Influenza virus infections in humans October 2018

This note is provided in order to clarify the differences among seasonal influenza, pandemic influenza, and zoonotic or variant influenza.

Seasonal influenza
Seasonal influenza viruses circulate and cause disease in humans every year. In temperate climates, disease tends to occur seasonally in the winter months, spreading from person-to-person through sneezing, coughing, or touching contaminated surfaces. Seasonal influenza viruses can cause mild to severe illness and even death, particularly in some high-risk individuals. Persons at increased risk for severe disease include pregnant women, the very young and very old, immune-compromised people, and people with chronic underlying medical conditions. Seasonal influenza viruses evolve continuously, which means that people can get infected multiple times throughout their lives. Therefore the components of seasonal influenza vaccines are reviewed frequently (currently biannually) and updated periodically to ensure continued effectiveness of the vaccines.

There are three large groupings or types of seasonal influenza viruses, labeled A, B, and C. Type A influenza viruses are further divided into subtypes according to the specific variety and combinations of two proteins that occur on the surface of the virus, the hemagglutinin or “H” protein and the neuraminidase or “N” protein. Currently, influenza A(H1N1) and A(H3N2) are the circulating seasonal influenza A virus subtypes. This seasonal A(H1N1) virus is the same virus that caused the 2009 influenza pandemic, as it is now circulating seasonally. In addition, there are two type B viruses that are also circulating as seasonal influenza viruses, which are named after the areas where they were first identified, Victoria lineage and Yamagata lineage. Type C influenza causes milder infections and is associated with sporadic cases and minor localized outbreaks. As influenza C poses much less of a disease burden than influenza A and B, only the latter two are included in seasonal influenza vaccines.

Pandemic influenza
A pandemic occurs when an influenza virus which was not previously circulating among humans and to which most people don't have immunity emerges and transmits among humans. These viruses may emerge, circulate and cause large outbreaks outside of the normal influenza season. As the majority of the population has no immunity to these viruses, the proportion of persons in a population getting infected may be quite large. Some pandemics may result in large numbers of severe infections while others will result in large numbers of milder infections, but the reasons behind these differences are not completely understood. The most notorious
pandemic for which data are available was the “Spanish Flu” in 1918-1919 which caused an estimated 20-50 million deaths worldwide. Subsequent pandemics in 1957 and 1968 resulted in many fewer deaths in spite of large portions of the world’s population being susceptible to infection.

In 2009, a strain of influenza A(H1N1) virus which had not ever been seen before, emerged, spread across the world and caused the 2009 H1N1 pandemic. This pandemic A(H1N1)2009 virus has been widely circulating across the globe since 2009, and is now established in human populations as a seasonal influenza virus, as described above. Currently there is no longer a pandemic virus circulating in the world.

**Zoonotic or variant influenza**
Humans can also be infected with influenza viruses that are routinely circulating in animals, such as avian influenza virus subtypes A(H5N1) and A(H9N2) and swine influenza virus subtypes A(H1N1) and (H3N2). Other species including horses and dogs also have their own varieties of influenza viruses. Even though these viruses may be named as the same subtype as viruses found in humans, all of these animal viruses are distinct from human influenza viruses and do not easily transmit between humans. Some may occasionally infect humans, however, and may cause disease ranging from mild conjunctivitis to severe pneumonia and even death. Usually these human infections of zoonotic influenza are acquired through direct contact with infected animals or contaminated environments, and do not spread very far among humans. If such a virus acquired the capacity to spread easily among people either through adaptation or acquisition of certain genes from human viruses, it could start an epidemic or a pandemic.

Over the past decades, there have been multiple instances of sporadic transmission of influenza viruses between animals and humans. When viruses of subtype A(H3N2) circulating in swine, began to infect people in the USA in 2011, they were labeled “variant” (with a “v” placed after the name of the virus) in order to distinguish them from human viruses of the same subtype\(^1\). The variant terminology is also used for other non-seasonal influenza viruses of a subtype shared with human seasonal influenza viruses, particularly viruses of the H1 and H3 subtypes circulating in swine, when these viruses are detected in humans\(^1\). For example, a non-seasonal influenza A(H1N1) virus detected in a human would be denoted as A(H1N1)v and a non-seasonal influenza A(H1N2) virus detected in humans would be denoted as A(H1N2)v. The current number of human infections with these variant viruses can be accessed on the Center for Disease Control web site at [https://www.cdc.gov/flu/swineflu/variant-cases-us.htm#table-infections](https://www.cdc.gov/flu/swineflu/variant-cases-us.htm#table-infections). Other animal viruses, e.g. avian influenza A(H5N1), A(H7N7), A(H7N9), and A(H9N2), infecting people are simply called “avian influenza”\(^2\)” or “zoonotic influenza” viruses.

When animal influenza viruses infect their natural animal host, they are named for that host, as in avian influenza viruses, swine influenza viruses, equine influenza viruses, etc. As such, the term “swine flu” refers to swine influenza viruses infecting swine, and is never used when such viruses infect people.

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