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Introduction to pandemic influenza through history

Youri Ghendon
World Health Organization, Geneva, Switzerland

Abstract. For the past 400 years, epidemics resembling influenza have been recorded in many countries. Epidemics from as early as the 16th Century in England and the 18th Century in the USA are recognizable as influenza, even in the absences of precise knowledge of their causative agents.

Key words: Control, Influenza, Pandemic

The influenza pandemic of 1918 was the largest in recent history, causing 20 million deaths worldwide. In more modern times since 1957 and 1968 influenza pandemic also killed a million people.

While the relationship between antigenic change and epidemic is complex, presumably involving multiple factors attributable to the host as well as to the viruses, antigenic drift or shift is the most readily identifiable marker of epidemic potential.

Although influenza pandemics cannot be predicted with certainty the plans for pandemic situations can be developed and can play an important role in the prompt and appropriate response when they occur.

In the year 412 BC Hippocrates described an epidemic that modern doctors believe was influenza, and history has recorded many influenza epidemics and pandemics since that time.

In the Middle Ages several widespread outbreaks that were probably influenza occurred in Europe. But the first epidemics that can be regarded with confidence as influenza were in 1173. However, the position of some medical historians that only epidemics which occurred in 1510 can be considered as unquestionable influenza epidemics [1]. In 1580 a severe pandemic occurred that was possibly the first global dissemination of influenza. It started in Asia and spared to Africa, Europe and America. Almost all of Europe was afflicted in six weeks and it was said that only one twentieth of the people escaped the illness. The case description of influenza was done during this epidemic and is similar to influenza illness seen currently.

In the eighteenth century there were 13 severe epidemics and in the nineteenth century there were 12, and probably 8 or 9 of these 25 were influenza pandemics in the modern sense. In the twentieth century there have been several pandemics: 1918, 1946, 1957, 1968 and 1977 due to emergence of new subtypes of influenza A virus.

The influenza viruses are unique in that they are able to circumvent immunity by gradually undergoing alteration of their two surface antigen – haemagglutinin and neuraminidase – by accommodation of a series of mutation (drift) and can also undergo a complete change in one or more of their surface antigens by genetic reassortment (shift). The shift variants of influenza virus are responsible for recent pandemics. It should be noted that the influenza viruses demonstrates only antigenic drift may also cause pandemics in the strictest epidemiological sense of the word. For example, worldwide epidemics occurred with the influenza A viruses of 1972, 1974 and 1975.

According to the dictionary definition, a pandemic is simply a widespread epidemic, but when referring to influenza a pandemic now signifies a worldwide epidemic caused by a new subtype of influenza A virus. Therefore only during the virological era can we recognize a pandemic with certainty. However, in the absence of virus identification, we can make an informed guess that if the epidemic originated in one place and from there spread worldwide with high morbidity, it was probably a pandemic. Also epidemics occurring during the warmer months of the year are a practically sure sign that they were pandemics; theses occurred in 1580, 1781, 1831 and 1918.

The greatest pandemic of the twentieth century was the pandemic of 1918, popularly known as Spanish flue owing to its high incidence in Spain, which is believed to have been caused by the 'swine' variant HlswN1 subtype of influenza virus.

The first wave of the pandemic of 1918 swept across North America in March and April 1918. The infection moved on to Europe, when it first reached epidemic levels in France in April 1918. Over the next several months, influenza spread throughout the whole of Europe. In the United States of America the 1918 influenza pandemic killed 550,000 people – 0.5% of the population, about ten times more the

number of Americans who died in the war [1, 2]. In Europe the influenza in England and Wales alone killed 200,000 people. In a few places such as Samoa and Alaska some 25% or more died. Throughout the world influenza pandemic 1918 killed 20 to 40 million people, and made one-quarter to one-half of the population sick. The 1918 influenza pandemic killed more people in less time than any other disease before or since.

In a vain effort to halt the spread of influenza during 1918 pandemic in the USA, in some cities officials closed dance halls, theatres, schools and even churches. There were placards on street cars and railroad stations asking people not to spit and all police wore masks. Police in Chicago were asked to arrest people who sneezed in the streets [2].

Since the 1918 pandemic, there have been two major global outbreaks of influenza A in the twentieth century: In 1957, influenza was induced by namely 'Asian' influenza virus A/H2N2, and in 1967, influenza was induced by namely 'Hong Kong' influenza virus – A/H3N2 – and two mild pandemics in 1946 and in 1977, induced by H1N1.

In 1946 there was a worldwide epidemic that was regarded as pandemic due to a new influenza virus subtype – H1N1. It was a mild pandemic and the excess of mortality was low. Influenza pandemic 1957 was not so bloodthirsty as in 1918, nevertheless in the USA alone 40,000 deaths were attributed to the 'Asian' influenza and the mortality was much the same in most countries. During the Hong Kong pandemic 1967 the mortality in the USA alone was estimated at around 30,000 deaths, 51 million Americans were ill and the total economic burden was 3.9 billion [3]. In Europe the mortality was estimated at 30,000 deaths in Britain alone [4].

The next notable event in the history of influenza was the reemergence in 1977 of the H1N1 influenza virus that had been prevalent from 1947 to 1957. It arose in China and spread world-wide but affected mostly people born after 1957. From 1977 to the present day it has continued to circulate along with H3N2 and B influenza viruses.

The minimal requirement for the generation of a pandemic seems to be the major change in external antigens. The severity of the 1957 pandemic when two external antigens changed, compared to the less dramatic pandemic in 1946 and 1967 when only haemagglutinin changed my reflect this fact.

What can we really do to control influenza pandemic? The main problem is that the real causative virus of pandemic influenza cannot be completely determined until at least the first phase of the pandemic is underway. If influenza surveillance is improved, especially in the areas in which most of the pandemic influenza viruses arise, the potential pandemic shift variants of influenza virus can be detected early. Nevertheless the period of time available for vaccine production from the potential pandemic strain of influenza virus will always be limited.

There is one example of an attempt to control pandemic influenza: In the USA in 1976 the cases of so-called swine influenza took place and a decision was made to control the potential influenza pandemic by mass vaccination. The sequence of events that constituted the response on this outbreak began with the initial recognition of the new virus and culminated in the production and use of a vaccine. But the time from the isolation of the influenza virus and the beginning of the Nationa Influenza Immunization Programme took approximately one year [5]. If it is influenza virus which really can induce pandemic influenza, at the beginning of a vaccination period, which is one year after the isolation of the virus, all people susceptible to this virus can develop influenza.

In the book Patterson [6], the author concluded: 'Pandemics have secured with a frequency of three per 100 years since 1700. There is no periodicity to the occurrence of pandemics and no basis for predicting where a new outbreak may arise'. Since 1889 pandemics of influenza have occurred at intervals of 28/29 and 10–11 years and in fact several suppositions on the possibility to predict the influenza pandemic on the basis of cyclical recurrence of the pandemic strains or solar activity, or other factors, are in fact only speculative. It is to be noted that the accounts of a Florentine family in the fourteen/fifteen centuries used the world 'influence' to suggest an unusual conjunction of planets at times of epidemics of coughs, colds and fevers. The word 'influenza' was thus derived as a description name for the epidemics due to 'influences'. In the twentieth century Hope-Simpson published an article [7] in which he suggests that antigenic shifts of influenza A virus and accordingly pandemic coincided with sunspot, and showed some examples of this from 1930 to 1970. But in 1979 sunspots activity took place but there was no pandemic. So we should be prepared for unforeseen influenza pandemic in any given year.

In the Middle Ages the Germans thought influenza was caused by eating too many sour applies and salt fish. Now we know much more about the agent induced influenza, but our knowledge on how to take control of pandemic influenza is practically at the same level as in the Middle Ages.

During the International Conference for the control of influenza in 1992, at Courcheval, attempts were made to work out several recommendations on pandemic planning [8]: Examples of these are as follows:

1. The enhanced surveillance of influence, especially in Southern China where most of the pandemic strains of influenza virus originated, in order to detect the emergence of the pandemic strain and isolate the pandemic strain of influenza virus as soon as possible.

2. The vaccine improvements are essential for optimal pandemic control, especially for the production of influenza vaccine in a short period of time. The possibility to use new substrate for vaccine production of new types of influenza vaccine for vaccination needs investigation.
3. The antivirals can play a major role in the early phases of a pandemic. Alternative agents to amantadine/rimantadine which have different mechanisms of antirival activity needs to be developed.
4. The national, regional and global plans on the control of pandemic influenza should be worked out.
5. Public and mass-media need to be involved in the control of pandemic at all stages.

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Address for correspondence: Dr Y. Chendon, World Health Organization, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland
Phone: +41 22 791 2656; Fax: +41 22 788 2937