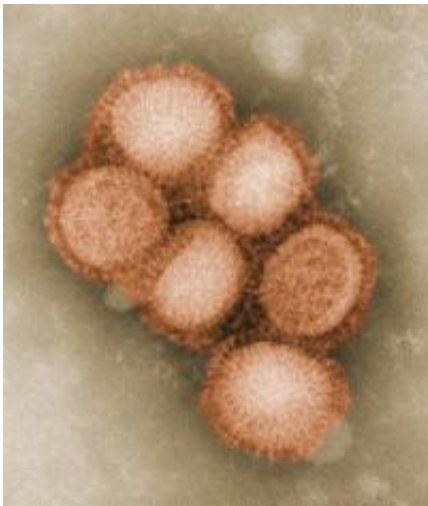


When well-known flu strains 'hook up' dangerous progeny can result

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Pictured is a negative stain electron microscope image of the H1N1 Influenza virus that was responsible for the 2009 flu pandemic. Credit: C. S. Goldsmith and A. Balish, CDC

A new University of Maryland-led study finds that 'sex' between the virus responsible for the 2009 flu pandemic (H1N1) and a common type of avian flu virus (H9N2) can produce offspring -- new combined flu viruses -- with the potential for creating a new influenza pandemic.

Of course, viruses don't actually have sex, but University of Maryland virologist Daniel Perez, who directed the new study, says new pandemic viruses are formed mainly through a process called reassortment, which

can best be described as viral [sexual reproduction](#). "In reassortment, two viruses enter the same cell; their [genetic material](#) is mixed; and new genetically distinct viruses emerge," explains Perez, an associate professor in the VA-MD Regional College of Veterinary Medicine, Maryland Campus.

According to Perez and his colleagues many factors are involved in the viability of new viruses that result from reassortment, but the most important is the compatibility of their two sets of viral genes to work together to form functional offspring. The importance of reassortment in the generation of viruses with pandemic potential, the scientists say, was demonstrated in 2009 when a novel H1N1 [influenza](#) (pH1N1) virus caused the first influenza pandemic in 40 years. That virus was identified as the product of a three way reassortment, between avian, swine, and human [influenza viruses](#).

In their current study, the researchers looked at the compatibility of the 2009 pandemic pH1N1 virus -- which has some [genetic characteristics](#) that may allow it to reassort more easily than other influenza viruses -- with an influenza strain known as H9N2.

Published in the *Proceedings of the National Academy of Sciences* (PNAS) the week of July 4-8, this new research builds on earlier findings by Perez and his team of the heightened communicability of the H1N1 virus as well as their work on the airborne communicability of H9N2. And it adds knowledge that may advance modern medicine's longstanding effort to learn how to predict when pandemic flu viruses will arise. An effort that in recent years has focused on study of H5, H7, and H9 subtypes of flu viruses because these all occasionally infect humans and, in the case of H5 viruses, can cause significant disease and death.

For their PNAS study, the researchers created four reassortant viruses

with one or two genes from the H9N2 virus and the rest of the genes from pH1N1. They used two different H9N2 viruses to provide the genes. One was a typical H9N2 isolated from a bird in Asia. The other was an avian isolate that had been adapted to infect and transmit in mammals.

Perez and colleagues looked at the growth characteristics of these four viruses and also their infectivity and transmissibility in ferrets. Ferrets are used as a model for human infections as they are susceptible to the same viruses and show similar signs of infection. All four viruses were able to grow to relatively high levels in cell culture. Similarly all four viruses infected ferrets and showed similar signs of disease and levels of replication. Additionally, they were all able to transmit to ferrets housed in the same cage and allowed physical contact. Finally, three of the four viruses were able to transmit to ferrets that were physically separated but shared the same air.

The new results are important for several reasons according to Perez. "Ours is the first study to show respiratory transmission of an H9 reassortant virus in mammals without prior adaptation. This is important because a new virus must be able to transmit via the respiratory route to impact the human population significantly. Secondly, adapting some of the genes to mammalian hosts allows for more efficient infection and transmission. Finally, these studies indicate that the pH1N1 and H9N2 influenza subtypes are highly compatible for reassortment with each other. And this compatibility means there is potential for the emergence of an H9 [influenza pandemic](#)."

More information: "Compatibility of H9N2 avian influenza surface genes and 2009 pandemic H1N1 internal genes for transmission in the ferret model," *PNAS*, July 4- 8, 2011.

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