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Influenza Pandemics
Part I: Definitions and Concepts
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Your Life Your Health
The Examiner
April 13, 2006

For the next several weeks, we are going to be discussing influenza pandemics. Today, we will lay the foundation for that discussion.

Influenza or "flu" is an infection of the respiratory tract that can affect millions of people every year. It is highly contagious and occurs mainly in the late fall, winter, or early spring. Influenza is spread from person-to-person through mists or sprays of infectious respiratory secretions caused by coughing and sneezing. Influenza affects all age groups and causes moderate to severe illness, loss of school and work, and complications such as pneumonia, hospitalization, and death. Each year approximately 36,000 Americans die because of influenza or influenza related pneumonia. Over 90% of the deaths occur in persons aged 65 years and older. Pneumonia and influenza together are the 6th most common cause of death in the United States.

Pandemic is from a Greek word “pan” which means “all,” and “demos” which means “people.” A pandemic is an outbreak of an infectious disease that spreads worldwide or at least across a large region. The recent emergence of the “bird flu,” also called “Avian Flu,” or H5N1, has created an alarm about a potential new pandemic. It must be stated clearly that at present, there is no pandemic of H5N1; it is only potential.

The chief reasons for the absence of a pandemic with this virus are:

1. At present, the virus is principally spread from animal (birds and chickens) to humans rather than from humans to humans. There is the potential, however, for the virus to mutate (change itself) to where it can be transmitted from human to human which would make it much more dangerous.
2. Cooking the meat of an infected animal destroys the virus which also limits its spread.

Pandemics of influenza are extreme infectious disease outbreaks. Although many infectious disease outbreaks such as Severe Acute Respiratory Syndrome (SARS), Ebola, HIV, or West Nile Virus can cause devastation, these infections are typically limited in their spread to either localized areas or regions, or to at-risk populations. Pandemic influenza, by contrast, is an explosive global event in which most, if not all, populations worldwide are at risk for infection and illness. In past pandemics, influenza viruses have spread worldwide within moths and are expected to spread even more quickly today given modern travel patterns.

In November, 2005, the United States Department of Health and Human Services (HHS) issued a lengthy report entitled *HHS Pandemic Influenza Plan*. This more than 490-page

document, is a strategic plan for preventing and/or control an outbreak of a world-wide flu infection. The following material is taken directly from the HHS Plan.

Influenza viruses

The agent of pandemic influenza is the influenza virus, which is also responsible for causing seasonal influenza, known by most persons as the flu. Seasonal influenza, a common disease characterized by symptoms such as fever, fatigue, body pain, headache, dry cough, and sore throat, affects large numbers of people each year. Although most people infected with flu recover, it is still responsible for approximately 36,000 deaths and 226,000 hospitalizations each year in the U.S.

Influenza viruses are negative-stranded RNA viruses that are divided into two types: "A" and "B" viruses. Influenza type C is not known to cause disease in humans and so is not applicable to this discussion. The remarkable variation of influenza strains- particularly type A- and their ability to cause annual epidemics of respiratory illness of varying intensity and severity, continue to be the focus of intense investigation.

Only type A viruses are known to cause pandemics. Type A viruses are further divided into subtypes bases on the specific hemagglutinin (H) and neuraminidase (N) proteins on the virus surface. Currently, two subtypes in the 20th century led to separate pandemics. For example, the 1918 pandemic resulted from the emergence and spread of the H1N1 virus while the 1968 pandemic was associated with the H3N2 virus. The 1957 pandemic was associated with the emergence and spread of the H2N2 virus; however, this virus subtype stopped circulating in 1968. Influenza pandemics are believed to have occurred for at least 300 years at unpredictable intervals.

Why influenza pandemics occur

An important feature of influenza viruses is their ability and propensity to modify (drift) or replace (shift) two key viral proteins, hemagglutinin and neuraminidase, on the viral surface. Because these proteins are the main targets for the immune system, changes in these proteins can have minor to profound effects on the antigenicity (ability of the human body to recognize the virus as a foreign substance and defend the body against it) of influenza viruses.

Drift

Influenza viruses can change through antigenic drift, which is a process in which mutations to the virus produce changed in the viral H or N. Drift is a continuous ongoing process that results in the emergence of new strain variants. The amount of change can be subtle or dramatic, but eventually one of the new variant strains becomes dominant, usually for a few years, until a new variant emerges and replaces it. In essence, drift affects the influenza viruses that are already in worldwide circulation. This process allows influenza viruses to change and re-infect people repeatedly through their lifetime and is the reason the influenza virus stains in vaccine must be updated each year.

Shift

In contrast to drift, pandemic viruses arise through a process known as antigenic shift. In this process, the surface existing viral H and N proteins are not modified, but are replaced by significantly different H and Ns. Since influenza A viruses that bear new (or move) H or H/N combinations are perceived by immune systems as new, most people do not have pre-existing antibody protection to these novel viruses. This is one of the reasons that pandemic viruses can have such severe impact on the health of populations.

Animal reservoirs

Novel (new) influenza viruses occasionally emerge among humans as part of the natural ecology and biology of influenza viruses. Wild birds are considered the reservoir for influenza viruses because more influenza A subtypes circulate among wild birds than humans or other animal species.

Normally, animal influenza viruses do not infect humans. However, avian influenza viruses can sometimes cross this barrier and directly infect humans. This was demonstrated in 1997, when an outbreak of avian influenza A (H5N1) viruses infected both domestic poultry and humans in Hong Kong, leading to 18 hospitalizations and 6 deaths. Since then, other outbreaks of avian viruses (such as H9N2 in 1999, H7N2 in 2002, H7N7 in 2003, and H5N1 again in 2004) have occurred and been found to directly infect people.

Fortunately, these avian viruses lacked the ability to spread easily from person-to-person and therefore did not precipitate larger outbreaks or a pandemic. Pandemic viruses can arise when some of the genes from animal influenza viruses mix or re-assort with some of the genes from human influenza viruses to create a new hybrid influenza virus. This can occur when a single animal (for example, a pig or possibly a person) is simultaneously co-infected by both a human influenza virus and an avian influenza virus.

In this situation, genes from the human and avian viruses can re-assort and create a virus with the surface proteins derived from the avian virus (hence, creating a new subtype) and the internal proteins derived from the human virus, enhancing the transmissibility of the hybrid virus. The process of re-assortment is not theoretical. Re-assorted viruses have been frequently identified and are thought to have been responsible for the 1957 and 1968 pandemic viruses.

Distinguishing pandemic from seasonal influenza

Several epidemiological features distinguish pandemic influenza form seasonal influenza. Pandemics of influenza are unusual events and their timing cannot be predicted. For example, only three pandemics occurred in the 20th century (1918, 1957, and 1968). The infrequency and unpredictable timing of these events is explained by the fact that

influenza pandemics occur only when a few (or novel) influenza A virus emerges and spreads globally.

By definition, most people have never been exposed to these viruses and therefore are susceptible to infection by them. In contrast, seasonal influenza virus stain variants are modified versions of influenza A viruses that are already in widespread circulation. Therefore, there is usually some level of pre-existing immunity to strain variants. Because of the frequent appearance of new variants, virus strains contained in seasonal inter-pandemic trivalent influenza vaccines must be updated annually.

Summary

Influenza pandemic has the potential to cause more death and illness than any other public health threat. If a pandemic influenza virus with similar virulence to the 1918 strain emerged today, in the absence of intervention, it is estimated that 1.9 million Americans could die and almost 10 million could be hospitalized over the course of the pandemic, which may evolve over a year or more. Although the timing, nature and severity of the next pandemic cannot be predicted with any certainty preparedness planning is imperative to lessen the impact of a pandemic.

The unique characteristics and events of a pandemic will stain local, state, and federal resources. It is unlikely that there will be sufficient personnel, equipment, and supplies to respond adequately to multiple areas of the country for a sustained period of time. Therefore, minimizing social and economic disruption will require a coordinated response. Governments, communities, and other public and private sector stakeholder will need to anticipate and prepare for a pandemic by defining roles and responsibilities and developing continuity of operations plans.

If we have a pandemic, the more you know about influenza the better you will be able to care for yourself and for those you love. Remember, it is your life and it is your health.