



CHEMICAL MIXTURES

Chemical Cocktails Are Mixed Pesticides More Potent?

Increasing evidence suggests that environmental chemicals that interact with the endocrine system harm the health of humans and animals. More recent studies suggest further that these chemicals act synergistically, meaning that their combined effect is greater than the sum of their individual effects. While few scientists doubt that endocrine disruptors can cause significant harm to humans and wildlife, there is a great deal of controversy over whether synergism is indeed part of the equation—and how researchers can go about finding out the truth of the matter.

In a paper published in the January–March 1999 issue of *Toxicology and Industrial Health*, Warren P. Porter, a professor of zoology at the University of Wisconsin in Madison, reported that mixtures of the pesticides aldicarb and atrazine and the fertilizer nitrate altered nervous system, endocrine, and immune system function in several strains of mice while each compound alone did not. In the study, mice were given drinking water laced with each of the eight possible combinations of the three chemicals in

concentrations approximating their maximum permissible concentration levels in groundwater. The researchers then examined aspects of behavior and physiology. The researchers distinguished between fall/winter and spring/summer experiments because the animals' hormones change with the seasons, which can affect metabolism of chemicals.

The most significant result involved the animals' ability to produce antibodies to foreign proteins. One group of mice exposed to aldicarb and nitrate during fall/winter had a tenfold increase in ability to make antibodies to foreign proteins. The increase in antibody production does not imply improved health, says Porter, because it may be occurring at the expense of some other aspect of immune function.

Unbound thyroxine (a thyroid hormone) increased by 25–50% in some of the treatment groups during spring/summer experiments, but the number of chemicals to which the mice were exposed made little difference in the results. "Thyroxine affects production of steroids in the adrenals; these can modify immune function," says Porter. Thyroxine can also have a profound impact on brain development. In behavioral experiments, most of the experiments resulted in suppressed aggression, although enhanced levels of aggression were also observed, he says.

There are two spiritual dangers in not owning a farm. One is the danger of supposing that breakfast comes from the grocery, and the other that heat comes from the furnace.

Aldo Leopold, *A Sand County Almanac*, 1949

A major implication of the study is that the U.S. chemical registration system has several shortcomings, says Porter. He points out there is virtually no testing of chemical mixtures, compounds are tested minus inert ingredients that go into commercial mixtures, end points include only cancer and mutations (but not immune, endocrine, nervous system, or development end points), and only single-exposure routes are used—a combination of oral, cutaneous, and respiratory routes is needed as well. Furthermore, he says, the tests do not include stresses from malnutrition, disease, or climate.

Ralph L. Cooper, chief of the Endocrinology Branch of the Reproductive Toxicology Division at the U.S. Environmental Protection Agency (EPA) National Health and Environmental Effects Research Laboratory, agrees that studies on chemical mixtures are lacking and emphasizes that the design of such studies creates special problems, particularly reproducibility. The difficulty of reproducing mixture studies is that when two variables (e.g., two chemicals) are combined, the amount of study work increases exponentially. "If you have four doses in one chemical, and four in the other, you end up with 16 treatment groups, so you have a large, cumbersome study," says Earl Gray, Jr., a research biologist with the EPA. "And four doses is often not enough to define the dose response. The interpretation requires some sophisticated statistical analyses."

Critics say Porter's results seem weak. Some point out that the differences between the spring/summer and fall/winter experiments were far greater than the differences between the treatment groups. "He ran a number of statistical tests, and only about 5% came out significant," says Cooper. "If the same set of experiments were done again, would a different 5% be significant? I couldn't get a sense of real synergy."

"We are dealing with very subtle responses in animals and possibly in people," says Porter, adding that the results may reflect different genetic vulnerabilities in some of the mice used in the study. Nonetheless, says Cooper, "The issues he raises are legitimate ones, and there is a ton of support in good peer-reviewed journal articles. The issue of developmental effects, sex differences, additivity, and the potential for synergism are all important questions in environmental toxicology." —David C. Holzman



Menacing mixtures? The synergistic effects of agricultural chemical mixtures on human health are controversial, and scientists agree that much more research on the issue is needed.

LAND USE

A Toxic House in the Country

Building on Former Farms

Families that bought land in the Barber Orchard subdivision near Waynesville, North Carolina, thought they were acquiring a piece of nirvana. Mountains rise all around; the air seems fresh and the water clean. But when one resident had his well water tested on the advice of a former orchard worker, the dream turned into a nightmare. The water was found to contain DDT, DDE, and benzene hydrochlorides, and the soil was contaminated with lead and arsenic—remnants of half a century of pesticide spraying on the former apple orchard. The U.S. Environmental Protection Agency has since sent in an emergency response team to remove the topsoil, and residents have been advised to outfit their water systems with carbon filters.

The dangers to farm workers and others living in agricultural communities from the misuse of pesticides have been well documented, but suburban homeowners may be surprised to learn that they, too, may be at potential risk from activities that took place on their property decades ago. Soil and water contamination of former agricultural areas has been recorded in virtually every region of the United States. Long Island made headlines in the 1970s when wells dug in former potato fields were found to be contaminated with aldicarb, a highly toxic carbamate insecticide. In Connecticut, hundreds of homes built on former tobacco fields have wells contaminated with the highly toxic pesticide ethylene dibromide. Wells in California's San Joaquin Valley have high concentrations of pesticides, as well as nitrates and nitrites. The herbicide atrazine has been found in 12% of wells tested by the state of Wisconsin.

Although no outbreaks of disease have been directly linked to pesticide contamination in residential wells, the possible health effects of these pesticides are many and varied. Pesticides can have numerous serious health effects, ranging from acute poisoning to cancers, neurological effects,

and interference with reproduction. Fetuses, infants, and children are particularly vulnerable to pesticides because their bodies cannot efficiently detoxify and eliminate chemicals and because they have more of their lifetime left in which to develop health complications after exposure.

Each year, an average of 1.3 million acres of rural land—including 370,000 acres of former cropland—is converted to development. Conversion is especially heavy near metropolitan areas where lack of profitability, increasing taxes, and escalating land prices are forcing many farmers to sell out. But for all the land that is being developed, both government and industry officials say there is no cause for alarm.



Suburban blight? Homeowners seeking the country life may get more than they bargained for when they build homes on former agricultural property.

“We have done extensive groundwater monitoring and we don't find a lot of drinking water wells that have pesticides,” says Tom Hoogheem, Environmental Stewardship Lead with Monsanto Corporation. “Of the ones that do have a problem, most of the wells are hand-dug [and thus lack a casing], have a casing that's cracked, or are improperly constructed, shallow wells.”

But critics say problems don't appear widespread only because no one is looking for them.

“No states require testing of private wells for pesticides, and county health departments typically screen only for microbiological contamination,” says Erick Umstead, research director for the nonprofit Agricultural Resources Center in Raleigh, North Carolina. “Problems are only detected when someone sinks a well, thinks the water tastes bad, and gets it tested.” But in the small concentrations that often appear in drinking water, pesticides are not always detectable to the taste.

Although it is up to consumers to request it, most states do offer free testing of well water for a variety of pesticides. If contamination is found, several treatment methods are available. Carbon filters can remove pesticides from water as long as the filters are properly maintained, and reverse osmosis systems will remove most nitrogen. For tainted soil, health officials recommend washing hands and wiping off feet before entering the house and avoiding heavy consumption of vegetables from backyard gardens. —**John S. Manuel**

Misleading Cigarette Labels

Researchers from the American Health Foundation in Valhalla, New York, say that Federal Trade Commission (FTC) measurements of tar and nicotine listed on cigarette packs are not a true indication of the amounts of the chemicals that people may inhale while smoking.

In the study, published in the 19 January 2000 issue of the *Journal of the National Cancer Institute*, researchers found that smokers of low-nicotine cigarettes inhaled over twice as much tar and nicotine as FTC machine tests predicted they would, and that smokers of medium-nicotine cigarettes inhaled nearly that much tar and nicotine. The researchers concluded that smokers who use the FTC ratings to choose a brand of cigarettes with lower amounts of carcinogens will not achieve the reduction anticipated.



Frogs and Fertilizers

Zoologists at Oregon State University have determined that several species of amphibians are harmed by concentrations of nitrates and nitrites that fall within Environmental Protection Agency standards for safe drinking water. Larval amphibians are especially affected by these by-products of nitrogen fertilizers.

The study, published in the December 1999 issue of *Environmental Toxicology and Chemistry*, focused on five amphibian species. When exposed to moderate amounts of nitrates and nitrites, some tadpoles and young frogs exhibited decreases in feeding and swimming activity, disequilibrium, physical abnormalities, paralysis, and death. Over half of one species, the Oregon spotted frog, died after 15 days of exposure to nitrites. The Oregon spotted frog has largely disappeared from its native range, most of which is commercial farmland. Study leader Andrew Blaustein says the effects of the compounds may be intensified by environmental factors such as acid rain and UV-B exposure.

Dioxin Sludge Rules

In December 1999 the U.S. Environmental Protection Agency proposed revised standards for concentrations of dioxin and dioxin-like compounds in treated sewage sludge that is recycled for use as fertilizer. The proposed rule would set an upper limit of 300 parts per trillion toxic equivalents for sludge that is used as fertilizer. The new rule would require all facilities to test sludge for dioxins before it is applied to the land, except waste treatment plants treating less than one million gallons per day and small businesses that prepare less than 290 dry metric tons of sewage sludge annually. Facilities that find amounts above the proposed limit would be required to monitor annually for dioxins; facilities finding less would have to monitor once every five years.

PESTICIDES

A Burning Question

Do Farmer-Set Fires Endanger Health?

Fall is burning season in the wheat fields of eastern Washington State. To prepare for planting in 1998, farmers burned about 229,000 acres of wheat stubble, an increase over recent years. Although a tighter state permitting system substantially reduced the acreage burned in 1999, clean air activists are concerned that the state has not tightened up enough.

The fires are used to help control crop diseases and to clear fields before using a relatively new farming technique called minimum tillage, which reduces soil erosion but requires machinery that can get clogged by heavy stubble. Nationally, fires are also used to clear stubble from grass seed fields in Idaho, rice fields in California, and sugarcane fields in Florida. In eastern Washington, grass growers stopped burning their fields in 1998 in accordance with an agreement with the state's Department of Ecology, which regulates agricultural burning in Washington. But the emphasis on minimum tillage, among other factors, has caused a larger number of wheat

fires to take grass's place.

Burning is a major source of air pollution in Spokane and surrounding areas. "It's a unique pollution, different from auto exhaust," says Patricia Hoffman, a veterinarian who heads Save Our Summers, a citizens group that opposes agricultural burning. "It's a high-concentration, high-intensity exposure for a short period. It's very dangerous for people with asthma or heart or lung problems."

Of Spokane County's approximately 500,000 residents, she says, about 40,000 have asthma and 3,000 have emphysema. These asthma rates are around twice the national average. Timothy Krautkraemer, age 10, is a Spokane asthma patient who stays indoors during the burning season. "He can't participate in activities that others participate in," says his father, Jeffrey. "It's pretty rough on a 10-year-old."



A hot issue. Farmers argue that agricultural burning is a necessary tool, but neighbors worry that the smoke may lead to health problems such as asthma, particularly in children.

The family has joined a federal lawsuit with another family and Save Our Summers against the Washington Department of Ecology. They argue that the burning constitutes discrimination against asthma sufferers, violating the Americans with Disabilities Act.

Michael McCarthy, a Spokane pulmonary pediatric specialist, says he's "totally convinced [the burning is] an extremely important public health problem." McCarthy believes the increased asthma rates are due to the smoke

AGRICULTURE

Debating Dursban

EPA Reviews Chlorpyrifos Risk

U.S. environmental officials say that one of the most widely used pesticides, Dursban, may be unsafe for people who are exposed to it either in home gardens or in crop fields. (Dursban is also often used in and around schools and hospitals, and in pet collars.) The U.S. Environmental Protection Agency (EPA) said in an October 1999 preliminary scientific assessment titled *Hazard Assessment of Organophosphates* that it is particularly concerned with the insecticide, which is made by Dow Chemical Company and applied more than 20 million times a year in the United States. "This preliminary risk assessment indicates that risks from the use of chlorpyrifos in residential settings, as well as its risks to applicators, are of concern," the EPA said in a statement released to the press. The EPA is largely concerned with the Dursban poisoning cases reported to federal officials: of 325 cases reported from 1993 to 1996, one-fourth required hospitalization.

Chlorpyrifos, the active ingredient in Dursban, is being reviewed under a process developed by the EPA and the U.S. Department of Agriculture's Tolerance Reassessment Advisory Committee to determine whether existing EPA daily dose and other requirements meet new safety standards mandated by the Food Quality Protection Act (FQPA) of 1996. The FQPA requires chemical companies to take extra safety steps with their products, such as significantly reducing acceptable levels of exposure in order to protect children and other vulnerable populations who may be particularly sensitive to adverse effects. Chlorpyrifos is one of the 9,000 chemicals the EPA is analyzing in households and in drinking water in order to further implement the FQPA.

Chlorpyrifos belongs to the class of chemicals known as organophosphates, which have been shown to negatively affect the human nervous system with symptoms such as blurred vision, muscle weakness, headaches, and memory problems. In addition to the acute poisoning of the neurologic system, chlorpyrifos has been associated with chronic neurobehavioral effects that include confusion, drowsiness, and depression. According to a 1994 survey of ready-to-eat foods conducted by the U.S. Food and Drug Administration (FDA), chlorpyrifos was the second most commonly detected pesticide in food. The FDA's sample included many foods eaten by infants and children. According to the EPA assessment, data from two human studies suggest that humans are as sensitive and possibly even more sensitive than animals to the effects of chlorpyrifos. The EPA also said that most Americans have at least a tiny amount of the chemical in their bodies.

Dow Chemical responded to the EPA's assessment with a letter stating that the EPA's analysis was misleading and based on fundamental scientific errors. William L. Chen, the study director and coauthor of Dow's response, wrote, "Three decades of use have shown that unless seriously misused, chlorpyrifos products have wide margins of safety that protect users and consumers, including infants and children." Dow's complaint is that the EPA is basing its assessment on information that is "not reflective of real world exposure and risk" and that "[m]any of the risk assessments conducted by the EPA were based on formulations and labels not currently available or utilized in the marketplace."

The EPA report outlined potential health risks but did not make any final decisions about restricting the use of Dursban or implementing the use of warning labels. The EPA plans to issue a final decision about use of the pesticide this summer. —**Lindsey A. Greene**

and a dry, dusty climate where frequent air inversions can cause smoke to linger for days.

While McCarthy admits he cannot prove that any particular patient has been injured by the smoke, he says his medical experience is persuasive. For example, he says, patients who travel during the burning season tell him, "As soon as I get out of Spokane, I feel better, and as soon as I get back, I feel worse." The evidence may be anecdotal, McCarthy adds, but "so many have told me this, it's become a reality for me."

Roe Roberts, an associate professor of health administration at Eastern Washington University in Spokane, studied the effects of grass-fire smoke in eastern Washington during the mid-1990s. Her research, published in the June 1998 issue of the *Journal of Environmental Health*, found that concentrations of smoke particles smaller than 2.5 microns in diameter correlated with weekend purchases of bronchodilators, which are used to open bronchial airways. Roberts says that because weekend purchases often represent emergency purchases, they provide an indirect measure of the effects of smoke on lung-disease patients.

Even some wheat growers recognize the problem. In the July 1999 issue of the trade journal *Wheat Life*, David Roseberry, past president of the Washington Association of

Wheat Growers, wrote, "Evidence affirming the negative consequences of inhaling smoke—all smoke, not just cigarette smoke—has been continuously building to a surprising extent."

Department of Ecology spokesman Larry Altose says the department recognizes that "smoke from agricultural fires is causing serious health problems and people are very interested in addressing this issue to bring it under control." The Washington Association of Wheat Growers signed an agreement with the Department of Ecology in February 1999 specifying a 50% decline in burning over seven years. Altose says permits are issued to farmers who show that burning is "necessary according to best management practices."

Hoffman says the 50% overall reduction mandated by the agreement will not protect public health because it was based on 1998 figures, when a record amount of acreage was burned. But Altose says the Department of Ecology believes the 50% reduction will make a big difference, especially when coupled with new "best management" practices used by farmers, which discourage the use of fire. "We've already seen burning decrease by 50% this fall," he says. —**David J. Tenenbaum**



American Farmland Trust

According to the American Farmland Trust (AFT), the United States has lost over 31 million acres of farmland since 1970. As the U.S. population grows and improvements in transportation and communication make suburban life more appealing, the loss of farmland could accelerate. If that happens, the United States could lose its position as one of the world's primary exporters of farm products—a situation that the AFT is working to prevent.

One way the group is communicating its message is through its Web site, located at <http://www.farmland.org/>. The site includes details of the group's policy efforts including the Competition for Land project, which seeks appropriate ways for governments to protect the nation's farmland without sacrificing the rights of the farmers that own it, and information on federal farm legislation such as bills to reauthorize the 1996 Farmland Protection Program, which provides funding to state, local, and tribal entities to purchase easements or other land in order to protect farmland from development.

The AFT is concerned not just with development but also with environmentally sound use of farmland. To this end, the site contains details of the group's \$10,000 Steward of the Land Award, which is awarded annually to a farmer who has worked to protect farmland and the environment. The AFT also sponsors scientific study through its academic research arm, the Center for Agriculture and the Environment, based at Northern Illinois University in De Kalb. The center's work, described on the site, includes an ongoing investigation of integrated pest management practices, which is being administered in conjunction with the U.S. Environmental Protection Agency, as well as the publication of several reports such as *Farming on the Edge*, a comprehensive look at the loss of prime and unique farmland in areas across the United States. —**Christopher G. Reuther**



Raw Eggs Are Ready to Eat

New food safety rules proposed by President Clinton in December 1999 could increase use of a pasteurization system that uses hot baths to kill *Salmonella* bacteria in raw eggs. An estimated 1 in 20,000 eggs is infected with *Salmonella*. Since the 1980s, *Salmonella* has affected more than 300,000 people annually in the United States. The rules are intended to halve *Salmonella* infections by 2005 and eliminate them by 2010.

The new rules encourage use of pasteurization by allowing egg producers to skip some *Salmonella* testing of their hens if eggs are pasteurized before being shipped to market. The pasteurized eggs, which will cost an extra 3¢ per egg, are due in several grocery chains in the eastern United States by the spring. The eggs, which will be safe to eat raw, will come with a Department of Agriculture seal to verify they have been sterilized.

Antibiotics on the Farm

In the 1950s researchers found that animals fed antibiotics grew faster than those that weren't, and the practice became routine in commercial livestock farming. On 8 December 1999, the Food and Drug Administration (FDA) issued a report stating that up to 5,000 Americans may have suffered longer-lasting food poisoning in 1998 because they caught an antibiotic-resistant strain of *Campylobacter* from eating chicken. The FDA formulated its estimate using a mathematical model that relates the prevalence of fluoroquinolone-resistant *Campylobacter* infections in people who ate chicken to the prevalence of the bacteria in the birds themselves.

Many public health experts say the use of antibiotics in food animals worsens the problem of bacterial resistance and antibiotic ineffectiveness, although the animal drug industry insists there is no serious risk to consumers. The FDA says its model could become a tool for assessing such risks in the future.

Friendly Phosphates

A new technology developed by Alan Goldstein of Alfred University and colleagues at the Idaho National Engineering and Environmental Laboratory may transform the way phosphate fertilizers, the second most widely used agricultural chemical, are produced, thereby reducing their damaging effects on the environment.

The new pellet-form fertilizer uses bacteria to convert raw phosphate ore into fertilizer in the soil, replacing the energy-intensive conventional smelting process, which currently consumes 1% of the total energy used in the United States. The new fertilizer releases soluble phosphate slowly in response to the growth of the bacteria. Farmers often have to overapply conventional phosphate fertilizers because they are easily washed away, often into groundwater or surface water, causing heavy algal growth that can destroy wetlands and marine ecosystems.

