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Introduction

An influenza pandemic is a global outbreak of disease that occurs when a new influenza A virus "emerges" in the human population, causes serious illness, and then spreads easily from person to person worldwide. Pandemics are different from seasonal outbreaks or "epidemics" of influenza. Seasonal outbreaks are caused by subtypes of influenza viruses that already circulate among people, whereas pandemic outbreaks are caused by new subtypes, by subtypes that have never circulated among people, or by subtypes that have not circulated among people for a long time. Past influenza pandemics have caused high levels of illness, death, social disruption, and economic loss.

Appearance (Emergence) of Pandemic Influenza Viruses

There are many different subtypes of influenza or "flu" viruses. The subtypes differ based upon proteins on the surface of the virus (the hemagglutinin or "HA" protein and the neuraminidase or "NA" protein).

Pandemic viruses emerge as a result of a process called "antigenic shift," which causes an abrupt major change in influenza A viruses. These changes are caused by new combinations of the H and N proteins on the surface of the virus. Such changes result in a new influenza A virus subtype. The emergence of a new influenza A virus subtype is the first step toward a pandemic; however, to cause a pandemic, a new virus subtype also must have the capacity to spread easily from person to person. Once a pandemic influenza virus emerges and spreads, it usually becomes established among people around the world or "circulates" for many years as seasonal epidemics of influenza. The U.S. Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) have large surveillance systems in place to monitor and detect influenza activity around the world, including the emergence of possible pandemic strains of influenza virus.

Influenza Pandemics during the 20th Century

During the 20th century, the emergence of several new influenza A virus subtypes caused three influenza pandemics, all of which spread around the world within a year of being detected.

- 1918-19, "Spanish flu," [A (H1N1)], caused the highest number of known influenza deaths.

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(However, the actual influenza virus subtype was not detected in the 1918-19 pandemic than 500,000 people died in the United States, and up to 50 million people may have worldwide. Many people died within the first few days after infection, and others died complications. Nearly half of those who died were young, healthy adults. Influenza A viruses still circulate today after being introduced again into the human population in

- 1957-58, "Asian flu," [A (H2N2)], caused about 70,000 deaths in the United States. Following its origin in China in late February 1957, the Asian flu spread to the United States by June 1957.
- 1968-69, "Hong Kong flu," [A (H3N2)], caused about 34,000 deaths in the United States. The virus was first detected in Hong Kong in early 1968 and spread to the United States 1 year later. Influenza A (H3N2) viruses still circulate today.

Both the 1957-58 and 1968-69 pandemics were caused by viruses containing a combination of human influenza virus and an avian influenza virus. The 1918-19 pandemic virus appears to have had an avian origin.

Vaccines to Protect Against Pandemic Influenza Viruses

A vaccine probably would not be available in the early stages of a pandemic. Scientists around the world are working together when developing a new vaccine against influenza to select the virus strain that would provide the best protection against that virus. Manufacturers then use the selected strain to develop a vaccine. Once a potential pandemic strain of influenza virus is identified, it takes several months before a vaccine is widely available. If a pandemic occurs, the U.S. government will work with many partner groups and health care providers, following recommendations guiding the early use of available vaccine.

Antiviral Medications to Prevent and Treat Pandemic Influenza

Four different influenza antiviral medications (amantadine, rimantadine, oseltamivir, and zanamivir) are approved by the U.S. Food and Drug Administration (FDA) for the treatment and/or prevention of influenza A viruses. All four usually work against influenza A viruses. However, the drugs may not always work, because influenza virus strains can become resistant to one or more of these medications. For example, studies have shown that some of the 2004 H5N1 viruses isolated from poultry and humans in Southeast Asia were resistant to two of the medications for influenza (amantadine and rimantadine).

More recently, testing of seasonal influenza A (H3N2) isolates from people in the United States during the current influenza season (2005-06) has shown that a high percentage of circulating viruses are resistant to amantadine and rimantadine. As a result, on January 14, 2006 CDC issued a Health Alert Notice recommending that neither amantadine nor rimantadine be used for the treatment or prevention of influenza A in the United States for the remainder of the 2005-06 influenza season. CDC and other health agencies will continue to monitor both seasonal and avian influenza viruses for resistance to antiviral medications.

Preparing for the Next Pandemic

Many scientists believe it is only a matter of time until the next influenza pandemic occurs. The next pandemic cannot be predicted, but modeling studies suggest that the impact of a pandemic in the United States could be substantial. In the absence of any control measures (vaccination or drug), it has been estimated that in the United States a "medium-level" pandemic could cause 89,000 to 203,000 and 734,000 hospitalizations, 18 to 42 million outpatient visits, and another 20 to 47 million people being sick. Between 15% and 35% of the U.S. population could be affected by an influenza pandemic. The economic impact could range between \$71.3 and \$166.5 billion.

Influenza pandemics are different from many of the threats for which public health and health-care agencies are currently planning:

- A pandemic will last much longer than most public health emergencies and may include multiple waves of influenza activity separated by months (in 20th century pandemics, a second wave of activity occurred 3 to 12 months after the first wave).
- The numbers of health-care workers and first responders available to work can be greatly reduced. They will be at high risk of illness through exposure in the community and in health-care settings, and some may have to miss work to care for ill family members.
- Resources in many locations could be limited, depending on the severity and spread of the influenza pandemic.

Because of these differences and the expected size of an influenza pandemic, it is important to preparedness activities that will permit a prompt and effective public health response. The U.S. Department of Health and Human Services (HHS) supports pandemic influenza activities in the areas of surveillance (detection), vaccine development and production, strategic stockpiling of antiviral medications, and risk communications. In May 2005, the U.S. Secretary of HHS created a multi-agency National Pandemic Preparedness and Response Task Group. This unified initiative involves CDC and other agencies (international, national, state, local and private) in planning for a potential pandemic. I have worked with organizations and professional associations at international, federal, state, and local levels to develop a comprehensive Pandemic Influenza Plan in conjunction with the President's National Pandemic Influenza Plan.

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Centers for Disease Control and Prevention, 1600 Clifton Rd, Atlanta, GA 30333, USA
Tel: 404-639-3311 • CDC Contact Center: 800-CDC-INFO • 888-232-6348 (TTY)

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