

Study confirms limited human-to-human spread of avian-flu virus in Indonesia in 2006

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In the first systematic, statistical analysis of its kind, infectious-disease-modeling experts at Fred Hutchinson Cancer Research Center confirm that the avian influenza A (H5N1) virus in 2006 spread between a small number of people within a family in Indonesia. The findings, by biostatistician Ira M. Longini Jr., Ph.D., and colleagues, appear online and will be published in the Sept. 1 print edition of *Emerging Infectious Diseases*, a journal of the Centers for Disease Control and Prevention.

Co-authors on the paper were biostatisticians M. Elizabeth (Betz) Halloran, M.D., D.Sc., and Yang Yang, Ph.D.; and epidemiologist Jonathan Sugimoto, M.H.S., a pre-doctoral research associate. All are within the Hutchinson Center's Public Health Sciences Division and Vaccine and Infectious Disease Institute.

The researchers based their findings on a cluster of eight flu cases within an extended family in northern Sumatra. Using a computerized disease-transmission model that took into account the number of infected cases, the number of people potentially exposed, the viral-incubation period and other parameters, the researchers produced the first statistical confirmation of humans contracting the disease from each other rather than from infected birds.

The cluster contained a chain of infection that involved a 10-year-old boy who probably caught the virus from his 37-year-old aunt, who had been exposed to dead poultry and chicken feces, the presumed source of infection. The boy then probably passed the virus to his father. The

possibility that the boy infected his father was supported by genetic sequencing data. Other person-to-person transmissions in the cluster are backed up with statistical data. All but one of the flu victims died, and all had had sustained close contact with other ill family members prior to getting sick – a factor considered crucial for transmission of this particular flu strain.

In an attempt to contain the spread of the virus, the local health authorities eventually placed more than 50 surviving relatives and close contacts under voluntary quarantine and all, except for pregnant women and infants, received antiviral medication as a precaution. “The containment strategy was implemented late in the game, so it could have been just luck that the virus burned out,” Longini said. “It went two generations and then just stopped, but it could have gotten out of control. The world really may have dodged a bullet with that one, and the next time we might not be so lucky,” he said.

Should a strain of avian flu acquire the ability to cause sustained human-to-human transmission, the results could be catastrophic, Longini said. “If not contained, the outbreak could spread worldwide through the global transportation network faster than the appropriate vaccine supply could be made available. That’s why it’s so important to ascertain whether human-to-human transmission is happening as well as the virulence of the strain.” The researchers estimated the secondary-attack rate of the virus in Indonesia – the risk of one infected person passing it to another – to be 29 percent, a level of infectiousness similar to statistical estimates for seasonal influenza A in the United States.

The researchers also aimed their statistical transmission-assessment technology at another large avian-flu cluster in eastern Turkey that in 2006 infected eight people, four of whom died. In this case, the researchers did not find statistical evidence of human-to-human transmission, most likely due to a lack of sufficient data. “There

probably was person-to-person spread there as well but we couldn't get all the information we needed for the analysis," Yang said.

The methods and software used in this research led to the development of a software application called TranStat, which will allow first responders to enter, store and perform real-time analysis of data from infectious-disease outbreaks. This tool soon will be available online free of charge via MIDAS, the Models of Infectious Disease Agent Study, which is supported by the National Institute of General Medical Sciences.

"We know the key to preventing a pandemic is early detection, containment and mitigation with antiviral therapy and this tool will enable those on the front lines, such as physicians, epidemiologists and other public-health officials, to carry that out efficiently," Halloran said. "The manuals on how to collect the necessary data are decades old. They are very outdated and incomplete. Often people on the front lines don't know what to do; they don't collect the correct data to assess whether transmission is occurring. TranStat will prompt people to gather precisely the data that needs to be collected to better understand and contain any infectious-disease spread, not just the avian flu," Sugimoto said.

If a smoldering disease cluster does flame out of control, the software also could be used to estimate the important characteristics of the virus – such as its transmissibility, secondary-attack rate and reproductive number – which would give public-health officials a better chance at slowing its spread until a vaccine or other effective control measures could be implemented. Yang and colleagues recently described the basis for the statistical methods used in the research in *The Annals of Applied Statistics*.

Source: Fred Hutchinson Cancer Research Center

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