence of long existing pollution on trace metal levels in a small tidal Mediterranean bay. Marine Pollution Bulletin 32:275-282.

Datta, A. K., M. Misra, S. L. North, and K. S. Kasprzak. 1992. Enhancement by nickel(II) and L-histidine of 2'-deoxyguanosine oxidation with hydrogen peroxide. Carcinogenesis 13:283-287.

Datta, A. K., S. L. North, and K. S. Kasprzak. 1994. Effect of nickel (II) and tetraglycine on hydroxylation of the guanine moiety in 2'-deoxyguanosine, DNA, and nucleohistone by hydrogen peroxide. Science of the Total Environment 148:207-216.

Dave, G., and R. Xiu. 1991. Toxicity of mercury, copper, nickel, lead, and cobalt to embryos and larvae of zebrafish, *Brachydanio rerio*. Archives of Environmental Contamination and Toxicology 21:126-134.

Donghua, L., and J. Wusheng. 1997. Effects of nickel sulfate on root growth. Pages 315-318 *in* P.N. Cheremisinoff, editor. Ecological issues and environmental impact assessment. Gulf Publishing Company, Houston, Texas.

Dongmann, G., and H. W. Nurnberg. 1982. Observations with *Thalassiosira rotula* (Menier) on the toxicity and accumulation of cadmium and nickel. Ecotoxicology and Environmental Safety 6:535-544.

Drbal, K., J. Elster, and J. Komarek. 1992. Heavy metals in water, ice and biological material from Spitsbergen, Svalbard. Polar Research 11:99-101.

Duke, J. M. 1980. Production and uses of nickel. Pages 51-65 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Eastin, W. C., Jr., and T. J. O'Shea. 1981. Effects of dietary nickel on mallards. Journal of Toxicology and Environmental Health 7:883-892.

Eisler, R. 1973. Annotated bibliography on biological effects of metals in aquatic environments (No. 1-567). U.S. Environmental Protection Agency Report EPA-R3-73-007. 287 pp.

Eisler, R. 1977a. Toxicity evaluation of a complex metal mixture to the softshell clam *Mya arenaria*. Marine Biology 43:265-276.

Eisler, R. 1977b. Acute toxicities of selected heavy metals to the softshell clam, *Mya arenaria*. Bulletin of Environmental Contamination and Toxicology 17:137-145.

Eisler, R. 1981. Trace metal concentrations in marine organisms. Pergamon Press, New York. 687 pp.

Eisler, R., M. M. Barry, R. L. Lapan, Jr., G. Telek, E. W. Davey, and A. E. Soper. 1978a. Metal survey of the marine clam *Pitar morrhuana* collected near a Rhode Island (USA) electroplating plant. Marine Biology 45:311-317.

Eisler, R., and R. J. Hennekey. 1977. Acute toxicities of Cd^{2+}, Cr^{+6}, Hg^{2+}, Ni^{2+} and Zn^{2+} to estuarine macrofauna. Archives of Environmental Contamination and Toxicology 6:315-323.

Eisler, R., D. J. O'Neill, Jr., and G. W. Thompson. 1978b. Third annotated bibliography on biological effects of metals in aquatic environments (No. 1293-2246). U.S. Environmental Protection Agency Report 600/3-78-005. 487 pp.

Eisler, R., R. M. Rossoll, and G. A. Gaboury. 1979. Fourth annotated bibliography on biological effects of metals in aquatic environments (No. 2247-3132). U.S. Environmental Protection Agency Report 600/3-79-084. 592 pp.

Eisler, R., and M. Wapner. 1975. Second annotated bibliography on biological effects of metals in aquatic environments (No. 568-1292). U.S. Environmental Protection Agency Report EPA-600/3-75-008. 400 pp.

Ellgaard, E. G., S. E. Ashley, A. E. Langford, and D. C. Harlin. 1995. Kinetic analysis of the swimming behavior of the goldfish, *Carassius auratus*, exposed to nickel; hypoactivity induced by sublethal concentrations. Bulletin of Environmental Contamination and Toxicology 55:929-936.

English, J. C., Parker, R. D. R., R. P. Sharma, and S. G. Oberg. 1981. Toxicokinetics of nickel in rats after intratracheal administration of a soluble and insoluble form. American Industrial Hygiene Association Journal 42:486-492.

Enserink, E. L., J. L. Maas-Diepeveen, and C. J. Van Leeuwen. 1991. Combined effects of metals: an ecotoxicological evaluation. Water Research 25:679-687.

Evans, D. H., K. E. Weingarten, and J. S. Walton. 1990. The effect of atropine on cadmium- and nickel-induced constriction of vascular smooth muscle of the dogfish shark ventral aorta. Toxicology 62:89-94.

Evans, D. H., and J. S. Walton. 1990. Muscarinic receptors are *not* involved in the nickel-induced constriction of vascular smooth muscle of the dogfish shark (*Squalus acanthias*) ventral aorta. Bulletin of the Mount Desert Island Biological Laboratory 29:122-123.

Evans, J. E., M. L. Miller, A. Andringa, and L. Hastings. 1995. Behavioral, histological, and neurochemical effects of nickel (II) on the rat olfactory system. Toxicology and Applied Pharmacology 130:209-220.

Foulds, G. A. 1995. Nickel 1991. Coordination Chemistry Reviews 142:153-255.

Frank, A., V. Galgan, A. Roos, M. Olsson, L. R. Petersson, and A. Bignet. 1992. Metal concentrations in seals from Swedish waters. Ambio 21:529-538.

Frank, R., K. I. Stonefield, and P. Suda. 1982. Impact of nickel contamination on the production of vegetables on an organic soil, Ontario, Canada, 1980-1981. The Science of the Total Environment 29:41-65.

Friedrich, A. R., and F. P. Filice. 1976. Uptake and accumulation of the nickel ion by *Mytilus edulis*. Bulletin of Environmental Contamination and Toxicology 16:750-755.

Furst, A., and S. B. Radding. 1980. An update of nickel carcinogenesis. Pages 585-600 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Ghazaly, K. S. 1992. Sublethal effects of nickel on carbohydrate metabolism, blood and mineral contents of *Tilapia nilotica*. Water, Air, and Soil Pollution 64:525-532.

Gilani, S. H., and M. Marano. 1980. Congenital abnormalities in nickel poisoning in chick embryos. Archives of Environmental Contamination and Toxicology 9:17-22.

Glooschenko, V., W. F. Weller, P. G. R. Smith, R. Alvo, and J. H. G. Archbold. 1992. Amphibian distribution with respect to pond water chemistry near Sudbury, Ontario. Canadian Journal of Fisheries and Aquatic Sciences 49 (Supplement 1):114-121.

Gochfeld, M., and J. Burger. 1987. Heavy metal concentrations in the liver of three duck species: influence of species and sex. Environmental Pollution 45:1-14.

Graham, J. A., D. E. Gardner, F. J. Miller, M. J. Daniels, and D. L. Coffin. 1975. Effect of nickel chloride on primary antibody production in the spleen. Environmental Health Perspectives 12:109-113.

Greig, R. A., A. Adams, and D. R. Wenzloff. 1977. Trace metal content of plankton and zooplankton collected from the New York Bight and Long Island Sound. Bulletin of Environmental Contamination and Toxicology 18:3-8.

Greig, R. A., and D. R. Wenzloff. 1977. Trace metals in finfish from the New York Bight and Long Island Sound. Marine Pollution Bulletin 8:198-200.

Greig, R. A., D. R. Wenzloff, C. L. MacKenzie, Jr., A. S. Merrill, and V. S. Zdanowicz. 1978. Trace metals in sea scallops, *Placopecten magellanicus*, from eastern United States. Bulletin of Environmental Contamination and Toxicology 19:326-334.

Gumgum, B., E. Unlu, Z. Tez, and Z. Gulsun. 1994. Heavy metal pollution in water, sediment and fish from the Tigris River in Turkey. Chemosphere 29:111-116.

Halbrook, R. S., A. Woolf, G. F. Hubert, Jr., S. Ross, and W. E. Braselton. 1996. Contaminant concentrations in Illinois mink and otter. Ecotoxicology 5:103-114.

Hartwig, A., I. Kruger, and D. Beyersmann. 1994. Mechanisms in nickel genotoxicity: the significance of interactions with DNA repair. Toxicology Letters 72:353-358.

Haspel, J., F. W. Sunderman, Jr., S. M. Hopfer, D. C. Henjum, P. W. Brandt-Rauf, I. B. Weinstein, S. Nishimura, Z. Yamaizumi, and M. R. Pincus. 1993. A nickel-binding serpin, *pNiXa*, induces maturation of *Xenopus* oocytes and shows synergism with oncogenic *ras*-p21 protein. Research Communications in Chemical Pathology and Pharmacology 79:131-140.

Hatcher, C. O., R. E. Ogawa, T. P. Poe, and J. R. P. French, III. 1992. Trace elements in lake sediment, macrozoobenthos, and fish near a coal ash disposal basin. Journal of Freshwater Ecology 7:257-269.

Hauptman, O., D. M. Albert, M. C. Plowman, S. M. Hopfer, and F. W. Sunderman, Jr. 1993. Ocular malformations of *Xenopus laevis* exposed to nickel during embryogenesis. Annals of Clinical and Laboratory Science 23:397-406.

Hausinger, R. P. 1993. Biochemistry of nickel. Plenum Press, New York. 280 pp.

Higgins, S. J. 1995. Nickel 1993. Coordination Chemistry Reviews 146:115-201.

Hillis, T. L., and G. H. Parker. 1993. Age and proximity to local ore-smelters as determinants of tissue metal levels in beaver (*Castor canadensis*) of the Sudbury (Ontario) area. Environmental Pollution 80:67-72.

Hirano, S., T. Shimada, J. Osugi, N. Kodama, and K. T. Suzuki. 1994. Pulmonary clearance and inflammatory potency of intratracheally instilled or acutely inhaled nickel sulfate in rats. Archives of Toxicology 68:548-554.

Ho, W., and A. Furst. 1973. Nickel excretion by rats following a single treatment. Proceedings of the Western Pharmacology Society 16:245-248.

Hoffman, D. J. 1979. Embryotoxic effects of crude oil containing nickel and vanadium in mallards. Bulletin of Environmental Contamination and Toxicology 23:203-206.

Hogan, G. R. 1985. Nickel acetate-induced mortality in mice of different ages. Bulletin of Environmental Contamination and Toxicology 34:446-450.

Hohansson, A., P. Camner, and B. Robertson. 1981. Effects of long-term nickel dust exposure on rabbit alveolar epithelium. Environmental Research 25:391-403.

Hopfer, S. M., M. C. Plowman, K. R. Sweeney, J. A. Bantle, and F. W. Sunderman, Jr. 1991. Teratogenicity of Ni^{2+} in *Xenopus*, assayed by the FETAX procedure. Biological Trace Element Research 29:203-216.

Horowitz, A., and B. J. Presley. 1977. Trace metal concentrations and partitioning in zooplankton, neuston, and benthos from the south Texas outer continental shelf. Archives of Environmental Contamination and Toxicology 5:241-255.

Howard, W., B. Leonard, W. Moody, and T. S. Kochhar. 1991. Induction of chromosome changes by metal compounds in cultured CHO cells. Toxicology Letters 56:179-186.

Hughes, K., M. E. Meek, P. K. L. Chan, J. Shedden, S. Bartlett, and L. J. Seed. 1994. Nickel and its compounds: evaluation of risks to health from environmental exposure in Canada. Journal of Environmental Science and Health. Part C, Environmental Carcinogenesis & Ecotoxicology Reviews 12:417-433.

Hutchinson, T. C., A. Fedorenko, J. Fitchko, A. Kuja, J. Van Loon, and J. Lichwa. 1975. Movement and compartmentation of nickel and copper in an aquatic ecosystem. Pages 89-105 *in* D. D. Hemphill, editor. Trace substances in environmental health - IX: proceedings of University of Missouri's 9th annual conference on trace substances in environmental health. University of Missouri, Columbia.

Ikarashi, Y., J. Momma, T. Tsuchiya, and A. Nakamura. 1996. Evaluation of skin sensitization potential of nickel, chromium, titanium and zirconium salts using guinea-pigs and mice. Biomaterials 17:2103-2108.

Ilback, N. G., J. Fohlman, and G. Friman. 1992. A common viral infection can change nickel target organ distribution. Toxicology and Applied Pharmacology 114:166-170.

International Agency for Research on Cancer (IARC). 1976. IARC monographs on the evaluation of the carcinogenic risk of chemicals to man: cadmium, nickel, some epoxides, miscellaneous industrial chemicals and general considerations on volatile anaesthetics. Volume 11. World Health Organization, IARC, Lyon, France. 306 pp.

Iscan, M., T. Coban, and B. C. Eke. 1992. Responses of hepatic xenobiotic metabolizing enzymes of mouse, rat and guinea-pig to nickel. Pharmacology & Toxicology 71:434-442.

Iscan, M., B. C. Eke, and T. Coban. 1993. Combined effects of cadmium and nickel on hepatic glutathione *S*-transferases in rats. Comparative Biochemistry and Physiology 104C:453-456.

Jenkins, D. W. 1980a. Biological monitoring of toxic trace metals: volume 1. Biological monitoring and surveillance. U.S. Environmental Protection Agency Report 600/3-80-089. 215 pp.

Jenkins, D. W. 1980b. Biological monitoring of toxic trace metals: volume 2. Toxic trace metals in plants and animals of the world. Part III. U.S. Environmental Protection Agency Report 600/3-80-092. 290 pp.

Jha, B. S., and M. M. Jha. 1995. Biochemical effects of nickel chloride on the liver and gonads of the freshwater climbing perch, *Anabas testudineus* (Bloch). Proceedings of the National Academy of Sciences, India. Section B. 65:39-46.

Johansson, A., T. Curstedt, and P. Camner. 1991. Lung lesions after combined inhalation of cobalt and nickel. Environmental Research 54:24-38.

Kalas, J. A., T. H. Ringsby, and S. Lierhagen. 1995. Metals and selenium from Norwegian areas close to Russian nickel smelters. Environmental Monitoring and Assessment 36:251-270.

Kariya, T., K. Kawase, H. Haga, and T. Tsuda. 1968. Studies on the post-mortem identification of the pollutant in the fish killed by water pollution--VII. Detection of nickel in the fish. Bulletin of the Japanese Society of Scientific Fisheries 34:385-390.

Kasprzak, K. S. 1987. Nickel. Advances in Modern Environmental Toxicology 11:145-183.

Kataev, G. D., J. Suomela, and P. Palokangas. 1994. Densities of microtine rodents along a pollution gradient from a copper-nickel smelter. Oecologia 97:491-498.

Khangarot, B. S., and P. K. Ray. 1990. Acute toxicity and toxic interaction of chromium and nickel to common guppy *Poecilia reticulata* (Peters). Bulletin of Environmental Contamination and Toxicology 44:832-839.

Kirchgessner, M., and A. Schnegg. 1980. Biochemical and physiological effects of nickel deficiency. Pages 635-652 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Kniep, T. J., G. Re, and T. Hernandez. 1974. Cadmium in an aquatic ecosystem: distribution and effects. Pages 173-177 *in* D. D. Hemphill, editor. Trace substances in environmental health - VIII: proceedings of University of Missouri's 8th annual conference on trace substances in environmental health. University of Missouri, Columbia.

Kobayashi, N., and K. Fujinaga. 1976. Synergism of inhibiting actions of heavy metals upon the fertilization and development of sea urchin eggs. Science and Engineering Reviews of Doshisha University 17:54-69.

Kramer, U., J. D. Cotter-Howells, J. M. Charnock, A. J. M. Baker, and J. A. C. Smith. 1996. Free histidine as a metal chelator in plants that accumulate nickel. Nature 379 (6566):635-638.

Kraus, M. L. 1989. Bioaccumulation of heavy metals in prefledgling tree swallows, *Tachycineta bicolor*. Bulletin of Environmental Contamination and Toxicology 43:407-414.

Langlois, C., and R. Langis. 1995. Presence of airborne contaminants in the wildlife of northern Quebec. The Science of the Total Environment 160/161:391-402.

Law, R. J., C. F. Fileman, A. D. Hopkins, J. R. Baker, J. Harwood, D. B. Jackson, S. Kennedy, A. R. Martin, and R. J. Morris. 1991. Concentrations of trace metals in the livers of marine mammals (seals, porpoises and dolphins) from waters around the British Isles. Marine Pollution Bulletin 22:183-191.

Law, R. J., B. R. Jones, J. R. Baker, S. Kennedy, R. Milne, and R. J. Morris. 1992. Trace metals in the livers of marine mammals from the Welsh coast and the Irish Sea. Marine Pollution Bulletin 24:296-304.

Law, R. J., R. L. Stringer, C. R. Allchin, and B. R. Jones. 1996. Metals and organochlorines in sperm whales (*Physeter macrocephalus*) stranded around the North Sea during the 1994/1995 winter. Marine Pollution Bulletin 32:72-77.

Lee, J., R. D. Reeves, R. P. Brooks, and T. Jaffre. 1978. The relation between nickel and citric acid in some nickel-accumulating plants. Phytochemistry 17:1033-1035.

Lee, L. H., and B. Lustigman. 1996. Effect of barium and nickel on the growth of *Anacystis nidulans*. Bulletin of Environmental Contamination and Toxicology 56:985-992.

Lee, Y. W., C. Pons, D. M. Tummolo, C. B. Klein, T. G. Rossman, and N. T. Christie. 1993. Mutagenicity of soluble and insoluble nickel compounds at the *gpt* locus in G12 Chinese hamster cells. Environmental and Molecular Mutagenesis 21:365-371.

Lepage, P., and G. H. Parker. 1988. Copper, nickel and iron levels in pelage of red squirrels living near the ore smelters at Sudbury, Ontario, Canada. Canadian Journal of Zoology 66:1631-1637.

Lin, K. C., and I. N. Chou. 1990. Studies on the mechanisms of Ni^{2+}-induced cell injury: I. Effects of Ni^{2+} on microtubules. Toxicology and Applied Pharmacology 106:209-221.

Ling, J. R., and R. M. Leach, Jr. 1979. Studies on nickel metabolism: interaction with other mineral elements. Poultry Science 58:591-596.

Luo, S. Q., M. C. Plowman, S. M. Hopfer, F. W. Sunderman, Jr. 1993. Mg^{2+}-deprivation enhances and Mg^{2+}-supplementation diminishes the embryotoxic and teratogenic effects of Ni^{2+}, Co^{2+}, Zn^{2+}, and Cd^{2+} for frog embryos in the FETAX assay. Annals of Clinical and Laboratory Science 23:121-129.

Lu, C. C., N. Matsumoto, and S. Iijima. 1981. Placental transfer and body distribution of nickel chloride in pregnant mice. Toxicology and Applied Pharmacology 59:409-413.

Manly, R., and W. O. George. 1977. The occurrence of some heavy metals in populations of the freshwater mussel *Anodonta anatina* (L.) from the River Thames. Environmental Pollution 14:139-154.

Mas, A., D. Holt, and M. Webb. 1985. The acute toxicity and teratogenicity of nickel in pregnant rats. Toxicology 35:47-57.

Mathews, T. D. 1994. Contaminants in recreationally important estuarine finfish from South Carolina. Bulletin of Environmental Contamination and Toxicology 53:412-419.

Mathur, A. K., T. S. S. Dikshith, M. M. Lal, and S. K. Tandon. 1978. Distribution of nickel and cytogenetic changes in poisoned rats. Toxicology 10:105-113.

Mears, H. C., and R. Eisler. 1977. Trace metals in liver from bluefish, tautog and tilefish in relation to body length. Chesapeake Science 18: 315-318.

Memon, A. R., S. Ito, and M. Yatazawa. 1980. Taxonomic characteristics in accumulating cobalt and nickel in the temperate forest vegetation of central Japan. Soil Science and Plant Nutrition 26:271-280.

Michot, T. C., T. W. Custer, A. J. Nault, and C. A. Mitchell. 1994. Environmental contaminants in redheads wintering in coastal Louisiana and Texas. Archives of Environmental Contamination and Toxicology 26:425-434.

Montgomery, M., Jr., M. Price, J. Thurston, G. L. de Castro, L.L. Cruz, and D. D. Zimmerman. 1978. Biological availability of pollutants to marine organisms. U.S. Environmental Protection Agency Report 600/3-78-035. 134 pp.

Morimoto, Y., Z. Nambu, I. Tanaka, T. Higashi, H. Yamato, H. Hori, S. Cho, and M. Kido. 1995. Effects of nickel oxide on the production of tumor necrosis factor by alveolar macrophages of rats. Biological Trace Element Research 48:287-296.

Mugiya, Y., T. Hakomori, and K. Hatsutori. 1991. Trace metal incorporation into otoliths and scales in goldfish, *Carassius auratus*. Comparative Biochemistry and Physiology 99C:327-331.

Munch, D. 1993. Concentration profiles of arsenic, cadmium, chromium, copper, lead, mercury, nickel, zinc, vanadium and polynuclear aromatic hydrocarbons (PAH) in forest soil beside an urban road. The Science of the Total Environment 138:47-55.

Munshower, F. F., and D. R. Neuman. 1979. Metals in soft tissues of mule deer and antelope. Bulletin of Environmental Contamination and Toxicology 22:827-832.

Murthy, R. C., and S. V. Chandra. 1979. Effect of interaction of manganese and nickel on their contents in various tissues of guinea pigs. Chemosphere 1:35-38.

Mushak, P. 1980. Metabolism and systemic toxicity of nickel. Pages 499-523 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Nath, K., and N. Kumar. 1989. Nickel-induced histopathological alterations in the gill architecture of a tropical freshwater perch, *Colisa fasciatus*. The Science of the Total Environment 80:293-296.

Nath, K., and N. Kumar. 1990. Gonadal histopathology following nickel intoxication in the giant gourami *Colisa fasciatus* (Bloch and Schneider), a freshwater tropical perch. Bulletin of Environmental Contamination and Toxicology 45:299-304.

National Research Council of Canada (NRCC). 1981. Effects of nickel in the Canadian environment. Publication No. NRCC 18568. Publications, NRCC/CNRC, Ottawa, Canada. 352 pp.

National Academy of Sciences (NAS). 1975. Medical and biological effects of environmental pollutants. Nickel. National Research Council, National Academy of Sciences, Washington, D.C. 277 pp.

Nebeker, A. V., C. Savonen, and D. G. Stevens. 1985. Sensitivity of rainbow trout early life stages to nickel chloride. Environmental Toxicology and Chemistry 4:233-239.

Niebuhr, E., R. M. Stern, E. Thomsen, and H. C. Wulf. 1980. Relative solubility of nickel welding fume fractions and their genotoxicity in sister chromatid exchange *in vitro*. Pages 129-132 *in* S. S. Brown and F. W. Sunderman, Jr., editors. Nickel toxicology. Academic Press, New York.

Nielsen, F. H. 1977. Nickel toxicity. Pages 129-146 *in* R. A. Goyer, and M. A. Mehlman, editors. Advances in modern toxicology. Volume 2. Toxicology of trace elements. Hemisphere Publishing Corporation, London.

Nielsen, F. H. 1980a. Interactions of nickel with essential minerals. Pages 611-634 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Nielsen, F. H. 1980b. Effect of form of iron on the interaction between nickel and iron in rats: growth and blood parameters. Journal of Nutrition 110:965-973.

Nielsen, F. H., D. R. Myron, S. H. Givand, and D. A. Ollerich. 1975a. Nickel deficiency and nickel-rhodium interaction in chicks. Journal of Nutrition 105:1607-1619.

Nielsen, F. H., D. R. Myron, S. H. Givand, T. J. Zimmerman, and D. A. Ollerich. 1975b. Nickel deficiency in rats. Journal of Nutrition 105:1620-1630.

Norseth, T. 1980. Cancer hazards caused by nickel and chromium exposure. Journal of Toxicology and Environmental Health 6:1219-1227.

Norseth, T. 1986. Nickel. Pages 462-481 *in* L. Friberg, G. F. Nordberg, and V. B. Vouk, editors. Handbook on the toxicology of metals. Second edition. Volume II: specific metals. Elsevier, Amsterdam.

Norseth, T., and M. Piscator. 1979. Nickel. Pages 541-553 *in* L. Friberg, G. F. Nordberg, and V. B. Vouk, editors. Handbook on the toxicology of metals. Elsevier/North-Holland Biomedical Press, New York.

Novelli, E. B., and N. L. Rodrigues. 1991. Nickel chloride: potential accumulation from the airway. Toxicokinetics in rats. Boletin de Estudios Medicos y Biologicos, Universidad Nacional Autonoma de Mexico 39:15-20.

Novelli, E. L. B., N. L. Rodrigues, and B. O. Ribas. 1995. Superoxide radical and toxicity of environmental nickel exposure. Human & Experimental Toxicology 14:248-251.

Nriagu, J. O., editor. 1980a. Nickel in the environment. John Wiley & Sons, New York. 833 pp.

Nriagu, J. O. 1980b. Global cycle and properties of nickel. Pages 1-26 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

O'Dell, G. D., W. J. Miller, W. A. King, S. L. Moore, and D. M. Blackmon. 1970. Nickel toxicity in the young bovine. Journal of Nutrition 100:1447-1453.

Ormrod, D. P., J. C. Hale, O. B. Allen, and P. J. Laffey. 1986. Joint action of particulate fall-out nickel and rooting medium nickel on soybean plants. Environmental Pollution 41A:277-291.

Oskarsson, A., M. C. Reid, and F. W. Sunderman, Jr. 1981. Effects of cobalt chloride, nickel chloride, and nickel subsulfide upon erythropoiesis in rats. Annals of Clinical and Laboratory Science 11:165-172.

Ottolenghi, A. D., J. K. Haseman, W. W. Payne, H. L. Falk, and H. N. MacFarland. 1974. Inhalation studies of nickel sulfide in pulmonary carcinogenesis of rats. Journal of the National Cancer Institute 54:1165-1172.

Outridge, P. M., and A. M. Scheuhammer. 1993. Bioaccumulation and toxicology of nickel: implications for wild mammals and birds. Environmental Reviews 1:172-197.

Palmer, J. B., and G. M. Rand. 1977. Trace metal concentrations in two shellfish species of commercial importance. Bulletin of Environmental Contamination and Toxicology 18:512-520.

Pankakoski, E., H. Hyvarinen, M. Jalkanen, and I. Koivisto. 1993. Accumulation of heavy metals in the mole in Finland. Environmental Pollution 80:9-16.

Pankakoski, E., I. Koivisto, H. Hyvarinen, and J. Terhivuo. 1994. Shrews as indicators of heavy metal pollution. Carnegie Museum of Natural History, Special Publication No. 18:137-149.

Patterson, J., and T. V. Fernandez. 1995. Influence of salinity on the total body burden of fish *Etroplus maculatus* exposed to Ni, Cu and their mixture. Indian Journal of Marine Sciences 24:211-214.

Pesch, G., B. Reynolds, and P. Rogerson. 1977. Trace metals in scallops from within and around two ocean disposal sites. Marine Pollution Bulletin 8:224-228.

Pickering, Q. H. 1974. Chronic toxicity of nickel to the fathead minnow. Journal Water Pollution Control Federation 46:760-765.

Pirrone, N., G. J. Keeler, J. O. Nriagu, and P. O. Warner. 1996. Historical trends of airborne trace metals in Detroit from 1971 to 1992. Water, Air, and Soil Pollution 88:145-165.

Plowman, M. C., S. Grbac-Ivankovic, J. Martin, S. M. Hopfer, and F. W. Sunderman, Jr. 1994. Malformations persist after metamorphosis of *Xenopus laevis* tadpoles exposed to Ni^{2+}, Co^{2+}, or Cd^{2+} in FETAX assays. Teratogenesis, Carcinogenesis, and Mutagenesis 14:135-144.

Proctor, J., and I. D. McGowan. 1976. Influence of magnesium on nickel toxicity. Nature 260:134.

Ranta, W. B., F. D. Tomassini, and E. Nieboer. 1978. Elevation of copper and nickel levels in primaries from black and mallard ducks collected in the Sudbury district, Ontario. Canadian Journal of Zoology 56:581-586.

Rencz, A. N., and W. W. Shilts. 1980. Nickel in soils and vegetation of glaciated terrains. Pages 151-188 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Richardson, D. H. S., P. J. Beckett, and E. Nieboer. 1980. Nickel in lichens, bryophytes, fungi and algae. Pages 367-406 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Ridgway, L. P., and D. A. Karnofsky. 1952. The effects of metals on the chick embryo: toxicity and production of abnormalities in development. Annals of the New York Academy of Sciences 55:203-215.

Rodriguez, R. E., M. Misra, B. A. Diwan, C. W. Riggs, and K. S. Kasprzak. 1996. Relative susceptibilities of C57BL/6X, (C57BL/6 X C3H/He)F_1, and C3H/He mice to acute toxicity and carcinogenicity of nickel subsulfide. Toxicology 107:131-140.

Rose, G. A., and G. H. Parker. 1983. Metal content of body tissues, diet items, and dung of ruffed grouse near the copper-nickel smelters at Sudbury, Ontario. Canadian Journal of Zoology 61:505-511.

Roth, I., and H. Hornung. 1977. Heavy metal concentrations in water, sediments, and fish from Mediterranean coastal area, Israel. Environmental Science & Technology 11:265-269.

Rutherford, J. E., and R. J. Mellow. 1994. The effects of an abandoned roast yard on the fish and macroinvertebrate communities of surrounding beaver ponds. Hydrobiologia 294:219-228.

Saiz-Salinas, J. I., J. M. Ruiz, and G. Frances-Zubillaga. 1996. Heavy metal levels in intertidal sediments and biota from the Bidasoa estuary. Marine Pollution Bulletin 32:69-71.

Samitz, M. H., and S. A. Katz. 1976. Nickel-epidermal interactions: diffusion and binding. Environmental Research 11:34-39.

Sarkar, B. 1980. Nickel in blood and kidney. Pages 79-84 *in* S. S. Brown and F. W. Sunderman, Jr., editors. Nickel toxicology. Academic Press, New York.

Scanlon, P. F. 1987. Heavy metals in small mammals in roadside environments: implications for food chains. The Science of the Total Environment 59:317-323.

Scheiner, D. M., S. A. Katz, and M. H. Samitz. 1976. Nickel levels in hair and nickel ingestion in guinea pigs. Environmental Research 12:355-357.

Schell, W. R., and A. Nevissi. 1977. Heavy metals from waste disposal in central Puget Sound. Environmental Science & Technology 11:887-893.

Schnegg, V. A., and M. Kirchgessner. 1976. Zur Toxizitat von alimentar verabreichtem Nickel. Landwirt-schaftliche Forschung 29:177-185.

Schroeder, H. A., and M. Mitchener. 1971. Toxic effects of trace elements on the reproduction of mice and rats. Archives of Environmental Health 23:102-106.

Schroeder, H. A., M. Mitchener, and A. P. Nason. 1974. Life-term effects of nickel in rats: survival, tumors, interactions with trace elements and tissue levels. Journal of Nutrition 104:239-243.

Schubauer-Berigan, M. K., J. R. Dierkes, P. D. Monson, and G. T. Ankley. 1993. pH-dependent toxicity of Cd, Cu, Ni, Pb, and Zn to *Ceriodaphnia dubia*, *Pimephales promelas*, *Hyalella azteca*, and *Lumbriculus variegatus*. Environmental Toxicology and Chemistry 12:1261-1266.

Scoullos, M., M. Dassenakis, and C. Zeri. 1996. Trace metal behaviour during summer in a stratified Mediterranean system: the Louros estuary (Greece). Water, Air, and Soil Pollution 88:269-295.

Segner, H., D. Lenz, W. Hanke, and G. Schuurmann. 1994. Cytotoxicity of metals toward rainbow trout R1 cell line. Environmental Toxicology and Water Quality 9:273-279.

Sevin, I. F. 1980. Nickel. Pages 263-291 *in* H. A. Waldron, editor. Metals in the environment. Academic Press, London.

Sharif, A. K. M., A. I. Mustafa, M. N. Amin, and S. Safiullah. 1993. Trace element concentrations in tropical marine fish from the Bay of Bengal. The Science of the Total Environment 138:223-234.

Shiber, J. G., and T. A. Shatila. 1978. Lead, cadmium, copper, nickel and iron in limpets, mussels and snails from the coast of Ras Beirut, Lebanon. Marine Environmental Research 1:125-134.

Sigel, H., and A. Sigel, editors. 1988. Metal ions in biological systems. Volume 23. Nickel and its role in biology. Marcel Dekker, New York. 488 pp.

Singh, S. M., and P. N. Ferns. 1978. Accumulation of heavy metals in rainbow trout *Salmo gairdneri* (Richardson) maintained on a diet containing activated sewage sludge. Journal of Fish Biology 13:277-286.

Sivertsen, T., H. L. Daae, A. Godal, and G. Sand. 1995. Ruminant uptake of nickel and other elements from industrial air pollution in the Norwegian-Russian border area. Environmental Pollution 90:75-81.

Smialowicz, R. J., R. R. Rogers, M. M. Riddle, and G. A. Stott. 1984. Immunologic effects of nickel: I. suppression of cellular and humoral immunity. Environmental Research 33:413-427.

Smith, G. J., and O. J. Rongstad. 1981. Heavy metals in mammals from two unmined copper-zinc deposits in Wisconsin. Bulletin of Environmental Contamination and Toxicology 27:28-33.

Snodgrass, W. J. 1980. Distribution and behavior of nickel in the aquatic environment. Pages 203-274 *in* J. O. Nriagu, editor. Nickel in the environment. John Wiley & Sons, New York.

Sparling, D. W., and T. P. Lowe. 1996. Metal concentrations of tadpoles in experimental ponds. Environmental Pollution 91:149-159.

Spears, J. W., E. E. Hatfield, and R. M. Forbes. 1979. Nickel for ruminants II. Influence of dietary nickel on performance and metabolic parameters. Journal of Animal Science 48:649-657.

Sreedevi, P., B. Sivaramakrishna, A. Suresh, and K. Radhakrishnaiah. 1992a. Effect of nickel on some aspects of protein metabolism in the gill and kidney of the freshwater fish, *Cyprinus carpio* L. Environmental Pollution 77:59-63.

Sreedevi, P., A. Suresh, B. Sivaramakrishna, B. Prabhavathi, and K. Radhakrishnaiah. 1992b. Bioaccumulation of nickel in the organs of the freshwater fish, *Cyprinus carpio*, and the freshwater mussel, *Lamellidens marginalis*, under lethal and sublethal nickel stress. Chemosphere 24:29-36.

Stangl, G.I., and M. Kirchgessner. 1996. Nickel deficiency alters liver lipid metabolism in rats. Journal of Nutrition 126:2466-2473.

Stangl, G.I., and M. Kirchgessner. 1997. Effect of nickel deficiency on fatty acid composition of total lipids and individual phospholipids in brain and erythrocytes of rats. Nutrition Research 17:137-147.

Stevens, J. B. 1991. Disposition of toxic metals in the agricultural food chain. 1. Steady-state bovine milk biotransfer factors. Environmental Science & Technology 25:1289-1294.

Stevens, J. B. 1992. Disposition of toxic metals in the agricultural food chain. 2. Steady-state bovine tissue biotransfer factors. Environmental Science & Technology 26:1915-1921.

Steyn, C. E., H. v. H. van der Watt, and A.S. Claassens. 1996. On the permissible concentration for South African soils. South African Journal of Science 92:359-362.

Stockand, J., A. Sultan, D. Molony, T. DuBose, Jr., and S. Sansom 1993. Interactions of cadmium and nickel with K channels of vascular smooth muscle. Toxicology and Applied Pharmacology 121:30-35.

Stoewsand, G. S., J. N. Telford, J. L. Anderson, C. A. Bache, W. H. Gutenmann, and D. J. Lisk. 1984. Toxicologic studies with Japanese quail fed winter wheat grown on municipal sludge-amended soil. Archives of Environmental Contamination and Toxicology 13:297-301.

Stohs, S. J., and D. Bagchi. 1995. Oxidative mechanisms in the toxicity of metal ions. Free Radical Biology & Medicine 18:321-336.

Stronkhorst, J. 1992. Trends in pollutants in blue mussel *Mytilus edulis* and flounder *Platichthys flesus* from two Dutch estuaries, 1985-1990. Marine Pollution Bulletin 24:250-258.

Sunderman, F. W., Jr. 1968. Nickel carcinogenesis. Diseases of the Chest 54 (6):41-48.

Sunderman, F. W. 1970. Nickel poisoning. Pages 387-396 *in* F. W. Sunderman and F. W. Sunderman, Jr., editors. Laboratory diagnosis of diseases caused by toxic agents. Warren H. Green, Inc., St. Louis, Missouri.

Sunderman, F. W., Jr. 1981. Recent research on nickel carcinogenesis. Environmental Health Perspectives 40:131-141.

Sunderman, F. W., Jr., A. Aito, A. Berlin, C. Bishop, E. Buringh, W. Davis, M. Gounar, P. C. Jacquignon, E. Mastromatteo, J. P. Rigaut, C. Rosenfeld, R. Saracci, and A. Sors, editors. 1984. Nickel in the human environment. IARC Scientific Publications No. 53. International Agency for Research on Cancer, Oxford University Press. 530 pp.

Sunderman, F. W., Jr., and A. J. Donnelly. 1965. Studies of nickel carcinogenesis metastasizing pulmonary tumors in rats induced by the inhalation of nickel carbonyl. The American Journal of Pathology 46:1027-1041.

Sunderman, F. W., Jr., B. L. Mongillo, M. C. Plowman, and S. M. Brennan. 1990. Uptake and release of $^{63}Ni^{2+}$ by *Xenopus* embryos during early cleavage stages. Biology of Metals 2:214-218.

Sunderman, F. W., Jr., S. Nomoto, R. Morang, M. W. Nechay, C. N. Burke, and S. W. Nielsen. 1972. Nickel deprivation in chicks. Journal of Nutrition 102:259-267.

Sunderman, F. W., Jr., M. C. Reid, L. M. Bibeau, and J. V. Linden. 1983. Nickel induction of microsomal heme oxygenase activity in rodents. Toxicology and Applied Pharmacology 68:87-95.

Sunderman, F. W., Jr., S. K. Shen, J. M. Mitchell, P. R. Allpass, and I. Damjanov. 1978. Embryotoxicity and fetal toxicity of nickel in rats. Toxicology and Applied Pharmacology 43:381-390.

Sunderman, F. W., Jr., S. K. Shen, M. C. Reid, and P. R. Allpass. 1980. Teratogenicity and embryotoxicity of nickel carbonyl in Syrian hamsters. Pages 113-116 *in* S. S. Brown and F. W. Sunderman, Jr., editors. Nickel toxicology. Academic Press, New York.

Sunderman, F. W., Jr., A. H. Varghese, O. S. Kroftova, S. Grbac-Ivankovic, J. Kotyza, A. K. Datta, M. Davis, W. Bal, and K. S. Kasprzak. 1996. Characterization of pNiXa, a serpin of *Xenopus laevis* oocytes and embryos, and its histidine-rich, Ni(II)-binding domain. Molecular Reproduction and Development 44:507-524.

Szefer, P., J. Pempkowiak, B. Skwarzec, R. Bojanowski, and E. Holm. 1993. Concentration of selected metals in penguins and other representative fauna of the Antarctica. The Science of the Total Environment 138:281-288.

Thatheyus, A. J., M. Selvanayagam, and S. S. Raja. 1992. Toxicity of nickel on protein content in tissues of *Cyprinus carpio communis* (Linn). Indian Journal of Environmental Health 34:236-238.

Thauer, R. K., G. Diekert, and P. Schonheit. 1980. Biological role of nickel. Trends in Biochemical Sciences 5:304-306.

Timourian, H., and G. Watchmaker. 1972. Nickel uptake by sea urchin embryos and their subsequent development. Journal of Experimental Zoology 182:379-387.

Timourian, H., and G. Watchmaker. 1977. Assay of sperm motility to study the effects of metal ions. Pages 523-536 *in* H. Drucker and R. E. Wildung, editors. Biological implications of metals in the environment. Proceedings of the fifteenth annual Hanford life sciences symposium at Richland, Washington, September 29-October 1, 1975. Energy Research and Development Administration Symposium Series 42, CONF-750929.

Tkeshelashvili, L. K., T. M. Reid, T. J. McBride, and L. A. Loeb. 1993. Nickel induces a signature mutation for oxygen free radical damage. Cancer Research 53:4172-4174.

Tomokuni, K., and M. Ichiba. 1990. Interaction between nickel and lead in relation to porphyrin metabolism in mice. Industrial Health (Kawasaki, Japan) 28:145-149.

Trefry, J. H., and B. J. Presley. 1976. Heavy metal transport from the Mississippi River to the Gulf of Mexico. Pages 39-76 *in* H. L. Windom and R. A. Duce, editors. Marine pollutant transfer. D. C. Heath, Lexington, Massachusetts.

U. S. Environmental Protection Agency (USEPA). 1975. Preliminary investigation of effects on the environment of boron, indium, nickel, selenium, tin, vanadium and their compounds. Volume III. Nickel. U.S. Environmental Protection Agency Report 560/2-75-005c. 89 pp.

U. S. Environmental Protection Agency (USEPA). 1980. Ambient water quality criteria for nickel. EPA Report 440/5-80-060. 206 pp.

U. S. Environmental Protection Agency (USEPA). 1985. Drinking water criteria document for nickel. EPA Report 600/X-84-193-1. 64 pp.

U. S. Environmental Protection Agency (USEPA). 1986. Health assessment document for nickel and nickel compounds. EPA Report 600/8-83/012FF. 460 pp.

U. S. Public Health Service (USPHS). 1977. Criteria for a recommended standard . . . occupational exposure to inorganic nickel. U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health. DHEW (NIOSH) Publication No. 77-164. 282 pp.

U. S. Public Health Service (USPHS). 1993. Toxicological profile for nickel. U.S. Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, Georgia. Report TP-92/14. 158 pp.

Vas, P. 1991. Trace metal levels in sharks from British and Atlantic waters. Marine Pollution Bulletin 22:67-72.

Villa, R. B., F. P. Osuna, and M. H. P. Cortes. 1993. Concentraciones de metales pesados en el tejida cardiaco, hepatio y renal de la vaquita *Phocoena sinus* (mammalia: phocoenidae). Anales del Instituto de Biologia, Universidad Nacional Autonoma de Mexico, Serie Zoologia 64:61-72.

Waseem, M., R. Bajpai, and J. L. Kaw. 1993. Reaction of pulmonary macrophages exposed to nickel and cadmium *in vitro*. Journal of Environmental Pathology, Toxicology and Oncology 12:47-54.

Weber, C. W., and B. L. Reid. 1968. Nickel toxicity in growing chicks. Journal of Nutrition 95:612-616.

Weber, C. W., and B. L. Reid. 1969. Nickel toxicity in young growing mice. Journal of Animal Science 28:620-623.

Whanger, P. D. 1973. Effects of dietary nickel on enzyme activities and mineral contents in rats. Toxicology and Applied Pharmacology 25:323-331.

Whitton, B. A., and F. H. A. Shehata. 1982. Influence of cobalt, nickel, copper and cadmium on the blue-green alga *Anacystis nidulans*. Environmental Pollution 27A:275-281.

Wiemeyer, S. N., R. M. Jrek, and J. F. Moore. 1986. Environmental contaminants in surrogates, foods, and feathers of California condors (*Gymnogyps californianus*). Environmental Monitoring and Assessment 6:91-111.

Wiemeyer, S. N., S. K. Schmeling, and A. Anderson. 1987. Environmental pollutant and necropsy data for ospreys from the eastern United States, 1975-1982. Journal of Wildlife Diseases 23:279-291.

Williams, S. L., D. B. Aulenbach, and N. L. Clesceri. 1977. Distribution of metals in lake sediments of the Adirondack region of New York state. Pages 153-166 *in* H. Drucker and R. E. Wildung, editors. Biological implications of metals in the environment. Proceedings of the fifteenth annual Hanford life sciences symposium at Richland, Washington, September 29-October 1, 1975. Energy Research and Development Administration Symposium Series 42, CONF-750929.

World Health Organization (WHO). 1991. Nickel. Environmental Health Criteria 108. 383 pp.

Wren, C. D. 1984. Distribution of metals in tissues of beaver, raccoon and otter from Ontario, Canada. The Science of the Total Environment 34:177-184.

Wren, C. D., K. L. Fischer, and P. M. Stokes. 1988. Levels of lead, cadmium and other elements in mink and otter from Ontario, Canada. Environmental Pollution 52:193-202.

Wren, C. D., H. R. MacCrimmon, and B. R. Loescher. 1983. Examination of bioaccumulation and biomagnification of metals in a precambrian shield lake. Water, Air, and Soil Pollution 19:277-292.

Biological Science Report USGS/BRD/BSR--1999-0002
March 1999

Contaminant Hazard Reviews
Report No. 35

CUMULATIVE INDEX TO CHEMICALS AND TO COMMON AND SCIENTIFIC NAMES OF SPECIES LISTED IN CONTAMINANT HAZARD REVIEWS 1 THROUGH 34

by
Ronald Eisler

Patuxent Wildlife Research Center
U.S. Geological Survey
Laurel, MD 20708

CONTENTS

Abstract

Abstract. The Contaminant Hazard Reviews (CHR) series—sponsored by the U.S. Geological Survey Patuxent Wildlife Research Center—synthesizes ecotoxicological data for selected environmental contaminants, with emphasis on hazards to native species of flora and fauna. From 1985 through 1998, 34 reviews were published in various report series of the U.S. Department of the Interior on agricultural pesticides (acrolein, atrazine, carbofuran, chlordane, chlorpyrifos, diazinon, diflubenzuron, famphur, fenvalerate, mirex, paraquat, toxaphene), metals and metalloids (arsenic, boron, cadmium, chromium, copper, lead, mercury, molybdenum, nickel, selenium, silver, tin, zinc), mammalian biocides (sodium monofluoroacetate), organic industrial and municipal wastes (dioxins, pentachlorophenol, polycyclic aromatic hydrocarbons, polychlorinated biphenyls), mining wastes (cyanide), and ionizing radiations. This current report is a cumulative index to the common and scientific names of all biological species listed in the first 34 reports in the CHR series, with individual species cross-referenced with contaminant hazard review and corresponding page numbers. A similar index for chemicals is included.

Key words: Index, mirex, cadmium, carbofuran, toxaphene, selenium, chromium, polychlorinated biphenyls, dioxins, diazinon, mercury, nickel, polycyclic aromatic hydrocarbons, arsenic, chlorpyrifos, lead, tin, pentachlorophenol, atrazine, molybdenum, boron, chlordane, paraquat, cyanide, fenvalerate, diflubenzuron, zinc, famphur, acrolein, radiation, sodium monofluoroacetate, silver, copper, wildlife, birds, mammals, amphibians, reptiles, fish, invertebrates, plants

---

Introduction

A series of 34 Contaminant Hazard Reviews (CHR) was published between 1985 and 1998 under the aegis of the Patuxent Wildlife Research Center in direct response to requests for information from environmental specialists of the U.S. Fish and Wildlife Service and other scientists and resource managers in the U.S. Department of the Interior. Each CHR synthesized ecological and toxicological information of a single environmental contaminant, with emphasis on native fishery and wildlife resources. Specifically, reviews were prepared on selected agricultural insecticides, herbicides, animal control agents, metals, metalloids, organic industrial wastes, mining wastes, and ionizing radiations. Financial support for the CHR series was provided by the U.S. Fish and Wildlife Service, the National Biological Survey, the National Biological Service, and, most recently, the U.S. Geological Survey (Table). Page 66 of this report provides information on obtaining copies of the CHR reports.

This report presents an index for all chemicals and chemical trade names listed in CHR's 1 through 34; a similar index is included for the common and scientific names of all biological species. This publication is the second index to the CHR series. The first index—CHR 16 (Eisler and Corley 1989)—listed the common and scientific names of species in CHR's 1 through 15 but did not include chemicals and chemical trade names. The current index issue—CHR 35—supersedes CHR 16. This index was also prepared at the request of environmental specialists of the U.S. Fish and Wildlife Service and various natural resource managers in the U.S. Department of the Interior. It should also be a useful resource to the many other users of the CHR reviews.

Table. Publications in the Contaminant Hazard Reviews (CHR) series by CHR number, subject, report series and number, and author(s).

CHR No.	Subject	Report series and number[a]	Author(s)
1	Mirex	FWS 85 (1.1)	Eisler (1985a)
2	Cadmium	FWS 85 (1.2)	Eisler (1985b)
3	Carbofuran	FWS 85 (1.3)	Eisler (1985c)
4	Toxaphene	FWS 85 (1.4)	Eisler and Jacknow (1985)
5	Selenium	FWS 85 (1.5)	Eisler (1985d)
6	Chromium	FWS 85 (1.6)	Eisler (1986a)
7	Polychlorinated Biphenyls	FWS 85 (1.7)	Eisler (1986b)
8	Dioxins	FWS 85 (1.8)	Eisler (1986c)
9	Diazinon	FWS 85 (1.9)	Eisler (1986d)
10	Mercury	FWS 85 (1.10)	Eisler (1987a)
11	Polycyclic Aromatic Hydrocarbons	FWS 85 (1.11)	Eisler (1987b)
12	Arsenic	FWS 85 (1.12)	Eisler (1988a)
13	Chlorpyrifos	FWS 85 (1.13)	Odenkirchen and Eisler (1988)
14	Lead	FWS 85 (1.14)	Eisler (1988b)
15	Tin	FWS 85 (1.15)	Eisler (1989a)
16	Index to Species	FWS 85 (1.16)	Eisler and Corley (1989)
17	Pentachlorophenol	FWS 85 (1.17)	Eisler (1989b)
18	Atrazine	FWS 85 (1.18)	Eisler (1989c)
19	Molybdenum	FWS 85 (1.19)	Eisler (1989d)
20	Boron	FWS 85 (1.20)	Eisler (1990a)
21	Chlordane	FWS 85 (1.21)	Eisler (1990b)
22	Paraquat	FWS 85 (1.22)	Eisler (1990c)
23	Cyanide	FWS 85 (1.23)	Eisler (1991)
24	Fenvalerate	FWS 2	Eisler (1992a)
25	Diflubenzuron	FWS 4	Eisler (1992b)
26	Zinc	FWS 10	Eisler (1993)
27	Famphur	NBSY 20	Eisler (1994a)
28	Acrolein	NBSY 23	Eisler (1994b)
29	Radiation	NBS 26	Eisler (1994c)
30	Sodium Monofluoroacetate (1080)	NBS 27	Eisler (1995)
31	Planar PCBs	NBS 31	Eisler and Belisle (1996)
32	Silver	NBS 32	Eisler (1996)
33	Copper	USGS 1997-0002	Eisler (1998a)
34	Nickel	USGS 1998-0001	Eisler (1998b)

[a]FWS = Biological Report series of the U.S. Fish and Wildlife Service (CHR 1 through 26); NBSY = Biological Report series of the U.S. National Biological Survey (CHR 27 and 28); NBS = Biological Report series of the U.S. National Biological Service (CHR 29-32); USGS = Biological Science Report series of the U.S. Geological Survey (CHR 33 and 34).

Index to Chemicals

All chemicals, chemical trade names, and other substances with known biological properties listed in CHR's 1 through 34—a total of 1,570—are presented in Section 1. Each listed chemical is followed by a **boldfaced number** between **1** and **34** (this number corresponds to the CHR report number listed in Table) and nonbolded numbers that designate the pages in that report.

Index to Species

Taxonomic nomenclatures for plants and animals are under constant revision. In this report, I elected to conform as much as possible to the systems and spellings used by Scott and Wasser (1980) for plants, Swain and Swain (1948) for insects, Turgeon et al. (1988) for aquatic mollusks, Williams et al. (1989) for decapod crustaceans, Pratt (1935) and Hyman (1940, 1951a, 1951b, 1955) for miscellaneous invertebrates, Robins et al.

(1991) for fishes, Ditmars (1966) for reptiles, Edwards (1974) and Howard and Moore (1991) for birds, and Nowak and Paradiso (1983) for mammals. Individual species are arranged alphabetically by scientific and common name (Section 2). Each scientific name is followed by a **boldfaced number** between **1** and **34** (this number corresponds to the CHR report number listed in Table) and nonbolded numbers that designate the pages in that report.

In total, 2,233 species of animals and plants were cited, of which only 23 (1.03%) were listed in at least 20 CHR reports. The most widely cited species included one species of plant (corn, *Zea mays*), two species of invertebrates (freshwater crustacean, *Daphnia magna*; American oyster, *Crassostrea virginica*), seven species of teleosts (channel catfish, *Ictalurus punctatus*; bluegill, *Lepomis macrochirus*; coho salmon, *Oncorhynchus kisutch*; rainbow trout, *Oncorhynchus mykiss*; fathead minnow, *Pimephales promelas*; brook trout, *Salvelinus fontinalis*; lake trout, *Salvelinus namaycush*), three species of birds (mallard, *Anas platyrhynchos*; domestic chicken, *Gallus* sp.; Japanese quail, *Coturnix japonica*), and ten species of mammals (cow, *Bos* spp.; domestic dog, *Canis familiaris*; guinea pig, *Cavia* spp.; domestic cat, *Felis domesticus*; human, *Homo sapiens*; hamster, *Cricetus* spp.; domestic mouse, *Mus* spp.; domestic sheep, *Ovis aries*; laboratory white rat, *Rattus* spp.; and domestic pig, *Sus* spp.). It is probable that these species are not representative of unusually sensitive or endangered species, but they can be considered appropriate sentinel organisms for many species of free-living wildlife.

Acknowledgments

I thank Henry C. Bourne for computer assistance; W. Nelson Beyer, Lynda J. Garrett, and Ann Zimmerman for technical review; Shannon E. Price and Beth A. Vairin for editorial services; and Susan M. Lauritzen and Natalie Gormanous Trahan for layout.

Literature Cited

Ditmars, R.L. 1966. Reptiles of the world. Macmillan, New York, N.Y. 321 pp. + 89 plates.

Edwards, E.P. 1974. A coded list of birds of the world. Ernest P. Edwards, Sweet Briar, Va. 174 pp.

Eisler, R. 1985a. Mirex hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.1), Contaminant Hazard Reviews Report 1. 42 pp.

Eisler, R. 1985b. Cadmium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.2), Contaminant Hazard Reviews Report 2. 46 pp.

Eisler, R. 1985c. Carbofuran hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.3), Contaminant Hazard Reviews Report 3. 36 pp.

Eisler, R. 1985d. Selenium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.5), Contaminant Hazard Reviews Report 5. 57 pp.

Eisler, R. 1986a. Chromium hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.6), Contaminant Hazard Reviews Report 6. 60 pp.

Eisler, R. 1986b. Polychlorinated biphenyl hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.7), Contaminant Hazard Reviews Report 7. 72 pp.

Eisler, R. 1986c. Dioxin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.8), Contaminant Hazard Reviews Report 8. 37 pp.

Eisler, R. 1986d. Diazinon hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.9), Contaminant Hazard Reviews Report 9. 37 pp.

Eisler, R. 1987a. Mercury hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.10), Contaminant Hazard Reviews Report 10. 90 pp.

Eisler, R. 1987b. Polycyclic aromatic hydrocarbon hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.11), Contaminant Hazard Reviews Report 11. 81 pp.

4

Eisler, R. 1988a. Arsenic hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.12), Contaminant Hazard Reviews Report 12. 92 pp.

Eisler, R. 1988b. Lead hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.14), Contaminant Hazard Reviews Report 14. 134 pp.

Eisler, R. 1989a. Tin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.15), Contaminant Hazard Reviews Report 15. 83 pp.

Eisler, R. 1989b. Pentachlorophenol hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.17), Contaminant Hazard Reviews Report 17. 72 pp.

Eisler, R. 1989c. Atrazine hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.18), Contaminant Hazard Reviews Report 18. 53 pp.

Eisler, R. 1989d. Molybdenum hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.19), Contaminant Hazard Reviews Report 19. 61 pp.

Eisler, 1990a. Boron hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.20), Contaminant Hazard Reviews Report 20. 32 pp.

Eisler, R. 1990b. Chlordane hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.21), Contaminant Hazard Reviews Report 21. 49 pp.

Eisler, R. 1990c. Paraquat hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.22), Contaminant Hazard Reviews Report 22. 28 pp.

Eisler, R. 1991. Cyanide hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.23), Contaminant Hazard Reviews Report 23. 55 pp.

Eisler, R. 1992a. Fenvalerate hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 2, Contaminant Hazard Reviews Report 24. 43 pp.

Eisler, R. 1992b. Diflubenzuron hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 4, Contaminant Hazard Reviews Report 25. 36 pp.

Eisler, R. 1993. Zinc hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 10, Contaminant Hazard Reviews Report 26. 106 pp.

Eisler, R. 1994a. Famphur hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. National Biological Survey Biological Report 20, Contaminant Hazard Reviews Report 27. 23 pp.

Eisler, R. 1994b. Acrolein hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. National Biological Survey Biological Report 23, Contaminant Hazard Reviews Report 28. 29 pp.

Eisler, R. 1994c. Radiation hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. National Biological Service Biological Report 26, Contaminant Hazard Reviews Report 29. 124 pp.

Eisler, R. 1995. Sodium monofluoroacetate (1080) hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. National Biological Service Biological Report 27, Contaminant Hazard Reviews Report 30. 47 pp.

Eisler, R. 1996. Silver hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. National Biological Service Biological Report 32, Contaminant Hazard Reviews Report 32. 44 pp.

Eisler, R. 1998a. Copper hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Geological Survey Biological Science Report USGS/BRD/BSR--1997-0002, Contaminant Hazard Reviews Report 33. 98 pp.

Eisler, R. 1998b. Nickel hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Geological Survey Biological Science Report USGS/BRD/BSR--1998-0001, Contaminant Hazard Reviews Report 34. 76 pp.

Eisler, R., and A.A. Belisle. 1996. Planar PCB hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. National Biological Service Biological Report 31, Contaminant Hazard Reviews Report 31. 75 pp.

Eisler, R., and J.H. Corley. 1989. Index to common and scientific names of species listed in Contaminant Hazard Reviews 1-15. U.S. Fish and Wildlife Service Biological Report 85 (1.16), Contaminant Hazard Reviews Report 16. 44 pp.

Eisler, R., and J. Jacknow. 1985. To xaphene hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.4), Contaminant Hazard Reviews Report 4. 26 pp.

Howard, R., and A. Moore. 1991. A complete checklist of the birds of the world. Second edition. Academic Press, New York. 622 pp.

Hyman, L.H. 1940. The invertebrates. Volume 1. Protozoa through ctenophora. McGraw-Hill, New York. 726 pp.

Hyman, L.H. 1951a. The invertebrates. Volume 2. Platyhelminthes and rhyncocoela. The acoelomate bilateria. McGraw-Hill, New York. 550 pp.

Hyman, L.H. 1951b. The invertebrates. Volume 3. Acanthocephala, aschelminthes, and entoprocta. The pseudocoelomate bilateria. McGraw-Hill, New York. 572 pp.

Hyman, L.H. 1955. The invertebrates. Volume 4. Echinodermata. The coelomate bilateria. McGraw-Hill, New York. 763 pp.

Nowak, R.M., and J.L. Paradiso. 1983. Walker's mammals of the world. Volumes I and II. Johns Hopkins University Press, Baltimore. xliv + 1362 pp.

Odenkirchen, E.W., and R. Eisler. 1988. Chlorpyrifos hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report 85 (1.13), Contaminant Hazard Reviews Report 13. 34 pp.

Pratt, H.S. 1935. A manual of the common invertebrate animals. P. Blakiston's Son and Company, Philadelphia. 854 pp.

Robins, C.R., R.M. Bailey, C.E. Bond, J.R. Brooker, E.A. Lachner, R.N. Lea, and W.B. Scott. 1991. Common and scientific names of fishes from the United States and Canada. Fifth edition. American Fisheries Society Special Publication 20. 183 pp.

Scott, T.G., and C.H. Wasser. 1980. Checklist of North American plants for wildlife biologists. The Wildlife Society, 7101 Wisconsin Ave. NW, Washington, DC. 58 pp.

Swain, R.B., and S.N. Swain. 1948. The insect guide. Doubleday, New York. 261 pp.

Turgeon, D.D., A.E. Bogan, E.V. Coan, W.K. Emerson, W.G. Lyons, W.L. Pratt, C.F.E. Roper, A. Scheltema, F.G.Thompson, and J.D. Williams. 1988. Common and scientific names of aquatic invertebrates from the United States and Canada: mollusks. American Fisheries Society Special Publication 16. 227 pp. + 12 plates.

Williams, A.B., L.G. Abele, D.L. Felder, H.H. Hobbs, Jr., R.B. Manning, P.A. McLaughlin, and I.P. Farfante. 1989. Common and scientific names of aquatic invertebrates from the United States and Canada: decapod crustaceans. American Fisheries Society Special Publication 17. 77 pp. + 4 plates.

NOTE: Page numbers given in this PDF match the page numbers in the published paper copy of the reports. They do not match the pagination in the PDF versions posted on our website. Information on individual terms can be retrieved by opening the reports listed for that term, and using the search function in your Adobe Acrobat reader.

Section 1: Index to Chemicals

Chemical and trade names of substances listed in the Contaminant Hazard Reviews (CHR) series. Substances are indexed by **CHR report number** and by page numbers within each CHR report.

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Section 2: Index to Species

Common and scientific names of plants and animals listed in the Contaminant Hazard Reviews (CHR) series. Individual species are indexed by scientific name, by **CHR report number** and by page numbers within each CHR report. References are provided from common names to scientific names.

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

67

68

69

70

71

72

73

74

75

76

77

78

CHR Report Number no.[d]	NTIS Order and Subject (year of publication)[b]	FWRS MIN Code[c]	Number and Price
1. Mirex (1985)	PB85-203081, PC A04	809680131	
2. Cadmium (1985)	PB86-116779, PC A04	809680132	
3. Carbofuran (1985)	PB86-126885, PC A03	809680133	
4. Toxaphene (1985)	PB86-127354, PC A03	809680134	
5. Selenium (1985)	PB86-137346, PC A04	809680135	
6. Chromium (1986)	PB86-141298, PC A04	809680136	
7. Polychlorinated Biphenyls (1986)	PB86-170057, PC A05	809680137	
8. Dioxins (1986)	PB86-173903, PC A03	809680138	
9. Diazinon (1986)	PB86-235074, PC A03	809680139	
10. Mercury (1987))	PB87-179115, PC A06	809680140	
11. Polycyclic Aromatic Hydrocarbons (1987)	PB87-189825, PC A05	809680141	
12. Arsenic (1988)	PB88-169404, PC A06	809680142	
13. Chlorpyrifos (1988)	PB88-187885, PC A03	809680143	
14. Lead (1988)	PB88-193081, PC A07	809680144	
15. Tin (1989)	PB89-139620, PC A05	809680145	
16. Index to Species (1989)	PB89-165161, PC A04	809680146	
17. Pentachlorophenol (1989)	PB89-187173, PC A05	809680147	
18. Atrazine (1989)	PB89-204671, PC A04	809680148	
19. Molybdenum (1989)	PB89-235998, PC A04	809680149	
20. Boron (1990)	PB90-240821, PC A03	809010009	
21. Chlordane (1990)	PB91-114223, PC A04	809110035	
22. Paraquat (1990)	PB91-114231, PC A03	809110036	
23. Cyanide (1991)	PB94-120144, PC A04	809220091	
24. Fenvalerate (1992)	PB92-205541, PC A03	809210027	
25. Diflubenzuron (1992)	PB94-120136, PC A03	809210022	
26. Zinc (1993)	PB93-197853, PC A06	809320139	
27. Famphur (1994)	PB94-156767, PC A03	809420253	
28. Acrolein (1994)	PB94-215910, PC AO3	809480099	
29. Radiation (1994)	PB95-192225, PC AO7	809520114	
30. Sodium Monofluoroacetate (1080) (1995)	PB95-189007, PC AO4	809520113	
31. Planar PCBs (1996)	PB97-150742, PC AO6	809780006	
32. Silver (1996)	PB98-112352, PC AO5	809780155	
33. Copper (1998)	ADA 347472, PC AO7	809880055	
34. Nickel (1998)	pending	809880089	

[a] Copies of individual reports, if available, may be obtained free from the author, Ronald Eisler, USGS Patuxent Wildlife Research Center, Laurel MD 20708-4017; telephone 301-497-5724; FAX 301-497-5744; email Ronald_Eisler@usgs.gov

79

[b] Printed supply exhausted of CHR 1-12, 14, 20, 22-24, and 26; photocopy will be supplied as staff time permits. A CD ROM disc of CHR 1-28 inclusive is in production and should become available in early 1999; please contact Librarian at PWRC (telephone 301-497-5550/5551; FAX 301-495-5545; email Wanda_Manning@usgs.gov or Lynda_Garrett@usgs.gov) for status and ordering.

[c] Copies may be purchased from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161 (telephone 800-553-6847 or 703-605-6000; FAX 703-605-6900; email orders@ntis.fedworld.gov; internet www.ntis.gov). NTIS order number and paper copy price code is given above; contact NTIS for microfiche price codes. Copies may also be purchased from the Defense Technical Information Center, 8725 Kingman Road, Suite 0944, Fort Belvoir, VA 22060-6218.

[d] Fish and Wildlife Reference Service, 5430 Grosvenor Lane, Bethesda MD 20814 (telephone 800-582-3421; FAX 301-564-4059; email fwrs@mail.fws.gov; internet www.fws.gov/search/fwrefser.html); use their MIN number for photocopy or microfiche.

NOTE: Mention of trade names or commercial products does not constitute endorsement or recommendation for use by the U. S. Government.

80