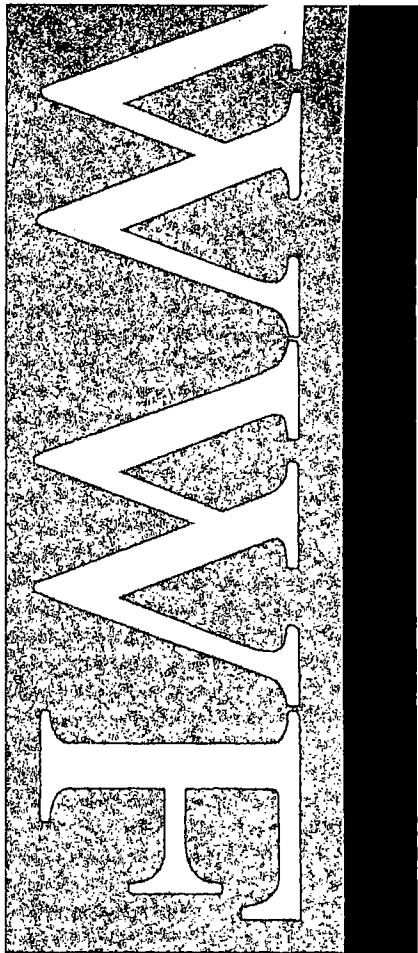




WWF

World Wildlife Fund

PHOTOCOPY
PRESERVATION

CONFRONTING THE HAZARDS

Confronting the hazards of harmful chemicals in the environment requires action on several fronts.

First, we must go beyond using the incidence of cancer and other gross health defects as the major criterion for determining research and regulatory priorities. Testing should be broadened to screen for hormonal activity and other endocrine-disrupting effects before chemicals are introduced into commerce. Testing should also be done on chemicals now in use and on persistent, bioaccumulative chemicals released in the past.

Second, we need a major, multi-disciplinary research initiative to investigate the effects of toxic chemicals on development in wildlife and humans. Research efforts in this area must be put into the mainstream and coordinated through institutions such as the Agency for Toxic Substances and Disease Registry, National Institute of Environmental Health Sciences, Environmental Protection Agency, National Academy of Sciences, or the proposed National Institute on the Environment. The evidence that we now have points toward frightening possibilities. We simply do not know what we need to know about the harmful effects of chemicals.

Third, we must begin collecting information from regions beyond North America and Europe. Little is known about the presence of toxic chemicals and their effects on wildlife in Latin America, Africa, and Asia. Obtaining this information is vital to protecting the world's biological diversity.

Fourth, because of the widespread use and particular hazards already associated with organochlorines, we need a strategy for assessing their impacts and opportunities for reducing their use. A task force such as that proposed by the Clinton administration, including representatives of government agencies, university-based researchers, and policy experts, could help insure that a comprehensive assessment of impacts and alternatives will lead to action by both the public and private sectors.

Fifth, neither the scientific community nor government agencies can afford to wait for answers to every research question before taking action. Efforts to reduce the hazards of toxic chemicals must proceed, using information provided by ongoing studies as the basis for creating new and more effective approaches for dealing with these chemicals.

Finally, although much research lies ahead in better understanding the effects of toxic chemicals, it is clear that prevention—using cleaner production processes and materials—is the best response. "It is vital," says Colborn, "that we focus attention on preventing pollution instead of simply trying to control it after it has been created. We must reconsider how we use materials in industry, agriculture, commerce, and our domestic lives. If we don't, we are putting the diversity of life on Earth on a fast track to extinction."⁹

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WORLD WILDLIFE FUND

WORLD WILDLIFE FUND IS THE LARGEST PRIVATE ORGANIZATION IN THE UNITED STATES THAT WORKS WORLDWIDE TO PROTECT ENDANGERED WILDLIFE AND WILDLANDS. WWF IS THE U.S. AFFILIATE OF THE INTERNATIONAL WWF FAMILY, WHICH HAS NATIONAL ORGANIZATIONS OR REPRESENTATIVES IN NEARLY 50 COUNTRIES.

REASSESSING POLLUTION

Wildlife, Humans, and Toxic Chemicals in the Environment



Photo by William Rossiter/WWF-I

The world's biological diversity cannot be conserved in an environment filled with harmful chemicals. Toxic chemicals move through water and air, into the earth and plants and animals, and have been detected in wildlife from the Arctic to Antarctica—in alligators, bald eagles, bottle-nosed dolphins, beluga whales, great blue herons, common seals, polar bears, sea turtles, and humans, among other species. Many species are threatened; so, too, is the fabric of life on this planet.



For decades, wildlife have sent warning signals about the dangers of chemical pollution. These dangers were first brought to widespread public attention in 1962 by Rachel Carson in her book *Silent Spring*.

In 1990, a report by World Wildlife Fund (WWF) and Canada's Institute for Research on Public Policy revealed a wide range of problems among 16 animal species in the Great Lakes region. This study, *Great Lakes, Great Legacy?*, noted reproductive and endocrine problems in bald eagles, beluga whales, lake trout, mink, snapping turtles, and other species. In each case, elevated concentrations of industrial chemicals and pesticides were found in the species.¹

THE WINGSPREAD STATEMENTS ON SYNTHETIC CHEMICALS

In July 1991, at the Wingspread Center in Racine, Wisconsin, WWF Senior Scientist Dr. Theo Colborn, who synthesized the wildlife research for *Great Lakes, Great Legacy?*, convened a work session of scientists representing a wide range of research specialties, from medical anthropology to wildlife toxicology, to share findings about the effects of chemicals on wildlife and human health, particularly the endocrine system, which controls development and reproduction.

Of particular concern to the Wingspread participants were "synthetic hormones," manmade chemicals that can mimic or interfere with the body's natural chemical messengers and disrupt normal development. Even tiny doses of these chemicals can have far-reaching effects on wildlife and humans. If present during the early stages of fetal development, especially when the major organs are still being formed and the brain is being programmed to control and respond to hormonal signals throughout life, synthetic hormones may trigger a cascade of damaging biochemical changes that affect development of the nervous, immune, endocrine, repro-

ductive, and digestive systems. These effects are usually irreversible.²

In a pioneering consensus statement that has had a broad impact on subsequent governmental and academic research and thinking about policy, the Wingspread conference participants declared, "We are certain of the following: A large number of manmade chemicals that have been released into the environment, as well as a few natural ones, have the potential to disrupt the endocrine system of animals, including humans."

As evidence continued to mount, a second Wingspread work session, "Environmentally Induced Alterations in Development: A Focus on Wildlife," was held in December 1993, producing an even stronger statement. "Declines in a number of species," participants declared, "are in progress on the North American continent. Some of these declines are related to exposure to manmade chemicals. Such declines are not solely a U.S. or North American problem but are occurring on a global scale....Populations of many long-lived species are declining, some to the verge of extinction, without society's knowledge."

CHEMICALS IN THE ENVIRONMENT

The manufacture and use of chemicals has grown rapidly since the end of World War II. Production of synthetic organic chemicals in the United States, as reported to the U.S. International Trade Commission, amounted to 197.5 billion kilograms in 1992—that is, 435 billion pounds, or more than 1,600 pounds for each person in the country.³ Chlorine-based chemicals are among the most common of the organic chemicals. There are now about 15,000 of them, which is more than 20 percent of all chemicals in U.S. commerce.⁴ They are used for many purposes: in drinking water, bleach, pesticides, pharmaceuticals, dry cleaning, and vinyl for building materials, cars, toys, and other products.

Although harmful effects have been associated with nonchlorinated chemicals—styrenes, phthalates, mercury, lead, cadmium, parathion, for example⁵—chlorine-based chemicals have been at the heart of recent controversy because of their widespread use and history. Many of the known or suspected "synthetic hormones" are chlorine-based. Some of the most notorious members of the chlorine family—for example, DDT and various PCBs—have been found to be so hazardous that their use has been highly restricted in the United States. The known and unknown effects of the many chlorine-based chemicals still in use have raised increasing concern and led to calls for the phaseout of many uses.

The Clinton Administration's recommendations for reauthorization of the Clean Water Act call for a task force on chlorine that would "develop a national strategy for substituting, reducing, or prohibiting the use of chlorine and chlorinated compounds." This strategy is to be based on a comprehensive assessment of the use and impacts of chlorine and alternatives to it in four key industries: pulp and paper, solvents, plastics, and publicly owned water treatment plants and drinking water systems.⁶

TESTING FOR HARMFUL EFFECTS

Underlying and amplifying the concern about chlorine and other chemicals is the fact that current methods of toxicity testing do not provide an adequate basis for establishing policies to safeguard against all of the harmful effects of chemicals. For more than two decades, scientists and government regulators have largely focused their attention on identifying and controlling chemicals that cause cancer, gene mutations, acute toxic effects, and visible birth defects. Even with this narrow focus, screening has not been comprehensive; although pesticides have been tested routinely, tens of thousands of industrial chemicals have never been

screened. Moreover, we do not have adequate data on what other consequences exposure to these chemicals in the environment may have for wildlife and humans.

Testing chemicals for developmental effects is problematic. The damage that researchers are now uncovering occurs before or soon after birth but in many cases does not become fully evident until adulthood. Moreover, the timing of exposure to "synthetic hormones," for example, can be crucial: Even a single exposure at a very low dose can have major effects if it occurs at a critical time. Although small doses of certain chemicals during fetal development can cause significant damage, much greater or accumulating doses later on may have no apparent impact; and thus adults may seem to escape harm while their offspring suffer it. This also means that short-lived chemicals could be as dangerous as those that persist in the environment.⁷

Risk assessment has generally been based on high-dose testing for a single "endpoint" such as cancer or mortality. This model does not work in the case of developmental disruption where the endpoints are numerous and unpredictable, and where one chemical is capable of causing many different effects. Cancer and mortality are relatively easy endpoints to monitor compared with functional losses such as learning disabilities, reproductive difficulties, and immune system problems, which can be manifested at different times in life and vary from slight to intense.⁸

In scientific literature, the Wingspread statements, and other forums, WWF's Colborn and other scientists have warned that ignoring the danger signals of damage to reproductive systems and deterioration of other essential functions could have devastating consequences for life on this planet. Current screening processes simply do not provide appropriate or adequate information for safeguarding the health of humans, wildlife, or the ecological systems on which we all depend.

■ ENVIRONMENT

Not So Fertile Ground

Some scientists fear that pollutants are damaging human reproductive systems

By MICHAEL D. LEMONICK

THE ALARM WENT OFF WITH RACHEL Carson's 1962 book *Silent Spring* and has been sounding ever since. We live, environmentalists warn, in a world laced with dangerous chemicals, from powerful pesticides to toxic industrial wastes like dioxin and PCBs. Despite periodic waves of public concern and efforts at government regulation (the 1972 banning of DDT in the U.S., for example), the chemicals are still found in small but measurable amounts in air, water, soil—and our own tissues. Many scientists have long argued that even tiny doses of pollutants can cause cancer in humans, but the contention is hotly disputed. Other researchers maintain that traces of man-made chemicals are no more likely to cause tumors than are the countless chemicals produced by Mother Nature.

Now, even as the cancer debate continues, environmental groups are pointing to a different, previously unrecognized threat. Chemical pollutants, they say, can interfere with one of the most basic of biological functions: the ability to reproduce. The chemicals allegedly disrupt the action of hormones, those all-important molecular messengers that regulate just about all bodily activities, including growth and reproduction. The result may be a variety of harmful effects that could decrease fertility. Among them: testicular cancer and reduced sperm counts in men, uterine abnormalities and miscarriages in women. While there is no hard evidence that pollution is affecting human fertility in the U.S. or anywhere else, the theory is likely to grab the attention of millions of couples who have trouble conceiving.

The Environmental Protection Agency is expected to raise the issue this week when it releases a major report on the effects of dioxin, one of the most ubiquitous of the suspect chemicals. Dioxin is the name given to a class of chlorine-containing compounds that are waste by-products of many industrial processes such as paper making and waste incineration. Although the release of dioxin has been curbed in recent years, traces of it still permeate the environment.

According to sources familiar with drafts of the EPA report, it will say that diox-

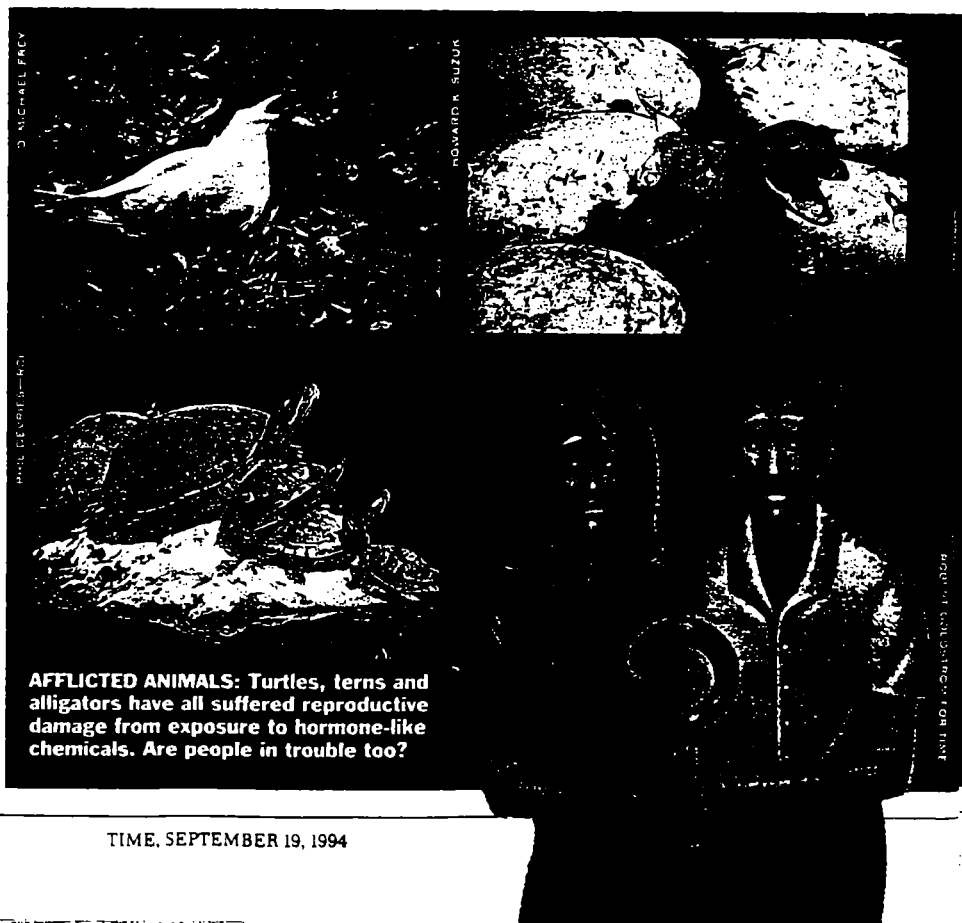
in remains a serious potential threat to human health and that possible links between the chemical and health problems, among them reproductive ills, should be further explored. "This study ranks with the Surgeon General's pronouncement that smoking causes lung cancer," says Sierra Club pollution expert George Colling, prematurely and hyperbolically, in the latest issue of the organization's monthly newspaper. And Peter deFur of the Environmental Defense Fund predicts that the document will lead to much tighter regulations, and in some cases even a ban, on the release of dioxin and related chemicals.

Well, maybe. But many scientists who have looked into hormone-disrupting chemicals say the issue is much more complex than environmental activists would have people believe. In high doses, the compounds in question, many of which contain chlorine, are clearly toxic and carcinogenic. On the other hand, the case that humans are being affected by very low concentrations remains far from certain. The existing evidence is largely circumstantial,

based on extrapolations from animal studies, laboratory work on the chemistry of dioxin and other molecules, and statistics on human disease that may or may not turn out to be accurate or relevant.

But most investigators agree that although the danger has not been proved, it is too plausible to ignore. The chain of reasoning goes something like this: animals exposed to high doses of these pollutants in the wild develop reproductive abnormalities. Animals exposed to low doses in the lab do too. Humans absorb comparable low doses simply by breathing, drinking and especially eating. Some of the suspect chemicals have physiological effects similar to those of estrogen and other sex hormones, or they at least interact with them; they might reasonably be expected to interfere with processes involving these hormones, such as the menstrual cycle and sperm production.

Finally, several hormone-related human disorders, including low sperm counts, testicular and breast cancers and endometriosis (a painful condition in



AFFLICTED ANIMALS: Turtles, terns and alligators have all suffered reproductive damage from exposure to hormone-like chemicals. Are people in trouble too?

which uterine cells migrate to other parts of the pelvic area), have arguably been on the rise in the decades since DDT, dioxin and the like first entered the food chain. Says Thomas Burke of the Johns Hopkins School of Public Health: "What we have now is identification of a potential hazard, and that's all we have. What the implications are we don't know yet, and we need to clarify that."

Suspicious about hormone disrupters were raised a few years ago by Theodora Colborn, a zoologist with the World Wildlife Fund who did a study on the reproductive health of Great Lakes wildlife in the late 1980s. Colborn discovered that the young of 16 predator species, including fish, birds, reptiles and mammals, were failing to survive to adulthood or could not reproduce if they did. All the animals ate fish from the Great Lakes, which were contaminated with a variety of hormone-like chemicals.

Colborn suspected a cause-and-effect relationship between pollution and fertility problems—and by extension a possible danger to humans. She began collecting human epidemiological studies, which suggested to her that human fetal exposure to such chemicals as PCBs could produce disorders affecting behavior, immune-system functioning, memory and learning. She also surveyed the literature on humans exposed to diethylstilbestrol, or DES, a synthetic drug that is related to estrogen. DES can be used to prevent miscarriage, treat prostate and breast cancer or reduce the



ECO-SLEUTH: Colborn set out to discover what was wrong with Great Lakes wildlife.

symptoms of menopause; it can even promote growth in sheep and cows. But in 1971, after studies linked its use by pregnant women with reproductive-system abnormalities, infertility and cancer in their offspring, the FDA decreed that DES should no longer be used to prevent miscarriage. In 1979 the drug was banned in livestock because traces were showing up in meat.

Since no one seemed to be studying the impact of chemicals on reproduction in any systematic way, Colborn organized a 1991 meeting in Racine, Wisconsin, and invited 21 scientists representing 17 disciplines ranging from toxicology to zoology to endocrinology. "No one seemed to know what the others were doing," she says. "Most of the people didn't know anyone

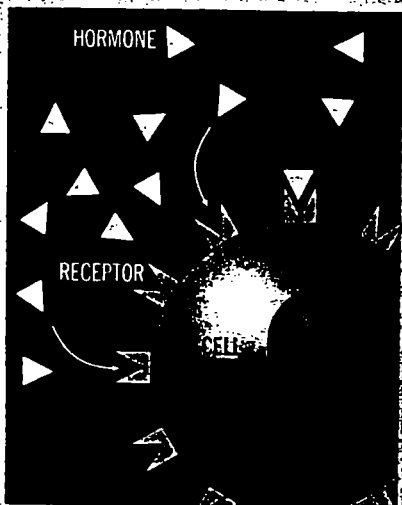
else in the room." Colborn also recalls that some of the participants were skeptical about the whole thing. Nonetheless, when they got down to discussing the problems Colborn and others had found in animals exposed to chemicals—thyroid damage, immune deficiencies, sexual abnormalities—a pattern emerged. Most of the problems involved malfunctions of the endocrine system that is responsible for producing hormones. Among the chemicals fingered by the group as probable culprits were DDT, kepone, triazine herbicides, certain PCBs and dioxins, styrenes and the alkyl phenols found in some detergents and plastics.

The conference gave rise to numerous collaborations, and participants began trading lab samples with one another and with a growing number of additional interested scientists. "We had gonads flying around the country," says Colborn. As the researchers compared notes, the evidence began to mount. During the mid-1980s, Colborn learned, mortality rates for alligator eggs in Lake Apopka, Florida, soared to 96%, in contrast to 57% in most Florida lakes. The almost certain cause: a 1980 chemical spill that included DDT. In 1993 researchers found that terns in PCB-contaminated Buzzard's Bay, Massachusetts, had reproductive-tract abnormalities including the presence of ovarian cells in male birds. Earlier studies had found similar problems with birds in California and the upper Midwest.

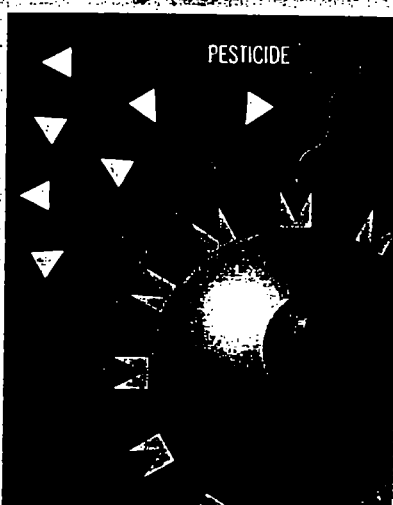
While most of these reports involve heavy doses of chemicals, evidence from laboratory studies suggests there are also effects at lower concentrations. Endocrinologist David Crews has discovered, for example, that small PCB doses can dramatically influence the ratio of male to female offspring in red-eared slider turtles. When University of Wisconsin toxicologist Richard Peterson investigated the impact of dioxin on male rats, he found that the dose needed to cause reproductive-system problems was relatively high. "But when we exposed pregnant rats to a dose 1/100th as large," he says, "we found the male offspring showed signs of reproductive dysfunction," including smaller sex organs, reduction in sperm counts and feminized sexual behavior. Peterson also found defects in lake-trout embryos exposed to dioxin.

What is especially disturbing about Peterson's work is that the levels of dioxin needed to do that kind of damage were as low as 64 nanograms per kg of body weight—only a little greater than the 5 or 10 nanograms of dioxin and comparable chemicals found in a typical kilogram of human tissue. It is not surprising that these compounds are so biologically active, since they are metabolized in a fashion similar to

CHEMICAL IMPOSTORS



1 Hormones are chemical messengers that regulate various processes in the body. The hormone's signal is received through receptors on the surface of or inside cells.



2 Chemicals from pesticides or other pollutants may mimic a hormone and attach to the receptors, either blocking the hormone's action or interfering with its effects.

TIME Diagram by Joe Lertola

natural chemicals. Says Linda Birnbaum of the EPA's Health Effects Research Laboratory, who was one of the driving forces behind the agency's decision to study dioxin: "You name almost every hormone system in the body, and dioxin interacts with it. And when you're dealing with hormones, they all talk to each other. When you ring one bell, many others chime."

But—and this is a big but—some species are more sensitive to dioxin than others. Just because rats and fish are affected in certain ways does not necessarily mean that humans will have comparable reactions. And doses that harm animals are not necessarily large enough to damage people. On the other hand, humans soak up many different chemicals, and the results may be cumulative.

Whatever the impact of pollutants on men and women, solid evidence is hard to come by. Even when a cause-and-effect relationship is established, as in major industrial accidents, the data are confusing. In the years after a large dioxin release in 1976 in Seveso, Italy, for example, the incidence of leukemias, lymphomas and soft-tissue cancers in men and gall-bladder and bile-duct cancers in women rose—but breast and endometrial cancers in women actually went down. Possible reason: dioxin may sometimes interfere with the hormone system in beneficial ways.

When scientists look for hormone disruption in the general population, the evidence is murkier still. Birthrates go up and down for many reasons that have nothing to do with pollution. While there are anecdotal reports that the number of infertile couples is on the rise, the phenomenon could be a result of their waiting too long to try for children. The incidence of testicular cancer is higher than it was two decades ago, but that could be because of better reporting. Even the strongest piece of evidence, a Danish study that seems to document a drop in sperm counts over the past 50 years, is considered inconclusive by some scientists.

None of these uncertainties will be cleared up quickly or easily. The fact that environmentalists and a group of concerned scientists have raised the issue of endangered fertility is likely to spur much-needed research. The evidence so far may not be strong enough to support sweeping government action, but it ought to prompt some companies to consider whether there are practical, economical ways to reduce their emissions of suspect chemicals. —Reported by J. Madeleine Nash/Chicago and Mia Schmiedeskamp/Washington

Keeping Cool About Risk

ALAR ON APPLES, RADON IN HOMES, ASBESTOS IN SCHOOLS: THE U.S. APPEARS to ricochet from one environmental crisis to another, with the result that policy aimed at reducing risks to human health frequently appears to make little economic or scientific sense. Even some environmentalists concur that decisions to rip asbestos out of school buildings were probably ill considered. In many cases, sealing the dangerous fibers in place would have provided a more prudent and less costly remedy. Similarly, while no one denies that homes with high levels of radon pose a health hazard requiring prompt attention, what about houses with much lower levels? Is it reasonable to urge that they too be radonproofed if there is no certainty that a danger exists?

Now environmentalists say dioxin and scores of other chemicals pose a threat to human fertility—as scary an issue as any policymakers have faced. But in the absence of conclusive evidence, what are policymakers to do? What measures can they take to handle a problem whose magnitude is unknown?

Predictably, attempts to whipsaw public opinion have already begun. Corporate lobbyists urge that action be put on hold until science resolves the unanswered questions. Environmentalists argue that evidence for harm is too strong to permit delay. The issue is especially tough because the chemicals under

scrutiny are found almost everywhere. Since many of them contain chlorine or are by-products of processes involving chlorine compounds, the environmental group Greenpeace has demanded a ban on all industrial uses of chlorine. The proposal seems appealingly simple, but it would be economically wrenching for companies and consumers alike.

With the escalating rhetoric, many professionals in the risk-assessment business are worried that once again emotion rather than common sense will drive the political process. "There is no free lunch," observes Tammy Tengs, a public-health specialist at Duke University. "When someone spends money in one place, that

Protesting in Belgium, Greenpeace demands a phaseout of chlorine

money is not available to spend on other things." She and her colleagues have calculated that tuberculosis treatment can extend a person's life by a year for less than \$10,000—surely a reasonable price tag. By contrast, extending a life by a year through asbestos removal costs nearly \$2 million, since relatively few people would die if the asbestos were left in place. That kind of benefit-risk analysis all too rarely informs the decisions made by government regulators.

As the EPA raises anew the dangers of dioxin, the agency needs to communicate its findings to the public in a calm and clear fashion. No one is eager to touch off the kind of hysteria that preceded the government's decision to move against Alar, the growth regulator once used by apple growers. When celebrities like Meryl Streep spoke out against Alar and the press fanned public fears, some schools and parents rushed to pluck apples out of the mouths of children. Yet all this happened before scientists had reached any consensus about Alar's dangers.

Rhetoric about dioxin may push the same kind of emotional buttons. The chemical becomes relatively concentrated in fat-rich foods—including human breast milk. Scientists estimate that a substantial fraction of an individual's lifetime burden of dioxin—as much as 12%—is accumulated during the first year of life. Nonetheless, the benefits of breast-feeding infants, the EPA and most everyone else would agree, far outweigh the hazards.

John Graham, director of the Harvard Center for Risk Analysis, suggests that people should strive to keep the perils posed by dioxin in perspective and remember other threats that are more easily averted. "Phantom risks and real risks compete not only for our resources but also for our attention," Graham observes. "It's a shame when a mother worries about toxic chemicals, and yet her kids are running around unvaccinated and without bicycle helmets."

—By J. Madeleine Nash



DANIEL GLENN/REUTERS-GAMMA LIAISON

SOCIETY

The Estrogen Complex

Science: Sperm counts down? Penises shriveled? Hey, Rush, don't blame it on feminists. It may be from chemical pollutants in water and food.

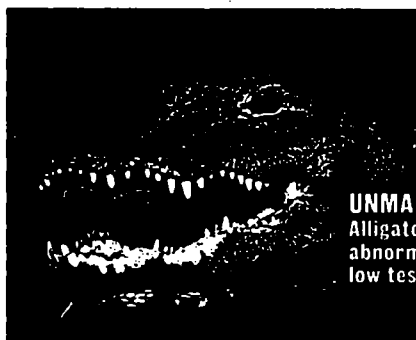
ALL LOUIS GUILLETTE WANTED TO do was to help figure out how many alligators could be hunted from Florida's Lake Apopka without making the population crash. But after years of wading (carefully) through the thigh-deep muck and sneaking up (warily) on alligator nests to snare the great reptiles with a noose, it dawned on him that the gators had bigger worries than winding up as pocketbooks. Male alligators' penises were only one quarter the normal size; their testosterone levels were so low they were probably sterile. Soon after, Guillette met a researcher who had seen similar effects on lab mice exposed to a cousin of the chemical DDE, formed when DDT decomposes. Not coincidentally, thousands of gallons of DDT-containing pesticide had spilled into Lake Apopka in 1980. Connecting the dots, Guillette said, "I think we have a problem here." By "we," he didn't mean alligators. Because people live in a sea of the same gender-bending chemicals, the University of Florida researcher recently told a congressional panel, "every man in this room is half the man his grandfather was."

It is a plot twist worthy of science fiction. Hundreds of the bedrock chemicals of the postwar age—PCBs used in the manufacture of electronics, pesticides such as endosulfan and atrazine, polycarbonate plastic found in many baby bottles and water jugs, chlorine compounds that bleach paper—resemble the human sex hormone estrogen. Although the compounds were concocted in the lab for purposes having nothing to do with human biology, their molecular structure turns out to be so similar to estrogen's that they fit into the same "receptors" in the body. (Contrary to popular belief, men as well as women produce estrogen, and so have receptors for the hormone.) The estrogen receptor can no more tell that it's being occupied by an impostor than a door lock can tell that a thief's skeleton key has been inserted. As a result, the estrogen mimics can trick the body into turning off, or ratcheting up, certain biochemical pathways—especially those in the reproductive system. The result: sexual development, in both males and females, gone seriously askew. Since the impostors find their way into the

soil, water and food supply, researching their effect on health "is a top priority for us," says Kenneth Olden, director of the National Institute of Environmental Health Sciences. "There's enough science out there to tell us we should be concerned."

For one thing, "half your grandfather" is no hyperbole. Since 1938, sperm counts of

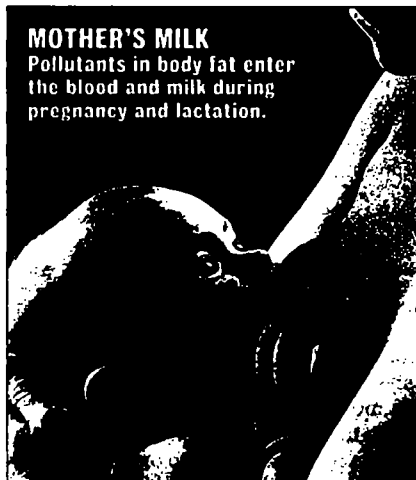
ground" levels of estrogenlike chemicals are responsible for the decline and fall of Western manhood, the case against high levels of the chemicals is clear-cut. In Michigan, estrogen mimics called PBBs accidentally got into cattle feed in 1973, and from there into beef. Women who ate the meat, and whose breast milk harbored high levels



JOE McDONALD—ANIMALS ANIMALS

UNMANNED

Alligators in a Florida lake have abnormally small penises and low testosterone levels.



MOTHER'S MILK

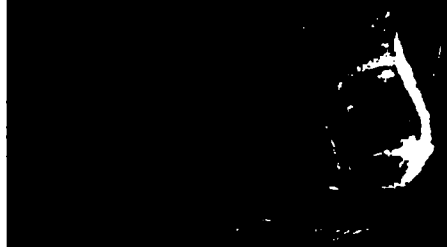
Pollutants in body fat enter the blood and milk during pregnancy and lactation.

DAG SUNDHEIM—IMAGE BANK

men in the United States and 20 other countries have plunged by an average of 50 percent, reported Danish endocrinologist Niels Skakkebaek in 1991. At the same time, testicular cancer has tripled. The trends could be a coincidence. But Skakkebaek suspects that the culprit in both the sparse sperm counts and the cancers may be men's exposure, as fetuses and newborns, to estrogenlike chemicals in their mothers' blood and milk.

While it's too soon to say that "back-

Gender Bender



AN ESTROGEN CRYSTAL

Hundreds of pollutants mimic estrogen's molecular shape. In males they may cause cancer and reproductive defects.

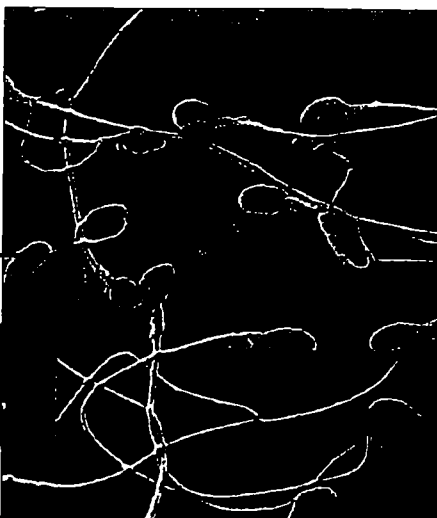
of PBBs, had sons with testicular malformations and undersized penises. And in the closest thing to a controlled study in such a tricky field, Chinese scientists have been studying 118 boys in Taiwan who were born to women exposed to a PCB spill in 1979. Compared with boys whose mothers were not exposed, the 118 suffered reproductive defects like those of the boys in Michigan. These abnormalities "were probably related to hormonal changes caused by toxic exposure," the scientists conclude.

Now physicians are analyzing studies that link estrogenlike pollutants to breast cancer and endometriosis, the painful inflammation of the uterine lining that often

causes infertility. Perhaps the oddest thing about endometriosis is that there were only 21 reported cases in the world 70 years ago; today there are 5 million in the United States alone. In a new German study, women with endometriosis were more likely than others to have high levels of PCBs in their blood. Some breast cancer may also have an environmental cause. Unusual amounts of DDE, the pesticide residue that seems to be leaving the alligators shortchanged, shows up in the tissue of women with breast cancer, according to a study last year by Mary Wolff of New York's Mount Sinai School of Medicine. Women with the greatest number of these DDE footprints were four times more likely to get breast cancer than women with the fewest such signs. The connection is plausible. This year the National Cancer Institute will begin a major study of the high rates of

genlike pesticides, have their own reproductive problems: more infertile females, sterile males, lower sperm counts and high estrogen levels. One male, says toxicologist Charles Facemire of the U.S. Fish and Wildlife Service, "had estrogen levels higher than most females."

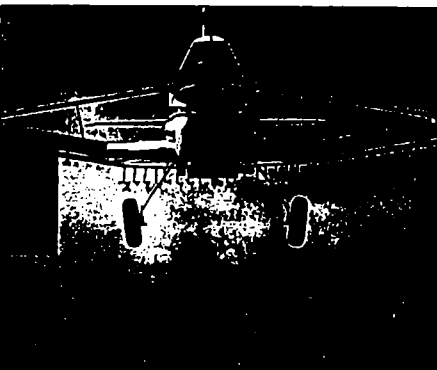
Despite such findings, "much of the evidence [about estrogen mimics] is circumstantial," says Thomas Goldsworthy of the Chemical Industry Institute of Toxicology. Although there is no question that the pollutants fit the body's estrogen receptors, there's still some wiggle room to argue that the chemicals do not switch on the same biological pathways that real estrogen



DAVID M. PHILLIPS - PHOTO RESEARCHERS

SHOOTING BLANKS

Men's sperm counts are down 50 percent since 1938, says one study.



ROBERTO VALLADARES - IMAGE BANK

CROP DUSTER

Among the chemicals that mimic estrogen are widely used pesticides.

breast cancer on New York's Long Island, assessing women's exposure to estrogen-like compounds in pesticides once used on the potato fields (and still in the aquifers) where suburbs now sprout.

Playing canary in the coal mine, wildlife "was the first to send signals that something was seriously wrong," says zoologist Theo Colborn of the World Wildlife Fund. Fish in places like the Great Lakes, where PCB and DDT concentrations are extremely high, and the terns and gulls that eat them, are becoming biochemical hermaphrodites: the males have reproductive parts of both sexes. Florida panthers, eating high on a food chain contaminated with estro-

does. Skeptics also ask why, if the ubiquitous estrogen impostors really trigger cancers and other diseases, rates of the illnesses are not higher. Lawmakers may not wait for an answer. In February, the Clinton administration called for an 18-month study of chlorine (a component in many estrogenlike chemicals) to assess its effects on human health and the environment, with an eye toward restricting or banning it. A bill in Congress would phase out chlorine in the paper and pulp industries over five years. Hell has no fury like a congressman who discovers he's not the man he thought he was.

SHARON BEGLEY with DANIEL GLICK

And Now the Good News

NOT ALL ESTROGENS, OR ESTROGEN impostors, twist sexual development and increase the risk of cancer. Just as there is good cholesterol and bad cholesterol, there is good estrogen and bad estrogen, forms of the hormone that differ by only a few molecules. As Devra Lee Davis, a senior scientist at the Department of Health and Human Services, puts it, "All estrogen is not equal." Her theory is that when the body manufactures estrogen, the hormone can be broken down by either of two biochemical pathways. One leads to a form called 16-hydroxyestrone, which can damage DNA and so is the form suspected of spurring breast and testicular cancers. The other leads to a form called 2-hydroxyestrone that does no harm, and may even do good.

Many edible plant products, such as French beans, soybeans and pomegranates, contain "phytoestrogens" that might combat cancer, suggests Kenneth Setchell of the Children's Hospital Medical Center in Washington. In his lab, rodents that are fed soy protein develop fewer tumors than those on a soy-free diet. This might help explain why women in Japan have low rates of breast cancer when they eat tofu, soy sauce and miso—all rich sources of good estrogen—but have "American" rates when they move to the United States and adopt a Western diet. Compounds in such "healthy" foods as broccoli, says Davis, might nudge estrogen down the path to the cancer-fighting form.

Last fall Victor Henderson of the University of Southern California reported a tantalizing link between estrogen and a lower risk of Alzheimer's disease: in a group of 2,418 postmenopausal women, those who took estrogen pills (for such problems as osteoporosis and hot flashes) were 40 percent less likely to develop this crippling dementia than those who did not take estrogen. In rats, estrogen helps make a "growth factor" that maintains and strengthens connections between neurons. It also helps produce an enzyme that speeds communications among neurons. The effect seems to be particularly strong in memory centers, the first to be ravaged by Alzheimer's.

'Toxins' 'Assault' on 'reproductive systems

By Anita Manning
USA TODAY

Pesticides, herbicides and other chemicals humans have been tossing around for 50 years could be wreaking havoc on the reproductive systems of people and animals.

No one's certain that chemicals are the culprit, but there's enough evidence of something going wrong to raise alarm bells. The topic is explored Sunday in a Discovery Channel documentary, *Assault on the Male*, airing 7-8 p.m. ET/PT. Though this show focuses on males, the problem affects both sexes.

In women, breast cancer and endometriosis are thought to be linked to chemicals in the environment that mimic the hormone estrogen.

In men, Danish researchers have reported a 50% drop in sperm count in Europe and the U.S. between 1938 and 1990, coinciding with a two- to fourfold increase in testicular cancer. Doctors say they're seeing growing numbers of infant boys born with undescended testicles or genital deformities.

Zoologist Theo Colborn, of the World Wildlife Fund, says chemicals appear to be acting on the endocrine system, which regulates metabolism, growth, and sexual development and functioning of animals and humans.

The chemicals, she says, "affect the embryo, fetus and newborn entirely different than they affect an adult, if they affect the adult at all. And the effects in the developing offspring are often irreversible and may not be seen until years after exposure in the womb."

In the late 1980s, Colborn studied fish and birds in the Great Lakes, where levels of DDT and PCB were high.

She found 16 species of birds, fish and mammals experiencing population



By Jim Sikarskie, Michigan State University

DAMAGING CONSEQUENCES: Scientists believed that the malformed beak of this Lake Erie bald eagle is a result of toxic chemicals in the environment.

decline and offspring with deformities ranging from eggs that didn't hatch to birds with crossed bills. Other red flags:

- At least 25% of the male alligators in Florida's Lake Apopka — site of a pesticide spill in 1980 — have low testosterone levels, high estrogen levels and penises one-fourth the normal size.

- Thyroid problems are seen in birds and fish in the Great Lakes.

- Demasculinization of male fish, birds and mammals and defeminization of female fish and birds is seen around the Great Lakes and below paper and pulp mills in the South.

- Immune system suppression has caused problems for dolphins on the Atlantic coast and in the Mediterranean.

In addition, Colborn says, "there are people walking around today who have been affected. If we don't reduce chem-

icals in the environment, we'll see widespread dysfunction."

But the issue is not clear-cut, says Dr. James Simon, endocrinologist at Georgetown University Medical Center, Washington, D.C. "Humans are not alligators," he says, adding the situation "requires far more investigation."

Sperm counts in men have dropped, says Dr. Michael Zinaman, of Loyola University of Chicago, who is conducting an Environmental Protection Agency study on the subject, "but I can't tell you what's caused that."

Still, there is enough evidence to warrant "big-time interest by our government to fund these studies," says Zinaman. "It would be devastating if the trend continued for the next 20 or 30 years. It would be a major issue for reproduction in developed countries."

Dr. John McLachlan, of the National Institute of Environmental Health Sciences, says research is going full-tilt on the effects of estrogens in the environment. "The thing we've spent most time on over years, going back to the early '70s, is trying to understand how estrogens alter sexual development, using DES," the drug given in the 1950s to prevent miscarriage in pregnant women.

The high doses of estrogen given to the women unintentionally set up a huge experiment, with humans as guinea pigs. The sons and daughters of women who took DES have suffered high rates of testicular or vaginal cancer, sterility and other reproductive problems.

"Part of the problem," McLachlan says, "is that it's all very new to us. So the concern that's expressed sometimes in the media and by groups is ahead of the data. As research scientists, we have a real urgency to develop the data as soon as possible, because it's hard to say what level of urgency is adequate."

"We know a potent estrogen like DES will affect lab animals, no doubt. We know the same potent chemical will affect the sexual development of humans. But whether these other molecules, which most people can agree are weakly estrogenic, can do the same thing is still an open issue."

Zoologist Louis Guillette, of the University of Florida, who has been studying Lake Apopka's alligators since the late 1980s, spoke earlier this year to a congressional panel on the potential effects of environmental estrogen.

"A guy said, 'I don't see what all this has to do with us,'" Guillette recalls. His response: "It means every man alive today is half the man his grandfather was."

"And the most important question is: Are our grandsons going to be half the men we are?"

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Los Angeles Times

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COLUMN ONE

Sexual Confusion in the Wild

■ From alligators to sea gulls, scientists say, pollution may be playing havoc with the hormones of animals. As a result, some males try to lay eggs. Some females nest together. Unchecked, certain species may risk extinction.

By MARLA CONE
TIMES ENVIRONMENTAL WRITER

WINTER GARDEN, Fla.—In the gender-bending waters of Lake Apopka, alligators aren't quite male. They aren't quite female either. They may be both. Or, neither.

This sexual confusion in the wild, discovered in this steamy Florida swamp last year, is so disturbing to scientists that they keep performing test after test on the scaly reptiles, trying to prove themselves wrong. But the more they look, the more evidence they find. In fact, hardly any young alligators with normal sexuality can be found in this vast lake on the suburban outskirts of Orlando.

Elsewhere around the world, the same astonishing phenomenon is turning up in a menagerie of fish, birds and other wild animals. Testosterone levels have plum-

THE GENDER WARP

Are chemicals blurring sexual identities?

■ First in a series

meted in some males, while females are super-charged with estrogen. Both sexes sometimes are born with a penis and ovaries, and some males wind up so gender-warped they try to produce eggs.

"Everything is really fouled up. It is indeed real, and it is scary," said Tim Gross, a University of Florida wildlife endocrinologist on the team that discovered the feminized alligators. "We didn't want to believe it, in all honesty."

This is no fluke of Mother Nature, no quirk of evolution. This is likely a legacy of pollution.

Wildlife scientists have uncovered persuasive evidence that artificial pesticides and industrial chemicals are infiltrating wombs and eggs, where they send false signals imitating or blocking hormones, which control sexuality. While the parents are unharmed, their embryo's sexual development is disrupted, and some male offspring are left chemically castrated and females sterile.

The potential consequences, if unabated,

Please see SEXES, A24

SEXES: No Fluke or Mother Nature

Continued from A1

are almost unthinkable.

If males aren't male and females aren't female, they cannot reproduce, and some outwardly healthy populations could be a generation away from extinction.

"Biologically, this is the most significant thing that could impair species and populations across the continent and across the globe," said Timothy Kubiak, chief of contaminant prevention and investigations at the U.S. Fish and Wildlife Service.

So far about 45 chemicals, many of them organochlorine pesticides widely used by farms and households to kill insects and weeds, have mimicked estrogen or inhibited testosterone in laboratory tests and in wild animals.

No one knows yet what this portends for humans—who often encounter the same chemical residues in their food and water. But since hormones play a role in the human body identical to other creatures, some scientists are alarmed by the potential of adults passing infertility and other reproductive defects such as prostate cancer on to their children.

The ability of these chemicals, called endocrine disrupters, to leave the parents unharmed but afflict the unborn is so alarming it was not even imagined by author Rachel Carson, who warned of pesticides run amok in her 1962 environmental classic, "Silent Spring."

The most insidious aspect is that the damage easily goes undetected; the animals look healthy, even to experts. Their bizarre sexuality is discovered only if their internal genitalia are examined or their hormones tested.

Although the threat of environmental hormones is newly recognized, many scientists and government agencies have already given it a rare urgency. Other researchers, however, remain skeptical, saying more evidence is needed to comprehend the scope of the threat and pinpoint the chemicals to blame.

Many of the scientists' findings are so new they have yet to be reviewed by their peers and published. Nonetheless, 21 biologists recently took the unprecedented step of warning in a position paper that "impacts on wildlife and laboratory animals . . . are of such a profound and insidious nature" that swift government action is warranted. In response, the National Academy of Sciences is hastily convening a panel to analyze the findings and guide research.

"My fear is that we will find more and more instances of this as we learn what to look for," said Ohio University reproductive biologist Brent Palmer, who found male cormorants in the Great Lakes and possibly some male frogs in California producing female egg proteins. "It doesn't seem like a few isolated incidents. The problem keeps snowballing and getting worse and worse."

Sexual Messengers

Estrogen and testosterone are the body's sexual messengers, ordering embryos how to grow. When a pregnant animal is exposed to even a



BILL GRAHAM / For The Times

'My fear is that we will find more and more instances of this as we learn what to look for. It doesn't seem like a few isolated incidents. The problem keeps snowballing and getting worse and worse.'

BRENT PALMER

Ohio University reproductive biologist

minuscule dose of a hormone during the onset of its embryo's sexual development, the gender of the offspring can be irreversibly altered, biologists say. In some cases, the father could be passing the defect to his young via his sperm or semen.

Because hormones also regulate the embryo's immune system and brain development, the offspring might also be prone to disease and behavioral disorders.

"It is the hand-me-down poison, from parents to offspring," said World Wildlife Fund senior scientist Theo Colborn.

Certainly, most populations of animals seem nowhere near collapse.

But many animals dependent on heavily polluted waters for their food are suffering serious reproductive defects that have been linked to environmental hormones—alligators and turtles in Lake Apopka, sea gulls and some fish off the coast of Southern California, great blue herons in British Columbia, terns in Massachusetts, sturgeon in the Missouri

River, trout in Great Britain, seals in the Netherlands, and an array of fish, birds and mammals in the Great Lakes.

"When it's bad enough to scare us, it's bad. And when I sit down and think about this, it scares me stiff," said Charles Facemire, a Fish and Wildlife Service toxicologist in Atlanta who has investigated contaminants for nearly 20 years.

Wildlife biologists also have begun studying whether hormone-disrupting chemicals are behind the unexplained declines of some creatures, such as frogs that are vanishing throughout much of the western United States, and several endangered and threatened species. Many bald eagles are failing to reproduce along the Great Lakes and the Pacific Northwest's Columbia River. In South Florida, a feud has erupted over whether environmental hormones are to blame for sperm and testicular disorders in the last living 30 to 50 Florida panthers.

Across the nation, the severity of

pollution has since the 1970s, birth defects in eagles, other animals prom, bans and cleanups. But suspect that smaller v pesticides and other ch, originally thought to be b, may be gradually depleting populations.

At the Great Lakes, 4 parts per million of polychlorinated biphenyls, or PCBs, will kill an eagle embryo. But a much tinier amount—perhaps measured in parts per billion—during a key stage of development might be enough to alter the newborn hormones and leave it sterile, experts say.

"If contaminants prevent an animal from reproducing, it will not replace itself," said zoologist David Crews at University of Texas, Austin, who created hermaphroditic pond turtles by painting eggs with 1 part per million of PCBs. "No normal animal will be born there."

To the U.S. Environmental Protection Agency, which regulates chemicals, most worrisome is the abundance of commercially sold substances that seem capable of altering hormones.

Among those are the world's most widely used herbicides, including alachlor, atrazine and 2,4-D. About 170 million pounds of the three herbicides are sprayed each year on U.S. corn, soybean and other crops, as well as garden and lawns. Nonylphenols, popular industrial compounds used in plastics and detergents, also were identified.

"A lot of these are things you can buy off the shelf at your local hardware store," Facemire said. "We're finding more all the time."

For many of these chemicals, evidence of their ability to tamper with hormones is based on laboratory tests. In wild animals, including Florida alligators, the most compelling proof has been detected in waters polluted with either DDT, a pesticide that blocks testosterone, or PCBs, which imitate estrogen. Used in enormous volumes until they were banned in the United States in the 1970s, these chemicals still pollute hundreds of lakes, streams and coastal waters.

Although the impact on animals is documented, the human implications remain highly theoretical. Some reproductive scientists suspect that exposure to environmental hormones could be lowering sperm counts in men and contributing to sharp increases in prostate and testicular cancer as well as breast cancer and endometriosis in women.

But veterinary toxicologist Stephen Safe of Texas A&M University is dubious. Although he acknowledges that the wildlife data in highly polluted waterways is convincing, he is skeptical about inferring any impact on humans or on wildlife in less contaminated areas. People, he argues, constantly are barraged with naturally occurring hormones in plants and food with no ill effects.

"The environment and organisms, including humans, have tremendous resiliency," said John McCarthy, vice president for science and regulatory affairs at the American Crop Protection Assn.

Please see SEXES, A2

Imitating Hormones

Hormone-imitating chemicals in the environment can cause infertility or other reproductive disorders that can devastate wildlife populations for generations. Here is how they work:

- **Pollutant accumulates:** A female animal eats food, such as fish, contaminated with an environmental pollutant that accumulates in her tissues.
- **False signal:** During an embryo's development, the pollutant from the mother invades a reproductive cell and binds to its receptor, which sends a false signal mimicking estrogen. To the cell, the signal from a fake hormone is indistinguishable from a natural one.
- **Proteins manufactured:** The signal turns on the manufacture of certain proteins, such as those that produce egg yolks. A male fetus could then develop both a penis and ovaries. Such an offspring would be unable to reproduce.

SEXES: Legacy of Pollution Suspected

Continued from A24

which represents pesticide manufacturers. "It doesn't mean you should go out and bombard them unnecessarily, but it just doesn't seem like we're going downhill fast and headed toward a crash in a generation or two."

But most scientists look to animals as sentinels for environmental quality and human health. Holding out for more proof before restricting the chemicals, Kubiak said, "is like waiting for the gangrene that started in your legs to go up your arms before cutting off your legs."

Gulls a Tip-Off

Few people were paying attention when the first hint of trouble arose more than 20 years ago, off the coast of Los Angeles.

Sea gulls on Santa Barbara Island—a major breeding area—were showing peculiar sexual behavior. Females were pairing up and sharing nests. Upon closer examination, two Southern California scientists found the reason.

They counted as many as 19 female gulls on the island for every male.

Where, they wondered, had all the males gone?

Because of the skewed gender ratio, the island's colony of Western gulls started to collapse, dropping from 3,000 pairs in the 1950s to about 700 by the mid-1970s.

Avian toxicologist Michael Fry of UC Davis had a theory.

He wondered if DDT, notorious for thinning the eggshells and killing the embryos of Southern California pelicans and cormorants, could be to blame for the missing males. Between 1950 and 1970, about 4 million pounds of the pesticide was pumped into the ocean at the Torrance headquarters of Montrose Chemical Corp.

Gulls, unlike pelicans and cormorants, had seemed to be unharmed by DDT. They had no visible birth defects or other physical disorders. But looking further, Fry was shocked to find many gulls had both testes and ovaries. To confirm his finding, he injected gull eggs from uncontaminated Mono Lake with amounts of DDT comparable to that found on Santa Barbara Island. In his laboratory, he crafted hermaphroditic birds.

"It turned out that DDT has two very different effects," Fry said. "In gulls, DDT in eggs caused abnormal development of the males. Chemical neuterization."

Fry's work—published in the journal *Science* in 1981—was the first evidence that environmental contaminants seemed to be feminizing wildlife.

While some scientists noted it, most shrugged it off.

At the time, common wisdom held that contamination that did not kill or maim animals was harmless. If an animal was alive, it was assumed to be healthy and fertile. Most biologists dismissed Fry's discovery as an inexplicable quirk at a uniquely contaminated spot.

3,000-Mile Parallels

But 3,000 miles away, Quebec scientist Glen Fox was intrigued. Fox, a Canadian government wildlife toxicologist, had noticed female herring gulls sharing nests at Lake Michigan and Lake Ontario—also contaminated with DDT as well as PCBs. He called the California toxicologist for help, and Fry found the identical half-male, half-female phenomenon. Still, their work was met with skepticism.

"I had a great difficulty convincing the scientific community that this was a real thing," Fry said.

Six years later, zoologist Theo Colborn was researching a book on Great Lakes wildlife for a conservation group when she began turning up studies indicating more than a dozen birds, fish and mammals were suffering ailments linked to heavy DDT and PCB contamination.

The oddest part, she thought, was that problems weren't showing up in adults that grew up in the 1960s and 1970s, when pollution had peaked. Instead, cormorants born more than a decade later had twisted, mutated bills, and the only healthy eaglets seemed to have parents that had just migrated to the lakes. Most young trout and other fish had disappeared, except for those that had been stocked.

"It was very evident that the problems affecting wildlife around the Great Lakes were not in the adult animals, but their offspring. The offspring that survived were not in very good shape," said Colborn, now a senior scientist with the World Wildlife Fund.

Tapping into an electronic data

base, Colborn pulled together hundreds of scientific reports from around the world. She learned that reproductive problems had been detected in almost every developed country since modern chemicals were introduced after World War II.

But because the reports came from scientists from a wide array of disciplines who rarely see or hear

runway.

H. Franklin Persival races his craft across the swamp's overgrown carpet of water lilies and pulls up to a pink nylon banner tied to a cypress. The banner means an alligator nest, spotted from the air, is hidden just offshore.

Grabbing a pair of wooden stakes, a wire loop, a magnet and some dental floss, Persival bounds

fivefold, which prompted the scientific team to begin exploring the cause. Apopka provides an ideal test case, since the population crash was fairly recent, and the research offers the most convincing proof so far that chemicals still are causing hormonal damage in wildlife.

The first breakthrough in finding why alligators are vanishing came in the fall of 1992, when endocrinologist Tim Gross, conducting routine sex typing on Apopka's turtles, couldn't tell males from females.

The following March, zoologist Louis Guillette Jr. and Gross examined 6-month-old alligators hatched in their laboratory from eggs from the lake. Males had the high estrogen and low testosterone typical of a female, while females had double the normal estrogen and were laying clutches that, instead of containing the usual one egg, had as many as seven, all dead. A few months later, the scientists confirmed sexual abnormalities in gators born in the wild—four of 12 had part-male, part-female genitals.

"It sent up signals and flags and fireworks and we knew something was going on there," said Guillette, director of the University of Florida's reproductive analysis laboratory. "... We now know that every single animal that we thought was a female in Lake Apopka had abnormal gonads."

DDE, a metabolite of DDT, was found in the tissues, and the team replicated the link in the laboratory when they painted eggs with minute amounts—as low as 10 parts per billion—and the young were born with abnormal hormones.

In comparison, not a single alligator at Lake Woodruff had hormonal or sexual defects.

Still unconvinced, the researchers returned to both lakes this summer. At night, they kicked around every imaginable theory, even an unlikely one they jokingly named the "shanty-town girl hypothesis"—that perhaps Lake Apopka is a magnet for poor, weak female gators. "We wanted to be 100% sure," Gross said, "before we opened our big mouths."

In August, they finally published their findings in a scientific journal, warning that their two years of studies "have only begun to address what we believe could be a serious, widespread threat to wildlife populations" and perhaps humans.

Vital questions remain. How is the damage physically passed from mother or father to embryo? How many chemicals are to blame, and at what concentrations?

"What we have is circumstantial evidence, but if you want to indict a certain chemical, we need a whole lot more evidence," Persival said. "Even if we then find what chemical it is, then what do we do about it?"

Gross suspects that "anything that eats anything off that lake potentially can be affected." But his fears go further. "I think Lake Apopka is just one case. I don't think it's even the worst case. Those [chemicals] have been used worldwide over a lot of environments."

Hundreds of species, from grebes at Southern California's Salton Sea to dolphins along the Atlantic Coast, suffer from mysterious ailments that could be linked to environmental hormones. Hoping to determine the national scope, Interior Secretary Bruce Babbitt is seeking federal research funds in 1996.

Perhaps future generations are in better shape today because DDT and PCB pollution levels have receded. Or is the worst yet to come because other chemicals that might be creating sexual chaos still are used?

The answers, scientists say, lie hidden in the unborn.

"The seeds for the next generation are already planted," Gross said, "and that is what's scary."

NEXT: The implications for humans.

'By the fall of 1988, it became very overwhelming that there was something really wrong. It was very evident that the problems . . . were not in the adult animals, but their offspring.'

ZOOLOGIST THEO COLBORN

about each other's work, no one had noticed the similarities.

"By the fall of 1988, it became very overwhelming that there was something really wrong," Colborn said. "As I put it all together, I had to do something with it."

Finally, in the summer of 1991,

onto the muddy banks. He deftly sidesteps saw-like blades of marsh grass, fist-sized spiders and mounds of fire ants, approaching a small clearing, where he finds a five-foot-wide nest woven like a basket from grasses and branches.

Quickly, Persival sets up a crude



RICH PEDRONCELLI / For The Times

'It turned out that DDT has two very different effects. In gulls, DDT in eggs caused abnormal development of the males. Chemical neuterization . . . I had a great difficulty convincing the scientific community that this was a real thing.'

MICHAEL FRY

Avian toxicologist, holding seabird eggshell in his UC Davis lab.

Colborn convened a meeting of 21 North American and European zoologists, pathologists, immunologists and other scientists researching the endocrine systems of humans and animals.

After three days, they issued an alarming six-page statement. "Many wildlife populations are already affected by these compounds," the scientists concluded. "It is urgent to move reproductive effects to the forefront. . . . A major research initiative on humans must be undertaken."

Last December, at a follow-up workshop, the warnings only intensified. Rarely does such a clear consensus emerge in science.

But even Fry had assumed the worst of the reproductive damage was over. PCBs and DDT were banned in the 1970s, and contamination levels in fish and wildlife have gradually decreased.

Then last year, when he visited New Bedford Harbor—a bird breeding area near Cape Cod contaminated with PCBs—11 of 15 terns he examined had the same bizarre sex organs he had seen in California a decade earlier.

His colleagues have become believers.

'A Big Whodunit'

As the sun rises over Florida's Lake Woodruff, three air boats slice through the tranquil morning mist, their engines roaring like Cessnas rising from a

radio-activated trap atop the nest, hoping the unsuspecting mother alligator will crawl through and get her snout snared.

The research is grueling in merciless 98-degree heat, but the six-man team stops its alligator rodeo only long enough to dodge late-afternoon lightning storms. They know they have little time to waste if they want to save the lake's alligators from extinction. So many questions, so few answers—"a big whodunit," says Persival, a National Biological Survey scientist.

Each summer, the team collects eggs, blood and tissue from alligators at both Lake Apopka and Lake Woodruff, a national refuge on the St. Johns River about 50 miles north of Orlando. Woodruff is considered a healthy lake, useful for comparing estrogen and testosterone in its alligators to those from Lake Apopka, one of Florida's most contaminated waterways.

In 1980, Tower Chemical Co. spilled a large quantity of Kelthane, a pesticide containing DDT, along Lake Apopka's banks. Fertilizers and insecticides routinely flow off nearby citrus groves and other farms, while little fresh water is allowed in. Even Hurricane Andrew took a swipe at Apopka and stirred up its polluted sediments.

"Everything that could happen to a lake has happened to this one," said University of Florida alligator biologist Ken Rice.

Since the early 1980s, alligator births at the lake have dropped

'I believe these animals have been feminized. I have no proof. I may be wrong, but if I am, I will really be surprised.'

—Charles Facemire, a U.S. Fish and Wildlife Service contaminants specialist.

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'There is no data in panthers supporting any of that, so I am very pessimistic that we have a problem as far as estrogenic chemicals having effects.'

—Michael Dunbar, wildlife research veterinarian for the Florida Game and Freshwater Fish Commission.

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Florida Panther: Debate Holds the Fate of the Species

■ **Sexuality:** Some researchers blame pesticides, others inbreeding, for the big cat's plight. Pollution would be more difficult and expensive to remedy.

By MARLA CONE
TIMES ENVIRONMENTAL WRITER

NAPLES, Fla.—Just past dawn, Florida Panther No. 52 is on the run, the beep from her radio collar growing steadily louder.

From the window of a Cessna, state biologist Darrell Land points out a spot, and the pilot spirals down, hovering above an emerald carpet of pines and palms. The sleek, tawny-colored cat is crouched below, checking out a herd of deer for breakfast.

"I'll be damned!" Land said, checking the panther through his binoculars. "That's the first one I've seen in months."

Three mornings a week, Land takes to the air to track these rare, nocturnal felines using radio signals, scribbling each cat's location and identification number on a green topographical map spread across his lap. Only 30 to 50 Florida panthers remain, making them one of the nation's most troubled endangered species.

For years, wildlife biologists have presumed the big cats are vanishing because the marshy forests surrounding the Everglades have been chewed up by South Florida's sprawling farms and suburbs. With so little space to roam, they inbreed, leading on reproductive defects such as low sperm counts.

But now biologists are wondering if another factor also has been playing a key role—chemicals that imitate hormones and feminize animals.

A scientific debate over the felines—whose protection already is a highly contentious subject in Florida—has erupted between those who think pesticides are at fault and those who blame development and inbreeding. At stake in this argument is the fate of the species.

"My argument is contaminants and theirs is inbreeding," said Charles Facemire, a U.S. Fish and Wildlife Service contaminants specialist. "I believe these animals have been feminized. I have no proof. I may be dead wrong, but if I am, I will really be surprised."

Male panthers may have abnormal estrogen levels—higher in some cases than many females. About 90% have large percentages of dead sperm, and more than half suffer from cryptorchidism—in which one or both testes fail to descend.

"All of those things have been shown to be caused by environmental estrogens or other endocrine-disrupting chemicals in other animals," Facemire said. "Every one of them."

But Michael Dunbar, wildlife research veterinarian for the Florida Game and Freshwater Fish Commission, disagrees.

"There is no data in panthers supporting any of that, so I am very pessimistic that we have a problem as far as estrogenic chemicals having effects," he said. "It is worth investigating, but people just have to use common sense about it. From what I see in the animals I am working with, it doesn't seem to be a problem."

A year ago, Dunbar compared panthers with abnormal testicles to normal ones and found no correlation to their hormones. Both had high estrogen, so Dunbar suspects that is normal in panthers compared to other large cats.

"If [environmental hormones] were a problem, we would be seeing more symptoms in many species there," Dunbar said. Raccoons, bobcats, deer and bear seem to have no similar sexual problems.

Facemire, however, said Florida officials are wedded to the inbreeding theory because it is easier to fix. The state wildlife agency is planning to import cougars from Texas to mate with Florida panthers and increase the gene pool. But those cats could be doomed to sire abnormal offspring, too, if Facemire's theory is correct.

If the panthers' problems are caused by estrogenic chemicals, a massive investigation and cleanup of pesticides and other contamination would have to be conducted in the Everglades and surrounding areas.

"These are highly charged, highly controversial issues," Facemire said. "Someone has to pay if we prove it's contaminants."

Although panthers roam the heart of a sugar and citrus belt, no one has tested the cats—or the raccoons and deer they feed on—for hormone-disrupting chemicals. DDT and other pesticides pollute nearby canals.

University of Florida wildlife endocrinologist Tim Gross said the most likely explanation is a combination of the two. "More than likely it's a pollution problem" behind the sperm abnormalities, while inbreeding probably causes the cryptorchidism, Gross said.

Land, however, is dubious that the sperm and testes disorders are even posing a problem in terms of births. He believes the panthers are recovering, based on the number of kittens he sees.

But the new generation of kittens could be infertile if pollution-caused problems have been passed from their parents. The true test will come when the young males are old enough to mate.

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Pollution's Effect on Sexual Development Fires Debate

■ **Health:** Some biologists blame chemicals for fertility problems, diseased organs. Others deny a problem exists.

By MARLA CONE
TIMES ENVIRONMENTAL WRITER

"Every man sitting in this room today is half the man his grandfather was. And the question is, are our children going to be half the men we are?"

In all likelihood, that alarming testimony—from a reproductive biologist at a congressional hearing on the hazards of pesticides—is hyperbole. Even so, it readily dramatizes the fears of many scientists that environmental pollution could be warping human sexual development.

Many biologists theorize that man-made pesticides and industrial chemicals that mimic hormones in the womb might be lowering

sperm counts, triggering diseases in ovaries, breasts, prostates and testes, and perhaps even retarding penis growth and causing children to reach puberty prematurely.

Such a link, however, remains

THE GENDER WARP

Are chemicals blurring sexual identities?

■ One in a series

highly speculative and fiercely debated, with some biologists maintaining that the small concentrations of man-made chemicals consumed by most people in their diet are harmless.

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BIOLOGY: Chemicals and Human Reproduction

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But scientists promoting the theory believe it could explain the puzzling array of trends in reproductive disorders that have surfaced since the advent of modern pesticides and industrial chemicals after World War II.

Sperm counts seem to have dropped by almost half in the past 50 years, according to the one highly disputed study on males in the general population. Endometriosis and breast cancer are detected in women in record numbers, and prostate and testicular cancer rates have at least doubled among men in industrialized nations in recent decades. Some fertility experts also believe more men are experiencing fertility problems.

"Although the possibilities for human health effects remain theoretical," there is a "growing sense that some diseases or dysfunctions" could be caused by pollutants that act like hormones, John McLachlan, scientific director of the National Institute of Environmental Health Sciences, reported in a journal last fall.

Every year, billions of pounds of pesticides and industrial compounds that imitate estrogen or inhibit testosterone—hormones vital to human sexuality and reproductive health—are sprayed on crops and yards and released into waterways in the United States.

These chemicals routinely contaminate food in small amounts, with a few—the pesticide DDT and industrial compounds called PCBs—so pervasive that every person on Earth is believed to carry at least a trace in their bodies. Fish in many waterways are tainted with DDT and PCBs, a contaminant called dioxin is found in some beef and other animal fat, and some produce contains small amounts of pesticide residues.

Already, there is evidence of these commonly used chemicals disrupting sexuality in animals.

If they can disrupt human hormones, that raises the possibility of infertility passing unrecognized from one generation to the next. Parents exposed to a slight amount of a man-made hormone in their food would be unharmed, but could transfer sperm problems or disease-causing defects to their children that wouldn't surface until sexual maturity.

"What the mother was exposed to . . . could have an effect on their children 30 years down the road," said Ohio University reproductive biologist Brent Palmer.

Everyone is running around saying the male is doomed. But the evidence does not support an effect in the overall human population. I'm not saying ignore it, but let's have some more information.'

STEPHEN SAFE
Texas A & M University toxicologist

"It is so insidious. The adults appear healthy, but our children may be the ones who wind up infertile."

Some toxicologists and chemical industry representatives say the threat to the general population is pure conjecture, raised by many scientists and environmental advocates to force restrictions on chemicals. They hope a panel about to be convened by the National Academy of Sciences will end the speculation within a few years.

"We're getting the estrogen scare of the week and it's making your head spin," said John McCarthy, vice president of science and regulatory affairs for the American Crop Protection Assn., which represents major pesticide manufacturers.

"Speculation is going on all over the place, especially when it comes to sperm counts. Will the real information please stand up? Let's take a look at the science and do this right."

Texas A & M University toxicologist Stephen Safe also is highly skeptical that the chemicals are affecting human health, explaining that people constantly are bombarded with potent, naturally occurring hormones in their food that seem to cause no ill effects.

"Everyone is running around saying the male is doomed. But the evidence does not support an effect in the overall human population," Safe said. "I'm not saying ignore it, but let's have some more information."

Much of the concern has grown out of the research on animals.

Studies on animals from Florida alligators to Southern California sea gulls that depend on highly contaminated waterways show these hormone-like pollutants are tampering with embryos, blurring the lines between the sexes in newborns. Tests on laboratory rats confirm that when pregnant animals are exposed, their offspring often are born with half-male, half-female sex organs and defective sperm.

The worries over human reproductive health stem from one basic rule of anatomy. People have the identical hormones—estrogen and testosterone—as a rat, a bird or an alligator, and their fetuses would seem just as vulnerable to damage from minute amounts of pollutants.

If not for the real-life saga of DES mothers, it might seem far-fetched to believe humans could pass sexual disorders on to their sons and daughters.

DES, or diethylstilbestrol, was a powerful synthetic estrogen prescribed to 3 million to 4 million women between 1948 and 1971 to prevent miscarriages. Although the mothers were unscathed, their daughters suffer a high incidence of ovarian abnormalities and vaginal cancer and their sons have abnormal rates of infertility and testicular disorders.

But DES is hundreds of times more potent in its estrogenic effects than most pesticides and industrial chemicals.

Toxicologists—even skeptics like Safe—agree the most vulnerable people are fishermen, Eskimos and other Native Americans whose diets rely heavily on

Hormones and Humans

Some scientists speculate that human fetuses exposed to environmental pollutants that mimic or block hormones might be born with reproductive disorders, many of which do not surface until adulthood. These are some of the suspected impacts on humans, based largely on animal studies.

LOW SPERM COUNTS

A study of medical records over 50 years shows that sperm counts have dropped by 40%. Researchers wonder if exposure of the fetus to pesticides and other chemicals that disrupt hormones may be a factor. Similar sperm problems have been noted in industrial workers exposed to high levels of dioxin, which is believed to block testosterone.

BREAST CANCER

Reports of this disease have increased by 1% per year over the past 50 years. Studies at Mt. Sinai School of Medicine have found high levels of DDT and PCBs in the tissue of women with breast cancer. Another recent study in California found no correlation. Some researchers believe chemicals that act as estrogens might promote breast cancer cells, but studies have been inconclusive.

OTHER CANCERS

Testicular cancer, which strikes young men, has tripled in the United States and England over the past three decades. Prostate cancer has doubled in some countries in 10 years. Researchers say exposure of a fetus to pollutants that act like estrogens could be a cause. Cells of men with testicular cancer resemble the primitive cells in embryos, which makes scientists believe their sexual development was interrupted in the fetal stage.

UNDESCENDED TESTICLES

This problem appears to be increasing among newborn boys, although there are no statistics available. Exposure to estrogenic chemicals in the environment could block development of male reproductive organs, causing cryptorchidism, or undescended testicles. In some cases this can lead to fertility problems.

HYPOSPADIAS

Young boys and infants can be afflicted with a urethra abnormality which, although rare, in extreme stages makes the penis resemble a vagina. This same type of "intersex" condition occurs in laboratory animals exposed to estrogenic chemicals during fetal development.

ENDOMETRIOSIS

This mysterious, painful disease afflicting 10% of women in their childbearing years appears to be increasing. Recent studies link it to exposure to dioxin and PCBs, both hormone-mimicking chemicals. Symptoms are the worst when a woman's estrogen level is highest. Many women who are infertile also have endometriosis.

EARLY PUBERTY

Girls are reaching puberty earlier, and some researchers suspect that exposure to environmental estrogens may be a cause. Studies on rodents exposed to DDT and other estrogenic chemicals show accelerated puberty.

Source: U.S. Environmental Protection Agency, National Institute of Environmental Health Sciences

fish and marine mammals gathered from waters contaminated with hormone-like chemicals.

Some of the nation's worst contamination has been found in sport fish caught close to Los Angeles County's shoreline and in harbors of the Great Lakes, which contain DDT and polychlorinated biphenyls, or PCBs. The compounds were used in large volumes until banned in the 1970s, but high concentrations remain in the environment.

The big unanswered question is whether an average person's diet, which is much more varied, contains large enough quantities of these and other man-made hormones to endanger an unborn child. And, do

nism that wards off small quantities?

Scientists are struggling with these questions, but the answers, in all likelihood, remain years away.

"We're certainly not having massive epidemics," said toxicologist Linda Birnbaum at the U.S. Environmental Protection Agency's health effects laboratory in North Carolina. "Whether we're having subtle effects is a more difficult question to answer."

Most people get a much smaller dose of the chemicals in their diets than wildlife such as alligators and birds, which often feed on fish from one polluted source during their entire lives.

"I have no doubt that when given an appropriate dosage level during the right phase of gestation, that you can see disruption of sexual development," said assistant EPA administrator Dr. Lynn Goldman. "But the doses that humans receive are lower. It is a leap to go from that evidence to a conclusion that sperm levels are being lowered due to these exposures."

So far, the most disturbing evidence that the general population may be at risk comes from rats studied at the University of Wisconsin. Mothers-to-be injected with a single, minute dose of one industrial pollutant, dioxin, during the onset of their embryo's sexual development gave birth to males with reduced sperm counts and malformed testicles.

The small dose given to the rodents—measured in parts per trillion—is not much higher than the average accumulation the EPA has found in human bodies. Dioxins, which are widely dispersed by the paper industry and in other manufacturing processes, apparently block testosterone development.

"If this work is correct, and I have no reason to think that it isn't, the real concern is the general population may be at risk," said Earl Gray, the EPA's chief of developmental reproduction and toxicology research. "This data is really critical because it's at such low doses."

Toxicologists suspect if people are harmed, the damage is much more subtle than what they are seeing in wildlife and lab animals. Gray said sons born to exposed parents might have a slight decrease in sperm count or shortened penises.

While reduced sperm probably would have a minimal effect on overall human populations, the result could be tragic for some individuals—the difference between fathering a child or not.

"For those men who already have low fertility or borderline fertility, this kind of an effect, if it's occurring, could render them infertile," said James Overstreet, a UC Davis obstetrics and gynecology professor who directs the Institute of Toxicology and Environmental Health.

Physicians in fertility clinics have long noticed what seems to be a decline in male fertility, but say the reasons could vary. More than 2 million couples are involuntarily childless, and between 1965 and 1982, infertility among young couples increased from 4% to 10%, according to a 1989 National Research Council report.

"I don't think we're going to go extinct," said Theo Colborn, senior scientist with the World Wildlife Fund. "But if we don't do something about this, life is going to be miserable."

The EPA is trying to pinpoint the risk so it can issue advice, especially to pregnant women. The most vulnerable stage is the first trimester when the fetus develops sexually.

One general warning, Birnbaum said, is to avoid eating fat—from beef, fish or any animal—because most pollutants accumulate there and it contributes to other health risks as well.

At this point, the EPA has not analyzed how much of these chemicals an average person consumes, a void which magnifies the uncertainty of how much risk the public might face.

The agency, for instance, doesn't know how much residue from a fungicide called vinclozolin people are eating in their fruits and vegetables. Rats exposed to high doses—100 parts per million per day during pregnancy—gave birth to half-male, half-female offspring, according to two recent EPA studies. Scientists suspect humans consume far less but have no proof.

Other than DDT and PCBs, most hormone disrupters, including vinclozolin, leave no trace in the human body. They could inflict hormonal damage on a fetus and pass through a parent's body without researchers knowing the person was exposed.

Since human experimentation is outlawed, toxicologists say tests on wildlife and lab animals are the

best—and sometimes only—forewarning they have.

"There is no absolute proof about a human connection, but that's the whole basis of biomedical research. You do work with non-human animals," said University of Texas, Austin, zoologist David Crews, who found small amounts of PCBs produced turtles born with both ovaries and testes.

Others argue, however, that the rodent and other animal data is irrelevant because humans may have a defense system animals lack.

Gray called that "the last line of defense" from people who have "almost a religious" belief that humans are better than animals.

"If humans are at all like rats," Gray said, "they have enough DDT in them to really have a reproductive effect."

Those skeptical of a human connection also point out that most environmental contaminants are hundreds

**'I don't think we're going to go extinct.
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THEO COLBORN

Senior scientist with the World Wildlife Fund

of times less powerful than the body's natural estrogen, estradiol. Numerous natural compounds in vegetables, called flavonoids, also are potent estrogen or estrogen inhibitors and may begin to harm us, he said.

"Just because something is estrogenic does not necessarily make it a hormone," said Safe of Texas A&M. "The important thing is what is our exposure?"

The most heated argument, however, is focusing on whether sperm counts are actually declining.

In 1992, reproductive biologists in Denmark thought they had an answer. After examining medical reports on almost 15,000 healthy, white men from many nations between 1938 and 1990, they found sperm concentrations were almost half what they had been—68 million per milliliter in 1990 compared with 113 million per milliliter in 1938.

The findings spurred concern that post-World War II chemicals and pesticides were to blame. For years, researchers already had been worried after small studies showed some industrial and farm workers handling large quantities experienced sperm problems.

But other researchers recently pointed out that the steepest sperm decline detected in the Danish study occurred in the 1940s and 1950s, before environmental contamination peaked.

"This data is very, very suspect," Safe said. "It looks like it is probably more fiction than fact."

Stil, many reproductive scientists call the data credible. Even if sperm counts are declining, proving the cause may be difficult. Men are exposed to a large number of factors that might be to blame, from hot tubs to venereal disease.

Research into breast cancer has been equally inconclusive. Four separate studies show high concentrations of DDT or PCBs in the tissues of women with breast cancer, but a study completed this year that was the largest of its type found no correlation. The debate continues.

"Here again, it's the classic case of one study says maybe and another study says no and another says 'Gee, we're not sure.' We need an answer," said McCarthy of the pesticide association.

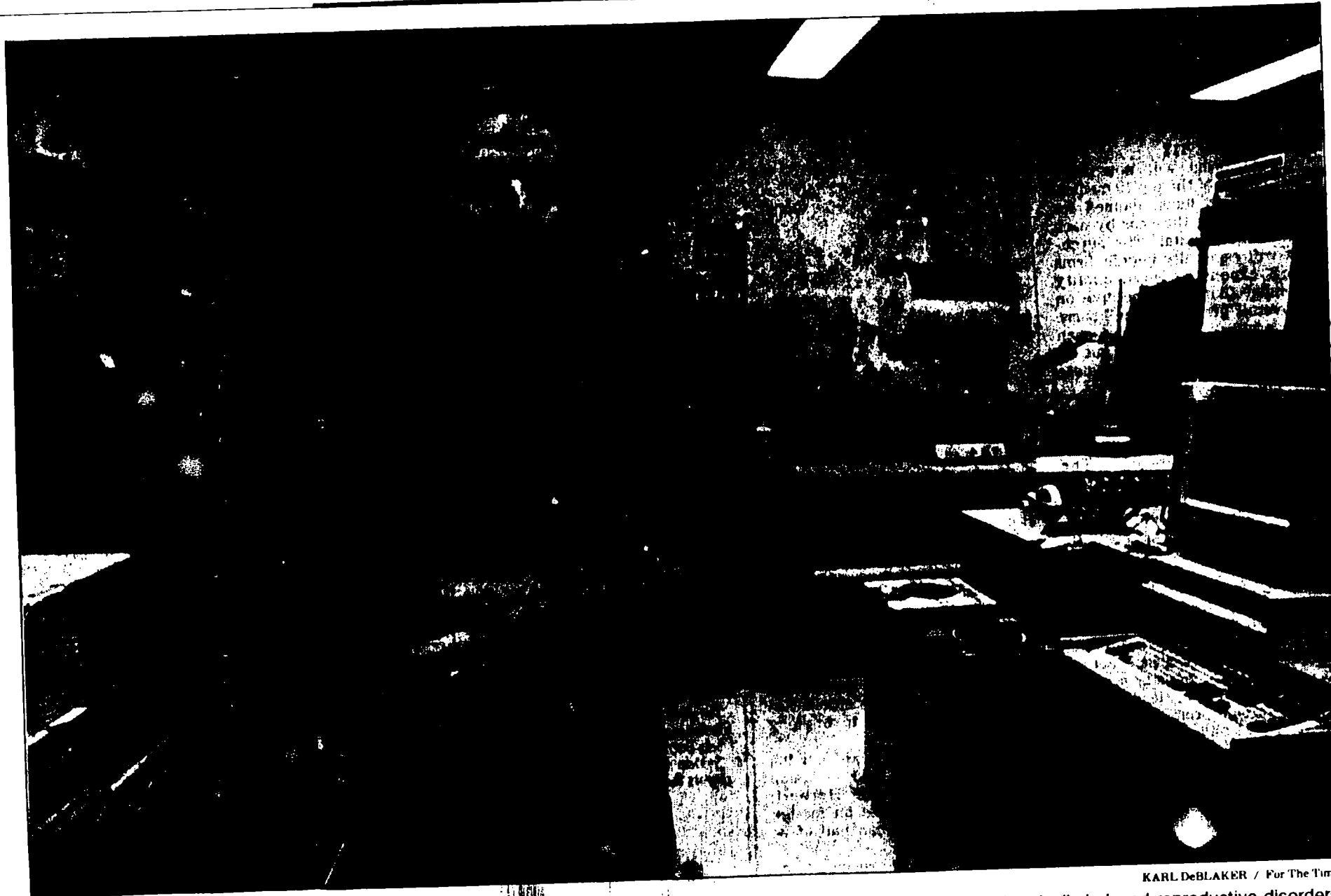
Health experts also are studying potential effects on disease immunity and brain development, since hormones control how the fetus develops its immune system and the behavioral part of its brain.

Women who ate fish two to three times a month for six years from Lake Michigan before pregnancy gave birth to babies with low birth weights, smaller heads and learning and behavioral defects, according to a 1984 study by two researchers at Wayne State University in Michigan.

"My concern is that we are dealing with a phenomenon in which the basic physiological processes can be affected," said Glen Fox, a toxicologist at the Canadian Wildlife Service. "You may not need large amounts of a substance to have an impact, particularly at the stage an embryo is developing."

"It has a potential to affect everybody. Not just the guy who applies a pesticide. Everybody."

THE GENDER WARP



KARL DeBLAKER / For The Times

Earl Gray, the EPA's chief of developmental reproduction and toxicology research, says humans could be at risk of chemically induced reproductive disorders.

Los Angeles Times

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Battle Looms on Chemicals That Disrupt Hormones

■ **Science:** Research finds threats at levels once thought safe. Cleanup of DDT off Palos Verdes is part of debate.

By MARLA CONE
TIMES ENVIRONMENTAL WRITER

WAUKEGAN, Ill.—After waiting nearly two decades to cleanse their lake-shore harbor of a million pounds of toxic waste, the people of this working-class suburb of Chicago were ready to party.

Setting sail on Lake Michigan aboard a cruise ship aptly named Celebration, local, state and federal dignitaries proclaimed the elaborate \$21-million cleanup of Waukegan Harbor officially complete this summer. The marina—for years stigmatized as the PCB contamination capital of the world—was declared safe for everyone who works and plays there.

But the celebration may have

come too soon.

Compelling new scientific evidence has emerged indicating that low concentrations of pesticides

THE GENDER WARP

Are chemicals blurring sexual identities?

■ Last in a series

and industrial chemicals once thought to be harmless can alter the hormones of wild animals, confusing their sexual identities and rendering them infertile.

The threat from these decades-old chemicals—most notably mas-

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CHEMICAL: EPA Weighs How Clean Is Clean Enough

Continued from A1

sive amounts of polychlorinated biphenyls (PCBs) in the Great Lakes and DDT off the shore of Los Angeles—has stoked a long-smoldering environmental debate: How clean is clean?

For years, how much pollution to remove from severely contaminated spots has been based largely on a single target—reducing the cancer risk to humans. But that may not be enough to defend bald eagles, trout, alligators and other animals from chemicals that imitate estrogen or block testosterone in the womb. Humans who eat contaminated fish and other food harvested from these areas also could be passing subtle reproductive problems such as low sperm counts to their children.

"In spite of government regulations and testing—which we all thought was adequate in all honesty—we are now finding effects that are much more subtle and much more intergenerational than we thought," said Tim Gross, a University of Florida endocrinologist who discovered part-male, part-female alligators and turtles in a Florida lake contaminated with DDT from a 1980 spill.

The concern over environmental hormones comes at a crucial time. In Southern California, federal officials are grappling with how to eliminate—or more likely contain—4 million pounds of the pesticide DDT dumped several decades ago in ocean waters off the Palos Verdes Peninsula.

Nationally, dozens of waterways from Washington's Puget Sound to South Florida's canals remain polluted with PCBs, compounds used as industrial insulators and lubricators, or DDT, even though they were banned in the United States in the 1970s.

"We have to address this enormous legacy," said Michael Gilbertson, a biologist with the International Joint Commission, a U.S.-Canadian government panel helping guide cleanup of the Great Lakes. "How are we going to come to terms with all these dump sites? What this work on estrogens shows us is we have a very long way to go."

Eliminating the potential for hormone-like effects is shaping up to be a political struggle.

The cost of even a basic cleanup job runs in the tens of millions of dollars and the projects take years. Expanding the scope to tackle lower concentrations of chemicals would push the price up and take even more time. Beyond that, raising new health and ecological concerns could cast a pall on a community's businesses and recreation, especially sport fishing.

"It's a legitimate question to ask how much it is going to cost and what are the benefits," said John McCarthy, vice president for science and regulatory affairs at the American Crop Protection Assn., which represents Dow, Monsanto and other major pesticide producers. "I know it's not popular to talk about economics when you're talking about health risks, but you've got to get real too."

Dealing with the legacies of the past, however, is only one contentious aspect of the battle emerging over environmental hormones.

To avoid saddling future generations with new problems, the U.S. Environmental Protection Agency and the chemical industry are wrestling with whether to restrict some of today's chemicals. About 25 popular insecticides, herbicides and fungicides—applied on millions of acres every year in the United States—have been shown in laboratory tests to imitate estrogen or inhibit testosterone.

Included are many pesticides, such as atrazine, endosulfan, EBDCs, parathion and dicofol, that help farmers protect and grow bountiful harvests of fruits, vegetables, grains and other crops worth billions of dollars annually. Some also are widely used for eliminating garden pests and weeds.

Seven industrial compounds—such as nonylphenol, used in plastics and detergents; styrene, an ingredient of rubber; and dioxins, a widely dispersed pollutant from paper mills and other manufacturing plants—are suspected of causing problems as well.

"One of the lessons we learned from DDT is that it is very hard to correct an error once you make it," said Dr. Lynn Goldman, assistant EPA administrator, who heads the Office of Prevention, Pesticides and Toxic Substances. "If you allow the use of a harmful compound . . . even after you take corrective action, you can see harmful effects for many years."

Several environmental groups

already are demanding a phaseout of chlorinated pesticides and other compounds, many of which are identified as man-made hormones. But manufacturers are urging the government to await clear scientific findings, which could take the National Academy of Sciences several years.

"There is a fair amount of advocacy science going on out there on this subject, and a lot of dueling Ph.Ds. Let's take a look at the science and do this right," said McCarthy of the crop association.

This fall, the EPA plans to propose new rules requiring manufacturers to test pesticides to determine their potential for disrupting the endocrine system that controls hormones, Goldman said. For example, manufacturers may have to check the testosterone of exposed rodents, or use a newly developed method of checking whether breast cancer cells, which are sensitive to estrogen, grow in test tubes when exposed to a pesticide.

But when it comes to non-pesticide chemicals—including some used in plastics—the government has much less authority, Goldman said. Under federal law, the EPA must first prove a chemical poses a likely public health risk before companies can be ordered to enhance testing. That, Goldman said, is a Catch-22 that could allow most industrial chemicals that alter hormones to escape tougher restrictions.

"We don't have a very good ability to predict which chemicals are likely to be endocrine disrupters," said Goldman, a former California epidemiologist and pediatrician. "That puts us at a great disadvantage. There are 70,000 chemicals on the inventory and of those, about 18,000 are of potential concern because they are in commerce to a significant extent."

Today's pesticides must be screened by their manufacturers on laboratory mice to gauge their risk of cancer, birth defects and reproductive effects. But they are not subjected to specific tests detecting hormonal changes. "Things can slip through the net," Goldman said, "and one of those things that can easily slip through are endocrine disrupters."

Each pesticide undergoes a "two-generation reproduction study," which exposes rats to various doses of chemicals in their food and then examines the offspring, and their offspring. But chemical industry officials acknowledge that the test is not sensitive enough to detect all troubling side effects.

For instance, in the case of a fungicide named vinclozolin, tests by the manufacturers, BASF Corp. and Grace-Sierra Crop Protection, did not discern reproductive defects in rats. But when the EPA performed more thorough tests, it found that the fungicide blocks the formation of testosterone in rodents and that offspring were born with half-male, half-female sex organs.

Toxicologist Chris Chaisson of TAS Inc., which designs tests for chemical manufacturers, said traditional two-generation studies often cannot detect malformed genitalia because the rats are exposed to fairly low doses of chemicals. She said the search for more reliable methods "is a huge issue internationally."

After testing pesticides, the EPA decides on a case-by-case basis whether the risk is great enough to impose new restrictions—"from changing instructions about how they are used all the way to suspension and cancellation," Goldman said.

Manufacturers say they will not oppose new testing requirements. But they are bracing for battle if such tests lead to new bans or severe restrictions on chemicals that they say are necessary to protect the nation's food supply from pests and weeds.

"This is not like a situation where we have to shut whole industries down because something terrible is happening to the environment," McCarthy said. "It doesn't mean that we should be insensitive, and it doesn't mean we shouldn't be vigilant. But I don't think the environment is unraveling."

Some pesticides have been indicted as hormone disrupters on the basis of results in test tubes or, as in the case of vinclozolin, fairly large doses fed to mice. But the true test, said pesticide industry consultant James Lamb, is to learn if the chemicals harm people or animals in amounts now in the environment, and if the risk is great enough to outweigh the benefits.

"Just because something causes a problem in a test tube doesn't

mean it poses a significant risk," said Lamb, a reproductive toxicologist formerly with the EPA. "That kind of test is very limited."

While a ban on all hormone disruptors is highly unlikely, some could face new restrictions or reformulation.

"We're not going to get rid of pesticides or plastics in our society," said David Crews, a zoologist at the University of Texas, Austin. "We will not allow loss of our quality of life. So we need to find out how to deactivate them or contain them so they don't have these impacts."

Generally, wildlife experts and industry agree on one point: No chemicals used today are as dangerous as DDT and PCBs, which accumulate in the environment and in body tissues and can reach poisonous levels.

"The new chemicals are entirely different," said McCarthy of the pesticide industry group. "Most are biodegradable. That's going to be a key difference in this whole debate."

Although many of the nation's waterways have improved since

the banning of DDT and PCBs, wildlife officials say buildup in many harbors, rivers and other hot spots remains severe enough to maim, kill or sterilize wild animals, especially fish-eating birds.

Along many Great Lakes' shorelines, bald eagles—a threatened species—still fail to reproduce and some cormorants are born with malformed, twisted beaks.

Beyond the political and financial ramifications, performing adequate cleanup has proved to be technically difficult.

In the case of Waukegan Harbor—on the nation's Superfund list of toxic sites named priorities for cleanup—the EPA took 12 years to reach agreement with Outboard Marine Corp. to pay for removing 1 million pounds of PCBs the boat manufacturer had dumped into the lake in the 1960s. It took five more years for the agency to design a strategy, remove and treat some waste, and bury the rest in a boat slip walled off from the rest of Lake Michigan.

Despite the \$21-million effort—which the EPA says removed 96% of the PCBs—a sister federal agency, the U.S. Fish and Wildlife

Service, maintains that the water is at least 100 times too contaminated to safeguard fish and birds, including some endangered and threatened species.

"A safe level of contamination? We're light-years away from that in any of the Great Lakes," said David Best, a biologist for the wildlife agency's Midwestern region who is exploring the impact of Great Lakes contamination on bald eagles. "There is no biologist that would say [Waukegan] harbor is clean enough to ensure the health of fish and wildlife."

The EPA allowed PCBs to remain in the harbor's sediments in concentrations as high as 50 parts per million, far greater than the 4 p.p.m. that kills a bald eagle's eggs. The Fish and Wildlife Service recommended cleaning the harbor to a level of 0.05 p.p.m., but the EPA rejected that option as impractical.

"A lot of times EPA and state regulatory agencies feel if they get it up to human health standards, that's enough for wildlife," said Donald Steffek, chief of contaminants for the wildlife service's western region. "But those cormorants or ospreys or eagles are out there 100% of the time eating those fish."

Returning to Waukegan Harbor to dredge more waste is considered unlikely, given the realities of money, politics and public sentiments.

Local residents generally are pleased and their harbor is more popular than ever because the water looks dramatically cleaner after the dredging and PCB concentrations have dropped. "Nobody worries about PCBs anymore," said one local Coast Guard auxiliary officer.

"People just don't want to know the truth," said Charles Facemire, an environmental toxicologist with the wildlife agency. "It scares the pants off them, especially this issue of endocrine disruption and how your children could be born with reproductive problems."

Gilbertson of the International Joint Commission said the EPA and state regulators overseeing cleanups have been "terribly slow" in realizing that potential reproductive damage to wildlife and people is important when setting cleanup goals. The EPA is much more focused on reducing human cancer risk from eating fish and on the outright mortality of animals.

"If the only consideration was to protect wildlife, that [harbor cleanup] would not be enough," said John Giesy, a Michigan State University fisheries and wildlife professor. "But that was purely a societal decision, a risk manage-

ment decision. EPA felt it was a decision they could live with."

Goldman, one of the highest ranking officials at the EPA, acknowledges that her agency should focus more on protecting the health of natural resources while regulating chemicals and cleaning up toxic waste. But she blames the failing on a need for better science to predict ecological impacts.

"The criticism is well-taken," she said. "In the absence of better tools, we go with the things we do know, like cancer. What is new is this general recognition of the connection between risks to wildlife and the risk to human health."

Goldman warned, however, that excavating old pollutants such as DDT and PCBs from the bottom of waterways sometimes can cause more contamination of the fish. "I may be that the best possible thing is to leave them buried," she said.

When it comes to tackling hormone-disrupting pollutants, the nation's most massive problem is in Los Angeles' own back yard.

From 1950 to 1970, DDT manufacturer Montrose Chemical Corp. of Torrance dumped several million pounds of the pesticide into county sewers that flow into the ocean off the Palos Verdes Peninsula. Due to a human cancer threat, warnings already have been issued on the peninsula and at Los Angeles Harbor advising against eating croaker and other fish caught to shore.

Their eggs poisoned by DDT, populations of brown pelicans, eagles and other birds plunged in the 1970s. Although most now appear to be recovering, scientists say fish and wildlife still are suffering some lingering reproductive effects.

Specific scientific evidence of the damage, however, has been kept confidential by U.S. Justice Department attorneys, who are suing Montrose and other industries to seek compensation for wildlife and habitat. The federal government is soon expected to announce a proposal for restoring the coastal resources that is bound to be costly.

Today, no one wants to retrace the mistakes that left such enduring environmental dilemmas.

"Industry has suffered greatly from DDT and other things that have come back to haunt them," said Glen Fox, a Canadian government biologist who has studied the impacts of Great Lakes pollution for two decades.

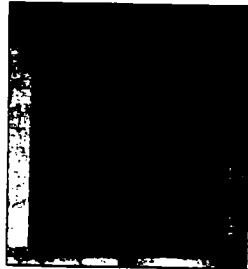
"They cannot afford to ignore a problem with a chemical that could affect your reproduction or your children's reproduction. They are so scared spineless of that sort of thing. If there was ever an issue industry would probably act on, it's this one."

Disruptive Pollutants		
CHEMICAL HERBICIDES		
Alachlor	Corn, peanuts, soybeans, sorghum	55 million to 70 million pounds
INSECTICIDES		
DDT, DDE	Banned in United States in 1973 because of severe impact on birds and fish	—
INDUSTRIAL ELEMENTS		
Dioxins	Industrial byproduct	—
Lead	Batteries, ammunition, paint	—
Mercury	Thermometers, batteries	160 million tons
PCBs	Banned in 1977. Were used as insulating material in electrical equipment and as hydraulic fluids	—

Los Angeles Times

THE GENDER WARP

Anatomy of a Cleanup

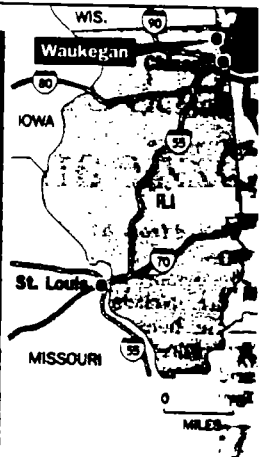
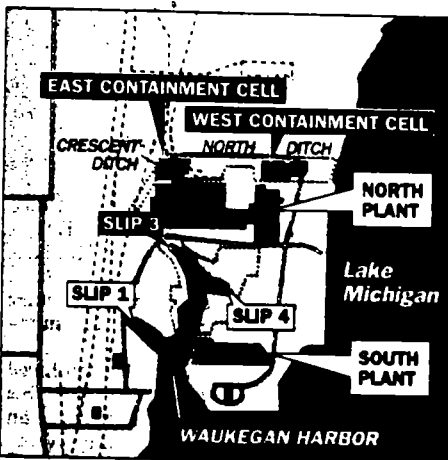


Cleaning up Waukegan Harbor, on Lake Michigan 35 miles north of Chicago, illustrates the difficulty of handling sites contaminated with toxic chemicals. After years of dumping by Outboard Marine Corp., the harbor had the worst contamination from polychlorinated biphenyls, or PCBs, in the United States.

The \$21-million cleanup, a high priority in the Superfund program, began in 1988 and was completed in 1993. Here is a look at how the process was accomplished:

1. One million pounds of PCB-laced sediment and soil were dredged from Slip 3—the main source of PCBs in the harbor—as well as Crescent Ditch and North Ditch.

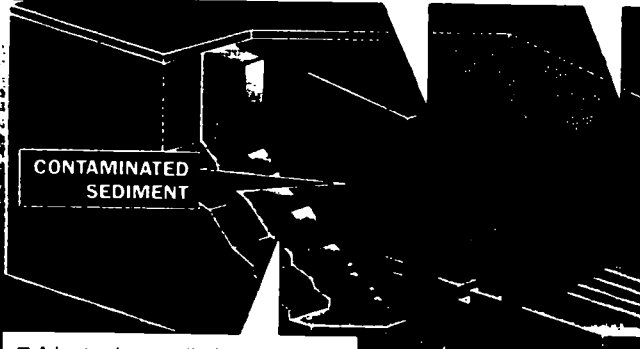
2. The materials were pumped into a holding pond and dried in the West Containment Cell.



3. Almost 13,000 tons were cooked at high temperatures in a mobile processor at the West Containment Cell that separated the PCBs from the sediment and concentrated the PCBs in an oil-based liquid. The liquid was hauled to an incinerator in Texas.

4. Slip 3 was turned into a huge containment cell to permanently hold untreated soils and sediments dredged from the harbor. The idea is to prevent lake water from flowing in.

■ A 290-foot cutoff wall was built at the mouth of the slip to cut it off from the rest of the harbor. The wall consists of two steel sheets 20 feet apart and anchored seven feet deep into the clay layer.



■ A large slurry wall, three feet thick, was connected to the cutoff wall to enclose the remainder of Slip 3.

■ A rock berm was constructed diagonally to the cutoff wall, extending 40 feet along the floor of the harbor.

■ An underwater layer of hard, silty clay was added between the steel sheets.

■ Steel braces were placed every 30 feet along the wall.

5. Hydraulic dredging removed 32,000 cubic yards of contaminated sediment from the upper harbor floor. The material was pumped into an intake pipe and discharged into the containment cell at Slip 3.

6. Two smaller containment cells were built to permanently hold wastes from the North Ditch and the treated sediment from the mobile cooking process.

7. Water in the cell is continuously monitored by wells. A water-treatment plant was built to clean any polluted water extracted from the cells.

8. A new boat slip was constructed in the harbor to replace the old one.

9. Once the sediment settles, Slip 3 will be sealed.



Private boat area at Waukegan Harbor.

TIM BOYLE/For The Times

Sources: U.S. Environmental Protection Agency

103D CONGRESS
2D SESSION

H. R. _____

IN THE HOUSE OF REPRESENTATIVES

Ms. MCKINNEY introduced the following bill; which was referred to the
Committee on _____

A BILL

To

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the "Farm Viability and
5 Pest Management Improvement Act of 1994: A National
6 Program for Pesticide Reduction".

7 **SEC. 2. FINDINGS.**

8 The Congress finds as follows:

9 (1) As documented by numerous reports by the
10 National Academy of Sciences, Office of Technology

1 Assessment, General Accounting Office and others
2 including, Alternative Agriculture, Soil and Water
3 Quality: An Agenda for Agriculture, Pesticides in
4 the Diets of Infants and Children, Pesticide Resist-
5 ance: Strategies and Tactics for Management,
6 Neurotoxicity: Identifying and Controlling Poisons of
7 the Nervous System, and Sustainable Agriculture:
8 Program Management, Accomplishments, and Op-
9 portunities, current regulatory approaches are insuf-
10 ficient to prevent pesticide-related pollution or to
11 quantify all risks associated with routine pesticide
12 use including worker exposure, residues in food,
13 wildlife impacts, ground and surface water contami-
14 nation, disruption of biological processes, and in-
15 creased pest resistance.

16 (2) As documented in the Office of Technology
17 Assessment report, Beneath the Bottom Line: Agri-
18 cultural Approaches to Reduce Agricultural Con-
19 tamination of Groundwater and the National Acad-
20 emy of Sciences report, Soil and Water Quality: An
21 Agency for Agriculture, a pollution prevention strat-
22 egy is effective for addressing pesticide-related pollu-
23 tion. Reducing pesticides at their source should be
24 the fundamental approach for pollution presentation
25 in farming and other pest management systems. A

1 pesticide reduction strategy as specified in this sec-
2 tion will provide significant improvements in public
3 health an environmental protection.

4 (3) As documented by the National Academy of
5 Sciences report, *Alternative Agriculture*, pesticide re-
6 duction can be achieved through widespread adop-
7 tion of integrated pest management and other prac-
8 tices and systems for agricultural sustainability.
9 Such practices can lower costs for farmers and pest
10 managers and in many cases increase quality, pro-
11 ductivity, and yields.

12 **SEC. 3. CONGRESSIONAL PURPOSES.**

13 The purpose of this Act is to foster a substantial re-
14 duction in pesticide use, and thereby reduce the public
15 health and environmental risks of the present level of
16 usage, while maintaining agricultural productivity and an
17 affordable food supply. It is the intent of Congress that
18 this Act be interpreted taking into account its text, the
19 pertinent Committee Reports, and other legislative his-
20 tory.

21 **SEC. 4. DEFINITION OF INTEGRATED PEST MANAGEMENT.**

22 Section 2 of the Federal Insecticide, Fungicide, and
23 Rodenticide Act (7 U.S.C. 136) is amended by adding at
24 the end the following subsection:

1 “(hh) INTEGRATED PEST MANAGEMENT SYSTEMS.—

2 The term ‘integrated pest management systems’ means
3 the use and integration of various pest control tactics in
4 the environment of a pest in a manner that—

5 “(1) complements and facilitates biological and
6 other natural controls of the pest;

7 “(2) reduces the use of chemical pesticides;

8 “(3) relies primarily on the use of nonchemical
9 pest management methods, with chemical pesticides
10 being used only as a last resort;

11 “(4) reduces injuries to the public health and
12 environment; and

13 “(5) is economically feasible, considering both
14 private and public costs.”.

15 **SEC. 5. PESTICIDE USE REDUCTION PROGRAM.**

16 (a) The Federal Insecticide, Fungicide, and
17 Rodenticide Act is amended—

18 (1) by redesignating sections 29, 30, and 31 (7
19 U.S.C. 136w-4, 136x, and 136y) as sections 30, 31,
20 and 32, respectively; and

21 (2) by inserting after section 28 the following
22 new section:

23 **“SEC. 29. PESTICIDE REDUCTION COUNCILS.**

24 “(a) REGIONAL PESTICIDE REDUCTION COUNCILS.—

“(1) ESTABLISHMENT.—Not later than 6 months after the date of the enactment of this section, the Administrator, in consultation with the Secretary, shall establish a pesticide reduction council in each region of the Environmental Protection Agency.

“(2) MEMBERSHIP.—The Administrator shall appoint members to each regional council who equally represent relevant Federal and State agencies, farmers, farm workers, university research and extension, nonprofit organizations, the private sector, regional institutions, and environmental and consumer organizations who are experts in the research, practice, and policy relevant to integrated pest management.

“(3) DUTIES.—Each regional council shall, within 6 months after establishment—

“(A) identify the most effective integrated pest management systems as defined in section 3 for individual cropping systems that have been demonstrated by farmers to—

“(i) use substantially less than the average volume of pesticides for the cropping system in the region;

1 “(ii) be practical and profitable for
2 the production of the crop within the re-
3 gion;

4 “(iii) decrease pesticide hazards to
5 workers, consumers, and the environment;
6 and

7 “(iv) make optimum use of cultural
8 and biological control practices to avoid
9 buildup of pest populations feasible in the
10 region;

11 “(B) within 6 months from the date of the
12 enactment of this Act, establish measurable
13 quantitative goals for the most technically fea-
14 sible and ecologically protective pesticide use re-
15 duction for individual cropping systems in the
16 region utilizing the IPM systems identified in
17 section 29(a)(3)(A); the goals shall be designed
18 to bring prevailing patterns of pesticide usage
19 into conformance with most effective integrated
20 pest management systems;

21 “(C) develop a regionwide plan for achiev-
22 ing the regional pesticide reduction goals estab-
23 lished in section 29(a)(3)(B) including rec-
24 ommendations for the roles of Federal and

1 State institutions and programs, as well as for
2 farmer-to-farmer demonstration programs;

3 “(D) identify research and technology
4 transfer needs specific to each cropping system
5 and region and recommend research and tech-
6 nology transfer priorities to the Secretary and
7 Administrator; and

8 “(E) identify government and industry
9 policies and practices that impede adoption of
10 integrated pest management systems and rec-
11 ommend policy changes to the Secretary and
12 Administrator to ensure such adoption.

13 “(b) ADMINISTRATOR’S AND SECRETARY’S DU-
14 TIES.—The Administrator and Secretary, in consultation
15 with the pesticide reduction councils, shall—

16 “(1) assess and approve the integrated pest
17 management systems and pesticide reduction plans
18 and goals identified and established by the regional
19 reduction councils;

20 “(2) develop and implement programs to assist
21 farmers in adopting integrated pest management
22 systems;

23 “(3) assess regional and national progress to-
24 ward reducing pesticide usage; and

1 “(4) review and revise regional pesticide reduc-
2 tion goals, if necessary, to achieve such goals.

3 “(c) REVIEW OF IPM SYSTEMS AND REDUCTION
4 GOALS.—Within 15 months of enactment of this section,
5 the Administrator, in consultation with the Secretary,
6 shall assess and approve of the pesticide reduction goals
7 and plans developed by each regional council. The Admin-
8 istrator shall evaluate the effectiveness of the integrated
9 pest management systems identified by the reduction
10 councils and further evaluate the goals and plans taking
11 into consideration pesticide use records and other relevant
12 information. If the Administrator determines that a reduc-
13 tion goals or plan established by a reduction council is in-
14 adequate to substantially reduce the risks of pesticides
15 within that region or that it underestimates the extent of
16 feasible pesticide reduction that can occur for that region,
17 the Administrator shall not approve the plan. If the goals
18 or plans for any region are not approved, each State with-
19 in the region shall be denied use of any pesticide under
20 section 24c and section 18 of the Federal Insecticide, Fun-
21 gicide, and Rodenticide Act until such time as the plan
22 is adequately approved.

23 “(d) PROGRAMS TO ASSIST FARMERS IN ADOPTING
24 IPM SYSTEMS.—Not later than 18 months after the date
25 of the enactment of this section, the Secretary, in con-

1 sultation with the Administrator and regional reduction
2 councils, shall develop and implement programs, based on
3 the plans developed by the reduction councils pursuant to
4 section 29(a)(3)(C), to assist farmers in adopting inte-
5 grated pest management systems and meeting regional re-
6 duction goals including farmer-to-farmer demonstrations
7 of effective IPM systems as identified in section
8 29(a)(3)(A).

9 “(e) ASSESSMENT OF PROGRESS.—

10 “(1) BASELINE.—The Administrator shall
11 measure annual progress toward meeting the re-
12 gional reduction goals. The goals shall be measured
13 against an averaged baseline reflecting pesticide ap-
14 plications in the 3 years immediately prior to the ap-
15 proval of the regional pesticide reduction plans dis-
16 cussed in section 29(a)(3)(C). The baseline shall be
17 derived from surveys of pesticide usage records for
18 that region and other information.

19 “(2) MID-TERM EVALUATION.—Within 3 years
20 of enactment of this Act, the Administrator shall as-
21 sess progress toward achievement of the pesticide re-
22 duction goals in each region. If the Administrator
23 determines that adequate progress toward a regional
24 goal or the overall purposes of the Act, has not been
25 made, the Secretary shall, within 1 year thereafter,

1 identify the barriers to further reductions in the re-
2 gion and develop and implement a plan to overcome
3 these barriers, taking into account the recommenda-
4 tions made by the reduction councils in subpara-
5 graphs (D) and (E) of section 29(a)(3).

6 “(3) ENFORCEMENT.—If, within 6 years of the
7 date of the enactment of this Act, the Administrator
8 determines, taking into account extenuating cir-
9 cumstances, such as extreme weather conditions,
10 that the goal or overall purposes of the Act have not
11 been met within a region, the Administrator shall,
12 after consultation with the Secretary, reduce or re-
13 strict the use of any pesticide deemed to contribute
14 significant risk to human health and the environ-
15 ment or amend the label of such a pesticide, as may
16 be necessary to achieve the regional reduction goals.

17 “(4) REVIEW AND REVISION OF GOALS.—The
18 Administrator, in consultation with the Secretary,
19 shall revise regional reduction goals in order to
20 achieve additional reductions in pesticide usage if
21 the Administrator determines that additional reduc-
22 tions are—

23 “(A) necessary to the protection of public
24 health or the environment; or

1 “(B) practical and feasible as a result of
2 improvements in pest management systems and
3 technologies.

4 “(f) FEE INCENTIVE.—Each registrant shall pay to
5 the Secretary an assessment equal to $\frac{2}{10}$ of 1 percent of
6 the sales value of any registered pesticide. A registrant
7 is not required to pay an assessment for pesticides reg-
8 istered and labeled for use in further manufacturing or
9 formulating of pesticide products. The proceeds of such
10 assessment shall be used for demonstration and extension
11 activities incurred under subsection (d) of this section.

12 “(g) NONAGRICULTURAL PESTICIDE REDUCTION.—

13 “(1) PUBLIC EDUCATION.—Not later than 1
14 year after the date of the enactment of this section,
15 the Administrator shall publish, and make available
16 to the public, educational materials concerning inte-
17 grated pest management systems for building and
18 landscape pests. The materials shall include informa-
19 tion on integrated pest management, pest identifica-
20 tion, threshold identification, least toxic treatment
21 options and timing, evaluation procedures, and other
22 relevant information.

23 “(2) PESTICIDE REDUCTION PLAN.—Not later
24 than 1 year after the date of the enactment of this
25 section, the Administrator shall establish a program

1 to set quantitative goals for reducing or eliminating,
2 to the extent practicable, the use of nonagricultural
3 pesticides and to carry out plans to achieve such
4 goals within 6 years. Highest priority shall be given
5 to reducing the use of insecticides, fungicides, and
6 herbicides used to control building and landscape
7 pests.

8 “(h) PESTICIDE USE BY FEDERAL AGENCIES.—Each
9 agency (as defined in section 551(1) of title 5, United
10 States Code, shall establish pesticide reduction goals and
11 develop and implement integrated pest management sys-
12 tems to achieve the goals. Such goals shall apply, at least,
13 to any Federal contract, grant, or cooperative agreement
14 entered into by such agency.

15 “(i) PROGRESS REPORTS.—The Administrator shall
16 publish and disseminate an annual assessment of progress
17 in advancing adoption of most effective integrated pest
18 management systems and achieving the overall purposes
19 of this section.”.

20 (b) Subsection (c) of section 11 of the Federal Insec-
21 ticide, Fungicide, and Rodenticide Act (7 U.S.C. 136i) is
22 amended to read as follows:

23 “(c) INSTRUCTION IN INTEGRATED PEST MANAGE-
24 MENT TECHNIQUES.—Standards prescribed by the Ad-
25 ministrator for the certification of applicators of pesticides

1 under subsection (a), and State plans submitted to the Ad-
2 ministrator under subsections (a) and (b), shall include
3 provisions requiring that individuals receive comprehensive
4 instruction in integrated pest management techniques, in-
5 cluding field experience, and be shown to be competent
6 with respect to the use of the techniques.”.

7 **SEC. 6. FEDERAL GOVERNMENT FOOD PURCHASES.**

8 (a) **DETERMINATION OF PERCENTAGE OF ORGANI-**
9 **CALLY PRODUCED FOOD.**—Not later than 1 year after the
10 date of the enactment of this section, and annually there-
11 after, the Secretary of Agriculture shall determine the per-
12 centage of food purchases throughout the United States
13 that are organically produced as defined in the Food, Agri-
14 culture and Conservation Trade Act (7 U.S.C. 6502(14)).

15 (b) **GOALS.**—

16 (1) **3-YEAR GOAL.**—Not later than 3 years after
17 the date of the enactment of this section, each agen-
18 cy (as defined in section 551(1) of title 5, United
19 States Code) shall develop a procurement plan that
20 ensures that the percentage of the agency’s pur-
21 chases of organically produced food meets or exceeds
22 the percentage determined under subsection (a).

23 (2) **6-YEAR GOAL.**—Not later than 6 years after
24 the date of the enactment of this section, each agen-
25 cy shall ensure that the percentage of the agency’s

1 purchases of organically produced food meets or ex-
2 ceeds twice the percentage determined under sub-
3 section (a).

4 **SEC. 7. PESTICIDE RECORDKEEPING AND REPORTING.**

5 (a) **IN GENERAL.**—The Federal Insecticide, Fun-
6 gicide, and Rodenticide Act is amended by inserting after
7 section 8 (7 U.S.C. 136f) the following new section:

8 **"SEC. 8a. PESTICIDE USE RECORDKEEPING AND REPORT-**
9 **ING.**

10 **"(a) REQUIREMENTS.—**

11 **"(1) IN GENERAL.**—The Secretary of Agri-
12 culture and the Administrator shall establish a na-
13 tional pesticide use recordkeeping and reporting sys-
14 tem for agricultural and nonagricultural applica-
15 tions.

16 **"(2) PERSONS REQUIRED TO KEEP RECORDS.—**
17 The following persons shall maintain records of pes-
18 ticide use:

19 **"(A)** Any person who uses a pesticide for
20 a commercial agricultural use.

21 **"(B)** Any person certified to apply a pes-
22 ticide classified as a restricted use pesticide
23 under section 3(d)(1)(C).

24 **"(C)** Any person engaged for hire in the
25 business of pest control.

1 “(3) INFORMATION.—The records required
2 under this section shall include the product name,
3 target pest, crop, or site being treated, including
4 total acreage or units treated, amount applied, date
5 and time of application, and the location of applica-
6 tion of each pesticide used. Records shall be main-
7 tained using a standard form as specified by the
8 Secretary.

9 “(4) ADDITIONAL RECORDS.—The Adminis-
10 trator shall establish such additional recordkeeping
11 requirements as necessary to evaluate adoption of
12 nonchemical pest management methods and changes
13 in pesticide usage patterns.

14 “(5) COPY OF RECORDS FROM APPLICATOR TO
15 PRINCIPAL.—Within 7 days of a pesticide applica-
16 tion, an applicator shall provide a copy of records
17 maintained under paragraph (1) to the person for
18 whom such application was provided.

19 “(6) RETENTION OF RECORDS.—Records re-
20 quired pursuant to this section shall be retained for
21 a period of at least 3 years following the application
22 of a pesticide.

23 “(7) COPY OF RECORDS FROM APPLICATOR TO
24 SECRETARY AND ADMINISTRATOR.—Every 6 months,
25 a person subject to the recordkeeping requirements

1 of this section shall report the pesticide use of the
2 person by providing copies of the records maintained
3 under paragraphs (3) and (4) to the Secretary and
4 the Administrator. An exception shall be made for a
5 person who meets the definition of paragraph (2)
6 and resides in a State that operates a comparable
7 pesticide use recordkeeping and reporting system as
8 determined by the Secretary. Such a person shall
9 submit records in accordance with the State pro-
10 gram.

11 “(8) COPY OF RECORDS FROM SECRETARY AND
12 ADMINISTRATOR TO STATES.—Not later than 3
13 months after receipt of the records, on the request
14 of a State, the Secretary and the Administrator shall
15 provide to the State copies of the records received
16 under paragraph (7).

17 “(9) COPY OF RECORDS FROM STATES TO SEC-
18 RETARY AND ADMINISTRATOR.—The Secretary and
19 Administrator shall identify those States with pes-
20 ticide recordkeeping and use reporting systems com-
21 parable to the national program established by this
22 Act. Every 6 months, such States shall be required
23 to submit individual pesticide records to the Admin-
24 istrator and Secretary.

25 “(b) PUBLIC ACCESS.—

1 “(1) IN GENERAL.—A record submitted to the
2 Secretary and the Administrator under subsection
3 (a)(7) shall be available to the public during normal
4 working hours at a location designated by the Sec-
5 retary and the Administrator, except that an em-
6 ployee of a Federal agency may not disclose the
7 identify of an individual grower.

8 “(2) DATABASE.—Not later than 1 year after
9 the date of enactment of this section, the Adminis-
10 trator shall establish and maintain in a computer
11 database a national pesticide use inventory based on
12 data submitted under subsection (a)(7). The Admin-
13 istrator shall make the data accessible by computer
14 telecommunication and other means to any inter-
15 ested person or organization.

16 “(c) HEALTH CARE PERSONNEL.—

17 “(1) IN GENERAL.—If a health professional de-
18 termines that pesticide information maintained
19 under this section is necessary to provide medical
20 treatment or first aid to an individual who may have
21 been exposed to the pesticides for which the informa-
22 tion is maintained, on request, a person required to
23 maintain records under subsection (a) shall promptly
24 provide the record and available label information to
25 the health professional.

1 “(2) EMERGENCIES.—In the case of an emer-
2 gency, the record information shall be provided im-
3 mediately or within 24 hours.

4 “(d) ENFORCEMENT AND PENALTIES.—The Sec-
5 retary, in consultation with the Administrator, shall be re-
6 sponsible for enforcement of subsections (a), (b), and (c).
7 A person who violates any such subsection during a crop
8 year shall—

9 “(1) in the case of the first offense, be subject
10 to a fine of not less than \$1,000;

11 “(2) in the case of the second offense, be sub-
12 ject to a fine of not less than \$5,000 and;

13 “(3) in the case of the third offense, be subject
14 to a fine of not less than \$20,000.

15 “(e) PILOT PROJECT.—

16 “(1) IN GENERAL.—Not later than 90 days
17 after the date of enactment of this section, the Sec-
18 retary and the Administrator shall establish a pilot
19 project to assess the feasibility of having pesticide
20 users subject to the reporting requirements of this
21 section submit such records using electronic or tele-
22 phonic means.

23 “(2) REPORT.—Not later than 270 days after
24 the date of enactment of this subsection, the Sec-
25 retary and the Administrator shall report to the

1 Congress on the findings of the study and make rec-
2 ommendations regarding widespread implementation
3 of electronic or telephonic submission of pesticide
4 use reports.

5 “(f) SURVEYS AND REPORTS.—

6 “(1) IN GENERAL.—The Secretary and the Ad-
7 ministrator shall utilize the data submitted under
8 subsection (a) to assess progress made towards
9 achieving the national pesticide reduction goals of
10 section 29 and in preparing the progress reports to
11 Congress required under section 29(h). Within 3
12 years of enactment and annually thereafter, the Sec-
13 retary and Administrator shall submit a report to
14 Congress assessing compliance with this provision of
15 the Act including the percentage of growers in com-
16 pliance and the number of enforcement actions
17 taken.

18 “(2) MEMORANDUM OF UNDERSTANDING.—The
19 Secretary and the Administrator shall enter a memo-
20 randum of understanding that defines the respective
21 responsibilities of the Secretary and the Adminis-
22 trator under this section in order to avoid duplica-
23 tion of efforts.

24 “(g) REGULATIONS.—Not later than 180 days after
25 the date of the enactment of this section, the Secretary

1 and the Administrator shall issue such regulations under
2 their respective authority, as are necessary to carry out
3 their respective duties under this section.”.

4 (b) CONFORMING AMENDMENTS.—

5 (1) Section 11 of the Federal Insecticide,
6 Rodenticide and Fungicide Act (7 U.S.C. 1361) is
7 amended—

8 (A) by striking subsection (d); and

9 (B) by redesignating subsection (e) as sub-
10 section (d).

11 (2) Section 1491 of the Food, Agriculture, Con-
12 servation, and Trade Act of 1990 (7 U.S.C. 136i-
13 1) is repealed.

14 SEC. 8. AGRICULTURE RESEARCH.

15 Section 20 of the Federal Insecticide, Fungicide and
16 Rodenticide Act (7 U.S.C. 136r) is amended by redesign-
17 ating subsections (b) and (c) as subsections (c) and (d)
18 and by adding a new subsection (b) to read as follows:

19 “(b)(1) AGRICULTURAL RESEARCH SERVICE AND
20 COOPERATIVE EXTENSION SERVICE.—No later than 6
21 months from the date of enactment of this section, the
22 Secretary of Agriculture shall ensure that the predominant
23 goal of all pest and weed management research and exten-
24 sion activities conducted within Agricultural Research
25 Service and the Cooperative Extension Service, respec-

1 tively, is development of and transfer of technology related
 2 to integrated pest management systems that reduce the
 3 use of or reliance on pesticides and are otherwise consist-
 4 ent with the goals of this Act and the purposes and prin-
 5 ciples set forth in sections 5801 and 5901 of title 7, Unit-
 6 ed States Code.

7 “(2) REPORT TO CONGRESS.—Within 2 years of en-
 8 actment of this section and biannually thereafter, the Sec-
 9 retary of Agriculture shall report to Congress the progress
 10 of the Agricultural Research Service and Cooperative Ex-
 11 tension Service in developing and transferring technology
 12 related to integrated pest management systems that re-
 13 duce the use of or reliance on pesticides and otherwise
 14 meet the goals of this Act.”.

15 **SEC. 9. GRANTS.**

16 Section 2 of the Act entitled “An Act to facilitate
 17 the work of the Department of Agriculture, and for other
 18 purposes” (7 U.S.C. 450i) is amended by adding at the
 19 end the following:

20 “(n) COMPETITIVE GRANTS.—

21 “(1) NATIONAL RESEARCH INITIATIVE.—Within
 22 6 months of enactment of this section, the Secretary
 23 of Agriculture shall ensure that the goal of pest
 24 management research conducted by the National Re-
 25 search Initiative in the areas of plant systems and

1 natural resources and environment is development of
2 biological, cultural and other nonchemical methods
3 of pest control that reduce the use of or reliance on
4 pesticides and are compatible with the goals of this
5 Act and the development of systems of sustainable
6 agriculture.

7 “(2) INTEGRATED PEST MANAGEMENT SYSTEMS
8 DEFINED.—For the purposes of this section, the
9 term ‘integrated pest management systems’ shall
10 have the same meaning as that term is defined in
11 section 2(hh) of the Federal Insecticide, Fungicide
12 and Rodenticide Act.

13 “(3) REGULATIONS AND COMMENT.—Not later
14 than 1 year from the date of enactment of this sec-
15 tion, the Secretary of Agriculture shall adopt regula-
16 tions establishing priorities and resource allocations
17 for competitive grants research in Integrated Pest
18 Management systems.

19 “(4) REVIEW PROCESS.—Not later than 1 year
20 from the date of enactment of this section, the Sec-
21 retary shall establish a 2-tier review process for com-
22 petitive grants to support integrated pest manage-
23 ment projects. The first tier shall be a scientific re-
24 view. The second tier shall be by an external review
25 panel consisting of at least one member of each of

1 the regional pesticide reduction councils, a farmer
2 involved in onfarm and educational outreach, a so-
3 cial scientist with expertise in technology assessment
4 and the structure of agriculture, and a representa-
5 tive of a nonprofit organization involved in agricul-
6 tural research or research policy with expertise in
7 assessing the social and environmental effects of
8 farming systems. The review panel shall assess an-
9 nually the progress of the competitive grants pro-
10 grams in developing integrated pest management
11 systems that reduce the use of or reliance on pes-
12 ticides and otherwise meet the goals of this Act and
13 the Food, Agriculture, Conservation, and Trade Act
14 of 1990.

15 “(5) COST-SHARE ASSISTANCE FOR IPM.—Not
16 later than 3 years from enactment of this section,
17 the Secretary shall ensure that no less than 10 per-
18 cent of Agricultural Conservation Program funding
19 shall be made available for the Integrated Crop
20 Management program. The Secretary shall also en-
21 sure that the Integrated Crop Management program
22 is available in every county and State and that the
23 Cooperative Extension Service provides the support
24 needed for its agents to be involved in developing

- 1 and reviewing Integrated Crop Management cost-
- 2 share assistance requests.”.



FARM VIABILITY AND PEST MANAGEMENT IMPROVEMENT ACT OF 1994

Summary

Before the end of the 103rd Congress, the Farm Viability and Pest Management Improvement Act of 1994 will be introduced in the House of Representatives by Representative Cynthia McKinney and others.

The Farm Viability and Pest Management Improvement Act of 1994 establishes a cohesive, national program to motivate users to reduce their use of and reliance on pesticides. It reflects growing concern about the risks of pesticides to humans and the environment and the interest of farmers in reducing their use of hazardous substances. It recognizes that comprehensive risk assessment and management -- while an important policy tool -- has not led to widespread adoption of profitable techniques that reduce risk and regenerate natural forms of biological pest management on farms.

The bill has two primary objectives: 1) to identify and feature farmers who are using integrated pest management and other systems that have substantially reduced their use of pesticides (and to assist other growers in achieving similar reductions); 2) to generate information and recommendations that will shift resources away from chemical-intensive pest management.

The bill is "farmer-friendly". It provides incentives and assistance rather than punishment, and it encourages farmers' autonomy while giving the public the information it needs to trust farm-level decisions. The Administrator of the EPA has enforcement authority only if a six year program promoting voluntary action has not resulted in reductions demonstrated to be feasible and cost-effective.

After the "short title" section of the bill, The Farm Viability and Pest Management Improvement Act of 1994 has eight major components:

Section 2 -- Findings cites prestigious national reports documenting the need for and feasibility of pesticide reduction.

Section 3 -- Congressional Purposes outlines the purpose of the Act: to foster reduction in pesticide use in order to reduce risk while maintaining agricultural productivity and an affordable food supply.

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Section 4 – Definition of Integrated Pest Management codifies a definition that returns to the original concept of IPM as systems-based, economically rational and relying on chemicals as a last resort.

Section 5 – Pesticide Use Reduction Program

- establishes multi-stakeholder councils in each EPA region to develop pesticide reduction plans and goals for the region and advise the Administrator and Secretary regarding research and technology transfer needs.
- requires the Administrator and the Secretary to assess and approve the regional pesticide reduction plans and goals and measure progress toward meeting the goals; makes granting of emergency exemptions for use of particularly hazardous pesticides contingent on adequate regional pesticide reduction plans.
- requires the Secretary to develop a program to assist farmers in adopting profitable integrated pest management systems which reduce pesticide use, including farmer to farmer demonstrations.
- requires the Administrator to produce educational materials and establish a program to encourage the reduction of pesticides used for non-agricultural purposes.
- requires federal agencies to establish goals for reduction in their own use of pesticides and develop and implement IPM.

Section 6 – Federal Government Food Purchases requires federal agencies that purchase food to gradually increase the percentage of the organic food they purchase as a market incentive for growers.

Section 7 – Pesticide Recordkeeping and Reporting requires the Secretary and Administrator to establish a system for reporting of pesticide usage which would protect growers' identity while allowing for detailed analysis of progress made towards reduction goals and identification of geographical areas of special concern.

Section 8 – Agricultural Research requires the Secretary to ensure that the goal of pest management research and extension activities is the development of IPM systems that reduce the use of and reliance on pesticides.

Section 9 – Funding for the Integrated Crop Management Program increases the funding available for the Integrated Crop Management Program, which has assisted growers in profitably reducing their pesticide use.

For further information on the Farm Viability and Pest Management Improvement Act of 1994, please call Gloria Butler in Representative McKinney's office (225-1605) or Polly Hoppin at World Wildlife Fund (778-9667).

FOR RELEASE: April 20, 1994

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**Leading Scientists Assess Widespread
Wildlife Decline**

Washington, D.C.-- World Wildlife Fund (WWF) today released a statement signed by 23 leading North American scientists, warning that in many cases wildlife and humans may have exceeded their capacity to compensate for exposure to chemicals. The scientists noted declines in a variety of North American wildlife populations, including beluga whales and bald eagles.

The scientists are certain that "populations of many long-lived species are declining, some to the verge of extinction, without society's knowledge. Some of these declines are related to exposure to man-made chemicals and their effects on the development of embryos."

"The embryo is the most sensitive life stage of animals to the hazards posed by chemicals," said Theo Colborn, a senior scientist at World Wildlife Fund.

The development of human and wildlife embryos is under the sensitive control of the endocrine system, which is fueled by hormones. Large quantities of endocrine-disrupting chemicals have been released into the environment. Exposure to these chemicals has been associated with immune and thyroid system disorders, disrupted sexual development, decreased fertility, gross birth deformities, and decreased hatching in birds, turtles

According to the scientists, man-made chemicals can affect a fetus by mimicking or interfering with natural hormones produced by the endocrine system and altering the embryo's development. The scientists concluded that the timing of the exposure during gestation, not necessarily the amount, determined the effect. Even a single, minute exposure could severely harm the developing offspring of wildlife and humans.

Endocrine-disrupting chemicals ignore geographic and ecological boundaries and can be found in rain and well water, lakes, oceans, and food products.

Chemicals have been found in troubled populations of alligators, bald eagles, Forster's terns, beluga whales, great blue herons, lake trout, wood ducks, and other species. These chemicals also have been detected in wildlife from the Arctic to Antarctica and in human beings as well.

The damage that researchers now are uncovering occurs before or soon after birth, if the animal survives, but often may not become fully evident until adulthood.

The scientists convened by WWF believe "traditional assessments of risks posed by single chemicals are not adequate for assessing the risks for embryos exposed to multiple chemicals."

The scientists issued the following recommendations:

- o Test chemicals before environmental release throughout a minimum of two generations for a wide variety of effects including reproductive, immunological, endocrinological, and neurological effects.
- o Raise awareness among legislators, scientists, public health officials and the general public about the danger of endocrine disrupting chemicals.
- o Undertake a major research effort and comprehensive assessment of wildlife declines and diseases caused by chemicals on a global basis.

U.S. Production of synthetic, organic chemicals amounted to 197.5 billion kilograms in 1992 (435 billion pounds), which translates to more than 1,600 pounds for each person in the country. Information about exposure to chemicals is scarce although companies are required to provide information about release of chemicals from their facilities.

World Wildlife Fund works in more than 100 countries to protect the abundance and diversity of life on earth.

**STATEMENT FROM THE WORK SESSION ON
CHEMICALLY-INDUCED ALTERATIONS IN SEXUAL
DEVELOPMENT: THE WILDLIFE/HUMAN CONNECTION**

THE PROBLEM

Many compounds introduced into the environment by human activity are capable of disrupting the endocrine system of animals, including fish, wildlife, and humans. The consequences of such disruption can be profound because of the crucial role hormones play in controlling development. Because of the increasing and pervasive contamination of the environment by compounds capable of such activity, a multidisciplinary group of experts gathered in retreat at Wingspread, Racine, Wisconsin, 26-28 July 1991 to assess what is known about the issue. Participants included experts in the fields of anthropology, ecology, comparative endocrinology, histopathology, immunology, mammalogy, medicine, law, psychiatry, psychoneuroendocrinology, reproductive physiology, toxicology, wildlife management, tumor biology, and zoology.

The purposes of the meeting were:

1. to integrate and evaluate findings from the diverse research disciplines concerning the magnitude of the problem of endocrine disruptors in the environment;
2. to identify the conclusions that can be drawn with confidence from existing data; and
3. to establish a research agenda that would clarify uncertainties remaining in the field.

CONSENSUS STATEMENT

The following consensus was reached by participants at the workshop.

1. *We are certain of the following:*

A large number of man-made chemicals that have been released into the environment, as well as a few natural ones, have the potential to disrupt the endocrine system of animals, including humans. Among these are the persistent, bioaccumulative, organohalogen compounds that include some pesticides (fungicides, herbicides, and insecticides) and industrial chemicals, other synthetic products, and some metals.¹

¹Chemicals known to disrupt the endocrine system include: DDT and its degradation products, DEHP (di(2-ethylhexyl)phthalate), dieldrin, HCB (hexachlorobenzene), kepone, kepone, lindane and other hexachlorocyclohexane congeners, methoxy-chlor, octachlorostyrene, synthetic pyrethroids, triazine herbicides, EBDC (fungicides, certain PCB congeners, 2,3,7,8-TCDD and other dioxins, 2,3,7,8-TCDF and

- Many wildlife populations are already affected by these compounds. The impacts include thyroid dysfunction in birds and fish; decreased fertility in birds, fish, shellfish, and mammals; decreased hatching success in birds, fish, and turtles; gross birth deformities in birds, fish, and turtles; metabolic abnormalities in birds, fish, and mammals; behavioral abnormalities in birds; demasculinization and feminization of male fish, birds and mammals; defeminization and masculinization of female fish and birds; and compromised immune systems in birds and mammals.
- The patterns of effects vary among species and among compounds. Four general points can nonetheless be made: (1) the chemicals of concern may have entirely different effects on the embryo, fetus, or perinatal organism than on the adult; (2) the effects are most often manifested in offspring, not in the exposed parent; (3) the timing of exposure in the developing organism is crucial in determining its character and future potential; and (4) although crucial exposure occurs during embryonic development, obvious manifestations may not occur until maturity.
- Laboratory studies corroborate the abnormal sexual development observed in the field and provide biological mechanisms to explain the observations in wildlife.
- Humans have been affected by compounds of this nature, too. The effects of DES (diethylstilbestrol), a synthetic therapeutic agent, like many of the compounds mentioned above, are estrogenic. Daughters born to mothers who took DES now suffer increased rates of vaginal clear cell adenocarcinoma, various genital tract abnormalities, abnormal pregnancies, and some changes in immune responses. Both sons and daughters exposed *in utero* experience congenital anomalies of their reproductive system and reduced fertility. The effects seen in *in utero* DES-exposed humans parallel those found in contaminated wildlife and laboratory animals, suggesting that humans may be at risk to the same environmental hazards as wildlife.

2. We estimate with confidence that:

- Some of the developmental impairments reported in humans today are seen in adult offspring of parents exposed to synthetic hormone

other furans, cadmium, lead, mercury, tributyltin and other organo-tin compounds, alkyl phenols (non-biodegradable detergents and anti-oxidants present in modified polystyrene and PVCs), styrene dimers and trimers, soy products, and laboratory animal and pet food products.

disruptors (agonists and antagonists) released in the environment. The concentrations of a number of synthetic sex hormone agonists and antagonists measured in the US human population today are well within the range and dosages at which effects are seen in wildlife populations. In fact, experimental results are being seen at the low end of current environmental concentrations.

- Unless the environmental load of synthetic hormone disruptors is abated and controlled, large scale dysfunction at the population level is possible. The scope and potential hazard to wildlife and humans are great because of the probability of repeated and/or constant exposure to numerous synthetic chemicals that are known to be endocrine disruptors.

- As attention is focused on this problem, more parallels in wildlife, laboratory, and human research will be revealed.

3. *Current models predict that:*

- The mechanisms by which these compounds have their impact vary, but they share the general properties of (1) mimicking the effects of natural hormones by recognizing their binding sites; (2) antagonizing the effect of these hormones by blocking their interaction with their physiological binding sites; (3) reacting directly and indirectly with the hormones in question; (4) by altering the natural pattern of synthesis of hormones; or (5) altering hormone receptor levels.

- Both exogenous (external source) and endogenous (internal source) androgens (male hormones) and estrogens (female hormones) can alter the development of brain function.

- Any perturbation of the endocrine system of a developing organism may alter the development of that organism: typically these effects are irreversible. For example, many sex-related characteristics are determined hormonally during a window of time in the early stages of development and can be influenced by small changes in hormone balance. Evidence suggests that sex-related characteristics, once imprinted, may be irreversible.

- Reproductive effects reported in wildlife should be of concern to humans dependent upon the same resources, e.g., contaminated fish. Food fish is a major pathway of exposure for birds. The avian (bird) model for organochlorine endocrine disruption is the best described to date. It also provides support for the wildlife/human connection because of similarities in the development of the avian and mammalian endocrine systems.

4. *There are many uncertainties in our predictions because:*

- The nature and extent of the effects of exposure on humans are not well established. Information is limited concerning the disposition of these contaminants within humans, especially data on concentrations of contaminants in embryos. This is compounded by the lack of measurable endpoints (biologic markers of exposure and effect) and the lack of multi-generational exposure studies that simulate ambient concentrations.
- While there are adequate quantitative data concerning reduction in reproductive success in wildlife, data are less robust concerning changes in behavior. The evidence, however, is sufficient to call for immediate efforts to fill these knowledge gaps.
- The potencies of many synthetic estrogenic compounds relative to natural estrogens have not been established. This is important because contemporary blood concentrations of some of the compounds of concern exceed those of internally produced estrogens.

5. *Our judgment is that:*

- Testing of products for regulatory purposes should be broadened to include hormonal activity *in vivo*. There is no substitute for animal studies for this aspect of testing.
- Screening assays for androgenicity and estrogenicity are available for those compounds that have direct hormonal effects. Regulations should require screening all new products and by-products for hormonal activity. If the material tests positive, further testing for functional teratogenicity (loss of function rather than obvious gross birth defects) using multigenerational studies should be required. This should apply to all persistent, bioaccumulative products released in the past as well.
- It is urgent to move reproductive effects and functional teratogenicity to the forefront when evaluating health risks. The cancer paradigm is insufficient because chemicals can cause severe health effects other than cancer.
- A more comprehensive inventory of these compounds is needed as they move through commerce and are eventually released to the environment. This information must be made more accessible. Information such as this affords the opportunity to reduce exposure through containment and manipulation of food chains. Rather than

separately regulating contaminants in water, air, and land, regulatory agencies should focus on the ecosystem as a whole.

- Banning the production and use of persistent chemicals has not solved the exposure problem. New approaches are needed to reduce exposure to synthetic chemicals already in the environment and prevent the release of new products with similar characteristics.
- Impacts on wildlife and laboratory animals as a result of exposure to these contaminants are of such a profound and insidious nature that a major research initiative on humans must be undertaken.
- The scientific and public health communities' general lack of awareness concerning the presence of hormonally active environmental chemicals, functional teratogenicity, and the concept of transgenerational exposure must be addressed. Because functional deficits are not visible at birth and may not be fully manifested until adulthood, they are often missed by physicians, parents, and the regulatory community, and the causal agent is never identified.

6. *To improve our predictive capability:*

- More basic research in the field of developmental biology of hormonally responsive organs is needed. For example, the amounts of specific endogenous hormones required to evoke a normal response must be established. Specific biologic markers of normal development per species, organ, and stage of development are needed. With this information, levels that elicit pathological changes can be established.
- Integrated cooperative research is needed to develop both wildlife and laboratory models for extrapolating risks to humans.
- The selection of a sentinel species at each trophic level in an ecosystem is needed for observing functional deficits, while at the same time describing the dynamics of a compound moving through the system.
- Measurable endpoints (biologic markers) as a result of exposure to exogenous endocrine disruptors are needed that include a range of effects at the molecular, cellular, organismal, and population levels. Molecular and cellular markers are important for the early monitoring of dysfunction. Normal levels and patterns of isoenzymes and hormones should be established.
- In mammals, exposure assessments are needed based on body burdens of a chemical that describe the concentration of a chemical

in an egg (ovum) which can be extrapolated to a dose of the chemical to the embryo, fetus, newborn, and adult. Hazard evaluations are needed that repeat in the laboratory what is being seen in the field. Subsequently, a gradient of doses for particular responses must be determined in the laboratory and then compared with exposure levels in wildlife populations.

- More descriptive field research is needed to explain the annual influx to areas of known pollution of migratory species that appear to maintain stable populations in spite of the relative vulnerability of their offspring.

- A reevaluation of the *in utero* DES-exposed population is required for a number of reasons. First, because the unregulated, large-volume releases of synthetic chemicals coincide with the use of DES, the results of the original DES studies may have been confounded by widespread exposure to other synthetic endocrine disruptors. Second, exposure to a hormone during fetal life may elevate responsiveness to the hormone during later life. As a result, the first wave of individuals exposed to DES *in utero* is just reaching the age where various cancers (vaginal, endometrial, breast, and prostate) may start appearing if the individuals are at a greater risk because of perinatal exposure to estrogen-like compounds. A threshold for DES adverse effects is needed. Even the lowest recorded dose has given rise to vaginal adenocarcinoma. DES exposure of fetal humans may provide the most-severe-effect model in the investigation of the less potent effects from environmental estrogens. Thus, the biological endpoints determined in *in utero* DES-exposed offspring will lead the investigation in humans following possible ambient exposures.

The effects of endocrine disruptors on longer-lived humans may not be as easily discerned as in shorter-lived laboratory or wildlife species. Therefore, early detection methods are needed to determine if human reproductive capability is declining. This is important from an individual level, as well as at the population level, because infertility is a subject of great concern and has psychological and economic impacts. Methods are now available to determine fertility rates in humans. New methods should involve more use of liver-enzyme-system activity screening, sperm counts, analyses of developmental abnormalities, and examination of histopathological lesions. These should be accompanied by more and better biomarkers of social and behavioral development, the use of multigenerational histories of individuals and their progeny, and congener-specific chemical analyses of reproductive tissues and products, including breast milk.

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From: Chemically Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection, Eds. T. Colborn and C. Clement, Princeton Scientific Publishing, Princeton, NJ 1992. Tel: 609-683-4750 or Fax: 609-683-0838

Consensus Statement

STATEMENT FROM THE WORK SESSION

on

ENVIRONMENTALLY INDUCED ALTERATIONS IN DEVELOPMENT:
A FOCUS ON WILDLIFEWingspread Conference Center
Racine, Wisconsin
December 10-12, 1993

THE PROBLEM

In the last five decades many wildlife populations across the North American continent have experienced severe and often sudden declines that in some cases have led to extirpation. While some of these declines are attributable to natural biological events such as epidemics caused by microbial pathogens and well-established human causes such as overharvesting, habitat changes, and introduction of exotic species, many of these declines have not been satisfactorily explained by these factors. During this time a number of man-made compounds were introduced into the environment that caused the declines of some wildlife populations through adult and embryonic mortality.

Many man-made contaminants can alter embryonic and early postnatal development. The consequences of this interference are irreversible, in some cases leading to early death, but in other cases not manifested until the individual reaches adulthood with resultant loss of fertility. Through subtle biochemical and physiological changes the contaminants interfere with the development of the reproductive, endocrine, immune, and nervous systems of embryos, and therefore are likely candidates for causing some of the declines and failure of wildlife populations to recover even after regulatory prohibition of activities involving these compounds. In light of this knowledge, 23 wildlife experts were gathered in retreat at Wingspread, Racine, Wisconsin, 10-12 December, 1993, to discuss the topic of "Environmentally Induced Alterations in Development: A Focus on Wildlife." Participants reported on their observations of alligators, bald eagles, beluga whales, boreal toads, bottle-nosed dolphins, Caspian terns, common terns, Florida panthers, Forster's terns, great blue herons, herring gulls, leopard frogs, old squaw ducks, polar bears, roseate terns, scoters, sea turtles, slider turtles, spectacled eiders, water fleas, white croakers, and wood ducks. Participants were expected to reach some conclusions concerning the nature, magnitude, and geographic scope of the problem on the North American continent.

CONSENSUS STATEMENT

The following consensus was reached by participants at the workshop.

1. *We are certain of the following:*

- Declines in a number of species and many taxa (including plants) are in progress on the North American continent. Some of these declines are related to exposure to man-made chemicals. Such declines are not solely a US or North American problem but are occurring on a global scale.

- There is a special cause for concern for long-lived species which may or may not (at this time) show overt signs of reproductive impairment. Examples of species that are near extirpation at the population level are those that are annually replenished by outside stock, not by intra-regional reproduction, such as Great Lakes lake trout and shoreline bald eagles, and Lake Apopka, FL alligators and turtles.
- Populations of many long-lived species are declining, some to the verge of extinction, without society's knowledge. The presence of breeding adults and even healthy young does not necessarily reflect a healthy population. Detailed population analysis is needed to determine whether offspring have the functional capacity to survive and reproduce.
- Wildlife are exposed to compounds that disrupt development of the reproductive, immune, nervous, and endocrine systems and thereby can lead to population instability. The pollutants of greatest concern affect cellular and molecular processes that regulate developmental, endocrine, and immunological functions. Hormones are natural substances that control normal development of all embryos and fetuses. Many of the contaminants mimic and/or interfere with female and male hormones, thereby modifying development and reproduction.
- The embryo is the most sensitive life stage of animals to the hazards posed by these chemicals.
- Current contamination in wildlife has reached levels in some regions at which there are known sublethal effects sufficient to impair populations. Unless the continuing release of man-made toxic chemicals is prohibited immediately in certain well-studied North American major aquatic systems, populations of important top predator species may become extirpated.
- Many persistent contaminants do not remain at the site of release. Chemical releases on one continent may not only affect animals on that continent but animals on other continents and in other hemispheres. They are carried as particulates or gases in the air, surface waters, groundwater, and ocean currents across or between continents and by animals that travel long distances from the site of contamination. The contaminant, therefore, can enter the food web in places remote from the site of release.
- It is no longer sufficient to approach population/species revitalization passively by providing appropriate habitat and expecting threatened or extirpated populations to recover. Contamination of apparently useful habitat is not always visible and may not cause overt lethality. Instead, contaminants may cause population-threatening changes in functionality. For example, populations may not be able to recover from infectious diseases because of immunosuppression; the inability to obtain sufficient food or avoid predators; the loss of parenting instinct because of neurotoxicological effects; or the result of abnormal sexual development of anatomy or behavior because of endocrine disruption.
- It has been difficult to document causal relationships between population declines and failures with the chemicals suspected to have caused them. The difficulty can only be successfully addressed through multidisciplinary research linking ecological, wildlife, human, and laboratory animal research and by building bridges between the human, veterinary, and environmental health sciences.

- Increased collaboration and exchange of information between wildlife, laboratory animal, and human investigations is essential. This requires a redefinition or broadening of the role of federal agencies and the institutionalization of causal investigations (environmental detective work). This work must be supported by federal agencies to investigate the declines and their causal relationships.
- Links have been made between some effects and specific man-made chemicals. Other chemical-effect linkages, which in fact may exist, have not been made for several reasons because (1) it is difficult to distinguish individual effects of the numerous man-made chemicals present in the environment because many have similar biological effects; (2) other biotic and abiotic factors play a role in population instability; (3) testing for the presence of such chemicals is so expensive; and (4) additional research is required to clarify these connections (see below).
- Currently, regulatory action depends upon knowledge of the specific physiological and/or biochemical endpoint of a chemical. However, we have yet to identify many biomarkers which are specifically diagnostic of a substance or an effect. Because few such biomarkers have been developed, there is clearly a need for more physiological and molecular-oriented biomarker-based research. However, we believe that the prerequisite of documenting the mode of toxic action and development of specific biomarkers to make cause and effect links before taking regulatory action leads to unnecessary delays that continue to result in injury and potential extirpation of more populations and species.
- The issues addressed in this statement are fundamental to the concepts of "biodiversity", "sustainable development", and "ecosystem health" and call for responsible global citizenship. They assume a preemptive, rather than a reactive, role for scientists, wildlife agencies, and environmental regulators (see below).

2. *We estimate with confidence that:*

- In many cases wildlife and humans have exceeded their capacity to compensate for exposure to chemicals.
- As more areas of the North American continent are surveyed and a wide variety of multigenerational consequences are taken into consideration, more evidence of damage will be revealed among wildlife and human populations. Many effects are taking place that are not easily observed, but they do exist. Too much attention has been directed toward the health of the current population, the directly exposed individuals, and not enough on the offspring. Our current regulatory focus on adult mortality is not sufficient to preserve reproductively successful populations. Rather, we must ensure that successive generations can reproduce.
- When an animal is exposed at the same time to many chemicals that individually are at non-toxic levels, additivity, antagonism, potentiation, and synergy can result in unpredictable consequences. Concomitant exposure to multiple chemicals can cause massive or subtle, but potentially tragic effects.
- When chemically induced syndromes have been identified in the past, it has been difficult to establish cause and effects relationships and to do so has frequently taken decades. The basic tenets of epidemiology have proved valuable in organizing information to infer causal

relationships. The tenets include (1) time order (exposure must precede the effect); (2) strength of association (relative risk); (3) specificity of a compound to an effect (does X lead to Y?); (4) consistency on replication (results are supported across studies, geographic areas, and over time); (5) coherence with biological theory (the relationship must be biologically plausible); and (6) performance on prediction (does the test stand up in the field?).

- Wildlife are reliable sentinels of effects of chemicals on human populations. Lesions at every level of biological organization provide parallels and excellent models for assessing the response of humans exposed to the same chemicals. Effects seen at the cellular to the population levels among wildlife populations should be an integral part of assessments of risk or injury to human health.

3. There are many uncertainties in our predictions because:

- The implications of cumulative exposure to the vast number of chemicals released in the environment are difficult to determine. Although data may become available on the mechanisms of action of certain chemicals, there is no way to account for the interaction of the large number of chemicals to which an animal is exposed.
- Regional differences in land-use practices, industrial activity, and geophysical characteristics must be factored into a cumulative, multimedia exposure model. Migratory species pose additional difficulties when determining sources of exposure.
- No systematic, coordinated effort has been undertaken to determine the geographic extent to which contaminants contribute to the degradation of wildlife populations. While there is evidence in areas where researchers have suspected and looked for wildlife damage, there are many more areas of the continent that have not yet been surveyed. Consequently, the magnitude of the damage is incompletely understood for major wildlife taxa.
- US and Canadian governmental agencies no longer appear willing to commit sufficient long-term, fiscal resources for documenting the effects of chemical exposure in wildlife. Until responsible parties are designated and given adequate appropriations to address wildlife health problems, biodiversity will continue to decline.

4. We believe that:

- Traditional assessments of risks posed by single chemicals are not adequate for assessing the risks for embryos exposed to multiple chemicals.
- The tenets of epidemiology have been successfully used to infer causal associations between certain syndromes and exposures to multiple chemicals.
- Model systems for characterizing wildlife population declines can help to determine the magnitude and scope of the problem. Initial efforts must concentrate on a suite of contaminants thought to have the most serious consequences. It is imperative to replicate the damage observed in the field under laboratory conditions in order to confirm cause and effect linkages.

- All chemicals licensed for environmental release should be tested throughout a minimum of two generations for a wide variety of effects including reproductive, immunological, endocrinological, and neurological endpoints.
- To abate the scope and severity of wildlife population declines, we must endeavor to bring the message into our homes, schools, and the political arena. Until more people understand the insidious nature of developmental toxicants, little will change. More popular press articles and other media should broadcast the message about the effects of developmental toxicants using the wildlife/human connection. A major popular press publication is needed to get the message to the public. Pressure must be exerted on legislators and public health officials to take action to restore damaged populations and to prevent further damage from occurring.

5. To improve our assessment of dangers posed by chemicals:

- A balanced and comprehensive assessment of wildlife declines and diseases caused by chemicals on a global basis is imperative. These assessments must include both retrospective as well as prospective information.
- Funding must be forthcoming to support interdisciplinary investigations, the use of non-traditional organisms (such as wildlife), and research that focuses on functionality in addition to obvious damage. It is imperative to establish a central coordinating office and interdisciplinary teams that can report on sites where subtle effects are occurring and be responsible for directing where field samples can be shipped for initial and rapid evaluation of effects and identification of suspected chemical causes.
- An electronic network should become available to wildlife biologists to improve networking and to increase opportunities for collaboration. In light of the strenuous and unpredictable nature of field research, networks could increase the maximum utilization of sampling and the power of each study.
- There is an urgent need to have integrated funding mechanisms established to facilitate these studies, possibly by creation of a National Institute of the Environment.

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Developmental Effects of Endocrine-Disrupting Chemicals in Wildlife and Humans

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Large numbers and large quantities of endocrine-disrupting chemicals have been released into the environment since World War II. Many of these chemicals can disturb development of the endocrine system and of the organs that respond to endocrine signals in organisms indirectly exposed during prenatal and/or early postnatal life: effects of exposure during development are permanent and irreversible. The risk to the developing organism can also stem from direct exposure of the offspring after birth or hatching. In addition, transgenerational exposure can result from the exposure of the mother to a chemical at any time throughout her life before producing offspring due to persistence of endocrine-disrupting chemicals in body fat, which is mobilized during egg laying or pregnancy and lactation. Mechanisms underlying the disruption of the development of vital systems, such as the endocrine, reproductive, and immune systems, are discussed with reference to wildlife, laboratory animals, and humans. **Key words:** developmental effects, diethylstilbestrol, differentiation, endocrine function, estrogen, fertility, hormones, organochlorines, pesticides, phenolics, reproductive function. *Environ Health Perspect* 101: 378-384 (1993)

Convincing evidence exists that a variety of pollutants, some of which can disrupt endocrine development in wildlife and laboratory animals, is found in rain water, well water, lakes, and oceans, as well as freshwater, marine, and terrestrial food products. This paper identifies the need for a greater awareness about the long-term health consequences associated with exposure to endocrine-disrupting chemicals during early life. Endocrine-disrupting effects are not currently considered in assessing risks to humans, domestic animals, and wildlife. Taking into consideration what is currently known about chemicals that disrupt the endocrine system, the effects 1) may be manifested in an entirely different way, and with permanent consequences, in the early embryo, fetus, and neonate from effects as a result of exposure only in adulthood; 2) can change the course of development and potential of offspring, with the outcome depending on the specific developmental period(s) of exposure; and 3) are often delayed and thus may not be fully or obviously expressed until the offspring reaches maturity or even middle age, even though critical

exposure occurred during early embryonic, fetal, or neonatal life.

In mammals as well as all other vertebrates, communication among cells is required for development to progress normally. Substances produced by one group of cells can direct the course of development and thus determine the future functioning of another group of cells (1). For example, a group of compounds, the steroid hormones produced by the mother's ovaries and adrenal glands, the placenta, and the fetal gonads and adrenal glands, has been identified as playing a major role in regulating developmental processes in many tissues (2). Organogenesis, a particularly vulnerable stage of development, begins in humans at the end of the second month of gestation. At this time the course of development of many tissues is regulated by endogenous steroid hormones along with other endocrine and paracrine factors (3).

It is now recognized that numerous endocrine-disrupting chemicals have been released into the environment in large quantities since World War II (Table 1). Some of these chemicals bind to intracellular receptor proteins for steroid hormones (4) and evoke hormonal effects in animals (5), humans (6), and cell culture (7,8). They thus interfere with the functioning of receptors whose normal role is to mediate the effects of the endogenous steroid hormones (9). Laboratory experiments have demonstrated that exposure of fetuses to endocrine-disrupting chemicals can profoundly disturb organ differentiation (10,11) because they can act as hormone agonists or antagonists. Organs that appear to be at particular risk for developmental abnormalities in offspring because of maternal exposure are those with receptors for gonadal hormones: in female fetuses this includes the mammary glands, fallopian tubes, uterus, cervix, and vagina, and in male fetuses it includes the prostate, seminal vesicles, epididymides, and testes. In both sexes the external genitalia, brain, skeleton, thyroid, liver, kidney, and immune system are also targets for steroid hormone action and are thus potential targets for endocrine-disrupting chemicals, although these chemicals may have multiple modes of action, in addition to acting as hormone agonists and antagonists, in different target tissues (11-15).

A major concern is the profound and permanent effects that exposure to endocrine disruptors during critical periods in development can have on the future well-being of wildlife and humans, although chronic exposure after maturity can also present a health risk. It is generally assumed that after maturity, exposure to endocrine disruptors does not permanently alter the functioning of hormone-responsive tissues. However, experimental studies in animals have shown permanent changes in brain (16) and vaginal epithelium (17) in females and prostate in males (18) after administration of estrogenic chemicals in adulthood. The possibility thus exists that chronic, low-level exposure to estrogenic chemicals in the environment after maturity can have effects in humans similar to those observed in laboratory animals administered estrogen (19).

Wildlife

Exposure to endocrine-disrupting chemicals in the environment has been associated with abnormal thyroid function in birds (20) and fish (21); decreased fertility in birds (22), fish (23), shellfish (24), and mammals (25); decreased hatching success in fish (26), birds (27), and turtles (28); demasculinization and feminization of male fish (29), birds (30), and mammals (31); defeminization and masculinization of female fish (32), gastropods (33), and birds (30); and alteration of immune function in birds (34) and mammals (35). These deleterious health effects have been observed in many areas where the presence of multiple man-made chemicals, such as byproducts of industrial chemical synthesis (chemical waste) and pesticides (36), has been established. The effects were not reported before the 1950s and are currently observed in many areas, such as the Great Lakes in North America. Although much of the data presented here is from studies conducted in and around the Great Lakes, it is important to note that the level of contamination in the Great Lakes region is no greater than some of the other major drainage basins in the United States (37).

Researchers from Guelph University report a 100% prevalence of thyroid enlargement in 2-4-year-old salmon in the Great Lakes. Moreover, in some Great Lakes salmon stocks, there is an extremely high prevalence of precocious sexual maturation in males (40-80% depending on the year), poor egg survival (<15%), and low egg thyroid hormone content (23). Multiple abnormalities, including behavioral

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changes, reproductive loss, and early mortality in offspring have been documented in bird species that feed on Great Lakes fish (38). Reproductive loss and early mortality have also been observed in offspring of confined mink that were fed Great Lakes fish (39).

The devastating effect of DDT on embryonic survival in bald eagles due to eggshell thinning and cracking has been known for some time (40). DDT was introduced on a large scale into the environment in the early 1940s. Restrictions on the use of DDT since 1972 have been only partially successful in reducing levels in the Great Lakes (36). Monitoring nesting sites along the Great Lakes shoreline indicates that while eggshell thinning has abated, embryonic and chick survival is not adequate to maintain stable populations. Recruitment is from inland populations that responded to the restrictions on DDT and other chemicals and that do not depend on contaminated fish in the Great Lakes as a primary food source. However, adult bald eagles that migrate to the shoreline have difficulty producing viable offspring after consuming fish and other food from the Great Lakes for 2 or more years (36). The shoreline has thus become a "black hole" for bald eagles that migrate from successful inland populations. Abandoned eggs hold as much as 10 times the critical concentration of DDT below which stable populations of bald eagles can be maintained (41). In addition to DDT, bald eagles carry elevated concentrations of other compounds that are known endocrine disruptors, such as chlordane, dieldrin, and polychlorinated biphenyls (PCBs) (41). Similar findings have been reported for bald eagles nesting along the Columbia River in Washington State (42).

There are several explanations for the continued elevated concentrations of endocrine-disrupting chemicals in wildlife tissues and the associated instability in wildlife populations, despite the fact that some of the chemicals have been regulated. First, many pesticides, such as DDT, are still manufactured abroad and used extensively in developing countries where there are limited safeguards or monitoring of use. There is now evidence that DDT, PCBs, and other chemicals that readily vaporize are being transported long distances over the globe via the atmosphere (43,44). For example, it is estimated that 90% of the PCBs entering Lake Superior, the largest of the Great Lakes, is derived from the atmosphere (36). Second, some chemicals are very persistent: DDT has a half-life of 57.5 years in temperate soils (45). PCBs were introduced in 1929, and production ceased in the United States in 1972. Many PCB residues which are

Table 1. Chemicals with widespread distribution in the environment reported to have reproductive and endocrine-disrupting effects

Chemical	Reference
Pesticides	
Herbicides	
2,4-D	(98,99)
2,4,5-T	(100)
Alachlor	(99,101)
Ametrole	(102,103)
Atrazine	(104-106)
Metribuzin	(107)
Nitrofen	(10)
Trifluralin	(108,109)
Fungicides	
Benomyl	(110)
Hexachlorobenzene	(111-114)
Mancosaz	(108)
Maneb	(115,116)
Metiram-complex	(117)
Tributyl tin	(118,119)
Zineb	(118)
Ziram	(99)
Insecticides	
B-HCH	(120)
Carbaryl	(100)
Chlordane	(121)
Dicofol	(30)
Dieldrin	(113)
DDT and metabolites	(30)
Endosulfan	(122; A. Soto, unpublished)
Heptachlor and H-epoxide	(113)
Lindane (γ-HCH)	(123)
Methomyl	(107)
Methoxychlor	(5,124)
Mirex	(A. Soto, unpublished)
Oxychlorane	(121)
Permethrin	(125)
Synthetic pyrethroids	(126)
Toxaphene	(A. Soto, unpublished)
Tranentachlor	(121)
Nematocides	
Aldicarb	(107)
OBEP	(10,98)
Industrial chemicals	
Cadmium	(127)
Dioxin (2,3,7,8-TCDD)	(85-87)
Lead	(128,129)
Mercury	(130)
PBBs	(131)
PCBs	(72,132,133)
Pentachlorophenol (PCP)	(134)
Polychlorinated biphenyls	(8)
Phthalates	(135-140)
Styrenes	(8,141,142)

endocrine disrupting and/or developmental toxicants have not been properly stored and are already dispersed in the environment. PCBs will be around over geologic time (46).

Effects of pollutants on the reproductive system, in addition to the well-documented reduction in eggshell thickness, became apparent in the late 1970s when histopathological examination of herring-

gull embryos and newly hatched chicks collected in Lake Ontario revealed oviducts and gonads resembling ovaries in male birds and abnormal development of the oviductal system in female birds (38). Follow-up laboratory studies using DDT and other pesticides which remain in wide use today (dicofol, kelthane, and methoxychlor) produced the same results in kestrels, western gulls, and California gulls (30,47). Today, adult female herring gulls have been observed tending double clutches in their nests in unstable populations (38). Elevated concentrations of DDT, its metabolite, DDE, PCBs, and other organochlorine residues have been found in eggs from these populations (48). It has not been determined whether half of the birds that are pairing are genotypic ♂ that had been feminized during embryonic development by environmental chemicals with estrogenic activity or whether they were all genotypic females showing abnormal behavior. Recent laboratory experiments with small mammals corroborate many of the anomalies cited above, although the effects vary among species among chemicals (5).

The DES Syndrome: A Model for Exposure to Estrogenic Chemicals in the Environment

Diethylstilbestrol (DES) is a synthetic estrogen that was used by physicians to prevent spontaneous abortions in women from 1948 until 1971, when its use for this purpose was banned. DES-exposed humans thus serve as a model for exposure during early life to any estrogenic chemical, including pollutants in the environment that are estrogen agonists. The primary model for determining estrogenic activity of a chemical is the stimulation of mitotic activity in the tissues of the female genital tract in early ontogeny, during puberty, and in the adult (49), although estrogen also affects other tissues in females and males (2,19). Daughters whose mothers took DES (1 million or more between 1960 and 1970) suffer reproductive organ dysfunction, abnormal pregnancies, a reduction in fertility, immune system disorders, and of depression (50,51). As young adults these women also suffer increased rates of vaginal clear-cell adenocarcinomas (52); this is a reproductive tract cancer found in women beginning in their fifties, but it is rare in women in their twenties (50,51). A major concern is that when women exposed *in utero* to estrogenic chemicals (DES and/or environmental pollutants that are estrogen agonists) reach the age at which the incidence of reproductive organ cancers normally increases, they will show a much higher incidence of cancer than unexposed individuals.

There is a substantial literature documenting the detrimental effects of exposure to DES during the critical period of organ differentiation in experimental studies using rodents. Animal models corroborate clinical studies in humans. For example, dysplastic changes in the rodent prostate (53) are comparable to those seen in still-born male offspring of women treated with DES (54). In female mice, DES exposure during early life leads to permanent cornification of the vaginal epithelium, which may be independent of effects on the brain-pituitary-ovarian axis (50,55,56). Significant impairment of immune function (particularly the T-cell system) has also been reported after exposure to DES during early life (57) as well as an increase in autoimmune diseases in women (58). These outcomes were typically not noticeable at birth and often not detected before maturity. For example, treatment of male rats with DES during the first month after birth [accessory reproductive organs are still developing (2)] did not result in observable malignancies at 6–9 months of age, but by 20 months (old age), squamous cell cancer was detected with involvement of the dorsolateral prostate (59). In female mice treated during early life with DES, an increase in sensitivity of mammary glands to carcinogens has been reported (60).

A variety of agricultural and industrial chemicals produced today (either within or outside the United States) are capable of binding to intracellular estrogen receptors either directly, such as *o,p'*-DDT (61), or after *in situ* conversion to an active metabolite. For example, the pesticide methoxychlor (62) is demethylated *in situ* to a more estrogenic bisphenolic compound (63). Pesticides such as *o,p'*-DDT, chlordecone (6), and components of plastics, such as nonylphenol (7), mimic the action of endogenous estrogens (and exogenous DES) both in laboratory animal models as well as in estrogen-sensitive cells in culture (8). A number of conditions in wildlife (reviewed earlier) parallel those reported in laboratory animals and humans exposed to DES during development.

It is worth noting that the estrogenicity of chlordecone was first detected in people working at a pesticide-producing plant (64), and although many effects of estrogenic chemicals may be primarily due to exposure during *in utero* development, chronic exposure throughout adulthood is also a concern. For example, in studies with male dogs, which show prostatic hyperplasia during aging, the disease only developed in castrated males treated with both androgen and estrogen, not androgen alone (18). Exposure of adult men to estrogen has been implicated in the etiology of prostate hyperplasia (19,65). Both prostate

cancer and benign prostatic hyperplasia in men and cancers of estrogen-responsive tissues in women (vaginal, cervical, endometrial, and breast) represent major medical problems faced by older people.

It is now suspected that increases in the incidence of numerous pathologies in men and women may be related to exposure to pesticides and other endocrine-disrupting chemicals that can mimic DES and are thus estrogen agonists. The clinical and experimental findings with DES show that consideration must be given to the following facts: 1) an increase in breast and prostatic cancer in the United States occurred between 1969 and 1986 (66), 2) a 400% increase in ectopic pregnancies occurred in the United States between 1970 and 1987 (67), 3) a doubling of the incidence of cryptorchidism occurred in the United Kingdom between 1970 and 1987 (68,69), and 4) an approximate 50% decrease in sperm count worldwide over the last 50 years (70). These trends may be a reflection of the increase from estrogenic pollutants in the environment. It has been suggested that the decrease in sperm count in men is the result of exposure during the fetal period of testicular differentiation to pollutants that have estrogenic activity (71). For example, an association between reduced sperm motility and PCBs in men with fertility problems has been reported (72); some PCBs are directly estrogenic while others become estrogenic after *in vivo* conversion, although the binding affinity of estrogen receptors for estrogenic PCBs is lower than that for estradiol-17 β (4).

Characterization of Endocrine-Disrupting Chemicals

Literally thousands of synthetic compounds, a number of which are endocrine disruptors, have been released in the environment, generating concern about their additive and synergistic effects. Also, many of the endocrine disruptors are persistent, lipophilic, and have low vapor pressures, which facilitates their widespread dispersal.

It is common to find PCBs, dioxins, DDT, and a number of other organochlorine pesticides together in human breast milk and adipose tissue (73,74). Of concern for humans, domestic animals, and wildlife are the likely additive effects due to exposure to these and other endocrine-disrupting chemicals either together or at different times in life. For example, possible exposure to multiple estrogenic chemicals may be related to the fact that not all offspring of DES-exposed mothers show abnormalities. Although genetic factors may partially account for this outcome, it is also possible that the most affected individuals are those whose mothers were exposed to endocrine-disrupting environ-

mental pollutants with estrogenic activity before or during treatment with DES. Many of the effects of endocrine disruptors that have been reported in wildlife are associated with the presence of a toxic contaminant in the mother due to exposure before egg production in birds and fish or pregnancy and lactation in mammals.

Evidence already exists that a number of organochlorine chemicals (such as dioxin, PCBs, and DDT) has reached concentrations in aquatic food sources that can lead to substantial functional deficits in animals that consume this food. Male rats fed Lake Ontario fish showed hyperreactivity to stress, and offspring of females fed Lake Ontario fish during pregnancy also expressed the same hyperreactive condition, although the offspring were never fed fish (75). In addition, offspring of women who ate two to three Lake Michigan fish a month for at least 6 years preceding their pregnancies were slightly preterm, had lower birth weight, smaller skull circumference, and cognitive, motor (hypotonicity and hyporeflexivity), and behavioral deficits at birth compared with offspring whose mothers did not eat fish (76). The effects were associated with the mothers' lifetime experience of eating fish, not just what they ate during pregnancy. These findings emphasize the importance of exposure of females to contaminants before pregnancy in terms of effects on their offspring.

Subsequent studies of the above cohort beginning at 6–7 months revealed delays in psychomotor development and poorer visual recognition compared with controls (77). When examined at 4 years of age, the children of women who had eaten fish in this study exhibited short-term memory problems, and 17 of the children became intractable and refused to cooperate during testing; they were the children of the mothers with the highest PCB concentrations (measured in their breast milk) in the study (78). The children's intractable behavior appears to be analogous to the behavior of the rats fed Lake Ontario fish. In another study using the infants of mothers who ate Lake Michigan fish and infants of mothers exposed to a PCB "farm incident," both cohorts experienced growth retardation and neurological effects which were related in a dose-dependent manner to umbilical cord serum PCB concentrations (reflecting the levels in fetal blood) (79). It remains to be determined whether the neurotoxic effects mentioned above are mediated through the endocrine system. It is recognized that endocrine-disrupting chemicals may act via multiple mechanisms, some of which may only operate during specific developmental periods (11,80,81).

Based on current breast milk concentrations nationwide, it is estimated that at least 50% and possibly more of the babies born in the United States are exposed to quantities of PCBs sufficient to cause neurological effects (82). These findings provide evidence that contemporary PCB exposure is above "any regulatory guideline" (82, 247). The possible immunological and endocrinological consequences remain to be determined in these cohorts. A major concern is that some of these consequences may not become apparent until young adulthood or even middle age.

Accumulation of pollutants increases the probability of repeated or constant exposure but, as the literature on dioxin shows, administration at only one time in development, rather than the more likely chronic exposure, can profoundly affect the embryo, fetus, or perinatal infant. Ample evidence exists from both *in vivo* and *in vitro* studies that dioxin can antagonize the action of estrogen in some estrogen target cells (83,84), although this effect does not appear to be due to dioxin binding to estrogen receptors (11). The fact that dioxin is antiestrogenic is important because the conversion of androgen to estrogen in some target cells plays a critical role in masculinization (2). For example, a series of studies describing the dose-related inhibition (dose range: 0.064–1.0 µg/kg/body weight to the dam) of masculinization and persistence of feminine traits in male rat offspring whose dams were fed one meal of dioxin during pregnancy at a critical period during sexual differentiation illustrates the vulnerability of the male rat fetus *in utero* to administration of only one low dose of dioxin to the dam. In these studies the effects were not fully manifested until the rats reached adulthood (85–87). These effects would be expected from either chronic, low-dose exposure to dioxin before pregnancy or to a single exposure during a critical time in pregnancy.

Dioxin accumulates in human tissue and is generally found in all tissues of people living in developed countries (88). However, only the toxic congeners of the dioxin family complex bioaccumulate in human breast milk (88). Similarly, these chemicals have also been found in follicular fluid obtained during *in vitro* fertilization procedures in women (89). Although direct correlations have not yet been reported between reproductive success and the presence of xenobiotics in the follicle, these substances could disrupt oocyte development (19,90,91).

Many endocrine-disrupting chemicals have been reported in the reproductive tissues of men and women (74). These lipid-soluble compounds appear to sequester in all fatty tissue in the body, so that organs and tissues with higher fat content hold

more of the compounds on a wet weight basis (73). Little is known about the concentrations in embryos and fetuses other than they appear to be similar to those in mothers (73,92). Of considerable concern is bioaccumulation of organochlorine chemicals in breast milk due to its high lipid content, which leads to a much higher concentration in breast milk than in maternal blood (73). It is well documented that the infant is exposed to higher concentrations of many of these chemicals during breastfeeding than at any other time in its life (74).

Consideration should also be given to the fact that man-made chemicals, such as DES, which bind to estrogen receptors in cells, do not bind to estrogen-binding plasma proteins (93). One function of estrogen-binding plasma proteins, such as sex-steroid binding globulin in humans, is to restrict entry of endogenous estrogen into cells (94). As a result of this affinity, only a small fraction of the total endogenous estrogen in blood is able to pass into cells. This is particularly important during pregnancy when the concentration of estrogen-binding plasma proteins increases dramatically (2,95). It is possible that estrogenlike chemicals may show low or no binding affinity to estrogen-binding plasma proteins. These chemicals may be able to freely enter cells (similar to DES), which would greatly increase their biological activity relative to similar blood concentrations of endogenous estrogen, most of which is inhibited from entering cells. This would contribute to the *in vivo* effectiveness of these pollutants, many of which show lower binding affinity to estrogen receptors than the most potent endogenous estrogen, estradiol-17β (4). Environmental pollutants with estrogenic activity are less potent agonists for the induction of proliferation of breast cancer cells *in vitro* (8).

Summary

The deleterious effects of endocrine-disrupting chemicals in the environment on the reproductive success of wildlife populations have been documented; this is not an isolated problem, and today many wildlife populations are at risk. At present, no coherent policy has been articulated to remedy this problem. This is due in part to the lack of knowledge concerning which of the many chemicals present in the environment are responsible for endocrine-disrupting effects. Regulatory agencies should recognize that the current endpoints of most tests to assess the risk of pesticides and other pollutants (carcinogenicity, acute toxicity, and immediate mutagenicity) have led to the misconception that these chemicals do not pose a threat to the health of wildlife, domestic animals, or

humans. Although the effects of mutagens can be seen immediately in terms of gross abnormalities, the consequences of fetal exposure to endocrine-disrupting chemicals would likely not be recognized until young adulthood, at which time abnormalities, particularly relating to the function of the reproductive system, become apparent.

Because endocrine-disrupting chemicals are in most cases neither mutagens nor acute toxicants at ambient concentrations, they may be released without proper caution into the environment. This may be partially remedied by screening for hormone agonistic and antagonistic activity using hormone-responsive cells in culture; this procedure identifies compounds that are endocrine disruptors because they are hormonally active (8). Although this procedure cannot rule out chemicals devoid of hormonal activity that may disrupt development through other mechanisms, it can at least rule out compounds like DDT, chlordane, alkylphenols, and some PCBs, which are estrogen agonists. It is also essential to continue to examine transgenerational effects in animal studies because some pollutants require metabolism *in vivo* to exert hormonal effects and because neurobehavioral and other developmental effects cannot be addressed with *in vitro* models (96,97).

Wildlife species have provided the model for maternal transfer of environmental endocrine-disrupting chemicals with their resulting suite of effects in offspring; experiments with laboratory animals have confirmed the findings. In humans, the DES model is clear and traceable. However, for clinicians and public health authorities, the implications of these findings regarding man-made endocrine disruptors present in air, water, and food for human health is just coming to light. Transgenerational exposure, hormonal activity, functionality, and delayed expression of effects must be addressed when determining the hazards of exposure to persistent chemicals already in the environment and of new chemicals that might be released in the future.

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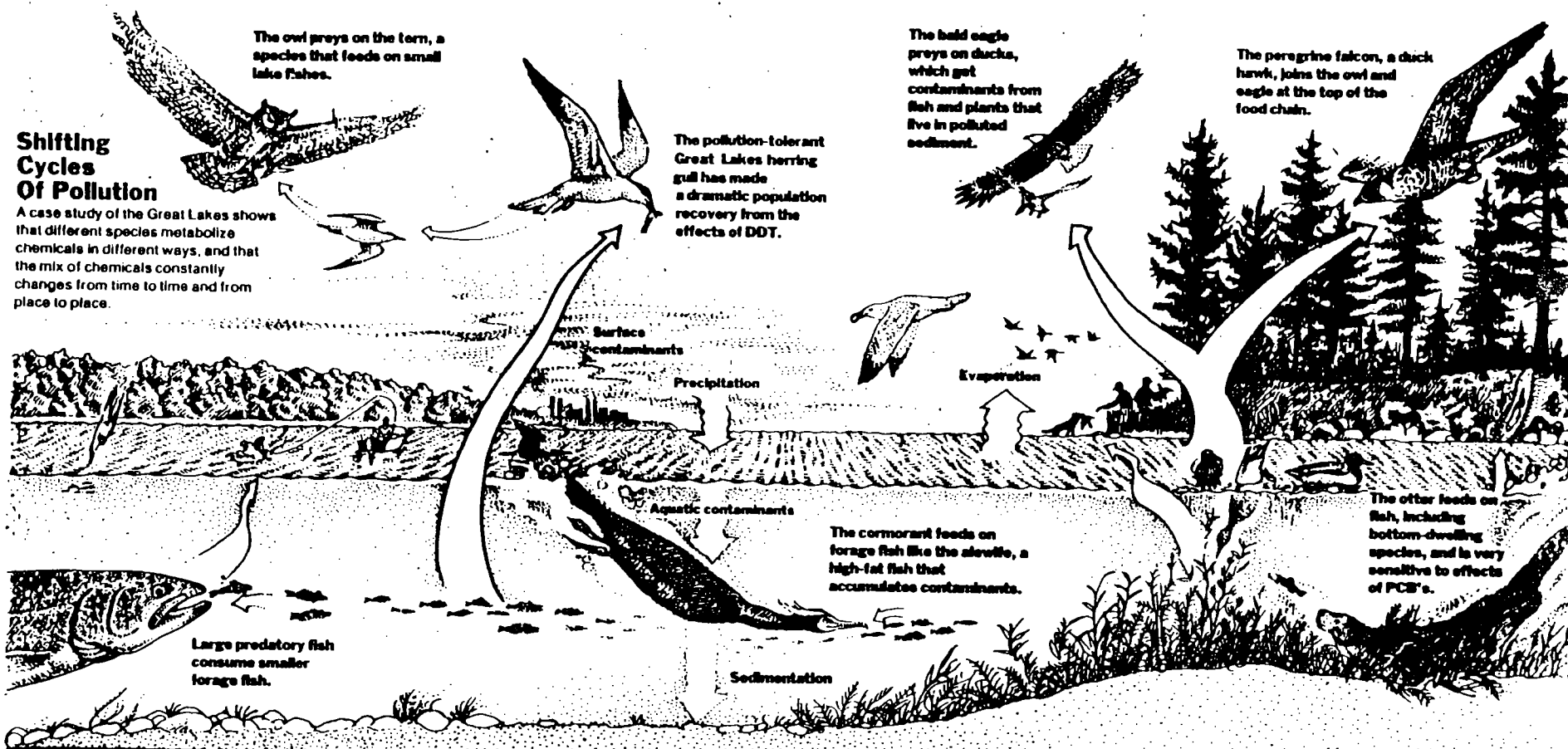
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Pesticides May Leave Legacy of Hormonal Chaos



Sources: Dr. William Bowerman/Michigan State University; U.S. Fish and Wildlife Service

The New York Times Illustration by Glenn Warr

By WILLIAM K. STEVENS

In a new wave of concern about synthetic chemicals in the environment, some biologists are warning that trace amounts of pesticides and other man-made substances may be interfering with the action of reproductive hormones and thereby damaging the fertility of various animal populations, including humans.

The evidence is far from conclusive. But the economic and political stakes are high; should the new fears prove justified, a large group of important industrial chemicals might have to be curbed.

At least 45 synthetic chemicals, most of them pesticides, have been found to be the kings of the

hormonal, or endocrine system, and for this reason they are known as endocrine disruptors. There is little doubt, many scientists agree, that when people or animals are exposed to large doses of these chemicals, as has happened in chemical spills or contamination of food, serious derangements of reproductive function sometimes result. Male alligators born in Florida's Lake Apopka after a large pesticide spill in 1986 were found to be incapable of producing sperm. In Taiwan, reproductive and other defects have been noted in the sons of women who in 1978 and 1979 ingested cooking oil contaminated with PCB's.

The question at issue is whether trace amounts of these chemicals that are widely distributed in the environment are exerting a less visible but pernicious effect on the reproductive fitness of many species of wildlife and possibly even humans.

Reproduction may be disrupted, but experts differ on damage.

For at least some wildlife populations, "I'd say we are on a fast track to extinction," said Dr. Theodora Colborn, a zoologist with the World Wildlife Fund, a conservation organization in Washington, who is a leading exponent of the view that endocrine disruptors pose a potentially serious threat. "You would see the same thing to happen with human populations."

Other experts disagree. "I don't think it is a huge problem at this point," said Dr. J. Goldsworthy, a

toxicologist with the Chemical Industry Institute of Technology, a nonprofit research organization at Research Triangle Park, N.C., that is largely supported by industry. Said Dr. Tom Orme, a Washington-based toxicologist with the American Council on Science and Health in New York, which has long held claims of harm from chemicals in the environment to be exaggerated: "We suspect there is a lot of baloney here. On the other hand, to develop the hard science to refute it is going to be a formidable task."

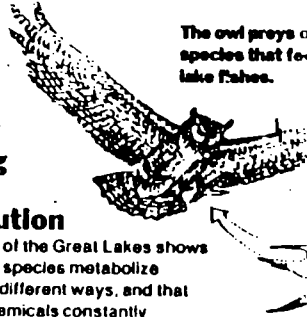
Still other experts view the issue as possibly serious but say it is too early to call it one way or the other. "We don't want to argue we've got a massive problem," said Dr. Larry Reller, the director of the Environmental Protection Agency's Health Effects Research Laboratory.

Continued on Page C6

Pestici

Shifting Cycles Of Pollution

A case study of the Great Lakes shows that different species metabolize chemicals in different ways, and that the mix of chemicals constantly changes from time to time and from place to place.

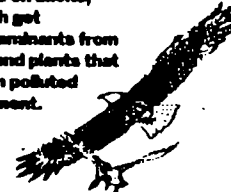


y Leave Legacy of Hormonal Chaos



The pollution-tolerant Great Lakes herring gull has made a dramatic population recovery from the effects of DDT.

The bald eagle preys on ducks, which get contaminants from fish and plants that live in polluted sediment.



The peregrine falcon, a duck hawk, joins the owl and eagle at the top of the food chain.



Surface contaminants

Precipitation

Evaporation

Industrial Chemicals May Disrupt Reproduction of Wildlife



World Wildlife Fund

Dr. Thomas Goldsworthy, left, of the Chemical Industry Institute of Technology; Dr. Lynn Goldman, center, of the Environmental Protection Agency; Dr. Theodora Colborn of the World Wildlife Fund.

Continued From Page C1

ry at Research Triangle Park. But he also said, "I don't think we want to argue there is no problem."

Although many biologists are convinced that endocrine disruptors are pervasive, they have not yet been able to assess the quantity and distribution of the chemicals in the environment. Nor is there any good survey to tell what burden of these chemicals is carried in the body fat of the general population.

But a number of studies suggest grounds for concern, particularly from the combined effects of several different chemicals acting in concert either to mimic or block the crucial effects of natural estrogens on sexual development in the fetus.

Dr. Ana M. Soto and Dr. Carlos Somerschn, biologists at Tufts University, have found that doses of estrogen-mimicking pesticides too small to have any effect individually on test-tube cultures of cells from breast-cancer tissue have a powerful effect when combined. Estrogens spur the growth of such cells. Other laboratory studies have shown that the synthetic chemicals can disrupt the reproductive development of mammal fetuses. And field investigations have traced reproductive dis-

In Great Lakes, birds have recovered as toxic burden fell.

orders in mammals and birds to the consumption of fish whose flesh contained the chemicals.

Dr. Colborn, Dr. Soto and others who are alarmed about endocrine disruptors say that all chemicals that reach the environment should be tested for their hormonal effect just as they are already tested for ability to cause cancer or mutations. Some environmentalists are calling for a phaseout of endocrine-disruptor chemicals, and already there is legislation before Congress to replace some chlorine compounds, many of which have been identified as endocrine disruptors, with feasible alternatives. The E.P.A. and the United States Fish and Wildlife Service have asked the National Academy of Sciences to investigate the problem. Meanwhile, those who are raising the alarm about endocrine disruptors have been energetic in seeking attention in the press and on television, where the subject has lately been explored, sometimes in apocalyptic tones.

The debate is in some ways a replay of "Silent Spring," Rachel Carson's landmark book published in 1962, in which she argued that fat-soluble pesticides in the bodies of birds were interfering with reproduction. Her thesis provoked a barrage of criticism, but biologists in time learned that many chlorinated hydrocarbons like DDT do indeed sabotage reproduction, for example by making the shells of birds' eggs too fragile.

Persistent Chemical Residues

DDT and similar pesticides like aldrin and dieldrin were banned long ago in the United States. But their residues persist in the environment, not the least because they remain in use in much of the world and are being transported to America on globe-girdling winds.

Moreover, there are many industrial chemicals that are hormonally active and that may find their way into the environment even though, unlike pesticides, they are not deliberately released. These include some members of a family of chemicals known as alkyl phenols, which Dr. Soto has found to have estrogen-like effects. These chemicals are used in plastics, including some food wrappings, as well as in several industrial processes, in paper and pulp production, textiles, hair colorings, spermicides and condom lubricants and as inert ingredients in pesticides. They are also used in industrial detergents, and their estrogenic components are released into the environment when the detergents break down. Dr. Soto has found that some of the chemicals can leach out of plastic containers and contaminate the con-



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World Wildlife Fund (WWF) is the largest private U.S. organization working worldwide to conserve nature. WWF works to preserve the biodiversity on Earth and the health of ecological systems by protecting critical species and their habitats, conserving wildlands by meeting human needs, and preventing pollution and reducing wasteful resource consumption.

**PHOTOCOPY
PRESERVATION**

For decades, wildlife have sent warning signals about the dangers of chemical pollution. These dangers were first brought to widespread public attention in 1962 by Rachel Carson in her book *Silent Spring*.

In 1990, a report by World Wildlife Fund (WWF) and Canada's Institute for Research on Public Policy revealed a wide range of problems among 16 animal species in the Great Lakes region. This study, *Great Lakes, Great Legacy?*, noted reproductive and endocrine problems in bald eagles, beluga whales, lake trout, mink, snapping turtles, and other species. In each case, elevated concentrations of industrial chemicals and pesticides were found in the species.¹

THE WINGSPREAD STATEMENTS ON SYNTHETIC CHEMICALS

In July 1991, at the Wingspread Center in Racine, Wisconsin, WWF Senior Scientist Dr. Theo Colborn, who synthesized the wildlife research for *Great Lakes, Great Legacy?*, convened a work session of scientists representing a wide range of research specialties, from medical anthropology to wildlife toxicology, to share findings about the effects of chemicals on wildlife and human health, particularly the endocrine system, which controls development and reproduction.

Of particular concern to the Wingspread participants were "synthetic hormones," manmade chemicals that can mimic or interfere with the body's natural chemical messengers and disrupt normal development. Even tiny doses of these chemicals can have far-reaching effects on wildlife and humans. If present during the early stages of fetal development, especially when the major organs are still being formed and the brain is being programmed to control and respond to hormonal signals throughout life, synthetic hormones may trigger a cascade of damaging biochemical changes that affect development of the nervous, immune, endocrine, repro-

ductive, and digestive systems. These effects are usually irreversible.²

In a pioneering consensus statement that has had a broad impact on subsequent governmental and academic research and thinking about policy, the Wingspread conference participants declared, "We are certain of the following: A large number of manmade chemicals that have been released into the environment, as well as a few natural ones, have the potential to disrupt the endocrine system of animals, including humans."

As evidence continued to mount, a second Wingspread work session, "Environmentally Induced Alterations in Development: A Focus on Wildlife," was held in December 1993, producing an even stronger statement. "Declines in a number of species," participants declared, "are in progress on the North American continent. Some of these declines are related to exposure to manmade chemicals. Such declines are not solely a U.S. or North American problem but are occurring on a global scale....Populations of many long-lived species are declining, some to the verge of extinction, without society's knowledge."

CHEMICALS IN THE ENVIRONMENT

The manufacture and use of chemicals has grown rapidly since the end of World War II. Production of synthetic organic chemicals in the United States, as reported to the U.S. International Trade Commission, amounted to 197.5 billion kilograms in 1992—that is, 435 billion pounds, or more than 1,600 pounds for each person in the country.³ Chlorine-based chemicals are among the most common of the organic chemicals. There are now about 15,000 of them, which is more than 20 percent of all chemicals in U.S. commerce.⁴ They are used for many purposes: in drinking water, bleach, pesticides, pharmaceuticals, dry cleaning, and vinyl for building materials, cars, toys, and other products.

Although harmful effects have been associated with nonchlorinated chemicals—styrenes, phthalates, mercury, lead, cadmium, parathion, for example⁵—chlorine-based chemicals have been at the heart of recent controversy because of their widespread use and history. Many of the known or suspected “synthetic hormones” are chlorine-based. Some of the most notorious members of the chlorine family—for example, DDT and various PCBs—have been found to be so hazardous that their use has been highly restricted in the United States. The known and unknown effects of the many chlorine-based chemicals still in use have raised increasing concern and led to calls for the phaseout of many uses.

The Clinton Administration’s recommendations for reauthorization of the Clean Water Act call for a task force on chlorine that would “develop a national strategy for substituting, reducing, or prohibiting the use of chlorine and chlorinated compounds.” This strategy is to be based on a comprehensive assessment of the use and impacts of chlorine and alternatives to it in four key industries: pulp and paper, solvents, plastics, and publicly owned water treatment plants and drinking water systems.⁶

TESTING FOR HARMFUL EFFECTS

Underlying and amplifying the concern about chlorine and other chemicals is the fact that current methods of toxicity testing do not provide an adequate basis for establishing policies to safeguard against all of the harmful effects of chemicals. For more than two decades, scientists and government regulators have largely focused their attention on identifying and controlling chemicals that cause cancer, gene mutations, acute toxic effects, and visible birth defects. Even with this narrow focus, screening has not been comprehensive; although pesticides have been tested routinely, tens of thousands of industrial chemicals have never been

screened. Moreover, we do not have adequate data on what other consequences exposure to these chemicals in the environment may have for wildlife and humans.

Testing chemicals for developmental effects is problematic. The damage that researchers are now uncovering occurs before or soon after birth but in many cases does not become fully evident until adulthood. Moreover, the timing of exposure to “synthetic hormones,” for example, can be crucial: Even a single exposure at a very low dose can have major effects if it occurs at a critical time. Although small doses of certain chemicals during fetal development can cause significant damage, much greater or accumulating doses later on may have no apparent impact; and thus adults may seem to escape harm while their offspring suffer it. This also means that short-lived chemicals could be as dangerous as those that persist in the environment.⁷

Risk assessment has generally been based on high-dose testing for a single “endpoint” such as cancer or mortality. This model does not work in the case of developmental disruption where the endpoints are numerous and unpredictable, and where one chemical is capable of causing many different effects. Cancer and mortality are relatively easy endpoints to monitor compared with functional losses such as learning disabilities, reproductive difficulties, and immune system problems, which can be manifested at different times in life and vary from slight to intense.⁸

In scientific literature, the Wingspread statements, and other forums, WWF’s Colborn and other scientists have warned that ignoring the danger signals of damage to reproductive systems and deterioration of other essential functions could have devastating consequences for life on this planet. Current screening processes simply do not provide appropriate or adequate information for safeguarding the health of humans, wildlife, or the ecological systems on which we all depend.

CONFRONTING THE HAZARDS

Confronting the hazards of harmful chemicals in the environment requires action on several fronts.

First, we must go beyond using the incidence of cancer and other gross health defects as the major criterion for determining research and regulatory priorities. Testing should be broadened to screen for hormonal activity and other endocrine-disrupting effects before chemicals are introduced into commerce. Testing should also be done on chemicals now in use and on persistent, bioaccumulative chemicals released in the past.

Second, we need a major, multi-disciplinary research initiative to investigate the effects of toxic chemicals on development in wildlife and humans. Research efforts in this area must be put into the mainstream and coordinated through institutions such as the Agency for Toxic Substances and Disease Registry, National Institute of Environmental Health Sciences, Environmental Protection Agency, National Academy of Sciences, or the proposed National Institute on the Environment. The evidence that we now have points toward frightening possibilities. We simply do not know what we need to know about the harmful effects of chemicals.

Third, we must begin collecting information from regions beyond North America and Europe. Little is known about the presence of toxic chemicals and their effects on wildlife in Latin America, Africa, and Asia. Obtaining this information is vital to protecting the world's biological diversity.

Fourth, because of the widespread use and particular hazards already associated with organochlorines, we need a strategy for assessing their impacts and opportunities for reducing their use. A task force such as that proposed by the Clinton administration, including representatives of government agencies, university-based researchers, and policy experts, could help insure that a comprehensive assessment of impacts and alternatives will lead to action by both the public and private sectors.

Fifth, neither the scientific community nor government agencies can afford to wait for answers to every research question before taking action. Efforts to reduce the hazards of toxic chemicals must proceed, using information provided by ongoing studies as the basis for creating new and more effective approaches for dealing with these chemicals.

Finally, although much research lies ahead in better understanding the effects of toxic chemicals, it is clear that prevention—using cleaner production processes and materials—is the best response. “It is vital,” says Colborn, “that we focus attention on preventing pollution instead of simply trying to control it after it has been created. We must reconsider how we use materials in industry, agriculture, commerce, and our domestic lives. If we don’t, we are putting the diversity of life on Earth on a fast track to extinction.”⁹

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SOCIETY

The Estrogen Complex

Science: Sperm counts down? Penises shriveled? Hey, Rush, don't blame it on feminists. It may be from chemical pollutants in water and food.

ALL LOUIS GUILLETTE WANTED to do was to help figure out how many alligators could be hunted from Florida's Lake Apopka without making the population crash. But after years of wading (carefully) through the thigh-deep muck and sneaking up (warily) on alligator nests to snare the great reptiles with a noose, it dawned on him that the gators had bigger worries than winding up as pocketbooks. Male alligators' penises were only one quarter the normal size; their testosterone levels were so low they were probably sterile. Soon after, Guillette met a researcher who had seen similar effects on lab mice exposed to a cousin of the chemical DDE, formed when DDT decomposes. Not coincidentally, thousands of gallons of DDT-containing pesticide had spilled into Lake Apopka in 1980. Connecting the dots, Guillette said, "I think we have a problem here." By "we," he didn't mean alligators. Because people live in a sea of the same gender-bending chemicals, the University of Florida researcher recently told a congressional panel, "every man in this room is half the man his grandfather was."

It is a plot twist worthy of science fiction. Hundreds of the bedrock chemicals of the postwar age—PCBs used in the manufacture of electronics, pesticides such as endosulfan and atrazine, polycarbonate plastic found in many baby bottles and water jugs, chlorine compounds that bleach paper—resemble the human sex hormone estrogen. Although the compounds were concocted in the lab for purposes having nothing to do with human biology, their molecular structure turns out to be so similar to estrogen's that they fit into the same "receptors" in the body. (Contrary to popular belief, men as well as women produce estrogen, and so have receptors for the hormone.) The estrogen receptor can no more tell that it's being occupied by an impostor than a door lock can tell that a thief's skeleton key has been inserted. As a result, the estrogen mimics can trick the body into turning off, or ratcheting up, certain biochemical pathways—especially those in the reproductive system. The result: sexual development, in both males and females, gone seriously askew. Since the impostors find their way into the

soil, water and food supply, researching their effect on health "is a top priority for us," says Kenneth Olden, director of the National Institute of Environmental Health Sciences. "There's enough science out there to tell us we should be concerned."

For one thing, "half your grandfather" is no hyperbole. Since 1938, sperm counts of

ground" levels of estrogenlike chemicals are responsible for the decline and fall of Western manhood, the case against high levels of the chemicals is clear-cut. In Michigan, estrogen mimics called PBBs accidentally got into cattle feed in 1973, and from there into beef. Women who ate the meat, and whose breast milk harbored high levels



JOE McDONALD—ANIMALS ANIMALS

UNMANNED

Alligators in a Florida lake have abnormally small penises and low testosterone levels.

MOTHER'S MILK

Pollutants in body fat enter the blood and milk during pregnancy and lactation.



DAG SUNDHOLM—IMAGE BANK

men in the United States and 20 other countries have plunged by an average of 50 percent, reported Danish endocrinologist Niels Skakkebaek in 1991. At the same time, testicular cancer has tripled. The trends could be a coincidence. But Skakkebaek suspects that the culprit in both the sparse sperm counts and the cancers may be men's exposure, as fetuses and newborns, to estrogenlike chemicals in their mothers' blood and milk.

While it's too soon to say that "back-

Gender Bender

AN ESTROGEN CRYSTAL

Hundreds of pollutants mimic estrogen's molecular shape. In males they may cause cancer and reproductive defects.

of PBBs, had sons with testicular malformations and undersized penises. And in the closest thing to a controlled study in such a tricky field, Chinese scientists have been studying 118 boys in Taiwan who were born to women exposed to a PCB spill in 1979. Compared with boys whose mothers were not exposed, the 118 suffered reproductive defects like those of the boys in Michigan. These abnormalities "were probably related to hormonal changes caused by toxic exposure," the scientists conclude.

Now physicians are analyzing studies that link estrogenlike pollutants to breast cancer and endometriosis, the painful inflammation of the uterine lining that often

causes infertility. Perhaps the oddest thing about endometriosis is that there were only 21 reported cases in the world 70 years ago; today there are 5 million in the United States alone. In a new German study, women with endometriosis were more likely than others to have high levels of PCBs in their blood. Some breast cancer may also have an environmental cause. Unusual amounts of DDE, the pesticide residue that seems to be leaving the alligators shortchanged, shows up in the tissue of women with breast cancer, according to a study last year by Mary Wolff of New York's Mount Sinai School of Medicine. Women with the greatest number of these DDE footprints were four times more likely to get breast cancer than women with the fewest such signs. The connection is plausible. This year the National Cancer Institute will begin a major study of the high rates of

genlike pesticides, have their own reproductive problems: more infertile females, sterile males, lower sperm counts and high estrogen levels. One male, says toxicologist Charles Facemire of the U.S. Fish and Wildlife Service, "had estrogen levels higher than most females."

Despite such findings, "much of the evidence [about estrogen mimics] is circumstantial," says Thomas Goldsworthy of the Chemical Industry Institute of Toxicology. Although there is no question that the pollutants fit the body's estrogen receptors, there's still some wiggle room to argue that the chemicals do not switch on the same biological pathways that real estrogen



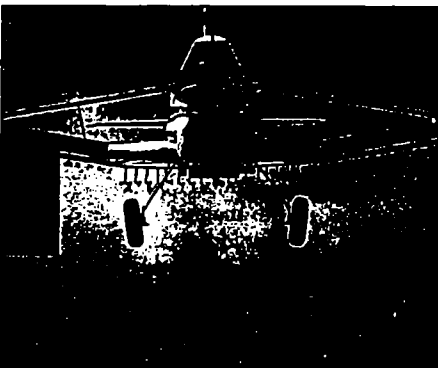
DAVID M. PHILLIPS—PHOTO RESEARCHERS

SHOOTING BLANKS

Men's sperm counts are down 50 percent since 1938, says one study.

CROP DUSTER

Among the chemicals that mimic estrogen are widely used pesticides.



ROBERTO VALLADARES—IMAGE BANK

breast cancer on New York's Long Island, assessing women's exposure to estrogen-like compounds in pesticides once used on the potato fields (and still in the aquifers) where suburbs now sprout.

Playing canary in the coal mine, wildlife "was the first to send signals that something was seriously wrong," says zoologist Theo Colborn of the World Wildlife Fund. Fish in places like the Great Lakes, where PCB and DDT concentrations are extremely high, and the terns and gulls that eat them, are becoming biochemical hermaphrodites: the males have reproductive parts of both sexes. Florida panthers, eating high on a food chain contaminated with estrogenlike pesticides, have their own reproductive problems: more infertile females, sterile males, lower sperm counts and high estrogen levels. One male, says toxicologist Charles Facemire of the U.S. Fish and Wildlife Service, "had estrogen levels higher than most females."

Does. Skeptics also ask why, if the ubiquitous estrogen impostors really trigger cancers and other diseases, rates of the illnesses are not higher. Lawmakers may not wait for an answer. In February, the Clinton administration called for an 18-month study of chlorine (a component in many estrogenlike chemicals) to assess its effects on human health and the environment, with an eye toward restricting or banning it. A bill in Congress would phase out chlorine in the paper and pulp industries over five years. Hell has no fury like a congressman who discovers he's not the man he thought he was.

SHARON BEGLEY with DANIEL GLICK

And Now the Good News

NOT ALL ESTROGENS, OR ESTROGEN impostors, twist sexual development and increase the risk of cancer. Just as there is good cholesterol and bad cholesterol, there is good estrogen and bad estrogen, forms of the hormone that differ by only a few molecules. As Devra Lee Davis, a senior scientist at the Department of Health and Human Services, puts it, "All estrogen is not equal." Her theory is that when the body manufactures estrogen, the hormone can be broken down by either of two biochemical pathways. One leads to a form called 16-hydroxyestrone, which can damage DNA and so is the form suspected of spurring breast and testicular cancers. The other leads to a form called 2-hydroxyestrone that does no harm, and may even do good.

Many edible plant products, such as French beans, soybeans and pomegranates, contain "phytoestrogens" that might combat cancer, suggests Kenneth Setchell of the Children's Hospital Medical Center in Washington. In his lab, rodents that are fed soy protein develop fewer tumors than those on a soy-free diet. This might help explain why women in Japan have low rates of breast cancer when they eat tofu, soy sauce and miso—all rich sources of good estrogen—but have "American" rates when they move to the United States and adopt a Western diet. Compounds in such "healthy" foods as broccoli, says Davis, might nudge estrogen down the path to the cancer-fighting form.

Last fall Victor Henderson of the University of Southern California reported a tantalizing link between estrogen and a lower risk of Alzheimer's disease: in a group of 2,418 postmenopausal women, those who took estrogen pills (for such problems as osteoporosis and hot flashes) were 40 percent less likely to develop this crippling dementia than those who did not take estrogen. In rats, estrogen helps make a "growth factor" that maintains and strengthens connections between neurons. It also helps produce an enzyme that speeds communications among neurons. The effect seems to be particularly strong in memory centers, the first to be ravaged by Alzheimer's.

■ ENVIRONMENT

Not So Fertile Ground

Some scientists fear that pollutants are damaging human reproductive systems

By MICHAEL D. LEMONICK

THE ALARM WENT OFF WITH RACHEL Carson's 1962 book *Silent Spring* and has been sounding ever since. We live, environmentalists warn, in a world laced with dangerous chemicals, from powerful pesticides to toxic industrial wastes like dioxin and PCBs. Despite periodic waves of public concern and efforts at government regulation (the 1972 banning of DDT in the U.S., for example), the chemicals are still found in small but measurable amounts in air, water, soil—and our own tissues. Many scientists have long argued that even tiny doses of pollutants can cause cancer in humans, but the contention is hotly disputed. Other researchers maintain that traces of man-made chemicals are no more likely to cause tumors than are the countless chemicals produced by Mother Nature.

Now, even as the cancer debate continues, environmental groups are pointing to a different, previously unrecognized threat. Chemical pollutants, they say, can interfere with one of the most basic of biological functions: the ability to reproduce. The chemicals allegedly disrupt the action of hormones, those all-important molecular messengers that regulate just about all bodily activities, including growth and reproduction. The result may be a variety of harmful effects that could decrease fertility. Among them: testicular cancer and reduced sperm counts in men, uterine abnormalities and miscarriages in women. While there is no hard evidence that pollution is affecting human fertility in the U.S. or anywhere else, the theory is likely to grab the attention of millions of couples who have trouble conceiving.

The Environmental Protection Agency is expected to raise the issue this week when it releases a major report on the effects of dioxin, one of the most ubiquitous of the suspect chemicals. Dioxin is the name given to a class of chlorine-containing compounds that are waste by-products of many industrial processes such as paper making and waste incineration. Although the release of dioxin has been curbed in recent years, traces of it still permeate the environment.

According to sources familiar with drafts of the EPA report, it will say that diox-

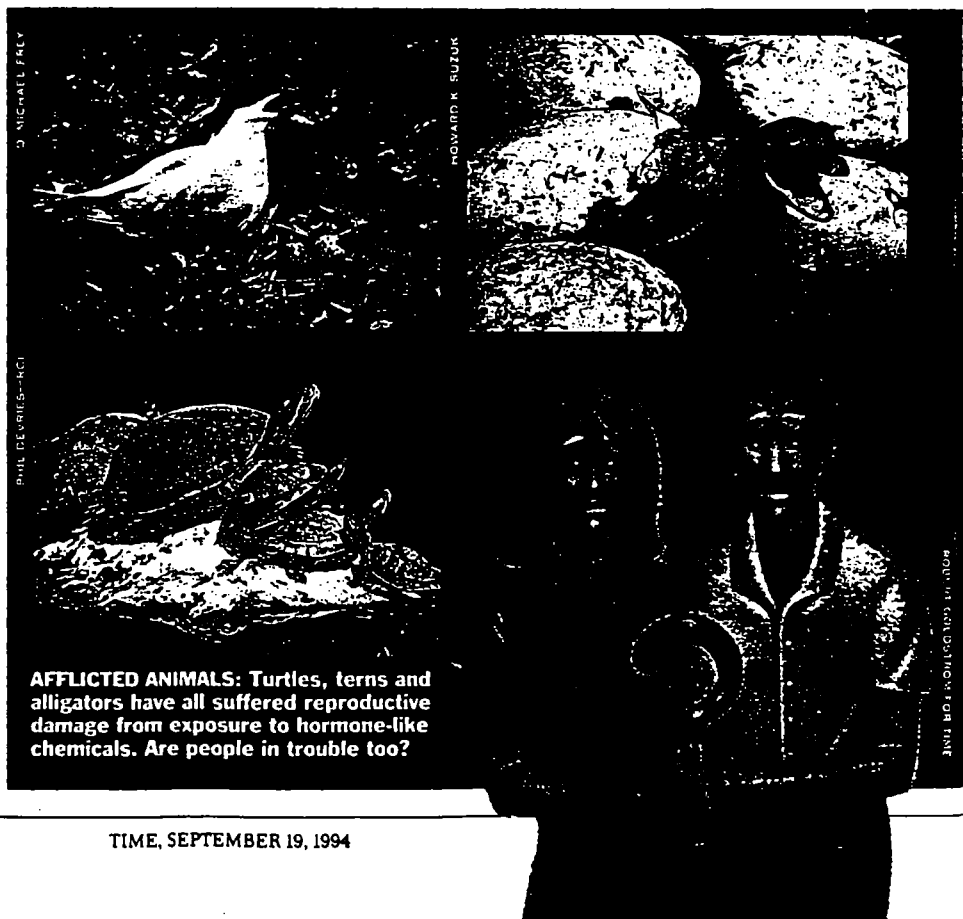
in remains a serious potential threat to human health and that possible links between the chemical and health problems, among them reproductive ills, should be further explored. "This study ranks with the Surgeon General's pronouncement that smoking causes lung cancer," says Sierra Club pollution expert George Colling, prematurely and hyperbolically, in the latest issue of the organization's monthly newspaper. And Peter deFur of the Environmental Defense Fund predicts that the document will lead to much tighter regulations, and in some cases even a ban, on the release of dioxin and related chemicals.

Well, maybe. But many scientists who have looked into hormone-disrupting chemicals say the issue is much more complex than environmental activists would have people believe. In high doses, the compounds in question, many of which contain chlorine, are clearly toxic and carcinogenic. On the other hand, the case that humans are being affected by very low concentrations remains far from certain. The existing evidence is largely circumstantial,

based on extrapolations from animal studies, laboratory work on the chemistry of dioxin and other molecules, and statistics on human disease that may or may not turn out to be accurate or relevant.

But most investigators agree that although the danger has not been proved, it is too plausible to ignore. The chain of reasoning goes something like this: animals exposed to high doses of these pollutants in the wild develop reproductive abnormalities. Animals exposed to low doses in the lab do too. Humans absorb comparable low doses simply by breathing, drinking and especially eating. Some of the suspect chemicals have physiological effects similar to those of estrogen and other sex hormones, or they at least interact with them; they might reasonably be expected to interfere with processes involving these hormones, such as the menstrual cycle and sperm production.

Finally, several hormone-related human disorders, including low sperm counts, testicular and breast cancers and endometriosis (a painful condition in



AFFLICTED ANIMALS: Turtles, terns and alligators have all suffered reproductive damage from exposure to hormone-like chemicals. Are people in trouble too?

which uterine cells migrate to other parts of the pelvic area), have arguably been on the rise in the decades since DDT, dioxin and the like first entered the food chain. Says Thomas Burke of the Johns Hopkins School of Public Health: "What we have now is identification of a potential hazard, and that's all we have. What the implications are we don't know yet, and we need to clarify that."

Suspicions about hormone disruptors were raised a few years ago by Theodora Colborn, a zoologist with the World Wildlife Fund who did a study on the reproductive health of Great Lakes wildlife in the late 1980s. Colborn discovered that the young of 16 predator species, including fish, birds, reptiles and mammals, were failing to survive to adulthood or could not reproduce if they did. All the animals ate fish from the Great Lakes, which were contaminated with a variety of hormone-like chemicals.

Colborn suspected a cause-and-effect relationship between pollution and fertility problems—and by extension a possible danger to humans. She began collecting human epidemiological studies, which suggested to her that human fetal exposure to such chemicals as PCBs could produce disorders affecting behavior, immune-system functioning, memory and learning. She also surveyed the literature on humans exposed to diethylstilbestrol, or DES, a synthetic drug that is related to estrogen. DES can be used to prevent miscarriage, treat prostate and breast cancer or reduce the



ECO-SLEUTH: Colborn set out to discover what was wrong with Great Lakes wildlife.

symptoms of menopause; it can even promote growth in sheep and cows. But in 1971, after studies linked its use by pregnant women with reproductive-system abnormalities, infertility and cancer in their offspring, the FDA decreed that DES should no longer be used to prevent miscarriage. In 1979 the drug was banned in livestock because traces were showing up in meat.

Since no one seemed to be studying the impact of chemicals on reproduction in any systematic way, Colborn organized a 1991 meeting in Racine, Wisconsin, and invited 21 scientists representing 17 disciplines ranging from toxicology to zoology to endocrinology. "No one seemed to know what the others were doing," she says. "Most of the people didn't know anyone

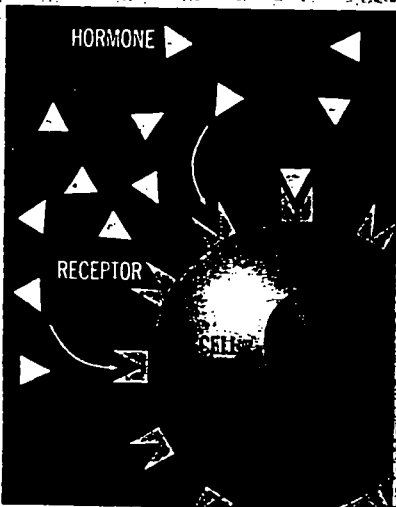
else in the room." Colborn also recalls that some of the participants were skeptical about the whole thing. Nonetheless, when they got down to discussing the problems Colborn and others had found in animals exposed to chemicals—thyroid damage, immune deficiencies, sexual abnormalities—a pattern emerged. Most of the problems involved malfunctions of the endocrine system that is responsible for producing hormones. Among the chemicals fingered by the group as probable culprits were DDT, kepone, triazine herbicides, certain PCBs and dioxins, styrenes and the alkyl phenols found in some detergents and plastics.

The conference gave rise to numerous collaborations, and participants began trading lab samples with one another and with a growing number of additional interested scientists. "We had gonads flying around the country," says Colborn. As the researchers compared notes, the evidence began to mount. During the mid-1980s, Colborn learned, mortality rates for alligator eggs in Lake Apopka, Florida, soared to 96%, in contrast to 57% in most Florida lakes. The almost certain cause: a 1980 chemical spill that included DDT. In 1993 researchers found that terns in PCB-contaminated Buzzard's Bay, Massachusetts, had reproductive-tract abnormalities including the presence of ovarian cells in male birds. Earlier studies had found similar problems with birds in California and the upper Midwest.

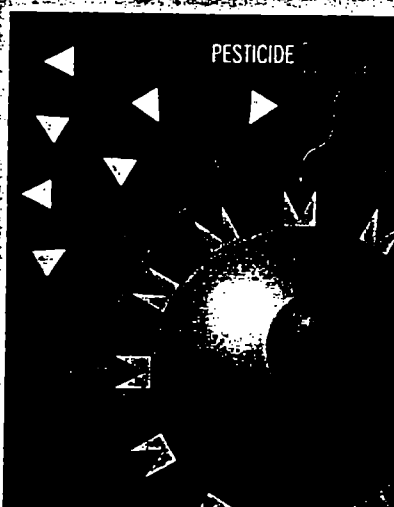
While most of these reports involve heavy doses of chemicals, evidence from laboratory studies suggests there are also effects at lower concentrations. Endocrinologist David Crews has discovered, for example, that small PCB doses can dramatically influence the ratio of male to female offspring in red-eared slider turtles. When University of Wisconsin toxicologist Richard Peterson investigated the impact of dioxin on male rats, he found that the dose needed to cause reproductive-system problems was relatively high. "But when we exposed pregnant rats to a dose 1/100th as large," he says, "we found the male offspring showed signs of reproductive dysfunction," including smaller sex organs, reduction in sperm counts and feminized sexual behavior. Peterson also found defects in lake-trout embryos exposed to dioxin.

What is especially disturbing about Peterson's work is that the levels of dioxin needed to do that kind of damage were as low as 64 nanograms per kg of body weight—only a little greater than the 5 or 10 nanograms of dioxin and comparable chemicals found in a typical kilogram of human tissue. It is not surprising that these compounds are so biologically active, since they are metabolized in a fashion similar to

CHEMICAL IMPOSTORS



1 Hormones are chemical messengers that regulate various processes in the body. The hormone's signal is received through receptors on the surface of or inside cells.



2 Chemicals from pesticides or other pollutants may mimic a hormone and attach to the receptors, either blocking the hormone's action or interfering with its effects.

natural chemicals. Says Linda Birnbaum of the EPA's Health Effects Research Laboratory, who was one of the driving forces behind the agency's decision to study dioxin: "You name almost every hormone system in the body, and dioxin interacts with it. And when you're dealing with hormones, they all talk to each other. When you ring one bell, many others chime."

But—and this is a big but—some species are more sensitive to dioxin than others. Just because rats and fish are affected in certain ways does not necessarily mean that humans will have comparable reactions. And doses that harm animals are not necessarily large enough to damage people. On the other hand, humans soak up many different chemicals, and the results may be cumulative.

Whatever the impact of pollutants on men and women, solid evidence is hard to come by. Even when a cause-and-effect relationship is established, as in major industrial accidents, the data are confusing. In the years after a large dioxin release in 1976 in Seveso, Italy, for example, the incidence of leukemias, lymphomas and soft-tissue cancers in men and gall-bladder and bile-duct cancers in women rose—but breast and endometrial cancers in women actually went down. Possible reason: dioxin may sometimes interfere with the hormone system in beneficial ways.

When scientists look for hormone disruption in the general population, the evidence is murkier still. Birthrates go up and down for many reasons that have nothing to do with pollution. While there are anecdotal reports that the number of infertile couples is on the rise, the phenomenon could be a result of their waiting too long to try for children. The incidence of testicular cancer is higher than it was two decades ago, but that could be because of better reporting. Even the strongest piece of evidence, a Danish study that seems to document a drop in sperm counts over the past 50 years, is considered inconclusive by some scientists.

None of these uncertainties will be cleared up quickly or easily. The fact that environmentalists and a group of concerned scientists have raised the issue of endangered fertility is likely to spur much-needed research. The evidence so far may not be strong enough to support sweeping government action, but it ought to prompt some companies to consider whether there are practical, economical ways to reduce their emissions of suspect chemicals. —*Reported by J. Madeleine Nash/Chicago and Mia Schmiedeskamp/Washington*

Keeping Cool About Risk

ALAR ON APPLES, RADON IN HOMES, ASBESTOS IN SCHOOLS: THE U.S. APPEARS to ricochet from one environmental crisis to another, with the result that policy aimed at reducing risks to human health frequently appears to make little economic or scientific sense. Even some environmentalists concur that decisions to rip asbestos out of school buildings were probably ill considered. In many cases, sealing the dangerous fibers in place would have provided a more prudent and less costly remedy. Similarly, while no one denies that homes with high levels of radon pose a health hazard requiring prompt attention, what about houses with much lower levels? Is it reasonable to urge that they too be radonproofed if there is no certainty that a danger exists?

Now environmentalists say dioxin and scores of other chemicals pose a threat to human fertility—as scary an issue as any policymakers have faced. But in the absence of conclusive evidence, what are policymakers to do? What measures can they take to handle a problem whose magnitude is unknown?

Predictably, attempts to whipaw public opinion have already begun. Corporate lobbyists urge that action be put on hold until science resolves the unanswered questions. Environmentalists argue that evidence for harm is too strong to permit delay. The issue is especially tough because the chemicals under

scrutiny are found almost everywhere. Since many of them contain chlorine or are by-products of processes involving chlorine compounds, the environmental group Greenpeace has demanded a ban on all industrial uses of chlorine. The proposal seems appealingly simple, but it would be economically wrenching for companies and consumers alike.

With the escalating rhetoric, many professionals in the risk-assessment business are worried that once again emotion rather than common sense will drive the political process. "There is no free lunch," observes Tammy Tengs, a public-health specialist at Duke University. "When someone spends money in one place, that

Protesting in Belgium, Greenpeace demands a phaseout of chlorine.

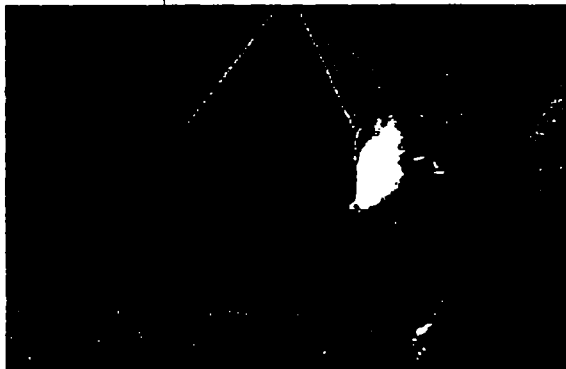
money is not available to spend on other things." She and her colleagues have calculated that tuberculosis treatment can extend a person's life by a year for less than \$10,000—surely a reasonable price tag. By contrast, extending a life by a year through asbestos removal costs nearly \$2 million, since relatively few people would die if the asbestos were left in place. That kind of benefit-risk analysis all too rarely informs the decisions made by government regulators.

As the EPA raises anew the dangers of dioxin, the agency needs to communicate its findings to the public in a calm and clear fashion. No one is eager to touch off the kind of hysteria that preceded the government's decision to move against Alar, the growth regulator once used by apple growers. When celebrities like Meryl Streep spoke out against Alar and the press fanned public fears, some schools and parents rushed to pluck apples out of the mouths of children. Yet all this happened before scientists had reached any consensus about Alar's dangers.

Rhetoric about dioxin may push the same kind of emotional buttons. The chemical becomes relatively concentrated in fat-rich foods—including human breast milk. Scientists estimate that a substantial fraction of an individual's lifetime burden of dioxin—as much as 12%—is accumulated during the first year of life. Nonetheless, the benefits of breast-feeding infants, the EPA and most everyone else would agree, far outweigh the hazards.

John Graham, director of the Harvard Center for Risk Analysis, suggests that people should strive to keep the perils posed by dioxin in perspective and remember other threats that are more easily averted. "Phantom risks and real risks compete not only for our resources but also for our attention," Graham observes. "It's a shame when a mother worries about toxic chemicals, and yet her kids are running around unvaccinated and without bicycle helmets."

—*By J. Madeleine Nash*



DANIEL GLEERENTS - GAMMA LIAISON

The Gender Bender

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Are environmental
"hormones" emasculating wildlife?

By JANET RALOFF

First in a two-part series

Mother Nature. The term conjures up images of a warm, nurturing, bountiful environment. But this sobriquet is proving increasingly apt for another reason — one that should offer anything but comfort.

New studies suggest that through pollution and other environmental factors, Mother Nature is exerting a feminizing hormonal influence on the animal kingdom.

Over the past 15 years, research has unmasked a number of "environmental hormones" — chemicals and pollutants that disrupt biological processes, often by mimicking the effects of naturally produced hormones such as the female hormone estrogen. On the ever-growing list of these agents are several restricted or banned pesticides — including DDT (and its even more toxic metabolite, DDE), kepone, heptachlor, dieldrin, mirex, and toxophene. Some polychlorinated biphenyls (PCBs) exhibit these disruptive properties, as do certain combustion pollutants, ingredients in plastics, and breakdown products of common detergents (SN: 7/3/93, p.10).

The hormonal activity of these chemicals usually bears little relationship to their intended function. Indeed, there is no way of predicting — based on structure or function — which compounds will exhibit a hormonal alter ego.

That fact troubles a number of scientists because such environmental hormones may be contributing to an increased risk of reproductive-system cancers in females. Moreover, prenatal exposure to hormone-like pollutants can derail the developmental processes that establish gender or ensure reproductive success.

While the health community has recently begun a host of studies to explore a possible link between estrogenic pollutants and cancers in women, few researchers have focused on the related reproductive risks such environmental hormones may pose for both sexes. That's unfortunate, says Theo Colborn, a zoologist with the World Wildlife Fund in Washington, D.C., because reproductive effects are likely to be "much more widespread."

Indeed, she notes, animal data are beginning to suggest that far smaller exposures are needed to trigger reproductive effects than to induce cancers.

And because some of these reproductive changes may be subtle, they could evade detection for decades — even a lifetime — unless hunted for explicitly.

Colborn has convened a number of symposia in the past few years for researchers who study reproductively impaired wildlife populations or laboratory animals exposed to environmental hormones. Most of these scientists, she says, describe the links they're finding between impaired reproduction and "hormonal" pollutants as sobering — if not downright scary.

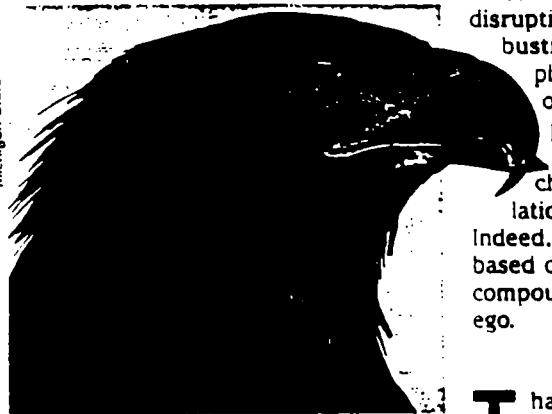
Indeed, she and many other environmental scientists worry that if hormone-like contaminants can feminize male animals, these ubiquitous pollutants may also underlie troubling reproductive-system trends being witnessed in men.

Some of the earliest data on unexpected reproductive risks posed by commercial chemicals came in the early 1950s. DDT, a potent and persistent organochlorine pesticide, was shown to cause the eggshells of many birds to thin. In fact, long after the compound was banned in 1972, DDT-thinned eggshells continued to put many embryonic birds — including bald eagles — at risk of being crushed to death.

DDT even wreaked havoc among birds resistant to eggshell thinning, such as sea gulls. Recognition of the extent of these problems, however, didn't emerge until decades after the initial reports of eggshell thinning.

Though heavily contaminated gull embryos managed to hatch, reproduction in gull colonies exposed to large amounts of DDT began to decline precipitously in the late 1960s. Biologists observed not only that many female gulls in these communities were sharing nests with other females — the so-called lesbian gulls — but also that the young within these communities bore grossly feminized reproductive tracts. Female gulls, which should have developed mature reproductive organs only on the left side, also carried

Michigan State Univ



Juvenile bald eagle collected in Michigan last year. Its life-threatening bill deformity may have been caused by exposure to estrogenic chemicals.

"We've been seeing many more deformities in recent years," reports David Best, a bald-eagle specialist with the U.S. Fish and Wildlife Service in East Lansing, Mich. "We've also seen some suggestion of deformities in the embryos [of eggs that didn't hatch]," he notes. Hatching rates within this population also fall below those seen in less polluted areas, such as inland Alaska. Reproduction in these birds starts to fall when PCBs in their bodies exceed 4 to 6 parts per million (ppm) or DDE exceeds 1 ppm. "We're finding very much higher levels than that around the Great Lakes," Best notes — such as eggs with PCB concentrations as high as 120 ppm.

vestigial oviducts on the right side. Many males also bore feminine characteristics, such as oviducts, recalls avian toxicologist D. Michael Fry of the University of California, Davis. Moreover, he notes, the males' left gonad "had tissues that were both ovarian and testicular — so it was an intersex, or hybrid, gonad."

To connect these effects with estrogenic pollutants, Fry and his colleagues conducted a number of experiments during the 1980s. In one, they injected eggs of contaminant-free gulls with estradiol or with an estrogenic pesticide such as DDT. When the hatchlings emerged, they exhibited the same array of feminized sex organs as DDT-contaminated Western gulls on Santa Barbara Island, off the coast of California.

In effect, DDT "chemically castrated" the males, Fry says. He suspects the males' likely lack of interest in mating explains not only why female gulls dominated Santa Barbara Island's breeding colony in the late 1960s and early 1970s, but also why the females cohabited.

More recently, Fry has turned his attention to the effects of other estrogenic pesticides and PCBs. This summer he began studying common terns, a relative of the gull. Fry studied male embryos from nests along New Bedford Harbor, Mass., located near a toxic waste site contaminated with PCBs. Only four of the 15 males that he analyzed appeared normal. The rest exhibited varying degrees of feminized sex organs.

When I never set out to do any toxicology," maintains Louis J. Guillette Jr., a reproductive endocrinologist at the University of Florida in Gainesville. But the team he heads has recently distinguished itself as one of the foremost in environmental-hormone toxicology. It all began six years ago, when the state of Florida asked him to find out what makes a good alligator egg.

Alligator ranching has become a multi-million-dollar industry in Florida, and ranchers wanted to know how many eggs they could harvest from the wild without jeopardizing the survival of this once-endangered species. So Guillette's team began surveying the hatching rate of eggs on various lakes: in all, more than 1,200 nests accounting for more than 50,000 alligator eggs.

It didn't take long, Guillette says, "before we realized there was something fundamentally different about one lake." It was Apopka, Florida's fourth largest freshwater body.

Whereas 70 to 80 percent of the eggs in most alligator nests hatched, between 80 and 95 percent of those from Apopka failed to hatch. Moreover, of the alligators that did hatch at Apopka, roughly half died within two weeks — a mortality rate at least 10 times that expected for such neonates.



Dunbar/PhotoDisc

Florida panthers. Researchers are investigating whether environmental hormones might help explain their testicular problems, puzzling sex-hormone concentrations, and falling fertility.

As one measure of the health of these animals, Guillette's team began two years ago to examine the fluid that leaks out of eggs at the time of hatching and to analyze it for estrogen and testosterone. In females, estrogen should predominate, whereas males should have more testosterone. Eggs from Lake Woodruff — with normal hatching rates — displayed those classic patterns.

Apopka eggs didn't. One group showed what at first appeared to be the normal female pattern. Another group appeared to be "superfemales," with ratios of estrogen to testosterone twice as high as normal. "We didn't have any group that looked like males," Guillette recalls.

It turns out that there were indeed males — the gators emerging from eggs exhibiting the standard female ratio of hormones. But the concentrations of the hormones contributing to that ratio were not normal. "These animals were making almost no testosterone and almost no estrogen," Guillette explains.

Six months later, the researchers returned to Lakes Woodruff and Apopka to measure hormones in the young. "We found exactly the same condition that we had seen in the eggs," he says — "females with about twice the estrogen typical of a female and almost no testosterone in the males."

Apopka's animals also possessed feminized internal reproductive organs. The males bore what looked like ovaries, for example, while follicles in the females possessed not only abnormal eggs, but also far too many eggs.

Last summer, Guillette's team collected more than 100 juvenile alligators — animals 2 to 8 years old — from each of five

lakes. Apopka's gators again distinguished themselves. The phallus on males was one-half to one-third the normal size, and the females' ovaries "looked burned out," Guillette says. Moreover, estrogen and testosterone production in all Apopka gators was minimal — as if, Guillette says, the ovaries and testes were indeed burned out.

What accounts for Apopka's feminized alligators? The culprit is estrogenic pesticides. Guillette testified at an Oct. 21 hearing before the House-Subcommittee on Health and the Environment. Tower Chemical Co. for years made the pesticide dicofol — a molecule that he says looks like DDT with an extra oxygen atom. Production methods at the plant, situated on the shore of Lake Apopka, weren't always ideal, Guillette says. Spills occurred and much of the dicofol was laced with up to 15 percent DDT or DDE. Tower's defunct plant is now a toxic waste site.

While high concentrations of DDT have been measured in Apopka gators, Guillette cautions that this doesn't prove DDT is responsible for the observed feminization. To test that link, his team this summer painted gator eggs from Lake Woodruff with concentrations of DDE and dicofol to produce tissue contamination typical of hatchlings from Lake Apopka.

Though not all their tests have been completed yet, Guillette told SCIENCE NEWS that "we're finding hormone levels in these hatchlings that are almost identical to those in Apopka hatchlings." He adds, "That's about the closest thing to proof science is ever likely to give."

In the meantime, Apopka's gators continue to suffer. Since a catastrophic

percent reduction in the number of juvenile anglers at the lake. And in a population of animals that can live to be 60 years old, that's not healthy, he says.

Another reluctant toxicologist, Brent Palmer of Ohio University in Athens, has begun studying a substance in the blood of egg-laying vertebrates that he suspects will one day prove a sensitive biomarker of exposure to estrogenic pollutants, at least in males. It's vitellogenin, the egg-yolk protein.

When stimulated by estrogen, the liver produces this protein, then dumps it into the blood. From there it circulates to the ovaries, where it is deposited in an egg. Though males can produce vitellogenin, usually only females possess sufficient estrogen to do so.

That's good, Guillette points out, because "if you have enough estrogen in a male to turn on vitellogenin, then you probably have enough to shut off the normal functioning of the testes."

Working with the red-eared slider, America's most common turtle, Palmer has demonstrated that DDT can turn on vitellogenin production in males. But DDT doesn't elicit the same broad suite of changes that estrogen does. For instance, it fails to trigger the liver's production of two other proteins and it turns on the production of some other substances that estrogen doesn't. "So even though DDT is mimicking estrogen in some ways," Palmer points out, "it's not *exactly* the same."

"Certainly, if we can find vitellogenin in

that's a sign they've been exposed to an environmental estrogen," he says. However, Palmer is not yet sure whether the converse also holds: that the lack of vitellogenin proves no estrogen was encountered. He says his new data "make me wonder if there might not still be an environmental estrogen present, just one that's having some other effect." Indeed, he says, interpreting the lack of vitellogenin "could prove a very sticky problem."

It's not a problem John Sumpter has had to cope with. The rainbow trout and carp that he and his colleagues have studied throughout the waterways of England and Wales have displayed plenty of vitellogenin — even the males.

Sumpter and Charles R. Tyler, biologists at Brunel University in Uxbridge, England, collaborated with scientists from Britain's Ministry of Agriculture,



Kent Krempke, FWS

Pallid sturgeon, an endangered fish native to the Missouri and Mississippi Rivers. Though most U.S. sturgeons aren't faring well, "there hasn't been any record of reproduction in the pallid sturgeon for 10 years," notes Richard Ruelle of the U.S. Fish and Wildlife Service in Pierre, S.D. Indeed, he says, any pallid sturgeon seen these days are usually 30 to 40 years old.

Altering the river — chiefly, damming and straightening its path — has reduced the fish's habitat. But the high concentrations of PCBs and DDT that have been found in some pallid sturgeon have led Ruelle to suspect that environmental estrogens might also be jeopardizing its reproductive health. Indeed, he notes, for 15 years researchers have reported that sturgeon gonads "aren't distinctly male or female anymore." Currently, Ruelle is awaiting lab results on vitellogenin in the gonadal tissues saved from sturgeon that were confiscated from anglers who caught the fish illegally.

EMFs — another environmental feminizer?

If electromagnetic fields (EMFs) can affect the amount of estrogen in animals — and their susceptibility to breast cancer (SN: 7/3/93, p.10) — might they also alter the fetal development of a male? Two studies investigating the topic suggest the answer may be a qualified yes.

Robert E. McGivern of Harbor-UCLA Medical Center in Torrance, Calif., and his co-workers exposed pregnant rats to low-level, pulsed magnetic fields twice daily for six days during the period when the fetal brain is undergoing sexual differentiation. In the January 1990 *TERATOLOGY*, the team reported finding that these low-frequency (15 hertz) prenatal exposures demasculinized the scent-marking behavior of mature males.

The study was notable for another reason, asserts McGivern, now at San Diego State University. Prenatal exposures led to "really huge" testes and prostate glands in the adult animal. The researchers have no explanation for the unexpected effect.

In 1972, researchers at the University of Manitoba in Winnipeg conducted a similar experiment. "We exposed male rats chronically to magnetic fields — either pre- or postnatally," notes study leader Klaus-Peter Ossenkopp, now at the University of Western Ontario in London. His team found that "if the rats were prenatally exposed, they developed heavier testicles. If you exposed them as adults, testicle size actually decreased."

"The reproductive system of the rat is built like a Sherman tank," McGivern says. As a result, he maintains, any disruption in the rat becomes interesting because the human is usually much more susceptible to the same things.

And because EMFs appear capable of altering susceptibility to estrogen-mediated tumors in female laboratory animals, Ossenkopp asserts, these findings may represent EMFs' male reproductive corollary.

Neither group has followed up on the work nor knows of others investigating the reproductive effects of EMFs.

Fisheries, and Food to measure vitellogenin concentrations in fish that were caged and suspended for three weeks in the river outfalls of 30 different sewage treatment plants.

In the January *CHEMISTRY AND ECOLOGY*, these researchers describe finding widely varied production of vitellogenin by the fish. However, "in all cases," they say, "exposure of trout to effluent resulted in a very pronounced increase (500- to 10,000-fold, depending on the site) in the blood plasma vitellogenin concentration." In some cases, male trout exhibited vitellogenin concentrations in their bloodstreams typical of mature females during egg production. Carp showed similar, though far smaller, increases.

Attempts to isolate the agent responsible for these increases proved fruitless. However, at least one of the researchers strongly suspected that ethynylestradiol (EE) — the main estrogenic compound in birth-control pills — was responsible for much of the vitellogenin effect they observed. He reasoned that women on the pill excreted the EE in their urine and that some share of this chemical may have passed through the water-treatment plants.

To test the theory, the researchers incubated fish in aquariums containing dilute concentrations of either estradiol — the animal kingdom's primary estrogen — or EE. Concentrations of EE as low as 0.1 nanogram per liter of water caused a significant spike in the animals' production of vitellogenin — proving EE "very

much more potent" than estradiol, Sumpter's team says. Indeed, they conclude, EE represents one of "the most potent of biologically active molecules."

Present in potable waters, however, EE must occur in concentrations below the limits of detection, the British team found. In fact, Sumpter notes, it was only after their research was completed that his team learned of another possible candidate: nonylphenols (SN: 7/3/93, p.12).

These are breakdown products of alkylphenol polyethoxylates (APEs), a class of surfactants first marketed in the 1940s. Today, APEs are used in detergents (including many U.S. dishwashing liquids), pesticides, herbicides, toiletries, and products that need to wet surfaces. Though the parent APEs are not estrogenic, Sumpter describes the nonylphenols as "directly estrogenic" — which means that they can bind to and activate the body's estrogen receptor.

Though nonylphenols occur in concentrations of more than 1 milligram per liter of water in poor-quality English rivers — especially downstream of textile mills — concentrations of 1 to 50 micrograms per liter ($\mu\text{g/l}$) are more typical of waters in England and Europe, Sumpter says. U.S. concentrations, by contrast, tend to fall below 1 $\mu\text{g/l}$.

"Because of their ubiquitous presence in the aquatic environment and the 'high' concentrations," Sumpter told *SCIENCE NEWS*, "we consider them a good candidate to account for the estrogenic effects [found in the study with trout and carp]." Though only perhaps 1/10,000 as potent as EE, nonylphenols "are pretty resistant to degradation and [they] bioaccumulate, which will increase the likelihood of them producing physiological effects," he argues.

But nonylphenols are not the only products formed by the breakdown of APEs. And because many of those others are not monitored, Sumpter says, "the total concentration of all the closely related degradation products remains unknown."

Environmental estrogens are also suspected of playing a role in reproductive problems plaguing the Florida panther, a species whose surviving members total only 30 to 50 animals.

Between 1985 and 1990, 67 percent of male Florida panthers were born with one or more undescended testes, a condition known as cryptorchidism. Just 10 years earlier, only 14 percent of males were cryptorchid, observes Charles Facemire, an ecological geneticist with the U.S. Fish and Wildlife Service in Atlanta. In addition, he notes, at least one non-cryptorchid male is sterile, and even some of the apparently normal males produce abnormal or deformed sperm.

Initially, these problems were assumed

to trace to a loss of genetic diversity in the heavily inbred species (SN: 9/25/93, p.200), Facemire says. But a few months ago, he and Mike Dunbar, a veterinarian with the Florida Game and Fresh Water Fish Commission in Gainesville, decided to investigate whether estrogenic contaminants might also be contributing to these reproductive problems.

Their initial blood sampling program turned up males with unusual steroid hormone ratios. For instance, one male had nearly twice as much estrogen as testosterone. (This animal should have had two to three times as much testosterone as estrogen.) At least two other males had similarly skewed ratios; both of them were also cryptorchid. Equally perplexing, at least one female had more testosterone than estrogen.

"We don't know enough about the species to know if these hormone levels might be normal under certain circumstances. But we don't think they are," Facemire says. Though genetic problems cannot be ruled out, he acknowledges, "I suspect we're going to find that the problems are due more to estrogenic chemicals in the environment."

Working under that assumption, Facemire's office has just issued a prohibition on the use of estrogenic chemicals — principally pesticides — in the 100 or so federally managed wildlife refuges in the southeastern United States. At the same time, Facemire's office has initiated four other investigations into possible effects of environmental hormones on wildlife — including one involving the prothonotary warbler in Alabama and another involving sea turtles in Georgia.

Nor are these the only animal studies linking reproductive changes with exposures to hormone-mimicking contaminants. Laboratory studies on fish at the University of Guelph in Ontario, for instance, have shown that white suckers exposed to papermill effluent — often rich in dioxins and related compounds — took longer to mature, developed smaller gonads, experienced reduced fertility, and had lower than normal concentrations of steroid hormones in their blood. Moreover, Glen Van Der Kraak and his co-workers reported at an international meeting on the topic in September 1990, male fish exposed to papermill wastes developed reduced secondary sex characteristics.

Other researchers have begun linking reproductive problems in salmon to relatively high concentrations of hormone-like contaminants. And at a conference sponsored by the U.S. and Canadian governments three years ago, PCBs in such fish were linked to dramatic declines in the reproduction of minks and otters around the Great Lakes.

Finally, University of Wisconsin scientists demonstrated two years ago that low prenatal exposures to dioxin feminized the behavior of male rats during

adolescence — and sharply reduced their production of sperm. Indeed, the researchers concluded, the developing male reproductive system appears to be more sensitive to the effects of this hormone-like toxicant than any other organ or organ-system studied (SN: 5/30/92, p.359).

"Because we're only just getting to the basics in this field," Palmer says, even simple questions about the reproductive effects of environmental hormones for most species must go unanswered. But he suspects that biologists are going to have to move fast in finding those answers if some contaminated populations are to survive.

Toxic-pollutant concentrations in the environment have dropped to where they can seldom kill most adult animals outright, he says. However, in some species, he fears, "We may have gotten to a point where the adults look healthy but are so reproductively impaired that that population may already be extinct — and we're just waiting for the last remaining adults to die [of old age]."

Jan. 22, *Environmental hormones and men*

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That Feminine Touch

Are men suffering from prenatal or childhood exposures to "hormonal" toxicants?

By JANET RALOFF

Second in a two-part series

Sex hormones orchestrate myriad biological activities throughout our lives, beginning with the initial signaling for certain fetal tissues to differentiate into structures that are quintessentially male or female.

But gender — both its physical expression and its characteristic behavior — traces more to the relative concentrations of various sex hormones circulating in the body than to the mere existence of certain dominant ones. For example, women produce some androgens, or male hormones. Indeed, a woman's body synthesizes estrogens from androgens such as testosterone. Similarly, though estradiol is the animal kingdom's primary estrogen, or feminizing hormone, it plays important roles in both men and women.

At no time does an imbalance of sex hormones produce more obvious results than during fetal development. Too much estrogen at the wrong moment can turn an organism with male genes into what to all outward appearances is a female. Similarly, an overabundance of androgens can produce the sex organs of a male in a fetus with the genes to be female.

Our genetic inheritance tends to oversee the production of sex hormones so that these mix-ups don't occur. But increasingly, scientists are finding, we have been seeding our environment with chemicals that can inadvertently alter or mimic the activity of feminizing hormones.

These agents are everywhere. Many — such as pesticides — contaminate our drinking water and foods. We unsuspectingly breathe others in urban air. A mother may even unwittingly pass some hormone-mimicking pollutants on to her child — via the blood she supplies a fetus before birth and the breast milk with which she later feeds her newborn (SN: 4/26/86, p.264).

A growing appreciation of the ubiquity of these "environmental hormones" has increased concern that large and un-

timely exposures to them may send gender-bending signals to males. In fact, some severely affected animal populations — principally birds, fish, and alligators — have already begun to exhibit the emasculating effects of these pollutants (SN: 1/8/94, p.24).

Researchers also have linked coincident declines in fertility in these and other populations to the pollutants' disruption of endocrine function.

Today, data tying similar reproductive abnormalities in humans to hormone-like pollutants remain scanty at best. However, signs are mounting that some males of our species may already have begun to suffer ill effects.

Early in human development, genetic programming must signal if a fetus is to be male. If it is, observes Richard M. Sharpe, a reproductive physiologist at the Medical Research Council's Center for Reproductive Biology in Edinburgh, Scotland, then the genes will "broadcast" certain chemical communications that result in the secretion of male hormones. These signals effectively flip a series of molecular "switches" that turn on male development.

If nothing happens — that is, no switches are flipped — a female will result. Explains Sharpe, feminine development "is what we call the default pathway."

Today, researchers still seek to identify the precise mechanisms of this female-to-male transformation. However, Sharpe says, animal studies show that if a fetus receives too much estrogen — for example, if its mother has been administered a natural or synthetic estrogen during the critical period when genes attempt to express masculinity — "then you disrupt



Produce sold in U.S. markets often contains trace residues of pesticides, some of which can affect hormone function. Studies show that a single peach, for example, can carry residues of up to six different pesticides (SN: 7/3/93, p.4).

this switch from female to male."

In humans, the male reproductive tract begins developing between about the seventh and 14th weeks of pregnancy. If external hormones appear sporadically or in low concentrations during this time, the disruptions they cause will not necessarily trigger a complete reversal of an individual's apparent gender. Rather, they may exert subtle changes, ones that play out later in life.

Nor are estrogens the only agents that can elicit gender-bending effects. Any chemical that blocks the activity of certain androgens can also foster feminization by preventing the developmental changes those androgens control. For instance, a male fetus depends on certain androgens to direct the development of its external genitalia.

With the growing ubiquity of pesticides and other pollutants possessing the functional attributes of female hormones, our environment effectively bathes us in a sea of estrogens. This realization has led Sharpe and endocrinologist Niels E. Skakkebaek to propose that estrogenic pollutants may underlie some disturbing trends affecting the male reproductive tract.

Last week, the pair chronicled these trends and their possible molecular underpinnings at "Estrogens in the Environment," a federally sponsored international conference in Washington, D.C.

harp rise in testicular cancer, notes Skakkebaek, chief of the University Department of Growth and Reproduction at Rigshospitalet in Copenhagen, Denmark. Some of the first data heralding this increase emerged in his country, which has maintained a national cancer registry since 1943.

There, the incidence of testicular cancer has more than tripled over the past 50 years, he observes. And the frightening thing, he says, is that the rate of increase continues to grow. Moreover, he notes, strong data demonstrate similar increases in Scotland, the United States, and other Scandinavian countries.

Sperm counts also have fallen in the last two generations. Skakkebaek and his co-workers conducted a meta-analysis of previously published studies on semen quality. The international data, from studies involving 14,947 men, indicate that the average density of sperm has fallen from 113 million per milliliter (ml) of semen in 1940 to just 66 million per ml in 1990.

In the January 1992 BRITISH MEDICAL JOURNAL, Skakkebaek's team noted that because the volume of semen available in these men at any given time has also dropped an average of 19 percent, the 50-year drop in sperm count has been more

should indicate. Another worrisome trend is the apparent increase in the incidence of undescended testicles in newborn males — a condition known as cryptorchidism. Though formed near the kidneys, both testicles should migrate down into the scrotum by birth. Few countries maintain registries on this condition, but Skakkebaek noted that two British studies have documented a near doubling of the number of boys born with at least one undescended testicle — from about 1.5 percent in the 1950s to 2.9 percent in the late 1970s.

Though undescended testicles usually complete their migration within a year or two after birth, some never do. Men with undescended testicles are unable to make sperm. Moreover, even individuals who were temporarily cryptorchid during infancy face an increased risk of fertility problems in adulthood, Sharpe notes.

Then there are hypospadias, congenital abnormalities of the urinary tract. During fetal development, the penis initially possesses an open groove down its entire length. Before birth, that opening should fuse closed to form an internal channel known as the urethra. Boys born with only partial fusion of that groove need surgery to correct the problem.

Birth registries in England and Wales

at least some of these trends may be related, Skakkebaek says. His own studies have identified an apparent link not only between undescended testicles at birth and testicular cancer in adulthood, but also between semen quality (such as low sperm counts or abnormal sperm) and testicular cancer.

Moreover, he points out, all these changes "could be the consequences of fetal events." Testicular cancer, undescended testicles, hypospadias, and poor-quality semen have been reported in the male offspring of women who during pregnancy received treatment with diethylstilbestrol (DES), a potent synthetic estrogen, he notes.

"We got more fuel for this estrogen hypothesis in late 1991," Skakkebaek recalls. It was then that he learned of work at the National Institute of Environmental Health Sciences in Research Triangle Park, N.C. This research showed that certain environmental contaminants can emulate the reproductive effects of estrogen and DES in male animals.

The previously unexplained male reproductive trends suddenly started to make sense, Sharpe says. It became clear "that a surprising number of chemicals that we've managed to pollute our environment with are estrogenic," he says.

Manliness: The Sertoli cell connection

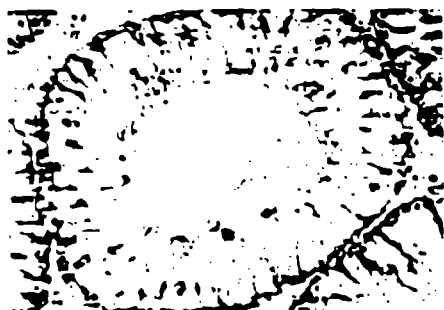
Early exposure to hormone-like pollutants may confuse or tinker with male development in a host of ways. One of the most obvious is by limiting the generation of Sertoli cells, says Richard M. Sharpe of the MRC's Center for Reproductive Biology in Edinburgh. In fact, he notes, production of these cells "is the very first change that happens when a fetus takes the male developmental pathway."

Named for the 19th century Italian physiologist who first described them, Sertoli cells reside within the testicles. In the fetus, these cells direct the development and descent of the testes, control the development of germ cells, and control the cells that secrete the hormones responsible for masculinization. Sertoli cells continue to play an important role in adulthood, when they nourish the early germ cells as they mature into sperm.

Throughout each sperm's 10-week maturation, Sharpe notes, "the Sertoli cells look after its every need."

As such, he says, "I would argue that the Sertoli cell is the most important cell in the male body."

Production of Sertoli cells continues beyond birth, although "for how many years, we're not quite sure," Sharpe says. Because each cell can nurture



Circular cross section of seminiferous tubule from rat testis. Wedged shoulder to shoulder along the outer edge and down toward the center of the tubule are Sertoli cells (stained brown). In adults, these cells nurture maturing sperm.

only a fixed number of sperm at one time, the fewer Sertoli cells that ultimately form, the smaller the testes will be—and the lower a man's production of sperm.

What's more, the number of Sertoli cells an individual produces can be limited by reducing his secretion of follicle-stimulating hormone (FSH). And, at least in young animals, FSH is "exquisitely sensitive to inhibition by exogenously administered estrogen," Sharpe and Niels Skakkebaek noted last year in the May 29 LANCET.

Mullerian inhibiting substance (MIS), another hormone, is produced by Sertoli cells. This hormone's primary role is to cause a regression of fetal structures known as Mullerian ducts. Because the failure of these ducts to regress has been associated with undescended testes, abnormalities in MIS production may play a role in cryptorchidism. Disturbance of MIS production could, therefore, impair normal testicular descent or other aspects of male reproductive development, Sharpe and Skakkebaek argue.

Though studies have shown that over the past five decades sperm counts have been falling—and cryptorchidism rising—Sharpe notes that "we have no data on what Sertoli cell [counts] were in men 50 years ago. So we have no way of proving that these changes are due to a drop in Sertoli cell number." However, he told SCIENCE NEWS, "that would be your prime suspicion."

At a meeting in Washington, D.C., last week, Sharpe said his laboratory is initiating a research program to identify the full cascade of physiological events that normally fixes an individual's manliness. In addition, his team will be looking to establish what factors can interfere with that process and when—and how that may ultimately play out in terms of reproductive success.

— J.A. Ratoff

chemicals that we started making in large quantities from the 1940s and '50s on-wards, and which are very resistant to eradication, including polychlorinated biphenyls (PCBs), DDT, and the break-down product of certain detergents.

I'm not trying to be alarmist, Sharpe told *Science News*, but when it comes to the male reproductive risks posed by hormone-like pollutants, "the data show there's reasonable cause for concern."

A paper in the October *ENVIRONMENTAL HEALTH-PERSPECTIVES* (EHP) lists 45 environmental contaminants or classes of agents that have been reported to cause changes in reproductive and hormone systems. They include eight herbicides, eight fungicides, 17 insecticides, two nematocides, and a miscellaneous category that includes metals, toxic industrial by-products, and commercial chemicals, such as styrenes.

Though releases of many substances on this list, including the toxic pesticides DDT, heptachlor, and kepone, have been banned or severely restricted in the United States, such compounds continue to pollute the environment.

Indeed, a pair of papers in the January *ENVIRONMENTAL SCIENCE AND TECHNOLOGY* (ES&T) reports on diverse occurrences of such organochlorine pesticides—from

Series Lake Baikal to those in sediments on a bay that provides water for Portland, Maine. These compounds even show up long distances from where they were used. For example, detectable levels of such pesticides appeared in an Antarctic penguin, a third ES&T paper reports.

Others of the listed organochlorines remain in widespread use. For instance, 2,4-D is the largest-selling broadleaf herbicide in North America, with some 60 million pounds of it and its chemical analogs applied annually in the United States alone. While this agent has not been shown to be directly estrogenic, work by Ana Soto, an endocrinologist at Tufts University School of Medicine in Boston and a coauthor of the EHP paper, has shown that nonylphenols are.

These compounds can leach out of some plastics (SN: 7/3/93, p.12) or form during the natural environmental degradation of certain surfactants known as nonylphenol polyethoxylates (SN: 11/8/94, p.24). Soto notes that an estimated 360 million pounds of these surfactants are sold in the United States each year for use in products ranging from dishwashing liquids to toiletries and pesticides.

Most of the agents of greatest immediate concern, however, are no longer allowed to enter the environment in large and relatively uncontrolled quantities. And this may contribute to a false sense of security about the threat these agents pose, argues another coauthor of the EHP paper, ecologist Theo Colborn of the World Wildlife Fund in Washington, D.C.

"My big concern now is that by lowering levels [of these pollutants] in the environment, the substances may be present in such small amounts that we cannot even trace them," Colborn told *Science News*. "They may be there, and we won't even know it."

Soto snarls that concern. "Most compounds with estrogenic effects are not present in the environment at levels that alone would produce an effect," she notes. However, unpublished studies by Soto now indicate that if humans are exposed to enough such chemicals, or if enough of them accumulate in the body, they can combine to cause undesirable effects.

For instance, Soto reported at the meeting last week, by taking 10 estrogenic chemicals and combining each of them at one-tenth of their effective dose, "you now have an effective dose."

Moreover, because chemical structure offers few clues to what may prove estrogenic, environmental hormones can be identified only by methodically testing,



I warned your dad about the female hormones in the water supply — but he won't listen.

one by one, the most widely used chemicals, she says.

Her lab, one of the few that does such testing, has just unmasked the estrogenic alter ego of three widely used pesticides: dieldrin, toxaphene, and endosulfan. Dieldrin and toxaphene are no longer legal in the United States, but "endosulfan remains the nation's most widely used pesticide," Soto says.

Nor are all environmental agents that affect reproduction estrogenic. For instance, benomyl, a systemic fungicide that's used on everything from rice and tomatoes to apples and grapes, "really affects the testes," Soto says; it causes the premature release of cells that would have become sperm. However, Soto notes, benomyl's not an estrogen. Other agents, like dioxin, may actually inhibit estrogen, she notes. Yet in rodents, dioxin feminizes — both physically and behaviorally — males exposed prenatally (SN: 5/30/92, p.359).

Society's preoccupation with cancer has led to regulations requiring that any new chemical be withheld from the marketplace until it passes screening tests that indicate it will not foster malignancies. No rules yet require a similar test of a new or existing chemical's ability to mimic or affect reproductive hormones.

The result of that omission, Soto charges, is that the economic cost-benefit analyses that today play an important role in determining which toxic chemicals remain on the market — and for how long — fail to capture the cost of exposing wildlife and its stewards to hormone-mimicking toxic chemicals.

"We have just begun to open the door of discovery concerning the noncancer health effects of the synthetic chemicals that in the last 50 years have become an integral part of our life," says Colborn. The take-home message from these new studies, she believes, is that "we need to take these effects as seriously as, if not more seriously than, cancer."

Indeed, argues Soto: "What is the economic cost of having a generation that cannot reproduce?"

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The role of chlorine — and its future

Biologist Theo Colborn of the World Wildlife Fund and her co-workers have compiled a list of 42 chemicals, or classes of chemicals that have been reported to affect the reproductive or hormone system. Twenty-three of the compounds — 55 percent — contain chlorine as an essential ingredient. Two others rely on a different halogen, or element in chlorine's chemical class: one on fluorine, the other on bromine.

Because many halogenated compounds are lipophilic (dissolve in fat) and resist breakdown, they tend to persist in the environment — often decades after their use has been banned — and to accumulate in body fat.

As a result, animals exposed to these ubiquitous contaminants frequently become walking, flying, or swimming reservoirs of toxic pollution. Indeed, at least 50 of the papers presented last October at the Ecological Effects of Arctic Airborne Contaminants meeting in Reykjavik, Iceland, dealt with the accumulation of such organochlorines in water and soil and throughout the food chain — from lichens, mosses, fish, and waterfowl to caribou, whales, and newborn harp seals.

Referring to such chlorinated chemicals, Tom Muir, a senior economist with Environment Canada in Burlington, Ontario, argues that "no other class of industrial — or natural — chemicals is known that exhibits so many detrimental properties at the same time. Put simply, the characteristics of chlorinated organic substances that give them useful technical properties are the same ones that make them persistent and/or toxic."

In a 67-page report — *Chlorine, Human Health, and the Environment* — released last October, Greenpeace USA argued that "no further organochlorine pollution should be permitted." Said Joe Thornton, the author, this "means phasing out the substance that is their root — chlorine, since whenever chlorine is used, organochlorines result."

Several other groups have issued similar, less-publicized recommendations. At its annual meeting in October 1992, the International Joint Commission (IJC) suggested that its patrons "sunset" — or begin commercially phasing out — persistent toxic chemicals. A federally appointed U.S.-Canadian board, IJC was established in 1909 to advise the U.S. and Canadian governments on how best to implement treaties and laws for preserving water quality in areas along their joint border. Though nonbinding, the commission's recommendations are taken seriously by both governments, notes Marty Bratzer in IJC's Windsor, Ontario, office.

While IJC has addressed a broad spectrum of persistent toxic agents, its recommendation specifically urges that the U.S. and Canadian governments "develop timetables to sunset the use of chlorine and chlorine-containing compounds as industrial feedstocks, and that the means of reducing or eliminating other uses be examined."

At a September 1992 meeting of the Paris Commission for the Prevention of Marine Pollution, ministers of 15 European nations also agreed that releases of halogenated organics and persistent toxic chemicals should be cut — "with the aim of their elimination."

And last Oct. 27, at its annual meeting, the American Public Health Association's governing council passed a resolution on these organics. It concluded



Provided by Chlorine Chemistry Council

According to a document issued by the Washington, D.C.-based Chlorine Institute, more than half of all commercially produced chemicals may rely on chlorine. Moreover, it says, the \$70 billion U.S. chlorine industry provides materials used in disinfecting 98 percent of U.S. drinking-water systems and in producing about 85 percent of all prescription drugs.

that "there should be a rebuttable presumption that chlorine-containing organic chemicals pose a significant risk. Therefore, before introducing new chemicals into commerce, using existing chemicals in new applications, or continuing to use these chemicals in the manufacturing processes or products beyond some future date, industry should either:

- demonstrate that the risk is not significant for a particular compound, use, or manufacturing process, or
- demonstrate that there are no substitutions, product reformulations, or changes in manufacturing processes that will result in a lower risk, or

- ensure that substitutes for existing products or changes in manufacturing processes will result in a lower risk."

Not surprisingly, the chemical industry has responded. Publicly it argues that such sweeping recommendations are not justified or go too far. Internally, however, many companies have begun evaluating what they can do to begin cutting their chlorine use and pollution.

Last October, in fact, Philip H. Brodsky, director of corporate research and environmental technology at Monsanto Co. in St. Louis, made new efforts to develop chlorine-cleanup and chlorine-substitution technologies the focus of his presentation before journalists at the Council for the Advancement of Science Writing.

And what of the scientists whose work Greenpeace cited to support a chlorine ban? Says Mary S. Wolff of the Mt. Sinai School of Medicine in New York City, whose team last year linked concentrations of DDT in the blood to a woman's risk of breast cancer (SN: 4/24/93, p.262): "I don't think any scientist would be against a ban on chlorinated organics." But does she support a ban on all chlorinated compounds? "No."

Calling for a chlorine ban "is an extremist position, and like most extremist positions, ridiculous," charges endocrinologist H. Leon Bradlow of Cornell University's Strang Cancer Prevention Center in New York City. He acknowledges that all toxic chemicals should be used judiciously and only when suitable nontoxic substitutes aren't available. However, he quips: "I think methylene chloride [an animal carcinogen] is a dandy solvent and would hate not to be able to use it."

Reproductive biologist Ana Soto of Tufts University Medical School also considers a chlorine ban an overly simplistic approach to regulation. Moreover, she notes, such a ban would not affect unchlorinated compounds such as nonylphenol — a substance whose estrogenicity she discovered when it leached out of plastics, destroying four months of endocrine research.

Soto also notes that, unlike chlorinated pesticides, some nonylphenol-containing products — such as spermicides used with contraceptive diaphragms and in many condoms — have been designed expressly for intimate contact with human reproductive tissue.

Adds toxicologist Devra Lee Davis with the Department of Health and Human Services in Washington, D.C., "We're not well served by blanket solutions to complicated problems." However, she asserts, "I'm glad I live in a democratic country where discussions, like those that Greenpeace has been leading on this chlorine issue, can be aired before the public." — J.A. Raloff

'Toxins' 'Assault' on reproductive systems

By Anita Manning
USA TODAY

Pesticides, herbicides and other chemicals humans have been tossing around for 50 years could be wreaking havoc on the reproductive systems of people and animals.

No one's certain that chemicals are the culprit, but there's enough evidence of something going wrong to raise alarm bells. The topic is explored Sunday in a Discovery Channel documentary, *Assault on the Male*, airing 7-8 p.m. ET/PT. Though this show focuses on males, the problem affects both sexes.

In women, breast cancer and endometriosis are thought to be linked to chemicals in the environment that mimic the hormone estrogen.

In men, Danish researchers have reported a 50% drop in sperm count in Europe and the U.S. between 1938 and 1990, coinciding with a two- to fourfold increase in testicular cancer. Doctors say they're seeing growing numbers of infant boys born with undescended testicles or genital deformities.

Zoologist Theo Colborn, of the World Wildlife Fund, says chemicals appear to be acting on the endocrine system, which regulates metabolism, growth, and sexual development and functioning of animals and humans.

The chemicals, she says, "affect the embryo, fetus and newborn entirely different than they affect an adult, if they affect the adult at all. And the effects in the developing offspring are often irreversible and may not be seen until years after exposure in the womb."

In the late 1980s, Colborn studied fish and birds in the Great Lakes, where levels of DDT and PCB were high.

She found 16 species of birds, fish and mammals experiencing population



By Jim Sikorskie, Michigan State University

DAMAGING CONSEQUENCES: Scientists believed that the malformed beak of this Lake Erie bald eagle is a result of toxic chemicals in the environment.

decline and offspring with deformities ranging from eggs that didn't hatch to birds with crossed bills. Other red flags:

- At least 25% of the male alligators in Florida's Lake Apopka — site of a pesticide spill in 1980 — have low testosterone levels, high estrogen levels and penises one-fourth the normal size.

- Thyroid problems are seen in birds and fish in the Great Lakes.

- Demasculinization of male fish, birds and mammals and defeminization of female fish and birds is seen around the Great Lakes and below paper and pulp mills in the South.

- Immune system suppression has caused problems for dolphins on the Atlantic coast and in the Mediterranean.

In addition, Colborn says, "there are people walking around today who have been affected. If we don't reduce chem-

icals in the environment, we'll see widespread dysfunction."

But the issue is not clear-cut, says Dr. James Simon, endocrinologist at Georgetown University Medical Center, Washington, D.C. "Humans are not alligators," he says, adding the situation "requires far more investigation."

Sperm counts in men have dropped, says Dr. Michael Zinaman, of Loyola University of Chicago, who is conducting an Environmental Protection Agency study on the subject, "but I can't tell you what's caused that."

Still, there is enough evidence to warrant "big-time interest by our government to fund these studies," says Zinaman. "It would be devastating if the trend continued for the next 20 or 30 years. It would be a major issue for reproduction in developed countries."

Dr. John McLachlan, of the National Institute of Environmental Health Sciences, says research is going full-tilt on the effects of estrogens in the environment. "The thing we've spent most time on over years, going back to the early '70s, is trying to understand how estrogens alter sexual development, using DES," the drug given in the 1950s to prevent miscarriage in pregnant women.

The high doses of estrogen given to the women unintentionally set up a huge experiment, with humans as guinea pigs. The sons and daughters of women who took DES have suffered high rates of testicular or vaginal cancer, sterility and other reproductive problems.

"Part of the problem," McLachlan says, "is that it's all very new to us. So the concern that's expressed sometimes in the media and by groups is ahead of the data. As research scientists, we have a real urgency to develop the data as soon as possible, because it's hard to say what level of urgency is adequate."

"We know a potent estrogen like DES will affect lab animals, no doubt. We know the same potent chemical will affect the sexual development of humans. But whether these other molecules, which most people can agree are weakly estrogenic, can do the same thing is still an open issue."

Zoologist Louis Guillette, of the University of Florida, who has been studying Lake Apopka's alligators since the late 1980s, spoke earlier this year to a congressional panel on the potential effects of environmental estrogen.

"A guy said, 'I don't see what all this has to do with us,'" Guillette recalls. His response: "It means every man alive today is half the man his grandfather was."

"And the most important question is: Are our grandsons going to be half the men we are?"

Thursday, September 1, 1994

USA Today

The Gender Bender

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Are environmental
"hormones" emasculating wildlife?

By JANET RALOFF

First in a two-part series

Mother Nature. The term conjures up images of a warm, nurturing, bountiful environment. But this sobriquet is proving increasingly apt for another reason — one that should offer anything but comfort.

New studies suggest that through pollution and other environmental factors, Mother Nature is exerting a feminizing hormonal influence on the animal kingdom.

Over the past 15 years, research has unmasked a number of "environmental hormones" — chemicals and pollutants that disrupt biological processes, often by mimicking the effects of naturally produced hormones such as the female hormone estrogen. On the ever-growing list of these agents are several restricted or banned pesticides — including DDT (and its even more toxic metabolite, DDE), kepone, heptachlor, dieldrin, mirex, and toxophene. Some polychlorinated biphenyls (PCBs) exhibit these disruptive properties, as do certain combustion pollutants, ingredients in plastics, and breakdown products of common detergents (SN: 7/3/93, p.10).

The hormonal activity of these chemicals usually bears little relationship to their intended function. Indeed, there is no way of predicting — based on structure or function — which compounds will exhibit a hormonal alter ego.

That fact troubles a number of scientists because such environmental hormones may be contributing to an increased risk of reproductive-system cancers in females. Moreover, prenatal exposure to hormone-like pollutants can derail the developmental processes that establish gender or ensure reproductive success.

While the health community has recently begun a host of studies to explore a possible link between estrogenic pollutants and cancers in women, few researchers have focused on the related reproductive risks such environmental hormones may pose for both sexes. That's unfortunate, says Theo Colborn, a zoologist with the World Wildlife Fund in Washington, D.C., because reproductive effects are likely to be "much more widespread."

Indeed, she notes, animal data are beginning to suggest that far smaller exposures are needed to trigger reproductive effects than to induce cancers.

And because some of these reproductive changes may be subtle, they could evade detection for decades — even a lifetime — unless hunted for explicitly.

Colborn has convened a number of symposia in the past few years for researchers who study reproductively impaired wildlife populations or laboratory animals exposed to environmental hormones. Most of these scientists, she says, describe the links they're finding between impaired reproduction and "hormonal" pollutants as sobering — if not downright scary.

Indeed, she and many other environmental scientists worry that if hormone-like contaminants can feminize male animals, these ubiquitous pollutants may also underlie troubling reproductive-system trends being witnessed in men.

Some of the earliest data on unexpected reproductive risks posed by commercial chemicals came in the early 1950s. DDT, a potent and persistent organochlorine pesticide, was shown to cause the eggshells of many birds to thin. In fact, long after the compound was banned in 1972, DDT-thinned eggshells continued to put many embryonic birds — including bald eagles — at risk of being crushed to death.

DDT even wreaked havoc among birds resistant to eggshell thinning, such as gulls. Recognition of the extent of the problems, however, didn't emerge until decades after the initial reports of eggshell thinning.

Though heavily contaminated gull embryos managed to hatch, reproduction in gull colonies exposed to large amounts of DDT began to decline precipitously in the late 1960s. Biologists observed not only that many female gulls in these communities were sharing nests with other females — the so-called lesbian gulls — but also that the young within these communities bore grossly feminized reproductive tracts. Female gulls, which should have developed mature reproductive organs only on the left side, also carried

Michigan State Univ



Juvenile bald eagle collected in Michigan last year. Its life-threatening bill deformity may have been caused by exposure to estrogenic chemicals.

"We've been seeing many more deformities in recent years," reports David Best, a bald-eagle specialist with the U.S. Fish and Wildlife Service in East Lansing, Mich. "We've also seen some suggestion of deformities in the embryos [of eggs that didn't hatch]," he notes. Hatching rates within this population also fall below those seen in less polluted areas, such as inland Alaska. Reproduction in these birds starts to fall when PCBs in their bodies exceed 4 to 6 parts per million (ppm) or DDE exceeds 1 ppm. "We're finding very much higher levels than that around the Great Lakes," Best notes — such as eggs with PCB concentrations as high as 120 ppm.

vestigial oviducts on the right side. Many males also bore feminine characteristics, such as oviducts, recalls avian toxicologist D. Michael Fry of the University of California, Davis. Moreover, he notes, the males' left gonad "had tissues that were both ovarian and testicular — so it was an intersex, or hybrid, gonad."

To connect these effects with estrogenic pollutants, Fry and his colleagues conducted a number of experiments during the 1980s. In one, they injected eggs of contaminant-free gulls with estradiol or with an estrogenic pesticide such as DDT. When the hatchlings emerged, they exhibited the same array of feminized sex organs as DDT-contaminated Western gulls on Santa Barbara Island, off the coast of California.

In effect, DDT "chemically castrated" the males, Fry says. He suspects the males' likely lack of interest in mating explains not only why female gulls dominated Santa Barbara Island's breeding colony in the late 1960s and early 1970s, but also why the females cohabited.

More recently, Fry has turned his attention to the effects of other estrogenic pesticides and PCBs. This summer he began studying common terns, a relative of the gull. Fry studied male embryos from nests along New Bedford Harbor, Mass., located near a toxic waste site contaminated with PCBs. Only four of the 15 males that he analyzed appeared normal. The rest exhibited varying degrees of feminized sex organs.

"I never set out to do any toxicology," maintains Louis J. Guillette Jr., a reproductive endocrinologist at the University of Florida in Gainesville. But the team he heads has recently distinguished itself as one of the foremost in environmental-hormone toxicology. It all began six years ago, when the state of Florida asked him to find out what makes a good alligator egg.

Alligator ranching has become a multi-million-dollar industry in Florida, and ranchers wanted to know how many eggs they could harvest from the wild without jeopardizing the survival of this once-endangered species. So Guillette's team began surveying the hatching rate of eggs on various lakes: in all, more than 1,200 nests accounting for more than 50,000 alligator eggs.

It didn't take long, Guillette says, "before we realized there was something fundamentally different about one lake." It was Apopka, Florida's fourth largest freshwater body.

Whereas 70 to 80 percent of the eggs in most alligator nests hatched, between 80 and 95 percent of those from Apopka failed to hatch. Moreover, of the alligators that did hatch at Apopka, roughly half died within two weeks — a mortality rate at least 10 times that expected for such neonates.



Florida panthers: Researchers are investigating whether environmental hormones might help explain their testicular problems, puzzling sex-hormone concentrations, and falling fertility.

As one measure of the health of these animals, Guillette's team began two years ago to examine the fluid that leaks out of eggs at the time of hatching and to analyze it for estrogen and testosterone. In females, estrogen should predominate, whereas males should have more testosterone. Eggs from Lake Woodruff — with normal hatching rates — displayed those classic patterns.

Apopka eggs didn't. One group showed what at first appeared to be the normal female pattern. Another group appeared to be "superfemales," with ratios of estrogen to testosterone twice as high as normal. "We didn't have any group that looked like males," Guillette recalls.

It turns out that there were indeed males — the gators emerging from eggs exhibiting the standard female ratio of hormones. But the concentrations of the hormones contributing to that ratio were not normal. "These animals were making almost no testosterone and almost no estrogen," Guillette explains.

Six months later, the researchers returned to Lakes Woodruff and Apopka to measure hormones in the young. "We found exactly the same condition that we had seen in the eggs," he says — "females with about twice the estrogen typical of a female and almost no testosterone in the males."

Apopka's animals also possessed feminized internal reproductive organs. The males bore what looked like ovaries, for example, while follicles in the females possessed not only abnormal eggs, but also far too many eggs.

Last summer, Guillette's team collected more than 100 juvenile alligators — animals 2 to 8 years old — from each of five

lakes. Apopka's gators again distinguished themselves. The phallus on males was one-half to one-third the normal size, and the females' ovaries "looked burned out," Guillette says. Moreover, estrogen and testosterone production in all Apopka gators was minimal — as if, Guillette says, the ovaries and testes were indeed burned out.

What accounts for Apopka's feminized alligators? The culprit is estrogenic pesticides, Guillette testified at an Oct. 21 hearing before the House-Subcommittee on Health and the Environment. Tower Chemical Co. for years made the pesticide dicofol — a molecule that he says looks like DDT with an extra oxygen atom. Production methods at the plant, situated on the shore of Lake Apopka, weren't always ideal, Guillette says. Spills occurred and much of the dicofol was laced with up to 15 percent DDT or DDE. Tower's defunct plant is now a toxic waste site.

While high concentrations of DDT have been measured in Apopka gators, Guillette cautions that this doesn't prove DDT is responsible for the observed feminization. To test that link, his team this summer painted gator eggs from Lake Woodruff with concentrations of DDE and dicofol to produce tissue contamination typical of hatchlings from Lake Apopka.

Though not all their tests have been completed yet, Guillette told SCIENCE News that "we're finding hormone levels in these hatchlings that are almost identical to those in Apopka hatchlings." He adds, "That's about the closest thing to proof science is ever likely to give."

In the meantime, Apopka's gators continue to suffer. Since a catastrophic

percent reduction in the number of juvenile alligators at the lake. And in a population of animals that can live to be 60 years old, that's not healthy, he says.

Another reluctant toxicologist, Brent Palmer of Ohio University in Athens, has begun studying a substance in the blood of egg-laying vertebrates that he suspects will one day prove a sensitive biomarker of exposure to estrogenic pollutants, at least in males. It's vitellogenin, the egg-yolk protein.

When stimulated by estrogen, the liver produces this protein, then dumps it into the blood. From there it circulates to the ovaries, where it is deposited in an egg. Though males can produce vitellogenin, usually only females possess sufficient estrogen to do so.

That's good, Guillette points out, because "if you have enough estrogen in a male to turn on vitellogenin, then you probably have enough to shut off the normal functioning of the testes."

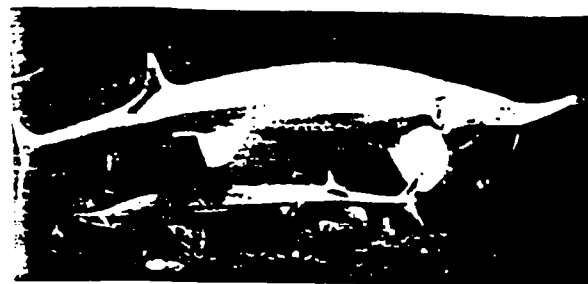
Working with the red-eared slider, America's most common turtle, Palmer has demonstrated that DDT can turn on vitellogenin production in males. But DDT doesn't elicit the same broad suite of changes that estrogen does. For instance, it fails to trigger the liver's production of two other proteins and it turns on the production of some other substances that estrogen doesn't. "So even though DDT is mimicking estrogen in some ways," Palmer points out, "it's not *exactly* the same."

"Certainly, if we can find vitellogenin in

that's a sign they've been exposed to an environmental estrogen," he says. However, Palmer is not yet sure whether the converse also holds: that the lack of vitellogenin proves no estrogen was encountered. He says his new data "make me wonder if there might not still be an environmental estrogen present, just one that's having some other effect." Indeed, he says, interpreting the lack of vitellogenin "could prove a very sticky problem."

It's not a problem John Sumpter has had to cope with. The rainbow trout and carp that he and his colleagues have studied throughout the waterways of England and Wales have displayed plenty of vitellogenin — even the males.

Sumpter and Charles R. Tyler, biologists at Brunel University in Uxbridge, England, collaborated with scientists from Britain's Ministry of Agriculture,



Kent Kneib, FWS

Pallid sturgeon, an endangered fish native to the Missouri and Mississippi Rivers. Though most U.S. sturgeons aren't faring well, "there hasn't been any record of reproduction in the pallid sturgeon for 10 years," notes Richard Ruelle of the U.S. Fish and Wildlife Service in Pierre, S.D. Indeed, he says, any pallid sturgeon seen these days are usually 30 to 40 years old.

Altering the river — chiefly, damming and straightening its path — has reduced the fish's habitat. But the high concentrations of PCBs and DDT that have been found in some pallid sturgeon have led Ruelle to suspect that environmental estrogens might also be jeopardizing its reproductive health. Indeed, he notes, for 15 years researchers have reported that sturgeon gonads "aren't distinctly male or female anymore." Currently, Ruelle is awaiting lab results on vitellogenin in the gonadal tissues saved from sturgeon that were confiscated from anglers who caught the fish illegally.

EMFs — another environmental feminizer?

If electromagnetic fields (EMFs) can affect the amount of estrogen in animals — and their susceptibility to breast cancer (SN: 7/3/93, p.10) — might they also alter the fetal development of a male? Two studies investigating the topic suggest the answer may be a qualified yes.

Robert E. McGivern of Harbor-UCLA Medical Center in Torrance, Calif., and his co-workers exposed pregnant rats to low-level, pulsed magnetic fields twice daily for six days during the period when the fetal brain is undergoing sexual differentiation. In the January 1990 *TERATOLOGY*, the team reported finding that these low-frequency (15 hertz) prenatal exposures demasculinized the scent-marking behavior of mature males.

The study was notable for another reason, asserts McGivern, now at San Diego State University. Prenatal exposures led to "really huge" testes and prostate glands in the adult animal. The researchers have no explanation for the unexpected effect.

In 1972, researchers at the University of Manitoba in Winnipeg conducted a similar experiment. "We exposed male rats chronically to magnetic fields — either pre- or postnatally," notes study leader Klaus-Peter Ossenkopp, now at the University of Western Ontario in London. His team found that "if the rats were prenatally exposed, they developed heavier testicles. If you exposed them as adults, testicle size actually decreased."

"The reproductive system of the rat is built like a Sherman tank," McGivern says. As a result, he maintains, any disruption in the rat becomes interesting because the human is usually much more susceptible to the same things.

And because EMFs appear capable of altering susceptibility to estrogen-mediated tumors in female laboratory animals, Ossenkopp asserts, these findings may represent EMFs' male reproductive corollary.

Neither group has followed up on the work, nor knows of others investigating the reproductive effects of EMFs.

Fisheries, and Food to measure vitellogenin concentrations in fish that were caged and suspended for three weeks in the river outfalls of 30 different sewage treatment plants.

In the January *CHEMISTRY AND ECOLOGY*, these researchers describe finding widely varied production of vitellogenin by the fish. However, "in all cases," they say, "exposure of trout to effluent resulted in a very pronounced increase (500- to 10,000-fold, depending on the site) in the blood plasma vitellogenin concentration." In some cases, male trout exhibited vitellogenin concentrations in their bloodstreams typical of mature females during egg production. Carp showed similar, though far smaller, increases.

Attempts to isolate the agent responsible for these increases proved fruitless. However, at least one of the researchers strongly suspected that ethynylestradiol (EE) — the main estrogenic compound in birth-control pills — was responsible for much of the vitellogenin effect they observed. He reasoned that women on the pill excreted the EE in their urine and that some share of this chemical may have passed through the water-treatment plants.

To test the theory, the researchers incubated fish in aquariums containing dilute concentrations of either estradiol — the animal kingdom's primary estrogen — or EE. Concentrations of EE as low as 0.1 nanogram per liter of water caused a significant spike in the animals' production of vitellogenin — proving EE "very

much more potent than estradiol. Sumpter's team says. Indeed, they conclude, EE represents one of "the most potent of biologically active molecules."

Present in potable waters, however, EE must occur in concentrations below the limits of detection, the British team found. In fact, Sumpter notes, it was only after their research was completed that his team learned of another possible candidate: nonylphenols (SN: 7/3/93, p.12).

These are breakdown products of alkylphenol polyethoxylates (APEs), a class of surfactants first marketed in the 1940s. Today, APEs are used in detergents (including many U.S. dishwashing liquids), pesticides, herbicides, toiletries, and products that need to wet surfaces. Though the parent APEs are not estrogenic, Sumpter describes the nonylphenols as "directly estrogenic" — which means that they can bind to and activate the body's estrogen receptor.

Though nonylphenols occur in concentrations of more than 1 milligram per liter of water in poor-quality English rivers — especially downstream of textile mills — concentrations of 1 to 50 micrograms per liter ($\mu\text{g/l}$) are more typical of waters in England and Europe, Sumpter says. U.S. concentrations, by contrast, tend to fall below 1 $\mu\text{g/l}$.

"Because of their ubiquitous presence in the aquatic environment and the 'high' concentrations," Sumpter told SCIENCE NEWS, "we consider them a good candidate to account for the estrogenic effects [found in the study with trout and carp]." Though only perhaps 1/10,000 as potent as EE, nonylphenols "are pretty resistant to degradation and [they] bioaccumulate, which will increase the likelihood of them producing physiological effects," he argues.

But nonylphenols are not the only products formed by the breakdown of APEs. And because many of those others are not monitored, Sumpter says, "the total concentration of all the closely related degradation products remains unknown."

Environmental estrogens are also suspected of playing a role in reproductive problems plaguing the Florida panther, a species whose surviving members total only 30 to 50 animals.

Between 1985 and 1990, 67 percent of male Florida panthers were born with one or more undescended testes, a condition known as cryptorchidism. Just 10 years earlier, only 14 percent of males were cryptorchid, observes Charles Facemire, an ecological geneticist with the U.S. Fish and Wildlife Service in Atlanta. In addition, he notes, at least one non-cryptorchid male is sterile, and even some of the apparently normal males produce abnormal or deformed sperm.

Initially, these problems were assumed

to trace to a loss of genetic diversity in the heavily inbred species (SN: 9/25/93, p.200), Facemire says. But a few months ago, he and Mike Dunbar, a veterinarian with the Florida Game and Fresh Water Fish Commission in Gainesville, decided to investigate whether estrogenic contaminants might also be contributing to these reproductive problems.

Their initial blood sampling program turned up males with unusual steroid hormone ratios. For instance, one male had nearly twice as much estrogen as testosterone. (This animal should have had two to three times as much testosterone as estrogen.) At least two other males had similarly skewed ratios; both of them were also cryptorchid. Equally perplexing, at least one female had more testosterone than estrogen.

"We don't know enough about the species to know if these hormone levels might be normal under certain circumstances. But we don't think they are," Facemire says. Though genetic problems cannot be ruled out, he acknowledges, "I suspect we're going to find that the problems are due more to estrogenic chemicals in the environment."

Working under that assumption, Facemire's office has just issued a prohibition on the use of estrogenic chemicals — principally pesticides — in the 100 or so federally managed wildlife refuges in the southeastern United States. At the same time, Facemire's office has initiated four other investigations into possible effects of environmental hormones on wildlife — including one involving the prothonotary warbler in Alabama and another involving sea turtles in Georgia.

Nor are these the only animal studies linking reproductive changes with exposures to hormone-mimicking contaminants. Laboratory studies on fish at the University of Guelph in Ontario, for instance, have shown that white suckers exposed to papermill effluent — often rich in dioxins and related compounds — took longer to mature, developed smaller gonads, experienced reduced fertility, and had lower than normal concentrations of steroid hormones in their blood. Moreover, Glen Van Der Kraak and his co-workers reported at an international meeting on the topic in September 1990, male fish exposed to papermill wastes developed reduced secondary sex characteristics.

Other researchers have begun linking reproductive problems in salmon to relatively high concentrations of hormone-like contaminants. And at a conference sponsored by the U.S. and Canadian governments three years ago, PCBs in such fish were linked to dramatic declines in the reproduction of minks and otters around the Great Lakes.

Finally, University of Wisconsin scientists demonstrated two years ago that low prenatal exposures to dioxin feminized the behavior of male rats during

adulthood — and sharply reduced their production of sperm. Indeed, the researchers concluded, the developing male reproductive system appears to be more sensitive to the effects of this hormone-like toxicant than any other organ or organ-system studied (SN: 5/30/92, p.359).

"Because we're only just getting to the basics in this field," Palmer says, even simple questions about the reproductive effects of environmental hormones for most species must go unanswered. But he suspects that biologists are going to have to move fast in finding those answers if some contaminated populations are to survive.

Toxic-pollutant concentrations in the environment have dropped to where they can seldom kill most adult animals outright, he says. However, in some species, he fears, "We may have gotten to a point where the adults look healthy but are so reproductively impaired that that population may already be extinct — and we're just waiting for the last remaining adults to die [of old age]."

Jan. 22: Environmental hormones and men

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That Feminine Touch

Are men suffering from prenatal or childhood exposures to "hormonal" toxicants?

By JANET RALOFF

Second in a two-part series

Sex hormones orchestrate myriad biological activities throughout our lives, beginning with the initial signaling for certain fetal tissues to differentiate into structures that are quintessentially male or female.

But gender — both its physical expression and its characteristic behavior — traces more to the relative concentrations of various sex hormones circulating in the body than to the mere existence of certain dominant ones. For example, women produce some androgens, or male hormones. Indeed, a woman's body synthesizes estrogens from androgens such as testosterone. Similarly, though estradiol is the animal kingdom's primary estrogen, or feminizing hormone, it plays important roles in both men and women.

At no time does an imbalance of sex hormones produce more obvious results than during fetal development. Too much estrogen at the wrong moment can turn an organism with male genes into what to all outward appearances is a female. Similarly, an overabundance of androgens can produce the sex organs of a male in a fetus with the genes to be female.

Our genetic inheritance tends to oversee the production of sex hormones so that these mix-ups don't occur. But increasingly, scientists are finding, we have been seeding our environment with chemicals that can inadvertently alter or mimic the activity of feminizing hormones.

These agents are everywhere. Many — such as pesticides — contaminate our drinking water and foods. We unsuspectingly breathe others in urban air. A mother may even unwittingly pass some hormone-mimicking pollutants on to her child — via the blood she supplies a fetus before birth and the breast milk with which she later feeds her newborn (SN: 4/26/86, p.264).

A growing appreciation of the ubiquity of these "environmental hormones" has increased concern that large and un-

timely exposures to them may send gender-bending signals to males. In fact, some severely affected animal populations — principally birds, fish, and alligators — have already begun to exhibit the emasculating effects of these pollutants (SN: 1/8/94, p.24).

Researchers also have linked coincident declines in fertility in these and other populations to the pollutants' disruption of endocrine function.

Today, data tying similar reproductive abnormalities in humans to hormone-like pollutants remain scanty at best. However, signs are mounting that some males of our species may already have begun to suffer ill effects.

Eariv in human development, genetic programming must signal if a fetus is to be male. If it is, observes Richard M. Sharpe, a reproductive physiologist at the Medical Research Council's Center for Reproductive Biology in Edinburgh, Scotland, then the genes will "broadcast" certain chemical communications that result in the secretion of male hormones. These signals effectively flip a series of molecular "switches" that turn on male development.

If nothing happens — that is, no switches are flipped — a female will result. Explains Sharpe, feminine development "is what we call the default pathway."

Today, researchers still seek to identify the precise mechanisms of this female-to-male transformation. However, Sharpe says, animal studies show that if a fetus receives too much estrogen — for example, if its mother has been administered a natural or synthetic estrogen during the critical period when genes attempt to express masculinity — "then you disrupt



Produce sold in U.S. markets often contains trace residues of pesticides, some of which can affect hormone function. Studies show that a single peach, for example, can carry residues of up to six different pesticides (SN: 7/3/93, p.4).

this switch from female to male."

In humans, the male reproductive tract begins developing between about the seventh and 14th weeks of pregnancy. If external hormones appear sporadically or in low concentrations during this time, the disruptions they cause will not necessarily trigger a complete reversal of an individual's apparent gender. Rather, they may exert subtle changes, ones that play out later in life.

Nor are estrogens the only agents that can elicit gender-bending effects. Any chemical that blocks the activity of certain androgens can also foster feminization by preventing the developmental changes those androgens control. For instance, a male fetus depends on certain androgens to direct the development of its external genitalia.

With the growing ubiquity of pesticides and other pollutants possessing the functional attributes of female hormones, our environment effectively bathes us in a sea of estrogens. This realization has led Sharpe and endocrinologist Niels E. Skakkebaek to propose that estrogenic pollutants may underlie some disturbing trends affecting the male reproductive tract.

Last week, the pair chronicled these trends and their possible molecular underpinnings at "Estrogens in the Environment," a federally sponsored international conference in Washington, D.C.

Manliness: The Sertoli cell connection

Early exposure to hormone-like pollutants may confuse or unnerve male development in a host of ways. One of the most obvious is by limiting the generation of Sertoli cells, says Richard M. Sharpe of the MRC's Center for Reproductive Biology in Edinburgh. In fact, the very first change that happens when a fetus takes the male developmental pathway.

Named for the 19th century Italian physiologist who first described them, Sertoli cells reside within the testes. In the fetus, these cells direct the development and descent of the testes, control the development of germ cells, and control the cells that secrete the hormones responsible for masculinization. Sertoli cells continue to play an important role in adulthood, when they nourish the early germ cells as they mature into sperm.

Throughout each sperm's 10-week maturation, Sharpe notes, the Sertoli cells look after its every need.

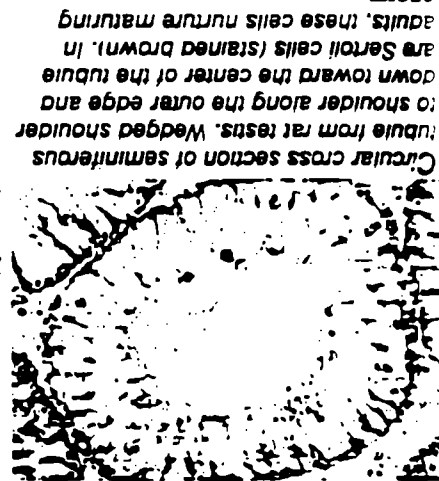
As such, he says, "I would argue that the Sertoli cell is the most important cell in the male body."

Production of Sertoli cells continues beyond birth, although "for now many years, we're not quite sure," Sharpe says. Because each cell can nurture

—noter worrisome trend is the apparent increase in the incidence of undescended testicles in newborn males — a condition known as cryptorchidism. Though formed near the kidneys, both testicles should migrate down into the scrotum by birth. Few countries maintain registries on this condition, but Skakkebaek noted that two British studies have documented a near doubling of the number of boys born with at least one undescended testicle — from about 1.5 percent in the 1950s to 2.9 percent in the late 1970s.

Though undescended testicles usually complete their migration within a year or two after birth, some never do. Men with undescended testicles are unable to make sperm. Moreover, even individuals who were temporarily cryptorchid during infancy face an increased risk of fertility problems in adulthood, Sharpe notes. Then there are hypospadias, congenital abnormalities of the urinary tract. During fetal development, the penis initially possesses an open groove down its entire length. Before birth, that opening should fuse closed to form an internal channel known as the urethra. Boys born with only partial fusion of that groove need surgery to correct the problem.

Birth registries in England and Wales



Medical Village

Circular cross section of seminiferous tubule from rat testis. Wedged shoulder to shoulder along the outer edge and down toward the center of the tubule are Sertoli cells (stained brown). In adults, these cells nurture maturing sperm.

What's more, the number of Sertoli cells an individual produces can be limited by reducing his secretion of follicle-stimulating hormone (FSH). And, at least in young animals, FSH is exquisitely sensitive to inhibition by exogenously administered estrogen. Sharpe and Niels Skakkebaek noted last year in the May 29 LANCET.

At least some of these trends may be related, Skakkebaek says. His own studies have identified an apparent link not only between undescended testicles and birth and testicular cancer in adulthood, but also between semen quality, such as low sperm counts or abnormal sperm, and testicular cancer.

Moreover, he points out, all these changes "could be the consequences of fetal events." Testicular cancer, undescended testicles, hypospadias, and poor-quality semen have been reported in the male offspring of women who during pregnancy received treatment with diethylstilbestrol (DES), a potent synthetic estrogen, he notes.

"We got more fuel for this estrogen hypothesis in late 1991," Skakkebaek recalls. It was then that he learned of work at the National Institute of Environmental Health Sciences in Research Triangle Park, N.C. This research showed that certain environmental contaminants can stimulate the reproductive effects of estrogen and DES in male animals.

The previously unexplained male reproductive trends suddenly started to make sense, Sharpe says. It became clear that a surprising number of chemicals — not just DES, but also a host of other chemicals — that we managed to pollute our environment with are estrogenic," he says.

Mullerian inhibiting substance (MIS), another hormone, is produced by Sertoli cells. This hormone's primary role is to cause a regression of fetal structures known as Mullerian ducts. Because the failure of these ducts to regress has been associated with undescended testes, abnormalities in MIS production may play a role in cryptorchidism. Disturbance of MIS production could, therefore, impact normal testicular descent or other aspects of male reproductive development, Sharpe and Skakkebaek argue.

Though studies have shown that over the past five decades sperm counts have been falling — and cryptorchidism rising — Sharpe notes that "we have no data on what Sertoli cell (counts) were in men 50 years ago. So we have no way of proving that these changes are due to a drop in Sertoli cell number." However, he told Science News, "that would be your prime suspicion."

At a meeting in Washington, D.C., last week, Sharpe said his laboratory is initiating a research program to identify the full cascade of physiological events that normally fixes an individual's male-ness. In addition, his team will be looking to establish what factors can interfere with that process and when — and how that may ultimately play out in terms of reproductive success.

— J.A. Rahoff

chemicals that we started making in large quantities from the 1940s and '50s on-wards, and which are very resistant to eradication, including polychlorinated biphenyls (PCBs), DDT, and the break-down product of certain detergents.

"I'm not trying to be alarmist," Sharpe told *Science News*, but when it comes to the male reproductive risks posed by hormone-like pollutants, "the data show there's reasonable cause for concern."

A paper in the October *ENVIRONMENTAL HEALTH-PERSPECTIVES* (EHP) lists 45 environmental contaminants or classes of agents that have been reported to cause changes in reproductive and hormone systems. They include eight herbicides, eight fungicides, 17 insecticides, two nematocides, and a miscellaneous category that includes metals, toxic industrial by-products, and commercial chemicals, such as styrenes.

Though releases of many substances on this list, including the toxic pesticides DDT, heptachlor, and kepone, have been banned or severely restricted in the United States, such compounds continue to pollute the environment.

Indeed, a pair of papers in the January *ENVIRONMENTAL SCIENCE AND TECHNOLOGY* (ES&T) reports on diverse occurrences of such organochlorine pesticides — from

Arctic rivers to sediments in Siberia's Lake Baikal to those in sediments in a bay that provides an harbor for Portland, Maine. These compounds even show up long distances from where they were used. For example, detectable levels of such pesticides appeared in an Antarctic penguin, a third ES&T paper reports.

Others on the listed organochlorines re-

main in widespread use. For instance, 2,4-D is the largest-selling broadleaf herbicide in North America, with some 60 million pounds of it and its chemical analogs applied annually in the United States alone. While this agent has not been shown to be directly estrogenic, work by Ana Soto, an endocrinologist at Tufts University School of Medicine in Boston and a coauthor of the EHP paper, has shown that nonylphenols are.

These compounds can leach out of some plastics (SN: 7/3/93, p.12) or form during the natural environmental degradation of certain surfactants known as nonylphenol polyethoxylates (SN: 1/8/94, p.24). Soto notes that an estimated 350 million pounds of these surfactants are sold in the United States each year for use in products ranging from dishwashing liquids to toiletries and pesticides.

Most of the agents of greatest immediate concern, however, are no longer allowed to enter the environment in large and relatively uncontrolled quantities. And this may contribute to a false sense of security about the threat these agents pose, argues another coauthor of the EHP paper, ecologist Theo Colborn of the World Wildlife Fund in Washington, D.C.

"My big concern now is that by lowering levels [of these pollutants] in the environment, the substances may be present in such small amounts that we cannot even trace them," Colborn told *Science News*. "They may be there, and we won't even know it."

Soto shares that concern. "Most compounds with estrogenic effects are not present in the environment at levels that alone would produce an effect," she notes. However, unpublished studies by Soto now indicate that if humans are exposed to enough such chemicals, or if enough of them accumulate in the body, they can combine to cause undesirable effects.

For instance, Soto reported at the meeting last week, by taking 10 estrogenic chemicals and combining each of them at one-tenth of their effective dose, "you now have an effective dose."

Moreover, because chemical structure offers few clues to what may prove estrogenic, environmental hormones can be identified only by methodically testing,



He warned your dad about the female hormones in the water supply — but he won't listen.

one by one, the most widely used chemicals, she says.

Her lab, one of the few that does such testing, has just unmasked the estrogenic water ego of three widely used pesticides: Dieldrin, toxaphene, and endosulfan. Dieldrin and toxaphene are no longer legal in the United States, but "endosulfan remains the nation's most widely used pesticide," Soto says.

Nor are all environmental agents that affect reproduction estrogenic. For instance, benomyl, a systemic fungicide that's used on everything from rice and tomatoes to apples and grapes, "really affects the testes," Soto says; it causes the premature release of cells that would have become sperm. However, Soto notes, benomyl's not an estrogen. Other agents, like dioxin, may actually inhibit estrogen, she notes. Yet in rodents, dioxin feminizes — both physically and behaviorally — males exposed prenatally (SN: 5/30/92, p.359).

Society's preoccupation with cancer has led to regulations requiring that any new chemical be withheld from the marketplace until it passes screening tests that indicate it will not foster malignancies. No rules yet require a similar test of a new or existing chemical's ability to mimic or affect reproductive hormones.

The result of that omission, Soto charges, is that the economic cost-benefit analyses that today play an important role in determining which toxic chemicals remain on the market — and for how long — fail to capture the cost of exposing wildlife and its stewards to hormone-mimicking toxic chemicals.

"We have just begun to open the door of discovery concerning the noncancer health effects of the synthetic chemicals that in the last 50 years have become an integral part of our life," says Colborn. The take-home message from these new studies, she believes, is that "we need to take these effects as seriously as, if not more seriously than, cancer."

Indeed, argues Soto: "What is the economic cost of having a generation that cannot reproduce?"

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The role of chlorine — and its future

Ecologist Theo Colborn of the World Wildlife Fund and her co-workers have compiled a list of 42 chemicals or classes of chemicals that have been reported to affect the reproductive or hormone system. Twenty-three of the compounds — 55 percent — contain chlorine as an essential ingredient. Two others rely on a different halogen, or element in chlorine's chemical class: one on fluorine, the other on bromine.

Because many halogenated compounds are lipophilic (dissolve in fat) and resist breakdown, they tend to persist in the environment — often decades after their use has been banned — and to accumulate in body fat.

As a result, animals exposed to these ubiquitous contaminants frequently become walking, flying, or swimming reservoirs of toxic pollution. Indeed, at least 50 of the papers presented last October at the Ecological Effects of Arctic Airborne Contaminants meeting in Reykjavik, Iceland, dealt with the accumulation of such organochlorines in water and soil and throughout the food chain — from lichens, mosses, fish, and waterfowl to caribou, whales, and newborn harp seals.

Referring to such chlorinated chemicals, Tom Muir, a senior economist with Environment Canada in Burlington, Ontario, argues that "no other class of industrial — or natural — chemicals is known that exhibits so many detrimental properties at the same time. Put simply, the characteristics of chlorinated organic substances that give them useful technical properties are the same ones that make them persistent and/or toxic."

In a 67-page report — *Chlorine, Human Health, and the Environment* — released last October, Greenpeace USA argued that "no further organochlorine pollution should be permitted." Said Joe Thornton, the author, this "means phasing out the substance that is their root — chlorine, since whenever chlorine is used, organochlorines result."

Several other groups have issued similar, less-publicized recommendations. At its annual meeting in October 1992, the International Joint Commission (IJC) suggested that its patrons "sunset" — or begin commercially phasing out — persistent toxic chemicals. A federally appointed U.S.-Canadian board, IJC was established in 1909 to advise the U.S. and Canadian governments on how best to implement treaties and laws for preserving water quality in areas along their joint border. Though nonbinding, the commission's recommendations are taken seriously by both governments, notes Marty Bratzer in IJC's Windsor, Ontario, office.

While IJC has addressed a broad spectrum of persistent toxic agents, its recommendation specifically urges that the U.S. and Canadian governments "develop timetables to sunset the use of chlorine and chlorine-containing compounds as industrial feedstocks, and that the means of reducing or eliminating other uses be examined."

At a September 1992 meeting of the Paris Commission for the Prevention of Marine Pollution, ministers of 15 European nations also agreed that releases of halogenated organics and persistent toxic chemicals should be cut — "with the aim of their elimination."

And last Oct. 27, at its annual meeting, the American Public Health Association's governing council passed a resolution on these organics. It concluded



Provided by Chlorine Chemistry Council

According to a document issued by the Washington, D.C.-based Chlorine Institute, more than half of all commercially produced chemicals may rely on chlorine. Moreover, it says, the \$70 billion U.S. chlorine industry provides materials used in disinfecting 98 percent of U.S. drinking-water systems and in producing about 85 percent of all prescription drugs.

that "there should be a rebuttable presumption that chlorine-containing organic chemicals pose a significant risk. Therefore, before introducing new chemicals into commerce, using existing chemicals in new applications, or continuing to use these chemicals in the manufacturing processes or products beyond some future date, industry should either:

- demonstrate that the risk is not significant for a particular compound, use, or manufacturing process, or
- demonstrate that there are no substitutions, product reformulations, or changes in manufacturing processes that will result in a lower risk, or

- ensure that substitutes for existing products or changes in manufacturing processes will result in a lower risk."

Not surprisingly, the chemical industry has responded. Publicly it argues that such sweeping recommendations are not justified or go too far. Internally, however, many companies have begun evaluating what they can do to begin cutting their chlorine use and pollution.

Last October, in fact, Philip H. Brodsky, director of corporate research and environmental technology at Monsanto Co. in St. Louis, made new efforts to develop chlorine-cleanup and chlorine-substitution technologies the focus of his presentation before journalists at the Council for the Advancement of Science Writing.

And what of the scientists whose work Greenpeace cited to support a chlorine ban? Says Mary S. Wolff of the Mt. Sinai School of Medicine in New York City whose team last year linked concentrations of DDT in the blood to a woman's risk of breast cancer (SN: 4/24/93, p.262): "I don't think any scientist would be against a ban on chlorinated organics." But does she support a ban on all chlorinated compounds? "No."

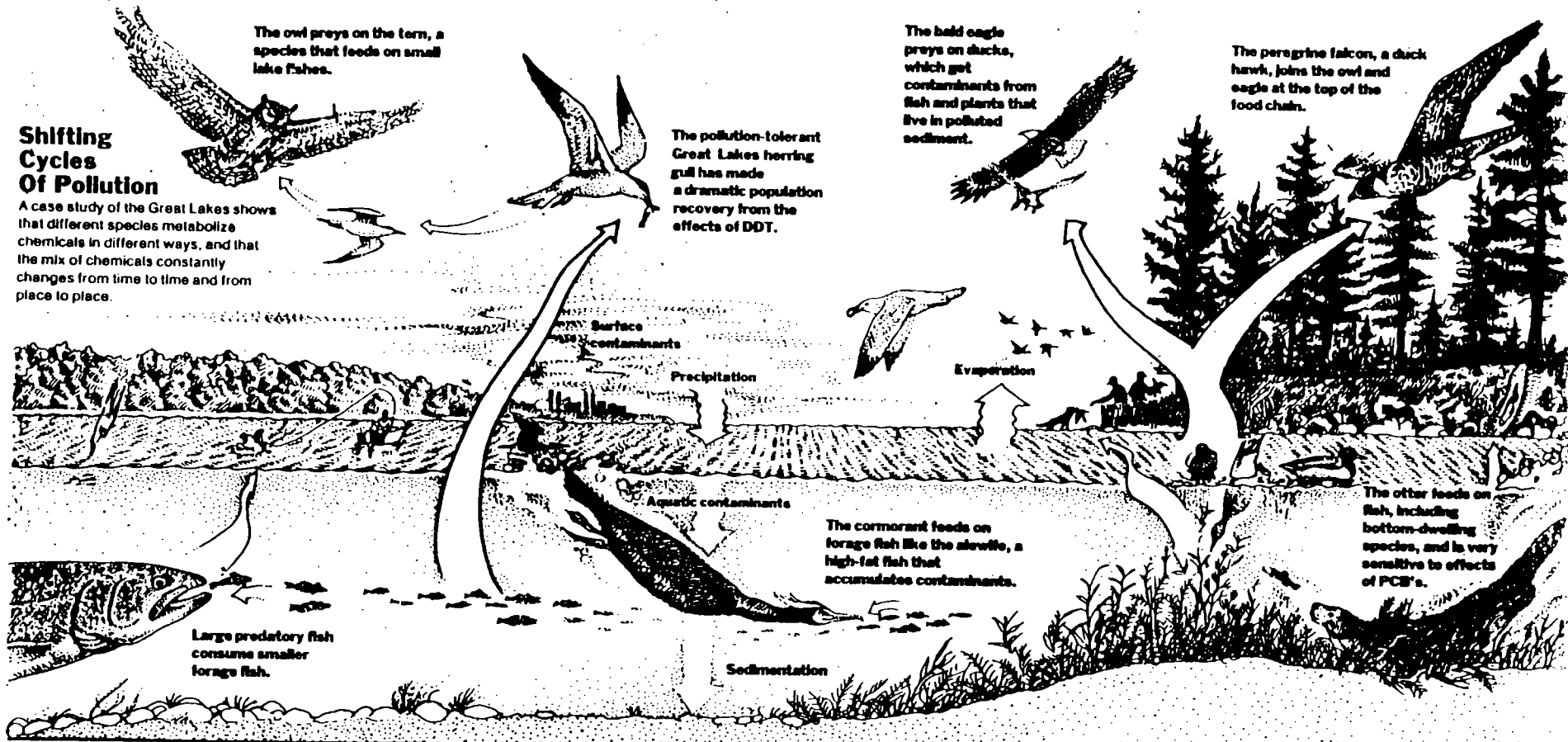
Calling for a chlorine ban "is an extremist position, and like most extremist positions, ridiculous," charges endocrinologist H. Leon Bradlow of Cornell University's Strang Cancer Prevention Center in New York City. He acknowledges that all toxic chemicals should be used judiciously and only when suitable nontoxic substitutes aren't available. However, he quips: "I think methylene chloride [an animal carcinogen] is a dandy solvent and would hate not to be able to use it."

Reproductive biologist Ana Soto of Tufts University Medical School also considers a chlorine ban an overly simplistic approach to regulation. Moreover, she notes, such a ban would not affect unchlorinated compounds such as nonylphenol — a substance whose estrogenicity she discovered when it leached out of plastics, destroying four months of endocrine research.

Soto also notes that, unlike chlorinated pesticides, some nonylphenol-containing products — such as spermicides used with contraceptive diaphragms and in many condoms — have been designed expressly for intimate contact with human reproductive tissue.

Adds toxicologist Devra Lee Davis with the Department of Health and Human Services in Washington, D.C., "We're not well served by blanket solutions to complicated problems." However, she asserts, "I'm glad I live in a democratic country where discussions, like those that Greenpeace has been leading on this chlorine issue, can be aired before the public." — J.A. Raloff

Pesticides May Leave Legacy of Hormonal Chaos



Sources: Dr. William Bowerman/Michigan State University, U.S. Fish and Wildlife Service

The New York Times' Illustration by Glenn Wolff

By WILLIAM K. STEVENS

IN a new wave of concern about synthetic chemicals in the environment, some biologists are warning that trace amounts of pesticides and other man-made substances may be interfering with the action of reproductive hormones and thereby damaging the fertility of various animal populations, including humans.

The evidence is far from conclusive. But the economic and political stakes are high; should the new fears prove justified, a large group of important industrial chemicals might have to be curbed.

At least 45 synthetic chemicals, of them pesticides, have been found to upset the workings of the

hormonal, or endocrine system, and for this reason they are known as endocrine disruptors. There is little doubt, many scientists agree, that when people or animals are exposed to large doses of these chemicals, as has happened in chemical spills or contamination of food, serious derangements of reproductive function sometimes result. Male alligators born in Florida's Lake Apopka after a large pesticide spill in 1980 were found to be incapable of producing sperm. In Taiwan, reproductive and other defects have been noted in the sons of women who in 1978 and 1979 ingested cooking oil contaminated with PCB's.

The question at issue is whether trace amounts of these chemicals that are now widely distributed in the environment are exerting a visible but still pernicious effect on the reproductive fitness of species and possibly even

Reproduction may be disrupted, but experts differ on damage.

For at least some wildlife populations, "I'd say we are on a fast track to extinction," said Dr. Theodora Colborn, a zoologist with the World Wildlife Fund, a conservation organization in Washington, who is a leading exponent of the view that endocrine disruptors pose a potentially serious threat. "You expect the same thing to happen with human populations."

Other experts disagree. "I don't think it is a huge problem at this point," said Dr. Thomas Goldsworthy, a

toxicologist with the Chemical Industry Institute of Technology, a nonprofit research organization at Research Triangle Park, N.C., that is largely supported by industry. Said Dr. Tom Orme, a Washington-based toxicologist with the American Council on Science and Health in New York, which has long held claims of harm from chemicals in the environment to be exaggerated: "We see there is a lot of baloney here. On the other hand, to develop the hard science to refute it is going to be a formidable task."

Still other experts view the issue as possibly serious but say it is too early to call it one way or the other. "We don't want to argue we've got a massive problem," said Dr. Larry Reller, the director of the Environmental Protection Agency's Health Effects Research Laboratory. Continued on Page C6

Pestici

Shifting Cycles Of Pollution

A case study of the Great Lakes shows that different species metabolize chemicals in different ways, and that the mix of chemicals constantly changes from time to time and from place to place.



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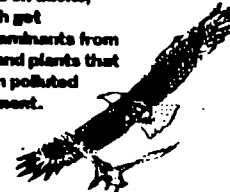
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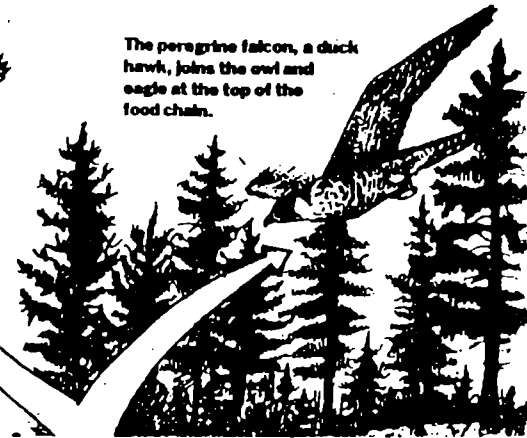
The pollution-tolerant Great Lakes herring gull has made a dramatic population recovery from the effects of DDT.

Surface
contaminants

The bald eagle preys on ducks, which get contaminants from fish and plants that live in polluted sediment.



The peregrine falcon, a duck hawk, joins the owl and eagle at the top of the food chain.



Evaporation

Industrial Chemicals May Disrupt Reproduction of Wildlife



World Wildlife Fund

Dr. Thomas Goldsworthy, left, of the Chemical Industry Institute of Technology; Dr. Lynn Goldman, center, of the Environmental Protection Agency; Dr. Theodora Colborn of the World Wildlife Fund.

Continued From Page C1

ry at Research Triangle Park. But he also said, "I don't think we want to argue there is no problem."

Although many biologists are convinced that endocrine disruptors are pervasive, they have not yet been able to assess the quantity and distribution of the chemicals in the environment. Nor is there any good survey to tell what burden of these chemicals is carried in the body fat of the general population.

But a number of studies suggest grounds for concern, particularly from the combined effects of several different chemicals acting in concert either to mimic or block the crucial effects of natural estrogens on sexual development in the fetus.

Dr. Ana M. Soto and Dr. Carlos Sonnenschein, biologists at Tufts University, have found that doses of estrogen-mimicking pesticides too small to have any effect individually on test-tube cultures of cells from breast-cancer tissue have a powerful effect when combined. Estrogens spur the growth of such cells. Other laboratory studies have shown that the synthetic chemicals can disrupt the reproductive development of mammal fetuses. And field investigations have traced reproductive dis-

In Great Lakes, birds have recovered as toxic burden fell.

orders in mammals and birds to the consumption of fish whose flesh contained the chemicals.

Dr. Colborn, Dr. Soto and others who are alarmed about endocrine disruptors say that all chemicals that reach the environment should be tested for their hormonal effect just as they are already tested for ability to cause cancer or mutations. Some environmentalists are calling for a phaseout of endocrine-disruptor chemicals, and already there is legislation before Congress to replace some chlorine compounds, many of which have been identified as endocrine disruptors, with feasible alternatives. The E.P.A. and the United States Fish and Wildlife Service have asked the National Academy of Sciences to investigate the problem. Meanwhile, those who are raising the alarm about endocrine disruptors have been energetic in seeking attention in the press and on television, where the subject has lately been explored, sometimes in apocalyptic tones.

The debate is in some ways a replay of "Silent Spring," Rachel Carson's landmark book published in 1962, in which she argued that fat-soluble pesticides in the bodies of birds were interfering with reproduction. Her thesis provoked a barrage of criticism, but biologists in time learned that many chlorinated hydrocarbons like DDT do indeed sabotage reproduction, for example by making the shells of birds' eggs too fragile.

Persistent Chemical Residues

DDT and similar pesticides like aldrin and dieldrin were banned long ago in the United States. But their residues persist in the environment, not the least because they remain in use in much of the world and are being transported to America on globe-girdling winds.

Moreover, there are many industrial chemicals that are hormonally active and that may find their way into the environment even though, unlike pesticides, they are not deliberately released. These include some members of a family of chemicals known as alkyl phenols, which Dr. Soto has found to have estrogen-like effects. These chemicals are used in plastics, including some food wrappings, as well as in several industrial processes, in paper and pulp production, textiles, hair colorings, spermicides and condom lubricants and as inert ingredients in pesticides. They are also used in industrial detergents, and their estrogenic components are released into the environment when the detergents break down. Dr. Soto has found that some of the chemicals can leach out of plastic containers and contaminate the contents.

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The Wildlife/Human Connection: Modernizing Risk Decisions

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THE WILDLIFE/HUMAN CONNECTION
A REPORT FOR THE U.S. ENVIRONMENTAL PROTECTION AGENCY
BY THE U.S. ENVIRONMENTAL PROTECTION AGENCY

The Wildlife/Human Connection

Key words: biodiversity, endocrine-disruptors, dioxin, exposure, functionality, hormones, PCBs, policy, risk, wildlife, xenobiotics.

This paper proposes that genetic and molecular ecotoxicology can play an important role in making policy and risk assessment decisions concerning xenobiotics. It calls for a greater awareness by ecotoxicologists to the effects in wildlife and humans resulting from transgenerational exposure to synthetic chemicals that interfere with gene expression and differentiation. The difficulty of recognizing these effects on the endocrine, immune, and nervous systems in developing embryos is described and suggests why effects of this nature have traditionally not been addressed when determining risk to synthetic chemicals. Specific examples are cited of environmental effects on hormonally responsive tissue in wildlife populations which could be used as models for assessing human exposure to synthetic chemicals. Evidence is presented that the environmental load of synthetic chemicals has reached critical levels where wildlife and human health are at risk.

This paper presents examples of environmental effects on hormonally responsive tissue in troubled wildlife populations that provide a model for assessing previously overlooked human health hazards associated with exposure to synthetic chemicals. The difficulty of recognizing these effects on the endocrine, immune, and nervous systems in wildlife and humans explains why the problems are usually not discovered until they become quantifiable at the population level. In the past, health effects of this nature were not addressed when determining the safety of synthetic chemicals. Consequently, endocrine-disrupting, synthetic chemicals once considered benign are now an integral part of the global ecosystem posing an emerging threat to biodiversity.

The number of synthetic chemicals that are capable of disrupting the endocrine system continues to grow as they are serendipitously(1,2) or deliberately(3) discovered. Among the list are fungicides, insecticides, herbicides, components in plastics and detergents, and other industrial products and by-products(4). These manmade chemicals look like, or interfere with, endogenously produced hormones, neurotransmitters, growth factors, and inhibiting substances. They invade the environment of the embryo and change its course of development(5). Effects not often expressed overtly in the parent are manifested as a second generation sequelae of changes in the architecture and function of the endocrine, immune, and nervous systems of

offspring exposed during critical periods of organ development(5).

A number of the endocrine disruptive effects reported in wildlife populations have been replicated in confined wild animals(6,7) and laboratory animals using single xenobiotics(8,3). However, in the real world, exposure involves multiple xenobiotics making causal links difficult. The effects are not necessarily expressed as gross physical defects that are visibly recognizable, but instead are expressed as loss of function which until recently have not been described. Consequently, with wildlife and humans, alike, a generation may pass before the effects become apparent, and only after the problem is widespread and has reached population proportion(9,10).

Many of the persistent endocrine-disrupting xenobiotics are found in the reproductive tissues of animals, including humans(11). However, recent findings that only one very low dose of dioxin administered during gestation can change the sexual development of rat offspring, demonstrate that a xenobiotic need not be persistent nor bioaccumulative in order to interfere with the development of vital systems. Timing of exposure during gestation is critical(8). These recent dioxin studies also emphasize the importance of broadening testing protocols for all chemicals destined to become a part of commerce that will come in contact with large numbers of wildlife and humans. Short-lived chemicals that "hit and run" might never be linked with in utero

damage unless they are carefully screened via multigenerational studies designed to detect functional changes. Unfortunately, the current substitutes for the older, more persistent, bioaccumulative chemicals such as the DDT and PCB analogs, have not been screened for their disruptive effects on the differentiation of organ systems.

A comprehensive review of the literature on the health status of birds, fishes, mammals, and reptiles in the northern hemisphere reveals widespread instability, decline, and extirpation among populations(12,13). Among those animals that can reproduce, however, aberrant development expressed in their offspring often goes unseen because the young are kept in seclusion, making it difficult to build a case for research in functional teratology. To date, some of the most convincing wildlife research on transgenerational loss of function has been accomplished during the breeding season among nesting colonies of egg-laying species(14, personal communication: Gross T, Guillette L, University Florida, turtles and alligators). Compared with the geographic scope and seriousness of the problem, however, there has been little support for research to determine the cause of the problems. Perhaps this is because infertility among adult animals that leads to population attrition is difficult to detect and does not catch the interest of public health authorities and funding sources compared with more obvious diseases such as cancer.

Follow-up studies on troubled wildlife populations have

revealed a number of conditions associated with reproductive success. Depending upon the species and study designs, these have been measured as reductions in embryo hatchability(15) and viability(16); chick(17) and fry survivorship(18); egg size and numbers(19); numbers of animals reaching sexual maturity(20); production of endogenous hormones, such as thyroid hormones(7,21), estrogen(22), testosterone(23,24), and retinols(7), as well as immune-competency. Increases in thyroid(25) and liver size(17); liver enzyme induction(17); highly carboxylated porphyrins(26); numbers of animals exhibiting sex reversal(6,27,28); spontaneous abortions(29); hermaphroditism(30); sex-linked birth defects (personal communication: Fry M, UC, Davis, crossed bill double-crested cormorants all were phenotypic females (n=>100); Kubiak, T, USFWS, Washington, DC, crossed bill bald eagles discovered in 1993 were females (n=3)); asymmetrical brains(31) and skulls(32); and unusual behavior(17,33) have been reported as well.

The above effects are not the result of mutations, but are epigenetic in nature. They are the result of changes in gene expression through many mechanisms, such as blockage, modulation, or improper timing, the results of which are unpredictable in most cases(34). Scientists and regulators have sought mutational answers to the problem because of the need for quantifiable standards for regulatory purposes and to respond to society's fixation on cancer. However, current standards and testing protocols for synthetic chemicals need to be reevaluated, opening

new research opportunities for molecular and genetic ecotoxicologists. Obviously more needs to be learned about the mechanism of action of endocrine disruption.

The large-scale mortality among dolphin, porpoise, seal, and whale populations commencing in 1987(35,36,37,38) has generated a number of questions. Why, suddenly in one year in widely disconnected geographic regions in the northern hemisphere should this occur? In this case, long-lived, toothed mammals that are obligate fish-eaters exhibited symptoms of immune incompetency and were affected by new strains of viruses, (one specific to dolphins, another to seals, and another to porpoises) or by naturally produced marine toxins(39).

In an effort to explain the sudden onset of marine mammal die-offs, it is important to keep in mind that mature animals in the first generation exposed to xenobiotics generally do not display obvious effects as a result of their exposure(40). If the transgenerational hypothesis holds, wide-scale immune-incompetency would not appear until the second generation(41,42). Were those mammals that succumbed in the recent die-offs second generation individuals whose endocrine and immune systems were constructed differently because of in utero exposure to xenobiotics? And were some of the older animals that died individuals whose immune systems had reached threshold levels of effect as the result of years of high-dose exposure? These animals held some of the highest concentrations of organochlorine chemicals ever reported.

A specific example of the possible result of exposure to elevated levels of endocrine-disrupting chemicals with biological effects similar to estrogens in utero is that of a bilateral hermaphroditic male beluga whale found dead and adrift in the St. Lawrence River in 1989(30,43). He was one of 41 male belugas from this population that have been necropsied over the past ten years. He was found to have intestinal ulcers and an inflamed pleura. His tooth history revealed that he was born before 1963. His mother was from an isolated population of belugas exposed to at least 20 years of unregulated dumping of a vast number of contaminants into the St. Lawrence River.

Table 1 provides an historical perspective on widespread exposure to xenobiotics for humans, a long-lived species, and may provide a clue to the marine mammal problem. PCBs were first manufactured and used in 1929, DDT in 1938. The 1940s are often referred to as the birth of the chemical revolution, driven by new technology during and immediately following World War II(44). It was during this period that humans (with a generation time of approximately 20 years) were first exposed to a vast number of chemicals. By the mid 1960s these individuals began to bear children and produced the first generation of humans exposed to xenobiotics in utero -- the first generation born with xenobiotics in their tissue. About 1980 this generation reached reproductive age.

In the case of long-lived marine mammals, the timing of the recent mass mortalities fits the above exposure model when

factoring in the delay between initial production and use of xenobiotics on land and their reaching the oceans, plus the tremendous dilution factor of the marine systems. The marine mammals that suffered the die-offs have generation times of approximately 10 to 15 years and are indigenous to highly contaminated enclosed aquatic regions, such as coastal waters and the Baltic and Mediterranean Seas.

In the past, human epidemiological studies designed to determine the outcome of exposure to a xenobiotic(s) have questioned only the health of the exposed individuals. It is not surprising that many human studies have failed to link adverse health effects with exposure to xenobiotics (Type II errors). The lesson learned from wildlife reveals the importance of considering the health of the offspring of the exposed individuals. For example, when seeking causal links for loss of fertility and/or immune competency among cohorts, the subjects' prenatal and early postnatal exposure must be considered (in other words, what was their parents exposure to xenobiotics?). Prenatal and perinatal exposure to xenobiotics probably have more influence on fertility than any other exposure throughout a lifetime. Functional deficits derived from in utero exposure in many cases may not correlate with only postnatal exposure. Most important, in light of the widespread distribution of these chemicals in the environment, it may be too late to find unexposed populations.

Evidence is building that xenobiotics are present in humans

at concentrations that are toxicologically relevant. For instance, female seals exposed to 27ug/kg/body weight (bw)/day PCB on a Wadden sea fish diet were less productive than seals exposed to 8ug/kg/bw/day on a North Atlantic fish diet(45). They experienced reduced plasma retinol and thyroid hormone levels, and fewer implantations. The Wadden Sea population of seals collapsed from 3,000 to 500 animals between 1950-1975. Female mink, animals who, like seals, also have delayed implantation, suffered similar and more severe effects when exposed to 25/ug/kg/bw/day PCBs(46). Similarly, it was estimated that the mothers of children who experienced impaired visual recognition memory at seven months and short term memory problems at 4 years were delivering a dose of >27 ug/kg/bw/day PCBs to their offspring(47). In the same study it was also estimated that the mothers (from Michigan, US) were exposed to 0.093 ug/kg/bw/day PCB throughout their life preceding pregnancy, which provides a model of the persistence of the PCBs. By comparison, 52.5% of Inuit women in eastern Arctic Canada participating in seven food consumption surveys are exposed to 0.25 to 3.25 ug/kg/bw/day PCB(48). Suckling infants consuming breast milk at the US average of 0.8 to 1 ppm PCB in milk fat are exposed to 5 ug/kg/bw/day PCB, 5 times the Allowable Daily Intake (ADI) set by the Food and Agricultural Organization for a 70 kg adult(49). The parents of the children in the Japanese rice oil incident (contaminated with PCBs and furans) were exposed to 63 ug/kg/bw/day PCB for three months(50), about 1000 times the

lifetime dose of the Michigan mothers.

The average US adult's body burden of dioxin (2,3,7,8-TCDD), is approximately 7 to 10 ppt. Dioxin's ability to induce cytochrome P-450 enzymes in rat liver hepatoma cells (H4IIE) has been used as a surrogate to describe its toxicity. Using dioxin as the standard for CP-450 activity on a weight to weight basis one can either measure directly or calculate (using equivalency factors times concentration) the toxicity of other dioxin-like compounds in tissue. The combined 2,3,7,8-TCDD, dioxin and furan isomers, and coplanar PCBs in the average adult's body are equivalent to 50 dioxin enzyme toxicity equivalents (TEQs). This is very close to the 64 ppt of pure 2,3,7,8-TCDD fed to pregnant rats whose male pups experienced abnormal sexual development, sperm count reduction, and behavioral changes(8). A recent French report found 5 coplanar PCB congeners (total 170 ppb) in human breast milk that on a H4IIE basis are equivalent to 6397 2,3,7,8-TCDD TEQs(51). The breast milk fat held 1.01 ppm total PCBs which is similar to the US average of 1 ppm. In addition, the milk held 307 ppbs of 5 PCB congeners (numbers 28(52), 52(53), 138(54), 153(52,54), 169(55)) that also disrupt the endocrine system or affect development. Double-crested cormorants exhibit significant increases in embryo mortality when their eggs hold approximately 100 dioxin TEQs using the H4IIE assay, with measurable losses commencing at about 40 or 50 TEQs(16).

A number of laboratory studies suggest that fertility among

human populations, like wildlife populations, when exposed to ubiquitous xenobiotics may be at risk. For example, in repeated trials it was demonstrated that the sperm of mature male rats exposed to PBCs postnatally through breast milk have difficulty penetrating ova or maintaining a viable zygote(56). In another study, pregnant rats fed one meal of dioxin (0.064, 0.16, 0.4, and 1.0 ug/kg/bw) on day 15 of gestation gave birth to male offspring who were demasculinized and feminized, as determined by morphological, biochemical, physiological, and behavioral parameters; their sperm count was also reduced 75%(8). Many of the effects were not measurable until the pups matured. In a follow-up study (1.0 ug/kg/bw) female pups exhibited morphological changes in external genitalia at birth and a sequelae of changes in the reproductive tract that were similar to effects reported in mice and humans exposed in utero to diethylstilbestrol (DES) (personal communication: Birnbaum, L, Gray LE, EPA, HERL, Research Triangle Park, 1993).

The motility of sperm from men experiencing fertility problems (<20 mill sperm/ml) was inversely proportional to the concentration of three PCB congeners in their semen; 2,4,5,2',4',5'-hexa-(no.153), 2,4,5,2',3',4'-hexa-(no.138), and 2,4,5,3',4'-pentachlorobiphenyl(no.114)(53). All three congeners are commonly found in human breast milk(57). Congener 153 comprises approximately 20% of the PCB body burden of people living in industrialized temperate areas and 40 to 50% of the body burden of native Americans living in eastern Arctic

Canada(58,59). A meta-analysis that reexamined 61 sperm count studies revealed that worldwide sperm count has decreased by approximately 50% since 1938(9). A doubling of cryptorchidism occurred in the UK between 1970 and 1987(60,61). Realizing that these effects could be the result of exposure to elevated estrogens during prenatal development, it has been suggested that the cause may be from environmental contaminants(62,63). A significant reduction in penis size at puberty, among other problems, has been associated with prenatal exposure to PCBs and furans among the offspring of women who consumed PCB contaminated rice oil in Taiwan(64).

Wildlife and humans are signalling problems at the population level that biodiversity is at risk. Addressing the problem with laboratory animal studies on a chemical by chemical basis will not work. The additive (personal communication: Ana Soto, Tufts University), synergistic, and other interactive(65) effects of chemicals already in the environment cannot be predicted. In order for ecotoxicology to meet these challenges it must: [1] be more aware of and develop protocols to assess functional damage in the field; [2] test in the laboratory the hypotheses generated in the field concerning causal links between wildlife damage and chemicals; [3] find early markers in developing tissue that predict long-term delayed effects on functionality for both wildlife and humans; [4] test the hypothesis that there are links between cell differentiation during development and cancer; [5] break disciplinary boundaries,

reach out, and collaborate with those responsible for public health; and [6] convince the policy/risk community that field data have a role in its deliberations. With this agenda in place ecotoxicology could bring a "real-world approach" to decision tables.

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