

Spotlight on Science at the Smithsonian

Bi-Weekly Newsletter | Vol. 4, No. 22 | 08 December 2006



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Smithsonian Under Secretary for Science



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- Dr. David Evans, Under Secretary for Science
- Theresa Mellendick, Editor, mellendickt@si.edu



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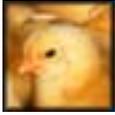


Shifting Genes Help
Track a Killer

Introduction from the Under Secretary for Science



In this installment of Spotlight on Science we feature the research of Smithsonian scientists working to understand the spread of avian flu. The deadly new strain H5N1 first emerged in Hong Kong in the 1990's. Since then it has devastated the poultry industry in Southeast Asia and infected birds as far away as Denmark. The number of human cases—and fatalities—is growing, raising fears of a global pandemic. Researchers from the National Zoo and Museum of Natural History are applying their knowledge of bird biology and molecular genetics to identify the pathways by which the virus is transported from one country to another by human trade and migratory birds. The better we understand these pathways, the better we will be able to control the disease's spread, and save the lives of its potential victims, both human and animal.



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Trade in live poultry and poultry products is key pathway by which the H5N1 avian flu virus has spread in Southeast Asia and elsewhere. It is the most likely means by which the virus will be introduced into the Western Hemisphere. Photo by Keith Weller, courtesy of the United States Department of Agriculture.

Predicting the Path of a Bird Flu Invasion

Since its first outbreak in Hong Kong in 1996, the deadly H5N1 strain of avian flu virus has spread to 52 countries in Asia, Africa, and Europe, killing more than 150 people and infecting untold numbers of wild and domestic birds. It has not yet reached the Western Hemisphere, but most experts believe that may just be a matter of time. Since the Asian outbreaks, wild bird migrations from Eastern Siberia into North America have been closely monitored to intercept disease-carrying flocks. But an exhaustive study by Smithsonian scientists and colleagues suggests that the disease will most likely get to the Americas by a completely different route: the international poultry trade. And it may enter the United States not from the north, but from the south.

The study was led by Marm Kilpatrick, of the Consortium for Conservation Medicine in New York, and included Smithsonian researchers Peter Marra and Robert Fleischer of the National Zoo and the National Museum of Natural history.

Using data from trade records, molecular biology, and decades of biological fieldwork, the researchers tracked the

spread of the disease by estimating the probable number of infected birds moving between countries via three distinct pathways: wild bird migrations, poultry exports, and international trade in captive wild birds, such as parrots and parakeets. They compared this with the international pattern of outbreaks over the past few years.

In Southeast Asia, outbreaks most closely followed the poultry trade. Elsewhere, the pattern was more complicated. The flu virus appears to have spread through Africa by a combination of trade and migration, with the virus jumping between domestic fowl and wild birds. In January 2006 unusually cold temperatures in Eastern Europe drove flocks of waterfowl westward in search of warmer weather. The birds brought the virus with them, introducing it to several western European countries.

Armed with this understanding of the spread of the flu virus so far, scientists hope to predict how it might continue to spread in the future. Very few bird species migrate between the eastern and western hemispheres. But there is a significant



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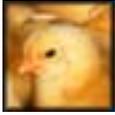
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trade in poultry and poultry products. And even if trade is halted from countries with reported poultry outbreaks, the virus's habit of moving between wild and domestic birds means infected birds could turn up with little warning in countries whose poultry flocks are thought to be disease-

free. Trade bans could also offer limited protection if the virus gained a foothold in a neighboring country that continued poultry imports, where it could be picked up by migratory birds, and then carried across international borders.



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A biologist swabs an emperor goose for avian influenza testing in Alaska. Though thousand of birds travel from Asia to North America across the Bering Straits each year, a more likely threat is migrants from the south infected by poultry imports. Photo by Donna Dewhurst, courtesy of the United States Geological Survey.

Dead Bird Birds Tell Tales

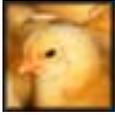
Water birds such as ducks geese and swans are prime reservoirs for many kinds of flu virus, but bird migrations don't usually pose much of a threat for long-distance spread of virulent strains. Sick birds normally can't fly very far. But the emerging highly pathogenic H5N1 virus appears to be different. Deadly as it is, it appears to be able to persist in migratory flocks long enough to be carried thousands of miles. This is one reason it is so dangerous.

Peter Marra at the Smithsonian's Migratory Bird Center is interested in the role of birds in spreading infectious disease, including insect-borne diseases such as West Nile Virus. For the current study, he focused his attention on the migratory routes by which the H5N1 could have spread through Eurasia and Africa, and how it might make the leap into the Americas.

Thousands of waterfowl of several species cross the Bering Straits each year in their annual migrations, mingling populations from Asia and North America. Because of the Asian origin of the bird flu outbreaks, surveillance to intercept the virus has concentrated on migratory stopovers such

as Alaska. But the numbers of Asian migrants traveling this route are dwarfed by the more than four million potential flu-carrying birds that cross the southern borders of the United States from wintering grounds in Latin America each year. No H5N1 outbreaks have yet been reported anywhere in Latin America or the western hemisphere, but if it enters via poultry imports, migrating waterfowl could quickly carry it north. This combination of poultry trade and wild migrants has been a potent mechanism for spreading the virus in Africa and Eurasia. Marra and his colleagues believe it is also the most likely way that it spread in the Americas.

Marra adds that only a tiny fraction of the birds in these incoming flocks would actually carry the flu virus, so wholesale testing of wild birds for early detection of the virus would probably not be worth the effort. A better approach would be to develop a system for reporting and testing sick and dead birds. Not only would this be a more efficient way of detecting birds infected with the H5N1 virus, but it could also turn up other emerging diseases not yet on our radar screen.



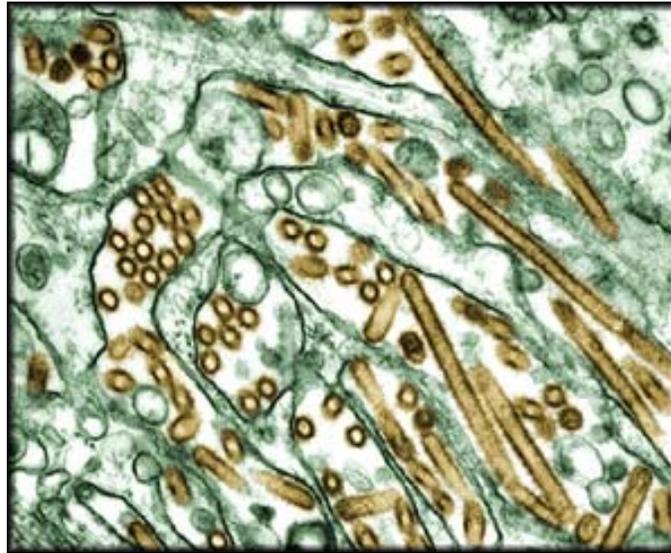
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Colorized transmission electron micrograph of Avian influenza A H5N1 viruses (seen in gold). Shifts in the viral genome have helped researchers fingerprint individual outbreaks and chart the pathways by which the disease spreads. Photo by Cynthia Goldsmith, courtesy of the Center for Disease Control.

Shifting Genes Help Track a Killer

Reference

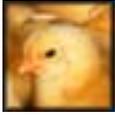
A. Marm Kilpatrick, Aleksei A. Chmura¹, David W. Gibbons, Robert C. Fleischer, Peter P. Marra, Peter Daszak, "Predicting the global spread of H5N1 avian influenza," *Proceedings of the National Academy of Sciences*, in press.

The lethal H5N1 avian flu virus can be passed from birds to humans, but it does not yet have the ability to pass from human to human. It is evolving extremely rapidly, however. As the virus has spread through Asia, Africa, and Europe over the past few years its genes have constantly changed. A shifty genome poses certain challenges for researchers—especially those hoping to develop a vaccine against the disease—but it also can help them trace its movements and track down the sources of outbreaks.

Robert Fleischer is head of the Genetics Program at the National Zoo and National Museum of Natural History. Most of the research in the Genetics Program is geared toward conservation biology and the study of evolution, but the program's methods are directly applicable to pressing questions such as the rapid spread of the avian flu.

For this study, Fleischer looked at DNA sequences from the HA gene of the H5N1 virus. This gene codes for the hemagglutinin molecule which protrudes

from the surface of the virus and is responsible for many of its distinctive properties. Using samples from 41 outbreaks across Asia, Africa and Europe, Fleischer constructed a family tree of the HA genes. In most cases, the lines of descent paralleled the pathways of the virus's spread the researchers had deduced based on trade and migratory data. But Fleischer's data also clarified some pathways that were unclear. For example, migrating birds enter Japan from both China and Korea; either could have been the source of Japan's two outbreaks of bird flu. But the genes of the Japanese virus most closely matched Korean sequences, so it was likely birds via Korea that introduced the flu to Japan. And in Europe, Italy and France both import poultry from Asia countries known to have suffered outbreaks. But the genetics of the viruses from Italian and French samples didn't match those of the Asian source countries. More likely, the virus was brought in by migrating birds from eastern Europe, where the viral genome was more similar.



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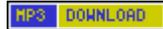
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