

New knowledge is the most valuable commodity on earth.  
The more truth we have to work with, the richer we become.  
Kurt Vonnegut (1922–2007)

CHEMICAL EXPOSURES

## Exploring Developmental Origins of Obesity

In the past 20 years, obesity rates across the developed world have skyrocketed. About one-third of U.S. adults are overweight and another third are obese, according to the National Institute of Diabetes and Digestive and Kidney Diseases. Similarly, more than one-third of U.S. children are overweight or at risk for overweight. The result is a host of health problems for millions of people, including diabetes, coronary heart disease, hypertension, hypercholesterolemia, gallbladder disease, and pregnancy complications. Researchers have typically blamed two main factors: reduced physical activity and increased caloric intake. But perhaps that's not all there is to it. In a session at the 2007 annual meeting of the American Association for the Advancement of Science titled "Obesity: Developmental Origins and Environmental Influences," scientists looked at

the question of whether prenatal chemical exposure may be predisposing some children to a life of obesity.

During the session, Frederick vom Saal, a professor of biological sciences at the University of Missouri–Columbia, described a link between bisphenol A and obesity. Bisphenol A is a major component of polycarbonate plastics found in the linings of cans and in baby bottles. It can leach from plastic when it is heated or there is a change in acid–base balance.

According to vom Saal, bisphenol A has exhibited endocrine disruption in animals and humans at ppb doses. "There are situations where bisphenol A is causing effects at a thousand times lower than the amount in the average human body," he said, adding that current global production of bisphenol A runs about 7 billion pounds per year.

In one of vom Saal's experiments, presented at the meeting, pregnant mice were fed doses of bisphenol A up to 10 times lower than what finds its way into the average human. Although the offspring did not meet the criteria for obesity, they did exhibit abnormal growth later in life. Other studies have linked similar doses

with cancer of the prostate and mammary gland in offspring.

Retha Newbold, a biologist with the Developmental Endocrinology Studies Group of the NIEHS Laboratory of Molecular Toxicology, focused her attention on diethylstilbestrol (DES), a potent estrogen widely prescribed from the 1940s to the 1970s for pregnancies at risk of miscarriage. The compound has been shown to cause impaired fertility, reproductive tract malformations, and a low incidence of cancer in the children of women who took the drug in pregnancy.

Newbold and her colleagues performed an experiment in which mice were exposed to DES in the womb or shortly after birth. DES-exposed mice were smaller than untreated controls after birth. However, when the animals reached puberty, the DES-treated mice became significantly larger than the controls. Activity levels and food consumption were similar for obese DES-treated mice and normal-weight controls. Yet DES mice accumulated more body fat and in some cases a more difficult time processing glucose.

In a third presentation during the session, Bruce Blumberg, an associate professor with the University of California, Irvine, Department of Developmental and Cell Biology, discussed how tributyltin alters gene expression to promote fat cell differentiation. Tributyltin is an organotin used as a heat stabilizer in the manufacture of polyvinyl chloride plastics that, like bisphenol A, may leach out of the plastic.

Testing of pure tributyltin showed that the compound altered receptor sensitivity at very high potency, and at similar levels to drugs that specifically target that receptor. "Prenatal tributyltin exposure causes permanent physiological changes in these animals that predisposes them to gaining weight," said Blumberg. "They were not treated with any more tributyltin after that prenatal exposure, they had a normal diet, normal exercise, and yet they were significantly fatter."  
–Graeme Stemp-Morlock



**A new line of thinking.** Evidence now suggests that a myriad of prenatal chemical exposures may predispose children to obesity later in life.

Image Source

## MARINE AND COASTAL SCIENCE

## Where Space and Ocean Meet

A variety of oceanborne microbes can sicken humans via seafood, drinking water, and swimming. At the February 2007 annual meeting of the American Association for the Advancement of Science, experts described new technologies for predicting hidden or nascent oceanborne hazards, often by satellite. Such predictions could prevent illness without causing economic losses that might otherwise occur—for example, when shellfish beds are shut down needlessly.

Location, time, and intensity of cholera epidemics can now be accurately predicted from satellite observations of sea surface temperature, sea surface height, and chlorophyll in the water, said Rita R. Colwell, a distinguished university professor at the University of Maryland. The correlations of disease with these environmental conditions are logical. Sea surface temperature and sunlight nurture phytoplankton, the food source for the copepods that carry *Vibrio cholerae*. Chlorophyll in the water indicates the presence of phytoplankton. Sea surface elevation is a proxy for the tides, which influence estuarine salinity; a high sea surface means pathogens can be washed into estuaries.

With enough warning, even people in the least stable situations—for example, in war-torn developing countries—could filter drinking water using low-tech devices, cutting the infection rate by 50%, said Colwell. She was the first to monitor and predict cholera epidemics in Bangladesh using satellites, as reported in the 15 February 2000 issue of *Proceedings of the National Academy of Sciences*.

Similarly, D. Jay Grimes, provost and vice president for academic affairs at the University of Southern Mississippi, is modeling prediction of health hazards from *V. parahaemolyticus* and *V. vulnificus* in the Gulf of Mexico and off the East Coast. In seawater or undercooked seafood these organisms can cause acute gastroenteritis and septicemia. *V. vulnificus* also infects wounds. Mortality is estimated at about 50–60% in compromised patients.

Grimes envisions a national surveillance system based on his model, which would integrate satellite measurements of sea surface temperature, chlorophyll, salinity, and turbidity. The multiplicity of parameters is needed because, for example, whereas temperature correlates well with the presence of the two microbes, it doesn't distinguish

between pathogenic and nonpathogenic *Vibrio* species. However, turbidity does appear to do so.

Many more potentially toxic species thrive in algal blooms. Two dozen such organisms are known to frequent the waters off the South Carolina coast, says Patrick J.P. Brown, a research specialist at the Hollings Marine Laboratory. Identifying which are in any given water sample at any given point in time is costly and time-consuming. The tab for analyzing one sample for 11 species using real-time polymerase chain reaction is about \$650, and microscope identification requires extensive training of personnel.

Brown has developed a highly sensitive DNA amplification technique he calls "species identity via chimeric amplification" (SIVCA) that can assay 11 species in a water sample for \$60. The technique has been successfully tested in the field, he says. This new tool will enable resource managers to make decisions on beach and shellfish bed closings and advisories much more quickly than current methods do.

Old-fashioned observation underpins high-tech efforts to anticipate domoic acid contamination in shellfish in the Pacific Northwest. This algal toxin can cause short-term memory loss, brain damage, and death. Recent research cruises established that the biggest blooms with the highest toxin levels are associated with offshore eddies or upwelling zones near coastal promontories, and that storm conditions tend to push the toxin-producing algae coastward.

Vera L. Trainer, program manager for the Harmful Algal Blooms Program at the Northwest Fisheries Science Center, has proposed placing early-warning moorings at these locations. These environmental sensing platforms are designed to record the presence and number of microorganisms and toxins using genetic and immunological techniques, respectively. This information could be integrated with data from various sensors and satellite images to serve as a reliable early warning for harmful algal blooms.

As the session concluded, Michael Moore, a senior research specialist at the Woods Hole Oceanographic Institution, noted that researchers have only begun to assess the scope of the hazards in oceans. Moore is documenting the diversity and prevalence of zoonotic organisms in marine mammals and seabirds. So far, in 116 individual birds and mammals, he has detected 79 of more than 200 known zoonotic bacteria capable of causing human disease. He was the first to detect a *Brucella*-like agent in birds and has also found moderate to high antibiotic resistance in bacteria from marine birds and animals. —David C. Holzman

## Satellites for Health

A two-year National Research Council study released in January 2007 states that 17 new Earth-observing satellite missions need to be funded over the next decade if important data on climate change, hurricanes, and shifting drought and rainfall patterns are to be gathered. The landmark report sets forth the actions deemed most crucial by a 100-member panel of scientists for NASA and NOAA over the next 10 years. Panel cochair Richard Anthes said a \$10 per capita investment in Earth-observing projects would pay for itself exponentially by improving weather forecasts, resource management, and hurricane preparedness. NASA's budget for satellite measurements and analysis has been cut by more than 30% over the past five years.



## Asia Buys In to Clean Energy

Two initiatives are under way to boost renewable energy sources in Asia. The first, in Nepal, calls for research into small-scale hydropower, biogas, and solar and wind power in an effort to reduce dependence on firewood, which negatively impacts indoor air quality, increases atmospheric pollution, and contributes to deforestation. In the second initiative, the leaders of 14 Asian countries, Australia, and New Zealand signed the Cebu Declaration on East Asian Energy Security in January 2007. The declaration calls for diversified energy sources, improved energy efficiency, and reduction of greenhouse gas emissions.

## Unsustainable Sustenance?

Low-birthweight babies are often fed a formula with extra nutrients and protein to help them catch up weight-wise and ensure they have adequate fat stores. A study in the 16 January 2007 issue of *Circulation* looked at newborns fed either fortified formula, regular formula, or breastmilk for the first nine months of their lives. At ages 6 to 8 years, the children fed enriched formula had significantly higher blood pressure than those in the other groups. The authors note that elevated blood pressure in childhood will probably carry over into adulthood and that lowering diastolic blood pressure at the population level by only 2 mm Hg could prevent nearly 100,000 heart attacks and strokes a year in the United States.



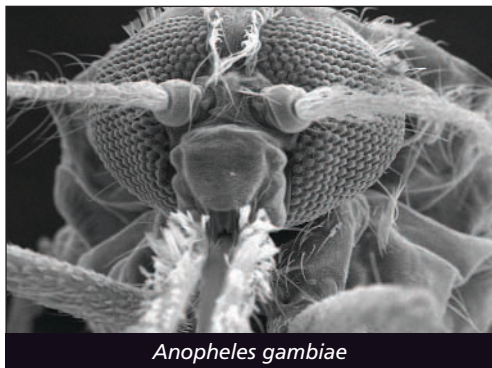
## INFECTIOUS DISEASE

## Safety Net for Malaria?

Pyrethroid-treated nets may be losing their effectiveness in preventing malaria, says a study in the February 2007 issue of *Emerging Infectious Diseases*. Mark Rowland, a senior lecturer at the London School of Hygiene and Tropical Medicine, and his colleagues found that treated nets killed only 30% of malaria-carrying *Anopheles gambiae* mosquitoes in an area of Benin where the *kdr* gene is highly prevalent; mosquitoes with this gene are less vulnerable to pyrethroids' neurotoxicity. In an area where *kdr* is rarely found, 98% of the mosquitoes were killed. "These findings are the first clear evidence of pyrethroids' failing to control an *An. gambiae* population that contains *kdr* resistance at high levels," the researchers write.

Treated nets are a primary means of fighting malaria in countries where the disease is endemic. "I think what we've identified here is the start of a problem which is going to get worse," says Rowland. "It may be that what we've uncovered at Benin exists elsewhere, but it hasn't been studied rigorously enough to prove that point."

WHO scientist Pierre Guillet says more study is necessary on actual malaria reduction conferred by treated nets, not just on the mortality of vectors, to draw broader conclusions about the impact of the *kdr* gene. The February paper also notes that in



*Anopheles gambiae*

Côte d'Ivoire, treated nets prevented malaria regardless of the prevalence of the *kdr* gene in mosquitoes—perhaps, Rowland speculates, because the *An. gambiae* mosquitoes there may be of a different type.

The insecticide both kills and repels mosquitoes, strengthening the physical barrier of the nets, which by itself is not enough to efficiently prevent malaria in real-life situations, explains Guillet. Volunteers in the study stayed in huts typical of the sort in which inhabitants of the region live. Even though treated nets were not lethal to mosquitoes with the *kdr* gene, they did deter 44% of the resistant mosquitoes from entering the huts.

According to Frank Collins, a professor of biological sciences at the University of Notre Dame, the implications of the study "are that resistance is going to emerge." New insecticides would not be the final answer, since mosquitoes probably would eventually develop resistance to them. This eventuality could be delayed, note Collins and Guillet, by treating nets with two insecticides, each with a different mechanism of action.

Even though such a strategy does not yet exist, and even in the face of developing resistance, treated nets remain vital, says Rowland: "Nets are still the best means of protection against malaria that we know of." The effort to provide treated nets has become a worldwide campaign. Nothing But Nets, founded by a diverse coalition of groups including the United Methodist Church and the National Basketball Association, is collecting money to buy and distribute nets in Africa. —Harvey Black

## SMOKING

## NRT in Pregnancy

Despite health warnings, at least 11% of U.S. women smoke during pregnancy. Smoking doubles the risk for low-birth-weight babies and raises the risk for preterm delivery and sudden infant death syndrome; premature and low-birthweight infants face increased odds for behavioral and learning problems and chronic disabilities such as cerebral palsy. Physicians typically have not viewed nicotine replacement therapy (NRT) as a safe alternative for pregnant women who can not or will not quit smoking. But a new study challenges that stance.

One reason physicians are reluctant to treat pregnant smokers with NRT stems from the findings of 20-year-old studies in which pregnant rats received nicotine doses well above those experienced by heavy smokers. Indeed, pregnant women would have to smoke up to 500 cigarettes a day to mirror those doses, according to Shabih Hasan, a neonatologist at the University of Calgary's Health Sciences Centre. In contrast, Hasan and colleagues treated pregnant rats with nicotine doses that replicate levels measured in the blood of pregnant women who smoke. The goal of Hasan's study was to

study the effects of nicotine on litter size and pup weight, given that fetal growth restriction is a known effect of maternal smoking.

At a nicotine dose of 2 mg/kg/day, both litter size and pup birth weights were normal. Even in the second and third trimesters, when clearance of nicotine slows, the rat mothers and fetuses stayed healthy. "High blood nicotine levels have no apparent effect on pregnancy in rats, including fetal weight gain," says Hasan, who reported the results in the 1 January 2007 issue of *Toxicology and Applied Pharmacology*.

Cigarette smoke contains 4,700 chemicals, including numerous toxicants and carcinogens. Hasan says short-term use of NRT during pregnancy could decrease exposure of mothers and fetuses to potentially more harmful components of cigarette smoke.

A Danish trial published in the December 2000 issue of *Obstetrics & Gynecology* provided some early clues to the safety of NRT on pregnancy. Half of 250 pregnant smokers received NRT as skin patches, and their babies' birth weights averaged 186 g higher than those born to women using placebo patches. Larger clinical studies are needed to monitor the safety and investigate the effectiveness of NRT in pregnant smokers, including long-term follow-up of mothers and babies, says Hasan.

"Logically, nicotine replacement should be safer than smoking, but there is no direct evidence that this is so," says Tim Coleman, an associate professor of primary care at the University of Nottingham. In March 2007, Coleman and his colleagues started recruiting more than 1,000 pregnant smokers in the United Kingdom for a double-blind, placebo-randomized trial of NRT in pregnancy. The trial, funded by the British National Health Service and the largest of its type ever conducted, will investigate the specific impact of nicotine on the developing human fetus and subsequently in infancy. Volunteers will receive nicotine or placebo skin patches and behavioral support to quit smoking. The women and babies will be followed for two years to evaluate medical and behavioral outcomes, according to the protocol described in the January 2007 *BMC Health Services Research*.

Meanwhile, pregnant smokers should not treat themselves with over-the-counter NRT products. "Unless blood, urine, and/or saliva levels of nicotine or its metabolites like cotinine are measured and closely monitored, women could inadvertently overdose themselves by continuing to smoke while using nicotine replacement products," Hasan cautions. Quitting smoking remains by far the best option. —Carol Potera

ehpnet

## Green Chemistry Institute

The Green Chemistry Institute (GCI) was formed in 1997 and became part of the American Chemical Society (ACS) in 2001. The institute works to advance the growth of green chemistry and green engineering, a movement to develop and implement manufacturing processes that are both economically sound and environmentally sustainable. Information on the institute's different activities and a wealth of resources are available at <http://chemistry.org/greenchemistryinstitute>.

The GCI site includes an overview of green chemistry and green engineering, and outlines 12 principles underlying each. The homepage also has a News section, divided into Green Chemistry Updates and Headlines Around the World. The updates link to information on ACS events (such as round-

tables, workshops, and meetings), announcements of new resources in the field, and other notable happenings. The Research section of the site has details about GCI funding opportunities and fellowships.

The Education section provides educational resources categorized by four levels: graduate, undergraduate, high school, and primary school. In the Undergraduate section, for example, are green engineering modules for chemical engineering courses that include problems and case studies that can be put into use in traditional classes. Also on offer is the ACS publication *Greener Approaches to Undergraduate Chemistry Experiments*, a collection of 14 laboratory activities that use green chemistry principles to investigate typical topics in undergraduate chemistry. The coursebook *Introduction to Green Chemistry* is also available in this section, as is a group of case studies based on the winners of the Presidential Green Chemistry Challenge Awards. A list of postsecondary schools in the United States and abroad that offer green chemistry programs is also featured in the Education section.

The Industrial Implementation section of the site offers a glimpse into resources the institute offers to companies. The GCI conducts professional training in green chemistry principles, applications, methods, tools, and techniques. It also provides technical assistance in the forms of opportunity assessments, databases of new technologies, and benchmarking. Finally, the institute furnishes companies ways to gain recognition for their green efforts through media and community outreach, the Presidential Green Chemistry Challenge Awards, and an annual Green Chemistry and Engineering Conference.

The International Cooperation section includes links to the 23 international chapters of the GCI. These chapters conduct educational programs in their countries, host green chemistry events, and produce publications. One of the three chapters in the United Kingdom has developed a green chemistry program targeted at consumers and retailers.

The Resources section of the GCI site indexes links under seven categories. Among other offerings in the Electronic Tools category is the Green Chemistry Resource Exchange, a searchable database of news articles, journal articles, reports, and presentations. By joining the exchange, visitors can add new entries to the database and receive updates on advances in the field. —Erin E. Dooley



ACS Green Chemistry Institute

## Tortillas Take a Tumble in Mexico

Demand for the grain-based fuel ethanol is dramatically increasing international prices for corn, leading to a food crunch in Mexico, where tortilla prices have tripled or quadrupled since last summer. The

27 January 2007

*Washington Post*

reports that

lower-class

Mexicans get

more than 40%

of their protein

from tortillas,

which also provide

an important source

of dietary fiber. The

price increase threatens to

result in a shift toward cheaper, less nutritious

foods. In an effort to stem the price increases,

Mexican president Felipe Calderón has instituted

an agreement with business leaders to cap

tortilla prices.



## Decline in Testosterone Levels

In a study notable for its large sample size and long duration, researchers from the New England Research Institutes report a substantial populationwide decline in testosterone levels over the past 20 years. The report on the Massachusetts Male Aging Study appears in the January 2007 issue of the *Journal of Clinical Endocrinology and Metabolism*. The decline appears unrelated to normal aging or to any health or environmental effects known to influence testosterone levels. Declines were measured at about 1.2% per year—about 17% overall between the years 1987 and 2004. Lower testosterone concentrations are linked with increases in age-related diseases, depression, and infertility.

## Amphibian Ark

Over the past decade, up to 170 species of frogs have become extinct due to the spread of *Chytrid* fungus, which affects amphibian respiratory and nervous systems. Close to 2,000 other species are threatened. In

February 2007,

the international

Amphibian Ark

project was

launched in

Atlanta, Georgia.

The project is

asking zoos,

aquariums, and

botanical gardens

to house

threatened frogs until the fungus can be controlled.

Amphibians are a key component of ecosystems,

eating insects that other animals do not.

Amphibians also are medically important; various

species produce compounds used in

pharmaceuticals. Fundraising will commence next

year to raise the estimated \$400–500 million it will

take to complete the project.

