A New World of Pollutant Effects

By JANET RALOFF

Over the past 4 years, a newly recognized environmental threat to health and reproduction has mushroomed into public prominence. Bearing the clumsy moniker "endocrine disrupters," these pollutants—including PCBs, DDT-breakdown products, dioxins, and certain plasticizers—can mimic or block the action of natural hormones.

By inappropriately turning genes on or off, these compounds can elicit a range of adverse effects. In humans, they may foster cancer in the breast or other reproductive organs. Prenatal exposures appear capable of altering brain development—with impacts on IQ and behavior that persist at least a decade, perhaps for life. Most surprisingly, in some exposed wildlife, creatures whose genes instruct them to be male have matured into individuals that look and act like females.

Minn. Pollution Control Agency

The newly recognized potential of these pollutants to wreak havoc in so many ways, together with their ubiquity, has given rise to a sense of humility among toxicologists. The compounds have been detected in pesticides, plastics, dental sealants, contraceptives, and dishwashing liquids, and they contaminate water, plants, wildlife, and foods. Explains John A. McLachlan, a pioneer in this field, researchers have traditionally hunted out carcinogens and other environmental toxicants that affect DNA. Such changes tend to "leave well-defined structural alterations," he says, "persistent footprints."

Scientists have observed a variety of internal chemical signals by which organisms trigger and modulate normal differentiation of cells, development of organs, immune responses, and neural activity.

"What I think endocrine disrupters have done is show us that they—and presumably other toxicants as well—can exert their damage by mimicking, blocking, or altering these natural signaling pathways," says McLachlan, who heads the Center for Bioenvironmental Research at Tulane and Xavier Universities in New Orleans.

Unfortunately, he notes, they do this without leaving footprints. Hormone disrupters are suspected of causing diverse abnormalities recently observed in wildlife, from extra limbs to altered sexual development, but the case is hard to prove.

McLachlan predicts that perhaps a decade from now, people who today study the immune, nervous, or hormone systems will be collaborating in a search for tests capable of pinpointing agents that can subtly alter communications within and between many—if not all—of these related systems.

These pseudohormones introduce "some profound challenges to toxicology," says Devra Lee Davis, a toxicologist with the World Resources Institute in Washington, D.C. For example, hormone mimics are "forcing us to rethink the notion of dose," she says. The traditional axiom that "the dose makes the poison" has been interpreted to mean that as exposures increase, so does the likelihood that a substance will do damage. However, she observes, several recent laboratory studies suggest that for some hormone mimics, lower doses can cause greater effects than larger ones.

In terms of risk, an exposure's "timing is going to turn out to be as critical as dose," she believes. At present, scientists can't reliably predict the critical windows of vulnerability to exposure or when the effects will appear. Aging is one of those "largely ignored" windows that will gain attention in coming years, predicts Susan L. Schantz, a neurotoxicologist at the University of Illinois at Urbana-Champaign.

At birth, the brain possesses a tremendous functional reserve—nerves that back each other up. Over time, as nerve cells die, that reserve shrinks. Other organs also suffer age-related declines in function as backup systems weaken. Those organs may be able to compensate for mild, chronic environmental assaults and remain symptomfree—until aging removes that protective backup. Moreover, says neurotoxicologist Bernard Weiss of the University of Rochester (N.Y.), early or chronic damage by pollutants may trigger the premature onset of infirmities that normally develop as reserves diminish.

For instance, concentrations of dopamine, a neurotransmitter made by brain cells, decline with age; PCBs can also decrease dopamine. So in PCB-exposed people, Schantz says, aging might trigger tremors and other effects resembling Parkinson's disease, a disorder of insufficient dopamine.

On the other hand, assaults by pollutants might cause immediate damage that is too subtle to distinguish from the variability typical of a population, notes toxicologist Linda S. Birnbaum of the Environmental Protection Agency in Research Triangle Park, N.C. For instance, PCB exposures, ubiquitous throughout the United States, may lower IQ by at least 5 points. This may not only limit the geniuses in a population but increase the number of intellectually handicapped needing social services, Weiss and Birnbaum point out.

Similarly, says Joan M. Cranmer of the University of Arkansas for Medical Sciences in Little Rock, dioxin exposures may boost the risk of mature-onset diabetes. If such exposures trigger the disease at a younger age, or in response to a smaller weight gain, they could have "calamitous" consequences for health care costs, she notes, and diminish the quality of life for increasing numbers of people.

In each case, the result may be a small, but economically important, populationwide drop in the functioning of exposed persons. To identify these problems, Birnbaum believes, toxicologists will have to measure change within entire populations, not just individuals.

History provides "no guide as to the magnitude or diversity of adverse effects [to anticipate]," Cranmer notes, because when it comes to many important toxicants, today's Baby Boomers "will be the first generation exposed from conception to grave." □

1972
Theory of punctuated equilibrium published

1973
Nuclear magnetic resonance used for medical diagnosis

1973
Foreign gene added to bacterium

1974
Chlorofluorocarbons recognized as threat to ozone layer

1974
Quark theory supported experimentally

1975
Sociobiology launched

1976
First cancer-causing gene identified

1977
Hydrothermal vent communities discovered on ocean floor

1978
Discovery of Lucy and her more than 4-million-year-old fossil cohorts

1978
First test-tube baby born

1979
Voyager 1 discovers volcanic activity on Jupiter's moon Io