



Too close for comfort. Chickens, such as these at a Nanjing market, may transmit H7N9 to people.

scale. China's National Avian Influenza Reference Laboratory in Harbin has collected more than 84,000 samples, 47,801 of which have been tested, says the lab's director, Chen Hualan. Only 39 were positive. Chen says that 19,978, or roughly 40%, of the processed samples involved serological tests, which look for antibodies that remain in the blood even after an animal clears the virus. Such tests are "crucial", Sims says, because they detect past infections. The remaining tests were on cloacal and tracheal swabs, which capture the virus if taken only within a 2- to 3-week window when infected birds shed the virus in feces and saliva.

Wild birds may play a role in the virus's spread as well. The H7N9 variants now in circulation most likely evolved by combining genes from viruses found in Beijing bramblings, Zhejiang ducks and Korean wild birds (*Science*, 12 April, p. 129). Over the last few weeks, researchers have collected 800 fecal samples from wild birds in wetlands in south-east China; they are now testing them, says Lei Fu-Min of the Institute of Zoology of the Chinese Academy of Sciences in Beijing. But so far, H7N9 has not been found in the wild save for a single infected pigeon.

One farmed pigeon also has tested positive, but all other infected birds—mainly chickens and ducks—were found for sale at marketplaces. Sims says he expects to find more infected birds at farms. "If you have the virus in a market," he says, "it's impossible to not have the virus somewhere on farms."

Chinese authorities have already culled more than 100,000 birds and have closed many of the live animal markets in affected areas. At a press conference last week, Michael O'Leary, the head of WHO's Beijing office, said that limited culling makes sense in places that have known infections but widespread culling—as was done with H7N7 and H7N1—does not. "I think in most situations it's premature to do that now," he said. That measure would be advisable, he said, if studies later show that the virus is easily transmitted in poultry.

If culling becomes the method of choice to control the disease and protect human health, it will be critical to offer fair reimbursement to farmers. Otherwise, "some farmers may hide their birds to prevent them from being killed," says Chen Huanchen, a veterinary scientist at Huazhong Agricultural University in Wuhan. Current compensation poli-

INFLUENZA

Despite Large Research Effort, H7N9 Continues to Baffle

SHANGHAI, CHINA—If the influenza virus known as H7N9 had a bumper sticker, it would read, "HUGE MYSTERY." Nearly a month after the first reported cases of people infected with the bird flu virus, many puzzles remain about how it made the jump to humans and adapted to us, how to prevent transmission, and how frequently an infection causes disease.

Public health experts have fitful nights about the virus touching off a pandemic. But even if that nightmare doesn't come true, H7N9 may be here to stay, says Les Sims, an animal disease consultant in Palm Grove, Australia. "The fact that we have the virus in markets in three [Chinese] provinces and beyond tells me it would be a very difficult job to eliminate and eradicate the virus," he says.

As *Science* went to press, the number of laboratory-confirmed human infections had risen to 108, with 22 fatalities. Around 10 international specialists arrived in Beijing last week to consult with the Chinese government; the group includes Keiji Fukuda, the top official for influenza at the World Health Organization (WHO).

A study published in *Eurosurveillance* on 18 April suggests that H7N9 has spread widely in domestic birds in China, under the radar, before passing to humans. The report's authors—including Shu Yuelong, the director of the Chinese National Influenza Center in Beijing, and Marion Koopmans and Ron Fouchier of Erasmus MC in Rotterdam, the Netherlands—compared

the diversity of genetic sequences in H7N9 isolates to the genetic changes documented during outbreaks of two other intensely studied H7 viruses: H7N1, which emerged in Italy in 1999, and H7N7, which swept the Netherlands in 2003. The number of mutations in different H7N9 isolates, which came from several locations in eastern China and were found in people at roughly the same time, led the researchers to conclude that the changes likely occurred in birds.

Now that the virus has been discovered, it has become an acid test for China's animal health infrastructure. Since the 2003 SARS episode and the near-simultaneous outbreak of H5N1, another bird flu strain, the country has focused on improving veterinary epidemiology, aided by training programs from the U.N. Food and Agriculture Organization (FAO). So far, "China is doing a fantastic job in reacting to this crisis," says Vincent Martin, head of animal health for FAO's Rome-based Emergency Prevention System for Transboundary Animal and Plant Pests and Diseases.

A plan issued on 9 April by China's Ministry of Agriculture—which did not respond to faxed questions—calls for collecting samples from every poultry market and slaughterhouse in provinces with confirmed human cases, along with more limited testing in all other provinces. Pig slaughterhouses are being targeted as well. It's a "logical" strategy, Sims says.

And it's being implemented on a massive

cies vary by locality; Shanghai announced before it began culling on 6 April that farmers would be compensated for at least 50% of their losses, but many other areas are adhering to a 2005 government standard of \$1.61 per bird, which is widely seen as too low.

Meanwhile, surveillance has turned up scant evidence of transmission between people. One case of possible transmission from father to son has received extensive media attention, but it's possible they both had contact with the same bird, said O'Leary. Contacts of confirmed cases are typically tested for the virus or antibodies to it only if they develop symptoms, says Shu, thus mild cases might be missed. In addition to making it difficult to detect instances of human-to-human transmission, subclinical infections in people obscure bird-to-human spread.

On the other hand, there has been no direct contact with poultry in more than half the reported cases, O'Leary said. That suggests an unknown route of transmission—although O'Leary noted that “it is often difficult to determine all the exposures that the person might have, particularly when they



Deadly serious. H7N9 has caused severe disease in more than 100 people.

are thinking back a bit in time.”

To better assess H7N9 spread and disease severity in people, Shu and his co-authors suggest monitoring for conjunctivitis, or “pink eye,” the most common symptom found in the 89 humans who became infected during the H7N7 outbreak in the Netherlands. They also advocate looking for H7N9 antibodies in sera of people exposed to infected humans or birds. This might pick up asymptomatic cases as well as people who cleared infections, helping to clarify how the virus spreads. If

many such “silent” cases were found, it also would mean that the 20% fatality rate seen so far exaggerates the virus's true threat. “We are going to collect sera samples from high risk groups such as poultry workers to assess the risk of human infection,” Shu wrote *Science* in an e-mail.

However, detecting H7N9 antibodies in human sera is difficult. Decades-old studies have shown that the most commonly used test for influenza antibodies—the hemagglutination inhibition assay—doesn't work well for gauging mammalian immune response to avian viruses. That's why many groups rely on microneutralization assays, a more cumbersome and time-consuming test for avian viruses in humans that requires growing large amounts of the pathogen, says Gregory Gray, an epidemiologist at the University of Florida in Gainesville. “We need better assays,” Gray says. It's only one of the many urgent challenges posed by a virus that 1 month ago was unknown.

—MARA HVISTENDAHL, DENNIS NORMILE,
AND JON COHEN

With reporting by Della Fu in Shanghai.

U.S. IMMIGRATION REFORM

More High-Tech Visas, More STEM Education Funds

Valentina Waters always got good grades in math and science. But college was out of the question: As one of 11 siblings, she needed to work after graduating from high school to help support her family.

More than a decade later, however, Waters is studying chemical engineering at Saddleback College in southern California and hopes to carve out a career in the pharmaceutical industry. Although born in Russia, she became a permanent U.S. resident last year. And her dream is being realized with funds from an unexpected source: fees that the U.S. government charges high-tech companies and universities that want to employ a foreign scientist or engineer. It's a pot of cash that could soon grow significantly.

Last week, a bipartisan group of U.S. senators unveiled a sweeping proposal to overhaul the nation's immigration policies. The bill would create new funding streams aimed at strengthening STEM (science, technol-

ogy, engineering, and mathematics) education and training programs for U.S. students like Waters and enrich existing mechanisms. It's based on the idea that companies that hire foreign-born STEM workers should also help expand the homegrown STEM workforce. The proposal would also make it much easier

“just completely broken,” Senator Marco Rubio (R-FL), one of the “Gang of Eight” senators behind the proposal, told reporters. The 844-page bill (S. 744) aims to fix it by, among other things, creating a path to citizenship for an estimated 11 million undocumented immigrants already in the United

States and beefing up border security. It would also, Rubio said, “prioritize recruitment of immigrant entrepreneurs, innovators, investors, [and] skilled workers.” However, the plan faces uncertain prospects in Congress.

The bill fundamentally alters how some 1 million people a year win the legal right to permanently live and work in the United States. Under current policies, nearly three-quarters receive their

permits, or “green cards,” as a result of family ties to people already in the country. Fewer than 15% receive green cards based on their education or skills. The proposal would move to a nearly 50-50 balance in coming decades



STEM at work. Saddleback College engineering students visit California State University, Fullerton, in program funded by visa fees.

for foreign-born scientists and engineers to live and work in the United States, especially if they earn an advanced STEM degree from an American university.

The existing U.S. immigration system is