

The Mutated Influenza Pig Virus Story

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In-depth Report: THE H1N1 SWINE FLU

PANDEMIC

The following text first published in December 2007 is relevant to the current debate and analysis on the H1N1 swine flu.

Posted on: December 23, 2007 4:06 PM, by revere

The recent report of a novel influenza virus in pigs, the H2N3 subtype, has been raised some alarm in certain quarters. I just read the paper itself (doi: 10.1073/pnas.0710286104) and then the account in CIDRAP News, which is both accurate and complete. I recommend it highly as a summary of this work. I have a bit to add, but first their concise summary of events leading to the investigation:

The discovery of the new virus began with an illness outbreak in pigs at a Missouri swine nursery in September 2006, according to the report. The pigs' lungs showed obvious signs of pneumonia, and tests showed the presence of an influenza gene, but the subtype could not be determined. Samples were submitted to the ARS [Agricultural Research Service] in Ames, where genetic sequencing and a search of a flu sequence database showed the virus subtype to be H2N3.

After the virus was subtyped, a record search revealed that another unidentified virus had been submitted in April 2006, from a 12-week-old pig at another Missouri swine farm, according to the report. Analysis by the ARS showed that this isolate too was an H2N3, and the two viruses were nearly identical.

The two outbreak sites are about 8 miles apart, according to Marie Gramer of the University of Minnesota College of Veterinary Medicine in St. Paul, a coauthor of the report. She said there was no connection between the two operations.

Phylogenetic analysis showed that the virus's hemagglutinin (HA) gene most closely matched the genes of H2 viruses isolated from North American mallard ducks, while the neuraminidase (NA) gene was closely related to that of an H4N3 virus found in blue-winged teal. Five of the other six genes were derived from swine flu viruses currently circulating in the United States, the scientists determined.

The source of the virus is unknown, but the likeliest possibility is pond water, which was used to clean barns and water the animals on both farms, according to the report. That transmission pathway has been described before. (Robert Roos, CIDRAP News)

influenza subtype, H2N2. H3N2 succeeded H2N2 as a circulating flu virus after the 1968 pandemic. Since that time only H1 and H3 subtypes have circulated, so if you are younger than 40 you've not had any exposure to an H2 flu virus. But this virus is in pigs, not humans. So what's the concern?

As most people know by now, flu viruses keep changing. They have more than one way to change and at least two of these, maybe three, have been involved in the changes that enabled the influenza virus to become a pandemic scourge in the last century. In the infamous 1918 Spanish flu, the virus appears to have jumped directly from birds to humans after some subtle and possibly minor genetic changes, but Mark and Adrian Gibbs have championed the idea the 1918 event was caused by homologous recombination between a human and swine virus, however, so some controversy remains. There is general agreement, however, that the 1957 and 1968 pandemics were the result of reassortment, that is, the swapping of entire segments of eight segments of the avian and human viruses. This virus seems to be a reassortant virus involving bird and pig viruses mixing and matching. The story, though, is a bit more complicated than this.

First the H2 part of the story. H2 influenza viruses continue to circulate in birds but there appear to be two lineages in birds, a Eurasian lineage and a North American one. The Eurasian H2 is more like the human H2 from the 1957 pandemic, but the new pig H2N3's H2 segment is more like the North American one seen in the H2N2 of mallard ducks. But it isn't identical. In particular, it differed at six places from the bird H2 and one of those places was position 226, known to be involved in the receptor binding determinant of the virus (for more on flu receptors see our posts here and here). Positions 226 and 228 are both important in differentiating "avian" from "human" receptors (but see the posts just linked for important qualifications regarding this too easy distinction) but only position 226 is changed to a more mammalian form in the new virus. The paper notes that in the 1957 pandemic, 226 changed first and then 228, so this pig version is like the early H2 virus in the 1957 pandemic but not yet like the full blown version with changes at both 226 and 228. Even if the virus had a full human type receptor, that isn't sufficient to make the virus into a transmissible human virus, since there is quite a bit of swine H1N1 with human receptors that doesn't circulate in humans.

The N3 was most like an N3 that currently circulates in blue-winged teals (an H4N3). An internal gene (PA) was similar to one found in mallards, but an H6N5, different than the H2N2 from mallards that contributed the H2. That leaves five more segments and they are characteristic of an influenza virus currently circulating in pigs, but the twist is that this virus is itself a triple reassortant of a bird, human and pig virus: PB1 is originally human, PB2 originally avian, and NP, M and NS swine. So the segments come from at least three different bird viruses, a human virus and a pig virus (possibly more).

This virus is also competent in more mammals than pigs. It was able to infect mice and ferrets and there was transmission to co-housed same species pigs or ferrets. It is thus mammalian adapted and there was serologic (blood antibody) evidence it continues to circulate in the pig stocks where it was isolated. No human illnesses have been reported among employees of these pig operations but antibody studies are only now underway so we don't yet know if there was any infection (albeit asymptomatic) in humans.

How big a deal is this? No one knows. Here are two views:

When asked whether the newfound virus currently represents a threat to humans, Gramer replied, "No more than any other influenza virus in the world. Transmission of flu from pigs to humans is likely rare. This flu itself is rare and we don't know if it is currently circulating in this farm or any other farm in the USA. We haven't found it again."

[snip]

Another expert, Michael T. Osterholm, PhD, MPH, generally concurred with Gray. "I think it's a potentially serious threat," said Osterholm, director of the University of Minnesota Center for Infectious Disease Research and Policy, publisher of CIDRAP News. "I think one of the problems we have is that we tend to think of influenza today, because of H5N1, as an Asian disease, with the roots of any future pandemic planted deep in Asia. But we have to be very careful because we don't know that."

Take your pick. I know which one I prefer. But wishing won't make it so.

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