

## Past and Present Influenza Pandemics

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Three influenza pandemics occurred in 20th century and each differed in terms of etiology, epidemiology and disease severity. The recent outbreak of swine flu (due to new H1N1 influenza virus) in March 2009 has been documented in the Mexico and southern part of USA followed by Europe and Asia. The virus is very contagious and has ability to spread from human to human. Symptoms of H1N1 influenza virus infection are similar to that of normal human flu. Patients suffering from swine flu need treatment with antivirals such as oseltamivir or zanamivir. Efforts to bring swine flu H1N1 vaccine are going on a large scale. Hopefully, vaccine will be available by 2009 end, till then preventive measures should be adapted to prevent spread of swine flu.

### Introduction

Influenza is an acute infectious disease caused by influenza virus which are divided into three genera Type A, B & C within the family of Orthomyxoviridae<sup>1</sup>. Influenza A and B virus are responsible for seasonal flu epidemics each year. Influenza type C infections cause a mild respiratory illness and are not thought to cause epidemics<sup>1,2</sup>.

Influenza A virus are divided into subtypes based on two proteins on the surface of the virus: the hemagglutinin (H) and the neuraminidase (N). There are 16 different hemagglutinin subtypes and 9 different neuraminidase subtypes, Influenza A virus can be further broken down into different strains. The current subtypes of influenza A virus found in people are A (H1N1) and A (H3N2). Influenza B virus are not divided into subtypes. Influenza B virus also can be further broken down into different strains. Influenza A (H1N1), A (H3N2), and influenza B strains are included in each year's influenza vaccine. Getting a flu vaccine can protect against influenza A and B virus. The flu vaccine does not protect against influenza C virus<sup>2,3</sup>.

There are several ways by which influenza virus changes and become pandemic. The small changes in the virus that happen continually over time are termed as antigenic drift. Antigenic drift produces new virus strains that may not be recognized by the body's immune system. This process works as follows: a person infected with a particular flu virus strain develops antibody against that virus. As newer virus strains appear, the antibodies against the older strains no longer recognize the "newer" virus, and reinfection can occur<sup>2,5</sup>. This is one of the main reasons why people can get the flu more than one time.

The other type of change is called "antigenic shift." Antigenic shift is an abrupt, major change in the influenza A virus, resulting in new hemagglutinin and/or new hemagglutinin and neuraminidase proteins in influenza virus that infect humans. Shift results in a new influenza A subtype. When shift happens, most people have little or no protection against the new virus. While influenza virus are changing by antigenic drift all the time, antigenic shift happens only occasionally. Type A virus undergo both kinds of changes; influenza type B virus change only by the more gradual process of antigenic drift<sup>1,2,5</sup>.

### Influenza Pandemics in the Past

A pandemic is a global disease outbreak. Though pandemics are rare but preordained events, they have occurred in past and indubitably will occur in future too. Prediction of next pandemics is always difficult. Influenza pandemics occur when a novel influenza strain, often previously an animal virus, mutates to allow human-to-human transmission. As there is no prior immunity, these pandemic strains rapidly sweep through populations causing high morbidity and mortality. Three pandemics occurred in the 20th century and each differed from the others with respect to etiologic agents, epidemiology, and disease severity<sup>5,6</sup>.

#### 1918-1919: Spanish Flu (H1N1)

Spanish influenza was the most serious of all the influenza pandemic which have occurred till date. Spanish flu infected approximately 20 to 40 percent of the worldwide population and causing about 40 million people worldwide<sup>5</sup>. Between September 1918 and April 1919, approximately 675,000 deaths from the flu occurred in the U.S. alone and about 17 million deaths in India. Most of the people suffered with Spanish flu died very quickly (within a day or two) and most of them among killed were young adults. Similarities in clinical presentations and pathologic features of influenza in human and swine suggested that pandemic human influenza in 1918 was actually adapted to the pigs<sup>6,7,8</sup>.

#### 1957-58: Asian Flu (H2N2)

In early 1957, the Asian influenza pandemic was first identified in the Far East. The virus entered U.S. with a series of small outbreaks over the summer of 1957. Immunity to this strain was rare in people less than 65 years of age, and a pandemic was predicted by that time. Unlike the virus that caused the 1918 pandemic, the 1957 pandemic virus was quickly identified, due to advances in science and technology. Vaccine was available in limited supply by August 1957. Infection rates were highest among school children, young adults, and pregnant women. Most influenza-and pneumonia-related deaths occurred between September 1957 and March 1958. Although the Asian flu pandemic was not as devastating as the Spanish flu, still it killed about 2 million people in which about 69,800 deaths were from U.S. alone<sup>6,7,8</sup>.

# **Review Article**

## **1968-69: Hong Kong Flu (H3N2)**

In early 1968, the Hong Kong influenza pandemic was first detected in Hong Kong and in September 1968 in USA. Deaths from this virus peaked in December 1968 and January 1969. This flu affected people over the age of 65. The same virus returned in 1970 and 1972. The number of deaths between September 1968 and March 1969 was 33,800, making it the mildest pandemic in the 20th century. Low death toll was because of earlier infections by the Asian flu virus might have provided some immunity against the Hong Kong flu. In addition several precautionary measures taken up by government (even closing of schools) and families<sup>6,7,8</sup>.

## **Present Influenza Pandemic Swine flu (new H1N1 2009)**

Recently in March 2009, an outbreak of influenza in North America was found which was caused by new strain of influenza A virus designated as Influenza H1N1 2009, which is a reassortment of swine, avian and human influenza virus. Influenza A (H1N1) subtypes virus have rarely predominated since 1957 pandemic. Though the reports are preliminary, as recent outbreak does not appear to be severe either in terms of the attack rate in communities or in the virulence of water itself. However there are significant changes in both the hemagglutinin and neuroaminidase protein of new virus<sup>4</sup>. These antigenic shift may make H1N1 2009 a significant pandemic potential. Pandemic influenza H1N1 has now been reported in over 170 countries and territories worldwide. Because hardly anyone has immunity to the new H1N1 virus, experts believe it will infect far more people than usual. About 77201 case of H1N1 2009 have been reported till July 1 2009 with 332 death worldwide. Out of these cases, 27717 cases were from USA and 104 cases from India.

The swine flu is caused by a novel influenza A (H1N1) virus that was originally known as "swine flu" because many of the genes in this new virus were very similar to influenza virus that normally occur in pigs in North America<sup>4,9</sup>. However, this new virus is actually quite different from the typical swine flu virus found in pigs; the virus responsible for the 2009 pandemic is termed H1N1 flu virus or novel H1N1 flu virus<sup>9</sup>.

## **Transmission of H1N1 virus in human**

It is transmitted similarly as the normal seasonal flu and can spread to other by exposure to infected droplets expelled by coughing or sneezing that can be inhaled, or that can contaminate hands or surfaces. Sometimes people may become infected by touching something with live flu virus on it and then touching their mouth or nose. Due to the ease with which the virus is spreading it is advisable to avoid public domains. The people who are infected should be admitted to isolation ward for treatment and their close contacts should be quarantined, so that spread of swine flu can be prevented. Personal hygiene as well as cleanliness should be maintained in order to avoid further carriage of this infectious virus<sup>6,9,11</sup>.

## **Symptoms and Diagnosis of Human influenza H1N1 infection**

The signs of infection with swine flu are similar to other forms of influenza, and may include high fever, coughing, headaches, pain in the muscles or joints pain, sore throat, chills, fatigue and runny nose. Diarrhoea, vomiting and neurological problems have also been reported in some cases.

Certain symptoms may require emergency medical attention. In children signs of respiratory distress, for instance, those might include blue lips and skin, dehydration, rapid breathing, excessive sleeping, seizures. In adults, shortness of breath, pain in the chest or abdomen, sudden dizziness or confusion may indicate the need for emergency care. In both children and adults, persistent vomiting or the return of flu-like symptoms that include a fever and cough may require medical attention<sup>6,7</sup>.

For diagnosis of H1N1, a nasopharyngeal swab, nasal swab, throat swab or nasal respiratory sample should be collected within the first five days of illness. The infection can be diagnosed using a polymerase chain reaction which is considered to be of gold standard for diagnosis of swine flu. There are commercially H1N1 detection kits from US based Applied Biosystems and Roche Diagnostics that can detect the human influenza H1N1 infection<sup>6,12</sup>.

## **Drug treatment and Vaccines for swine flu:**

Antivirals are commonly used for the treatment of treatment of seasonal influenza<sup>1</sup>. For H1N1 treatment, antivirals such as Oseltamivir<sup>10</sup> and Zanamivir have shown susceptibility. Roche, Innovator company of Oseltamivir have limited licensing agreement in India and is available in capsule (100 mg) and syrup (50 mg/5ml). Zanamivir is manufactured by Glaxowellcome and it is available as dry powder for inhalation<sup>9</sup>.

Currently two vaccines (TIV & LAIV) are available for seasonal flu but these vaccines do not have any efficacy against new H1N1 strain. The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP)—an advisory committee to CDC—recommended that novel H1N1 flu vaccine will be made available by end of 2009 first for the following five groups: Pregnant women, Health care workers and emergency medical responders, People caring for infants under 6 months of age Children and young adults from 6 months to 24 years, People aged 25 to 64 years with underlying medical conditions (e.g. asthma, diabetes)<sup>7</sup>.

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