4. CORRELATION OF EXPOSURE AND EFFECT

4.1 Effects on Humans

Cases of accidental and suicidal poisoning of humans by DDT are described in Section 3.1. All the reported cases of human poisoning involved ingestion. The earliest symptom of poisoning was hyperesthesia of the mouth and lower part of the face, which was followed by paresthesia of the same area and of the tongue, and an objective disturbance of equilibrium, paresthesia of the extremities, confusion, malaise, headache, fatigue, and delayed vomiting. Convulsions occurred only in severe poisoning.

In many cases of poisoning, quantitative information on exposure is not available, and the cases are often complicated by simultaneous ingestion of solvents (Hayes 1959). Poisoning incidents in which the effects were clearly caused by DDT are tabulated in Table 3.1.1. Table 3.2.1 summarizes the effects of one or a few oral doses of DDT on volunteers. These data form the primary basis for the following numerical estimates of toxic doses derived by Hayes (1975):

Largest nonfatal dose	285 mg/kg
Smallest dose with serious effect	16 mg/kg
Median clinical ED50	10 mg/kg
Smallest dose with clinical effect	6 mg/kg

The acute oral LD50 for DDT in humans has been estimated to be about 250 mg/kg (Gosselin et al 1976).

Three studies in which groups of volunteers were exposed to small oral doses of DDT, DDE, or DDE daily for long periods are described in

Section 3.2. In the two studies by Hayes (1956, 1971), 21 men were exposed to technical DDT or p,p'-DDT for up to 2 years at a dose level of 35 mg/day (about 0.5 mg/kg/day). No adverse effects were detected by a variety of tests, although two men were removed from one study because of illnesses (hepatitis and myocardial infarction), which the authors did not attribute to the effect of DDT. The third study involved only four men (Morgan and Roan 1971).

Table 4.1.1 summarizes studies of workers occupationally exposed to DDT, which are described more fully in Section 3.3. Although precise measures of the degree of exposure to DDT are rarely available, the concentrations of DDT and its metabolities in tissues were measured in several studies. The quantitative relationships between the intake of DDT, the storage of p,p'-DDT and p,p'-DDE in the tissues, and the excretion of p,p'-DDA in the urine are summarized in Section 1.5. These relationships are complicated by several factors including the slow conversion of p,p'-DDT to p,p'-DDE and the long retention of DDE in the body, the effects of intermittent exposure, and the effects of drugs and other pesticides in reducing storage of DDT and DDE. Nevertheless, measurements of tissue residues can be used to derive rough estimates of the exposure of persons during the preceding months. Where appropriate, these estimates are included in Table 4.1.1.

Only a few of the studies listed in Table 4.1.1 involved workers whose exposures were exclusively or primarily to DDT. Although some of these workers had tissue residue levels equivalent to mean intakes of DDT as high as 42 mg/day, no clinical effects were reported except for

skin and eye irritation and equivocal neurologic abnormalities (Ortelee 1958, Laws et al 1967, WHO 1973). The most pronounced effects were increased metabolism of drugs and steroids, indicative of induction of hepatic microsomal enzymes (Kolmodin-Hedmar 1973a,b; Poland et al 1970), and an increase in chromatid aberrations in lymphocytes of DDT workers relative to controls (Rabello et al 1975). These effects were found in workers with mean residues in blood of 1.0 ppm, equivalent to a daily intake of about 18 mg of DDT.

The other studies listed in Table 4.1.1 were complicated by the simultaneous exposure of the workers to other pesticides. In a few cases, measured changes were correlated with blood levels of DDT or DDE. These changes included increased levels of serum LDH and decreased serum creatinine phosphokinase (Morgan and Roan 1974), increased blood pressure and serum cholesterol (Sandifer et al 1972), and increased levels of SGOT (Warnick and Carter 1972). The last effect was observed in a group with mean residue level (DDT plus DDE) in serum of 61 ppb. This is the lowest tissue level statistically associated with a measured biologic effect in occupationally exposed workers in the reported studies.

In addition to the reported effects listed in Table 4.1.1, several other effects were reported in workers exposed simultaneously to DDT and to other pesticides (see Section 3.3). These effects include dermatitis, a variety of psychologic symptoms, gastritis, hepatitis, disorders of pregnancy and childbirth, myocardial dystrophy, abnormal EKG, vascular effects, hepatic cirrhosis, and abnormal EEG. However,

none of these or other effects can be ascribed unequivocally to exposure to DDT, and in most cases the degree of exposure was not reported.

Few data are available that can be used to assess the possibility that DDT has carcinogenic, teratogenic, or mutagenic effects in the human population or affects human reproduction. Seven studies have been reported in which levels of DDT and DDE in tissues taken at autopsy have been related to cause of death. In three of these studies, residue levels of DDT and DDE were significantly higher in cancer victims than in persons dying of other causes. No such association was found in the four other studies. Considered in toto, these findings fail to prove or disprove a cause-and-effect relationship.

Workers exposed for up to 19 years showed no indication of excess cancer incidence (Laws et al 1967), but the sample size (35) was too small to be the basis for definite conclusions. A significant increase in chromatid aberrations was reported in DDT workers with tissue residues equivalent to daily intakes of 6-27 mg (Rabello et al 1975). In one study, DDE levels in whole blood were much higher in premature infants than in full-term infants (O'Leary et al 1972). Nikitina (1974) reported an increased frequency of miscarriages and other abnormalities of pregnancy, together with reduced birth weight of infants, in female vineyard workers whose milk contained 0.12 ppm DDT (equivalent to daily intakes of 1-2 mg DDT). Although these workers were exposed to other pesticides in addition to DDT, this study commands attention as the only study found of occupationally exposed females.

4.2 Effects on Experimental Animals

Table 4.2.1 summarizes the reported effects of dietary exposure to DDT and its principal metabolites on animals. Teratogenic, carcinogenic, and mutagenic effects are listed in Tables 4.3.1., 4.3.2., and 4.3.3, respectively. In Table 4.2.1, primary emphasis is on studies involving repeated or long-term oral exposure. Some biochemical and functional effects resulting from short-term exposures to relatively high doses are not included in Table 4.2.1 but are discussed in Sections 2.2 and 2.3.4. No studies were found on the effects of DDT on animals exposed by the dermal or respiratory routes.

The most pronounced effects of exposure to DDT at high dietary levels were on the liver and the central nervous system. Dietary levels reported to be associated with reduced lifespan were 400 ppm in rats, 250 ppm in mice, and 1,000 ppm in hamsters. At these dietary levels, many animals suffered from tremors and convulsions, and most had lesions of the liver observed at autopsy, although some survived for the normal lifespan (Fitzhugh and Nelson 1947, Tomatis et al 1972, Agthe et al 1970).

In animals exposed to DDT at dietary concentrations between 25 and 250 ppm, the most consistent effects were increased liver weight, histopathologic changes in the liver (observable at autopsy), and reproduction, primarily due to preweaning mortality of offspring. Reproduction was reported to be normal in mice exposed at dietary levels of 25 ppm or less, but the data on rats are inconsistent. Although Ottoboni (1969) reported normal reproductive performance in rats exposed

at 200 ppm, several other investigators found adverse effects on reproduction at dietary levels of 50-100 ppm. Green (1969) reported severe effects, which were especially marked in the second generation, in animals exposed at a dietary concentration as low as 7 ppm.

Histopathologic changes were observed in the livers of rats exposed to DDT at dietary levels as low as 5 ppm (Ortega et al 1956a,b; Ortega 1962; Kunze et al 1949), and liver tumors occurred in mice exposed at 2 ppm (see Section 4.3). Immunosuppressive effects were detected in rabbits given DDT at 0.92 and 2.1 mg/kg/day (Street and Sharma 1974, 1975). Otherwise, the only reported significant effects at dietary levels below 10 ppm were the induction of hepatic microsomal enzymes and effects on behavior.

Several studies have shown increased microsomal enzyme activity in rats exposed to DDT at dietary levels between 0.9 and 4 ppm (Hoffmann et al 1969, Schwabe and Wendling 1967, Street et al 1969, Kinoshita et al 1966, Gillett 1968). No significant effects were evident after exposure at 0.5 or 0.2 ppm (Hoffmann et al 1969, Kinoshita et al 1966).

Exposure of male mice to DDT at 7 ppm in the diet for 10 days resulted in a reduction in aggressive behavior (Peterle and Peterle 1971). Exposure of pregnant mice to DDT in drinking water at concentrations of 1.0 or 0.1 ppb led to a significant reduction in the aggressiveness of their male offspring when tested at the age of 55 days; no effects were reported at 0.01 ppb (Scudder and Richardson 1970). These are by far the lowest exposure levels at which effects of DDT were reported to have been detected in experimental animals.

Only one report of an experiment involving long-term exposure of mammals to DDE was found. In this experiment, male mice exposed to DDE at 125 or 250 ppm throughout life suffered a high incidence of myocardial necrosis, in addition to the liver tumors discussed below (Tomatis et al 1974a).

4.1 Teratogenic, Carcinogenic, and Mutagenic Effects

Table 4.3.1 summarizes the experiments on teratogenesis, which are described in Section 2.4. There is no indication that DDT was teratogenic at doses tested (1-50 mg/kg).

Table 4.3.2 summarizes the experiments on carcinogenesis described in Section 2.5. DDT induced liver tumors in rats in two of the three experiments that were reported in sufficient detail for evaluation (Fitzhugh and Nelson 1947, Rossi et al 1977). In one experiment, 4 of 15 tumors in exposed rats were diagnosed as "low grade hepatic cell carcinomas" and the remainder as "nodular adenomatiod hyperplasia." In the other experiment, the tumors were classified as "neoplastic nodules".

DDT has been shown to be carcinogenic in mice in at least 11 experiments, many of which involved exposure for up to six generations, several dose levels or dosage regimens, or several routes of exposure (Table 4.3.2). The principal site of action was the liver, but an increased incidence of tumors of the lung and lymphatic system was reported in several experiments. The liver tumors showed a low degree of malignancy as judged by histopathologic characteristics, but were

readily transplantable and metatasized in a small fraction of cases (Tomatis and Turusov 1975).

Although dietary levels of 50-250 ppm were used in most experiments, DDT induced liver tumors in male CF1 mice at levels as low as 2 and 10 ppm (Tomatis et al 1972). At a dietary level of 250 ppm, DDT induced liver tumors in mice exposed for only 15 or 30 weeks early in life (Tomatis et al 1974b).

In one experiment, mice were exposed to DDD or DDE at 250 ppm or to both chemicals, each at 125 ppm. The mice exposed to DDD developed a high incidence of lung tumors, whereas those exposed to DDE developed a high incidence of liver tumors. In this experiment, DDE appeared to be more active in inducing liver tumors than DDT itself (Tomatis et al 1974a). Preliminary results of a more recent experiment indicate that DDE induced liver tumors in B6C3F1 mice, in circumstances in which technical DDT showed no significant effects (NCI 1978).

Table 4.3.3 summarizes the experiments on mutagenesis described in Section 2.5. DDT, DDE, and DDE have been reported to cause chromosome damage, primarily breaks and gaps, in a number of experiments, both in vivo and in vitro. These experiments have involved cells from several mammalian species, including man. On the other hand, DDT and DDE have given consistently negative results in bacterial mutagenesis bioassays involving systems sensitive to both base-pair substitutions and frame-shift mutations. In other mutagenicity tests, including dominant lethal assays in mice and Drosophila and host-mediated assays, DDT, DDD, and DDE have sometimes given positive results. Other tests

have provided inconclusive or negative results.

Most of the reported experiments on the mutagenicity of DDT involved short exposures at relatively high doses, and dose-response relations were not always clear. However, statistically significant increases in the frequency of chromosome damage in vitro have been reported at concentrations in the range 0.2-10 ppm (Lessa et al 1976, Palmer et al 1972). This range overlaps that of serum concentrations of DDT and DDE found in occupationally exposed workers (Table 4.1.1).

4.4 Summary

DDT is converted by mammals via DDD or DDE to a number of other metabolites and is excreted primarily as DDA in the urine. In most mammals, metabolism to DDE is only a minor pathway, but p,p'-DDE is retained in the tissues much more strongly than DDT or other metabolites. p,p'-DDE is also the most stable metabolite in the environment and may be found in small quantities in some samples of technical DDT.

After mammals are exposed to technical DDT, DDT, DDD, and DDE are circulated in their blood and are stored in their tissues, primarily in the fat. After ingestion, humans store DDT and DDE in their tissues at much higher concentrations than those measured in experimental animals exposed at comparable levels. Consequently, target tissues in humans are exposed at concentrations of DDT and DDE proportionately higher than in experimental animals that ingest comparable quantities.

Although several incidents of poisoning after accidental ingestion have been reported, DDT has relatively low toxicity for humans. The estimated LD50 is about 250 mg/kg and the median dose for clinical effects is about 10 mg/kg. Workers exposed for long periods to technical DDT and absorbing 18-42 mg/day, as reflected by residue concentrations up to 1.1 ppm in blood and 650 ppm in fat, showed only minor or equivocal clinical signs. However, tests on these workers showed elevated activity of hepatic microsomal enzymes. Other changes statistically associated with blood concentrations of DDT and DDE include increased levels of serum LDH and SGOT, decreased levels of serum CPK, and

increased blood pressure and serum cholesterol.

Although a few workers who were exposed to DDT for up to 19 years have been studied, the available reports are inadequate for determining whether DDT may have carcinogenic or teratogenic effects in humans. Workers with mean blood residues of 1.0 ppm (equivalent to a daily intake of about 18 mg of DDT) showed a significantly higher frequency of chromatid aberrations than less exposed controls. Female workers exposed to DDT and other pesticides are reported to have suffered a significantly higher frequency of miscarriages and prepartum and postpartum disorders than less exposed controls.

In experimental animals, exposure to DDT and its metabolites has caused a wide variety of toxic effects, especially on the liver and CNS, on several other organs and a number of enzyme systems. DDT and its metabolites also affect the levels of steriod hormones circulating in the blood and bound to hormone receptors, and adversely affect reproduction in exposed mammals. The o,p' isomers of DDT and DDE are estrogenic and have irreversible effects on the development of animals exposed early in life. DDT has been reported to be immunosuppressive in rabbits.

At exposure levels below 10 ppm in the diet, the principal reported effects of DDT and its metabolites have been induction of hepatic microsomal enzymes and effects on behavior. Microsomal enzyme activity was increased by exposure to DDT at 0.9-4 ppm in the diet, but not at 0.2 or 0.5 ppm. Three experiments have shown that prenatal or neonatal exposure of mice to DDT causes changes in their behavior later in life. One of these experiments involved exposure at concentrations as

low as 0.1 ppm in drinking water.

DDT is carcinogenic in mice, increasing the incidence of tumors primarily in the liver, but also in the lungs and lymphatic system in some experiments. In one experiment, DDT increased the incidence of liver tumors in mice exposed for their lifetime to only 2 ppm in the diet. Tissue levels of DDT in these mice were comparable to or lower than those reported in several studies of occupationally exposed workers. DDD and DDE are also carcinogenic in mice, causing liver and lung tumors; DDE is more effective than DDT itself. In two experiments with rats, DDT induced liver tumors (or "neoplastic nodules") with a low degree of malignancy. DDD has also been reported to be carcinogenic in rats. Three experiments involving exposure of hamsters to DDT have given negative results for carcinogenicity. DDT also interacts with other carcinogens in mice and rats, increasing the incidence of tumors in some experiments and decreasing it in others.

There is no reported evidence that DDT is teratogenic in mammals. Experiments investigating the mutagenicity of DDT and its metabolites have yielded a complex mixture of positive and negative results. DDT and DDE have given consistently negative results in bacterial mutagenesis bioassays. On the other hand, DDT, DDD, and DDE have been reported to cause chromosome damage in a number of experiments, both in vivo and in vitro. In two experiments, chromosome damage was reported to be evident after exposure to DDT at concentrations in the range of 0.2-10 ppm, a range which overlaps the serum concentrations of DDT and DDE found in occupationally exposed workers.

TABLE 4.1.1

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE OF DDT

Formulation	Duration and Route of Exposure	Tissue Levels of DDT, DDE, and DDA	Reported Effects	Reference
Mainly dust (manufacture and formulation)	0.4-8 yr dermal, respiratory, some oral	0.1-7.5 ppm DDA in urine (equivalent to DDT intake of 14-42 mg/d)	Skin and eye irritation, slight hand tremor in 5/40, enlarged liver in 1	Ortelee 1958
Chips, flakes, dust	Mean 14.4 yr dermal, respiratory	Mean 0.573 ppm p,p'-DDT and 0.506 ppm p,p'-DDE in serum (equivalent to DDT intake of 18 mg/d)	Serum half-life of phenylbutazone 19% less than in controls, urinary excretion of 6-beta-hydroxycortisol increased by 57%	Poland et al 1970
Not reported	2 mo - 10 yr unknown	0.16-3.25 ppm total residues in plasma (equivalent to DDT intake of 6-27 mg/d)	Chromatid aberrations in 12.2% of lymphocytes vs 8.8% in lower exposure group and 2.2% in unexposed controls (0.02-0.04 ppm total residues in plasma)	Rabello et al 1975
Chips, flakes, dust	11-19 yr dermal, respiratory	0.11-2.20 ppm total residues in serum, 38-646 ppm total residues in fat, 0-2.7 ppm DDA in urine (equivalent to DDT intake of 4-18 mg/d)	No effects attributable to exposure	Laws et al 1967

TABLE 4.1.1 (continued)

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO DDT

Forumlation	Duration and Route of Exposure	Tissue Levels of DDT, DDE, and DDA	Reported Effects	Reference
Spray	5-15 yr dermal, respiratory	Mean 1.11 ppm in blood (equivalent to DDT intake of 9 mg/d) vs 0.26 ppm in controls	Slight differences in knee reflex, tremor, performance of Romberg tests; not confirmed in a second examination	WHO 1973
Unknown (formulation and application)	5-22 yr unknown	0-167 ppb p,p'-DDT and 26-222 ppb DDE in serum	Increased serum LDH and decreased serum CPK in group with highest residues (104-222 ppb DDE)	Morgan and Roan 1974
Not reported	1-20 yr unknown (also exposed to BHC and "Benzilan")	-	Abnormal EEG in 21.9% of workers	Mayersdorf and Israeli 1974
Not stated (vineyard application)	Unknown (also exposed to sulfur, methyl parathion, and copper sulfate)	Mean 0.12 ppm in maternal milk and 0.19 ppm in placentas (4.8 and 5.4 times levels in controls, respectively)	Increased frequency of miscarriages, toxemia of pregnancy, uterine inertia, postpartum hemorrhage; reduced birth weight of infants; histopathologic changes in placentas	Nikitiana 1974

TABLE 4.1.1 (continued)

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO DDT

Formulation	Duration of Route of Exposure	Tissue Levels of DDT, DDE, and DDA	Reported Effects	Reference
Spray	Unknown (also exposed to lindane and other pesticides)	Mean 33 ppb DDE in plasma	Decreased half-life of antipyrine and phenylbutazone in plasma, hyper-alpha-HDL lipoproteinemia	Kolmodin et al 1969, Kolmodin and Hedman 1973a,b
-	Mean 12 yr Unknown (also exposed to organophosphate and carbamate pesticides	-	Increased levels of SGPT and cholesterol in groups exposed to organochlorine pesticides; correlation between blood pressure, serum cholesterol, and plasma DDT and DDE; no effects considered clinically significant	Sandifer et al 1972
-	"Chronically exposed" to DDT and various other pesticides	-	Elevated levels of several amino acids in plasma and elevated levels of SGOT, alkaline phosphatase, serum osmolality, and creatinine relative to controls	Tocci et al 1969

TABLE 4.1.1 (continued)

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE OF DDT

Formulation	Duration and Route of Exposure	Tissue Levels of DDT, DDE, and DDA	Reported Effects	Reference
-	Not stated (occupationally exposed to various pesticides)	Mean 9.2 ppb p,p'-DDT and 29.3 ppb p,p'-DDE	Significant correlation between SGOT levels, number of band cells and serum DDE levels; other parameters not associated with DDE	Warnick and Carter 1972
Spray	6-13 yr dermal, respiratory	"Approximately 3 times that of controls" from general population	Minor differences in results of some neurologic tests; not confirmed in a second examination	WHO 1973

TABLE 4.2.1

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Rat	1,000 ppm o,p'-DDT 6 mo	-	Reduced growth, fertility; reduced fecundity of offspring	Clement and Okey 1974
"	800 ppm technical DDT 2 yr	-	Increased mortality, liver lesions	Fitzhugh and Nelson 1947, Fitzhugh 1948
"	600 ppm technical DDT 2 yr	-	Increased mortality, increased liver and kidney weights, liver lesions, reduction in preweaning survival of offspring, no survival of offspring in second generation	Fitzhugh and Nelson 1947, Fitzhugh 1948
"	500 ppm p,p'-DDT 6 mo	-	Death of all offspring within 10 d of birth	Clement and Okey 1974
"	400 ppm technical DDT 2 yr	1,000 ppm in fat	Increased mortality, increased liver weight, liver changes	Fitzhugh and Nelson 1947, Fitzhugh 1948
"	350 ppm 33-60 wk	-	No increase in histopathologic changes in liver relative to controls	Cameron and Cheng 1951
"	250 or 500 ppm technical DDT 8 wk	-	Increased liver weight, proliferation of smooth endoplasmic reticulum, atypical mitochondria	Kimbrough et al 1971

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Rat	20 mg/kg/d 4-5 wk	-	Changes in frequency and amplitude of EEG, slight ataxia	Farkas et al 1968
"	200 ppm technical DDT 2 yr	160-310 ppm in fat	Increased liver weight in females, liver lesions	Fitzhugh and Nelson 1947, Fitzhugh 1948
"	200 ppm p,p'-DDT 6 mo	-	Severe depression of growth in offspring	Clement and Okey 1974
"	200 ppm o,p'-DDT 6 mo	-	No effects on growth or subsequent reproductive performance of offspring	"
"	200 ppm technical DDT 2 generations	-	Normal reproduction, increase in liver weight, increase in incidence of ring-tail	Ottoboni 1969
"	150 ppm 8-36 wk	-	Reproductive failure	Jonsson et al 1975
"	100 ppm technical DDT 2 yr	100-130 ppm in fat	Mild liver lesions, reduction in pre-weaning survival of offspring	Fitzhugh and Nelson 1947, Fitzhugh 1948
"	75 ppm 8-36 wk	-	Reduction in number of females producing litters, no effect on litter size	Jonsson et al 1975

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Rat	50 ppm technical DDT 2 generations	-	Reduction in preweaning survival of offspring	Fitzhugh 1948
"	25 ppm 2 yr	-	Increased liver weight in males	Treon and Cleveland 1955
"	20 or 200 ppm technical DDT 31 d	-	Reduction in histamine-containing mast cells in mesenteries; reduction in severity of anaphylactic shock	Gabliks et al 1975
"	20 or 200 ppm o,p'-DDT 6 mo	-	No effects on reproductive performance of offspring	Clement and Okey 1974
"	20 ppm p,p'-DDT 6 mo	-	No effects on reproduction	"
"	20 ppm technical DDT 2 generations	-	Increased reproductive lifespan relative to controls, increase in incidence of ringtail	Ottoboni 1969
"	15 ppm p,p'-DDT, o,p'-DDT, or technical DDT 2 generations	-	No effects on reproductive performance	Duby et al 1971

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Rat	10 ppm technical DDT 2 yr	120-270 ppm in fat	Liver lesions, no effects on reproduction	Fitzhugh 1948
"	1 mg/kg single dose	9.4 ppm in fat	Increased activity of hepatic microsomal enzymes	Gerboth and Schwabe 1964
"	7 ppm 2 generations	-	Marked reduction in fertility and in survival of offspring from 1st generation; no conceptions in rats in 2nd generation	Green 1969
"	0.5 mg/kg/d 14 d	10.8 ppm in fat	Increase in hepatic microsomal enzyme activity	Schwabe and Wendling 1967
"	5 or 50 ppm 3 mo	-	Increased activity in hepatic microsomal enzymes	Hart and Fouts 1965
"	5 ppm 4-6 mo	-	"Liver injury"	Kunze et al 1949
"	5 or 15 ppm 2-18 mo	-	Histopathologic changes in liver in males, proliferation of SER, concentric membrane arrays	Ortega et al 1956, Ortega 1962
"	4, 8, 16, or 32 ppm technical DDT 14 d	-	Increased hepatic p-nitroanisole metabolism	Hoffmann et al 1969

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Rat	2.5, 12.5, or 25 ppm 3 generations	-	Slight increase in mortality of offspring at all three dose levels, no effects on number of pregnancies or size of litters	Treon and Cleveland 1955
"	0.2 mg/kg/d 14 d	2.56 ppm in fat	Nonsignificant increase in hepatic microsomal enzyme activity	Schwabe and Wendling 1967
"	1 or 2.5 ppm o,p'-DDT 168 d	-	No significant effects on reproduction	Wrenn et al 1970
"	1 ppm 175 d	-	No effects on reproductive performance	Duby et al 1971
"	1 ppm 14 d	-	Estimated dietary threshold for induction of hepatic microsomal enzyme activity	Street et al 1969
"	1, 5, 25, and 50 ppm 1 wk	-	Induction of hepatic microsomal enzymes; N-demethylase activity increased to 2.3 times control level after 1 wk at 1 ppm	Kinoshita et al 1966
"	1 or 2.5 ppm o,p'-DDT through pregnancy and lactation	-	No significant effects on reproductive performance	Wrenn et al 1970
"	0.9 ppm -	-	Estimated dietary threshold for induction of hepatic microsomal enzymes	Gillett et al 1968

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Rat	0.5 or 2 ppm technical DDT 14 d	-	No increase in liver weight or increase in p-nitroanisole metabolism	Hoffman et al 1967
"	0.2 ppm 1-13 wk	-	No significant increase in hepatic microsomal enzyme activity	Kinoshita et al 1968
Mouse	250 ppm p,p'-DDE lifespan	78-434 ppm DDE in fat	Reduced lifespan, high incidence of liver tumors, myocardial necrosis in 22/53 males	Tomatis et al 1974
"	125 ppm p,p'-DDE plus 125 ppm p,p'-DDD lifespan	17-222 ppm DDE, 0-5.4 ppm DDD in fat	Reduced lifespan, high incidence of liver tumors, mycardial necrosis in 11/56 males	"
"	250 ppm p,p'-DDD lifespan	0.5-5.6 ppm DDD in fat	Reduced lifespan, increased incidence of lung and liver tumors	"
"	250 ppm technical DDT 2 generations	271-629 ppm DDT, 6-37 ppm DDE in fat	Reduced lifespan, convulsions, tremors, increased incidence of liver tumors, increased preweaning mortality of offspring	Tomatis et al 1972
"	250 ppm 6 generations	-	Severe adverse effects on reproduction, primarily on lactation and survival of offspring	Keplinger et 1970

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Mouse	250 ppm technical DDT 4 generations	-	Reduced lifespan in females, convulsions, gastrointestional bleeding, increased incidence of liver tumors, no effect on reproductive performance	Terracini et al 1973a,b
"	25 or 50 mg/kg/d technical DDT 10 d	-	Reduction in accumulation of testosterone and 5-alpha-dihydrotestosterone by anterior prostate	Lloyd et al 1974
"	46 mg/kg/d p,p'-DDT until weaning, then 140 ppm 18 mo	-	Increased incidence of liver tumors	Innes et al 1969
"	100 ppm 6 generations	-	Slight reduction in lactation and survival of offspring	Keplinger et al 1970
"	100 ppm p,p'-DDT 2 yr	-	Increased incidence of liver tumors	Thorpe and Walker 1973, Walker et al 1973
"	10 or 20 mg/kg single dose	-	Changes in electroshock seizure patterns, increase in exploratory behavior, decrease in habituation	Sobotka 1971

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Mouse	10 mg/kg technical DDT daily by oral intubation or twice/mo sc 80 wk	-	Tremors and convulsions after 40 wk, no increase in mortality, increased incidence of corneal opacity, increased incidence of tumors	Kashyap et al 1977
"	50 ppm technical DDT 2 generations	-	Increased incidence of liver tumors	Tomatis et al 1972
"	50 ppm p,p'-DDT 2 yr	-	"	Walker et al 1973
"	25 ppm 6 generations	-	No effects on reproduction	Kelpinger et al 1970
"	2.5 mg/kg/d single dose during pregnancy	-	Delayed acquisition of conditioned avoidance responses by offspring at age 32-37 d	Al-Hachim and Fink 1967, 1968
"	20 ppm technical DDT 2 generations	-	No observed effects	Terracini et al 1973a
"	10 ppm technical DDT 2 generations	-	Increased incidence of liver tumors	Tomatis et al 1972

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Mouse	7 ppm technical DDT 120 d	-	No effects on reproduction	Ware and Good 1967
"	7 ppm technical DDT 10 d	-	Decrease in aggressive behavior and loss of dominance in males	Peterle and Peterle 1971
"	2.8-3.0 ppm technical DDT 5 generations	5-11 ppm in fat	Increase in incidence of lung and other tumors, leukemia; no effects on reproductive success or motility	Tarjan and Kemeny 1969
"	0.1 or 1.0 ppb in drinking water 8 wk during and after pregnancy	-	Significant decrease in aggressive behavior of male offspring at age 35 d	Scudder and Richardson 1970
"	0.01 ppb in drinking water 8 wk during and after pregnancy	-	No effects on agressive behavior of male offspring	"
Hamster	500 or 1,000 ppm p,p'-DDT 90 wk	-	Nervousness, convulsions, reduced lifespan	Agthe et al 1970
"	250 ppm p,p'-DDT 6 wk	60 ppm in fat	Decreased hexobarbital sleeping time, increased rate of metabolism of radiolabeled DDT	Gingell and Wallcave 1973

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Hamster	250, 500, or 1,000 ppm technical DDT 18 mo	-	Increased liver weight, increase activity of glucose-6-phosphate dehydrogenase, increased lifespan	Graillot et al 1975
"	125, 250, or 500 ppm lifespan	-	No effects on growth or survival rates	Cabral and Shubik 1977
Dog	3,200 ppm technical DDT 39-49 mo	-	Liver damage	Lehman 1952, 1965
"	2,000 ppm technical DDT 34-49 ppm	-	Minor liver damage	"
"	400 ppm technical DDT 39-49 mo	-	No observed effects	"
"	12 mg/kg/d p,p'-DDT 14 mo	3 ppb in blood, 32 ppm in fat at time of mating	Moderate increase in serum alkaline phosphatase, diminished libido in males, delayed estrus in females, reduction in mammary development and milk production, infertility, increased infant and maternal mortality	Deichmann et al 1971, Deichmann and MacDonald 1971

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Tissue Levels	Reported Effects	Reference
Dog	1, 5, or 10 mg/kg/d technical DDT 3 generations	-	Earlier onset of estrus in exposed females than in controls; reproduction otherwise normal	Ottoboni et al 1977
Rabbit	0.92, 2.1, or 6.5 mg/kg/d p,p'-DDT 28 d	-	Increased spleen weight, decreased count of plasma cells in popliteal lymph nodes, reduction in germinal centers in spleen, atrophy of thymus cortex	Street and Sharma 1974
Rhesus monkey	200 ppm technical DDT or p,p'-DDT 3.5-7.5 yr	256-472 ppm DDT in fat	No observed effects attributable to exposure	Durham et al 1963
"	50 ppm technical DDT 1.6 yr	100-198 ppm DDT in fat	"	"
Sheep	250 ppm technical DDT 10-16 wk	-	Increased hepatic microsomal enzyme activity	Cecil et al 1975

TABLE 4.3.1

EXPERIMENTS INVOLVING ORAL ADMINISTRATION OF DDT TO ANIMALS IN WHICH TERATOGENIC EFFECTS WERE SOUGHT

Species	Dose and Time of Administration*	Reported Effects	Reference
Rabbit	50 mg/kg p,p'-DDT d 7, 8, and 9	Premature delivery, increase in resorptions, decreased intrauterine growth, no congenital abnormalities	Hart et al 1971
Mouse	1 mg/kg p,p'-DDT d 10, 12, and 17	Morphologic changes in gonads and reduction in fertility of offspring, especially females; no gross teratogenic effects	McLachlan and Dixon 1972
Rat	7 ppm in diet before and thoughout pregnancy	Marked decrease in fertility, small increase in resorption, no increase in frequency of congenital abnormalities	Green 1969

*Day of pregnancy

TABLE 4.3.2

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Reported Effects	Reference
Rat, male (Osborne-Mendel)	1,647 or 3,294 ppm technical DDD 78 wk	Combination follicular-cell carcinomas and follicular-cell adenomas	NCI 1978
Rat, female (Osborne-Mendel)	850 or 1,700 ppm technical DDD 78 wk	No evidence of carcinogenicity	"
Rate, male (Osborne-Mendel)	839 or 437 ppm technical DDE 78 wk	"	"
"	100, 200, 400, 600, or 800 ppm technical DDT 2 yr	Reduced survival; 4 liver carcinomas and 11 liver nodules in 75 exposed rats vs 0 in controls	Fitzhugh and Nelson 1947
"	642 or 321 ppm technical DDT 78 wk	No evidence of carcinogenicity	NCI 1978
Rat	600 ppm o,p'-DDD 24-469 d	Interstitial cell testicular tumors in 2/3 rats surviving 348-469 d	Lacassagne and Hurst 1965
Rat (Wistar)	500 ppm technical DDT 2 yr	Increased incidence of liver tumors (neoplastic nodules) in both sexes	Rossi et al 1977

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Reported Effects	Reference
Rat, female (Osborne-Mendel)	242 or 457 ppm technical DDE 78 wk	No evidence of carcinogenicity	NCI 1978
"	210 or 420 ppm technical DDT 78 wk	"	"
Rat (Osborne-Mendel)	80 or 200 ppm recrystallized DDT up to 2 yr	Bronchogenic carcinomas in 8/60 rats at 80 ppm vs 2/60 in controls and 0 in rats at 200 ppm; not confirmed in other groups given DDT with other pesticides	Deichmann et al 1967, Radomski et al 1965
Mouse, male and female (B6C3F1)	411 or 822 ppm technical DDD 78 wk	No evidence of carcinogenicity	NCI 1978
"	147 or 253 ppm technical DDE 78 wk	Hepatocellular carcinomas	"
Mouse (CF1)	250 ppm technical DDT 6 generations lifespan	Increased incidence of liver cell tumors in both sexes	Turusov et al 1973
"	250 ppm p,p'-DDE 2 yr	Increased incidence of liver cell tumors in both sexes; tumor incidence greater and occurrence earlier than in animals exposed to DDT or p,p'-DDD at 250 ppm	Tomatis et al 1974a

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Reported Effects	Reference
Mouse (CF1)	250 ppm p,p'-DDD 2 yr	Increased incidence of liver cell tumors and lung adenomas in both sexes	Tomatis et al 1974a
"	125 ppm p,p'-DDE plus 125 ppm p,p'-DDD 2 yr	Increase in liver cell tumors in both sexes; incidence and time of occurrence of tumors intermediate between those of groups fed 250 ppm DDE and 250 ppm DDD	"
"	250 ppm technical DDT 2 yr	Decreased lifespan, increased incidence of liver cell tumors in both sexes, metastases from 2 tumors	Tomatis et al 1972
Mouse (BALB/c)	250 ppm technical DDT 4 generations lifespan	Reduced lifespan in females, increased incidence of liver cell tumors in both sexes, tumors successfully transplanted	Terracini et al 1973a,b
Mouse (CF1)	250 ppm technical DDT 15 or 30 wk followed by observation for 50-150 wk	Increase in liver cell tumors in all 6 exposed groups; tumor incidence dependent on length of exposure early in life; increase in size and multiplicity of tumors with age	Tomatis et al 1974b
Mouse (ICR)	250 ppm -	Focal hepatic hyperplasia developing into hepatic cellular adenoma, negative test for alpha-fetoprotein	Kuwabara and Takayama 1974

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Reported Effects	Reference
Mouse (CF1)	200 ppm p,p'-DDT 2 yr	Increase in liver tumors in both sexes	Stevenson 1974
Mouse, female (B6C3F1)	87 or 174 ppm technical DDT 78 wk	No evidence of carcinogenicity	
Mouse (2 hybrid strains)	46.4 mg/kg/d p,p'-DDT prior to weaning, then 140 ppm in diet 18 mo	Increased incidence of liver tumors in both strains and of lymphomas in females of one strain	Innes et al 1969
Mouse (Swiss)	100 ppm technical DDT in diet or 10 mg/kg/d by intubation 80 wk	Increase in malignant lymphomas, lung adenomas, and hepatocellular carcinomas	Kashyap et al 1977
Mouse (CF1)	100 ppm p,p'-DDT 110 wk	Increased incidence of liver tumors in both sexes	Thorpe and Walker 1973, Reuber 1974
"	50 or 100 ppm p,p'-DDT 2 yr	In both sexes, dose-related increases in liver tumors and increases in age-adjusted incidence of lung tumors	Walker et al 1972, Hunt 1974

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Reported Effects	Reference
Mouse (A)	50 ppm in oil (exact dose unspecified) 6-12 mo	Increase in pulmonary adenomas, increase in number of tumors per mouse	Shabad et al 1973
Mouse (CF1)	50 ppm p,p'-DDT with 5 ppm HEOD 2 yr	Increased incidence of liver tumors in both sexes, relative to controls and to mice fed 50 ppm DDT alone	Walker et al 1973, Epstein 1975
Mouse, male (B6C3F1)	22 or 43 ppm technical DDT 78 wk	No evidence of carcinogenicity	NCI 1978
Mouse (A)	10 ppm in oil (exact dose unspecified) 5 generations	Increase in pulmonary adenomas in parental mice and in all 5 subsequent generations, increased number of tumors per mouse	Shabad et al 1973
Mouse	2.8-3.0 ppm 5 generations	Increased incidence of leukemia and of lung carcinomas and other tumors, especially in 2nd-5th generations	Tarjan and Kemeny 1969
Mouse (BALB/c)	2 or 20 ppm technical DDT 4 generations	No significant increase in tumors in either sex	Terracini et al 1973a,b

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF DDT TO ANIMALS

Species	Concentration and Duration	Reported Effects	Reference
Mouse (CF1)	2, 10, or 50 ppm technical DDT 6 generations	Increased incidence of liver cell tumors in males; nonsignificant increases in females	Turusov et al 1973
"	2, 10, or 50 ppm technical DDT 2 generations	Increased incidence of lung tumors in males; increased incidence of liver cell tumors in exposed males (67/127 at 50 ppm, 52/104 at 10 ppm, 57/124 at 2 ppm, 25/113 in controls); nonsignificant increases in females; metastases from 2 tumors in exposed mice	Tomatis et al 1972
Hamster	500 or 1,000 ppm p,p'-DDT 90 wk	No significant increase in tumors	Agthe et al 1970
"	250, 500, and 1,000 ppm 18 mo	Decreased incidence of lymphosarcomas; other tumors not listed	Graillot et al 1975
"	100, 250, or 500 ppm lifespan	No increase in tumors	Cabral and Shubik 1977

TABLE 4.3.3

SUMMARY OF MUTAGENIC EFFECTS OF DDT AND METABOLITES

Substance	Species or System	Strain	Dose	Reported Effects	Reference
Technical DDT	Salmonella typhimurium	TA 1535 TA 1536 TA 1537 TA 1538	20 µg/plate	No increase in revertants without rat liver microsomal preparations	Shirasu et al 1976
DDT	"	"	2,500 µg/plate	No increase in revertants with or without rat liver microsomal preparations	Marshall et al 1975
DDE	"	"	1,000 µg/plate	"	"
p,p'-DDT, p,p'-DDE	"	-	Not stated	No increase in revertants with mouse liver microsomal preparations	Van Dijck and Van de Voorde 1976
p,p'-DDE	"	TA 1535 TA 1537 TA 98 TA 100	5,000 µg/plate	No increase in revertants with or without rat liver microsomal preparations	McCann et al 1975
Technical DDT	Escherichia coli	B/r try WP2, WP2 try hcr	20 µg/plate	No increase in revertants without rat liver microsomal preparations	Shirasu et al 1976

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF DDT AND METABOLITES

Substance	Species or System	Strain	Dose	Reported Effects	Reference
Technical DDT	Bacillus subtilis	H17 Rec^+ M45 Rec^-	20 µg/plate	No increase in recombination mutants	Shirasu et al 1976
"	Neurospora crassa	Heterokaryon 12	750 mg/ 100 ml	Nonsignificant increase in recessive lethal mutants	Clark 1974
DDT, DDD, DDE, DDA	Salmonella typhimurium in NMRl mice (host-mediated assay)	-	500 mg/kg	No significant increase in mutation frequency	Buselmaier et al 1972
"	Serratia marcescens in NMRl Mice (host-mediated assay)	-	Not stated	DDD strongly mutagenic, DDT, DDE, and DDA inactive; DDD not mutagenic when applied directly to S. marcescens	"
Technical DDT	Neurospora crassa in Swiss mice (host-mediated assay)	Heterokaryon 12	150 mg/kg 2 oral doses	Nonsignificant increase in mutants	Clark 1974
p,p'-DDT p,p'-DDD, or p,p'-DDE	Rat-kangaroo cells	-	10 µg/ml	Chromosomal aberrations in 22.4, 15.5, and 13.7% of cells exposed to DDT, DDD, and DDE, respectively, vs 2.1% in controls	Palmer et al 1972

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF DDT AND METABOLITES

Substance	Species of System	Strain	Dose	Reported Effects	Reference
o,p'-DDT, o,p'-DDD, or o,p'-DDE	Rat-kangaroo cells	-	10 µg/ml	Chromosomal aberrations in 8.9, 8.3, and 5.9% of cells exposed to DDT, DDD, and DDE, respectively, vs 2.1% in controls	Palmer et al 1972
p,p'-DDT, p,p'-DDD, p,p'-DDE, p,p'-DDA	Mouse embryo cells	-	2.8-42.6 µM	Cell transformations (DDD most active); transformed cells not malignant	Langenbach and Gingell 1975
p,p'-DDT	Chinese hamster cells	V79	30-45 µg/ml	Nonsignificant increase in forward mutations, nonsignificant increase in cytogenetic abnormalities	Kelly-Garvert and Legator 1973
p,p'-DDE	"	"	25-40 µg/ml	Significant increase in forward mutations (to 8-azaguanine resistance), significant increase in cytogenetic abnormalities (exchanges)	"
p,p'-DDT, p,p'-DDD, p,p'-DDE, p,p'-DDA	"	B14 E28	12-100 µg/ml	Marked increase in chromosome gaps and breaks in cells exposed to DDT or DDD, increase in gaps in cells exposed to DDA, DDE intermediate in activity; dose-dependent effects for all 4 compounds	Mahr and Miltenburger 1976

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF DDT AND METABOLITES

Substance	Species or System	Strain	Dose	Reported Effects	Reference
DDT	Chinese hamster cells	V79	0.1-3.0 mM	Negative results in alkaline elution assay in vitro for DNA damage, with rat liver microsomal activation	Swenberg et al 1976
Technical DDT	Human lymphocytes	-	0.06-15.6 µg/ml	Significant increase in chromosome aberrations (chromatid gaps and breaks) at 0.2, 4.0, and 8.7 ug/ml DDT but not at higher concentrations	Lessa et al 1975
"	Drosophila melanogaster	Canton-S	1 µg on food medium	Dominant lethal mutations in early spermatid and spermatocte stages, nondisjunction of X and Y chromosomes, shift in sex ratio; no increase in recessive lethal mutations	Clark 1974
DDT	"	-	-	No increase in recessive lethal mutations	Luers 1953
p,p'-DDT, p,p'-DDD, p,p'-DDE, p,p'-DDA, p,p'-DDOM	"	Berlin wild K	0.2-3.7 mM	Significant increase in sex-linked recessive lethal mutants exposed to DDA or DDT, no effect with DDD, DDE, or DDOM	Vogel 1972
p,p'-DDT	Rat	Osborne-Meldel	50, 100, or 200 mg/kg single dose ip or 40, 80, or 100 mg/kg/d x 5 d ip	No significant increase in chromosomal aberrations in bone-marrow cells	Legator et al 1973

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF DDT AND METABOLITES

Substance	Species or System	Strain	Dose	Reported Effects	Reference
p,p'-DDT	Rat	-	25, 50, or 100 mg/kg single dose oral intubation or 20, 40, or 80 mg/kg/d x 5 d ip	Significant increase in dead implants in females mated to males exposed at 100 mg/kg (dominant lethal assay); no significant effects at lower doses	Palmer et al 1973
Technical DDT	Mouse	CF1	250 ppm 5 generations	No evidence of greater incidence of recessive invisible mutations in descendants of exposed mice relative to controls	Wallace et al 1976
"	"	Swiss	150 mg/kg x 2 oral doses, or 100 mg/kg 2x weekly for 10 wk	Dominant lethal mutations in early spermatid and spermatocyte stages, reduced number of implants/female and increased number of dead implants; chromosome breakage, stickiness, and nondisjunction in spermatocytes	Clark 1974
DDT, DDE, DDD, DDA	"	NMRI	1,200 mg/kg	Inconclusive results in dominant lethal assay	Buselmaier et al 1972
DDT	"	ICR/Ha	105-130 mg/kg ip or 10-100 mg/kg/d x 48 d	No significant increase in dead implants (dominant lethal assay)	Epstein et al 1972

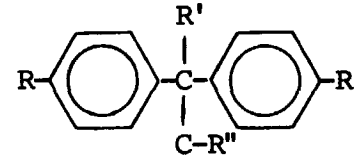
TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF DDT AND METABOLITES

Substance	Species or System	Strain	Dose	Reported Effects	Reference
DDT	Mouse	BALB/c	- ip 3 wk	Significant dose-related increase in frequency of chromosomal stickiness and deletions	Johnson and Jalal 1973
"	"	"	25, 50, 100, or 250 mg/kg single dose ip	Significant dose-related increase in frequency of deletions in bone marrow cells, no increase in gaps or stickiness	Larsen and Jalal 1973, 1975
"	"	-	10 mg/kg	Significant increase in chromosomal aberrations (stickiness, rearrangements) in bone marrow cells	Markaryan 1966
"	"	C57Bl x C3H	10 or 25 mg/kg ip	No increase in sperm abnormalities	Wyrobeck and Bruce 1975

TABLE 5.1

STRUCTURE OF DDT AND ITS ANALOGS* OF THE FORM:



MANY OF THE COMPOUNDS ALSO EXIST AS o,p'-ISOMERS AND OTHER ISOMERS

Abbreviated Name	Chemical Name	R	R'	R"
DDT	1,1,1-trichloro-2,2-bis-(p-chlorophenyl) ethane	-Cl	-H	$-Cl_3$
DDE	1,1-dichloro-2,2-bis-(p-chlorophenyl) ethylene	-Cl	None	$-Cl_2$
DDD**	1,1-dichloro-2,2-bis-(p-chlorophenyl)ethane	-Cl	-H	$-HCl_2$
DDMU	1-chloro-2,2-bis-(p-chlorophenyl) ethylene	-Cl	None	-HCl
DDMS	1-chloro-2,2-bis-(p-chlorophenyl) ethane	-Cl	-H	$-H_2Cl$
DDNU	2,2-bis(p-chlorophenyl) ethylene	-Cl	None	$-H_2$
DDOH	2,2-bis(p-chlorophenyl) ethanol	-Cl	-H	$-H_2OH$
DDA	2,2-bis(p-chlorophenyl) acetic acid	-Cl	-H	-OOH

* Each is a recognized metabolite of DDT in the rat.

**As an insecticide, this compound has the approved name of TDE, and it has been sold under the name Rothane; as a drug, it is called mitotane.

Adapted from WHO 1977

TABLE 5.2

PHYSICAL AND CHEMICAL PROPERTIES OF DDT

Appearance	Colorless crystals or white to slightly off-white powder
Empirical formula	$C_{14}H_9Cl_5$
Formula weight	354.49
Melting point	108.5-109 C
Boiling point	260 C
Vapor pressure	1.5×10^{-7} mm Hg at 20 C
Octanol/water partition coefficient	4.96
Solubility	Practically insoluble in water Solubility in 100 ml of: acetone = 58 g benzene = 78 g benzyl benzoate = 42 g carbon tetrachloride = 45 g chlorobenzene = 74 g cyclohexanone = 116 g 95% alc. = 2 g ethyl ether = 28 g gasoline = 10 g isopropanol = 3 g kerosene = 8-10 g morpholine = 75 g peanut oil = 11 g pine oil = 10-16 g tetralin = 61 g tributyl phosphate = 50 g freely soluble in pyridine, dioxane Solubility in organic solvents increases with a rise in temperature
Stability	Stable to light and oxidation

From Condensed Chemical Directory 1977, Merck Index 1976, Handbook of Chemistry and Physics 1976

TABLE 5.3

SYNONYMS AND TRADE NAMES FOR DDT

Dichlorodiphenyltrichloroethane
Dicophane
Chlorophenothane
1,1,1-Trichloro-2,2-bis(p-chlorophenyl) ethane)
1,1'-(2,2,2-Trichloroethylidene)bis(4-chlorobenzene)
alpha,alpha-bis(p-Chlorophenyl),beta,beta,beta-trichloroethane
Pentachlorin
p,p'-DDT
Gesarol
Neocid

From Condensed Chemical Dictionary 1977, Merck 1976