An historical overview
of
pandemic influenza

Alan W. Hampson
Influenza—this much studied and least understood of diseases—is not only a disease but for some of us a way of life.

Once challenged with its virus, the investigator, unlike the patient, is chronically stricken and is doomed to a lifetime of servitude to its whims—and endless debates with his colleagues—unless he is rescued by the early attainment of a high administrative position or seduced by the largesse of cancer virology.

A neuropathic sequel of this affliction is a delusion in which influenza suddenly becomes comprehensible. The investigator then becomes totally inaccessible to human communication until the next pandemic occurs, after which either he is restored abruptly to sanity or is led away muttering something about a "new hypothesis."

Perhaps for this reason, the student of influenza is constantly looking back over his shoulder and asking "what happened"? in the hope that understanding of past events will alert him to the catastrophes of the future.

Ed Kilbourne 1973
Defining a Pandemic

WHO 'description' to 2009:
“An influenza pandemic occurs when a new influenza virus appears against which the human population has no immunity, resulting in several simultaneous epidemics worldwide with enormous numbers of deaths and illness.”

WHO 2010:
“An influenza pandemic occurs when a new influenza virus emerges and spreads around the world, and most people do not have immunity. Viruses that have caused past pandemics typically originated from animal influenza viruses.”

CDC current web page:
“An influenza pandemic is a global outbreak of a new influenza A virus. Pandemics happen when new (novel) influenza A viruses emerge which are able to infect people easily and spread from person to person in an efficient and sustained way.”
Difficulties in Determining Historical Pandemics

Accuracy of disease description - pre 16th century largely by lay people.

No way of knowing that the infectious agent was influenza or novel could there have been coronaviruses or paramyxoviruses involved?

Lack of geographically representative data limits of the 'known' world limited non-Western information available

Until the mid-eighteenth century population density was restricted, travel was limited and slow - early outbreaks sometimes 'diffused' rather than spread rapidly
Contemporary Literature (last 30-40 years)

The Chronicle of Influenza Epidemics

W.I.B. Beveridge
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Abstract - Epidemics that were probably influenza have been reported throughout recorded history. There are 13 fairly recent epidemics during the 18th century and 13 during the 19th century. Probably 8 of these 26 were influenza epidemics. In the 20th century there have been 4 pandemics (1918/19, 1975/76, 1980/81, 1977) due to the emergence of new strains of influenza A virus. The great pandemic of 1918/19 caused an estimated 20 million deaths. Between pandemics usually there have been epidemic-sized waves at intervals of two to three years and a trickle of sporadic cases every year. The morbidity and mortality rates have varied greatly from epidemic to epidemic and from place to place. Generally the mortality has been lowest in people over 60 years of age, but, except for 1918/19, the mortality has been predominantly in old people.

PANDEMIC AND EPIDEMIC INFLUENZA, 1830-1848

K. David Patterson
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Abstract - Four major influenza epidemics were recorded in Europe during the 1830s-1840s. In 1836-1837, influenza diffusion was largely from the Mediterranean to northern Europe. Vomiting and its epidemics spread rapidly and caused very high death rates, especially among alcoholics. The epidemic influenza of 1840 has been some of the most difficult to understand.

Introduction to pandemic influenza through history

Youyi Ghendos
World Health Organization, Geneva, Switzerland

The 1918 Influenza Pandemic: Insights for the 21st Century

Gerald F. Pyle

The 1918-1919-1920 influenza pandemic was among the most deadly events recorded in human history. It killed an estimated 50 million people. Moreover, recent genomic analysis has shown that the pandemic strain was derived from a previous strain of influenza, 1889-1890, and that it began in China in 1889 and moved to Japan in 1890, then to the West in 1890, and finally to Europe in 1890. In the winter of 1890, the strain spread rapidly to the Americas, reaching Mexico in 1890. From Mexico, the strain spread to the rest of the world, reaching Europe in 1890, the Middle East in 1890, the United States in 1890, and the rest of the world in 1890.

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Summary

Influenza pandemics and epidemics have apparently occurred since at least the Middle Ages. When pandemics appear, 50% or more of an affected population can be infected in a single year, and the number of deaths caused by influenza can dramatically exceed what is normally expected. Since 1500 there appear to have been 13 or more influenza pandemics. In the past 120 years there were

Review

Reviewing the History of Pandemic Influenza: Understanding Patterns of Emergence and Transmission

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Academic Editor: Lawrence S. Young
Received: 8 August 2016; Accepted: 20 November 2016; Published: 6 December 2016

Abstract: For centuries, novel strains of influenza have emerged to produce human pandemics, causing widespread illness, death, and disruption. There have been four influenza pandemics in the past hundred years. During this time, globalization processes, alongside advances in medicine and epidemiology, have altered the way these pandemics occur. Drawing on international case
Early Source Literature

A HISTORY OF EPIDEMICS IN BRITAIN
Charles Creighton

A HISTORY OF EPIDEMICS

PANDEMIC INFLUENZA 1700–1900

ANNALS OF INFLUENZA OR EPIDEMIC CATARRHAL FEVER IN GREAT BRITAIN FROM 1540 TO 1837.

HANDBOOK OF GEOGRAPHICAL AND HISTORICAL PATHOLOGY.
Early Source Literature

- Webster, N. (1799). *A brief history of epidemic and pestilent diseases: with the principle phenomena of the physical world, which precede and accompany them, and observations deduced from the facts stated*. Hudson & Goodwin, Hartford.


Criteria Used for Selection of Probable Pandemics

- Clinical disease with fever and respiratory symptoms lasting a few days, with full recovery or death
- Sudden outbreak onset
- High morbidity
- Low overall case fatality rate but usually increased overall mortality
  - Evidence of deaths from pneumonia
- Outbreak duration 1-2 mo. in major towns
- Spread (throughout a continent or the known world)
  - Evidence of disease in at least 2 geographically separated regions
- People of all ages, classes and walks of life affected
- Sometimes unseasonal outbreaks
First generally agreed pandemics were those of 1510 or 1580.


Morens and Taubenberger 2010
Infl Other Resp Vir. 4 327-337
Beveridge 1991
Hist Phil Life Sci 13 223-35
Sixteenth Century Pandemics

1510:
- Spread from Africa to Europe summer of 1510, northward spread to Baltic states.
- High attack rates, low mortality restricted to children.
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1557-8
- Westward spread Asia to Europe
- High mortality (pleurisy, fatal peripneumony)
  - High mortality in pregnant women
  - English parish registries show xs deaths 1558-1560
Sixteenth Century Pandemics

1580

- Global with rapid spread
- High mortality

From “The Diffusion of Influenza Patterns and Paradigms” Pyle 1986
# Influenza in the 17th Century

## No evidence of pandemics recorded!

- Several large-scale European epidemics but without directional spread

- Development of influenza-like activity in the Americas
  - 1617 ILI outbreak in Chile spreading throughout South & North America and the Caribbean

- Beginning of a period of semi-autonomous American Influenza

- 152 year absence of recorded pandemic activity (1580-1732)
Eighteenth Century Pandemics

- 1732-3
  - East to West spread
  - May have been a second wave of 1729-30 outbreaks
  - High morbidity and mortality
  - Period of heightened influenza activity

- 1761-2
  - Listed only by Taubenberger & Morens (2009)
  - Possible origin in the Americas

From “The Diffusion of Influenza Patterns and Paradigms” Pyle 1986
Eighteenth Century Pandemics

- **1781-82** (?1780 origin)
  - Started in China, spread through Russia to Europe, India & North America.
  - Very high morbidity, low mortality except records from London.

- During the 1700s an association between human and equine influenza outbreaks was often recorded

From "The Diffusion of Influenza Patterns and Paradigms" Pyle 1986
Nineteenth Century Pandemics

1830-1833
- Originated in China then Russia to Europe and globally.
- Two waves, higher mortality in second wave, older people spared.
- Third wave or separate pandemic 1836-7

1847-8
- Pandemic recorded in Europe North America, West Indies & Brazil. Possible origin recorded as Ottoman Empire or Russia.
- High morbidity (25-50% in Paris) high mortality in the UK.
- Suggestions that infection around this time may have been sparing against 1918-19 pandemic.

From “The Diffusion of Influenza Patterns and Paradigms” Pyle 1986
1889-92(93) ('Russian Flu')

- First reported in Central Asia (Uzbekistan) ~May 1889, summer lull then spread rapidly from Russia along transportation networks (rail).
- Reached the Americas December, Australia in March 1890.
- High morbidity, modest mortality in first wave.
- Two or three subsequent waves, mortality higher in second wave.
- Subsequent serology indicates H3 subtype (possibly with N8)

From "The Diffusion of Influenza Patterns and Paradigms" Pyle 1986
The authors note increasing access to web-based information such as all issues of Lancet 1823 to present.
Twentieth Century Pandemics

- 1918-19 'Spanish Flu'
- 1947
  - originally considered to be a pandemic but in reality a major antigenic drift variant not a change of sub-type.
- 1957-58 'Asian Flu'
- 1968-69 'Hong Kong Flu'
- 1977-78 'Russian Flu'
Global mortality estimates continue to grow - now 50-100 million

Origins still debated
  - Geographic
    - Clinical reports 1916–17 (UK, France) Oxford 2002
    - USA Kansas March 1918 (Crosby 1989, Barry 2004)
  - Viral
    - Taubenberger et al 2005 propose direct avian source
    - Evolutionary clock analysis (Worobey et al 2014) suggests earlier ~1907 evolution of the HA, and development by reassortment

Initial spread commencing spring 1918 Kansas (Camp Funston)
Global mortality estimates continue to grow - now 50-100 million

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Initial spread commencing spring 1918 Kansas (Camp Funston)
Twentieth Century Pandemic 1: 1918-19

- Unusual 'W' shaped mortality curve
  - Three waves of differing mortality
Twentieth Century Pandemic 1: 1918-19

- Unusual 'W' shaped mortality curve

Deaths from pneumonia & influenza in USA in 3 influenza pandemics

Dowdle (1999) Bull WHO. 77 (10), 820