ehp ENVIRONMENTAL HEALTH PERSPECTIVES

DECEMBER 2006
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Build a Personal Sensor

Pyrethroid Panic?

What's the Plan?

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STUDENT EDITION

The role of biology today, like the role of every other science, is simply to describe, and when it explains it does not mean that it arrives at finality; it only means that some descriptions are so charged with significance that they expose the relationship of cause and effect.
Donald Culross Peattie (1898–1964)

CHEMICAL EXPOSURES

Prostate Cancer and Early BPA Exposure

In animal models, estrogens can drive carcinogenesis of the prostate and have long been suspected of playing a role in human prostate cancer. Scientists have hypothesized that prenatal exposure to estrogen-like compounds, including monomeric bisphenol A (BPA), may account for recent increases in rates of prostate cancer. Now a rat study by Gail Prins of the University of Illinois at Chicago Department of Urology, Shuk-Mei Ho of the University of Cincinnati Department of Environmental Health, and their colleagues provides the first evidence of a direct link between low-dose BPA exposure during development and later prostate cancer.

BPA initially was synthesized for use in estrogenic-type drugs. BPA also is used as a cross-linking compound in the manufacture of polycarbonate plastics and epoxy resins. It leaches from food and beverage containers and from dental sealants, although the latter currently are not thought to be a major source of exposure. Today, this hormonally active chemical is widespread in the environment, with detectable serum levels present in approximately 90% of humans in the United States and other industrialized countries, by Prins's estimate. BPA concentrations measured in placental and fetal tissues may be fivefold higher than maternal serum levels, with higher levels found in male fetuses compared to females, according to Prins.

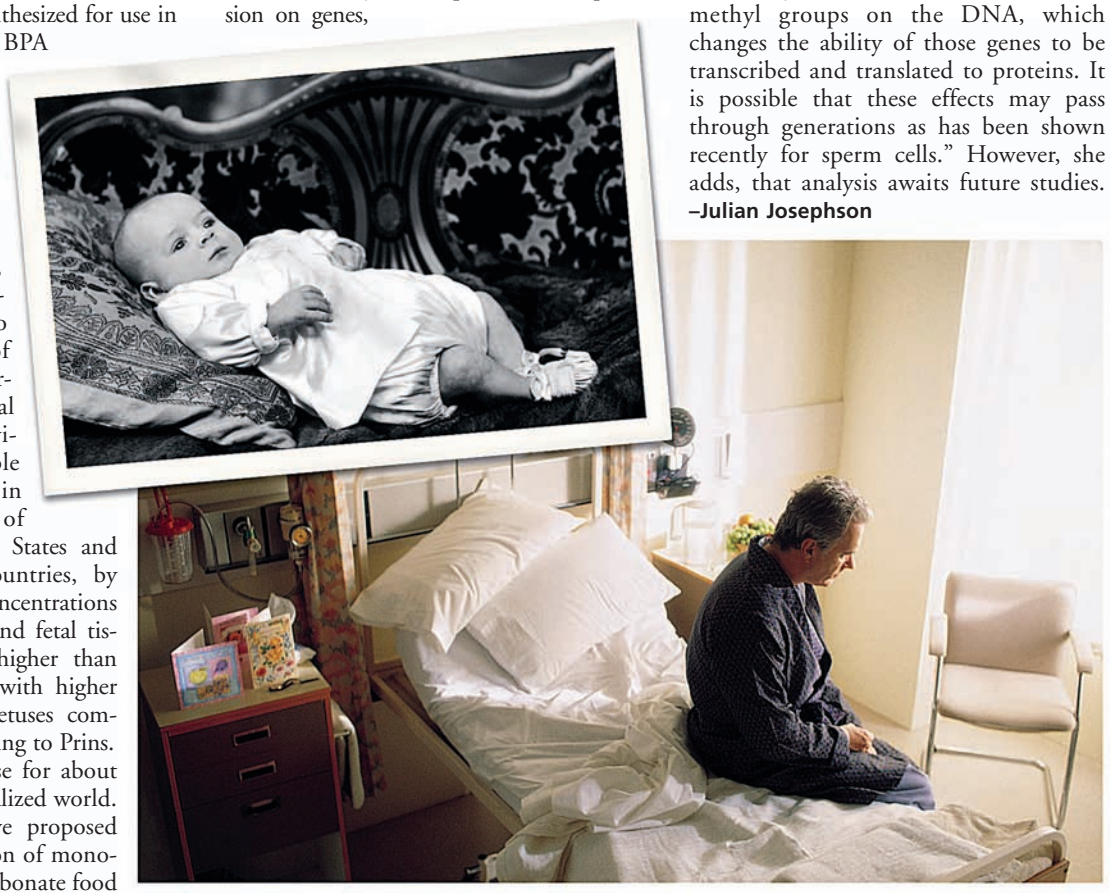
BPA has been in use for about 50 years in the industrialized world. Some investigators have proposed that widespread ingestion of monomeric BPA from polycarbonate food and drink containers might partially explain recent increases in prostate cancer rates. According to the American Cancer Society, rates have been on the rise since 1975. With the 1987 introduction of prostate-specific antigen testing, the newly enhanced ability to diagnose the disease caused incidence to spike to 240 age-adjusted cases per 100,000 men by 1992. After this "catch-up" period, rates dropped for three years, but are now back on the rise.

In the study, described in the 1 June 2006 issue of *Cancer Research,* groups of newborn rats were given high or low doses of estradiol or an environmentally relevant dose of BPA. The findings provide a molecular underpinning for potential long-term effects by showing changes in methyl groups on DNA that are responsible for turning genes on or off. For example, one key prostate gene that normally fuels cell growth during development stayed turned on in the prostates of male rats exposed to BPA or elevated estradiol from birth, says Prins. Such epigenetic alterations may leave a permanent impression on genes, possibly sensitizing the animal to developing diseases later in life.

One must exercise caution, however, in extrapolating the current rat findings to humans. How might one conduct an analogous program of research on men? The researchers consider such a program virtually impossible because 50 years or more typically would be required for results of early exposure to BPA to show up as prostate cancer.

Indeed, Rebecca Sokol, a professor of medicine at the University of Southern California, cautions against extrapolating human effects from rat studies. She does, however, note that unlike strong carcinogens that damage DNA profoundly, BPA appears to cause subtle changes that may pass from one generation to the next. She asks whether something is happening to alter genes seemingly without changing the genetic code itself.

Says Prins, "Our evidence shows that in an animal model, some genes are altered by the addition or removal of methyl groups on the DNA, which changes the ability of those genes to be transcribed and translated to proteins. It is possible that these effects may pass through generations as has been shown recently for sperm cells." However, she adds, that analysis awaits future studies.
–Julian Josephson



Disease through the ages. New rat data link BPA exposure during critical periods of early development to later prostate cancer, raising compelling questions for research in humans.

Digital Vision; inset: Eclectic Collections

Policy

WHO/ILSI Affiliation Sustained

The International Life Sciences Institute (ILSI) is set to be honored for its Physical Activity and Nutrition program as part of the September 2006 National Congress on Accelerating Improvement in Childhood Obesity in Washington, DC. The program is being singled out for its innovative approaches to educating children, parents, and caregivers about managing child obesity. However, such praise contrasts sharply with criticism that was leveled at ILSI just months ago.

At a 27 January 2006 meeting in Geneva, the WHO Executive Board reviewed ILSI's NGO status, along with that of several other NGOs, as part of the WHO's standard three-year review cycle. The National Resources Defense Council, an environmental action group, was calling for the WHO to sever its relationship with ILSI, based on the fact that ILSI's membership includes representatives of major multinational corporations with a vested interest in public health matters.

The board ultimately decided to maintain official relations with ILSI, describing its role as "a knowledge resource base for the application of leading-edge science and knowledge transfer in the fields of food and chemical safety." ILSI is therefore still permitted to attend WHO governing body meetings and make statements at these meetings. Although this presence does not come with voting privileges, it affords such an organization valuable "insider" status. However, this latest decision by the Executive Board does exclude any collaboration by ILSI on normative activities, defined as "setting microbiological or chemical standards for food and water."

According to Harvey Anderson, who chairs ILSI's Board of Trustees, the organization has never taken part in such activities anyway. While its strongest critics accuse ILSI of working behind the scenes to present information that would shape public policy to corporate advantage, Anderson points out that ILSI functions according to a nonprofit charter bound by U.S. regulations, with a board dominated by members not affiliated with any vested interest, who would readily vote down such lobbying.

"ILSI is overrun by lawyers making damn sure everybody holds to the charter," he explains, noting that representatives like himself—a nutritional sciences professor at the University of Toronto—are unpaid volunteers devoting a great deal of time and energy to what they regard as a research endeavour.

"ILSI has gathered some of the top scientists from around the world to work with industry and work with government and work with their colleagues on issues that need this kind of cooperative approach," says Anderson. "We publish our research and reports in journals that require peer review by their standards and by scientists of their choice."

Observers such as Jennifer Sass, a scientist with the Natural Resources Defense Council, insist that this approach nevertheless yields skewed science. Her group drafted a letter of protest that was circulated by hand at the Geneva meeting, citing examples of ILSI's undue influence in shaping the conclusions of scientific studies on issues such as the role of sugar in diet and the designation of cancer-causing agents.

"Their documents come out in one direction, which is always somewhere between 'everything's okay' and 'we need more study,'" she says, referring to ILSI's participation in a 1998 study that denied finding evidence of a direct link between sugar intake and lifestyle-related diseases. According to Sass, that conclusion conflicts with the results from a 1990 WHO study group, which recommended health policy targets that reflect the increased risks of chronic diseases caused by dietary patterns that include high sugar intake.

"They never come out as 'this is a big problem and we should do something about it,'" says Sass, adding that governments can perpetuate a misrepresentation of this research by condoning ILSI's approach.

Similar complaints voiced in the 1990s were followed by a 2001 report by the WHO Tobacco-Free Initiative on how member tobacco companies had used ILSI to muster seemingly unbiased scientific opinions aimed at quashing WHO tobacco control efforts. ILSI vehemently denied these allegations and, Anderson says, worked with the WHO to provide assurances of transparency about how ILSI operates.

Derek Yach, now head of the Rockefeller Foundation's Program on Global Health, led that WHO initiative and closely watched ILSI's response. "Part of the problem lies with the UN agencies themselves, or in this case the WHO," he concludes, noting that these bodies have yet to take many of the protective measures recommended by the report. "You can blame the corporations," he says, "but you also need to place blame on not having very clear, very transparent review of conflict-of-interest procedures internally." **–Tim Lougheed**

Tracking Toxicants in Canadians

Health Canada announced in May 2006 that it would begin a national biomonitoring program to measure levels of toxic chemicals in the bodies of Canadians. The announcement came as the NGO Environmental Defense prepared to release the results of its own tests, the first look at the amounts of chemicals showing up in Canadian adults and children. That study found 46 of 68 chemicals tested for, with an average of 32 chemicals appearing in adults and 23 in children. Compounds such as polychlorinated biphenyls and DDT were found in children born years after these chemicals were banned. It is not yet known whether the new program, set to begin in late 2007, will be permanent.

Citizens Want Free Access to Research Findings

The results of an online Harris poll released 1 June 2006 show that 82% of U.S. adults believe the findings of federally funded research should be available for free online, and that 62% believe free access would lead to quicker discoveries that positively impact health. Heather Joseph, executive director of the Scholarly Publishing and Academic Resources Coalition, commented, "The public recognizes its stake in open sharing of resources, and the Harris data gives voice to their stand." Senators John Cornyn (R–Texas) and Joseph Lieberman (D–Connecticut) recently introduced the Federal Research Public Access Act of 2006, which would require federal agencies that fund over $100 million in external research per year to make their study results publicly available online.

Roadside Meth Risk

According to the National Advisory Council on Drug Abuse, every pound of methamphetamine produced means 5 to 7 pounds of toxic materials. Now roadside cleanup volunteers and maintenance workers are being educated about the dangers of picking up litter tossed out when meth labs clean house. People coming across such materials can experience skin burns or lung damage from touching or inhaling fumes from meth waste. Several state and local agencies have created brochures and videos to educate their workers. Hints indicating a roadside meth dump site include bottles with rubber hoses attached, the smell of ammonia, and coffee filters stained red or containing a white powdery residue.

Top to bottom: AP Photo/*Daily Post-Athenian*, Ben Benton; AP Photo/Ben Curtis

INFECTIOUS DISEASE

A Deadly MIF

Up to 2 million children die each year from malaria, with about half dying from malaria-induced anemia. Scientists aren't sure why some malaria patients develop this life-threatening complication and others don't. A study published in the 15 May 2006 *Journal of Experimental Medicine* suggests the blame rests in part on macrophage migration inhibitory factor (MIF), an immune cytokine produced by white blood cells.

Unraveling a life-threatening complication. A genotyping project at Macha Mission Hospital in Zambia, where director Phil Thuma (center) conducts pediatric rounds, aims to prevent malaria-induced anemia in children.

The paper's authors suspected that MIF might suppress bone marrow activity, because polymorphisms of the *MIF* gene increase susceptibility to different inflammatory and infectious disorders. "MIF appears to be part of an over-exuberant response on the part of the immune system in a number of diseases, so it was a logical choice for us to look at," says coauthor Michael A. McDevitt, a hematologist at the Johns Hopkins University School of Medicine. The team infected mice that were genetically modified to lack the *Mif* gene with malaria parasites. About one-third of those mice survived, compared to only 9% of the normal mice.

MIF doesn't act alone, the researchers discovered when they took progenitor cells from the bone marrow of mice and allowed the cells to grow both with and without MIF and two other immune factors, TNFα and IFNγ. Applied alone in low concentrations, none of the immune factors seriously damaged the bone marrow cells. "But when we added all three together at the same low levels, we witnessed a synergistic poisoning of bone marrow," says McDevitt.

MIF probably prevents cells in the bone marrow from responding to erythropoietin, the hormone that triggers red blood cell production, says coauthor Richard Bucala, an immunologist and rheumatologist at Yale University School of Medicine. Some people's immune system may make too much MIF in response to malarial infection. About 30% of the population in Africa, where malaria is rampant, produces excessive MIF protein, earlier studies have shown.

MIF isn't the only cause of malarial anemia. The *Plasmodium* parasite destroys red blood cells, and the spleen also removes infected and even some uninfected cells. "The pathogenesis of [malarial] anemia has been a mystery for a long time," says Peter J. Hotez, a parasitologist at George Wash*ington University*. *"This mouse* study adds to the evidence . . . that MIF impedes the production of red blood cells."

Understanding the mechanisms behind malarial anemia could help direct future therapies. MIF is the key therapeutic target, because blocking it alone protects the cells, whereas blocking TNFα or IFNγ alone doesn't, explains Bucala. Since the blood transfusions needed to treat severe anemia are often difficult for many poor families to find or afford, researchers hope to determine early on which children need immediate care to prevent the anemia.

To that end, Bucala and colleagues are collaborating on a project with Macha Mission Hospital in Zambia to assess the frequency of *MIF* polymorphisms in children with malarial anemia. They use a new, inexpensive method to identify the polymorphism in just 2 hours, letting them know whether a child will likely need a transfusion. In Zambia, children have a well-baby visit soon after birth, and it is possible every baby could get genotyped, says Bucala, who adds, "Then the mother would know that if her child develops fever in the rainy season, she should go to the hospital quickly." **–Tina Adler**

ENVIRONMENTAL DISEASE

Ozone: Good, Bad, or Indifferent?

Following up on their eye-catching finding that the human body generates its own ozone for beneficial purposes, a team of U.S. and British researchers now describe specific processes through which ozone can react with cholesterol and contribute to atherosclerosis, or hardening of the arteries. Whether the ozone involved comes from within the body or from the environment remains unclear, however, and the team's findings remain controversial on several counts.

In earlier work, Paul Wentworth, Jr., a chemistry professor at The Scripps Research Institute, and colleagues concluded that self-generated ozone is used by the immune system's antibodies and neutrophils to destroy bacteria and fungi. They published a study in 2003 showing that ozone can damage the vascular system by contributing to atherosclerosis. They also noted the same process may play a role in diseases such as lupus, multiple sclerosis, and rheumatoid arthritis.

The mechanism by which such damage occurs wasn't clear in the 2003 study, however. Some of that information was filled in with a report published 13 June 2006 in *Biochemistry*. Through a series of *in vitro* tests, the team exposed human and mouse cells to two by-products of ozone's interaction with cholesterol, atheronal-A and atheronal-B. They found that one, the other, or both atheronals accelerate the normal conversion of monocytes to macrophages, are rapidly taken up by macrophages, hasten the inflammatory response on and increase the stickiness of the interior arterial walls, and contribute to the formation of arterial plaques.

Numerous questions remain about the research protocols (such as a lack of controls to prove that ozone was the oxidant at work) and conclusions regarding the body's self-generation of ozone (such as whether cells are likely to expend so much energy to produce their own ozone), says William Pryor, director of the Biodynamics Institute at Louisiana State University. Further, there is little solid evidence that environmental ozone plays a role in this specific process, although exposure to atmospheric ozone has been implicated in a number of cardiovascular problems, including heart attack and changes in heart rhythm.

Wentworth acknowledges that increased cholesterol ingestion may be the most important driving factor in the atherosclerotic damage his team found—many of the harmful atheronal processes occurred only when "bad" LDL cholesterol was present. Still, this line of inquiry may contribute to better insights about the complex relationships between the body's normal functions, reactive oxygen species including ozone, and cardiovascular damage, leading even its critics to say this concept deserves attention, analysis, and more research. **–Bob Weinhold**

Rick Bucala/Yale University

ehpnet

Collaborative on Health and the Environment Toxicant and Disease Database

From huge industrial spills to exposure to everyday products, there are a number of ways people come in contact with potentially hazardous chemicals. To help educate those wanting more in-depth information about the health effects of chemicals, the Collaborative on Health and the Environment (CHE) has developed the CHE Toxicant and Disease Database, available online at http://database.healthandenvironment.org/.

The CHE was formed in 2002 as a project of the nonprofit health and environmental research institute Commonweal with a mission to foster a greater understanding of the links between human health and the environment. The database, which summarizes links between chemical contaminants and approximately 180 human diseases and conditions, has been enhanced recently with new search features and a directory of links to other resources that would be of interest to visitors to the CHE site.

Background information on the theory behind the database project is available through a link in the text paragraph near the top of the homepage. Here, visitors can learn about the nature of gene–environment interactions and their impacts on human health; the lack of toxicity data on many of the 80,000-plus chemicals that have been developed, distributed, and discarded over the past 50 years; and the difficulties encountered in assessing the risk of chemical exposures. This page also describes where the information in the database came from, how chemicals are categorized, and what limitations there are to the database.

The homepage features an alphabetical listing of diseases and conditions—ranging from abnormal sperm to Wilm's tumor—that can potentially be triggered by exposure to environmental chemicals. Each disease or condition links to a page listing its chemically related causes. These causes are grouped by the strength of evidence—strong, good, or limited—of the relationship between the health effect and the chemical. Each page also cites references. Choosing one of the listed chemical causes brings up a record of all of the diseases and conditions linked to that chemical.

The database can be searched using one of the pull-down lists at the right of the homepage. There are options for searching by any of 25 disease categories, by individual disease, or by any of dozens of toxicants. Searches can also be performed by Chemical Abstract Service number and by keyword.

The directory available through the Links to Other Databases and Resources link cites 17 databases, including ones hosted by the NIEHS, the CDC, the EPA, the ATSDR, and the International Agency for Research on Cancer. Other resources listed include the CDC's *National Report on Human Exposure to Environmental Chemicals*, the National Toxicology Program and its *11th Report on Carcinogens*, the California Office of Environmental Health Hazard Assessment, and *EHP*. **–Erin E. Dooley**

Cairo Hails New Fleet of Eco-Cabs

Cairo is known for its poor air quality, with its near-permanent haze a mix of industrial emissions, desert sand, and car exhaust fumes. In March 2006, a small fleet of new taxis hit the streets of Egypt's capital city. Unlike their predecessors, the 150 new yellow Hyundais and Volkswagens feature catalytic converters to filter their exhaust, along with air conditioning and seat belts. A scheme laid out by Egyptian prime minister Ahmed Nazif calls for a total of 1,500 new taxis to be available by the end of 2006. *The Christian Science Monitor* reported on 1 June 2006 that the Egyptian government is also considering fueling the vehicles with natural gas.

Living Low Poses Risk

Although only 2.2% of the world's land area is less than 10 meters above sea level, 10% of the world's population—some 600 million people—lives at these low elevations. Of these, 60% live in urban areas. A report in the April 2006 news bulletin *Tiempo* by researchers from The Earth Institute at Columbia University states these people are at risk from rising sea levels and increasingly strong storms due to climate change. Geographical location isn't the only factor that determines vulnerability, however. Although the United States has more urban areas in low-elevation coastal zones than any other country, low-income countries and those designated as Least Developed Countries have fewer resources to rebound from the effects of climate variability.

A Plan for Farm Plastics

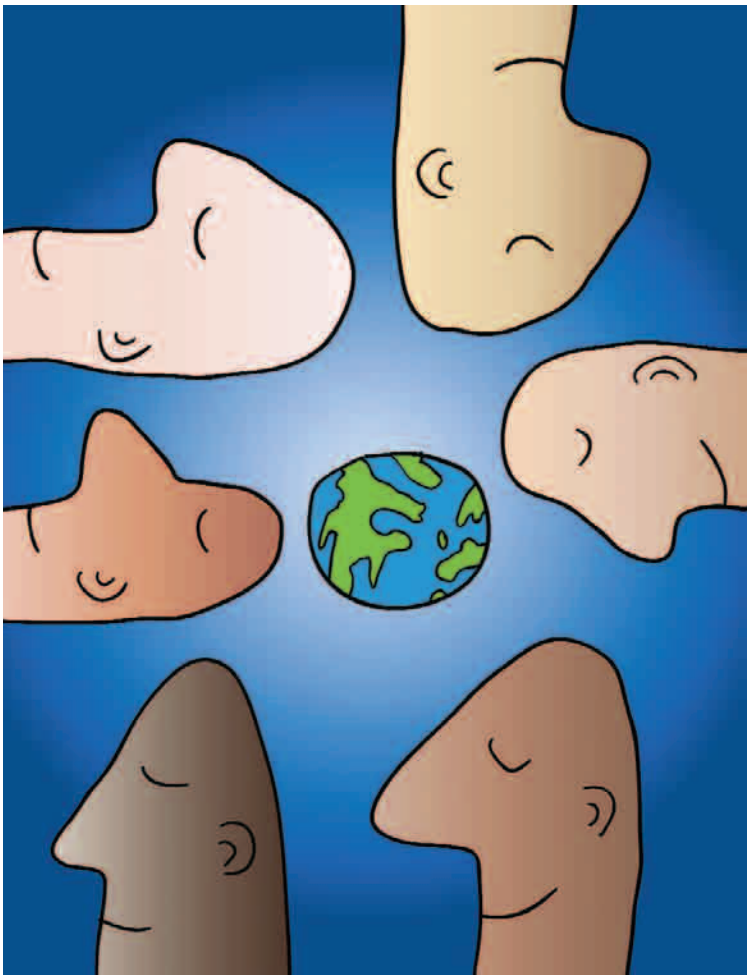
Farmers use "ag plastics" for a wide variety of purposes—dairy and silage bags, coverings for crops, wrappings for hay bales, and more—and thousands of tons are burned, buried, or dumped annually. Now Cornell University researcher Lois Levitan is developing a pilot program to collect and recycle used plastic film sheeting from New York dairies and nurseries.

Levitan reports that about half of discarded ag plastic is burned, which generates emissions of dioxin and other hazardous chemicals. Other waste plastic is often plowed into the ground, where it can become a breeding place for insect pests as well as trap and choke wildlife. Levitan suggests recycling plastics into fence posts, plastic lumber, garbage bags, and other uses, or converting the plastic resin content to a fuel.

Top to bottom: Art Explosion; CHE; Patricia Marroquin/Shutterstock

RTP Leaders Unite to Advance Environmental Health

When North Carolina's Research Triangle Foundation provided 509 acres of land to the U.S. Surgeon General's Office in 1967 as the site for the newly established Division of Environmental Health Sciences, the area was probably not foreseen as a hub for companies, institutions, and government agencies working on issues related to environmental health. Then, just two years later, the Division of Environmental Health Sciences was elevated to institute status to form the NIEHS. Since that time, the area now known as Research Triangle Park (RTP) has expanded into a nucleus of intellectual activity in environmental health sciences that includes the National Toxicology Program, the laboratories of the U.S. EPA, the CIIT Centers for Health Research, and environmental research programs at Duke University, the University of North Carolina–Chapel Hill, and North Carolina State University, among other institutions and nonprofit organizations.



These organizations are now taking advantage of a unique opportunity to solidify RTP's reputation as the epicenter for environmental health science research in the United States by creating a forum for discussion and debate of the important public health issues related to environment and health. Prominent individuals in the RTP community—including former North Carolina governor James Hunt, former NIEHS director Kenneth Olden, and William Roper, chief executive officer of the North Carolina Health Care System and former head of the CDC—have been working to bring thought leaders together on these issues in a new initiative that has been dubbed the Research Triangle Environmental Health Collaborative.

The mission of the collaborative is to connect organizations and institutions; link research and policy; and join government, academia, industry, and public interest groups for the purpose of mutually considering, discussing, and debating the grand challenges in environmental health at the regional, national, and international levels. Says Olden, "When I came to the NIEHS many years ago, I realized the talent base we have here in RTP. The major environmental health research institutions are all here, the intellectual resources of the major research universities, and also the companies that have evolved around this. No place else in the world can boast this concentration of minds working on environmental public health issues. So we thought that it follows that if you can help to focus these talents in the areas where perhaps the most change can be effected, real progress might be made."

An Idea Made Real

According to David P. Brown, director of scientific research program development for Constella Group, a professional health consulting service that is facilitating the effort with support from the NIEHS, the collaborative has applied for nonprofit 501(c)(3) status. "Once created, the collaborative will provide those in government, academia, and the private sector with a neutral forum to host candid discussions and to provide advice on the most significant issues facing environmental health and related public policy," says Brown.

"Constella is proud to work with the NIEHS and other organizations and be at the genesis of creating a forum to discuss exciting, groundbreaking issues in environmental health," says Donald A. Holzworth, Constella Group's chairman and CEO. "By articulating this vision for a public–private partnership focused on environmental health, we have a unique opportunity to participate in creating a global forum to build awareness and education around these critical issues."

Olden chairs the collaborative's Executive Committee, which currently comprises representatives from academia and the private sector. The other members include William Greenlee, president and CEO of the CIIT Centers for Health Research; David Hinton, Nicholas Professor of Environmental Quality at Duke University's Nicholas School of the Environment and Earth Sciences; Ernest Hodgson, a professor of environmental and molecular toxicology at North Carolina State University; Rich Cohn, vice president of the Center for Health Research at Constella Group; and Edward Baker, director of the Institute for Public Health at the University of North Carolina–Chapel Hill.

Committee members hope that leaders of nonprofit organizations and public interest groups in RTP will join the collaborative as well.

A First Step

The collaborative has already received $30,000 in initial funding from the NIEHS to host its first Environmental Health Summit, planned for the spring of

Miroslaw Pieprzyk/iStockphoto

2007 in RTP. This meeting will bring together environmental and public health leaders from around the world to identify today's foremost environmental health challenges. Participants, who may include former EPA administrators Carol Browner and William Reilly, will also seek to address these challenges from a solution-oriented perspective, emphasizing research needs, policy changes, education, and prevention/intervention programs.

The Environmental Health Summit is just one activity through which the collaborative plans to address important issues. The collaborative will help facilitate the goals of the NIEHS and the EPA by organizing meetings, helping to attract new scientists, and serving as a clearinghouse for environmental health science–related activities and events in the RTP area. The collaborative may also provide expert advice and review as well as a neutral forum for discussions on science and policy.

Other activities will include promoting RTP as a desirable scientific, research, and business destination in an effort to lure more environmental health science organizations to the area, as well as supporting the convergence of government, academia, and nonprofit interests to generate an attractive economic environment for business growth for private companies. The group will showcase academic institutions' key environmental programs, including those supported by the federal government, and will facilitate interaction between academia, government, nonprofit foundations, public interest groups, and private organizations in a collegial environment. The collaborative also plans to facilitate multipartner efforts in grant development to generate new research programs. Finally, the collaborative will serve as an interorganizational think tank comprising environmental, health, and policy leaders from associations, foundations, and nonprofit organizations.

For additional information about the collaborative, please contact David Brown at dabrown@constellagroup.com.
–Luz Claudio

Martha S. Young © 2006 Baylor College of Medicine

BEYOND THE BENCH

An Integrative Curriculum: Science by Design

With our increased awareness of the need to understand human–environment interactions, it is more critical than ever to spark and nourish children's interest in science. Now an NIEHS-sponsored program at the Baylor College of Medicine Center for Educational Outreach is responding to this educational challenge by offering the ECOS (Environment as a Context for Opportunities in Schools) project, a teacher professional development and curriculum implementation project with an integrative approach that focuses on strengthening science teaching and learning at the elementary school level.

Established in 2000, the ECOS project was created by a team of educators, scientists, and health specialists to connect environmental health science with health, reading/language arts, mathematics, and social studies for Houston-area elementary schools. Two distinct educational series for grades K–2 and 3–5, developed previously with funding from the NIEHS and the National Center for Research Resources, were first implemented in six schools. Later, a charter school and four more elementary schools were added to the project. Both series of curriculum materials include interactive class lessons and engaging adventure storybooks illustrated by T. Lewis, co-creator of the syndicated comic strip and animated movie *Over the Hedge*.

Teaching the teachers. ECOS participants learn to implement curricula that examine topics such as the processes involved in creating everyday objects from natural resources (large photo) and the physical properties of water (inset).

"My World and Me," the module developed for students in grades K–2, contains two units, "Living Things and Their Needs" and "Resources and the Environment," each with 10 sequential series of lessons, an illustrated storybook for each student that teaches science and health concepts while relating the adventures of Tillena Lou Turtle, and a "read aloud" big book for classroom use. An accompanying teacher's guide to hands-on activities stresses inquiry-based lessons such as observing an earthworm, identifying its needs, and building an appropriate habitat in a terrarium made of a plastic soda bottle.

The "My World" (formerly "My Health, My World") series has four units on integrative topics for students in grades 3–5: "Air," "Water," "Global Resources," and "Food." Each unit includes a storybook featuring the adventures of squirrels Riff and Rosie, an *Explorations* mini-magazine for each student to share with family members, an activity guide for teachers, and supplements (for reading/language arts and mathematics) related to the storybook. Typical language arts activities include "finding the main idea" and writing about cause-and-effect relationships. Math activities focus on developing basic skills using science information related to a specific unit—for example, estimating metric measures, solving number puzzles, and creating and using graphs.

The program also provides support and training for teachers to help maximize the effectiveness of the curriculum. New teacher enrollees receive two days of professional

development including an overview of the curriculum content, a complete package of instructions, classroom activity kits, and training in conducting the different activities in the classroom units. Those already participating in the program receive additional training in enrichment activities scheduled several times throughout the academic year.

Both series are designed to be flexible and accommodate a variety of teaching methods and styles; the program designers note that schools have begun customizing unit activities to fit their own educational needs and priorities. Nancy Moreno, associate director of the Center for Educational Outreach and the ECOS project principal investigator, says customization shows that teachers are actively involved in the planning process for the project's implementation in their schools, and are intellectually invested in it. For example, she describes how the "Water" unit, initially designed for use in 2nd grade to meet science standards for that grade level, is now being used in 4th-grade classes in some schools because it better fits requirements for that grade level. "Since the materials are not grade level–specific, teachers can adjust them up or down by using suggestions and extensions that are provided in the teacher's guide," she explains.

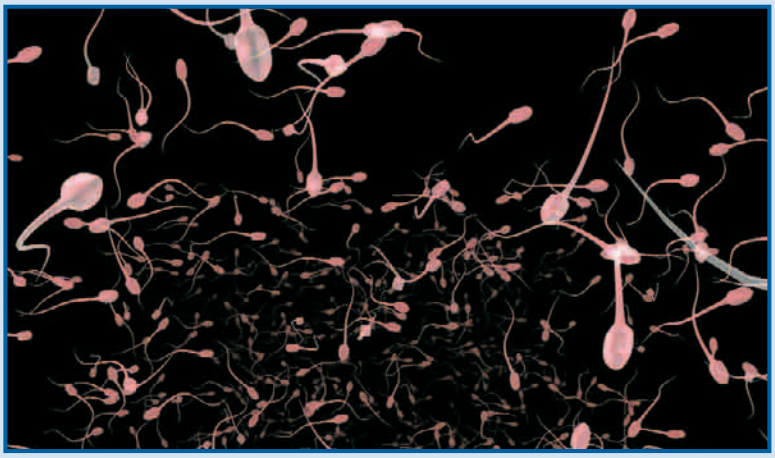
ECOS project participation is also having a positive impact on overall science learning for both students and teachers. The program developers have measured student knowledge using tools such as pre- and post-tests and essay assignments, and have observed a noticeable increase in student performance, especially among Spanish-speaking students, at all grade levels. Participating teachers have also shown gains in content knowledge when taking similar types of assessments.

"The ECOS project is an example of how scientific research institutions can collaborate effectively with local schools to improve science teaching and learning," says Moreno. "Shortcuts do not work. However, when scientists, science educators, school administrators, and classroom teachers work together, the nature of science instruction received by students changes profoundly. The payoffs from this approach are beginning to be visible in the ECOS project."

More information on the project, including ordering information, is available at http://www.ccit.bcm.tmc.edu/ceo/. The project, which has received such honors as finalist status for the State of Texas Environmental Excellence Award, is developing new units to integrate science inquiry into schoolwork. Coming up in the next school year is a unit for 5th graders that focuses on alcohol as a chemical that can interact with the human body. **–Tanya Tillett**

Headliners
NIEHS-Supported Research

Reproductive Health



Sperm DNA Changes as Men Age

Wyrobek AJ, Eskenazi B, Young S, Arnheim N, Tiemann-Boege I, Jabs EW, et al. 2006. Advancing age has differential effects on DNA damage, chromatin integrity, gene mutations, and aneuploidies in sperm. Proc Natl Acad Sci U S A 103:9601–9606.

In the past several decades, more men and women have been postponing parenthood. Fatherhood among men aged 35–49 has increased 40%, while there has been a 20% decline in births fathered by men under age 30. Although it has long been accepted that women face reproductive challenges with age, the consequences of delaying fatherhood have been less understood. Now NIEHS grantees Andrew J. Wyrobek of Lawrence Livermore National Laboratory and Brenda Eskenazi of the University of California, Berkeley, School of Public Health, with their colleagues, have produced new research that suggests that, like women, men too have a "biological clock," but one that causes a more gradual change in fertility.

Obstetrician/gynecologists have known for quite a while that as women age, their risk of miscarriage increases, as does the risk of having children with Down syndrome or other genetic defects. Advanced paternal age has also been implicated in a range of reproductive and genetic abnormalities, from reduced fertility to some diseases of complex etiology such as schizophrenia. This research team has previously reported that as men age, their sperm counts decline and their sperm become less active. However, the mechanisms for the effect of older paternal age on genetic defects are not well understood.

In this study, the researchers analyzed the sperm of 97 men after an average of 5.1 days of sexual abstinence. The men were nonsmokers aged 22–80 who were in generally good health. The researchers used flow cytometry and statistical analysis to observe associations between a subject's age, his semen quality, and genomic abnormalities in his sperm such as DNA fragmentation, aneuploidy, diploidy, and mutations related to achondroplasia and Apert syndrome.

Increased age of the men was not associated with the same genetic defects seen in older women; for instance, there was no increased risk of fathering a child with Down syndrome. But some older fathers did have an increased risk of having children with achondroplasia, and according to the published results, "a small fraction of men are at increased risk for transmitting multiple genetic and chromosomal defects." The authors caution that their findings are preliminary and are based on a small number of tests in a small population of men. However, they believe their findings suggest that as men age, they may have more difficulty fathering children. **–Jerry Phelps**

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Monitoring Environmental Exposures
Now It's Personal

Most diseases are thought to arise from the combined effects of genes and the environment. While great strides have been made in our understanding of human genetics, the contribution of environmental exposures to disease remains poorly understood. This lack of understanding impedes real progress in identifying genetically susceptible people whose responses to environmental agents are severe or unique relative to the general population. If identified, targeted prevention and treatment strategies might be applied to these groups, with potentially lifesaving results. Without more personal exposure information, however, scientists have a limited ability to identify pollution-susceptibility genes that elevate disease risk.

This mismatch between exposure and genetic research slows the identification of environmental factors that—if altered or removed—could even prevent some diseases from occurring in the first place.

"Genes aren't modifiable," explains Frederica Perera, a professor of environmental health sciences at the Mailman School of Public Health of Columbia University. "So, these environmental components in diet, food, water, and air are the only ones we can act on for disease prevention."

Exposure is, at a core level, the instance of environmental stimuli such as chemicals, infectious agents, diet, and lifestyle factors interacting with the human body. But studying human exposures poses difficult challenges. Scientists studying the effects of chemical pollutants can't ethically dose people, so they often base their dose–response estimates on animal models. Further, they base their estimates of human exposure on indirect measures taken from a person's home or work environment, along with assumptions about individual behaviors that influence the risk of coming into contact with a given pollutant. In a typical study, epidemiologists might use census figures, questionnaires, and general environmental monitoring data (such as samples of water from a household tap or soil in a schoolyard) to estimate how much of a given chemical an individual has come into contact with, and for how long.

But while these studies approximate population-level exposures, they provide little information about real exposures to individual people. And because of this, scientists know little about how specific pollutants—particularly in combination with each other, with diet, and with physical activity—affect any individual's response to the pollutant.

With a clear need for progress, exposure assessment has recently come under the spotlight. This year, the NIEHS launched the Exposure Biology Program (EBP), a four-year effort with two overarching goals: to improve exposure assessment technology, and to identify biomarkers for common pathogenic mechanisms that reflect the human response to environmental agents. Such biomarkers could include changes in metabolites, proteins, or DNA that reflect the individual's genetic susceptibility to environmental harm.

"Right now we don't really understand how exposure levels translate to human health risk, so our goal is to fill that gap," says EBP coordinator Brenda Weis, a senior scientific advisor at NIEHS. "We need to get a better measure of exposure at the point of human contact, and we need to integrate those measures with biological response measures derived from samples taken directly from exposed people. So, this is a more 'medical' approach to exposure assessment—in the sense that measures are taken on a personal level—rather than the broader, ecological approaches we've been using so far."

The Genes and Environment Initiative

The EBP is part of the larger DHHS Genes and Environment Initiative (GEI), which was established on 8 February 2006. This initiative links the EBP with a complementary genome association program, led by the National Human Genome Research Institute (NHGRI), which is dedicated to finding genetic risk factors for environmental diseases.

NIEHS director David Schwartz and NHGRI director Francis Collins initially hatched the idea for a joint collaboration two years ago. At first, the two scientists proposed assembling a vast cohort of 1 million Americans for a 10-year prospective study of gene–environment interactions in health. However, that plan has not yet materialized, because of its high anticipated cost—estimated at up to $3 billion—and also because experts at both agencies felt that policies for genetic privacy and other social issues needed to be further developed before such a large study could be undertaken.

The GEI was therefore proposed as a more limited effort encompassing smaller population studies and fewer diseases. "Schwartz will head the exposure piece while Collins will head up the GEI's genome association studies," Weis explains. "The idea was to unite our mutual expertise—we worked for a long time on the concept, and we wound up with forty million dollars in annual funding for four years."

NIH director Elias Zerhouni said of the GEI upon its launch that "[this initiative] would not have been possible a year or two ago." Recent years have given rise to medical and computational advances that make detailed studies of gene–environment interactions increasingly more feasible. The cost of genotyping, for instance, meaning the identification of specific genetic variants at one or more loci in an individual, has dropped by more than 100-fold, making the initiative's genome association component more affordable. Environmental sensors that monitor individual pollution exposures, physical activity patterns, and corresponding physiological responses have also met with rapid progress, bringing goals for personalized exposure assessment within reach.

Through the EBP, Weis says, the NIEHS will develop technologies that produce more precise measures of exposure, and with that, better biomarkers of physiological response. The NHGRI, meanwhile, plans to apply those biomarkers toward genome association studies in specific illnesses, such as cancer, respiratory ailments, and heart disease. "We'll also offer input on the [biomarkers of] exposure that the scientists select," says Teri Manolio, a senior advisor at the NHGRI managing GEI-related activities. "We need to be sure they relate to genetics as well as environment." Through the combined efforts of both institutes, adds Weis, the GEI will accelerate progress on gene–environment research and lay the technical and social foundations for larger studies in the future.

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Outside impacts on inside systems. Measuring responses to factors such as sun exposure and allergies may provide important information about the health impact of environmental stress.

It's a combo deal. Any given person has a highly unique suite of exposures, making individual-level exposure assessment a must for teasing out how factors such as diet and physical activity influence people's responses to particular pollutants.

A step forward on the NIEHS's exposure assessment agenda occurred on 16–17 May 2006, when academic, government, and industry experts convened in Greensboro, North Carolina, for the NIH Exposure Biology Workshop, hosted by the NIEHS and the NHGRI. At the workshop, experts deliberated the pitfalls and promises of exposure assessment, and produced a series of recommendations for optimizing sensor technology and biomarker development.

The meeting was remarkably interdisciplinary, participants say. "I'm used to going to meetings where I know everyone," says Martyn Smith, a professor of toxicology at the University of California, Berkeley, who was in attendance. "But I didn't know many of the people there, and I think that's a good thing. There needs to be more interaction between the engineers who design exposure instruments and we in environmental health who apply them in the field."

New Sensations

Among the tools used to monitor exposures now are laser-based sensors that assess population exposures to industrial stack emissions, wearable dosimeters that measure chemicals and radiation (generally in occupational settings), accelerometers that measure physical activity, and biosensors that can detect specific analytes in the body.

New technologies to assess personal exposures are being conceptualized, but developments are moving slowly. A research article by Weis and colleagues published in the July 2005 issue of *EHP* outlines current, ongoing efforts. The article describes promising applications that link geographic information system (GIS) technology with fate and transport models to derive individual exposure metrics for pesticides, drinking water contaminants, and air pollutants. The article further reports that researchers have used GIS with Global Positioning System (GPS) technology to define activity patterns that could conceivably be linked to environmental data for exposure assessment. However, sources contacted for the present article were unaware of any existing GIS applications for environmental epidemiology research.

Some of the most exciting sensing opportunities have come from military and biomedical research. The military has produced sensors that detect biological warfare agents such as anthrax down to the level of a single spore. Medical researchers, meanwhile, have developed biosensors that detect isolated binding events in single cells, in addition to variables like heart rate, respiratory function, and changes in enzyme levels. "We have a glaring, obvious opportunity to adapt these tools for environmental exposure assessment," says David Walt, a professor of chemistry at Tufts University. "We can use them to monitor the ambient environment as well as personal exposure. We now have the capability to take all those measurements and link them together."

Future sensing opportunities are nothing short of extraordinary. Subjects could be injected with nanoscale biosensors that light up when they detect exposure-induced molecular changes. "After a period of time, a blood sample could be taken, the biosensors could be fished out, and you'd see precisely what you'd been exposed to," Walt speculates. "The techniques are available now, but they haven't been addressed to environmental exposure." Some biosensors outfitted with microtransducers could relay information about cellular changes with electronic signals, he adds. "And in those

Left to right: Bora Ucak/iStockphoto, fiflweson/iStockphoto

Phoning in the facts. New sensor technologies will make use of cell phones and similar apparatus to continuously monitor individuals as they go about daily life, recording data on physical activity, environmental exposures, and measures such as heart rate and respiration.

cases you might not even have to take the blood sample—you could read an integrated signal of all the particles in an interrogation zone right through the skin."

William Haskell, a professor at the Stanford University School of Medicine, proposes to create a portable device that measures physical activity, pollution exposure, and other variables simultaneously in real time. The sensing instruments, he suggests, could be loaded onto a GPS-enabled cell phone into which subjects could record their diet and other pertinent information using the keypad.

Haskell is collaborating on the concept with Stephen Intille, a research scientist at the Massachusetts Institute of Technology who's been developing wireless motion sensors to measure a variety of human behaviors. Their immediate goal is to create cell phone–adaptable software that distinguishes whether someone is walking, riding a bike, working in the yard, or doing something else, all according to how their physical motions affect heart rate, and how they accelerate and decelerate over time. That capability, along with GPS and sensors that detect chemicals in the cell phone's immediate vicinity, could give scientists unprecedented access to the locations, activities, diets, and chemical exposures of individuals in a given cohort.

What would scientists do with that information? "Say you were a pediatrician in Los Angeles," Haskell proposes, "and you wanted to understand what triggers asthma in kids. With these more advanced technologies you could plot their activity patterns against pollution exposure levels. That would allow you to draw a personal profile that, upon being transmitted by the cell phone, could be automatically downloaded onto a server. We could use that information to determine the specific components in air pollution that trigger asthma in high-risk individuals. We have the technical capability to do this now; it's just a matter of pulling the resources together for this particular purpose."

Future sensors, scientists say, need to be even faster, cheaper, and more portable than they are now. Participants at the May workshop called for more collaboration with sensor developers, and clear lines of communication regarding the specific measurements needed to move exposure assessment forward. Along these lines, "high-benefit" opportunities are expected in lab-on-a-chip platforms (which analyze pollutants in the field as opposed to in the laboratory) and multiplexed sensors that monitor multiple pollutants simultaneously.

Fingering the Biomarkers

The chief goal, of course, is to link exposure measurements to biomarkers that reflect a physiological response. John Groopman, who chairs the Department of Environmental Health Sciences at the Johns Hopkins Bloomberg School of Public Health, argues that scientists should first seek biomarkers for diseases with known links to the environment. "And certainly a number of lung-related effects fulfill that criteria," he says.

Weis agrees, and points out that the EBP's first project, an airway disease project launched in 2006, will investigate the impacts of cigarette smoke, ozone, cockroach dander, and lipopolysaccharide (found on the cell walls of Gram-negative bacteria) on two processes related to respiratory disease: inflammation and oxidative stress. "It would be really informative to find a panel of biomarkers that's specific to each of these agents," she says.

Scientists will begin by searching for putative biomarkers in animals that can be further investigated in people going about their daily business who will be outfitted with personal exposure monitors. Another goal is to use exposure agents to find biomarkers that distinguish different types of asthma—for instance, using an immune response triggered by cockroach dander to distinguish allergenic asthma from nonallergenic asthmatic reactions caused by other environmental agents. "People with different types of asthma could be treated with therapies tailored to their type of asthma," Weis explains. "But we need to understand the mechanistic differences between the various manifestations of the disease. We want to better understand those mechanisms so we can improve treatment and prevention options."

Focusing on inflammation and oxidative stress makes additional sense because both pathways are also common to other ailments, including cancer and heart disease. But scientists studying these pathways must consider their normal equilibrium, stresses Martha Monick, a research scientist

Left to right: Radu Razvan/Shutterstock; Paul-Andre Belle-Isle/Shutterstock

at the University of Iowa. Inflammation and oxidative stress normally protect the body from pathogens and are only toxic when overstimulated, she says, and that natural variability should be considered during the exposure assessment. Moreover, she adds, the inflammatory response to environmental factors can, in some cases, merely exacerbate preexisting conditions with nonenvironmental origins. For instance, atherosclerosis, a progressive vascular disease with an underlying basis in genetics, can be aggravated by exposure to cigarette smoke and air pollutants such as particulate matter. "So it would be helpful to have biomarkers for exposures that prolong a disease in addition to those that might cause it," she says.

EBP workshop participants stressed that metabolomic, proteomic, and genomic methods offer new opportunities for biomarker development. DNA and protein adducts in particular could provide windows into the body's long-term "memory" of previous exposures, they suggested. Metabolite profiles, meanwhile, could offer shorter-term measures of environmental response. Perera explains, "The DNA and protein adducts in peripheral blood—at least for polycyclic aromatic hydrocarbons in settings of constant exposure—have lifetimes on the order of several months. The metabolite profiles are likely to be more short-lived."

Bruce Hammock, a professor of entomology and toxicology at the University of California, Davis, says metabolomics—like the other "omic" sciences—has benefited from economies of scale that have dramatically reduced analytical costs. He says the growing capacity to measure dozens, even hundreds, of metabolites simultaneously opens doors for two types of research.

The first involves an unbiased interrogation of all measurable metabolites induced by a particular environmental exposure. This global approach could yield biomarkers linking the exposure to entirely new and perhaps unexpected diseases. "Say we're studying air pollution and asthma," Smith says. "Recent evidence shows airborne particulates play an important role in heart disease, so if you focus just on asthma, then you might miss that additional connection."

With the second type of research, scientists could investigate specific metabolic pathways linked to a specific ailment—for instance, air pollution–induced inflammation and heart disease. This hypothesis-driven method would allow scientists to backtrack along the exposure response to biomarkers that offer clues to underlying physiology.

Another point to consider, Groopman adds, is that mass spectrometry is 1,000-fold more sensitive today than it was 15 to 20 years ago, which makes it possible to detect ever-smaller concentrations of chemicals in a given sample. Scientists who previously might have detected a pollutant in the blood of just a few subjects might now find it at very low levels in many more, he says. And by linking those pollutant analyses with corresponding gene, protein, and metabolite profiles in exposed people, it might finally be possible to assess the health effects of low-level chemical mixtures, which has long been a holy grail for environmental health scientists.

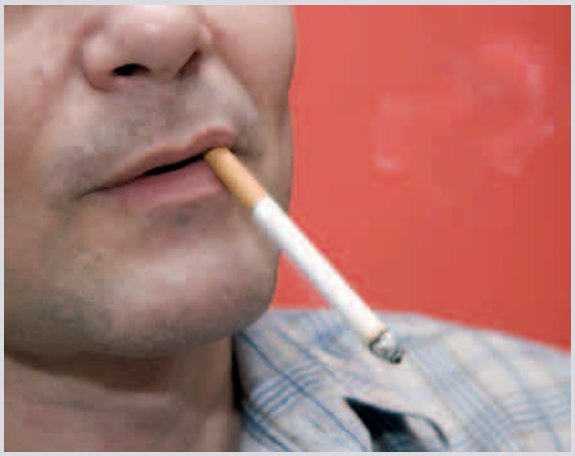
Social Concerns and Regulatory Implications

As it stands now, the coming era of personal exposure assessment is poised for takeoff. Dialogue, collaboration, and the promise of funding have brought a preliminary vision into focus, and the next several years will see increasingly refined technologies applied to the field. But exposure assessment's new direction also raises some difficult questions. In the not-too-distant future, thousands of people could be enrolled in highly invasive studies, their pollutant levels, diets, movements, and physical activities all monitored in real time with wireless sensors linked to growing databases. Kathy Hudson, who directs the Genetics and Public Policy Center in Washington, DC, says, "We're talking about peering into people's private lives in a very profound way, so the question is whether they will accept that intrusion into their personal space."

Who would participate in these studies? "Certainly highly motivated people," Weis answers. "Parents who have kids with asthma would be more likely to enroll. We're trying to address this issue now—we know data collection devices would have to be portable and easy to carry around."

Linda Sheldon, the acting director for human exposure and atmospheric sciences at the EPA, suggests researchers need to reach out to prospective communities and listen to their concerns. "You have to work with community groups and help them understand how this knowledge can benefit them and society in general," she says. "And you really need to focus on people who are interested in the environment and its impacts on their health and the health of their kids."

Beyond the recruitment challenges, gene–environment research in general raises questions about genetic privacy. Could subjects be harmed by relinquishing genetic information to the public? Hudson



Making the connection. A major goal of exposure biology is to identify specific biomarkers of exposure to agents such as vehicular air pollution and environmental tobacco smoke, then link them to mechanisms of disease.

Elena Elisseeva

says there's little evidence to suggest individuals are more concerned about disclosing their genotypes than they are about disclosing the dietary and lifestyle factors already used in health research. But she concedes the GEI and future larger-scale projects are breaking new ground in this area.

"For all these data to be used to expand our knowledge of disease, they have to be widely available," Hudson says. "So, we have to consider the kinds of access and uses we want to prevent. On the one hand, we want that [gene–environment] information to be available, but on the other hand we don't want those who give of themselves to research to put themselves at risk."

Hudson says researchers also need to consider the consequences of their findings. For instance, she asks, how and at what point are correlations that link exposure and environmental disease relayed back to the public? Who pays for the removal of confirmed risk factors and the treatment of identified health conditions? What obligations do researchers have to communicate findings to their cohorts? "You really have to think carefully about all these outcomes," Hudson says.

Over time, findings that emerge from exposure assessment's growing alliance with genetics could produce social benefits by improved regulation. Sheldon says that whereas the EPA built its success on addressing "the big, obvious pollution problems," it is now facing more subtle issues such as understanding and managing health risks from low-level pollutant mixtures to which most people are exposed.

"We need more precise tools to understand the problems we face now," Hudson says. "Once these chemicals pass into the body, the effects may be different in different people—we need to get a better handle on the sequence of events that ultimately leads to a health outcome."

Ultimately, this could help us improve the safety factors we use in risk assessment as well as truly understand the risks. "The findings may not translate immediately," says Sheldon, "but as the science builds up it will have an impact."

Moving Forward

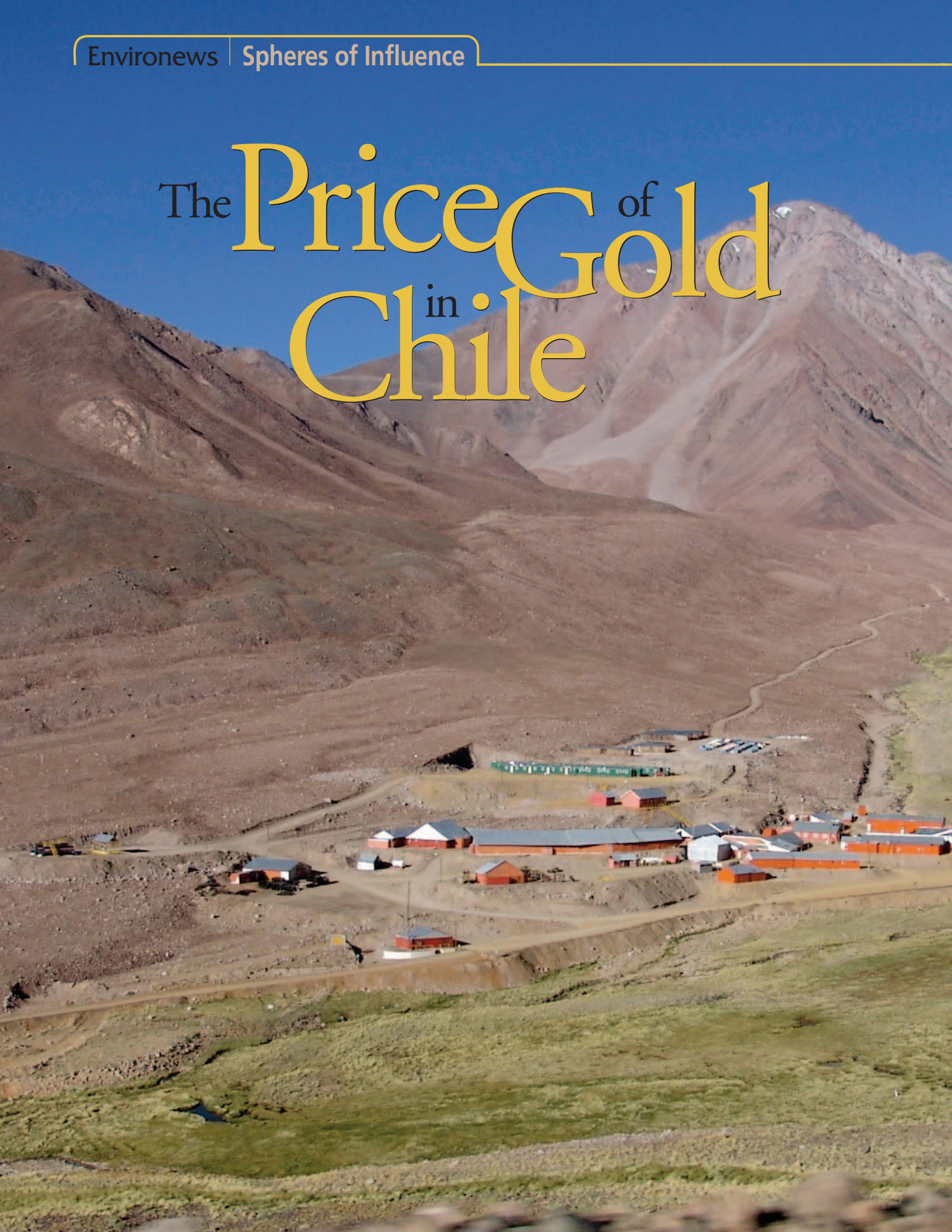
As the EBP moves forward, a GEI Subcommittee on Exposure Biology made up of experts from throughout the NIH is meeting on a biweekly basis in Bethesda to discuss priorities and progress. According to Weis, discussions emphasize fiscal year 2007 research initiatives in environmental sensors and biomarker development, which will address assessment needs for environmental pollutants, diet, physical activity, and even psychosocial stressors. Meanwhile, a counterpart GEI Genetics Subcommittee is addressing ongoing issues related to the initiative's genome association studies. Both subcommittees are open to all NIH staff.

Summing up, Perera suggests that emerging advances in exposure assessment will allow researchers to make better use of population resources.

"Everyone's excited about moving on to this next level," she says. "Researchers like us are eager to do more with our cohorts, and to find new molecular links between exposure and disease. This is all really about identifying preventable environmental exposures and their role in diseases that are extremely prevalent in our society."

Charles W. Schmidt

The Price of Gold in Chile



Straddling the Chilean–Argentine border high in the Andes, near a field of glaciers, lies an ore body that by mining industry estimates is large enough to yield 750,000 ounces of gold, 30 million ounces of silver, and 5,000 tons of tradable copper concentrate (typically consisting of 25–30% copper) every year for 20 years. Whether these valuable metals would stay in the ground, at least for the foreseeable future, or be extracted in an open pit mine is the topic of an ongoing tug-of-war between environmentalists and Canada's Barrick Gold Corporation, the claim holder and one of the world's largest gold miners.

MiningWatch Canada

Source of gold—and contention. Glaciers along the Chilean–Argentine border (above) narrowly missed being relocated to permit open pit gold mining at the Pascua-Lama site. At left is a mining exploration camp in the same area. Environmentalists continue to oppose the proposed mine.

Just about any new extractive industry proposal will attract protests, says Vincent Borg, Barrick Gold's senior vice president of corporate communications. He says Pascua-Lama, as the proposed mine is called, has been a target of environmentalists' wrath just because it's the latest large mine on the drawing table. But the Pascua-Lama case includes a few unique twists: perhaps 5% of the metals lie under glaciers, the site sits on land in two countries, and as gold and silver mines go, it is at a high altitude, a little over 15,000 feet above sea level. Tremors from regional earthquakes also are no stranger to Huasco Valley. According to the USGS, the region saw 6.7-magnitude earthquakes in 2006 and 2002, while a 6.8-magnitude event occurred in 2003.

By now, hoops have been jumped through, most i's dotted and t's crossed, protests conducted, and appeals exhausted. Just about all of the major players on this issue, for and against, say that the mine will almost certainly open in the near future. However, some activists are grasping at a thin thread of hope that new appeals to Chilean regulatory agencies, as well as other legal maneuvers could halt the project.

> What concerns me is that this particular mine has a very high resource value. That can drive people to assuming and making promises about a project that just realistically can't be upheld.
>
> *— Jim Kuipers, Kuipers and Associates LLC*

Initial Concerns

Much of the initial attention on Pascua-Lama focused on the issue of the glaciers that cover a portion of the site's deposits. To get at some of the metal deposits, Barrick Gold at one time planned to relocate parts of three of the smaller glaciers, called Toro 1, Toro 2, and Esperanza.

Melt from all of the glaciers—which developed during the last ice age, don't fully renew each winter, and have already diminished by 50–70% over the last 20 years—feeds primary sources of water used by local farmers and other inhabitants. The prospect of destroying glaciers, especially ones that indigenous people depend on so heavily, drew a flurry of attention from local activists and environmental groups in Chile and Argentina and from abroad. But Borg argues that these three glaciers are so small compared to the surrounding glaciers that they contribute little to the Huasco Valley watershed—less than 0.5%, by Barrick Gold's estimate.

All that said, the whole glacier issue is now moot anyway, according to Borg: "The glaciers will not be moved as part of the actual project that was approved." That's because new Chilean president Michelle Bachelet said during her campaign and after taking office that she wouldn't allow the glaciers to be touched. So the deposits that currently lie under these glaciers will stay put, Borg says, even if the ice covering them should disappear naturally later in the project.

Despite the glaciers' surviving the mine unscathed, local groups worry that, like problematic mines in locations elsewhere, this mine will contaminate local water supplies, says David Modersbach, an independent activist who lives in Rosario, Argentina. Water impacts are usually the most troublesome issue associated with all types of mining, but especially with hard-rock mines like Pascua-Lama.

Potential Water Problems

The water problems associated with hard-rock mining are essentially twofold: those associated with exposing buried rock, and those associated with accidents involving chemicals such as cyanide, mercury, and ammonia, which modern hard-rock miners use to extract gold and silver from pulverized rock. According to the U.S. EPA, mines can also affect waterways in other, more subtle ways, by altering natural drainage patterns, impounding water, diverting streams, and a host of other practices.

Acid mine drainage forms when the sulfide minerals in which gold and silver hide mix with specialized bacteria, air, and water. These acidic waters also can leak from natural rock formations, although in vastly smaller quantities. When sulfides are churned up and exposed to air, then introduced to water, they produce sulfuric acid, a medium in which these bacteria thrive. The nurtured bacteria oxidize the minerals further, resulting in a chain reaction that can produce water acidic enough to dissolve iron tools.

Unconstrained acid mine drainage can damage ecosystems when it finds its way into waterways and groundwater alike. It can also pepper waterways with potentially toxic metals—such as arsenic, lead, cadmium, mercury, zinc, iron, copper, aluminum, manganese, and chromium—that the acidic water leaches from the rock it flows through. Acid mine drainage has cost hundreds of millions of dollars to remediate in the past two decades alone, according to EPA estimates. Ideally acid mine drainage is controlled, usually by sequestering the depleted ore ("tailings") and waste rock behind dams and other enclosures designed to prevent water from flowing through the sulfide minerals.

The other hazard that hard-rock mines pose to waterways is inadvertent releases of cyanide. Like virtually all gold or silver mines nowadays, Pascua-Lama will use cyanide to strip minute flecks of gold and silver from ore. In the "vat leach" process planned for Pascua-Lama, ore is pulverized and poured into enormous vats. Sodium cyanide solution—the annual use of a typical mine is measured in hundreds of tons—is mixed with the pulverized ore. Cyanide trickling through the ore collects gold and silver particles, forming water-soluble gold– or silver–cyanide compounds. The tailings are deposited in vast pools and held in place by dams.

According to Borg, the Pascua-Lama project has included in its design significant facilities to minimize the possibility of surface and subterranean water coming in contact with waste rock as well as a comprehensive system of passive and active barriers to collect, store, treat, and reuse any water that does come in contact with the waste rock. This will ensure the quality of the water downstream of the project. The mine will also include

state-of-the-art facilities for controlling acid mine drainage, for handling cyanide (including wide, well-constructed roads for cyanide transport vehicles), and for monitoring water quality.

But according to a U.S. government mining expert who is familiar with the Pascua-Lama site and who asked not to be identified, the altitude and terrain of the site present unique challenges. In more hospitable locales, even the most up-to-date acid mine drainage prevention technologies, tailings holdings facilities, and cyanide handling schemes have failed, he says. In the past three decades, several tailings dams around the world have collapsed, and many more have leaked leftover cyanide and trace heavy metals leached from the ore. In some cases, even when enclosures have worked well, acid mine drainage has appeared from unanticipated spots outside the enclosures.

For the Pascua-Lama operation, the source says, the company would need "great engineering" to prevent the environmental damage that hard-rock mines often inflict. Once the mine closes, he says, restoring the site will be especially difficult because ecosystems at such high altitudes are fragile and slow-growing.

Besides dam failure, there is the possibility of cyanide tanker trucks crashing into or near waterways, dumping hundreds of gallons of cyanide into bodies of water. It is the prospect of just this kind of spill that most worries local residents, especially farmers, says Antonia Fortt, an environmental engineer at the Santiago office of Oceana, a Washington, DC–based environmental group. "On the Chilean side they are going to build their roads for the trucks of the mine just next to the river. These trucks will carry not just explosives and other materials, but also cyanide. We have had accidents with cyanide before, here in Chile," she says. "If we have a spill of cyanide, it would be just a disaster."

Fortt also notes that the trip will be precarious because of the mine's extreme elevation; trucks will be pummeled by seasonal high winds near the summit. Further, she says, the company's plan to dump waste rock at the headwaters of the Estrecho River could be equally, albeit more gradually, damaging if the rocks start generating acid.

The Question of Environmental Impact

Many modern mines in developed countries—including U.S. sites in states such as Montana, Idaho, and Alaska—are getting better at mitigating the environmental risks posed by mines, says Jim Kuipers, an independent mining consultant and mining facility inspector for Kuipers and Associates LLC of Butte, Montana. "In a case like Pascua-Lama it is more difficult to predict what will happen in that kind of circumstance," he says. Further, he adds, "It is fair to say that the ability to control it may be much more difficult just because of the climate, the topography, and issues like that."

A few other mines have operated, with mixed success, in similarly strenuous environments, Kuipers says, and learning from them will be critical in properly designing this mine.

Kuipers also voices concerns about the speed of the Pascua-Lama permitting process, which took just 18 months compared to an average of 4-plus years for a U.S. mine. He says Chile holds mining companies to much lower standards, explaining, "If this site were in the United States, I think it would warrant a much harder look from the permitting standpoint: a full-blown environmental impact statement, adequate opportunity for public opinion, not just from the opposition standpoint but from a technical standpoint. . . . You would want very competent agencies with experienced people looking at it. And even then I would expect you would still have problems with this mine, but hopefully you would have foreseen those problems and identified ways to deal with them. But in this case I don't see any way they could have possibly done this, as quickly as it has been escorted through the permitting process."

Adds Kuipers, "What concerns me is that this particular mine has a very high resource value. That can drive people to assuming and making promises about a project that just realistically can't be upheld."

Besides the mine's state-of-the-art facilities, Borg says that if the quality of the water drops below Chilean and Argentine standards, the company will stop operations until the problem can be fixed. The catch, warns Joan Kuyek, national coordinator for the Ottawa-based watchdog group MiningWatch Canada, is that other than the mining company's good word, there is not much to compel it to adhere to this agreement.

Pascua-Lama, like other mines in the region, doesn't have to provide a financial guarantee that it will protect surrounding terrain or restore the site to pre-mine conditions. In most of the developed world, including the United States and Canada, mining companies must post reclamation bonds, typically for tens of millions of dollars, to ensure that a detailed and periodically updated mining closure plan is followed. Borg says a reclamation bond will not be posted for Pascua-Lama; instead, he says, "The most significant aspects of the closure requirements will be built into the project from the beginning of construction."

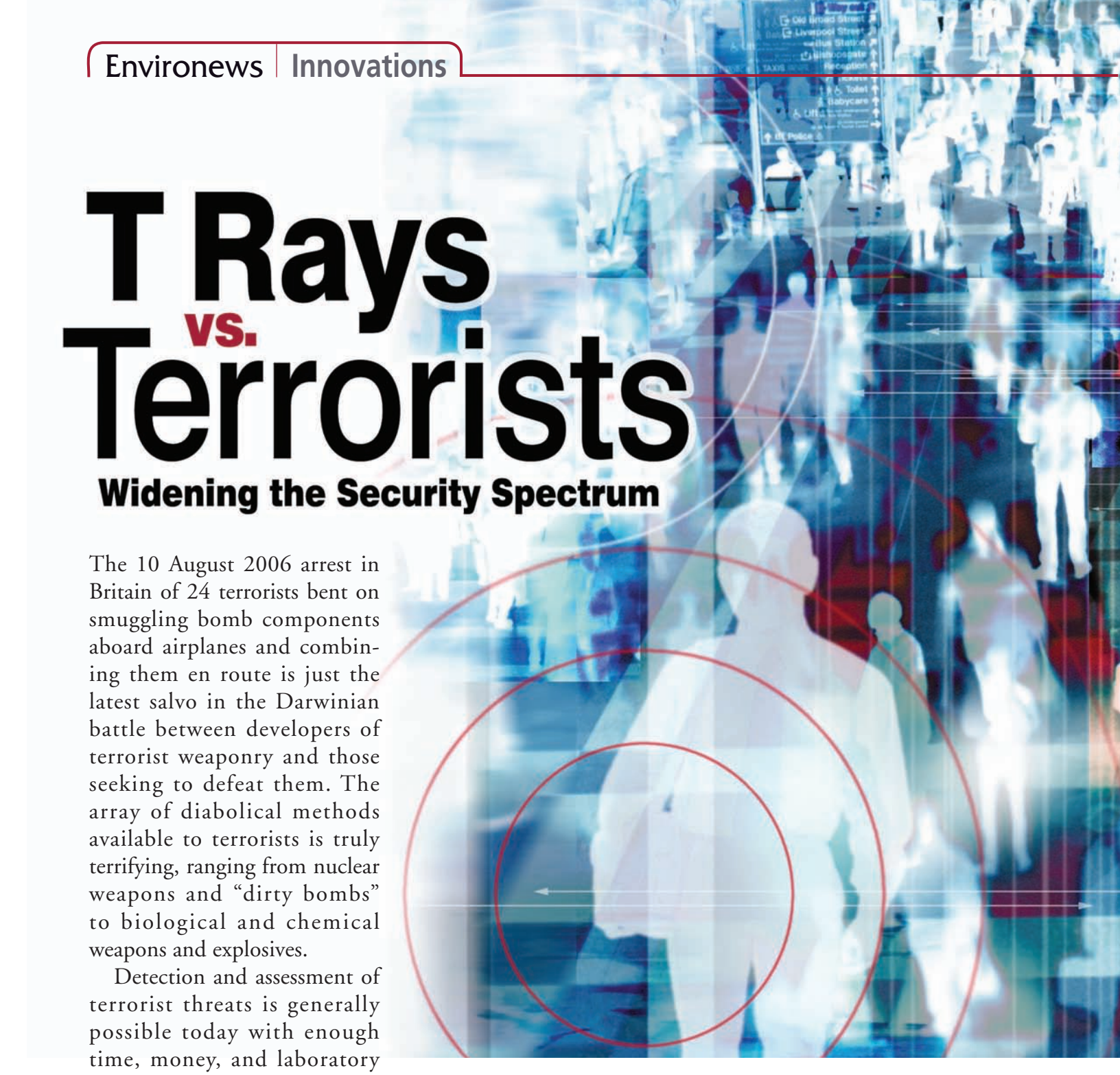
A Test Case

Many of the activists who oppose this mine say that they consider Pascua-Lama—for which 75% of the deposits lie in Chile and 25% lie in Argentina—a test case for future mines in pristine environments in the Andes in Argentina and Chile and on the long border that divides them. The Treaty of Mining Integration between the countries allowing such dual-country operations was ratified in 2000 and signed into law in 2004.

On 13 June 2006 the Chilean National Environmental Commission agreed to endorse 2 of 46 complaints filed against the decision to allow the Pascua-Lama project to proceed. A week later, a Chilean court returned two of Barrick Gold's Pascua Lama mining leases to a prospector who had agreed to sell them but had never received full payment from the company. The leases are listed as Barrick's property in a 2004 protocol to the Treaty of Mining Integration; there is a slim chance that the recent ruling would therefore invalidate this protocol, according to an analysis published 26 June 2006 in the Chilean newspaper *El Mostrador*.

In the meantime, barring any further legal action, the company plans to begin construction at Pascua-Lama in September 2006, with production slated to begin three years later. At this point activists are not optimistic about the future of the region. "If everything goes okay with this one, the gold companies could start to exploit all of the Andes to the south," says Fortt. "It's very likely that all other further projects could be approved for them, and they could get all of their environmental permits. If so, we don't think we will be able to stop other companies from coming. Through all the valley, agriculture has been developed. If they are allowed to destroy the valley—which is so pure—what keeps them from doing it anywhere else?"

Scott Fields



T Rays vs. Terrorists

Widening the Security Spectrum

The 10 August 2006 arrest in Britain of 24 terrorists bent on smuggling bomb components aboard airplanes and combining them en route is just the latest salvo in the Darwinian battle between developers of terrorist weaponry and those seeking to defeat them. The array of diabolical methods available to terrorists is truly terrifying, ranging from nuclear weapons and "dirty bombs" to biological and chemical weapons and explosives.

Detection and assessment of terrorist threats is generally possible today with enough time, money, and laboratory equipment, but the ideal technology would be fast, accurate, cheap, easy to use, and portable or able to remotely detect threats, with an emphasis on prevention. No technology now exhibits all these virtues, but under the pressure of terrorists' inventiveness, researchers are working steadily to develop and apply improved systems.

Now researchers at Argonne National Laboratory are getting promising results from experiments using "T rays," the terahertz (THz) part of the electromagnetic spectrum. In March 2006 Argonne announced that a research team there had shown for the first time that T rays can be used to identify explosives and poison gas precursors. The Argonne team also successfully used millimeter-wave radar to remotely detect airborne chemicals and the effects of radiation in the air. These results are currently being written up for publication.

Chris Reuther/EHP, Digital Vision

T rays and millimeter waves are at the low-energy end of the electromagnetic spectrum, between microwaves and infrared frequencies. According to Nachappa "Sami" Gopalsami, a senior electrical engineer at Argonne and a lead researcher on the THz sensor project, the general characteristics of T rays and millimeter waves are the same. "But," he says, "new physics and phenomena are beginning to be explored as we move up in frequencies."

Although many detection techniques currently in use are based on electromagnetic radiation and mass spectrometry, T rays and millimeter waves have not previously been used in this context, mainly due to an inability to generate broadband pulses in these frequencies. In the Argonne experiments, however, THz spectrometry sensors provided unambiguous identification of explosive chemicals, including TNT and plastic explosives. Gopalsami says this method is "highly specific" and will eliminate interference from confounding elements.

The Argonne team has been collaborating with researchers at Dartmouth College, Sandia National Laboratory, Sarnoff Corporation, and AOZT Finn-Trade of St. Petersburg, Russia. Funding has come from the U.S. Air Force, the Department of Energy, and the Department of Defense. But although national security imperatives are the driving force behind current research, many of the resulting technologies could also prove useful in environmental health applications.

Being able to remotely detect and identify chemicals will be helpful in monitoring gas pipeline leaks, chemical plants, vehicle emissions, and the like. Gopalsami says the T ray technology can detect some of the most important environmental hazards including ozone, volatile organics, and cyanide compounds. Medical applications, particularly imaging techniques for body tissues and teeth, are also in the offing, especially because the THz zone

is on the opposite end of the electromagnetic spectrum from X rays, and thus of lower energy and far less damaging to living tissue.

Detection Difficulties

Technical problems plague many existing detection methods. For example, X rays can penetrate almost anything but can harm the object being studied, and in living organisms they may damage DNA and cause cancer. Laser and other optical instruments are less harmful, but their performance can be affected by wind, humidity, fog, and smoke.

Just tracking terrorists' movements is a nightmare. In a paper presented at the March 2002 Conference on Technology for Preventing Terrorism, David Dye of Lawrence Livermore National Laboratory noted that the United States has 7,606 miles of land border and some 12,452 miles of coastline. Further, Dye reported, 633.7 million people entered the United States at the nation's 361 ports of entry. Even in the months just after September 11, the Coast Guard boarded only about 35% of the 5,112 vessels entering U.S. ports. Wrote Dye, "The government simply cannot perform 633.7 million hand searches every year, no matter how great the threat."

"Our biggest concern is explosives," says Nico Melendez, a spokesman for the Transportation Security Administration (TSA). Melendez says the TSA started airport screening for explosives using what's called an "air shower" system in the summer of 2004. In this system, passengers step into a booth-like portal that releases puffs of air aimed at their clothing and skin. An air sample is then collected and analyzed by an ion mobility spectrometer, which compares the air's components against a database containing spectrographic profiles of target chemicals such as TNT, C-4, and Semtex. According to a 24 May 2006 press release from the Port of Portland (Oregon), 28 airports in the United States are now using air shower portals.

THz waves are also useful for passenger screening because they can penetrate beneath clothing to detect hidden weapons. Peter Adrian, a senior analyst with business consultancy Frost & Sullivan, says, "One of the historical problems with gas sensors [including ion mobility spectrometers] is that they can be affected by extraneous environmental factors." Conventional mobility spectrometers searching for explosives and trace levels of chemical warfare agents can't always pick the target signal out of the "noise" of the many other chemicals in the environment, such as perfumes, and may be susceptible to false positives, causing delays and passenger frustration.

Hair-raising experience? One technology now used for airport security comprises portals in which puffs of air are blown at passengers and then analyzed to detect trace amounts of explosives. THz waves add the advantage of penetrating clothing, and offer a high probability of detection with few false alarms.

Faster and more accurate identification of questionable materials is crucial to effective protection from terrorism. With too many false positives, people will become desensitized to the danger. At the same time, a false negative means the system has failed, with potentially devastating consequences. The TSA is currently funding Argonne research into replacing the ion mobility spectrometer with THz spectrometry, says Gopalsami, who adds that with proper funding the device could be taken into the field in two years.

Putting T Rays to the Task

Argonne's THz spectrometry technology measures the rotation of a molecule in the vapor or gas phase. Every molecule's rotational pattern is unique, and exciting a molecule with T ray frequencies reveals the "fingerprint" for that molecule. A spectral identification algorithm uses the information to determine the specific compound being examined by matching it with a spectral library. One disadvantage of THz spectrometry, says Gopalsami, is that to be detected a molecule must be polar, or asymmetrical; methane, for example, cannot be

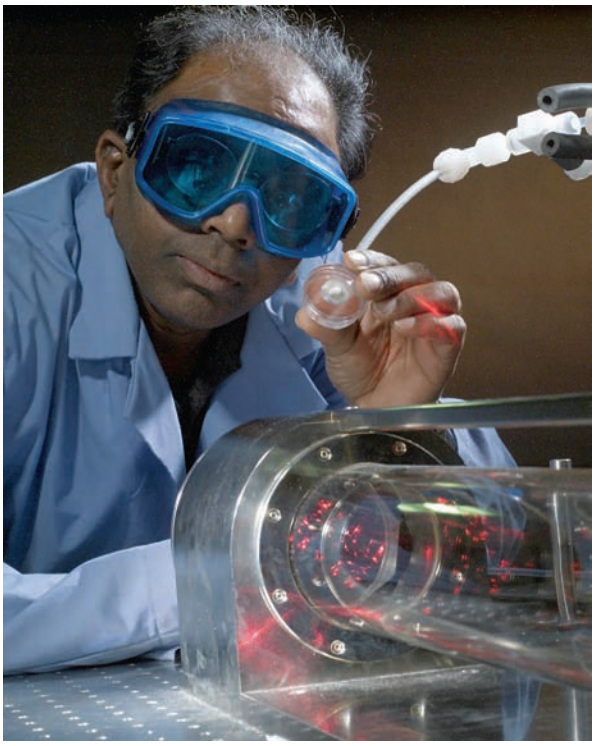
Top to bottom: Digital Vision; AP Photo/Joe Giblin

detected this way because it is nonpolar, or symmetrical.

Quick and accurate identification of a molecule is easiest when the molecules are rotating unimpeded in gas or vapor form under pressures well below normal atmospheric pressure, so that collisions between molecules are decreased. This is easy to establish in a laboratory, but difficult in field conditions. However, the Argonne researchers were able to overcome this handicap with millimeter-wave frequencies, which are less sensitive to atmospheric conditions; their longer wavelengths (relative to cloud particles) cause less reflection and scattering of the millimeter waves. "Additionally," says Gopalsami, "there are gaps or windows in the millimeter-wave spectrum in which common molecules in air are mostly transparent to the millimeter waves." Using millimeter-wave frequencies, the team identified airborne poison gas chemicals from 60 meters away and chemicals related to nuclear weapons from 600 meters.

A major issue for counterterrorist sensor development is whether a sensor must have a physical sample or whether it can detect and analyze a substance at a distance. The former are called "point sensors," and the latter are "remote" or "standoff" detectors. Chemical, biological, and explosive materials generally require a point sensor. However, in an experiment with AOZT Finn-Trade, the Argonne team was able to tell when a nuclear power plant 9 kilometers away was in operation or idle by measuring radiation-induced changes in the air around the plant. Those changes were observable using microwave radar, but the team is also experimenting with millimeter-wave radar to achieve higher sensitivity of detection.

Bioweapons also pose serious risks, and the development of sensors capable of rapid remote detection has been slow. The litany of known and possible biological agents is frightening, among them the viruses that cause smallpox, anthrax, plague, and Ebola hemorrhagic fever. Further, in an article in the 2006 special issue of *EMBO Reports*, authors Jonathan Tucker and Craig Hooper described how advances in protein engineering could make so-called fusion toxins another front-runner for terrorists. These custom-made "designer" poisons unite two or more naturally occurring toxins, such as ricin and botulinum, to create a toxin significantly more toxic than either parent. Not only that, but unless counterterrorist researchers can stay abreast of possible combinations, a fusion toxin could be invisible to a sensor looking for a match in a preexisting library.



One in a billion. Sami Gopalsami demonstrates an instrument in Argonne's Terahertz Test Facility that can detect chemicals at the part-per-billion level.

For bioweapon detection, Argonne researchers are working on a sensor based on dielectric properties of molecules. Dielectric materials are nonconducting and exhibit a complex property called a dielectric constant that can be measured by resonator techniques. Furthermore, they resonate at particular frequencies. DNA appears to resonate strongly in the THz region; therefore, the dielectric approach may eventually enable early detection of biological molecules without the use of more complex and much slower biochips that rely on analytical tools such as polymerase chain reaction.

As new technologies are developed, they will not necessarily eliminate older methods. "It's hard to make a categorical statement that one approach is better than the others," says Dye. Because the range of terrorist weapons is so broad, he adds, "You'll end up with niche applications." In the swirl of national security challenges, however, using a new part of the electromagnetic spectrum offers rich promise for thwarting the terrorist arsenal—and likely will produce benefits for environmental health as well.

Valerie J. Brown

Suggested Reading

Brower JL. 2005. The Terrorist Threat and Its Implications for Sensor Technologies. Presented at: Advances in Sensing with Security Applications; 17–30 July 2005; Il Ciocco, Italy. Available: http://www.nato-asi.org/sensors2005/papers/brower.pdf.

Dye DH. 2002. Sensors for screening and surveillance. Presented at: Conference on Technology for Preventing Terrorism; 12–13 March 2002; Stanford, CA. Report UCRL-JC-147479.

Gopalsami N, Raptis AC. Resonance-enhanced dielectric sensing of chemical and biological species. Presented at: Biological Threat Reduction Conference 2003; 19–21 March 2003; Albuquerque, NM.

Siegel PH. 2004. Terahertz technology in biology and medicine. IEEE Trans Microw Theory Tech 52(10):2438–2447.

Tucker JB, Hopper C. 2006. Protein engineering: security implications. EMBO Rep 7(SI):S14–S17.

Argonne National Laboratory

Pyrethroids in the Home

Nondietary Pesticide Exposure in Children

Because pyrethroid pesticides are often used in conventional agriculture, people are routinely exposed to trace amounts in foods. Similar exposure to organophosphorus (OP) pesticides has been described previously in results from the Children's Pesticide Exposure Study, an investigation of pesticide exposures among 23 Seattle children aged 3–11. Unlike OP pesticides, however, pyrethroids are also approved for residential use. The latest findings from this study show that residential use of pyrethroids appears to be a more significant source of exposure to this class of pesticides than diet [***EHP* 114:1419–1423; Lu et al.**].

With the phaseout of residential use of the commonly used OP pesticides chlorpyrifos and diazinon, home use of pyrethroids has increased. Depending on the compound and the dose, pyrethroids may affect neurological development, disrupt hormones, induce cancer, and suppress the immune system. However, little is known about the extent and effects of human exposure.

Close to the source. New data show that OP pesticides used in the home contribute more to children's exposure than diet.

Using samples collected during the summer of 2003, researchers at Emory University and the CDC determined urinary pyrethroid metabolite levels during 15 consecutive days for each child. During days 1–3 and 9–15, the children consumed foods prepared from conventionally grown crops. On days 4–8, organic items were substituted for plant-based foods such as fruits, vegetables, pasta, and cereal.

During the entire 15-day sampling period, the dominant metabolite seen was PBA, a nonspecific metabolite of permethrin, cypermethrin, and deltamethrin. PBA was detected in 82% of samples and had the highest median concentration, 0.45 µg/L. *trans*-DCCA and *cis*-DCCA, metabolites of permethrin, cypermethrin, and cyfluthrin, were also common, detected in 71% and 35% of all samples, respectively. Concentrations of *cis*-DCCA were too low to quantify; the median *trans*-DCCA concentration was 0.38 µg/L. The metabolites FPBA, derived from cyfluthrin, and DBCA, derived from deltamethrin, were each detected in only 2% of samples.

Comparing metabolites between dietary phases, the researchers saw no apparent trend. However, seven children in families that reported using pyrethroid pesticides had significantly higher levels of PBA and *trans*-DCCA than the other children and accounted for most of the FPBA-containing samples and all of the DBCA-containing samples. Interestingly, the older children experienced higher exposure than the younger ones. Typically younger children have higher exposure due to behaviors such as mouthing items and playing on floors, but the older children in this study spent time at sports facilities where pyrethroids may have been used.

The researchers conclude that an organic diet alone is unlikely to dramatically decrease a child's exposure to pyrethroids the way it does exposure to OP pesticides. Limiting residential use of pyrethroids and preventing children's contact with treated areas are very likely the best measures for decreasing their exposure to these pesticides. **–Julia R. Barrett**

Heavy Traffic Can Be a Pain in the . . . Ear?

Vehicle Emissions Linked to Otitis Media

Traffic is a major source of air pollutants, and more studies are looking at the role of traffic-related air pollution in children's health. Researchers report in this issue that young children exposed to higher levels of traffic pollution have a greater incidence of otitis media (middle ear infections) than those exposed to lower levels [***EHP* 114:1414–1418; Brauer et al.**]. In 2002, the same team found that such pollution increased the risk for asthma and upper respiratory tract infections in young children. Now they focus on otitis media because upper respiratory tract infections often progress to ear infections, which are one of the leading reasons for visits to doctors and the use of antibiotics in childhood.

The new study involved approximately 3,700 Dutch children and 650 German children surveyed from birth to age 2 years. Researchers in those countries monitored the concentrations of three common traffic-related pollutants (nitrogen dioxide, particulate matter less than 2.5 µm in diameter, and elemental carbon) at 40 different sites in each country, then used those data to estimate exposures at each child's residence. The levels of pollutants measured were similar in both countries and fell within a range commonly experienced by people living in industrialized nations. Information about doctor-diagnosed otitis media came from questionnaires answered by parents.

Aural pollution? Traffic pollution is linked to increases in cases of ear infection in children.

Both groups of children showed an increase in otitis media in association with greater traffic pollution exposure. By age 2, a third of the children had experienced otitis media at least once. The adjusted odds ratios of contracting otitis media associated with modest increases in exposure to the different air pollutants ranged from 1.09 to 1.24, and the risk of ear infections was similar for each of the three pollutants measured. Although environmental tobacco smoke has been linked to otitis media in studies by other researchers, exposure to this agent did not alter the associations between traffic pollution and otitis media observed in this study.

Otitis media has been estimated to cost the U.S. health care system $3–5 billion yearly. These findings, the first to link traffic pollution to otitis media, represent an additional consequence of air pollution. Protecting children from exposure to vehicular emissions—for example, by building major roadways away from residential zones, improving automobile emission standards, and driving less—may reduce the risk of otitis media. **–Carol Potera**

Top to bottom: Rebecca Ellis/iStockphoto; Photodisc

A Lethal Change in the Weather

Temperature Extremes and Premature Mortality

Extremely hot and cold days can be fatal to certain vulnerable populations, as the more than 160 deaths in two weeks during California's July 2006 heat wave clearly showed. The elderly and lower-income individuals are generally acknowledged to be most vulnerable to the effects of temperature extremes, but relatively little is known about how such extremes combine with underlying medical conditions to increase mortality risks. Now, a team from the Harvard School of Public Health has analyzed millions of death records from 50 U.S. cities to identify factors that increase the risk of dying on extremely hot or cold days [***EHP* 114:1331–1336; Medina-Ramón et al.**]. The study is the first of its size to identify specific diseases that produce the largest relative mortality increases on extreme temperature days.

The researchers examined approximately 7.8 million death records for the period 1989 through 2000. They defined extreme temperatures for each city as the coldest 1% of daytime highs and the warmest 1% of nighttime lows. These are the most physically challenging conditions, with people unable to warm up even in the daytime or cool off even at night. The data were analyzed using a case-only approach, a technique borrowed from genetic research that allows the identification of time-invariant factors (such as gender) that modify the effect of a time-variant risk factor (such as weather). This approach allowed the researchers to compare the individual characteristics of those dying under extreme weather conditions with those dying on other days.

The study's large sample size provided enough statistical power for researchers to see how a variety of individual characteristics, including presence of chronic conditions, affected vulnerability to weather extremes for a specific cause of death. For example, previous studies had already shown that blacks are more likely than whites to die on a hot day, but the authors found that susceptibility in this subgroup was more pronounced when death was due to cardiovascular disease. Conversely, the elderly and diabetics were more vulnerable to heat when the primary cause of death was *not* due to cardiovascular disease. The researchers also found a large increase in vulnerability to heat in individuals who suffered from atrial fibrillation, a finding that has not previously been reported. Cardiovascular deaths, especially cardiac arrest deaths, also showed a greater relative increase on extremely cold days.

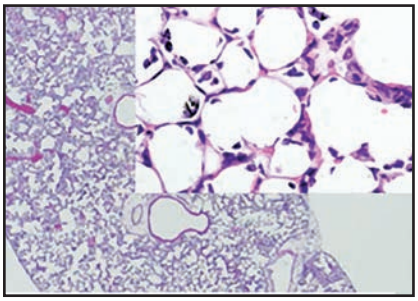
Hot science. Identifying disease risks related to extreme temps can help officials target services such as fan distribution to those most at risk.

The authors note that public health officials can target appropriate health services and infrastructure by knowing which subpopulations are particularly at risk from temperature extremes as well as the most common mortality causes that may affect them. This kind of information will be even more important as some subgroups (such as diabetics and the elderly) increase as a percentage of the population at large, and as global warming raises the probability of higher maximum temperatures. **–Nancy Bazilchuk**

Tiny Intensifiers

Nanoparticles Worsen Lung Effects of Bacterial Endotoxin

Exposure to particulate matter in the air, especially extremely fine particles, has been associated with increased morbidity and mortality from lung and cardiovascular disease. Effects grow more significant with decreasing particle size. However, the size-related effects of nanoparticles—particles less than 100 nm (0.1 μm) in diameter—on pulmonary inflammatory conditions have not been fully investigated. This month a team of Japanese investigators reports that nanoparticles can increase lung inflammation associated with bacterial endotoxin, or lipopolysaccharide (LPS) [***EHP* 114:1325–1330; Inoue et al.**].



Nanoparticles in inflamed lung tissue

Inhalation of particles with a mass median aerodynamic diameter of 10 μm or less is associated with increased hospitalization for asthma, bronchiolar irritation, and lower respiratory tract infections, while exposure to particles 2.5 μm and smaller, including common carbon-cored pollutants from diesel exhaust, exhibit a stronger epidemiological link to death from cardiopulmonary and respiratory effects. Particles even smaller, 0.1 μm or less, are thought to move beyond the respiratory system, perhaps reaching the blood stream. The tiniest particles are not just smaller than other pollutants; they have more surface area for a given weight—imagine the difference between the surface area of a solid glass cube compared to that of an equal weight of fine glass beads. Both the small size of nanoparticles and the high surface area that they present to cells may contribute to their effects.

For the current study the researchers used ultrafine carbon black, a form of elemental carbon used in the printing industry, to explore how exposure to nanoparticles impacted antigen-related inflammation of airways in mice. Using carbon black formulations with diameters of 14 nm and 56 nm, they looked at how LPS's effects changed in the context of nanoparticles in the airway.

The effects of the nanoparticles by themselves was slight, while exposure to LPS alone increased by 12-fold the number of cells harvested by bronchoalveolar lavage (a measure of airway inflammation). However, simultaneous exposure to LPS and to 14-nm particles amplified the effect to yield a 20-fold increase. Simultaneous exposure to LPS and to 56-nm particles resulted in a smaller, statistically insignificant boost in the effects of LPS.

It was not just cell infiltration that was affected. Histology showed that lung exposure to a mixture of 14-nm particles, which had only minor effects themselves, and LPS led to recruitment of neutrophils in the parenchyma, the actual respiratory surface of the lung. LPS-driven oxidative stress and expression of chemokines and cytokines also were amplified in the presence of these small particles, and changes in blood coagulatory factors were seen as well. The larger 56-nm particles increased the effects of LPS in some but not all assays.

Taken together, these observations suggest that ultrafine carbon-cored particles, perhaps including those present in vehicle exhaust, can make respiratory damage from commonly encountered bacterial endotoxins even worse. **–Victoria McGovern**

Top to bottom: Associated Press; Inoue et al.