



Where you deliver water and how is a powerful tool.

Philip Schmuck

quoted in *Conservation Foundation Newsletter*, May 1979

### HAZARDOUS WASTE

## Wasting Away in the South Pacific

A two-year survey of 13 Pacific Island countries has found stockpiles of hazardous chemicals and more than 50 contaminated sites throughout the South Pacific region. The South Pacific Regional Environment Programme (SPREP), the Samoa-based international environmental organization that carried out the survey, estimates the cost of cleaning up the sites at \$5–10 million. A report of the survey, titled *Management of Persistent Organic Pollutants in Pacific Island Countries*, was released in August 2000.

SPREP environmental waste management coordinator Bruce Graham says that 200 sites were inspected during the survey. Surplus chemicals were found at 142 of these sites, and of those, contamination was suspected at 112. The chemicals found included pesticides, polychlorinated biphenyls (PCBs), general industrial chemicals, medical wastes, laboratory chemicals, oil, bitumen, timber treatment chemicals,

and fertilizers, any of which may cause adverse health effects in people and animals and may render a location unusable for other purposes such as farming or building. Graham says that urgent action is needed at sites where agricultural chemicals are improperly stored in Fiji, the Federated States of Micronesia, the Solomon Islands, and Kiribati. Immediate work on these sites would probably cost about \$60,000, Graham says.

The survey was undertaken by SPREP to study toxic waste in its member nations, many of which lack the financial resources to address these problems on their own. Some member nations, such as the Federated States of Micronesia, the Marshall Islands, and Palau, are former “trust territories” of the United States, held in trust following World War II until they could achieve independence. Since shedding that status in the mid-1970s, they no longer receive funding or support from the U.S. Environmental Protection Agency (EPA). Since then, says Carl Goldstein, the EPA Region 9 program coordinator for American Samoa, the Pacific Island nations have fallen behind in monitoring and response to hazardous waste sites.

“As far as this kind of activity goes, the South Pacific nations have insufficient resources—funding and manpower—to address and correct these highly technical and costly problems,” says Goldstein, adding that the SPREP report is “an important first step toward comprehensive hazardous waste management in the South Pacific.”

The report recommends that some 131 tons of PCBs and 42 tons of pesticides be removed from the islands to sites where they can be disposed of safely. Agricultural pesticides pose some of the most urgent problems; the report describes one site in the Solomon Islands where children’s fingerprints were found in improperly stored DDT. The report also identifies 11 sites where island groundwater has been contaminated by oil spills. This poses particular problems in the Pacific Islands, where fresh water sources are mainly limited to rainfall and groundwater.

While improved storage facilities may be sufficient to resolve problems at many of the sites with surplus agricultural chemicals, the question of how to deal with PCBs—particularly where to put them—may be somewhat trickier. Goldstein points out that the United States will not accept PCBs from foreign countries, including the former trust territories, and suggests that Europe or Australia may be more likely disposal sites.

The report has reminded many Pacific Island countries of the importance of ratifying the Basel Convention, which governs the shipment of hazardous waste between countries, and the Waigani Convention, which specifically controls hazardous waste movement within the Pacific Islands. Although many island nations have signed on to the Waigani Convention, they have been slow to ratify it largely due to reservations regarding its provisions for pollution prevention.

However, says Graham, ratification of these conventions would greatly ease the way for offshore disposal. He adds, “It also allows countries to tap into the extensive technical expertise and support available through the Basel Secretariat.”

Although the costs of addressing these toxic sites may appear daunting to island nations, many of which have small or nonexistent environmental budgets, Graham appears optimistic about securing funding from outside national and international sources to pay for the work. “I expect to be able to announce a significant funding package early next year,” he says. —John F. Lauerman



**No island is an island . . .** at least when it comes to toxic waste. New surveys show that the Pacific Islands have not escaped the scourge of stockpiles of chemicals and other contaminants.

Corel: Inesis; South Pacific Regional Environment Programme

## MARINE SCIENCE

## Finding *Pfiesteria* Fast

Science is slowly gaining ground on the still-mysterious *Pfiesteria*, a toxic dinoflagellate blamed for human illness and massive fish kills in two U.S. states during the past decade. Aiding researchers are recent breakthroughs that let them identify *Pfiesteria* more quickly and accurately.

Parke A. Rublee, a professor of biology at the University of North Carolina at Greensboro, working with JoAnn M. Burkholder, a professor of marine science at North Carolina State University, first developed rapid techniques to identify *Pfiesteria*. Their polymerase chain reaction (PCR) assay, available in 1998, is used in monitoring efforts by several states. Recently, a team led by David W. Oldach, an assistant professor of medicine at the University of Maryland School of Medicine in Baltimore, used a technique known as the heteroduplex mobility assay (HMA) to identify ribosomal gene sequences from *Pfiesteria* species. With that information, they developed other PCR assays for *Pfiesteria* species that are nearly 100% accurate in identifying their presence in water and sediment samples.

*Pfiesteria* was first identified in 1988 but didn't draw much attention until it was tagged as the culprit in a series of fish die-offs throughout the 1990s that killed over one billion fish, mostly in North Carolina but also in Maryland. *Pfiesteria* also is a suspect in fish kills elsewhere along the Eastern seaboard. Some people who worked near or with water or sediment in fish kill areas have suffered short- and long-term symptoms believed to be linked to *Pfiesteria* such as memory loss, learning impairment, breathing difficulty, nausea, lethargy, and skin lesions. (These symptoms match health problems sustained by laboratory staff working with toxic *Pfiesteria* cultures until such efforts were restricted to biohazard III containment facilities.)

Before the breakthroughs with HMA and PCR, investigators needed nearly two weeks using a scanning electron microscope and thecal plate analysis to confirm whether *Pfiesteria* was in a water sample. With improved PCR, that time has been slashed to as little as two hours of lab time, and even faster equipment that can work in the lab or the field is coming on the market. If other toxic algae are believed to be present, HMA (which takes about 48 hours) can then be used to assess which species are present in the water sample, and novel HMA patterns representing other organisms can then be targeted

for sequencing analyses. Though the technique allows rapid identification of *Pfiesteria*, it isn't foolproof; still, public health officials are better equipped to decide quickly if they need to warn water users of a possible hazard.

To develop the technique, Oldach's team gathered water samples from an outbreak area, then filtered them to extract material suspected to contain *Pfiesteria*. Together with Rublee and Burkholder, they used PCR assay to amplify a region of the microbes' DNA, as described in the 11 April 2000 issue of *Proceedings of the National Academy of Sciences*. Using a special gel apparatus, they then ran an HMA, which works off the fact that DNA heteroduplexes—nucleic acid molecules composed of two chains, with each derived from a different parent molecule—migrate more slowly through the gel than homoduplexes. With HMA, a "signature" sequence pattern was identified that was present in all of the toxic *Pfiesteria* cultures assessed, as well as in water samples collected during *Pfiesteria*-related fish kills.

Through this approach, the investigators were able to overcome the problem that pure *Pfiesteria* cultures were not yet available for DNA sequencing procedures, and that some cultures (particularly those in which toxicity was maintained through the regular introduction of live fish prey) are contaminated by other eukaryotic organisms. Once the HMA-generated partial sequence information was available, the investigators were able to complete ribosomal gene sequencing work for these and related organisms, and to develop highly specific PCR assays for *P. piscicida* and *P. shumwayae* sp. nov., as reported in the November 2000 issue of *Applied and Environmental Microbiology*.

But HMA and PCR still can't determine whether *Pfiesteria* species are in a toxic stage. Burkholder has shown that these dinoflagellates morph through many stages—only some of which are toxic to humans or fish—during their complex life cycles. A toxic phase can develop and vanish in a matter of hours—or weeks. Only the fish bioassay, an expensive, multistep procedure, can tell whether *Pfiesteria* from estuarine waters is in actively toxic mode. HMA and PCR also can't pinpoint how many *Pfiesteria* cells are in the water or sediment. (It takes about 100 actively toxic *Pfiesteria* cells per milliliter of water to cause fish health problems, and about 300 cells per milliliter to kill fish.) And researchers are still trying to identify the actual toxin and triggering mechanisms involved in *Pfiesteria* toxicity. Until these factors are identified, monitoring for the two species alone will provide only a few pieces of the puzzle needed for confirmation of a toxic *Pfiesteria* event. —Bob Weinhold

## New Antibacterial Warnings

On 19 September 2000, the U.S. Food and Drug Administration proposed that systemic antibacterial drugs sold for human use be labeled with warnings against the emergence of drug-resistant strains of bacteria. The proposal is intended to encourage physicians to prescribe these drugs only when clinically indicated and to counsel their patients on the need to take the drugs exactly as prescribed.

The new labeling would include reminders that antibacterials do not treat viral infections and that the type of bacteria being treated should be considered when choosing the best drug. A final rule on this proposal would apply to all new systemic antibacterial drugs as well as to drugs that have already been approved and are on the market.



## UN Driving Motor Vehicle Regs

A United Nations agreement to develop globally uniform motor vehicle regulations took effect on 28 August 2000. The regulations will provide greater environmental protection, energy efficiency, vehicle safety, and pollution reduction. Although approved in 1998, the agreement could not be enacted until it was signed by eight member nations. In July, the Russian Federation became the eighth country to sign the agreement; the United States was the first.

The U.S. Environmental Protection Agency and Department of Transportation were key players in developing the agreement, which will take into account the best available and most cost-effective technologies as well as public health considerations. Current levels of environmental protection and vehicle safety will not be compromised in the quest for uniformity, according to UN officials, who also emphasize that regulatory activities will be conducted in an open manner. The other six signers are Canada, Japan, France, England, the European Union, and Germany.

## Have Your Plate and Eat It Too

New cafeteria tableware may not only serve food but also help to provide future food. Tableware made developed by EarthShell Corporation, made mainly of limestone and potato starch, degrades relatively quickly into compost.

In a pilot study at the U.S. Department of the Interior cafeteria in Washington, D.C., EarthShell plates and bowls were mixed with food scraps, leaves, and grass clippings to produce a compost mixture. After six months, no traces of the products were found in the compost. When using the finished compost for growing cucumbers, U.S. Department of Agriculture scientists found it comparable to commercial potting mixtures.





## PHARMACEUTICALS

## Prescription for Mutant Prevention

In the battle against drug-resistant microbes, it might be necessary to change the rules governing what constitutes an effective antibiotic. The standard, says Paul Tulkens, a professor of pharmacology at Catholic University in Louvain, Belgium, is for manufacturers to create antibiotics that achieve a minimum inhibitory concentration (MIC), the amount of antibiotic required to inhibit growth of—but not necessarily kill—a given bacterium *in vitro*. Tulkens claims a better system would target a so-called mutant prevention concentration (MPC), the amount required to prevent emergence of mutant, resistant strains *in vitro* by actually killing the bacterium.

This concept was first developed by scientists at the Public Health Research Institute in New York. In a paper published in the September 2000 issue of *Antimicrobial Agents and Chemotherapy*, they wrote, “[W]e have defined a drug concentration threshold above which bacterial cells require the presence of two or more resistance mutations for growth. . . . [A]dministration of antibiotic above the [MPC] threshold . . . should severely restrict selection of resistant mutants.”

“Inhibition doesn’t go far enough,” Tulkens argued during a presentation at the September 2000 Interscience Conference on Antimicrobial Agents and Chemotherapy. “You want to go beyond inhibition to kill the microbes.” Tulkens says that newer antibiotics such as moxifloxacin and gatifloxacin are not only capable of achieving acceptable MIC at low doses, but also go on to kill the bugs, preventing the bacteria from developing defenses against the new compounds; in effect, they achieve MPC.

The need for drugs that combat resistance is urgent, Tulkens says, especially in a world in which resistance to beta-lactam antibiotics (the penicillin family) is as high as 80% among some pneumonia-causing microbes. For example, Tulkens says, *Streptococcus pneumoniae* resistance or decreased sensitivity to beta-lactams can be as high as 40% in some regions of North America, 60% in southern Europe, 36% in Latin America, and 67% in the Asia-Pacific region. Resistant strains of *Moraxella catarrhalis* are found over 80% of the time in North America and 50–80% of the time in Latin America. And *Haemophilus influenzae* resistance is found in up to 30% of strains in Europe.

Exactly how well the MPC concept will be accepted will take time to see, says Donald Low,

head of the Department of Microbiology at the University of Toronto. In order for regulatory agencies such as the U.S. Food and Drug Administration (FDA) to accept MPC, he says, clinical trials must show that such drugs correlate not only with clinical efficacy but with the prevention of resistance.



**Darwinian drugs?** A new theory suggests that antimicrobial agents’ propensity for inducing resistance should be considered in drug formulations.

But the concept of MPC has not penetrated the FDA. Mark Goldberger, director of the FDA Division of Special Pathogen and Immunologic Drug Products, says, “I don’t believe that there has been any discussion of [MPC as a] major criterion for approval.” Goldberger notes, however, that drug submissions to the FDA do contain microbiologic data, which generally includes information on the drug’s ability to generate resistant organisms. “Although a favorable result in such testing is encouraging,” he says, “it must be viewed in the context of overall efficacy and safety.” —Ed Susman

## DRUG ABUSE

## Leading to Drug Abuse

Exposure to lead during childhood poses many risks, such as anemia, behavioral problems, and neurologic consequences. Heavier cocaine use among drug users might be added to the roster, according to a research team led by psychologist Jack R. Nation at Texas A&M University in College Station. He posits that childhood lead exposure reduces the release of dopamine in the brain, requiring higher drug doses to experience euphoric effects. The team reports in the September 2000 issue of *Pharmacology, Biochemistry, and Behavior* that rat pups exposed to lead in the womb and during lactation required larger doses of cocaine to achieve a high. “Lead may induce a sort of tolerance or may alter sensitivity to drug abuse,” Nation says.

Nation and colleagues administered 8- and 16-milligram (mg) doses of lead by gavage to adult female rats starting 30 days before breeding them. Dosing continued through pregnancy and the birth and nursing of pups, ending at weaning. A control group received no lead. The 8-mg dose yielded a blood lead concentration in the mothers of some 20 micrograms per deciliter, comparable to the level often found in urban human populations.

At 30 and 90 days after birth, the researchers gave the pups cocaine doses of 1.25, 2.5, or 5.0 mg per kilogram of body weight. Unexposed rats responded to the drug at all doses, but rats whose mothers received the higher lead dose needed the highest cocaine dose to show a response. In the rats, the observed changes in sensitivity lasted more than a year—a period analogous to 20–30 years in humans, Nation says. And the neurologic effects lasted even after lead residues cleared the soft tissues, indicating that changes may be permanent. The pups’ blood lead concentrations at the times of cocaine dosing were comparable to those common in urban children, who by socioeconomic circumstance may also be at greater risk of drug use.

Nation hypothesizes that lead may reduce production of the neurotransmitter dopamine and thereby change sensitivity in exposed people,

though he acknowledges that other mechanisms are possible. For one, lead may simply damage the central nervous system outright, explains Michael T. Bardo, director of graduate studies in psychology at the University of Kentucky in Lexington. The mechanism is readily testable by measuring dopamine release in the brain’s “reward” center, or nucleus accumbens, while rats are performing a behavioral task, he says.

Nation observed a similar effect in previous studies of exposure to cadmium—prevalent in tobacco smoke—in unborn rats, though the mechanism of action is likely wholly different, since cadmium may not penetrate the blood-brain barrier. “If these contaminants are promoting drug use,” Nation says, “then you have a relatively high public health risk.”

But other researchers say the jury is still out on how—and whether—lead or other environmental agents may affect drug use. Although reasonably good evidence supports the notion that lowered dopamine concentrations may prompt an individual to use more of a drug to get high, other studies suggest that reduced dopamine concentrations may actually decrease the likelihood of drug abuse. Stephen M. Lasley, a neurotoxicologist at the University of Illinois College of Medicine at Peoria says it is just as likely that lead exposure may actually hamper a habit from forming because a first-time user may not experience a high. “It may take greater intake initially to establish a habit,” he says.

The idea that lead is involved in drug use dates to morphine studies in the 1970s, according to Deborah Cory-Slechta, head of environmental medicine at the University of Rochester School of Medicine and Dentistry. Although she says “there’s good evidence that the dopamine system is clearly targeted by lead,” she says she’d like to see more proof, preferably drug self-administration studies—the gold standard of behavioral work—to be convinced there’s a clear association with drug use.

It’s unlikely that exposure to lead would automatically lead to taking drugs because various sociocultural and psychologic factors are involved in the initiation of drug use, Bardo says. However, he adds, if exposure to lead increases the subsequent drug intake in an individual prone to substance abuse, then one would expect that the risk of dangers associated with overdose, such as heart attack and cocaine-induced psychosis, would be increased. —Julie Wakefield

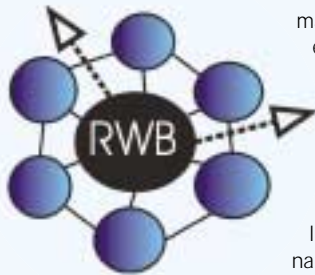


## Regional Workbench

The NIEHS has developed the Binational Border Research in Disease and Geospatial Research (BRIDGE) Program to address environmental problems associated with the rapid industrial and population growth affecting Texas, Arizona, California, New Mexico, and the six Mexican states across the border. With implementation planned for fiscal year 2002, the BRIDGE Program will blend multidisciplinary biomedical and nonbiomedical research, community outreach, and technology transfer in a strong partnership of federal and environmental agencies to help eliminate the growing environmental problems along the border. Among the region's problems is a strong need for sustainable development measures.

As a step toward establishing a consortium to address these issues, the NIEHS cosponsored the Binational Conference on Environmental Research and Policy on 12–13 June 2000 in San Diego. The purpose of this conference was to provide NIEHS leaders with a strategic agenda and criteria for supporting future research on border region environmental problems. The conference was also intended as a starting point for a coalition of border universities and industrial and civic partners.

To further this coalition, conference co-organizer Keith Pezzoli and colleagues have developed the Regional Workbench (RWB) Web site, located at <http://regionalworkbench.org/>. The RWB is a collaborative, Web-based network of researchers and community partners dedicated to furthering the goals of sustainable development. The RWB site links projects, searchable topic maps, data guides, tutorials, and interactive tools for conceptualizing, designing, conducting, and sharing multidisciplinary research. The RWB also provides a mode of communication among universities, industry, government, and community-based organizations, enabling researchers to network with the end users of their research.



Visitors can click on the Knowledge Clusters link on the main page to read more about subtopics such as industrial ecology, urban and regional planning, social capital and community development, and quality of life and health. Each subtopic link leads to a directory of online resources. For instance, under the Industrial Ecology and Systems of Innovation link, visitors can access the Environmental Defense Scorecard, which lists the top environmental issues in specific areas and includes a database of local pollution problems searchable by geographic area or company name. This same link also leads viewers to a new interactive mapping tool developed by the San Diego Association of

Governments that lets planners and decision makers see where businesses representing different industries are clustered in San Diego County. Under the Urban and Regional Planning subtopic, visitors can access the National Neighborhood Coalition, an organization that promotes public policies to strengthen the role of the community and neighborhood-based nonprofits, and that fosters efforts to build healthy, sustainable communities. The Quality of Life/Health subtopic includes a link to the San Diego County Quality of Life program, described as "a progressive approach to strategic planning, integration, and improvement of client centered services."

The Social Capital and Community Development subtopic provides a link to the U.S. Department of Commerce Technology Opportunities Program, a merit-based grant program that has yielded practical applications for new telecommunications and information technologies to serve the public. This subtopic also contains a link to the Digital Divide Web site describing federal efforts to provide all Americans with access to Internet technology, which has become crucial to economic growth and advancement. Such efforts include the establishment of community computer centers and the recycling and reuse of old computers.

Back on the main page, the Research Guide link leads to a wealth of data sources, data mining tools, organizational contacts, Internet links, references to existing research and scholarly literature, and specific suggestions for individual and team research projects. Links include the Border EcoWeb, the Commission for Environmental Cooperation/North American Integrated Information System, and SanGIS, a San Diego-based partnership that is responsible for the maintenance of and access to regional geographic databases.

According to the home page, although the RWB's geographic focus is now on the U.S.–Mexico border, especially Southern California and Baja California, the ultimate goal of the project is to create a global network of regionally based research collaboratives seeking the knowledge, methods, and practice necessary to engender sustainable development. The hope is that students will gain hands-on experience in a manner that emphasizes not only multidisciplinary scholarship but also civic-minded workforce development. –Lindsey A. Greene

## USDA Says What's Organic

On 20 December 2000, U.S. Agriculture Secretary Dan Glickman announced national standards for organic foods, describing them as "the strictest, most comprehensive organic standards in the world." The standards apply to every step of organic food production and ban synthetic pesticides and fertilizers, sewer sludge fertilizers, irradiation, and genetic engineering from use with organic products. The new rules also set expectations for soil conservation and enrichment.



The standards take effect on 19 February 2001 and establish four labeling categories determined by the percentage of organic ingredients in the product. Only products that adhere to the new rules will be allowed to use the term "organic" in their labeling. The regulations are intended to replace the various organic production standards set by states and private agencies.

## Heavy Calcium Issue

A study by researchers at the University of Florida in Gainesville has determined that despite regulatory efforts and widespread publicity addressing the risks of lead exposure from calcium supplements, many supplements still on the market contain detectable amounts of lead. The study examined 23 calcium formulations and found concentrations of lead as high as 3.4 micrograms per dose in the 1,500-milligram daily dose recommended for women trying to prevent or treat osteoporosis.

In the study, published in the 20 September 2000 issue of *JAMA*, the researchers stated that although the amounts of lead found were small, they could pose a potential risk to certain people who take larger-than-usual doses of calcium, such as those with chronic renal failure. They stress that consumers should look for supplements that have been tested for lead content.

## Cleaning Up Paradise

In August 1999, the European Union (EU) launched a program to assist eight South Pacific Island nations in managing their solid waste. On these islands, where space is at a premium, landfills are overflowing, and dumping of wastes including plastic and paper packaging, glass bottles, foam containers, scrap metal, and chemical and industrial refuse is uncontrolled.

As part of the program, a video titled "Waste World" was produced that documents the extent of the problems created by poor waste disposal practices—these problems include water contamination, increases in disease-carrying pests, and potential loss of tourism revenue. The video also features options for controlling the problem such as reducing the islands' reliance on imported goods and creating public awareness of the issue.