



AVIAN INFLUENZA

Evidence Points to Migratory Birds in H5N1 Spread

With the H5N1 avian influenza virus racing across the globe, scientists are debating new evidence on the role of migratory birds. As *Science* went to press, the virus had just been confirmed in a third African nation, Niger, one of the world's poorest countries. It had spread further in Europe and Asia, with 13 countries confirming outbreaks in just the past 2 months. And France reported the European Union's first outbreak in domestic poultry.

Increasingly, scientists are attributing this remarkably fast spread to migratory birds, but dissenters remain. One set of data that points to a role for wild birds comes from recent, unpublished analyses of influenza viruses recovered from outbreaks stretching from Russia and Kazakhstan to Nigeria, Iraq, and Turkey. A World Health Organization report issued last week,* which drew upon these analyses, concluded that all of the viruses involved in these outbreaks appear to be related to the strain identified from Qinghai Lake in northwestern China, where an outbreak killed 6000 wild birds last spring. And instead of the constant evolution typical of avian viruses, the Qinghai variant appears to have remained unusually stable for nearly a year. "This finding raises the possibility that the virus—in its highly pathogenic form—has now adapted to at least some species of migratory waterfowl and is ... traveling with these birds along their migratory routes," the WHO report concludes.

That case is strengthened by the first documented identification of the H5N1 virus in healthy migratory birds, reported in the 21 February issue of the *Proceedings of the National Academy of Sciences (PNAS)*. Some researchers have expressed skepticism that migratory birds play a major role in the spread of H5N1, arguing that infected birds would die before traveling very far (*Science*, 21 October 2005, p. 426). The new findings, from a collaboration led by Yi Guan, a virologist at the University of Hong Kong, and virologist Robert Webster of St. Jude Children's Research Hospital in Memphis, Tennessee, suggest that's not always the case. Since early 2003, the team has collected more than 13,000 cloacal and fecal samples from migratory birds at Mai Po Marshes in Hong Kong and

Poyang Lake in Jiangxi Province, China. In early 2005, they isolated the H5N1 virus from six apparently healthy migratory ducks at Poyang Lake. The team also collected serologic samples from 1092 captured migratory ducks and found that 3.1% had antibodies to H5N1, indicating a prior infection.

The group's findings confirm that wild birds can carry the virus great distances. Their sequencing analyses show that the viruses iso-



Investigation. A veterinarian looks for signs of bird flu infection in a swan, found dead earlier in the day, at a lab in Arras in northern France on 22 February.

lated from Qinghai Lake are genetically linked to the two strains recovered from the wild ducks at Poyang Lake. Guan says this doesn't mean ducks from Poyang carried the virus to Qinghai but does suggest that these viruses are circulating among migratory birds.

Guan and his colleagues also have data suggesting that once an outbreak is established, the main route of transmission appears to be through poultry. The group has regularly sam-

pled poultry brought to markets in six provinces in southeastern China since 2000. Among the more than 51,000 birds studied, they found the virus in 1.8% of all ducks and 1.9% of all geese, as well as 0.26% of chickens. Sequencing of 121 influenza samples collected from birds in China, Indonesia, Malaysia, and Vietnam showed that the viruses fall into regional sub-lineages. Viruses recovered from wild ducks at China's Poyang Lake were related to two sub-lineages from different regions in southern China. Guan says that together, this suggests that the viruses have been endemic among ducks and geese in different regions long enough to evolve distinct phylogenetic signatures and that circulation among poultry, not

reintroduction from wild birds, is keeping the virus going in China. If migratory birds had repeatedly seeded the outbreaks, there would likely be fewer distinct regional differences in the viruses. Guan adds that this conclusion offers hope that the cycle of transmission can be broken if the virus is eradicated from poultry flocks.

The WHO report and *PNAS* study don't convince everyone that wild birds explain H5N1's alarming spread. "There is no single bird species that migrates due west-east," notes Richard Thomas, a spokesperson for Birdlife International. Guan counters that the spread could involve a complex interaction of humans transporting poultry and the movements of dozens of species of wild birds. "It is not easy to trace this step by step," he says.

The difficulty is seen in Europe, where dead swans symbolize the spread of the virus. Because they obviously succumb to the virus, no one thinks swans are carrying it great distances. "Swans become infected by other aquatic [bird] species," says Albert Osterhaus, a virologist at Erasmus University Medical Center in Rotterdam, the Netherlands. But he admits that as yet, surveillance efforts in Europe have not found H5N1 in any healthy wild birds. "We do not, at this moment, have the complete epidemiological picture," Osterhaus says. He adds that more surveillance of wild birds is needed along with lab experiments to study the behavior of the virus in different migratory species.

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