

Researchers identify key step bird flu virus takes to spread readily in humans

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Since it first appeared in Hong Kong in 1997, the H5N1 avian flu virus has been slowly evolving into a pathogen better equipped to infect humans. The final form of the virus, biomedical researchers fear, will be a highly pathogenic strain of influenza that spreads easily among humans.

Now, in a new study a team of researchers from the University of Wisconsin-Madison report the identification of a key step the virus must take to facilitate the easy transmission of the virus from person to person.

Writing today (Oct. 4, 2007) in the journal *Public Library of Science Pathogens*, a team of researchers led by virologist Yoshihiro Kawaoka of the UW-Madison School of Veterinary Medicine has identified a single change in a viral protein that facilitates the virus' ability to infect the cells of the upper respiratory system in mammals. By adapting to the upper respiratory system, the virus is capable of infecting a wider range of cell types and is more easily spread, potentially setting the stage for a flu pandemic.

"The viruses that are in circulation now are much more mammalian-like than the ones circulating in 1997," says Kawaoka, an internationally recognized authority on influenza. "The viruses that are circulating in Africa and Europe are the ones closest to becoming a human virus."

As its name implies, bird flu first arises in chickens and other birds.

Humans and other animals in close contact with the birds may be infected, and the virus begins to adapt to new host animals, a process that may take years as small changes accumulate. Over time, an avian virus may gather enough genetic change to spread easily, as experts believe was the case with the 1918 Spanish flu, an event that killed at least 30 million people worldwide.

In the new study, which was conducted in mice, the Wisconsin team identified a single change in a viral surface protein that enabled the H5N1 virus to settle into the upper respiratory system, which "may provide a platform for the adaptation of avian H5N1 viruses to humans and for efficient person-to-person virus transmission."

Other currently undetermined changes are required for the virus to become a human pathogen of pandemic proportions, Kawaoka explains, but establishing itself in the upper respiratory system is necessary as that enables easy transmission of the virus through coughing and sneezing.

To date, more than 250 H5N1 human infections worldwide have been reported. Of those, more than 150 have been fatal, but so far efficient human-to-human transmission has not occurred. Most infections have occurred as a result of humans being in close contact with birds such as chickens that have the virus.

According to Kawaoka, the avian virus can be at home in the lungs of humans and other mammals as the cells of the lower respiratory system have receptors that enable the virus to establish itself. Temperatures in the lungs are also higher and thus more amenable to the efficient growth of the virus.

The new study involved two different viruses isolated from a single patient - one from the lungs, the other from the upper respiratory system. The virus from the upper respiratory system exhibited a single

amino acid change in one of the key proteins for amplification of influenza virus genes.

The single change identified by the Wisconsin study, says Kawaoka, promotes better virus replication at lower temperatures, such as those found in the upper respiratory system, and in a wider range of cell types.

"This change is needed, but not sufficient," Kawaoka explains. "There are other viral factors needed to cause a viral pandemic" strain of bird flu.

However, Kawaoka and other flu researchers are convinced it is only a matter of time, as more humans and other animals are exposed to the virus, before H5N1 virus takes those steps and evolves into a virus capable of causing a pandemic.

Source: University of Wisconsin-Madison

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