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Nuclear Energy: Is Perception Reality?

Particles Size Makes All the Difference

Human Body Systems The Domino Effect?

NIEHS
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STUDENT EDITION

[Nuclear energy] requires a social commitment, and perhaps even a stability of the society, over very long times to maintain the expertise, the quality assurance, the vigilance that will keep us out of trouble.
Alvin M. Weinberg
Science, 7 July 1972

INFECTIOUS DISEASE

In Disaster's Wake: Tsunami Lung

When the Asian tsumani struck on 26 December 2004, health authorities braced for an onslaught of waterborne illnesses including malaria and cholera, which often follow such disasters. But saltwater flooded the freshwater breeding grounds of the mosquitoes that spread malaria, and relief agencies quickly distributed bottled water, thwarting a cholera epidemic. Instead, a type of aspiration pneumonia named "tsunami lung" emerged and afflicted some survivors.

New concerns in devastation's wake. Some survivors of the tsunami that struck South Asia on 26 December 2004 are experiencing a new peril—mud and bacteria they inhaled as they were swept along with the waves has led to a type of aspiration pneumonia called "tsunami lung."

Tsunami lung occurs when people being swept by tsunami waves inhale saltwater contaminated with mud and bacteria. The resulting pneumonia-like infections normally are treated with antibiotics. However, the 2004 tsunami "wiped out the medical infrastructure, and antibiotics were not available to treat infections in the early stages," says David Systrom, a pulmonologist at Massachusetts General Hospital in Boston. Consequently, victims' lung infections festered, entered the bloodstream, and spread to the brain, producing abscesses and neurological problems such as paralysis.

Systrom and colleagues volunteered to work on a medical disaster team with Project HOPE (Health Opportunities for People Everywhere) aboard the hospital ship U.S. Naval Ship *Mercy* off the coast of Banda Aceh, Sumatra. When they arrived three weeks after the tsunami hit, "we saw infections not seen in the United States since before the development of antibiotics," says Systrom. Among them were about 25 cases of tsunami lung. "No one expected the number of tsunami lung cases we saw," says Systrom. "It was not on the radar screen."

The diagnosis of tsunami lung requires a chest radiograph and computed tomography scan of the brain to confirm abscesses. This sophisticated equipment was available on the hospital ship. "Only the most severe cases with central nervous system involvement made it to the ship," says Systrom. The team suspects that hundreds of milder cases went unreported.

In the 23 June 2005 issue of the *New England Journal of Medicine*, the team describes the case of a 17-year-old girl who aspirated water and mud while engulfed by a wave and carried about half a mile. She developed pneumonia two weeks later and was treated at a local clinic with unknown medicines. A week later, the right side of her face drooped, her right arm and leg became paralyzed, and she stopped talking.

A chest radiograph revealed air and pus outside the lining of the lung (a condition known as hydropneumothorax), and a brain scan showed four abscesses. After the doctors treated her with a combination of intravenous antibiotics (imipenem until the stock of that drug ran out, then vancomycin, ceftazadime, and metronidazole), her speech and facial movement recovered first. When she moved her right leg and arm for the first time, she "burst into peals of laughter," according to the report. She was transferred to an International Committee of the Red Cross–Crescent field hospital. "I suspect she'll fully recover," says Sydney Cash, a neurologist at Massachusetts General Hospital and member of the team, who has since received pictures of her walking.

A combination of microbes likely contributes to tsunami lung, but no lab facility was available to culture and identify those found in the Indonesian patients before the *Mercy* arrived. However, in a letter published in the 4 April 2005 issue of *The Medical Journal of Australia*, Anthony Allworth, director of infectious diseases at Royal Brisbane and Women's Hospital, describes culturing *Burkholderia pseudomallei* from two tsunami lung patients in a land-based hospital and *Nocardia* species from a third.

B. pseudomallei lives in the Asian soil and water. Mark Pasternack, an infectious disease specialist at Massachusetts General Hospital who also served on the *Mercy*, says, "You do not have to directly aspirate *Burkholderia* to produce pneumonia. . . . After the tsunami, people had soft tissue injuries from being forced into objects, so they could have gotten *Burkholderia* from wounds or aspiration."

Cash echoes this thought: "Natural disasters produce odd combinations of pathogens and unexpected ways for the body to be damaged that lead to unexpected clinical circumstances. [Medical disaster physicians need to] keep an open mind and expect the unexpected."

Could an infection like tsunami lung emerge in victims of Hurricane Katrina? Probably not, speculates Pasternack. Although the water sweeping the Gulf Coast area may have been contaminated, "it was not forced down peoples' lungs by high-speed waves," he says. Therefore, aspiration pneumonia and its complications are unlikely to appear commonly during the Gulf Coast relief efforts. **–Carol Potera**

Tim A. Hetherington/Panos

RADIATION

Any Dose Is Too High

Any exposure to radiation may cause cell damage that could lead to cancer, according to a June 2005 report from the National Research Council. The risk noted by the report, though small, is a third higher than the risk of 8.46 cancers per 10,000 people exposed to 1 rem (or 10 millisieverts [mSv]) currently used by U.S. regulators. The report contradicts critics who believe there is a threshold below which radiation is harmless; it also fails to support those who say low doses of radiation cause greater health damage per unit dose than high levels.

The seventh Biological Effects of Ionizing Radiation (BEIR) report, sponsored by several federal agencies, assessed and updated the health risks from low linear energy transfer (low-LET) radiation, which deposits little energy in a cell and thus tends to cause little damage. The last BEIR report that addressed these health risks was published in 1990.

Richard Monson, a professor of epidemiology at the Harvard School of Public Health and chair of the group that conducted the study, says, "We judged that the most reasonable shape is a line through the origin." Simply put, this means any low-LET ionizing radiation may increase the risk of a cell becoming cancerous—there is no threshold below which there is no risk—and as exposure increases, so does the health risk. Researchers refer to this straight line as the linear-no-threshold model.

Less than 20% of people's low-level radiation exposure comes from anthropogenic sources. The Earth and cosmic sources emit the remainder. Nearly 80% of human-induced exposure comes from medical procedures, about 15% from products like tobacco and building materials, and around 5% from exposure at work.

For the purpose of the BEIR VII report, the authoring committee defined low-LET radiation as levels up to about 100 mSv. For comparison, a chest X ray averages around 0.1 mSv. The committee concluded it's likely that about 1 out of 100 people would develop a tumor or leukemia from exposure to 100 mSv above background. Of that same 100 people, experts would expect 42 to develop cancers for other reasons, but at the press conference marking the release of the report, the committee said it did not fully exclude the possibility of some radiation exposure being a factor in those cases.

The BEIR VII report employed statistical data to draw its conclusions and reviewed studies of people exposed at work and in medical settings. It also relied heavily on data from the Japanese atomic bomb survivors.

As these survivors age, more is revealed about the relationship between radiation exposure and eventual health outcomes. Investigators have also improved their estimate of the levels of exposure this population received. But critics question the heavy reliance on the Japanese survivors because of the "healthy survivor" effect—those who survived the bombing might have been hardier than those who died early on, potentially skewing the results.

Many researchers say the latest report helps reaffirm the general accuracy of federal standards in place for limiting health risks from low-level radiation. "We believe the data are more convincing than fifteen years ago and show that the radiation protection standards we use are reasonable," says Monson.

Mike Boyd, a health physicist who works on setting and updating those standards for the Environmental Protection Agency, concurs. "I don't think we'll be changing any federal standards," he says. "I'm not willing to say there will be no impact. This report will go into our estimation of risk and could lead to refinements, but generally standards should stay the same."

Although most scientists agree the report incorporated the majority of pertinent data up through 2003, information about low-LET radiation continues to emerge. One hypothesis under investigation, says biologist Andrew Wyrobek of Lawrence Livermore National Laboratory, is the possible adaptive response cells developed over eons of natural exposure. Other hypotheses include genetic instability (the idea that some cells already have genetic mutations and are thus more prone to becoming cancerous, given the incentive) and the "bystander effect" (in which cells respond adversely to nearby irradiation although they themselves weren't hit directly). These concepts were among those reviewed for the BEIR VII report but were not incorporated into the risk estimates.

Most experts agree that the BEIR VII report won't be the last in the series. "Right now there is just a lot we don't know about how cells react to very low doses of radiation," says Wyrobek. "But with multiple exposures from more and more people undergoing medical diagnostics in the low-dose range, and increased amounts of radioactive waste, it's important to understand these ranges better." Says Boyd, "I will be excited to see some future academy report after we find out more about how radiation affects cells at very low doses."

–Sarah Todd Davidson

Smoke-Free Beijing Olympics

WHO officials announced in April 2005 that the 2008 Beijing Olympic Games will be smoke-free, a ban the city's mayor has personally endorsed. Experts say the move signals an official effort by China to heighten awareness of the dangers of smoking among its population, of whom 360 million smoke. The 2000 Sydney Olympics were smoke-free, but smoking was permitted at some venues of the 2004 Athens games.

China is a signatory of the WHO Framework Convention on Tobacco Control, yet as the world's largest tobacco producer it faces challenges in reducing smoking among its population. Sharing cigarettes is a form of social courtesy, and 67% of Chinese males smoke. The WHO estimates at least 1.3 million Chinese die each year from smoking-related illnesses.

Nuclear Cleanup Slowdown

In 2002, the U.S. DOE began an accelerated cleanup program for nuclear waste aimed at reducing cleanup costs by $50 billion and shortening the timeline by 35 years. In July 2005, the GAO released a review of this program which found that progress is varied among the 16 cleanup activities measured. The DOE is ahead of schedule on packaging nuclear materials for disposal, disposing of low-level waste, and removing buildings, but lags on the tougher and costlier tasks of disposing of transuranic and radioactive tank wastes and closing tanks that contained radioactive waste. Because of these factors the DOE is not likely to achieve its full estimated cost and time reduction. The GAO advised the agency to revise its performance reporting and better highlight critical activities that will help it meet its goals.

Flush with Progress

The homeless population of Vancouver, British Columbia, has doubled in recent years. Now high populations of homeless persons and drug abusers have created an unsanitary problem for the city—streets, alleys, and parking lots around the downtown are habitually used as outdoor toilets. The city is now purchasing several new high-tech, self-cleaning bathroom booths—at up to $300,000 apiece—to be installed in critical areas, with an urban anthropologist to pinpoint major problem spots. The city is looking at a stainless steel model that cleans and dries every surface of its interior after each use.

Top to bottom: International Olympic Committee, City of Vancouver

INFORMATION TECHNOLOGY

This Is YourAir Calling

Consider the following scenario: You're making last-minute preparations the night before a planned day of outdoor activities. Suddenly your cell phone rings. It's not a friend or relative, but a text message warning you that air pollution levels will spike near your destination the next day. If you suffered from asthma or heart disease, this would be crucial information—high levels of air pollution can trigger life-threatening reactions in vulnerable people. With prior knowledge of the risk, you might take steps to limit your exposure and protect your health.

Thanks to a pilot project called YourAir, subscribers in some areas of London, England, are getting just this type of service. Coordinated by the European Space Agency (ESA) and Cambridge Environmental Research Consultants (CERC), YourAir calls subscribers with text message alerts on evenings before high levels of ozone, nitrogen dioxide, and particulates are predicted in their locations.

YourAir currently serves Central London and the boroughs of Croydon, Camden, and Wakefield. Iarla Kilbane-Dawe, a senior scientist with CERC, predicts the service will cover all of London and its population of 7 million by next year. The effort was developed as a demonstration service of ESA's PROMOTE project, which uses real-time atmospheric data to improve quality of life and public decision making.

Subscribers to the free service are recruited through newspaper ads. They provide CERC with a street address or postcode, and are alerted only when pollution levels in that area are expected to rise. According to Kilbane-Dawe, YourAir integrates measurements of transboundary pollution movements generated by an ESA satellite with weather forecasts and knowledge of local traffic patterns. Through this approach, citizens get high-resolution air quality predictions at the street-by-street level.

YourAir also has a web-based interface, located at http://www.cerc.co.uk/YourAir/index.asp, that provides air quality predictions for all of Central London. With upcoming improvements to the site, Kilbane-Dawe says "you'll be able to zoom in, pan, and scroll the air quality map and even look at air quality in the vicinity of individual houses."

A key goal of the first-of-its-kind service is to enhance the medical community's predictive capacity. For instance, pharmacies are more likely to run out of inhalers when pollution levels rise, and better air quality predictions might alert them to stock up in advance. "Air pollution alerts are a growth area," Kilbane-Dawe says. "We think we'll have air pollution issues in London for another twenty years at least." **–Charles W. Schmidt**

Get the message? A pilot project in the United Kingdom sends text messages to people at risk for complications from severe air pollution, warning of days when it might be safer to stay inside.

ALLERGIES

The Radical Theory of Sneezing

Anyone with common seasonal allergies knows perfectly well what's causing their misery: pollen! And allergists know why pollen makes people sneeze: the body's immune system is releasing a lot of inflammatory cells, including neutrophils and eosinophils, in response to the invading pollen proteins. However, new research reveals that it's more than just pollen's proteins wreaking havoc on human airways.

Earlier work had shown that the inflammatory cells the body spews out in response to pollen harbor enzymes called NADPH oxidases. Now researchers report in the August 2005 *Journal of Clinical Investigation* that even before the immune system cranks up, NADPH oxidases in pollen itself generate a type of free radical known as reactive oxygen species (ROS), which interfere with cell signaling pathways and cause the immune system to overreact.

"We demonstrate for the first time to our knowledge that pollen extracts from weeds, trees, and grasses have intrinsic NADPH oxidase activity that induces ROS in airway epithelium within minutes," the team writes. ROS are formed when NADPH oxidases interact with cells lining the airways. The result is oxidative stress, which health experts suspect exacerbates asthma and allergies. Pollen's double whammy causes the often quick, intense allergic reaction seen in sensitized patients, explains lead author Istvan Boldogh, a molecular biologist at the University of Texas Medical Branch at Galveston.

The surprising new findings reveal that "pollen is more active than we thought," says J. David Lambeth, a molecular biologist at Emory University School of Medicine, who wrote a commentary on the study for the same journal. "We knew that pollen can make the body make free radicals, but this study shows that pollen takes an active role in making free radicals itself," he says.

Plant cells were known to contain NADPH oxidases similar to those found in white blood cells in humans and other mammals. Among other important functions, the oxidases protect the plant against pathogens. However, researchers had not tested pollen for NADPH oxidases, says Boldogh. He and his colleagues uncovered pollen's double-barreled effect on lungs by exposing sensitized mice to different forms of pollen, some with excess NADPH oxidases added, others that were NADPH-free. When they eliminated the NADPH oxidase activity, the mice had little or no inflammation in their airways and produced few of the cells that indicate an allergic response. When the researchers tested the effects of pollen extracts on cells taken from the lining of the lung, they found that adding NADPH oxidase increased the intracellular levels of free radicals.

Patients may someday use an inhaler containing antioxidants to counter ROS and minimize the effects of pollen, says Boldogh. The team's recent studies show that a combination of the antioxidants ascorbic acid and *N*-acetyl-L-cysteine prevents airway inflammation in pollen-exposed mice.

But antioxidants available now clear from the lungs too quickly to be effective in people, so companies are looking into developing longer-lasting products, Boldogh says. However, the group warns against developing treatments for patients based on its single study, noting that the results are circumstantial and need to be established in patients, work the team is now attempting. **–Tina Adler**

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Greener Education Materials for Chemists

Green chemistry aims in part to help clean up chemical processing by reducing or eliminating toxic elements from production and use. One university at the forefront of the movement is the University of Oregon, which has developed a website, Greener Education Materials for Chemists (GEMS), to educate teachers on introducing green chemistry concepts to their students. Although the site, located at http://greenchem.uoregon.edu/gems.html, currently contains only materials for university-level education, the developers hope to eventually include content for K–12 teachers.

The site consists of a database of print resources, which visitors can search using free text or by selecting search terms from seven categories, including chemistry concepts, laboratory techniques, green chemistry principles, and chemistry subdisciplines. Each item in the database has an overview that summarizes its content and its connection to green chemistry as well as contact information for the person that contributed the material to the database.

The different types of material that are currently available on the site, which is partially funded by the National Science Foundation, include laboratory exercises, lecture materials, course syllabi, and multimedia content. To aid educators in determining which materials best suit their needs, threaded discussions will soon be included for each item. Here educators will be able to discuss how they integrated materials into their lesson plans and relate their success in using them.

The site, unveiled in June 2005 at an American Chemical Society meeting, was developed by a partnership between the university's Green Chemistry Group and Center for Educational Technologies. Students and high school teachers were involved in the design of the site, as were more than 100 college instructors who attended national green chemistry education workshops at the university. The site's developers have provided information on the site advising people how to contribute material to the database. They are also looking for educators to evaluate materials, test laboratory procedures, and adapt content for varying age groups. The developers want the website to be as inclusive as possible so it can serve as many grade levels and subject areas as possible.

A link to information about the university's Green Chemistry Center is sited in the toolbar at the top of the homepage. Here visitors can find an overview of the program's work in developing undergraduate green chemistry curricula, the history of the program, and media coverage. A description of *Green Organic Chemistry: Tools, Strategies and Laboratory Experiments*, a textbook/laboratory manual released in 2004 for the undergraduate organic chemistry laboratory, is available from this page as well. **–Erin E. Dooley**

Heavy Metals in Ayurvedic Meds

Health Canada has issued a warning to consumers following a 15 December 2004 *JAMA* report that 1 in 5 Ayurvedic medicinal products made in South Asia and sold in the Boston area contained potentially harmful levels of lead, mercury, or arsenic. Ayurveda (Sanskrit for "science of life") often employs heavy metals because of their purported therapeutic properties.

Although none of the products tested are authorized for sale in Canada, the agency suspects some are sold there nonetheless. The agency tested one product, sold as a blood purifier for skin diseases and digestive problems, and found more than 40 times the allowable concentration of arsenic. Health Canada is reviewing the *JAMA* findings and assessing availability of the products in Canada, with results posted on the agency's website.

Ecolabeling for Fisheries

As concern over the fate of wild marine fish stocks grows, the UN Food and Agriculture Organization took action in March 2005 by adopting a set of voluntary guidelines for the ecolabeling of fish products. These guidelines advise governments and organizations that oversee or plan to implement labels for fish and fishery products from well-managed marine capture fisheries. Included are minimum requirements and criteria for determining whether a fishery should be certified to use the ecolabel, based on the agency's Code of Conduct for Responsible Fisheries. The guidelines, acknowledging the financial and technical challenges faced by developing nations in managing their fisheries, call for support in these areas to help these countries implement and benefit from the program.

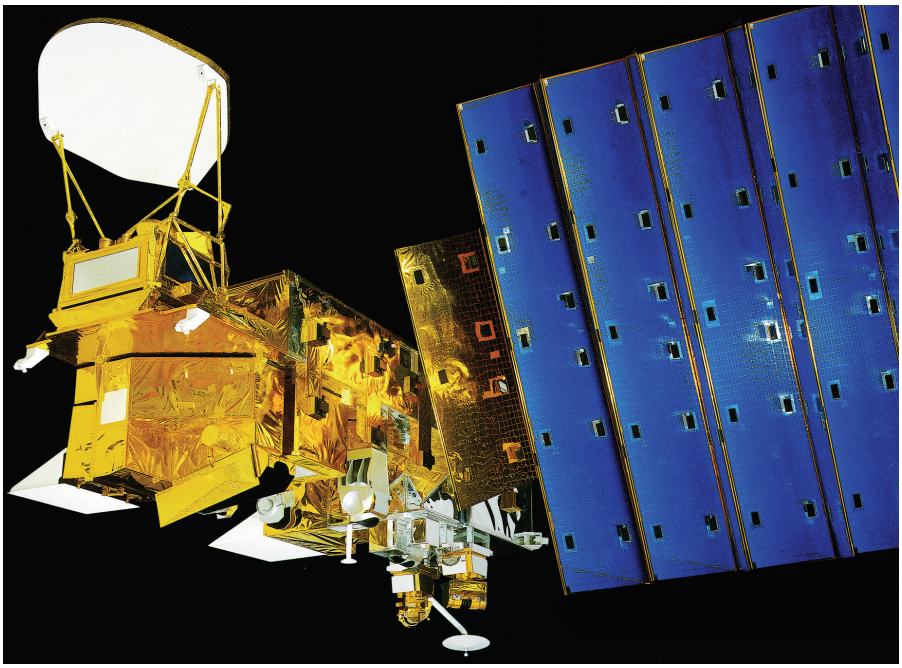
Wildfire Pollution Widespread

Research by the U.S. National Center for Atmospheric Research in the 14 June 2005 issue of *Geophysical Research Letters* shows that particularly intense wildfires in Alaska and Canada during the summer of 2004 emitted as much carbon monoxide as human activities in the continental United States during the same period. The fires also boosted ground-level ozone across the northern continental United States, even increasing levels of this pollutant by 10% as far away as Europe. The researchers used a novel combination of satellite-based observing instruments, computer models, and numerical techniques to help them distinguish between fire-generated carbon monoxide and that from other sources.

Top to bottom: Health Canada; GEMS; Digital Vision

Global Earth Observations for Health

Every day, Earth-observing satellites outfitted with remote-sensing technology generate vast data streams that scientists use to study the biosphere—the part of the Earth and its atmosphere that can support life. These orbiting systems are rapidly advancing studies of climate change, weather, and other global phenomena. Now experts are looking for ways to put them to work in the field of environmental health research.



Eyes in the sky. Earth-observing satellites such as Aqua (above) are being used to monitor problems including air pollution, weather, and climate change. A recent meeting at the NIEHS brought together scientists from a broad range of disciplines to discuss how satellite data might be brought to bear on addressing issues of human health.

Recently, the NIEHS and the U.S. Environmental Protection Agency (EPA) united health and Earth scientists in a workshop charged with two key objectives. The first was to determine if observations of air quality and climate from space could be used as public health tools for research, policy decisions, and environmental and health planning. The second was to engage the NIEHS extramural research community in dialogue with remote-sensing data producers and organizers including the National Oceanic and Atmospheric Administration, the National Aeronautics and Space Administration, and the EPA. Together these experts explored ways to use Earth observation data in studies of air pollution and health.

The NIEHS and Earth Observations

The workshop, titled "Global Earth Observations: Application to Air Quality and Health," was held at the NIEHS campus on 1–2 August 2005, and was attended by several dozen academic and government scientists. "Health researchers already use ground-based measurements of air pollution [to assess human exposures], and the workshop provided a mechanism for them to consider if addition of remote-sensed data would improve their exposure assessment and analysis of disease outcomes," says Sally Tinkle, a program administrator with the Cellular, Organs, and Systems Pathobiology Branch of the NIEHS Division of Extramural Research and Training. Tinkle, together with NIEHS program analysts Mary Gant and Mike Humble and EPA representatives Gary Foley, Valerie Garcia, and Andy Bond, organized the event and provided NIEHS scientific support.

The NIEHS plays a growing role in the use of this technology, in part through its membership in the U.S. Group on Earth Observations (USGEO), a standing committee that reports to the National Science and Technology Council's Committee on Environment and Natural Resources. The USGEO recently drafted a 10-year strategic plan for applying Earth observations to health and environmental research, which was released by the White House on 6 April 2005. Tinkle is the NIEHS's USGEO representative, and Gant leads the USGEO's User Interface Working Group.

At the August workshop, speakers covered issues ranging from the strength and adequacy of remote-sensing data to new directions in satellite research, coverage with land-based monitoring networks, and the challenges of using spatial data to address air quality and health outcomes. Participants also split into working groups to identify potential demonstration projects for remote sensing in three areas of health research: respiratory disease, cardiovascular disease, and developmental biology. Outcomes in all three areas have been linked to air pollution.

An Emphasis on Feasibility

Despite an initial focus on user needs in the area of remote-sensing data architecture—the way data are organized, stored, and made available to users—the workshop dialogue shifted frequently to feasibility issues. While the health scientists present found the technology intriguing, they raised questions about its potential for human exposure assessment.

Resolution limits were of particular concern. Remote sensing's spatial resolution, for instance, is rarely less than a square kilometer, although there is increasing evidence that air pollution levels vary at much finer scales of resolution (for instance, city blocks). Temporal resolution can also be problematic, especially for polar-orbiting satellites, whose positions remain fixed as the Earth rotates beneath them (this is less of a problem for geostationary satellites, which orbit in sync with a particular location and thus image that area all the time).

Discussions also addressed methods for averaging pollution concentrations measured from space. Remote sensors measure pollution in atmospheric columns that extend to the outer edge of the stratosphere. Humans, however, are exposed to pollutants close to the Earth's surface.

Finally, participants discussed limits on remote particulate measurements, which don't extend below the 10-micron level and cannot distinguish between chemical species on particle surfaces. "All these factors contribute to the uncertainty of linking remote-sensing data to human effects," says workshop participant Raymond Hoff, a professor of physics at The University of Maryland, Baltimore County.

NASA

According to Tinkle, feasibility discussions exposed the need for demonstration studies that layer remote-sensing data over existing ground-based pollution data sets. "This would permit us to determine if the addition of remote-sensing data improves the correlation of air pollution with adverse health events—such as asthma exacerbation and myocardial arrhythmias, for instance—in the area of respiratory and cardiovascular disease," she says.

Working Group Conclusions

Peggy Reynolds, an investigator with the Environmental Health Investigations Branch of the California Department of Health Services, moderated the working group on respiratory disease. During breakout sessions, participants identified key data needs in this area. They included improved measures for data quality assurance and control, validated correlations with health outcomes, and confirmation that remote-sensing data accurately represent exposures on the ground. Participants speculated that remote sensing could help fill gaps in existing exposure data and suggested a demonstration project that correlates asthma prevalence with remote-sensed measures of airborne particulates and bioallergens.

Diane Gold, an associate professor at the Harvard University School of Public Health, moderated the cardiovascular disease working group. Participants in this group identified "applications," or health outcomes, that might be served by remote-sensing data. Among them were myocardial infarction, arrhythmia, heart failure, hypertension, and stroke, in addition to a number of subclinical outcomes such as blood pressure changes and heart rate variability. Population-level application areas were also identified; they included hospital admissions and emergency room visits. Participants concluded that resolution limits might not pose problems for chronic applications, but that acute events like myocardial infarction and stroke would be better served by higher-resolution technology.

The developmental biology working group, moderated by Beate Ritz, an associate professor of epidemiology at the University of California, Los Angeles, identified several uses of remote-sensing data to assess developmental outcomes; they included critical windows of vulnerability that occur before, during, and following parturition; acute versus chronic pollutant exposure dynamics; and the interaction of maternal and fetal genetic susceptibilities. Participants also identified data needs such as adequate temporal and spatial resolution in pollution measures, and improved identification and quantification of chemical species in air pollution.

The workshop prompted Earth and health scientists to begin a dialogue to develop web-based pilot studies that integrate existing remote-sensing data with ground-based analyses as a preliminary step toward this broader validation. The workshop generated significant enthusiasm for collaboration between NIEHS extramural researchers and scientists at the participating agencies and for the possible use of remote-sensing air quality and climate data to improve public health. Ideally, space-based measures will produce new views of air pollution and the extent of human exposure, possibly leading to better opportunities to protect public health.

–Charles W. Schmidt

A virtual journey to real health. The Veggie-Mon website uses a cartoon character (inset) to introduce students to concepts of good diet, nutrition, and healthy lifestyle choices. In one activity, students take a virtual journey along Tobacco Road and read billboards with messages about smoking.

Veggie-mon.org

BEYOND THE BENCH

Online and On Track with Veggie-Mon

Too much computer time may not be good for kids, but sometimes surfing the Internet can be a wholesome activity, especially when it involves websites that help children learn how to make informed choices about their own health. One such site is the Veggie-Mon website at http://www.veggie-mon.org/. Created in 2000 by the Community Outreach and Education Program (COEP) of The Center for Research on Environmental Disease, a joint NIEHS center of The University of Texas M.D. Anderson Cancer Center and The University of Texas at Austin, the Veggie-Mon website has informed thousands of kids about the choices they can make to lead a healthy life.

The Veggie-Mon site introduces concepts of environmental risk factors and disease prevention to elementary- and middle-school students in a compelling and comprehensible way. "The goal of the site is to inform students, even young ones, that they can have an important and long-term impact on their own health by reducing their exposure to environmental risk factors and improving their diet," says COEP director Robin Fuchs-Young.

The homepage offers three portals, one for students in grades 4–6, one for students in grades 7–8, and one for teachers. Both student portals present information on three main topics: nutrition, sun and ultraviolet (UV) exposure, and tobacco use. According to Fuchs-Young, these are among the most important environmental risks faced by school-age children, and are also some of the risks that are most easily mitigated.

Each visitor is accompanied through the different sections by Veggie-Mon himself, a character reminiscent of a walking, talking artichoke who offers site navigation tips and provides extra details on the information presented. Each of the three sections has information that is both informative and fun. Along the way, Veggie-Mon encounters different acquaintances who help him explain the subject matter.

In the Nutrition section, students meet Strawberry Girl, an advocate of healthy eating habits. Here students can learn how to make healthy food choices through an illustrated food pyramid, and can also find recipes for delicious, wholesome snacks like a strawberry banana blast or a peanut butter and honey sandwich.

The Sun and UV section features Sunspot, a character who discusses some of the dangers of too much sunlight. In this section, students learn how fish research is helping scientists study the connection between sun exposure and skin cancer, and they can also take Sunspot's quiz to gauge how much they've learned.

In the Tobacco Road section, students meet Igna-Ray-Mouse, a misinformed rodent who has decided to smoke. Here they can take a virtual journey down Tobacco Road with Igna-Ray-Mouse and learn how advertising messages and peer pressure may be used to try to convince them to smoke. At each fork in the road, evidence is presented to prove that choosing to smoke is a bad idea.

Other tools on the site include a submission form to send questions to real scientists, a glossary, and a "laboratory" with instructions for simple experiments that students can conduct themselves. Each section also includes age-appropriate games and puzzles.

Teachers have their own features on the site. In a password-protected area, they can access lesson plans and provide feedback on how the website has helped them with classroom activities. Educators also contribute directly to the development of the website. During a 4- to 6-week educator fellowship held each summer at The Center for Research on Environmental Disease, teachers from grades K–12 help the COEP staff translate center research findings into age-appropriate content.

The COEP regularly revises the Veggie-Mon website to improve its usefulness for both students and teachers. Next up for the site is an exercise unit for the Nutrition section that will offer suggestions for fun and safe activities as well as information on healthy weight maintenance. **–Tanya Tillett**

Headliners | Uterine Leiomyoma

NIEHS-Supported Research

Corbis

Genetic Reprogramming and Benign Uterine Tumors

Cook JD, Davis BJ, Cai SL, Barrett JC, Conti CJ, Walker CL. 2005. Interaction between genetic susceptibility and early-life environmental exposure determines tumor-suppressor-gene penetrance. Proc Natl Acad Sci USA 102:8644–8649.

Uterine leiomyomas (fibroids) are common benign tumors in the muscle tissue of the uterus. Previous research has suggested a link between environmental exposures and uterine fibroids. NIEHS grantee Cheryl Lyn Walker and colleagues at The University of Texas M.D. Anderson Cancer Center were interested in how such exposures contribute to uterine fibroids. They propose that early-life exposure to xenoestrogens may alter genetic programming during development, setting the stage for an adverse response to later natural estrogen stimulation.

Uterine fibroids occur in up to 77% of women, can cause severe menstrual bleeding and pelvic discomfort, and result in more than 200,000 hysterectomies each year in the United States alone; although "benign," they are far from harmless. Lesions causing symptoms range in size from 1 to 20 centimeters. Data indicate that 25% of white women have problematic lesions. Black women have about a threefold higher risk of developing fibroids and, in general, their clinical symptoms are worse.

Diethylstilbestrol (DES), a xenoestrogen, is one environmental exposure that has been posited as contributing to uterine fibroids. To determine the actions of this chemical, Walker and colleagues studied rats with a genetic predisposition to developing uterine fibroids, exposing some of them to DES during their first week of life. By age 16 months, the DES-exposed animals had almost a 95% incidence of tumor formation, while the unexposed animals had a 64% incidence. There were more tumors in each affected DES-exposed animal, and the tumors were larger in size and more invasive, compared to controls.

The researchers determined that DES did not cause a mutation in estrogen-responsive genes, but rather caused them to become "reprogrammed" so that they responded differently to natural estrogen stimulation later in life. These findings indicate that reprogramming of genes during the developmental period as a consequence of xenoestrogenic exposure can interact with a preexisting genetic condition to increase the formation and severity of uterine fibroids. If additional research confirms these results, this study's findings could have implications for other hormonally mediated cancers such as those of the breast and prostate. **–Jerry Phelps**

Brand X/Alamy

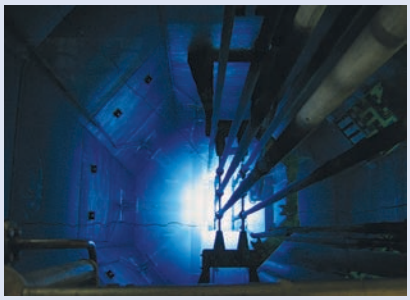
POWER SURGE

Renewed Interest in Nuclear Energy

Just past its 50th birthday, commercial nuclear energy is experiencing a tentative rejuvenation that could result in a greater role as a global source of electricity. Skeptics still harbor many of the objections that have slowed or stopped the construction of new nuclear power plants, but rising concerns about the cost and security of energy supplies and global climate change have reframed the debate in terms more favorable for nuclear power advocates.

As a result, the question of whether governments should encourage the construction of new nuclear power plants is no longer off the table in developed countries such as Australia, the United Kingdom, and the United States. For other developed countries such as France and Japan, and for countries with fast-growing economies such as China and India, nuclear energy has remained a central component of energy policy. For example, to achieve its goal of generating 4% of electricity from nuclear power, China plans to add more than 30 new nuclear plants by 2020 to the 11 currently in operation or under construction. India's goal is to supply 25% of its electricity from nuclear power by 2050.

Worldwide there are now 440 nuclear power reactors operating in 31 countries and producing a combined capacity of 367 gigawatts electric, or about 16% of the world's supply of electricity. The Vienna-based International Atomic Energy Agency (IAEA)—the agency of the United Nations chartered to promote cooperation on nuclear issues—estimates that at least 60 new nuclear plants will be constructed in the next 15 years. Given the world's growing demand for electricity, however, this added capacity will still account for only 17% of global electricity use.



The core of the matter. The view looking down into a research reactor core in Chile shows the fuel elements and control rods hanging in a water pool.

Kirstie Hansen/IAEA

Environmental Conundrum

One central issue facing policy makers and electric utilities is the question of how to meet the rapidly growing worldwide demand for electricity while not increasing global greenhouse gas emissions. The U.S. Department of Energy's Energy Information Administration tracks world energy trends and projects a 75% increase in global electricity use between 2000 and 2020. By 2050 a tripling of use is probable. Electricity production currently is responsible for an estimated one-third of all greenhouse gas emissions.

In terms of human welfare, this growth in electricity usage is desirable as reflected in the strong correlation between electricity consumption per capita and the United Nations' human development index, which combines indicators of health, education, and economic

Full steam ahead. Construction is well under way on China's first experimental fast breeder reactor, located in Tuoli.

prosperity. Overall energy consumption per capita in the developing world is less than one-fifth that in the developed world, and as developing countries industrialize, they will tend to seek the least expensive supply to meet their electricity needs. In most cases this means coal-fired plants, which produce significantly more greenhouse gases—primarily carbon dioxide—than other carbon-based sources such as natural gas–fired generators. Nuclear and noncarbon-based renewable sources such as wind and solar power do not directly create greenhouse gases.

Global climate change and the 2005 entry into force of the Kyoto Protocol to the United Nations Framework Convention on Climate Change have spurred new thinking about the potential value of nuclear energy by both environmental groups and the nuclear energy industry. Recently, several prominent environmentalists have publicly supported nuclear energy, including former Anglican bishop Hugh Montefiore, a longtime trustee of Friends of the Earth, and Patrick Moore, cofounder of Greenpeace.

Their support has alienated them from many in their former organizations, but indicates a more nuanced challenge to nuclear energy by some environmental activists, who are perhaps more willing to consider the nuclear option but still do not think it's the wisest choice. Organizations such as the Natural Resources Defense Council and the Union of Concerned Scientists now talk in terms of the proper role of government in energy policy and ensuring the safe operation of nuclear plants, rather than whether nuclear power should even be considered.

Minds Differ

The potential for building new nuclear power plants is quite different in different countries. For example, the role of nuclear power is unlikely to change substantially in countries with a flat demand for electricity, such as Japan, which now relies on nuclear power for 30% of its electric capacity and expects to see a population decline, or France, with a stable population and a power industry that is 80% nuclear. On the other hand, the United States, which currently operates 103 nuclear power plants and relies on nuclear energy for 20% of its electricity, expects to see a rising population and consequent greater demand. Developing countries offer the potential for considerably more use of nuclear power, especially as much of their populations will be urban, providing a concentrated market for large electric-generating plants.

So in answer to the question of whether nuclear power makes economic sense, it simply depends—"in some countries it does, in others it does not," says Alan McDonald, a staff expert in planning and economic studies at the IAEA. "In countries like China and India, you need [every source of power] you can get. Asia has major pollution problems and energy needs. Sometimes it seems to be a matter of national preferences. In countries like Austria and Denmark, nuclear power is anathema; in others like Germany, opinions may be changing. In the United States, Wall Street is very skeptical and will watch developments closely."

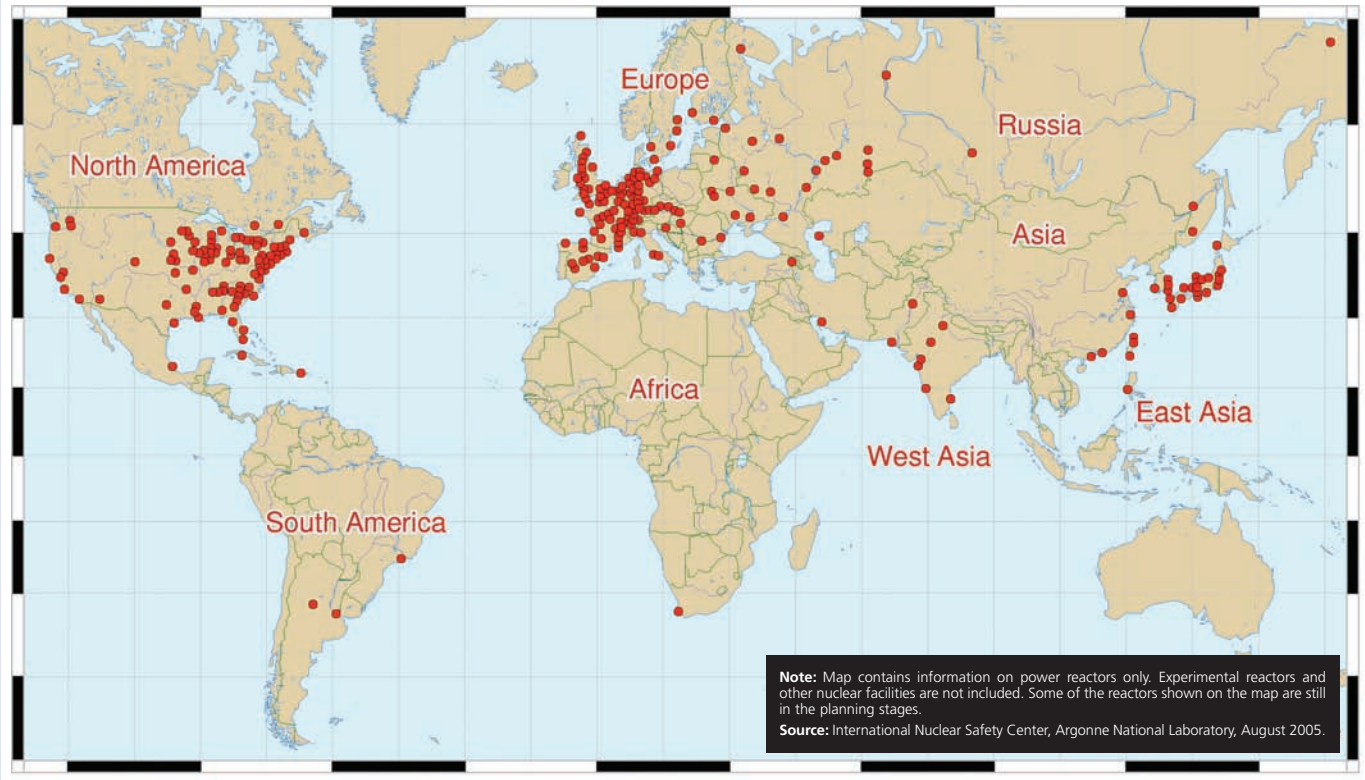
Relative costs of nuclear energy vary depending on what options and factors are being considered, but in general, McDonald says, the up-front costs of nuclear energy are very high while the cost of operation is relatively low. Thus, countries with government-owned electric utilities have an advantage in new power plant construction because they can fund investments more easily than investor-owned utilities, which are subject to the capital markets and the demand for rapid returns on investments.

"Until the Kyoto Protocol, the environmental value of nuclear energy could not be translated into financial terms," says McDonald. "But now, obtaining greenhouse gas emission permits for a new coal-fired plant in Europe can cost more than the coal itself. Although the United States is not bound by Kyoto, U.S. investors may see the writing on the wall. If the treaty is changed and nuclear power

Terror target? Some critics' reservations about nuclear energy revolve around the fear that reactors and their contents may pose an attractive target for terrorists.

Top to bottom: Petr Pavlicek/IAEA; imagebroker/Alamy

Locations of Nuclear Power Plants Worldwide



becomes part of the international market mechanism that allows credit for clean energy sources and the trading of carbon emission credits, that would be a big incentive."

But more nuclear power doesn't come without potential security threats of another sort. "If the world sees a big increase in nuclear energy, there will be an increased risk of [nuclear arms] proliferation—all things being equal," McDonald notes. Indeed, the director general of the IAEA, Mohamed ElBaradei, says that recent revelations about undeclared uranium enrichment activities and reprocessing of spent fuel, along with the discovery of an international illicit market in nuclear technologies, underlines the need for improved controls. On 7 October 2005 ElBaradei and the IAEA were awarded the 2005 Nobel Peace Prize for their efforts to stop the spread of nuclear weapons and prevent North Korea and Iran from acquiring nuclear arms.

In response to the threat of proliferation, the IAEA has developed a model Additional Protocol that signatories can add to their IAEA Safeguards Agreements, which address questions of traceability and verification of nuclear materials. The Additional Protocol strengthens safeguards, protects nuclear materials and facilities, and bolsters the systems of nuclear export controls. So far more than 100 countries have added the protocol to their agreements. The IAEA further proposes that future reactor technologies be designed to be more resistant to proliferation, and that the international enrichment and reprocessing of nuclear fuel be centralized in a few countries under a structure that guarantees supply to member nations.

An Industry with a Storied Past

The question of whether nuclear energy should play a significant role in future electric power generation cannot be separated from its history, the role played by governments, or the nuclear fuel cycle itself. The cycle has always been a focus of concern, from the potential hazards of uranium mining operations, through the processing of uranium into fuel, to the controlled fission process in the reactor core, and finally to the disposal or reprocessing of the fuel and related waste products.

The civilian nuclear power industry was created through U.S. government–electric utility industry cooperation that officially began with the Atomic Energy Act of 1954. Until that point, all U.S. atomic energy resources had been devoted to military activities. President Dwight Eisenhower's "Atoms for Peace" speech to the United Nations in December 1953 led to the U.S. government's financial and technical support of commercial nuclear energy. The government also enacted the Price-Anderson Act of 1957, requiring nuclear power operators to carry the maximum insurance offered by private insurance companies but also limiting their liability—a stipulation demanded by the utility companies before they would invest in building nuclear power plants.

The U.S. Navy first developed the now widely used pressurized-water reactor for propulsion in submarines. This design became the basis for the first commercial nuclear plant at Shippingport, Pennsylvania, which began operation in 1957. In the Soviet Union, reactors designed for producing plutonium for weapons were modified and new ones developed to generate heat and electricity. The first such reactor began producing electricity for the city of Obninsk in 1954.

The fostering of nuclear energy was woven into many U.S. foreign policy initiatives during the early days of the Cold War. The United States sponsored the creation of the IAEA as the global manager of nuclear technology and materials, it supported international research reactors and isotopes for nuclear medicine and agriculture, and it helped create a nuclear energy industry in Europe, where coal production was declining and other sources of electric power were limited.

The U.S. commercial nuclear power industry flourished from the mid-1960s through the early 1970s, although the power

plants operating then were not economical compared to other sources at the time. Nuclear energy advocates argued that, with moderate and selective government assistance, the technology could cross the economic threshold into widespread acceptance by the utility industry. The U.S. Atomic Energy Commission—which then combined the functions of today's Nuclear Regulatory Commission (NRC) and Department of Energy—estimated that the United States would exhaust its oil and coal supplies within 100 years and that nuclear energy was the best replacement for fossil fuels in electricity production. The commission optimistically estimated that by 2000 as much as two-thirds of the nation's electric power could come from nuclear energy.

The peak year for achieving this scenario in the United States was 1973, when 50 orders were placed for new nuclear plants, although in the following years leading up to 1979, cancellations began to exceed new orders. Then, in March 1979, a series of operator errors and miscommunications led to the partial core meltdown in the pressurized-water reactor at Three Mile Island Unit 2. The accident did not result in major damage outside of the core and primary cooling system, and according to all official estimates, the radiation released during the accident was minimal, well below levels that have been associated with health effects from radiation exposure. However, a panicked evacuation of nearby residents took place, followed by extensive investigations and a government-subsidized 10-year cleanup effort. The notoriety of the accident, combined with the high cost of construction, slow regulatory processes, and political opposition, essentially halted the growth of the U.S. nuclear industry. Although numerous nuclear power plants that had been under construction at the time eventually came online, no new U.S. plants were ordered.

Nuclear fallout. A researcher buys food samples from a local farmer for radionuclide analysis during the International Chernobyl Assessment Project. A recent IAEA report states, though, that the greatest long-term health impact from the accident is psychological trauma.

Building on the past. Construction of new nuclear plants continues worldwide. Although stalled in the United States, renewed interest and the need for energy may bring this power source back online.

The devastating accident at Chernobyl Unit 4 in April 1986 could have been the death knell of the industry worldwide. The steam explosion, fire, and nuclear fuel melting at the site were the result of a flawed reactor design operated by inadequately trained personnel who violated safety procedures. The reactor design widely used for nuclear power in the Soviet Union did not include the containment system used with most Western reactors, and so substantial quantities of radioactive material, dust, and gases escaped into the atmosphere.

The Chernobyl site is now entombed in a concrete structure known as the Sarcophagus, but it is not stable for the long term and is not air- or watertight (a major new Sarcophagus is planned, but funding is slow to materialize). The accident was a deeply traumatic experience for the 350,000 people who relocated from the area. A 30-square-kilometer area around the site remains closed because of high levels of contamination. About 50 people were killed in the initial accident and emergency response. A September 2005 IAEA report, *Chernobyl's Legacy: Health, Environmental, and Socio-Economic Impacts and Recommendations to the Governments of Belarus, the Russian Federation, and Ukraine*, estimates that around 4,000 people have died or will die as the result of exposure related to the accident. The report observes that "mental health is the largest public health problem created by the accident," referring to affected residents' subsequent poverty, substance abuse problems, and "paralyzing fatalism," manifested as negative self-assessments of health, belief in a shortened life expectancy, lack of initiative, and dependency on assistance from the state.

Even with the resulting public outcry against nuclear power, the world did not halt new construction of nuclear power plants. However, some European countries such as Belgium, Germany, and Sweden began to reconsider their plans for nuclear energy, and eventually developed policies to phase out existing plants. Now some of these countries are under the gun to find replacement energy sources. Sweden, for example, aims to be nuclear-free by 2010, having taken a second reactor offline in June 2005 (the first was closed in 1999).

Top to bottom: Elisabeth Zeiler/IAEA; imagebroker/Alamy

But the remaining 10 plants still supply about half of Sweden's domestic energy production, according to the World Nuclear Association.

New/Old Thinking

An influential 2003 report out of the Massachusetts Institute of Technology (MIT), *The Future of Nuclear Power: An Interdisciplinary MIT Study*, spelled out the major areas of concern surrounding nuclear energy and proposed a plan that the authors hoped would allow the United States to resume development of nuclear power in order to reduce greenhouse gas emissions. The study identified the four critical problems that must be overcome for nuclear power to succeed—cost, safety, waste, and proliferation. It also offered policy recommendations for making the nuclear energy option commercially viable, including steps to lower cost and a limited production tax credit to "first movers," private sector investors who build and then operate new nuclear plants.

"Our recommendations are basically holding up," says study cochair Ernest Moniz, who is codirector of MIT's Laboratory for Energy and the Environment and former undersecretary for energy during the Clinton administration. "On the positive side, new regulatory approaches are being developed, the industry's intent is to build a new reactor, there are more open discussions with environmental groups, and the Energy Policy Act became law," he says. "On the negative side, the situation with spent fuel management is worse—Yucca Mountain casts a shadow over any decision. And the nonproliferation situation in Iran is a real problem."

The fate of Nevada's Yucca Mountain nuclear burial site is unclear. In the face of sustained resistance from the state and citizens groups, the federal government has slowed in its effort to build a long-term geological repository for commercial spent fuel and high-level radioactive waste. Opposition to the Yucca Mountain project is based on a long history of Nevada being a nuclear weapons testing grounds, resentment at becoming a repository for toxic waste generated elsewhere in the country, and concerns that the site is not geologically stable enough to guarantee that the radioactivity will remain confined over the required 10,000-year span. But several more such sites will be needed in future decades if a significant number of new nuclear power plants are built.

Moniz says the MIT study endorses a robust research and development program and tax credits for the nuclear industry. This is because, in the past, there has been considerable regulatory uncertainty, causing prohibitively high financial risk for utility investors. In addition, the true cost of burning carbon-based fuels has not been internalized, meaning that if the health and environmental costs of pollution and greenhouse gases could be factored in, nuclear energy would be very competitive. As a result, public subsidy of noncarbon-based energy sources is justified.

The comprehensive Energy Policy Act of 2005 that Moniz cites provides loan guarantees to develop energy technologies, including nuclear power, that avoid, reduce, or sequester greenhouse gases. It also provides a tax credit of 1.8¢ per kilowatt hour for 6,000 megawatts of capacity at new nuclear power plants (equivalent to the output of about six new plants). Important to the industry, the act provides investment protection against delays in licensing and startup that are beyond the control of industry, including litigation.

The act also provides several billion dollars for nuclear energy research and development, which translates into work on a more cost-efficient and inherently safer generation of reactors known as Generation IV. These reactors achieve greater safety through passive technologies that automatically shut down the reactor in an emergency, bypassing the risk of operator error (humans still control the normal operation and shutdown of these reactors). They are also more efficient and relatively more cost-effective than their

Iran moves ahead. (above) Construction of the Bushehr nuclear power plant, being built under an agreement with Russia, is under way in Iran. (right) Journalists examine a scale model of the Bushehr plant during a visit to the construction site.

Kaveh Kazemi/Panos Pictures

A yucky situation. Yucca Mountain, in the Mojave Desert of Nevada, is the site Congress designated as a geologic repository for the nation's spent nuclear fuel and high-level radioactive waste. However, the project has been fraught with technical problems and public opposition.

Generation III predecessors. In another bow to the environment, the act funds construction of a cogeneration reactor that will produce both electricity and hydrogen, which advocates hope will be a new, carbon-free fuel for automobiles—the single largest source of greenhouse gas emissions.

Finally, the act funds a central nuclear energy program of the Bush administration: Nuclear Power 2010. The program was unveiled in 2002 as a government–industry cost-sharing plan to identify three sites for new nuclear power plants, develop Generation III reactors, and develop a single-license process with the NRC for approval of both plant construction and operation, thereby removing much of the delay and uncertainty for investors.

In response, three consortia of electric utility companies, reactor suppliers, and construction firms have made proposals. None are yet committed to building a new nuclear plant. The consortia are led by Dominion Resources, Exelon and Entergy (via the NuStart Energy Development consortium), and the Tennessee Valley Authority. These consortia represent operators of 67 of the nation's nuclear plants, and their proposals have all focused on building a new plant on sites where plants already operate—in much the same way that a consortium of 10 electric utilities built the Yankee Rowe plant, one of the first commercial nuclear plants, in the 1950s.

The consortia embrace a number of different reactor vendors and designs, some of which have already been certified by the NRC. The final decision on building a nuclear power plant will depend on factors as they stand later this decade, including the power market, the status of permanent spent fuel storage, and the ability of the participants to obtain financing without adversely affecting their credit ratings.

Concerned Parties

"The industry's interest is very real," says Russ Bell, a senior project manager for new plant development at the Nuclear Energy Institute, a utility trade association. "The utilities are [participating in consortia and spending money on preliminary designs and siting plans] because the economics are turning in favor of nuclear, especially over the long term. [The Kyoto Protocol] is not driving us, but it makes sense and there is increasing concern about pollution in the United States and more stringent environmental regulations."

Bell says the industry is getting what it needs from the Energy Policy Act and is looking to government to do no more than jumpstart new builds after so much time has passed. He acknowledges the long time horizon for building new plants in the United States. Assuming that any of the consortia meet the 2010 goal of being

Vive la nuclear! France has embraced nuclear energy and now obtains 80% of its electricity from nuclear power.

Top to bottom: U.S. DOE; images-of-france/Alamy

licensed to build and operate a plant, another four to five years will pass before construction is complete and electricity flows. Meanwhile, the electric utility industry will continue to improve operating performance of existing nuclear power plants and apply for license extensions.

Originally licensed for 40 years, the first operating license issued by the NRC will expire in 2006, approximately 10% will expire by the end of 2010, and more than 40% will expire by 2015. The decision to seek license renewal is strictly voluntary, and nuclear power plant owners must decide whether they are likely to satisfy NRC requirements and whether license renewal is more cost-effective than shutting down and pursuing other sources of energy. The NRC has now granted 35 plants the right to operate for another 20 years. Three-quarters of the nation's plants have received, have applied for, or are expected to apply for an extension.

The question of plant life extension can bring the relationship between nuclear energy and greenhouse gases into sharp focus. For example, the governors of nine Northeast states have proposed an agreement to cap greenhouse gas emissions from all power plants in their states. Two nuclear power plants in the region, one in Vermont and one in New Jersey, are up for life extension, yet if these plants are shut down, the result would be increased reliance on carbon-based fuels. This could potentially triple greenhouse gas emissions in Vermont and double them in New Jersey, according to the 14 September 2005 edition of *The New York Times*.

"We are not fundamentally opposed to nuclear power," says David Lochbaum, a nuclear safety engineer at the Union of Concerned Scientists, "but there are better choices. In addition, we now have spent nuclear fuel in storage places where it is not meant to be. It's not a health threat yet, but it could be."

Lochbaum is also concerned about the oversight role played by the NRC. "The NRC budget has been cut for a decade," he notes. "It is understaffed to support a nuclear resurgence. And the industry still has operational troubles at some plants."

These concerns are echoed by Thomas Cochran, director of the nuclear program at the Natural Resources Defense Council and an advisory committee member on the MIT study. "The Energy Policy Act was the result of successful lobbying by the nuclear industry," he says. "They will probably build a few plants and then the issue is, are you back to where you are today?" Cochran does not believe that the subsidy or the economics will work for nuclear power. "It's not helpful to just say you are for or against nuclear," he says. "Ultimately you must make a decision on real policy to address global warming, and a carbon tax is the best way."

The objective of a carbon tax would be to internalize the environmental costs and hope for an open competitive market for energy. "To balance the energy market, you either tax a pollutant or regulate it," says Cochran. "If public policy was made correctly, it would help the nuclear industry."

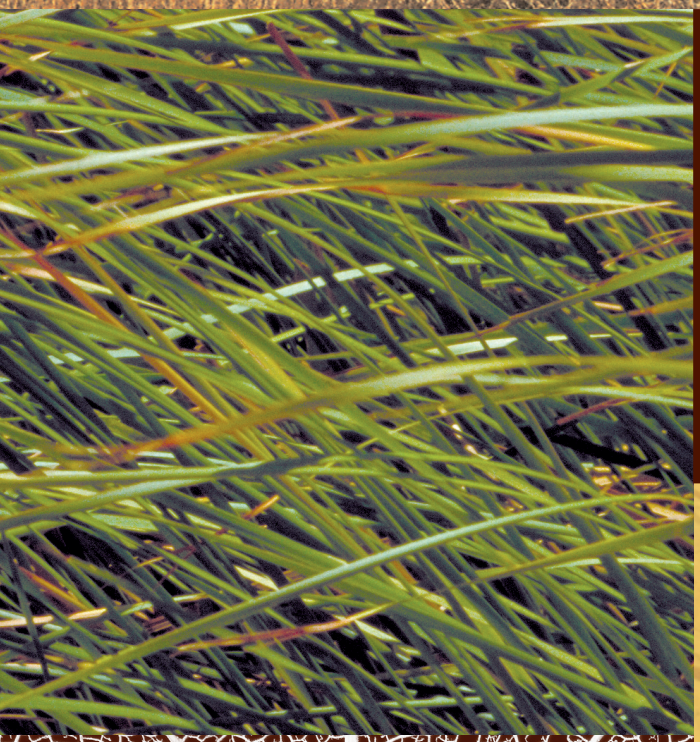
Is there a real, economically justified "nuclear resurgence," or simply a steady growth in some regions to meet rising demand for electricity? Nothing happens quickly in the world of power plant construction. Yet major investments by government and industry can change the bases of electricity supplies in the time frame of a decade or two. France closed its last coal mine in 2004, and its transition from 15% to 80% nuclear-based electricity was accomplished in 20 years. A sense of optimism and urgency now surrounds the question of whether to pursue nuclear power. How this translates into results should unfold at a brisk, measurable pace.

W. Conard Holton

Nuclear microcosm. Many nations have an ambivalent relationship with nuclear energy. (above) A family walks along the beach in Kenting, China, with National Nuclear Power Station No. 3 behind them. Until recently, the waste from this power station was shipped to a controversial storage facility on nearby Orchid (Lanyu) Island. (below) Masked student protestors voice their opposition at an antinuclear rally.

Chris Stowers/Panos Pictures

Harvesting the Potential of BIO



Clockwise from top: Corbis; Taglia and Incolla; Linda Bair/iStockphoto; Taglia and Incolla

As fossil fuel prices and consumption both continue rising, the search is on for alternative fuels. Fuel for vehicles is taking center stage, now that 67% of U.S. petroleum consumption goes toward fueling vehicles, according to the U.S. Department of Energy (DOE). Could biomass energy derived from plant matter supply a significant percentage of future transportation fuel?

MASS

The answer is yes, according to *Biomass as Feedstock for a Bioenergy and Bioproducts Industry: the Technical Feasibility of a Billion-Ton Annual Supply*, a report funded by the DOE and the U.S. Department of Agriculture (USDA) and issued by Oak Ridge National Laboratory in April 2005.

Biomass Today

The report defines biomass as all plant-derived molecules, including grain, starch, sugar, oil, and waste products, as well as the plant structural components cellulose, hemicellulose, and lignin. Fossil fuels and animal matter are excluded. While the diversity of resources is a strength of biomass, it also raises a problem: different facilities are needed to convert the array of molecules from biomass into the hydrocarbons needed for transportation fuel. Furthermore, large changes in infrastructure

would be needed to harvest the various potential sources.

The report gives an overview of the biomass situation today in the United States. About 190 million dry tons of biomass feedstock are consumed annually. Biomass accounts for about 3% of total U.S. energy supplies, and has recently surpassed hydropower as the largest renewable energy source. A great deal of biomass is waste material that is both produced and consumed by industry. For example, forest-products firms (including paper companies) use 96 million dry tons of biomass, largely to power their factories. Currently, 3.4 billion gallons of ethanol are blended into gasoline each year; that amount could soar to 80 billion gallons by 2030.

The report states that by 2030, American acreage could produce enough biomass to displace at least 30% of the country's current consumption of petroleum fuels with some changes in land use and agricultural and forestry practices, and up to 50% with advanced conversion technologies. This calculates to up to 1.366 billion tons of biomass produced annually.

Lynn Wright, who formerly worked in Oak Ridge National Laboratory's biomass program and now consults to it, says the report was a response to a common question from the energy industry. "We were hearing from people with connections to oil companies that they hardly considered it worth their while to think about biomass unless we could show that it could supply as much as a billion dry tons per year," she says.

The *Billion-Ton* report does not attempt to assess the economic viability of large-scale biomass energy, and Wright explains that it's difficult at best to predict the relative price of fossil fuels and the various sources of biomass in 25 years. Today, she says, when prices are measured by energy content (British thermal units), energy from switchgrass or corn stover, the residue that remains in the field after a grain crop is harvested, is cheaper than energy from oil but more expensive than energy from coal.

Boosting Production

According to the report, wood could grow to supply 368 million dry tons of biomass by 2030. The supply could expand with enhanced collection of urban tree trimmings and construction waste, and greater efforts to prevent forest fires by clearing deadwood from forests.

But transportation and processing costs may keep wood expensive, cautions report coauthor Bryce Stokes, program leader of vegetation management and protection research at the USDA Forest Service. He says, "We still have to overcome some economic and conversion efficiency barriers . . . to make wood competitive" in transportation fuels. Woody biomass will seem more competitive, he adds, if the benefits of improving forest heath, reducing fire risk, and recycling carbon from the atmosphere are held in view.

Farms could potentially contribute a far larger quantity of biomass (998 million dry tons), and much of that may come from corn stover and perennial crops managed with no-till production techniques and collected with advanced harvesting equipment. However, Wally Wilhelm, a plant physiologist with the USDA Agricultural Research Service, says it is unlikely that all land will ever be switched to no tillage. "Use of no-tillage methods and producing crops without tillage is far more complex than simply not passing over the field with a plow or disk," he explains. "It takes time and skill, and trial and error, to become proficient at no-till farming. Not all farmers are willing, nor have the flexibility—the money in the bank—to pursue the knowledge and skill."

Corn grain is currently the source of most of the ethanol used as motor fuel in the United States today. Corn production has been growing by 1.7 bushels per acre per year for 30 to 40 years, says Achim Dobermann, a professor of soil science and nutrient management at the University of Nebraska. Dobermann says irrigated cornfields in Nebraska could produce 250 to 350 bushels per acre.

These yields require intensive inputs, especially in the form of nitrogen fertilizer, which is usually derived from natural gas. Farmers already manage nitrogen closely, due to its price and potential for polluting groundwater, but ever-higher yields will force them to work even harder to carefully manage nitrogen. "It requires a more fine-tuned type of management," says Dobermann. "You can't just go in and apply anhydrous ammonia [a common nitrogen fertilizer] in the fall and take off for vacation." Instead, he suggests multiple nitrogen applications, timed and placed when and where the crop needs it.

More Mass, Sustainably

If biomass harvesting is to be sustainable, it must not diminish soil's fertility (its ability to supply nutrients for plant growth) or other properties influencing productivity. A market for stover creates an incentive for farmers to remove more after the harvest. But crop residue left in the fields reduces soil erosion; it also improves soil fertility and structure through the addition of organic carbon, which fuels microbial activity that drives the cycling of nutrients and structures in productive lands.

Estimates of how much stover must remain on the fields if erosion is to be controlled rely on the concept of a tolerable amount of soil loss, as defined for particular soils by the USDA Natural Resource Conservation Service. But this amounts to "an educated guess," says Wilhelm. "The assumption is that if we keep losses below the tolerable level, we should not notice a significant impact on productivity." Erosion is affected by farming practices, soil types, and weather, and Wilhelm says it's "a very good question" whether it's possible to predict what level of stover removal will hold soil organic carbon loss below tolerable levels.

Because crop residue is converted into organic matter that maintains soil structure, Wilhelm says levels of organic matter may be a good metric of soil health and the amount of stover that must be retained on or in the soil to sustain productivity. Wilhelm, who is leading a project to develop guidelines for sustainable removal of corn stover, says extensive biomass extraction raises the danger that soil organic carbon will be "mined" rather than be treated as the irreplaceable resource that it is. He adds that stakeholders must work together to develop systems that enhance the use of renewable sources of energy and produce renewable energy in a sustainable manner.

A Question of Impact

One of the key arguments over biomass energy concerns the net energy contribution of biomass—how much energy is gained from the crop. For example, David Pimentel, a professor of ecology and agriculture at Cornell University, and Tad Patzek, a professor of civil and environmental engineering at the University of California, Berkeley, published calculations in the March 2005 issue of *Natural Resources Research* showing that ethanol derived from corn contains only 71% of the energy used to grow, harvest, and convert the grain into ethanol. At the other end of the spectrum, calculations by federal researchers Hosein Shapouri, James A. Duffield, and Michael Wang in the July 2002 *Agricultural Economic Report Number 814* showed a net energy gain of up to 130–140%.

Pimentel and Patzek based their calculations on average U.S. corn production

output for 2003—140 bushels per acre. As to the assertions put forth in the *Billion-Ton* report, Pimentel contends that providing enough biomass to cover 30% of current U.S. gasoline and diesel use would require a land area greater than that of the United States. He believes the actual U.S. biomass capacity is about half the 1.366 billion tons cited in the report.

But calculating net energy efficiency is difficult, says Robert Anex, an associate professor of agricultural and biosystems engineering at Iowa State University who studies life-cycle assessments of biomass resources. "One must account for all of the resources that are used, all of the product created, and also those resources that are saved via substitution of the biomass product for some other probably petroleum-based product," he says. "This involves many assumptions about how crops are grown, harvested, and converted, but also what resource use is avoided." This, he says, is why these sorts of measures are often contentious.

Biomass advocates such as Thomas Foust, biomass program technology manager at the DOE National Renewable Energy Laboratory, say more biomass should become available if agricultural productivity continues its steady rise and improvements in conversion technologies are made—for example, ethanol production per bushel of corn has grown by about 25% in the past 25 years. Furthermore, Foust says that net energy balances for ethanol are not that useful, and the real metric should be imported oil displacement, which can be as high as 6 to 1 for ethanol.

The environmental health impact of gathering 1 billion tons of biomass through whatever means—a plan that could affect hundreds of millions of acres—must also be investigated thoroughly. For example, the impact of harvesting biomass from millions of acres of farmland now set aside under the USDA Conservation Reserve Program remains to be studied. One higher-production scenario in the *Billion-Ton* report assumes that 60 million acres would be shifted from a combination of Conservation Reserve Program land, pasture land, and commodity crop production in order to produce woody and grass crops as a source of biomass. The land used to produce wood and grass crops would provide bird and mammal habitat similar to the Conservation Reserve Program but would be harvested more frequently.

Donald Waller, a professor of botany and environmental studies at the University of Wisconsin–Madison, raises other questions about the impact of boosted biomass energy production on forest health. While noting that the report does not call for building roads in roadless forests or removing biomass from wilderness areas, he warns of broad ecological consequences from removing massive amounts of tree biomass and thus essential nutrients. "In most forests, the old growth is dominated by decomposers in terms of species number and complexity," he says. "Deadwood is there in far greater quantity than live wood."

Waller emphasizes the importance of leaving behind "biological legacies"—standing dead trees, live trees, and tree material on the ground. "You can't take it all away without seriously diminishing the ecosystem functions and the plant and animals that live there," he says.

Achieving Critical Mass

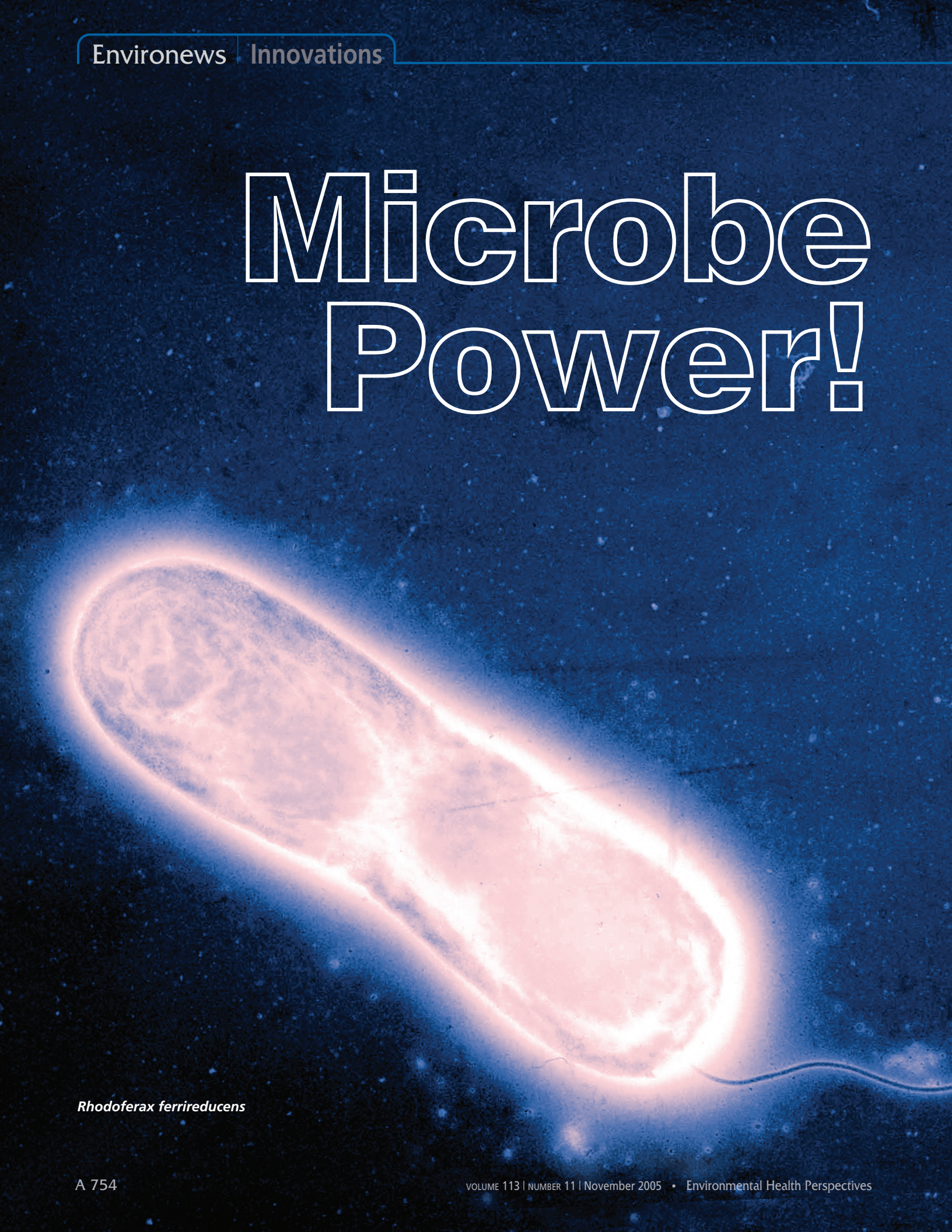
In the face of tight fossil fuel supplies, the federal government is moving ahead with plans to expand biomass output. The National Renewable Energy Laboratory, for example, has a considerable effort working to improve biomass conversion into liquid fuel. Wright suggests putting more effort into pilot projects that use large amounts of biomass. "I think it would help a great deal to get some demonstrations in place on the part of farmers and power producers," she says.

Government subsidies similar to the tax credits already offered to build wind power towers and install solar energy panels may be another way to enhance the appeal of biomass. In the 17 October 2005 issue of *Newsweek*, Frances Beinecke, executive director and incoming president of the Natural Resources Defense Council, says, "We think subsidies or assistance from the federal government should go to the new technologies that need to come to the market. . . . Biofuels are definitely part of the renewables portfolio. There's growing interest in the agricultural sector, because that way we could have homegrown fuels."

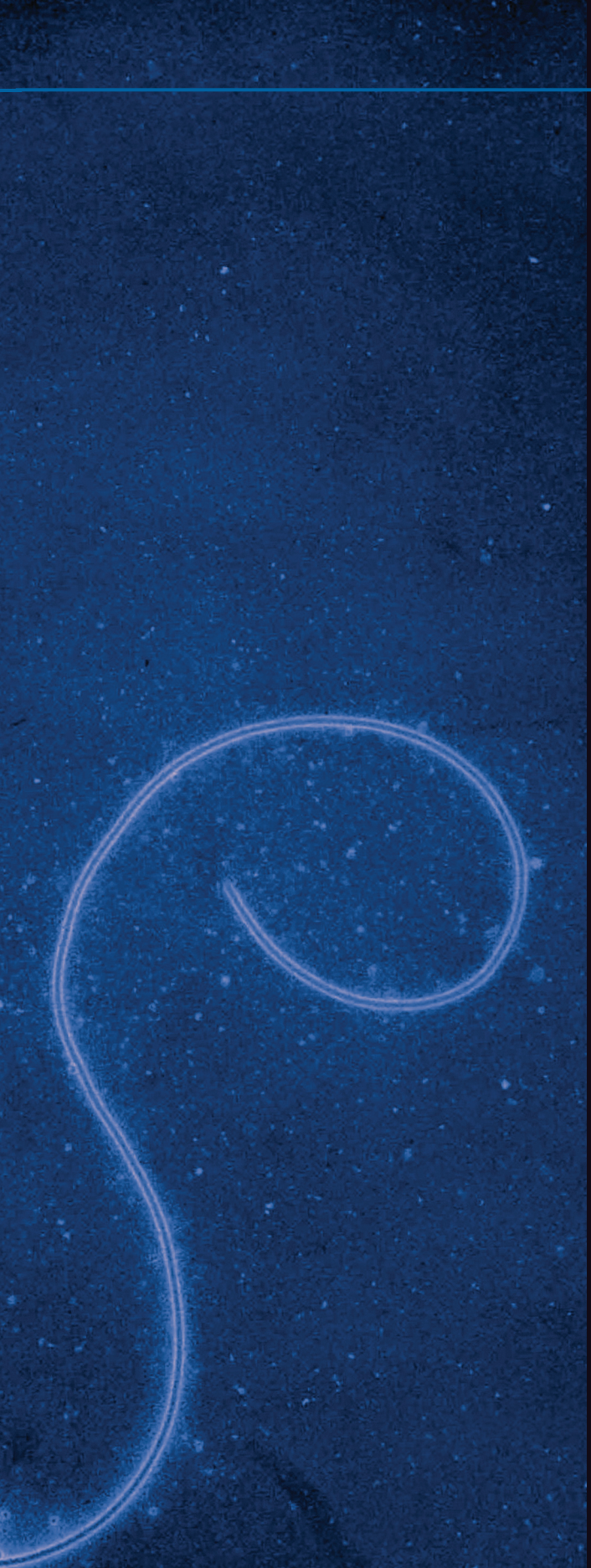
The energy business may be at a turning point. After years of concern about funding levels for alternative energy research, the prices of oil and natural gas have changed the equation, says Wright: "If prices stay high, I don't think the government will have to do very much [to jumpstart the biomass bandwagon]."

David J. Tenenbaum

Microbe Power!



Rhodoferax ferrireducens



Claudia V. Johnson/University of Massachusetts Amherst, Chris Reuther/EHP

Increasingly, problems of rising energy demands, dwindling resources, and pollution concerns are being mitigated by turning waste into usable products. Now some researchers are eyeing organic wastes from homes, food processing, and other sources as an energy feedstock—bacteria including *Rhodoferax* and *Geobacter* are being harnessed in devices called microbial fuel cells (MFCs) to break down organic waste products, converting the energy of their chemical bonds into electricity and hydrogen.

Significant Energy Resource

In the United States, 46 trillion liters of household wastewater are treated annually, according to an article by Bruce Logan, director of the Hydrogen Energy Center at The Pennsylvania State University, in the 1 May 2004 issue of *Environmental Science & Technology*. This costs $25 billion, and the electricity required—mostly for aeration—constitutes 1.5% of the electricity used in the nation, says Lars Angenent, an assistant professor in the Department of Chemical Engineering at Washington University in St. Louis. According to Angenent, most of that energy could be saved by treating wastewater using MFCs. He says one of these devices could produce enough extra energy to power 900 homes by treating the wastes from a single large food processing plant. According to Logan, MFCs would cut the cost of aerating activated sludge in wastewater by as much as 50% of the electricity usage, and should generate 50–90% less solids to be disposed of.

Logan put this potential in context in his 1 May 2004 article when he wrote that the United States consumed 97 quads (short for "quadrillion British thermal units") of total energy in 2002; of this, 13 quads were generated electricity. Should hydrogen become the transportation fuel of choice, as many believe it will—with most hydrogen produced ultimately from fossil fuels—another 12 quads would be required to make hydrogen from water, he wrote.

According to Logan, all the U.S. household wastewater produced in one year contains 0.11 quad organic matter, livestock production wastewater contains 0.3 quad, and food processing wastewater possibly 0.1 quad. Though small, these amounts are potentially significant, says Scott Sklar, the former executive director of the Solar Energy Industries Association and current president of The Stella Group, an energy generation marketing and policy analysis firm. There will be no one-size-fits-all solution to the nation's energy problems, he says. Instead, energy will come from many sources, many of them small sources, and power will be created through a patchwork of technologies tailored to local circumstances and needs.

MFCs could also become important energy sources in the lesser developed parts of the world, says Logan. These fuel cells used locally produced fuel, and their power output can be managed locally. "Microbial fuel cells [appear] destined, at least at this moment, to utilize some energy resources that are not otherwise available on an industrial scale, like sea bottom sediments, or some biomass from waste," says Plamen Atanassov, an assistant professor of chemical engineering at the University of New Mexico. One candidate bacterium for MFCs, *Rhodoferax ferrireducens*, was first isolated from sediments collected in Oyster Bay, Virginia; *Geobacter metallireducens* was first isolated from sediments from the Potomac River.

Breakthroughs Boost Prospects

MFCs go back to the early 1900s, says Angenent. It was at a 1996 American Chemical Society meeting titled "Emerging Technologies in Hazardous Waste Management" that Korean scientists Byung Hong Kim and Doo-Hong Park first described the use of a "mediator-less biofuel cell" to treat wastewater. Breakthroughs in the last five years have suggested fresh promise for this technology.

One breakthrough was the discovery, reported in the 18 January 2002 issue of *Science* by Derek Lovley, a professor in the Department of Microbiology at the University of Massachusetts Amherst, that *Geobacter* produces electricity. That followed the discovery by German and Australian researchers, published in *Bacteriology* in July 1998 (issue 14), that in certain iron-reducing bacteria, the cytochromes—specialized

Skimming the surface. Bruce Logan and colleagues at Penn State have begun demonstrating that MFCs can produce electricity directly from wastewater, potentially cutting both power costs and solid wastes.

enzymes known to transfer electrons to other proteins—span the outer cell membrane, enabling direct transfer of electrons to external metals and the creation of a circuit. This is the ultimate source of electricity in MFCs. These discoveries opened up the possibility of engineering both the bacteria and the electrodes in the MFC to improve electron transfer.

In the 23 June 2005 issue of *Nature*, Lovley announced the discovery of "nanowires," literally tiny wires produced by *Geobacter*, which the bacterium presumably uses to transfer electrons. This discovery opened up further possibilities for electron transfer. He also published a study in the Octobe 2003 issue of *Nature Biotechnology* showing that *Rhodoferax* provides a constant flow of electrons while oxidizing glucose at 80% electron efficiency—a boon for drawing power from carbohydrates.

Still another breakthrough was the discovery, published by Park and University of Michigan molecular biologist J. Greg Zeikus in the June 2002 issue of *Applied Microbiology and Biotechnology*, that one could increase power output in MFCs by about sixfold by using mixed microbial communities rather than pure cultures. This is a big advantage for harvesting energy from wastewater, which is microbially diverse, says Angenent. The question of exactly why this is so is an area Angenent plans to address in future research.

The technology has also seen the benefit of engineering advances. A year ago, in unpublished research, Angenent combined the "upflow" system used in methane digesters with the MFC technology to eliminate the need for mechanical pumping and mixing. In the upflow system, wastewater is piped from above the fuel cell, down, around, and then upwards into the bottom of the anode powered by gravity—the opposite of a syphon. Thus, pumping and mixing become unnecessary.

The first microbial fuel cells produced between 1 and 40 milliwatts per square meter (mW/m^2) of anode electrode surface area, says Logan. In just the past year, he says, his laboratory has generated power in the range of up to 500 mW/m^2 using domestic wastewater and 1,500 mW/m^2 with glucose and air. He adds that researchers in Belgium recently achieved 3,600 mW/m^2 using glucose, although they needed a nonrenewable chemical instead of air for their process.

Electric versus Hydrogen

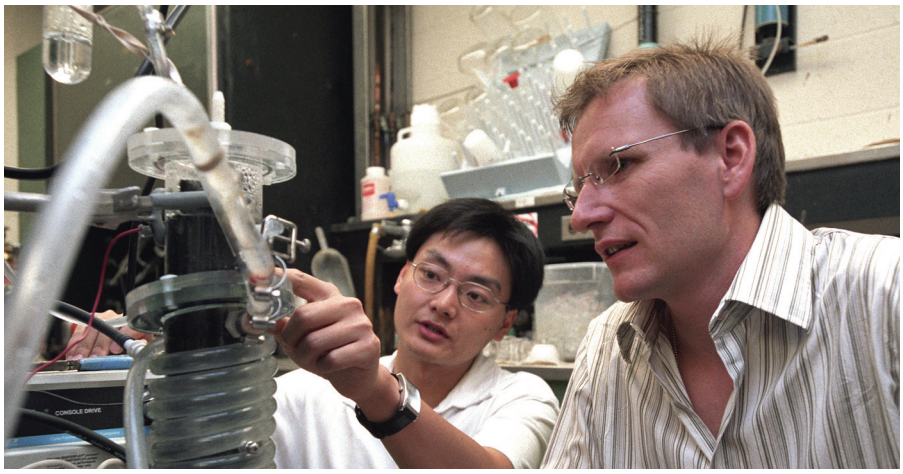
MFCs generate electricity, but can be modified to produce hydrogen instead. In both systems, the source of electricity is the chemical energy contained in the bonds of organic compounds. Bacteria, living in biofilms on the anode, break down the organics, separating electrons from protons. These electrons and protons then travel to the cathode, the former via an external wire, the latter by diffusing through the electrolyte, a substance that does not conduct electricity.

In the electricity-generating MFCs, the protons and electrons combine at the cathode with oxygen to form water. This "uses up" the electrons, allowing more to keep flowing from the anode to the cathode.

In the MFC modified to produce hydrogen, the cathode is kept free of oxygen. But in order to make hydrogen, a thermodynamic barrier must be breached. To overcome this barrier, Logan uses a power source to add voltage into the circuit.

The hydrogen MFC appears to be twice as efficient as the electricity-producing cells, says Logan, because in the latter some oxygen leaks back into the anode. However, adding the voltage in the hydrogen-producing system requires about one-sixth of the energy that is produced as hydrogen. Further losses occur if the hydrogen is converted into other forms of energy. Bottom line: in terms of efficiency for electricity as a final product, neither electricity nor hydrogen production possesses a clear advantage.

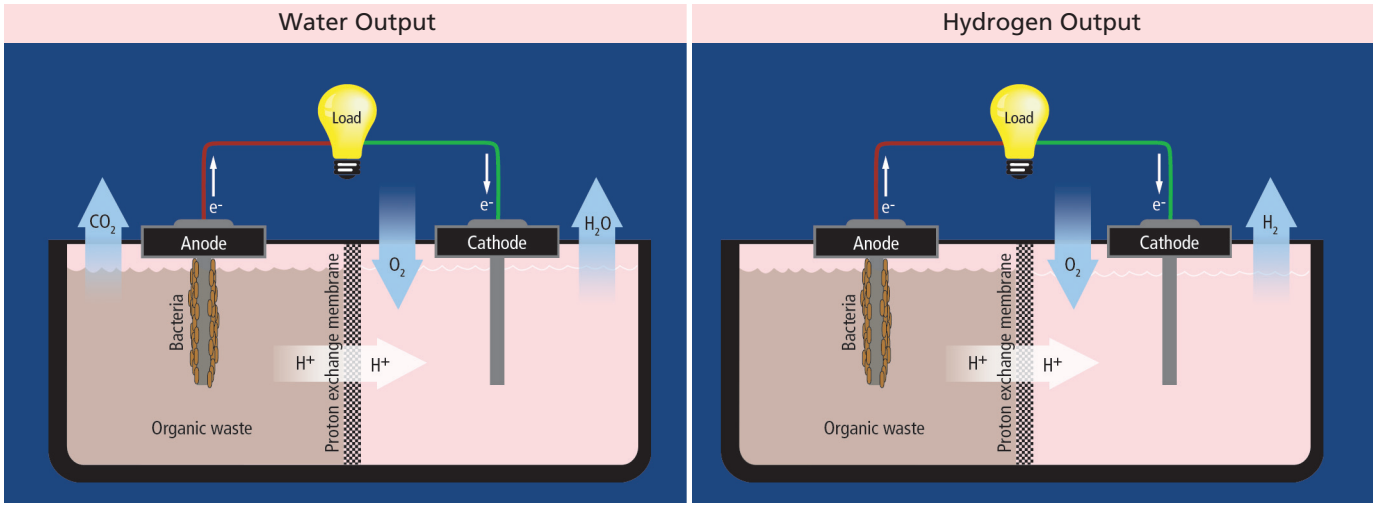
The main benefit of hydrogen-producing MFCs is that they would provide additional options to fit production to energy needs, says Logan. For example, hydrogen could be stored to make off-peak electricity or for use as a transportation fuel. "But if you just want to use electricity locally, you are



Big plans for small microbes. Jason He (left) and Lars Angenent inspect their MFC. In Derek Lovley's lab (right), a model SUV is powered by marine geobatteries.

Clockwise from top: Greg Grieco/The Pennsylvania State University; Derek Lovley; David Kipler/Washington University in St. Louis

Microbial Fuel Cells: The Basics



probably better off making electricity to start with," he says.

Many Technological Challenges

MFC technology is still strictly at the laboratory scale. "[It] doesn't have its own design principals, and borrows from neighboring technologies," says Atanassov. "It is absolutely premature to even address [questions of design]."

The cathode oxygen in electricity-producing devices creates a big challenge for MFCs. A "proton exchange membrane" separates anode from cathode, allowing protons to pass, but blocking the larger oxygen molecules from diffusing to the anode. However, some oxygen manages to cross the proton exchange membrane into the anode, where it takes electrons that would otherwise flow in the circuit, reducing the power, says Lovley.

The low power density of MFCs is also a major problem. Researchers working on MFCs measure power density in W/m^2, while those working on conventional fuel cells measure power density in W/cm^2, a highly illustrative disparity, says Atanassov. That low power density of MFCs means electrodes—which aren't cheap—must be exceptionally bulky.

Power density is a function of the interface between the microbes and the electrodes, says Harold Bright, a program manager in the Office of Naval Research, which is funding studies on MFCs. "We have fairly slow electron transfer from the bacteria into the electrode."

Scale-up for commercial uses adds to the challenges. The current laboratory-scale prototypes use materials that aren't sturdy enough to be used in a commercial system, such as carbon paper and carbon cloth electrodes. Further, experimental MFCs, now smaller than a beer mug, would need to be as big as a mansion (in large part to compensate for the low power density), undoubtedly greatly increasing the distance between anode and cathode. That, in turn, would slow diffusion of hydrogen from the former to the latter, damping efficiency.

To be competitive with methane digester technology, MFCs' practical predecessor, the power density must more than double the maximum achieved so far, to 8,500 mW/m^2, says Angenent. And for this, he says, "another breakthrough is required."

Advances in microbiology and electrode technology leading to higher rates of electron transfer could improve power density; bacteria could be engineered for better electron transfer. Lovley has been systematically deleting genes for outer membrane cytochromes in order to discern which cytochrome was essential for electricity production. "Now we can determine if engineering *Geobacter* to produce more of this cytochrome and/or modifying the electrode to better interact with the cytochrome will result in more power production," he says.

There is ample room for improvement. "If *Geobacter* could transfer electrons to electrodes as fast as it can to its natural electron acceptor, ferric iron, the rate of electron flow—that is, the current—could possibly be ten thousand times higher," says Lovley.

The use of wastes as cost-free substrates will further improve economics, says Logan. Wastes are ideal since their disposal, he says, "is already an economic burden."

Currently, there is virtually no government funding for MFCs except for use in applications such as remote sensors, which are funded by the Navy, the Department of Energy, and the Defense Advanced Research Projects Agency. "The current laboratory systems that we build cost way too much money for the amount of electricity we get back," Logan admits. "[But] the same was true of solar energy fifty years ago." Now solar has become an important—if still small—contributor to the nation's energy supply, and Logan predicts that MFCs will follow suit.

David C. Holzman

Suggested Reading

Holmes DE, Nicoll JS, Bond DR, Lovley DR. 2004. Potential role of a novel psychrotolerant member of the family *Geobacteraceae*, *Geopsychrobacter electrodiphilus* gen. nov., sp. nov., in electricity production by a marine sediment fuel cell. Appl Environ Microbiol 70:6023–6030.

Liu H, Grot S, Logan BE. 2005. Electrochemically assisted microbial production of hydrogen from acetate. Environ Sci Technol 39:4317–4320.

Logan BE. 2004. Extracting hydrogen and electricity from renewable resources [review]. Environ Sci Technol 38:160A–167A.

Reguera G, McCarthy KD, Mehta T, Nicoll JS, Tuominen MT, Lovley DR. 2005. Extracellular electron transfer via microbial nanowires. Nature 435:1098–1101.

Chris Reuther/EHP

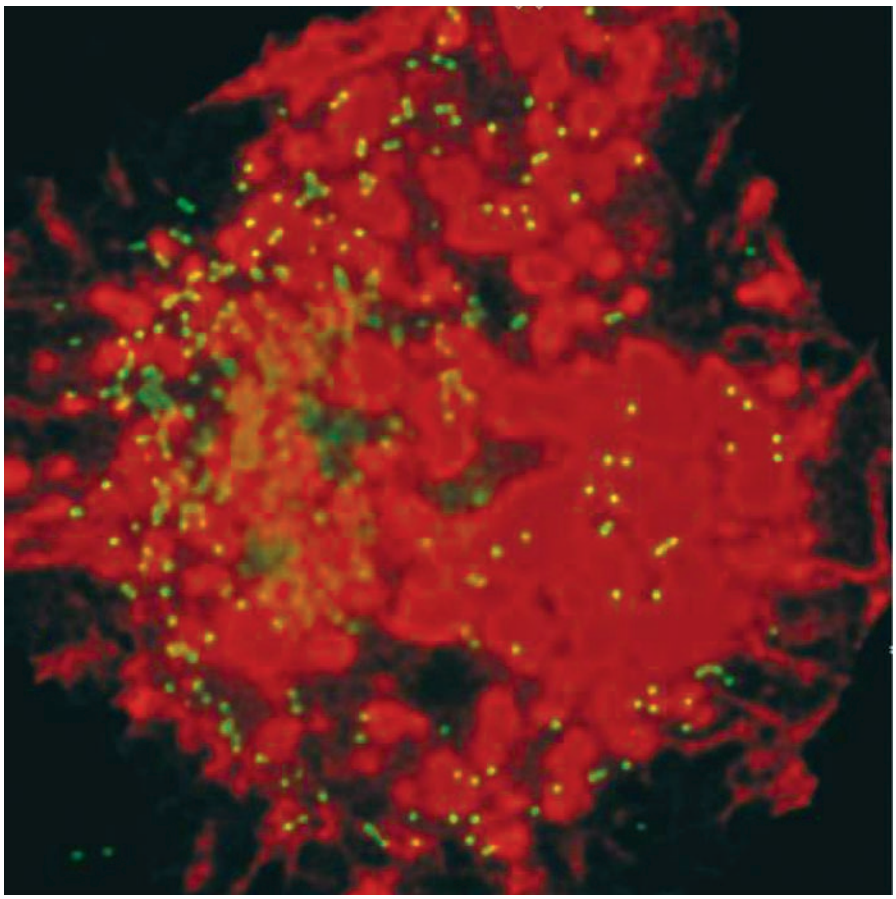
Particles in Practice

How Ultrafines Disseminate in the Body

Ultrafine particles (UFPs), those less than 100 nanometers in diameter, have existed for millennia in natural settings. But with the significant increase in UFPs resulting from human activities in the past few centuries (largely through combustion processes) and the potential for a deluge of nanoparticles as that industry gears up, are ancient human bodily defenses up to the substantial new hazards they now face? Findings by a team of Swiss, German, and Canadian researchers suggest that animals may be largely defenseless against the rapid dissemination of UFPs into cells throughout the body [***EHP* 113:1555–1560**]. Their findings, which include the first evidence of how individual particles are distributed within the lung, raise some concerns, especially since UFPs often end up in locations within cells where the tiny particles can impair many cellular functions.

General knowledge about the rapid penetration of UFPs into various body organs has surfaced in the past few years, but the specific distribution and mechanisms remain largely unknown. To explore the distribution, the research team performed two parallel sets of experiments.

In the first set of experiments, they investigated the spread of titanium dioxide UFPs in rats after a 1-hour inhalation of an aerosol containing the material. The team then evaluated lung tissue taken from the rats either 1 or 24 hours after inhalation.



Ultrafine infusion. A series of recent experiments demonstrates that ultrafine particles are widely disseminated in a variety of cells. A micrograph of one such experiment shows 0.2-micrometer fluorescent polystyrene particles (green) taken up by a macrophage (red).

Geiser et al.

They found that on average, 24% of the inhaled titanium dioxide they detected had penetrated cells throughout the lung and the bloodstream just 1 hour after inhalation. Within cells in different lung compartments, there was no difference in the 1-hour and 24-hour samples, suggesting that UFPs can easily move between compartments. The team continues to investigate what happens with the remaining 76% of the particles and with those that enter the bloodstream. There is evidence the particles spread throughout the body.

Of the particles they did find, 79.3% lodged in cells on the inner surface of airways and alveoli, 11.3% were within capillaries, 4.8% were within connective tissue, and 4.6% were within epithelial or endothelial cells. The researchers were surprised to find that most of the particles in the cellular cytoplasm were not attached to the membrane, as would have been expected if the particles had been encapsulated through endocytosis or phagocytosis. Floating in the cytoplasm, the particles can access many of the structures within the cell, such as the nucleus and mitochondria, increasing the potential toxicity of the particles.

In the second set of experiments, the researchers explored the movement of three sizes of fluorescent polystyrene UFPs and of gold UFPs after the particles were introduced to cultures of swine macrophages and human red blood cells. They found all three particle sizes (1.0, 0.2, and 0.078 micrometer) penetrated the swine macrophages, though in perplexingly different proportions—only 21% of the macrophages contained the medium size, while 77% contained the smallest and 56% contained the largest. In human red blood cells, they found the smallest and medium sizes, but not the largest.

The experiments did not offer evidence about exactly how the tiny, insoluble particles disseminate so extensively and rapidly into so many different cells, but the researchers note that other experiments have demonstrated a number of possible mechanisms. The researchers also note their findings are specific to just the few substances they studied, and differ in some ways from those for iridium, one of the few other materials evaluated in some detail. **–Bob Weinhold**

Testing the Additivity Assumption

Chemical Mixtures and Thyroid Function

It is well established that many environmental contaminants can disrupt thyroid hormone (TH) homeostasis, which is vital during fetal development and for a variety of physiological processes in adults. Among known TH disruptors are polychlorinated biphenyls (PCBs), dioxins, and dibenzofurans, all members of the polyhalogenated aromatic hydrocarbon (PHAH) chemical family. Little is known, however, about how mixtures of such chemicals at typical environmental exposure levels may disrupt TH functions. Nor is it clear whether effects are additive, synergistic, or antagonistic—that is, whether there is interaction between constituent chemicals, whether their cumulative influence is more than the sum of its parts, or whether they cancel each other out. With respect to risk assessment, the U.S. Environmental Protection Agency's default assumption is that the effects of chemicals in

mixtures are additive. Now a team of researchers has tested the additivity assumption and found that it is relatively robust at exposure levels typical for humans [***EHP* 113:1549–1554**].

Over a four-day period the team exposed young female rats to six different doses of a combination of 18 PHAHs comprising 2 dioxins, 4 dibenzofurans, and 12 PCBs. The team determined dose–response information for each constituent chemical before the mixture was tested. The concentration of each chemical in the mixture reflected typical concentrations measured in breast milk and in fish and other foods. The mixture was also formulated so that even at the highest mixture doses, the rats' exposure to each constituent chemical was at or below the known no-observed-effect level for that chemical.

The mixture reduced the rats' serum thyroxine (T_4; the most common form of circulating TH) in a dose-dependent manner. At lower doses the effects were additive. At higher doses T_4 declined by as much as 50%, and the effects were mildly synergistic—about twice what was predicted by additivity—so that even in the upper range the effects as predicted by the additivity hypothesis came close to actual results.

Significantly, the study also showed that the mixture exerted an effect on T_4 even though concentrations of its constituent chemicals were at least an order of magnitude below their known effective doses. This indicates that considering individual chemicals in isolation may not predict their effects in mixtures because, even though chemicals may not be potent enough by themselves to cause effects, the cumulative effects of low doses of many chemicals may be enough to do so.

The multiple functions of TH, such as its role in fetal development and its regulation of metabolism and heart rate, make it vulnerable at many points. The team estimates that there could be as many as five distinct mechanisms by which chemicals exert antithyroid effects for which a reduction in circulating T_4 is the common end point.

Several factors temper the study results. One is that this study was a series of short-term exposures that did not encompass all the chemicals' varied half-lives. The results therefore cannot be directly extrapolated to the effects of chronic exposures and may be subject to confounding by pharmacokinetic differences. Another is that thyroid disruption mechanisms in rats may not be identical to those in humans. The team is now working on testing how a more complex chemical mixture may interact with dietary iodine insufficiency to produce thyrotoxic effects. **–Valerie J. Brown**

Cadmium and Kidneys

Low-Level Exposure and Effects in Women

Widespread exposure to the heavy metal cadmium occurs through both natural and industry-related sources. The general population is likely to encounter low-level chronic exposure through smoking and from dietary sources, particularly shellfish, grains, and vegetables. In 1999 an ongoing population-based Swedish study, Women's Health in the Lund Area, was expanded to include low-level cadmium exposure. Analysis of the data collected now reveals a small but significant kidney response to low-level cadmium exposure [***EHP* 113:1627–1631**]. This suggests that low-level cadmium exposure may pose a significant public health risk.

Owing to extremely slow excretion, cadmium accumulates in the body, especially in the kidneys. Kidney damage is the primary consequence, but most toxicity data are from exposures in occupational settings or severely polluted areas. The effects of low-level exposure are less certain.

A primary function of the kidney is to filter excess water and metabolic by-products from the blood for urinary excretion. This filtration occurs in more than 1 million nephrons, each of which contains a blood capillary (the glomerulus) intertwined with a urine-collecting tubule. In the current study, researchers assessed glomerular and tubular fitness by measuring kidney function markers in blood and urine, respectively. Blood testing also revealed ongoing cadmium exposure, and urinalysis indicated cadmium body burden.

The team analyzed data, including blood and urine samples, collected from 820 women aged 54–63 years. Blood levels of creatinine and cystatin C were measured in 742 participants to calculate glomerular function. Urinary concentrations of calcium, human complex-forming protein, and *N*-acetyl-β-D-glucosaminidase—all markers of tubule function—were available for 813 women. The researchers additionally collected data on medications taken, smoking history, lead exposure, and incidence of diabetes and hypertension to control for potential confounding factors.

Cadmium concentrations were similar or slightly higher compared with previous data from Sweden and much lower than concentrations reported for populations in highly polluted areas in Europe and Japan. Current or former smokers had cadmium concentrations

Cadmium connection. A new study shows that kidneys respond to even low-level chronic cadmium exposure such as that obtained from smoking and eating grains.

Photodisc

that were 90% higher in blood and 40% higher in urine than concentrations measured in participants who never smoked. Consequently, multivariate analyses were conducted on data from all participants as one group and from those who had never smoked as another group.

Cadmium concentrations were positively associated with the tubular function markers, indicating some damage to the tubules. Increased cadmium was also associated with decreased creatinine clearance, reflecting a reduced glomerular filtration rate. The lowest-observed-effect level for increased tubular markers was a mean urinary cadmium concentration of 0.6 microgram per liter, which is lower than previously reported. A reduction in glomerular filtration rate was associated with a minimum mean urinary cadmium concentration of 0.86 microgram per liter.

The researchers speculate that effect levels might be even lower for people with diabetes, a disease carrying high risk of kidney damage similar to that caused by cadmium exposure. Although the effects of low-level cadmium exposure are clinically minor, they should be viewed as early indicators of potential severe health effects, according to the researchers. Given the size of the exposed population, there may be a significant public health risk, and efforts beyond smoking cessation programs are needed to reduce exposure. **–Julia R. Barrett**

Indoor Air Complaints

VOCs May Not Be Cause of Acute Effects

Over the past few decades, researchers have been trying to pin down the specific chemical culprits behind increasing complaints of poor air quality inside offices and other buildings. Among the many chemicals suspected so far have been volatile organic compounds (VOCs) and ozone, prominent pollutants in indoor environments. But VOCs alone, or in combination with ozone, may not be the prime source of acute health problems, says a team of New Jersey investigators [***EHP* 113:1542–1548**]. Instead, they found that psychological stress was a more salient factor, but they acknowledge that a number of limitations in their study preclude applying this finding to all indoor air complaints.

The study investigated the short-term acute health effects of exposure to ozone, a mixture of 23 VOCs, and stress. The research was conducted in a controlled chamber into which either a relatively high level of the VOC mixture (26 milligrams per cubic meter), the VOCs plus moderate concentrations of ozone (40 parts per billion), or clean air with a low one-minute spike of VOCs (about 2.5 milligrams per cubic meter) was introduced. In the middle of each three-hour test session half of the volunteer subjects had to make a four-minute speech on a controversial subject as a stress test, while the other half performed simple arithmetic problems. The test sessions were held one week apart.

The researchers evaluated stress by measuring cortisol secretions in saliva. To assess health effects, they evaluated selected performance measures, as well as 33 observed and self-reported physical and behavioral indicators, such as headache, nausea, eye irritation, nervousness, and leg cramps.

They found the challenge of public speaking induced a significant increase in the subjects' measures of stress. However, even with that increase in stress, no significant increase in health symptoms or reduction in neurobehavioral performance was linked to the exposures to VOCs either alone or combined with ozone, despite sharp increases in many secondary pollutants resulting when ozone was added to the VOC mixture.

The 130 female volunteers exposed to each air mixture constituted the largest group evaluated in a study of this kind, and the researchers determined the numbers were of sufficient power to produce significant findings. However, all the subjects were healthy, young (mean age 27.2 years), and well educated (mean education of 15.2 years), demographically limiting the applicability of the findings.

In addition, the team acknowledges that its testing, while extensive, didn't represent many aspects of a typical office building. For instance, the test chamber did not include carpet, many office furniture materials, and other normal interior accoutrements that might interact with VOCs and ozone. The mix of VOCs, although extensive, likely didn't represent the mix in many buildings. Further, the ventilation rate in the test chamber was substantially higher than in many buildings at which complaints have been lodged.

Further, the public speaking challenge, although successful at inducing stress, wasn't representative of the multiple complex stressors experienced in a typical work day. And the testing period was very short, providing no information on the potential chronic effects that may be induced by longer-term exposures to chemicals and stress. Nonetheless, the findings are helpful in pinning down the relative contribution, or lack thereof, of certain mixtures and concentrations of VOCs and ozone to poor indoor air quality. **–Bob Weinhold**

Maybe it's nerves. A study of indoor air pollutants and stress (induced by public speaking) shows that stress, not VOCs, may be a larger culprit behind sick building complaints.

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