

LIVESTOCK ISSUES

On Hens and Needles

Asian governments alarmed at the unprecedented spread of the deadly H5N1 avian influenza virus are seeking relief in a controversial vaccination program. The Thai government announced in February 2005 that it would join China and Indonesia in vaccinating select healthy ducks and chickens. Vietnam also is considering a vaccination program.

Vaccinations can lessen the risk of influenza by reducing the birds' chances of infection and minimizing the amount of virus shed through nasal secretions and feces by those that do become infected. But vaccinated chickens can still become infected while showing no symptoms of disease (chickens that have not been vaccinated typically die within 48 hours of infection). For that reason, many countries—including Japan, one of Thailand's biggest poultry markets—ban imports of vaccinated chickens. Countries therefore usually vaccinate poultry against influenza only as a last resort.

"The concern is that if a vaccine is used, it will be harder to identify the virus," says epidemiologist Mark Katz of the Centers for Disease Control and Prevention, "and it's not a guarantee that vaccination will completely eliminate the shedding of virus."

Asian farmers, though, are running out of options. Mass culling has done little to stem the epidemic. More than 120 million chickens in Vietnam, Thailand, and China died or were destroyed during a three-month period early in 2004. A 2 September 2004 article in *Nature* says many Thai farmers are turning to ineffective black-market vaccines to avoid killing their birds. But black-market vaccines can contain viruses that have not been properly inactivated, and may spur the evolution of even more dangerous strains.

Moreover, the virus poses the serious threat of sparking a worldwide human pandemic. H5N1 is highly virulent in humans, with a

death rate of more than 60%. What's kept the virus in check among humans so far is its inability to spread readily from person to person. Fewer than 10 of the 79 confirmed human cases are thought to have resulted for person-to-person contact—most victims handled infected poultry. Scientists believe, though, that H5N1 could mutate into a strain that spreads as easily among humans as the common cold.

"If you put less virus back into the environment, there's less chance of transmission," says David Swayne, laboratory director at the U.S. Department of Agriculture's Southeast Poultry Research Laboratory. "The negatives of vaccination are small if it's used properly."

The best prospects for containing avian flu come from using vaccines in conjunc-

tion with rigorous surveillance, quarantines, escape-proof poultry coops, and disinfection of poultry handlers and their equipment. Through much of Southeast Asia, though, low budgets and a weak infrastructure hinder such commonsense measures. Millions of peasants, each raising a dozen chickens in their backyard, are simply beyond the reach of government efforts.

Yet another barrier to stemming the epidemic is the reluctance that developing countries have to reporting news that could hurt their economies. Mainland China, where scientists believe the virus first emerged before 1997, acknowledged avian flu for the first time only in 2004, after outbreaks were reported in several neighboring countries. Chinese scholars later admitted in an article published 16 February 2004 in *Newsweek International* that the virus was rampant in several provinces as early as 2001.

H5N1 has become so entrenched in some regions of Southeast Asia that it has now established a permanent ecological niche in poultry, according to a January 2005 World Health Organization report, *Avian Influenza: Assessing the Pandemic Threat*. "The chance of complete eradication in the near future is very unlikely," Swayne says.

Still, Swayne sees reason for hope. In a 7 March 2005 review he wrote for the International Society for Infectious Disease, he deemed the commonly used inactivated AI vaccine effective, along with two new vaccines developed for use in Chinese poultry. And government-sponsored vaccination programs such as those in China and Thailand reduce the risk of farmers using black-market vaccines.

Juan Lubroth, a veterinarian specializing in infectious diseases with the Food and Agriculture Organization of the United Nations, agrees with Swayne that progress is being made in the fight against H5N1, albeit slowly. "I think we'll have a few years to deal with this virus," Lubroth says. "But during that time, I think we'll strengthen the veterinary structure in Asia. Ultimately, it will be good for the production of other livestock." —**Cynthia Washam**



Preventive medicine? Several Asian governments have begun vaccinating healthy poultry in hopes of averting the spread of avian flu, but some scientists have concerns about the effectiveness of such programs.

INFECTIOUS DISEASE

ExPECTing the Worst

Dramatic media reports have alerted the public to the dangers of foodborne pathogens such as *Salmonella* and *Escherichia coli* O157:H7. But less-publicized microbes may soon become serious public health threats as well. Two foodborne bacteria, extraintestinal pathogenic *E. coli* (ExPEC) and antimicrobial-resistant *Campylobacter*, are becoming more prevalent, according to studies published in the 1 April 2005 *Journal of Infectious Diseases*.

ExPEC causes millions of urinary tract infections and an estimated 36,000 sepsis deaths each year in the United States alone, and untold numbers globally. ExPEC can live in the gut, but—unlike other classes of *E. coli*—causes infection only if it travels to other parts of the body. ExPEC can live in the intestine for weeks without causing symptoms before inducing illness elsewhere in the body, says Kirk Smith, supervisor of the Foodborne, Vectorborne, and Zoonotic Disease Unit of the Minnesota Department of Health. This delay in onset can create the illusion that an infection is caused by something other than a foodborne pathogen.

In the first *Journal of Infectious Diseases* paper, Smith and colleagues at the University of Minnesota–Twin Cities report their analysis of *E. coli* contamination in foods they bought at 10 Minneapolis–St. Paul markets between 2001 and 2003. They found *E. coli* in 24% of the 1,648 items sampled, including 92% of poultry items, 69% of beef and pork items, and 9% of ready-to-eat foods such as produce, cheeses, and delicatessen items. Almost half of the *E. coli* found in poultry products was ExPEC; about one-fifth of the *E. coli* from beef and pork and a small percentage of that from ready-to-eat foods was ExPEC.

The number of *E. coli* organisms found in each food sample was relatively low, says Sita Tatini, a professor emeritus of food science and nutrition at the University of Minnesota and senior author of the paper. However, ExPEC's virulence factors—the properties that permit it to infect tissue—allow even a small number of bacteria to cause disease, Tatini says.

The scientists also found that 94% of poultry samples contaminated with *E. coli* contained a strain that was resistant to at least one antibiotic. They isolated resistant strains from 85% of *E. coli*-contaminated beef and pork and from 27% of *E. coli*-contaminated ready-to-eat items.

The second paper focused on drug-resistant strains of *Campylobacter*. Kåre Mølbak,

director of the Department of Epidemiology at the Statens Serum Institut in Copenhagen, examined the clinical effects of human infection with *Campylobacter* strains resistant to quinolones and erythromycin.

By accessing the Danish government's national registry of patient admissions and discharges, Mølbak and his colleagues were able to track the outcomes of about 3,500 people who were diagnosed with *Campylobacter* infections between 1996 and 2000. Within 30 days of infection, patients with quinolone-resistant infections were more than six times as likely as patients infected with susceptible strains to die or suffer an invasive illness such as meningitis, abscess, pancreatitis, or hepatitis. Within 90 days of infection, patients with erythromycin-resistant infections were more than five times as likely to die or to be diagnosed with an invasive illness.

Antibiotic overuse by people is just one reason why we're now seeing more antibiotic-resistant microbes, says Wondwossen Abebe Gebreyes, an assistant professor of food safety and molecular epidemiology at North Carolina State University in Raleigh. Farmers in many countries use antibiotics not only to treat or prevent infection but also to promote growth of healthy animals. Fluoroquinolones have been used in human medicine since the 1980s, but it was not until farmers began to use them to treat animal infection in the 1990s that resistant bacterial strains appeared. In some countries, quinolone-resistant *Campylobacter* species are now more common than quinolone-susceptible strains.

In Denmark, the prevalence of *Campylobacter* species resistant to macrolide-class antibiotics such as erythromycin has dropped since 1998, when all growth promoters, including macrolides, were banned from use in livestock. "That's really good news," says Mølbak, "because that suggests that if you change the policy—for example, improve hygiene and management practices rather than give the animals antibiotics—then you are able to reverse the situation." Use of fluoroquinolones is limited but not banned in Danish livestock.

Indeed, in most countries, antibiotic use on farms is on the rise, and so is antibiotic-resistant bacterial infection in humans, says Martin Blaser, chair of medicine at New York University and president-elect of the Infectious Diseases Society of America. Resistance has "been recognized as a cost of antibiotic use for more than fifty years," Blaser says. "As a society, we're using more and more [antibiotics], so it's not surprising that resistance is growing."

—Melissa Lee Phillips

Seaweed for Safety

Researchers from Oregon State University and Northeastern University have found that certain red seaweeds including *Portieria hornemannii* and *Acrosiphonia coalita* can detoxify organic pollutants such as TNT and polycyclic aromatic hydrocarbons 5–10 times faster than any known terrestrial plant. TNT is found at the sites of sunken warships, while polycyclic aromatic hydrocarbons are emitted from watercraft. The scientists, who presented their research at the 2005 annual meeting of the American Association for the Advancement of Science, see their discovery possibly playing a role in seafood safety, with marine seaweeds being planted around aquaculture beds to protect oysters, clams, and other bioaccumulators from contamination.



Nations' Environmental Efforts Ranked

In January 2005 the second Environmental Sustainability Index was released, ranking 146 nations on their environmental stewardship efforts. Prepared by researchers at Yale and Columbia, the index is based on 75 measures, including hazardous waste generation, pesticide consumption, participation in international environmental agreements, and carbon emissions. The first index, which came out in 2002, was a wakeup call for countries, inspiring some to improve their performance. South Korea, for example, moved up 13 spots between the first and second indexes.

Finland, Norway, and Uruguay took the top three positions, while the United States ranked 45th. The lowest-ranking country was North Korea. The report cited a significant correlation between higher ranking and countries having open political systems and effective governments.

Sustainable Wildcrafting in Nepal

In Nepal, approximately 15,000 tons of medicinal plants are collected for export each year by villagers who often receive less than a living wage for their work and are encouraged by unscrupulous buyers to strip plant supplies. A coalition of Nepalese and U.S. product buyers, advocacy groups, and donors was set up in 2002 to promote sustainable collection among villagers and responsible buying among western purchasers, with certification as one incentive. These efforts are paying off: in January 2005 the Federation of Community Forestry Users, Nepal, received certification from the Rainforest Alliance for its handmade paper and herbal products. The federation's members manage community forests by sustainable principles and supply wildcrafted ingredients to the international herbal, medicinal, and natural products industries.



ASTHMA

A Gut Reaction to Antibiotics

Is the explosive rise in asthma and allergies being seen especially in children partially related to antibiotic use? Epidemiologic studies have found strong connections between antibiotic treatment and the later development of asthma and allergies. Yet, until recently, no studies had looked at how the two are linked. Now researchers at the University of Michigan in Ann Arbor have created a mouse model that offers clues to the mechanism behind the association.

Immunologist Gary Huffnagle and colleagues are the first to demonstrate in a mouse model that the disruption of beneficial intestinal bacteria by antibiotics allows yeast to take hold and flourish. They developed their mouse model specifically to study the relationship between antibiotic use and allergies. When mice inhale fungal spores known to trigger allergies in people, the allergic reaction is more potent in mice with an overgrowth of yeast in their guts.

In their studies, the Michigan researchers first treat mice for several days with the broad-spectrum antibiotic cefoperazone to destroy the gut flora. Then the mice are fed *Candida albicans*, a yeast that commonly lives in people. "This represents the clinical scenario of getting a yeast infection after taking antibiotics," says Huffnagle. Next, the mice are exposed nasally to spores of the mold *Aspergillus fumigatus* (a major indoor contaminant) and to egg white protein.

Results are showing that both allergens produce significant increases in inflammation-related white blood cells in the lungs of the

mice, and they elevate blood levels of key markers of allergic reactions, including IgE, interleukin-5, and interleukin-13. Mice not treated with antibiotics show much milder reactions to the allergens. The team's latest report appears in the January 2005 issue of *Infection and Immunity*. Future work with the model will investigate the actions of other antibiotics (such as amoxicillin) and allergens (such as pollen and dust mites).

How do changes in gut flora influence respiratory allergies? The answer likely involves oral tolerance, Huffnagle theorizes. Upon ingestion of allergens, the oral mucosa generate regulatory T cells, which circulate to the respiratory tract, where they suppress allergic reactions. "We live in a dirty world, and we swallow mold spores, pollen, dust, and other allergens constantly," says Huffnagle. These oral allergens trigger immune responses that instruct the rest of the body to be more tolerant of allergens so allergic reactions don't occur. Moreover, other studies have indicated that mice lacking gut flora cannot generate oral tolerance. When the gut flora are restored, oral tolerance returns.

Huffnagle plans to evaluate over-the-counter probiotics—concentrated supplements of beneficial bacteria—to identify which, if any, work best for replenishing gut flora. "[Probiotics are a] relatively new concept, and there's not a lot of precedent for their use now," says infectious disease specialist Bruce Klein of the University of Wisconsin–Madison. If future studies show that probiotics do replace flora, Klein adds, physicians may be inclined to recommend their use. Eating yogurt with live cultures also remains a good way to replenish gut flora following a course of antibiotics. —Carol Potera

NEUROLOGY

Triple Threat Activates Neurons

Scientists from the Marine Biological Laboratory in Woods Hole, Massachusetts, have reported on a potentially sinister synergy, showing that a combination of three common pollutants—bromoform, chloroform, and tetrachloroethylene—alters nerve cell development, whereas the toxicants alone or in pairs do not. The discovery is an intriguing first step toward understanding whether this trio of pollutants is linked to neurological disorders such as autism.

Carol Reinisch, an expert in chemical-induced neurotoxicity, had read in the scientific literature about the contamination of municipal drinking water in Brick Township, New Jersey, and its possible connection to higher autism rates in local children. Chemical wastes dumped at the town's landfill over the years had contaminated nearby wells with bromoform, chloroform, and tetrachloroethylene, and in 1983, the U.S. Environmental Protection Agency declared the landfill a Superfund site. In the 1990s, autism rates in the town started rising, and researchers from the Centers for Disease Control and the Agency for Toxic Substances and Disease Registry began to investigate in

1998. Although the incidence of autism was twice the national average, the federal scientists concluded in 2000 that the levels of individual well water contaminants were too low to adversely impact children's health.

Reinisch wondered whether the synergistic effect of the chemicals would tell a different story. Her lab was already using a surf clam (*Spisula solidissima*) embryo model to assess how polychlorinated biphenyls affect embryonic neuronal development. The transparency of the embryos and the fact that most basic molecular processes involved in early development are conserved across species make the surf clam a good model for such studies. She and her colleagues began studying the three well-water contaminants in combination.

When tested alone or in pairs, the toxicants produced no significant changes,



Brain teaser. The embryo of the surf clam yields intriguing clues to a potential neuronal threat.

even at levels 1,000 times those in the mixture. But the trio acted synergistically to upregulate a regulatory subunit of cAMP-dependent protein kinase, a ubiquitous protein involved in neurologic pathways and a key regulator of neuronal growth in the clam embryo model. The clam embryos also showed increased cilia movement. The study appears in the January 2005 issue of *Environmental Toxicology and Pharmacology*.

"The fact that several events are speeded up is abnormal," says Reinisch. Coauthor Jill Kreiling, a developmental biologist, adds, "We found something unusual going on neurologically, but we cannot say this is causing autism."

Now the team is testing the mixture in zebrafish embryos, and their preliminary results parallel those for clam embryos. They hope others will undertake experiments in mice, rats, and higher mammals in order to confirm the association.

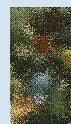
Studying mixtures of toxicants yields a more accurate picture of how contaminants work in the environment. "Most risk assessments look at single chemicals acting on single target organs with single outcomes, but that's not the way [exposures] work in nature," says Nigel Fields, a research program manager at the Environmental Protection Agency, which funded Reinisch's project. —Carol Potera

ehpnet

West Bengal & Bangladesh Arsenic Crisis Information Centre

Bangladesh and the neighboring Indian state of West Bengal are the site of what has been called the largest mass poisoning in history: millions of people here are drinking water that is heavily contaminated with arsenic. Researchers, engineers, and others who wish to learn more about this public health crisis can access the latest information and research at the West Bengal & Bangladesh Arsenic Crisis Information Centre, located at <http://bicn.com/acic/>. The page is a service of the Bangladesh International Community News website.

The homepage of the site features a color-coded map showing the levels of arsenic contamination across the region. More than half of Bangladesh's 10 million drinking water tubewells are contaminated with arsenic in concentrations exceeding World Health Organization guidelines. The United Nations Development Programme estimates that 20,000 people may die of arsenic-related disease each year; how-



**west bengal & bangladesh
arsenic crisis information centre**

ever, the numbers are hard to calculate because of the long time it takes for some cancers to emerge. If caught early enough, arsenic poisoning can be reversed with safe drinking water, nutritious foods, and time—three things most people of the region have little of.

The fully searchable site comprises pages of links to news and research articles, data sets, and online forums. Arsenic-crisis and WaterForum are Yahoo group forums that are available to anyone with access to the Internet. Participants may discuss, among other topics, arsenic geochemistry, remediation options, health effects, and related groundwater and surface water issues.

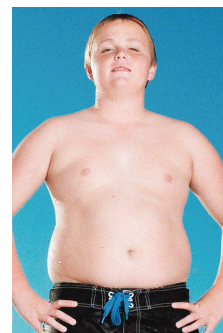
Other pages are devoted to reports, project documents, reference materials, and organizations and individuals from around the world who are involved in the arsenic crisis or related work. For example, a team at Harvard and the Massachusetts Institute of Technology is working to consolidate arsenic data, study the hydro-geochemistry of groundwater, and identify feasible, effective water treatment options for villagers, among other projects.

One page, Water Treatment & Alternative Supplies, specifically links to information on a variety of water treatment projects. Included here are sections on arsenic removal technology verification projects, removal technology providers and projects, alternative water supply technology providers and projects, and field test kits and other measurement-related resources. On another page, Health Effects & Medical Info, visitors will find suggestions for a homemade ointment to ease the suffering of the cracked palms and feet that can accompany chronic arsenic poisoning.

Visitors can also subscribe to *Arsenic Crisis News* through the site. This free newsletter covers such topics as arsenic geochemistry, water treatment technologies, epidemiology, disease mechanisms, and medical treatments. The site provides a list of arsenic-related conferences as well as a bibliography of books and other media, along with ordering information for these resources. —Erin E. Dooley

Obesity Cuts Longevity

The surge of obesity, especially among children and adolescents, could shorten life expectancy in the United States by 2–5 years, reversing the steady rise in longevity of the past two centuries, says a data analysis published in the 17 March 2005 *New England Journal of Medicine*. The predictions are based on data from the Third National Health and Nutrition Examination Survey and previously published reports on estimated years of life lost from obesity. Current trends indicate that rates of obesity will continue to rise, and that ever-younger age groups will be affected. The surge in obesity has already triggered a sharp rise in type 2 ("adult-onset") diabetes mellitus in children.



EU Holds Firm on REACH

On 4 April 2005 the European Commission announced its plan to introduce its controversial Registration, Evaluation, and Authorisation of Chemicals (REACH) policy for consideration by the European Parliament. The policy calls for the chemical industry to provide safety data for 30,000 chemicals. Business leaders, citing costs for testing, had urged the commission to require rigorous testing only for the 4,000–5,000 chemicals that pose the greatest risks. An impact study published 27 April 2005 did confirm that the policy could be pricey for businesses. But EU environment commissioner Stavros Dimas said he is convinced that the plan strikes the proper balance between protecting environmental and human health and protecting business interests. REACH was first proposed in October 2003 [see "REACHing for Chemical Safety," *EHP* 111:A766–A769 (2003)]. A final decision is expected in early 2006.

CFCs: A Dying Breed

China and Venezuela have pledged to phase out the use and production of chlorofluorocarbons (CFCs) by the end of 2007, two years earlier than required by the Montréal Protocol on Substances that Deplete the Ozone Layer. A total of US\$26.5 million from the protocol's Multilateral Fund has been allocated to finance the phaseouts. With these pledges, production of more than 100,000 tons of CFCs will be eliminated each year, and the use of CFCs in developing countries will end. China is the world's largest producer and consumer of CFCs, which are used as coolants, solvents, and propellants.

Protection against further degradation of the ozone layer should prevent millions of cases of skin cancer and cataracts resulting from harmful ultraviolet rays reaching the Earth's surface. The phaseout also means fewer emissions contributing to global warming.

