An Avian Flu Jumps to People

While researchers monitor U.S. pigs for potentially dangerous changes in swine influenza virus (see main text), recent events on the other side of the world have sounded an even more urgent alarm. Last month in Hong Kong, a 33-year-old man died and his 9-year-old son fell seriously ill after contracting an avian influenza virus from a source that remains mysterious.

Initial genetic sequencing suggests that the virus may be descended from one found in wild birds. If so, it could be difficult to contain. In all previously known cases of an avian flu jumping to humans, the source is believed to have been poultry. But “this virus hasn’t been seen in domestic poultry,” says Robert Webster, director of the World Health Organization’s (WHO’s) collaborating laboratory on animal influenza at St. Jude Children’s Research Hospital in Memphis, Tennessee. However, authorities have not ruled out the possibility that the virus came from chickens on a relative’s farm in mainland China.

Most flu viruses are adapted for a particular group of animals, although pigs can mix and match viruses from birds and humans. And on seemingly rare occasions, flu viruses have jumped the species barrier from other animals to humans. The last two human influenza pandemics, or worldwide flu epidemics, were caused by viruses that incorporated both human and avian flu genes. Because humans have no immunity to many strains of avian influenza, such viruses have deadly potential if they acquire the ability to infect human cells and move easily from one human host to another. However, Hong Kong health officials say that thus far there is no indication that the latest avian virus can spread from person to person.

All the same, WHO has declared an influenza alert, and its collaborating laboratories have moved into high gear. “We don’t know what the consequence of this virus will be. I wouldn’t trust it,” says Webster. He points out that in the most similar case known—an avian influenza virus that jumped from chickens to humans in 1997, infecting 18 people in Hong Kong and killing six—there was a 6-month lag between the first death and those that followed.

Further complicating the current case is the fact that the Hong Kong family had recently visited relatives who keep chickens in Fujian Province in mainland China. The man’s 8-year-old daughter died from an undiagnosed respiratory infection while there. And the deaths in this family coincide with an unidentified virus sweeping nearby Guangdong Province, infecting more than 500 people and killing at least seven. Researchers aren’t sure if the family has the same illness as those in Guangdong. Webster says the nature of the Guangdong outbreak is still unknown, but “WHO has a team investigating there now.”

The virus in the 1997 avian flu outbreak, labeled H5N1 for the particular forms of its surface molecules (“H” stands for hemagglutinin and “N” for neuraminidase), didn’t spread beyond those who’d had direct contact with infected birds. All 1.4 million chickens in Hong Kong were slaughtered with the hope of stamping out the virus (Science, 16 January 1998, pp. 324 and 393). But despite the massive slaughter, the virus survived—perhaps in backyard poultry or in other domestic or wild bird hosts—and has continued to evolve. The latest virus, also an H5N1 subtype, is believed to be its most recent descendant.

The HA molecule of the new virus is most similar to that of the 1997 H5N1, says Klaus Stöhr, director of the WHO influenza program in Geneva, but its overall genetic makeup most resembles that of a recently discovered relative that infected migratory wildfowl. That H5N1 virus felled ducks, geese, swans, greater flamingos, and wild little egrets in a Hong Kong park beginning last November. This means that the deadly H5N1 may already have spread. “It suggests [that] the virus is not necessarily confined to that park in Hong Kong, because it was found in free-roaming waterfowl,” Stöhr says.

It is unusual to see waterfowl sick with the flu, Stöhr says. Avian influenza viruses usually bind to receptors in the intestinal tract of their wild bird hosts and cause no symptoms. “The surprise was to find a highly pathogenic virus in waterfowl—the natural host for influenza,” says Stöhr. Domestic poultry do harbor low-pathogenic influenza strains. A highly pathogenic H5N1 virus, such as the 1997 Hong Kong virus, typically becomes deadly by mutating so that it can bind to cells throughout the bird’s body, rather than just in the intestinal tract. Then it can cause systemic and fatal disease in domestic poultry such as chickens and turkeys, explains Terrence Tumpey, an avian influenza expert at the U.S. Department of Agriculture’s Southeast Poultry Research Laboratory in Athens, Georgia. No one knows how such a virus might acquire the ability to infect humans, however, as avian influenza viruses typically bind to cell receptors not known to exist in people.

Now that another H5N1 influenza virus has crossed into the human population, public health experts are taking no chances. All the chickens in Hong Kong are undergoing vaccination for the virus, and a large number of already infected or potentially infected birds are being slaughtered. The park where the infected wild and exotic birds died was closed and disinfected, and the wild birds were killed.

WHO is helping coordinate preliminary work on a vaccine, e-mailing the viral sequence to its collaborating labs around the world. However, the virus is so virulent that it kills chick embryos within 2 to 3 days, making it impossible to use eggs to produce the vaccine, as is usually done, Stöhr says. Rather, labs will have to use the viral sequence to create a less virulent form of the virus in tissue culture, and then put this virus into eggs for vaccine production. “We are desperately working on a vaccine through reverse genetics,” says Webster.

“The goal is to make available a vaccine strain to all vaccine companies,” Stöhr adds—and so to have a vaccine available should this species-hopping virus manage an even more alarming leap: from one human host to the next.

—B.W.