

# Good news! Avian Flu Pandemic

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Studies Suggest Avian Flu Pandemic Isn't Imminent

<http://www.nytimes.com/2006/03/23/science/23flu.html>

By NICHOLAS WADE

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Two groups of researchers, in Japan and in Holland, say they have discovered why the avian flu virus is rarely if ever transmitted from one person to another.

The reason, the researchers propose, is that the cells bearing the type of receptor the avian virus is known to favor are clustered in the deepest branches of the human respiratory tract, keeping it from spreading by coughs and sneezes. Human flu viruses typically infect cells in the upper respiratory tract.

The avian virus would need to accumulate many mutations in its genetic material before it could become a pandemic strain, said Yoshihiro Kawaoka, a virologist at the University of Tokyo and the University of Wisconsin.

According to a University of Wisconsin news release approved by Dr. Kawaoka, "The finding suggests that scientists and public health agencies worldwide may have more time to prepare for an eventual pandemic."

Dr. Kawaoka's finding is published in today's issue of Nature, and a similar finding, by Thijs Kuiken and colleagues at the Erasmus Medical Center in Rotterdam, appears in this week's Science.

Flu experts already knew that people who contract the current avian flu virus, a type known as A(H5N1) or H5 for short, are infected in the lower lung.

Paul A. Offit, a virologist at the Children's Hospital of Philadelphia, said the new reports helped explain why the H5 virus, though it can infect people, does not easily spread from one person to another.

Virologists agree that a flu pandemic will happen sooner or later as one of the 16 types of flu virus in the animal world, probably one that infects birds, will manage to switch hosts, and grow and spread in humans. But they differ over whether H5 is the likeliest candidate to make such a switch. Previous pandemics have been caused only by H1- (the

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1918 pandemic), H2- (the 1957 Asian flu) or H3-type viruses (the Hong Kong flu of 1968).

The H5 strain of avian flu has so far failed to develop a pandemic form. Some virologists fear it may need only better transmissibility. The new findings suggest that the virus could acquire such a property by switching its preference from the cell receptor found in the lower lung, known as alpha 2-3, to the receptor found on cells in the upper airways, known as alpha 2-6.

A team of scientists at the Scripps Research Institute reported in Science last week that only a couple of mutations might be needed to enable the H5 virus to make this switch to the alpha 2-6 receptor. This is the about same number of mutations made by the H1, H2 and H3 viruses when they adapted to infect people. Since viruses mutate fast, a two-mutation step is not such a big hurdle.

Because the H5 virus has killed about half of the 187 people it has infected, "a lot of its genes are already optimized for virulence," said James C. Paulson, a member of the Scripps team. For H5 to become pandemic, "the key gene that needs to be mutated is the HA gene," he said, referring to the hemagglutinin gene that makes the protein probe used by the virus to latch onto a cell's receptor sites.

Though H5 may seem only a couple of steps from transmissibility among people, many virologists believe mutations in several other genes would be necessary as well, even though those changes are not yet well understood.

Viruses find it difficult to switch hosts, and though they may quite often cause outbreaks in just a few individuals, "viruses that produce a self-sustaining chain of transmission in the new host appear rare," Dr. Kawaoka writes in the current Annual Review of Microbiology. "Most of these transfers are dead ends," he said.

The H5 virus has been present in the human population since the late 1950's, said Dr. Offit of Children's Hospital, but has never acquired the full set of mutations needed to set off a pandemic. Such epidemiological evidence "should make us feel safe that there's a substantial barrier," he said, noting the small number of people who have been infected.

Dr. Offit said it was a good thing to worry about the next flu pandemic, given that about three can be expected every century. "What's not good is to try to sell the public on their fear of pandemic flu being this particular bird flu, since if it's not, crying wolf will lose you credibility," he said.

Peter Palese, a virologist at the Mount Sinai School of Medicine, said he did not believe the H5 virus could infect people except when they were exposed to large doses, for example, by sleeping in the same room as chickens. "I feel strongly that H5 has been around in humans for a long time and never caused a pandemic, suggesting that this is not the virus which is likely to be the next pandemic," he said.

But like Dr. Offit, Dr. Palese said he fully supported plans for better preparations for the next flu pandemic, whatever its source. "People have to understand we are not really prepared should it come," he said.

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