From the Lab to the Land

A major challenge in environmental health research is the question of technology transfer, or how to turn basic research findings into useful technology that deals with the critical issues confronting the world's public and environmental health. The NIEHS Superfund Basic Research Program (SBRP) has been responding to the challenge of technology transfer since its founding in 1986. At the SBRP annual meeting held 3–6 November 2002 in Tucson, Arizona, participants had the opportunity to learn about some of the groundbreaking work coming out of the program, and about how findings are being applied in new and profitable ways.

Established under the Superfund Amendments and Reauthorization Act of 1986, the SBRP was intended to be a means for improving scientists' ability to identify, assess, and evaluate the potential health effects of exposure to hazardous waste, and for developing innovative chemical, biological, and physical remediation technologies. "[The SBRP] is designed to provide research in making decisions—decisions about cleanup and decisions about assessing risk, determining how best to deal with the uncertainty of exposure and related health consequences primarily in people," says William Suk, deputy director of extramural research at the NIEHS and director of the SBRP. "It is interdisciplinary, and an absolutely outstanding example of how to bring top-notch people together from a variety of disciplines to answer hard questions and develop different approaches."

The SBRP supports peer-reviewed research in 19 university-based programs, with participation by a total of 70 collaborating institutions.The program also supports training of graduate students and postdoctoral researchers. The SBRP had a fiscal year 2002 budget of about $45 million.

Technology Transfer at the Heart of the Program

Each university program focuses on one central research theme, pulling in collaborators from an assortment of disciplines—from ecology, to epidemiology, to toxicology—to work together on multifaceted projects. In one such project, Milton Gordon, a University of Washington specialist in phytoremediation, and Lee Newman, a research scientist at the Savannah River Ecology Laboratory in South Carolina, developed a genetically modified poplar tree that could be planted around polluted sites to metabolize chlorinated solvents into carbon dioxide and water. They brought in plant biologists, toxicologists, botanists, and other experts to help develop the tree. Gordon credits the SBRP with bringing together the people, including microbiologists, hydrologists, and others, who each contributed a piece of the puzzle and provided an invaluable resource through their subject matter expertise.

"[The cleanup of chlorinated solvents] is a vital issue because 25% of the water supplies in the United States have traces of chlorinated solvents," he says. "Poplar trees work like green 'livers' and break these substances down into harmless components. When we get approval for the use of genetically engineered trees outside of the lab, we'll be able to increase the efficiency of the process several hundredfold."

In another project, Michael Hooper, a specialist in wildlife biomarker research at Texas Tech University, a part of the University of Washington center, was one of the leaders in a study of the Rocky Mountain Arsenal National Wildlife Refuge. This study used biomonitoring of indigenous wildlife species to do two things: assess the bioavailability of the contaminants on the site and determine, in effect, how clean is clean enough when it comes to remediating a site.

The 27-square-mile site outside of Denver, Colorado is a former military installation where chemical and incendiary weapons were produced, stored, and later demilitarized, and where several companies leased facilities to produce a range of organochlorine insecticides (including dieldrin, a possible carcinogen), herbicides, and other chemicals. The site was placed on the Superfund National Priorities List in 1982. Following the discovery of a bald eagle winter roosting area on the site in 1986, Congress designated the site as a future refuge.

Hooper's project involved setting up nesting boxes throughout the site, and studying dieldrin uptake in starlings. The studies showed that starlings nesting in areas of relatively low contamination showed no apparent effects. This indicated that on-site burial of contaminated soil would be an adequate method, from a wildlife health perspective, for dealing with the pollution, even though it did not completely eradicate the contamination.

"Traditional [remediation] procedures might have involved digging up the contaminated soil, then hauling it away for burning to remove the organochlorines. . . . Trucking in clean soils would have damaged the pristine refuge areas from where they were taken, and would have caused further damage through the road-building needed to accommodate these huge trucks," Hooper says. He estimates probably $3 million was saved immediately by not having to

From refuse to refuge. Researchers study the effects of dieldrin contamination on starlings at the Rocky Mountain Arsenal National Wildlife Refuge, where the chemical was formerly produced.

Large photo, inset left: Michael Hooper

Remediation plant. Genetically modified poplar trees, which can take up chlorinated solvents, are developed to remediate polluted sites.

study any further soils for backfill, and probably many more millions were saved by not having to build access roads and use heavy equipment to extract pure soil.

Hooper's other Rocky Mountain Arsenal research on badgers—the predators highest on the food chain at this site—helped show that the potential for exposure and uptake was not as great as laboratory studies had indicated, revealing that it was not necessary to remove all traces of contamination. "Instead of going by lab studies on dogs, rats, and other animals," he says, "we were able to base our decisions on wildlife living on-site."

Hooper has done similar work near Butte, Montana, where ore removed from the Berkeley Pit was smelted for copper, leaving residual contamination with copper, lead, zinc, arsenic, and cadmium. "This is a one-hundred-square-mile site," he says, "with a variety of habitats, so it was difficult to get a handle on it. The modeling done to assess risk suggested arsenic as the most significant threat, but we were able to show that lead was the greatest risk. That leads to a whole different approach to dealing with the problem than relying on lab studies."

Ronald Scrudato, director of the Environmental Research Center at the State University of New York Oswego, was involved in a technology transfer and outreach program involving the Mohawk nation and potential health impacts from sites along the St. Lawrence River and other nearby waterways. These sites were contaminated with industrial pollutants including polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), and PCB/PAH mixtures. Scrudato says there were several sites of concern, including a former General Motors facility (a designated federal Superfund site), and studies were needed to assess risk and impact on the area's resources, including fish and humans living near the contaminated sites.

"The SBRP is geared toward a broader understanding of the effects of inactive hazardous waste sites on the local environment and human health," he says. "The program provided us with the resources to address specific examples with the appropriate technology, and of perhaps equal importance, outreach and transfer of that information into the community that was being impacted."

Researchers were able to study a variety of cleanup technologies, including the use of supercritical fluids to extract and destroy PCBs in contaminated soil. An extensive study by G-Yull Rhee of the New York State Department of Health looked at how indigenous microbes attack PCBs in soil.

"Rhee's study revealed that you need a minimum [pollutant] concentration of about forty to fifty parts per million," Scrudato explains. "Otherwise, anaerobes aren't interested. But perhaps more importantly, it also showed that bacteria preferentially attack certain PCBs and not others. That leads to a group of PCBs that are not degradable by bacteria, and which results in a different mix of PCBs from what was originally in the soil." This leftover mix is less susceptible to biodegradation. Furthermore, says Scrudato, "These lower-chlorinated PCBs are more volatile and more soluble than the original PCBs, which makes them more available to fish and [thus to] humans. Also, we found that, if conditions are favorable, degradation occurs quickly to a certain level, then flattens out for an extended period of time. That was important to learn for future decontamination issues."

Scrudato says neither study received funding beyond their bench-scale level, but that a great deal of the knowledge and technology was transferred to the Mohawk

Studying and sharing. PCB-contaminated sites along the St. Lawrence River offered the SBRP the opportunity to study cleanup technologies and to transfer this knowledge to the Mohawk nation, whose members live along the river's banks.

Top to bottom: Milton Gordon; Corbis

nation, which has since initiated a variety of additional studies on the sites.

"We tried to provide a measure of self-sufficiency, so that when we left, the local residents could go out and get funding from other sources for additional studies," he says. "That put the Mohawk nation in more control of their own destiny, in addition to providing the impetus for higher education among many on the reservation."

The Money Crunch

If there's a problem with the SBRP, Scrudato feels, it arises out of the inescapable conflict between the need for immediate remediation of environmental situations that threaten human health and the need to understand as completely as possible how these potential health impacts play out over the long term.

Studies focusing on effects on human health "can be very subtle and may take a long time to discern," he points out. "Yet Superfund sites are being remediated while research is still going on. During the ten-year period we were at [the Mohawk site of] Akwesasne, many sites were dredged and remediated to levels that were guessed at because the research hadn't been concluded. We spend millions in remediation when we don't know what a safe level is, and ten years from now, we're going to have to go back and re-remediate many of those sites."

Across the board, says A. Jay Gandolfi, director of the SBRP program at the University of Arizona, principal investigators agree that program funding constraints are the major limiting factor. "There just isn't enough money in the [SBRP] to cover all the research people want to do and the associated technology transfer," he says.

"Money is always an issue," agrees Suk. "I think we would have needed more than one hundred million dollars to fund everything of worth we saw in our last review. That's probably not going to happen, but I think we have a record of doing a lot with what we do have."

Indeed, according to Suk, the program's effects are wide-reaching: "SBRP has had a major impact on the infrastructure of the environmental health sciences," he says. "It has had impact on how science is done and how it is communicated to a variety of audiences and stakeholders. It has had an impact on how research is translated into the hands of those who need it and need it now. It has had an impact on community outreach and how research findings are communicated to communities and how information is fed back to researchers so that their work has greater meaning and impact." **–Lance Frazer**

Headliners | Aging

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Heme Deficiency Effects Offer Clue to Alzheimer Disease

Atamna H, Killilea DW, Killilea AN, Ames BN. 2002. Heme deficiency may be a factor in the mitochondrial and neuronal decay of aging. *Proc Natl Acad Sci U S A*. 99(23):14807–14812.

Normal aging of the brain and the neurodegeneration caused by Alzheimer disease (AD) share several pathological changes, including mitochondrial dysfunction, oxidative stress, and loss of iron homeostasis. Synthesis of heme—the major intracellular functional form of iron—declines with age. Heme functions in hemoglobin and in a variety of enzymes and promotes the growth of nerve tissue. NIEHS grantee Bruce Ames and colleagues at the Children's Hospital Oakland Research Institute in Oakland, California, investigated the effect of a decline in heme on nerve cell function.

The investigators induced heme deficiency in a nerve cell culture system. The results of the study showed that heme deficiency in brain cells deterred normal mitochondrial function, stimulated oxidative stress and damage by activating synthesis of nitric oxide, altered amyloid proteins, and inhibited zinc and iron homeostasis. The metabolic changes that resulted from the heme deficiency were similar to those seen in dysfunctional neurons in patients with AD. In particular, in this model of heme deficiency, iron was the last parameter to change.

These findings are consistent, the authors say, with the hypothesis that an alteration in heme metabolism is the driving force for iron to accumulate in the cell. A marked increase in zinc and iron is associated with extracellular plaques found in AD patients, suggesting a disruption of metal homeostasis.

Common reasons for heme deficiency are iron and vitamin B_6 deficiencies, aging, and exposure to toxic metals such as aluminum. In addition, degradation of heme by heme oxygenase, which increases with age and in the brains of AD patients, may be a factor in changes in the metabolism of iron and heme with age. Therefore, heme deficiency may be an important and preventable part of the neurodegenerative process. **–Jerry Phelps**