INFECTIOUS DISEASES

Stopping Asia's Avian Flu: A Worrisome Third Outbreak

Tokyo—Health officials are racing to contain an avian influenza outbreak that surfaced in South Korea in December, then in Japan and Vietnam early this month. It is virulent, they say: After making an unusual leap to humans, it has infected and killed at least five people in Vietnam. Ten more suspect cases in Vietnam are under investigation. Researchers have not yet determined the virus's DNA sequence or its source. But authorities in the region, using the only tool available, have killed more than 3 million potentially exposed chickens to slow its spread.

Although the virus appears to be transmitted only by birds and not person-to-person,

health authorities are watching it nervously. The more virus in circulation, the greater the chance it could reassort "into something with the lethality of the avian flu and the transmissibility of a human flu," says Ilaria Capua, a virologist at Italy's National Reference Laboratory for Avian Influenza, a part of the Istituto Zooprofilattico Sperimentale delle Venezie in Padua. The potential for this deadly combination is "frightening," says Capua, whose lab is also affiliated with the

Paris-based World Organization for Animal Health (OIE, from its French name). A more infectious variant could touch off a pandemic.

The virus behind these fears is known as influenza A subtype H5N1. Subtypes are categorized by the forms of two surface glycoproteins, hemagglutinin (H) and neuraminidase (N). H5N1 first surfaced in poultry in Hong Kong in 1997, when it jumped the species barrier into humans, killing six of the 18 people it infected. Humans have limited immunity to avian viruses, which means "this virus is bad in humans," says Robert Webster, a flu expert at St. Jude Children's Research Hospital in Memphis, Tennessee.

The reappearance of H5N1 was no surprise. Webster and others have been warning that it could touch off a pandemic ever since it first appeared in Hong Kong. The territory contained the outbreak by slaughtering all of the city's 1.4 million chickens and ducks. But experts have long believed that there are one or more animal reservoirs. "This virus is out there in large amounts somewhere," Webster says.

An evolved variant showed up in wild birds in Hong Kong parks in late 2002. Then in February 2003, a variant nearly identical to the wild bird form was isolated from a Hong Kong man, who died, and his son, who became seriously ill but recovered. The man's daughter had died of an undiagnosed respiratory illness while the family was visiting relatives in China's Fujian Province (*Science*, 7 March 2003, p. 1504). The source was never pinned down. But Kennedy Shortridge, a virologist and now a professor emeritus at the University of Hong Kong who was involved in the 1997 investigations, says that the evidence all pointed to "the existence of natural reservoirs in southern China." China has claimed in reports to OIE never to have had



Rising toll. Children have been hard hit by the return of avian flu type H5N1, which first caused an outbreak in 1997.

any large-scale outbreaks of avian influenza.

The appearance of H5N1 in South Korea, Japan, and Vietnam shows that the virus is spreading. But whether it was spread by migratory birds or infected poultry or poultry products is not clear. Webster developed a vaccine for the 1997 variant, but it's not known if it would have any effect on this latest version.

Outbreaks of highly pathogenic avian influenza are increasing in frequency and severity, Capua warns. There were only 17 outbreaks in the 40 years from 1959 to 1998, she says. But there have been six in the 6 years from 1997 to 2003—not counting the latest incidents.

Capua suspects a combination of factors. The most important may be a phenomenal growth in demand for poultry, leading to denser concentrations of larger poultry farms without appropriate biological safeguards. Once an infection is introduced into this environment, "it spreads very rapidly and is very difficult to get rid of," she says. Even if the virus is successfully contained this winter, Capua believes it is only a matter of time before it reappears. **–DENNIS NORMILE**

ScienceScope

Royal Society Says Panel Needed for Bioweapons Treaty

LONDON—The U.K.'s Royal Society (RS) this week called for the creation of an independent scientific body that would help give teeth to the Biological and Toxin Weapons Convention. The treaty, which came into force in 1975, has been called a paper tiger because it failed to prevent signatories such as the Soviet Union and Iraq from pursuing advanced weapons programs. Negotiations over a protocol to strengthen the treaty bogged down in 2001.

The RS argues that a science panel could advise governments on developing new countermeasures to threats and improving approaches for verifying treaty compliance. But the idea may be ahead of its time. With nations nowhere near a consensus on how to fortify the treaty, diplomats may have little use for scientific advice. Says one analyst, "The climate is just not ripe." The next treaty-review conference is set for 2006. –RICHARD STONE

-RICHARD STON

Scientists Trek to South Dakota to Push Homestake

Some physicists and politicians are trying to rescue a drowning plan to convert an abandoned South Dakota gold mine into the world's deepest underground laboratory. State Governor Mike Rounds (R) last week announced that he had signed a long-delayed deal with Barrick Gold Corp. to transfer its flooding Homestake mine in Lead to state ownership, protecting the company from legal liability. A team of scientists led by Jordan Goodman, physics department chair at the University of Maryland, College Park, traveled to the state this week to help drum up support for the plan, which must be approved by the state legislature.

In 2001, physicists launched an ambitious effort to transform Homestake into a \$300 million state-of-the-art buried lab for astrophysics and other experiments that need shelter from cosmic radiation. The push all but died last year, after efforts to negotiate a transfer agreement stalled and the company announced that it was turning off pumps that kept the century-old mine dry (*Science*, 6 June 2003, p. 1486). That led some key scientists to abandon the idea and back competing sites in Washington, Minnesota, and California.

Homestake backers hope the new deal will resuscitate support. They note that a National Science Foundation advisory panel has already endorsed the South Dakota mine as the best available option. But the agency is probably years away from deciding whether it wants to push for any underground laboratory, and Congress is even further from funding one. –DAVID MALAKOFF Green Party and a strong critic of GM crops, outlined her proposal for a new law regulating genetic technologies. Although the proposal would allow farmers to plant E.U.approved crops, it would also hold them liable for any contamination of the crops of neighboring organic farmers with GM pollen or seeds. Such a rule would not only discourage farmers from planting the crops commercially, says Heinz Saedler of the Max Planck Institute for Plant Breeding Research in Cologne, but would also strongly discourage scientists from conducting field trials of new crops. The proposal may still be modified before it is officially introduced to the Bundestag in February, and Saedler predicts that the current form would face strong opposition in the upper house of parliament, where the opposition Christian Democrats hold a majority. **-GRETCHEN VOGEL**

Experts Recommend a Cautious Approach

To lessen the chance that genetically modified organisms (GMOs) might harm humans or the environment, researchers have come up with ways to isolate engineered species. Transgenic crops' pollen is hobbled so it doesn't spread herbicide-resistance genes to weeds, for example, and growth-enhanced salmon have been sterilized to prevent them from competing with native species if they escape from their ocean pens.

Such approaches may not be good enough, according to a report^{*} from the National Academy of Sciences (NAS) released

this week. No biological barrier to gene flow—called bioconfinement—is likely to be completely effective, and thus multiple safeguards are needed. But most approaches are untested, the report adds, and it calls for more research into devising and evaluating bioconfinement strategies.

A second report[†] out this week, from the Pew Initiative on Food and Biotechnology, points out the need to clarify regulations of GM arthropods. Such bugs have the potential to disrupt transmission of malaria and other diseases, but it's not clear which U.S. government agencies will oversee their day

agencies will oversee their development.

Not all GMOs will need to be confined, the NAS panel found. Those engineered with benign traits, such as plumper fruit, should be safe. The need for bioconfinement is greater if GMOs contain worrisome traits or are released in droves. Researchers will need to evaluate GMOs individually, defining how much bioconfinement is enough to reduce the chance of gene flow to an acceptable level. "The issue is how unlikely it has to be," says David Andow of the University

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of Minnesota, Twin Cities (UMTC).

Getting confinement right is important, the panel notes, because in most cases there are few options for detecting escapes or dealing with their consequences. Better markers, sampling strategies, and monitoring methods should be developed. In addition, bioconfinement techniques themselves need greater scrutiny, especially field testing, the report concludes. "There are few cases where people have looked at the long-term reliability of these methods," says committee member Anne Kapuscinski of UMTC. And because

> multiple defenses will likely be needed, funding should be boosted to develop and evaluate new methods, say Kapuscinski and others. When it comes to the state of bioconfinement technology today, says Steven Strauss of Oregon State University in Corvallis, "basically we're at square one."

> Also at the starting block, according to the Pew Initiative, is the regulatory system for transgenic arthropods. Researchers hope to control plant pests by creating sterile insects or stop the transmission of

malaria by introducing disease-resistant mosquitoes. Although the U.S. Department of Agriculture has a regulatory pathway for plant pests, it's not clear who has authority for other kinds of GM arthropods. "It's a quagmire," says molecular geneticist David O'Brochta of the University of Maryland, College Park.

A more glaring problem is the lack of a clearly defined risk-assessment procedure for GM arthropods, says Ravi Durvasula of Yale School of Public Health, who's trying to prevent the kissing bug from transmitting Chagas disease. These issues, the report says, should be worked out before GM arthropods are ready to be released.

-ERIK STOKSTAD

ScienceScope

GAO to Investigate NIH Consulting Rules

Troubled by possible conflicts of interest at the National Institutes of Health (NIH), three House Democrats want the U.S. General Accounting Office (GAO) to examine the extent of consulting at NIH and its disclosure policies.

A December *Los Angeles Times* story described millions of dollars in consulting fees paid by companies to some highranking NIH researchers and suggested that the deals often posed conflicts of interest (*Science*, 19 December 2003, p. 2046). NIH is now reviewing its policies and was scheduled to discuss them this week at a Senate hearing.

In a 16 January letter to GAO, Henry Waxman (D–CA), John Dingell (D–MI), and Sherrod Brown (D–OH) also ask the agency—Congress's investigative arm to see how NIH's procedures compare with those of other science agencies and evaluate how NIH is responding to the furor kicked up by the media coverage. GAO is likely to take on the study, but its reports typically take months or more to complete.

-JOCELYN KAISER

UNC, NIEHS Plan Environmental Gene Bank

Environmental health researchers are hoping to enroll 20,000 volunteers in a new DNA biobank aimed at ferreting out links among genes, toxic exposures, and disease.

The project, announced last week by the National Institute of Environmental Health Sciences (NIEHS) and the University of North Carolina, Chapel Hill (UNC), will recruit patients from university clinics. Unlike some other large biobanks in Iceland and elsewhere, the registry will collect only subjects' blood, not health information. But coded names and addresses will be retained so subjects can later be invited to participate in clinical studies, says Perry Blackshear, NIEHS director of clinical research. Researchers at NIEHS and UNC are particularly interested in studying genes suspected to play a role, for example, in repairing DNA, metabolizing toxicants and drugs, and modulating responses to air pollutants. Outside researchers can also apply: "We plan to make it available to all noncommercial investigators," Blackshear says.

In an 8-month pilot project with 600 patients, about 80% agreed to donate their DNA. Based on that, it could take just 2 to 4 years to build the repository, Blackshear says, at a cost of under \$1 million.

-JOCELYN KAISER



Risky? Concern about making the kissing bug a GM target.

^{*} Biological Confinement of Genetically Engineered

Organisms, National Research Council, 2004. [†] Bugs in the System? Pew Initiative on Food and Biotechnology, 2004.