1950s pandemic influenza virus remains a health threat, particularly to those under 50

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December 3, 2013) St. Jude Children's Research Hospital scientists have evidence that descendants of the H2N2 avian influenza A virus that killed millions worldwide in the 1950s still pose a threat to human health, particularly to those under 50. The research has been published in an advance online edition of the *Journal of Virology*.

The study included 22 H2N2 avian viruses collected from domestic poultry and wild aquatic birds between 1961 and 2008, making it the most comprehensive analysis yet of avian H2N2 viruses.

Researchers reported the viruses could infect human respiratory cells. Several strains also infected and spread among ferrets, which are susceptible to the same flu viruses as humans. Based on those and other indicators, one virus was classified as posing a high risk for triggering a pandemic.

Researchers found evidence the viruses were susceptible to current antiviral medications and could likely be controlled with an available prototype vaccine.

Such protection was unavailable in 1957 when an H2N2 virus that included genes from avian flu viruses emerged. Federal health officials estimate the 1957-58 pandemic killed 1 to 2 million people worldwide. While the H2N2 strain disappeared from flu viruses circulating in humans in 1968, it has persisted in the world's bird population.

"This study suggests H2N2 has the characteristics necessary to re-emerge as a significant threat to human health in part because most individuals under the age of 50 lack immunity to the virus," said corresponding author Robert Webster, Ph.D., a member of the St. Jude Department of Infectious Diseases. "This highlights the importance of continued surveillance of viruses circulating in animals and additional research to enhance our ability to identify viruses that are emerging health threats."

The research stems from the institution's role as a National Institute of Allergy and Infectious Diseases Center of Excellence for Influenza Research and Surveillance. St. Jude is also home to the only World Health Organization Collaborating Center focused on the spread of animal flu viruses to humans.

Historically, pandemic flu viruses arise when bird and human flu viruses swap genes. The mixing can result in novel viruses capable of spreading efficiently in humans and against which the human immune system is unprepared. "One school of thought regarding emerging flu viruses is that in more than 100 years, only three of the 18 subtypes of influenza A have caused pandemics. The H2 subtype is one," Webster said. The H2N2 viruses in this study remained genetically similar to the 1957 pandemic strain.

Along with being able to infect human trachea and other mammalian cells growing in the laboratory, five viruses also infected ferrets, according to researchers. Ferrets are a reliable model for studying flu's spread in humans. The five strains were among the nine H2N2 viruses that researchers tested in ferrets.

Three of the strains demonstrated a surprising ability to spread among ferrets housed in the same cage. The strains included the Dk/HK319/79 virus, which researchers classified as having high pandemic potential.

The virus was isolated in 1979 from a duck in Hong Kong. The other viruses were classified as having low to intermediate pandemic potential. None of the viruses studied in ferrets spread via airborne transmission.

In addition, none of the viruses showed changes in the two viral proteins viewed as indicators of avian flu virus adaptation to human infection and transmission. Those markers are the hemagglutinin (HA) protein that the virus uses to infect cells and the PB2 protein, which is required for viral replication. The viruses in this study had HA and PB2 proteins with a preference for infecting avian, rather than human cells.

"While these viruses genetically look very avian, this study shows they can behave like mammalian viruses and replicate in multiple mammalian models of flu," said the study's first author, Jeremy Jones, Ph.D., a postdoctoral fellow in Webster's laboratory. "That is troubling because some of the original H2N2 pandemic viruses looked avian when the pandemic began in 1957, but in a few short months, all of the isolated viruses had picked up the genetic signatures of adaptation to humans. Our results suggest the same could happen if the H2N2 viruses again crossed from birds into humans."

Work is underway at St. Jude to identify other changes that are critical to the ability of avian flu viruses to infect and replicate in mammalian cells, Jones said.

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