

MOLECULAR BIOLOGY

## Tobacco's Secret Weapon

It is almost universally understood that tobacco is bad for your health, but tobacco's specific role in triggering disease processes is still unclear. Now a component of tobacco has been shown to function in chemical reactions that are thought to contribute to secondary cardiovascular disease, kidney failure, and cancer in diabetics, and to neurological diseases. The compound, nornicotine, is naturally present in tobacco and is also a metabolite of nicotine, forming about 10% of nicotine breakdown products in the body. Combustion is not necessary to produce nornicotine, so it can enter the body not only through inhaling smoke but also through chewing tobacco and wearing nicotine patches.

The research, by chemistry professor Kim D. Janda and graduate student Tobin J. Dickerson of the Skaggs Institute for Chemical Biology at The Scripps Research Institute in La Jolla, California, was published in the 12 November 2002 issue of *Proceedings of the National Academy of Sciences*. Janda and Dickerson showed that nornicotine binds to glucose to form compounds that react further

with proteins. The resulting products, called glycotoxins, interfere with protein function. The entire process, termed a Maillard reaction, ultimately forms compounds called advanced glycation end products (AGEs). Maillard reactions and AGEs have been well known in food chemistry for many years; they are created by cooking proteins and sugars at high heat and by the simple breakdown of food over time. Tobacco curing also creates conditions favorable to AGE formation. The human body makes variable amounts of AGEs, and exogenous factors such as tobacco use and dietary habits may greatly raise levels in blood.

AGEs have been implicated not only in diabetes-related diseases but also in neurological conditions such as Alzheimer disease and amyotrophic lateral sclerosis. There is speculation that glycation reactions and oxidative stress work synergistically, and some evidence suggests that AGEs can damage DNA. The ability of nornicotine to undergo Maillard chemistry suggests there may be a direct chemical link between tobacco use and disease.

Dickerson and Janda first showed *in vitro* that nornicotine does in fact engage in intermediate Maillard reactions. They then developed an antibody that could detect a range of nicotine-related proteins, including nornicotine-modified

Risk varies inversely with knowledge.  
Irving Fisher, *The Theory of Interest*, 1930

proteins. They tested the antibody against serum samples from 10 smokers and 10 nonsmokers. Because the antibody could detect more than just nornicotine-modified proteins, it also reacted to proteins in the nonsmokers' plasma. But the signal generated by the proteins in the smokers' plasma was about 50% greater than that generated by proteins in the nonsmokers' plasma. The researchers attributed this to the presence of nornicotine-modified proteins, which they believe would lead to AGE formation *in vivo*.

Dickerson and Janda investigated nornicotine as part of their study of the biochemical mechanisms of addictive drugs. Because nornicotine stays in the bloodstream much longer than nicotine, they think it may not only generate AGEs but may also contribute to nicotine dependence.

The Janda-Dickerson research builds on a study by Anthony Cerami and others reported in the 9 December 1997 issue of *Proceedings of the National Academy of Sciences*. This study showed that aqueous extracts of cigarette smoke contained glycotoxins that formed AGEs *in vitro*.

"All this work helps us to understand the influence of exogenous factors such as smoking and diet in human disease," says Jaime Uribarri, an associate professor of medicine at the Mount Sinai School of Medicine. A team led by Uribarri has demonstrated that dietary glycotoxins significantly raise AGE blood levels in patients with kidney failure.

Establishing nornicotine's ability to trigger an immune response and to alter the function of proteins are "two nice findings" strengthening the evidence for its connection to disease processes, says Yousef Al-Abed, a chemist at the North Shore Long Island Jewish Research Institute in Manhasset, New York, who was part of the 1997 Cerami team.

Dickerson and Janda also tested the nornicotine AGEs against steroid compounds, and found that the AGEs chemically modified the steroids. They speculate that this may affect both the toxicity and function of important drugs such as prednisone, which is widely used to control severe allergic and asthmatic reactions. —Valerie J. Brown



**Culprit uncovered.** New research indicates that a component of tobacco called nornicotine is a factor in causing illnesses including cancer, neurological disease, and cardiovascular disease.

Corbis

## AIR POLLUTION

## Far-Reaching Effects of Fine Particles

Sulfate aerosols—fine particles generated from sulfur dioxide (SO<sub>2</sub>) emissions by power plants located primarily in the Northern Hemisphere—may alter rainfall patterns and contribute to drought thousands of miles away. This would help explain the devastating drought in the Sahel region of Africa, according to atmospheric scientists Leon Rotstajn of CSIRO Atmospheric Research in Aspendale, Victoria, Australia, and Ulrike Lohmann of Dalhousie University in Halifax, Nova Scotia.

The strength of Rotstajn and Lohmann's work, published in the August (number 15) 2002 issue of *Journal of Climate*, lies in their backing up their model with "careful analysis of satellite estimates of cloud properties and observed precipitation trends," says William Collins, cochair of the Atmospheric Model Working Group at the National Center for Atmospheric Research in Boulder, Colorado. Rotstajn and Lohmann collected SO<sub>2</sub> emissions data from various countries and cloud property data from satellites. Then they ran sophisticated computer climate models to illustrate and evaluate how sulfate aerosols influenced rainfall patterns between 1900 and 1998.

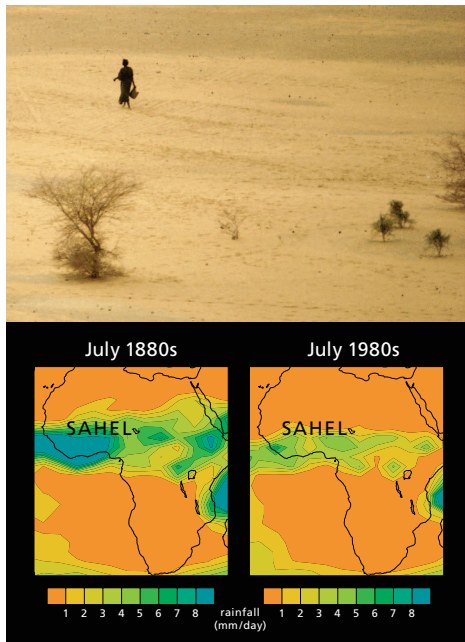
One prominent feature emerged from the model when anthropogenic SO<sub>2</sub> emissions were added—an extended drying trend in the Sahel region of northwestern Africa. Indeed, from the late 1960s into the 1980s, a severe drought plagued the Sahel. During the same period, SO<sub>2</sub> emissions grew rapidly in North America—from

about 20 million tons in 1960 to about 30 million tons in 1980 in the United States alone, according to the U.S. Environmental Protection Agency, because of growth in industrialization with little government control of pollution. In the 1990s, the return of rainfall to the Sahel—which brought only limited amelioration of the drought—coincided with a drop in SO<sub>2</sub> emissions by industrialized countries. According to the Environmental Protection Agency, total SO<sub>2</sub> emissions in the United States were 39% lower in 1996 than in 1970.

Rotstajn and Lohmann propose that the drought may be the result of sulfate aerosols in northern industrialized countries indirectly forcing African monsoons south of the Sahel. The sulfate aerosols serve as tiny nuclei on which cloud droplets form. A large number of tiny cloud droplets collectively acts as a shield to reflect solar radiation back into space, which cools polluted areas. According to Rotstajn, the cooling of the oceans in the Northern Hemisphere shifts circulation patterns and

drives tropical rainstorms to move southward. "Moist air rises over warmer waters, leading to cloud formation and rainfall," he says. Meteorology records confirm that since the mid-1980s—coincident with the partial recovery of rainfall in the Sahel—the Northern Hemisphere has warmed even more strongly than the Southern Hemisphere.

The Sahel has experienced the most substantial and sustained lack of rainfall recorded anywhere in the world. Scientists trying to understand the cause of the paralyzing drought have blamed overfarming and overgrazing of the land by its residents. Certainly, other factors likely contribute to the ongoing drought, says Rotstajn, but he is hopeful that "cleaner air in the future will mean greater rainfall in the region." —Carol Potera



**From dust to dust.** A new model suggests that drought, such as that afflicting Africa's Sahel region, is a result of industrial pollution in the Northern Hemisphere.

## Asthma Case Won in Japan

An October 2002 court decision awarded almost ¥80 million—US\$638,000—in a suit filed against the Japanese national government, the Tokyo municipal government and highway authority, and seven auto makers. Of an original 99 plaintiffs, the Tokyo District Court ruled that pollution from roadways caused or exacerbated asthma in 7 who lived within 50 meters of high-traffic roadways in central Tokyo. The auto makers named in the case were cleared of any responsibility, but Judge Toshifumi Takahashi said they could have predicted harmful diesel emission-related health effects as far back as 1973 (when Japan established standards for pollutants) and that they have a social duty to reduce harmful vehicle emissions.



## Slovakia Inks First Kyoto Deal

Although the Kyoto Protocol to reduce greenhouse gas emissions is not yet in effect, the first emissions credit deal has been brokered under the trading framework set up by the agreement. In December 2002, the Slovakian government sold greenhouse gas emissions credits equal to 200,000 metric tons of CO<sub>2</sub> to an undisclosed Japanese buyer. Slovakian engineering company Menert LLS is helping to generate this supply of credits by switching its operations from coal to natural gas and by capturing waste heat at industrial plants to produce electricity.

## Liking Lichens Even More

Lichens, which absorb the nutrients they need from the air and thus mirror air pollution conditions, have been used as biomonitors for over a century. Now Brigham Young University biologists have demonstrated for the first time that lichens take in pollutants in patterns that exactly reflect the concentrations present in the air, making them even more accurate gauges of airborne pollution than originally thought. The authors say that if further studies corroborate their findings, lichens could replace conventional air sampling equipment, which is often expensive to purchase and maintain. The report was published in volume 36, issue 36/37 (2002) of *Atmospheric Environment*.



## ENERGY

## The Deregulation Debate

In 1996 the Federal Energy Regulatory Commission (FERC) issued a landmark order designed to foster competition in the wholesale electricity industry. Order 888 required that electric generating utilities open their transmission grids—the wholesale market—to any company that could supply electricity. Under retail competition, customers could choose their electricity provider. But recent analyses show that Order 888 has in some cases had worse environmental repercussions than anticipated.

Restructuring has led utilities to dramatically cut spending on energy efficiency measures. From \$2.4 billion in 1995, they reduced spending to \$1.4 billion in 1999, according to the Department of Energy as cited in *A Retrospective Review of FERC's Environmental Impact Statement on Open Transmission Access*, a 2002 report of the Commission for Environmental Cooperation. This body was set up under the North American Free Trade Act to examine the impact of changes in electric restructuring in North America.

The cutbacks come, says *Retrospective Review* coauthor Tim Woolf, because of industry concerns over increased competition in the retail electricity business. Although retail competition is currently the law in just 17 states, utilities fear the trend will spread nationwide. In the past, utilities were able to regain the costs of

energy efficiency spending—such as promotions for efficient appliances and energy audits—in their rates. Under retail competition, that wouldn't happen: "Utilities worry if they spent money on customers to improve their efficiency, that customer could sign up with another generator, and the utility would never see the benefits," says Woolf.

Furthermore, as utilities curtail their efforts to boost electricity efficiency, coal-fired electricity generation is growing sharply in the Midwest and South, because coal remains cheaper than alternatives such as natural gas. This growth was not predicted by FERC, says Woolf.

*Retrospective Review* found that the increase in coal-fired electricity generation resulted in 5.4% more nitrogen oxide (NO<sub>x</sub>) emissions than FERC expected. NO<sub>x</sub>, which results from combustion, leads to the formation of ozone and particulates. These secondary by-products are associated with a number of health effects, including premature death, exacerbation of asthma, and cardiovascular problems, says Jonathan Levy, an assistant professor of environmental health and risk assessment at the Harvard School of Public Health. The review also notes that FERC

underestimated emissions of the greenhouse gas carbon dioxide by about 8%, and probably underestimated mercury emissions as well, as coal-fired power plants are a major source of that pollutant.

Assessing the impact of the NO<sub>x</sub> increase is difficult. However, Levy says a 5.4% increase is substantial and that "it could be something of concern." —Harvey Black



## RESEARCH INITIATIVES

## Geology and Health

If you don't consider geologists to be environmental health experts, think again. Earth scientists collect data on some of the planet's naturally occurring health hazards—including pathogens, radon, arsenic, coal, zinc, volcanic releases, dust, cadmium, and asbestos—and work with public health and biomedical scientists to mitigate the effects of these potent pollutants. These contributions to environmental health research were the topic of an April 2003 meeting, "Natural Science and Public Health: Prescription for a Better Environment."

In rural villages across the world, geologists are linking environmental contaminants to local diseases. William Orem, a USGS geochemist from Reston, Virginia, has been studying Balkan endemic nephropathy (BEN), which occurs in certain areas in the Balkans. BEN patients have a high incidence of renal and pelvic cancer. Orem and his colleagues have linked the disease to well water contaminated with organic compounds leached from low-rank (softer) coal deposits known as Pliocene lignites. Their investigation expanded in 2002

to Wyoming, the Dakotas, and Louisiana, where they are finding communities underlain by low-rank coal deposits that have contaminated drinking water and high rates of renal and pelvic cancer.

In their pursuit of pathogens, USGS scientists are investigating when and where West Nile virus will strike next, reported Stephen Guptill, a USGS geographer from Reston. The virus is spread by mosquitoes to humans, birds, and other animals; uninfected mosquitoes pick it up when they feed on infected birds. Communities where bird infections occurred early in the mosquito season were 2–20 times more likely than other communities to have human cases of the disease, Guptill and colleagues wrote in the April 2003 issue of *Emerging Infectious Diseases*. They tested and released thousands of birds of more than 150 species in 2001 and 2002. They think the primary bird carriers may be one of the species that the virus doesn't sicken.

In the wake of West Nile virus's cross-country march is a trail of insecticides used to kill the mosquito vectors. Stephen Terracciano, a USGS hydrologist from Coram, New York, reported on a Long Island pilot program begun in 2000 to monitor the fate of insecticides. He and his

colleagues are in the process of measuring concentrations of a broad screen of pesticides in the water with a lipid-containing, semipermeable membrane kit that mimics how pesticides are absorbed by fish.

Fish have also caught the attention of scientists with the Biomonitoring of Environmental Status and Trends (BEST) Program, a USGS project to characterize the effects of environmental contaminants on the health of biota and their habitats. Since 1995, researchers have assessed fish health in large rivers to see whether they are affected by contaminants. Thus far the program has sampled the Mississippi, Rio Grande, Columbia, and Yukon basins, reported Tim Bartish, a USGS biologist in Fort Collins, Colorado.

Results have documented a gonadal anomaly in which egg cells are found in the testes of male smallmouth and largemouth bass. At one site on the Mississippi River downstream of Minneapolis–St. Paul, 70% of bass collected were affected, compared to a rate of less than 10% found elsewhere. The specific causes and biological significance of this condition are not known.

For more on the USGS environmental health program, visit <http://health.usgs.gov/>. —Tina Adler

## ehpnet Environment Public Health Tracking

Until recently, the United States had no integrated network to assess local and state data to determine exposures and health effects linked to environmental hazards. But now the National Center for Environmental Health of the U.S. Centers for Disease Control and Prevention (CDC) is laying the groundwork for what is planned to become a nationwide environmental public health tracking network.

In 2002, the agency awarded the first round of grants for this program, totaling \$17.5 million, to 17 states, 3 local health departments, and 3 schools of public health to begin building a network that is standards-based, allows direct electronic reporting and linking, and is compatible with other public health systems. The program's website, <http://www.cdc.gov/nceh/tracking/>, is an information resource on this project.

The At A Glance page describes how the program came into being, outlines its mission and goals, and provides an overview of the program grants that have been awarded to date. Grantees are working on three different types of projects: planning and capacity building, enhancement and demonstration (which involves strengthening existing programs and establishing concrete data linkages to build support for electronic reporting programs and their use in policy development), and establishing university centers of excellence. A color-coded map shows the locations of different types of currently funded activities throughout the nation. This page also lists examples of the external partners—nongovernmental organizations and government agencies—that are involved with the project and gives a snapshot of future planned activities.

The Funded Programs & Contacts page lists links to information on each of the currently funded programs. The New Mexico Department of Health program page, for example, describes the program's goals, how the program components are to be developed, and partners with whom the department will work to build their program, which in this case include the New Mexico Environmental Department, the Indian Health Service, the City of Albuquerque Environmental Health Department, and the Bernalillo County Environmental Health Department.

Links on the homepage lead to information on the CDC's Biomonitoring Program and the Environmental Public Health Indicators (EHPI) Project. The goal of the Biomonitoring Program is to prevent environmental disease by assessing exposures from a number of sources (including acute emergencies that can result in fatalities), identifying at-risk populations, and monitoring exposure trends over time. This program produces the *National Report on Human Exposure to Environmental Chemicals*. The 2003 report, available on the site, features biomonitoring exposure data for 116 environmental chemicals that were measured over the period 1999–2000 by the National Health and Nutrition Examination Survey [also see "Body of Evidence," p. A394 this issue]. The EHPI Project is a result of work by the CDC and the Council of State and Territorial Epidemiologists to develop a list of priority areas and indicators that need to be evaluated to bridge the gap in the understanding of environmentally related diseases and the possible hazards and exposures that may trigger them. Visitors can find a list of all core indicators identified, including measures and potential data sources.

The Resources link on the homepage leads to a list of nine other environmental and public health tracking resources. These include the CDC National Electronic Disease Surveillance System, the National Association of County and City Health Officials' *Protocol for Assessing Community Excellence in Environmental Health*, the Pew Commission report titled *America's Environmental Health Gap: Why the Country Needs a Nationwide Health Tracking Network*, and the website for Trust for America's Health, a nonprofit group working to protect communities, especially those at high risk for environmental and other public health threats. —Erin E. Dooley



## Too Many Home Alone?

Michigan State and Stanford researchers have found that in 76 countries rich in threatened native species—including Australia, Brazil, China, Kenya, and the United States—the number of households grew by 3.1% annually over the period 1985–2000, compared with a population increase of only 1.8%. The average number of people in each household fell from 4.7 to 4.0. Had the number remained at 4.7 per household, the scientists estimate there would have been 155 million fewer households.

Given the same size population, the scientists say, more households require more energy, construction materials, and building sites, which in turn contributes to deforestation and habitat fragmentation. They project that if this trend continues, 233 million households will be added in these countries by 2015.



## Border 2012

On 4 April 2003, the United States and Mexico finalized a 10-year cooperative environmental and public health plan called Border 2012. Almost 12 million people live and work in the 2,000-mile border area between the two countries, with 90% residing in 14 binational "sister" cities. State, local, and tribal government input helped shape the program, which focuses on a bottom-up approach to prioritize and reduce each locality's most pressing health concerns, including pesticide and other chemical exposures, waterborne diseases, respiratory problems, and air, water, and soil pollution.

## Muddy Waters for GM Fish

In its January 2003 report on the science and regulation of genetically modified (GM) fish, the Pew Initiative on Food and Biotechnology asks whether the FDA process for evaluating these biotechnology products—the same as that used for approving animal drugs—is sufficient to regulate the potential environmental impacts of these fish. Concerns include gene flow (the spread of novel traits from GM fish into wild populations that could harm the resilience of aquatic ecosystems) and the possibility of GM fish outcompeting wild species for food and other resources. The report, while making no recommendations, says the FDA regulations do not address environmental risks, and points out that the confidential approval process does not allow for public input. The report further questions whether the FDA has sufficient authority and expertise to review the safety of GM fish.

