# Zeroing in on Brain Toxins

Almost everyone is now sensitized to the possibility that some manmade substances in the environment, such as pesticides, may have a role in causing cancer. But cancer isn't the only possible risk of these compounds, according to a report released last week by the National Research Council (NRC). The report, "Environmental Neurotoxicity," zeroes in on a new, little understood threat: the possibility that some environmental substances contribute to degenerative neurological diseases such as Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis (Lou Gehrig's disease). The report calls for far more extensive testing of pesticides and other chemicals to determine their potential for toxic effects on the human nervous system—a call that's being resisted by industry but may be heeded in Congress.

The NRC report builds on research over the past decade suggesting that unspecified environmental toxins may play a role in degenerative brain diseases. "It seems plausible that some fraction of chronic neurodegenerative diseases may reflect the long-term consequence of those exposures, just as some fraction of cancer reflects the long-term consequence of chemical exposure," says epidemiologist Philip Landrigan of the Mt. Sinai School of Medicine, who chaired the NRC panel. Perhaps the most dramatic case was an epidemic of a Parkinson's-like illness a decade ago in California among users of a synthetic heroin. Later research showed that a toxic metabolite of the drug was attacking the same brain structures that are affected in Parkinson's disease, raising suspicions that ordinary cases of the disease might also be due to an environmental toxin.

In spite of such suggestive findings, few of the roughly 70,000 chemicals in commercial use have been tested for neurotoxicity, according to the NRC report. Currently, the only products the Environmental Protection Agency (EPA) requires industry to test for neurotoxicity are those the agency designates "high volume"—meaning they're produced in quantities of more than 100,000 kilograms per year or are so widespread that many workers or consumers are likely to come in contact with them, says Suzanne McMaster, an EPA neurotoxicologist. That category includes fewer than 20% of the chemicals EPA licenses. For "low-volume" chemicals, the EPA tries to estimate neurotoxicity by the structure-activity relationship (SAR) method, which is based on a comparison of a chemical's structure to that of a known neurotoxin or nervous-system receptor molecule.

That's not good enough, says the report, which calls the SAR method a "poor basis for predicting neurotoxic potential." The report's rejection of the SAR method is news, according to NRC committee member W. Kent Anger, a behavioral neurotoxicologist at the Oregon Health Sciences University in Portland: "I don't think an authoritative source has said that before." Instead of relying on SARs, the report suggests that the EPA should routinely put chemicals through a three-tiered neurotoxicological testing battery consisting of an initial screen, dose-response studies, and mechanism studies. "With the tiered-testing battery we laid out, there's a reasonable hope of catching most neurotoxins," says Landrigan.

Spokespeople for industry, however, don't think an elaborate new testing scheme is needed for all chemicals. "There's a huge world of chemicals, some of which deserve rigorous testing, others that don't," says Roger O. McClellan, president of the Chemical Industry Institute of Toxicology. Extensive neurotoxicity testing, he says, might be impractically expensive for substances not likely to find a large market. He suggests that the EPA and industry look for a middle ground between SARs and extensive testing.

But some members of Congress think additional surveillance of environmental neurotoxicity would be a good thing. Sponsors of a bill called the "Safety of Pesticides in Food Act," which would require tougher scrutiny of pesticides for neurotoxicity, carcinogenic effects, and reproductive toxicity, are hailing the report. Senator Edward M. Kennedy (D–MA), sponsor of the Senate version, said in a statement last week: "This report makes clear how little we know about the health consequences of the thousands of toxic chemicals that permeate our high-tech society. The most ominous finding is that current risk assessment methods are not sensitive enough to detect real and avoidable risks lurking in our environment." Kennedy and the bill's other supporters think the NRC report may be just the ammunition they need to win the support of reluctant colleagues. ■ RICHARD STONE

# Malaria Vaccine on Trial at Last?

Army medical researchers are planning to seek permission in the next month to test a controversial malaria vaccine in U.S. volunteers. The vaccine was devised in the mid-1980s by Manuel Patarroyo, director of the Institute of Immunology at the Hospital of San Juan de Dios in Bogota, Colombia, and has since received much attention in the media—not all of it flattering. If the Food and Drug Administration (FDA) clears the project, and if a series of two ethical and one scientific review boards gives the nod, Jerry Sadoff, W. Ripley Ballou, and Daniel Gordon at the Walter Reed Army Institute of Research in Washington, D.C. hope to begin recruiting Army personnel for clinical trials as soon as this spring.

The vaccine has made its way to center stage in part because any medication that holds out the hope of reducing the number of new cases of malaria each year (currently around 270 million) deserves attention. Patarroyo himself has fanned this hope by injecting more than 20,000 volunteer patients in Brazil, Columbia, and Venezuela and arguing that the vaccine is protecting 70% or more, an extraordinarily good result. But the Patarroyo vaccine has also been making the news because of the controversy those claims have generated. Many scientists in North America and Europe remain unpersuaded of the vaccine's efficacy. Among the skeptics is Britain's Medical Research Council (MRC), which—as *The New Scientist* has reported—has twice turned down a request by researcher Brian Greenwood to mount field tests in The Gambia, in western Africa. The reason for the refusal: The MRC has concluded that the available data on Patarroyo's vaccine are not adequate to justify the council's support for an experiment in humans.

Indeed, other scientists, including a group at the U.S. Centers for Disease Control (CDC), have had difficulty replicating the animal experiments that preceded human trials of Patarroyo's vaccine. Carlos Campbell, chief of CDC's malaria research lab, says that while there is "enormous interest" in the Patarroyo vaccine, the "details are still not clear." Two vaccine tests with animals have proved "stone cold negative," says Campbell—"ours [at CDC] and one by Socrates Herrera," a colleague of Patarroyo's in Colombia. Patarroyo's human results, meanwhile, are meeting with skepticism because he has not published results of any experiment in which treated volunteers are compared with "controls" receiving a placebo, nor have any of the published experiments used "double-blind" methods to mask the identity of the treated patients.