

INFLUENZA: Notes about the Disease

The influenza virus is a wily microbe that causes epidemics of variable intensity every year. Among the vaccine-preventable diseases, “flu” is the only one for which a new vaccine has to be reformulated annually because of the ability of the virus to change over time. True influenza—a respiratory and systemic disease stemming from infection with an influenza virus—should not be confused with milder illnesses caused by other viruses and referred to with common names like “intestinal flu” or “24-hour flu.”

There are three major types of influenza virus: A, B, and C. The type C virus is of minor importance. The A and B viruses undergo minor mutations (or “drifts”) in their surface antigenic proteins on a continuous basis, thus necessitating the updating of the flu vaccine each year to protect against the changing strains. Additionally, the type A virus unpredictably goes through a major antigenic change (“shift”) from time to time, resulting in a new virus with pandemic potential.

Type A viruses are classified based on the composition of the hemagglutinin (H) and neuraminidase (N) antigens on their surfaces. They also acquire place names based on the geographic location where they were first identified. The current flu vaccine contains representatives of the most recent drifts of the A(H3N2), A(H1N1), and B viruses. The H3N2 virus first appeared in 1968 as the “Hong Kong” influenza virus, and the H1N1 virus mysteriously showed up in 1977 as the “Russian” flu virus. Both of these influenza A viruses are now known to be descendents of the human H1N1 virus that caused the deadly 1918-19 “Spanish” flu pandemic; the A/H2N2 “Asian” virus that circulated between 1957 and 1968 was also a descendent of the 1918 A/H1N1 strain. However, the 1977 H1N1 virus closely resembled the H1N1 strain that “disappeared” 20 years earlier when the H2N2 virus first appeared. (Where did this virus spend two decades essentially unchanged—in some USSR deep freeze?)¹

Certain animal groups (most importantly birds) can be infected with their own influenza A virus strains. One thing that makes birds so important is that viruses representing all 16 type A hemagglutinins can be found in various avian species, particularly feral aquatic birds. Some influenza viruses (e.g., H5 and H7) are particularly virulent for domestic fowl when they become infected through direct or indirect contact with wild birds. In 1997, 18 cases of H5N1 avian influenza were documented in humans in Hong Kong; a third of these were fatal. After all poultry in the Hong Kong commercial poultry industry were slaughtered (>1 million birds), no additional human cases of H5N1 disease were detected until 2003, although a couple of other avian viruses (H9N2 and H7N7) caused a few cases of human disease. Since 2003, >200 human cases of H5N1 flu with a case-fatality ratio exceeding 50% have been reported to the World Health Organization; almost all these cases seem to have been contracted via contact with birds or their excreta, but direct human-to-human transmission has not been ruled out in a few situations.²

Antigenic shifts in influenza A viruses can occur as a result of “reassortment” of the genome sequences of two different flu viruses simultaneously infecting a single host—perhaps a human, but quite possibly a pig or other animal. This process seems to explain how the viruses causing the pandemics of 1957 and 1968 arose from reassortment of one or both of the human H and N antigenic surface proteins of the, respectively, H1N1 and H2N2 human viruses extant at the times with circulating avian influenza virus proteins. However, the H1N1 virus that sprang up in 1918—though apparently from an avian source—did not originate from reassortment with any avian virus around at that time. The mystery of its origin remains unsolved. It simultaneously initiated separate lineages of H1N1 human and porcine viruses.³

The public health importance of influenza is enormous. The 40-50 million deaths worldwide resulting from the 1918-19 “Spanish” flu pandemic made that the worst pandemic of all types and times. Even today, in the United States there are, on average, about 36,000 deaths related to influenza *each year*.⁴ The possibility that the H5N1 avian influenza virus—or some other avian strain—might undergo reassortment or otherwise change to a virus capable of effective human-to-human transmission cannot be ignored, even though the starting day, month, or year of the next influenza pandemic can-

not be predicted. However, the inevitability of the next flu pandemic has stimulated the formulation of both national⁵ and state⁶ plans for dealing with this prospect. As part of the NC Pandemic Influenza Plan, documented **infection of a human with a novel influenza virus** is reportable immediately to the General Communicable Disease Control Branch. Also, because of concern by the Council of State and Territorial Epidemiologists about the prominence of pediatric influenza-related deaths during the 2003-04 season, CSTE recommended that reporting of **influenza-related deaths in persons under 18 years of age** be added to each state's list of reportable diseases and conditions.⁷ Accordingly, pediatric flu deaths are also now reportable in NC.

1. ED Kilbourne, "Influenza Pandemics of the 20th Century," *Emerg Infect Dis* 12 (2006): 9-14, www.cdc.gov/ncidod/EID/vol12no01/pdfs/05-1254.pdf.
2. "Epidemic and Pandemic Alert and Response: Avian influenza," *WHO*, 2007, www.who.int/csr/disease/avian_influenza/en/.
3. JK Taubenberger, Dm Morens, "1918 Influenza: The Mother of All Pandemics," *Emerg Infect Dis* 12 (2006): 15-22, www.cdc.gov/ncidod/eid/vol12no01/pdfs/05-0979.pdf.
4. AS Fauci, "Emerging and Re-Emerging Infectious Diseases: Influenza as a Prototype of the Host-Pathogen Balancing Act," *Cell* 124 (2006): 665-70, http://www3.niaid.nih.gov/about/directors/pdf/2-23-06_Cell.pdf.
5. "HHS Pandemic Influenza Plan," *US Department of Health and Human Services*, 2006, www.hhs.gov/pandemicflu/plan/.
6. "NC Pandemic Influenza Plan," *Epidemiology in NC*, 2007, www.epi.state.nc.us/epi/gcdc/pandemic.html.
7. "Influenza-Associated Pediatric Mortality," *Council of State and Territorial Epidemiologists Position Statement 04-ID-04*, www.cste.org/ps/2004pdf/04-ID-04-final.pdf.