



An historical overview of pandemic influenza

Alan W. Hampson

The History of Pandemics - Why Bother?

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

Early Source Literature

A HISTORY OF EPIDEMICS

PANDEMIC INFLUENZA 1700-1900

A Study in Historical Epidemiology

K. DAVID PATTERSON

BUTTER & LITTLEFIELD
Publishers

A HISTORY OF EPIDEMICS IN BRITAIN

Charles Creighton

ANNALS

INFLUENZA

OR
EPIDEMIC CATARRHAL FEVER

IN
GREAT BRITAIN

FROM 1510 TO 1837.

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CH UNDERWOOD
& AOVENALL

VOLUME TWO
OF THE PLAGUE TO THE PRESENT TIME

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Publishers - Bookellers - Since 1873

HANDBOOK OF GEOGRAPHICAL AND HISTORICAL PATHOLOGY.

BY
DR. AUGUST HIRSCH,
Professor of Medicine in the University of Berlin.

Volume I.—Acute Infective Diseases.

REVISED FROM THE SECOND GERMAN EDITION

BY
CHARLES CREIGHTON, M.D.

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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. Hartsford
- Thompson, T. (1852). *Annals of Influenza or Catarrhal Fever in Great Britain from 1510 to 1837.* The Sydenham Society. London
- Hirsh A. (1881). *Handbook of Biographical and Historical Pathology, vol 11 (translated by Creighton).* New Sydenham Society, London
- Wilson, J.C. & Da Costa, J.M. (1881). *Influenza. In a treatise on the continued fevers.* William Wood & Co. New York.
- Thompson, E.S. (1890). *Influenza.* Percival & Co. London
- Creighton, C. (1894). *A history of Epidemics in Britain.* Cambridge University Press
- Finkler, D. (1898). *Influenza in Twentieth Century Practice.* Stedman, T.L. Ed.d. Vol XV. Sampson Low, Marston & Co London

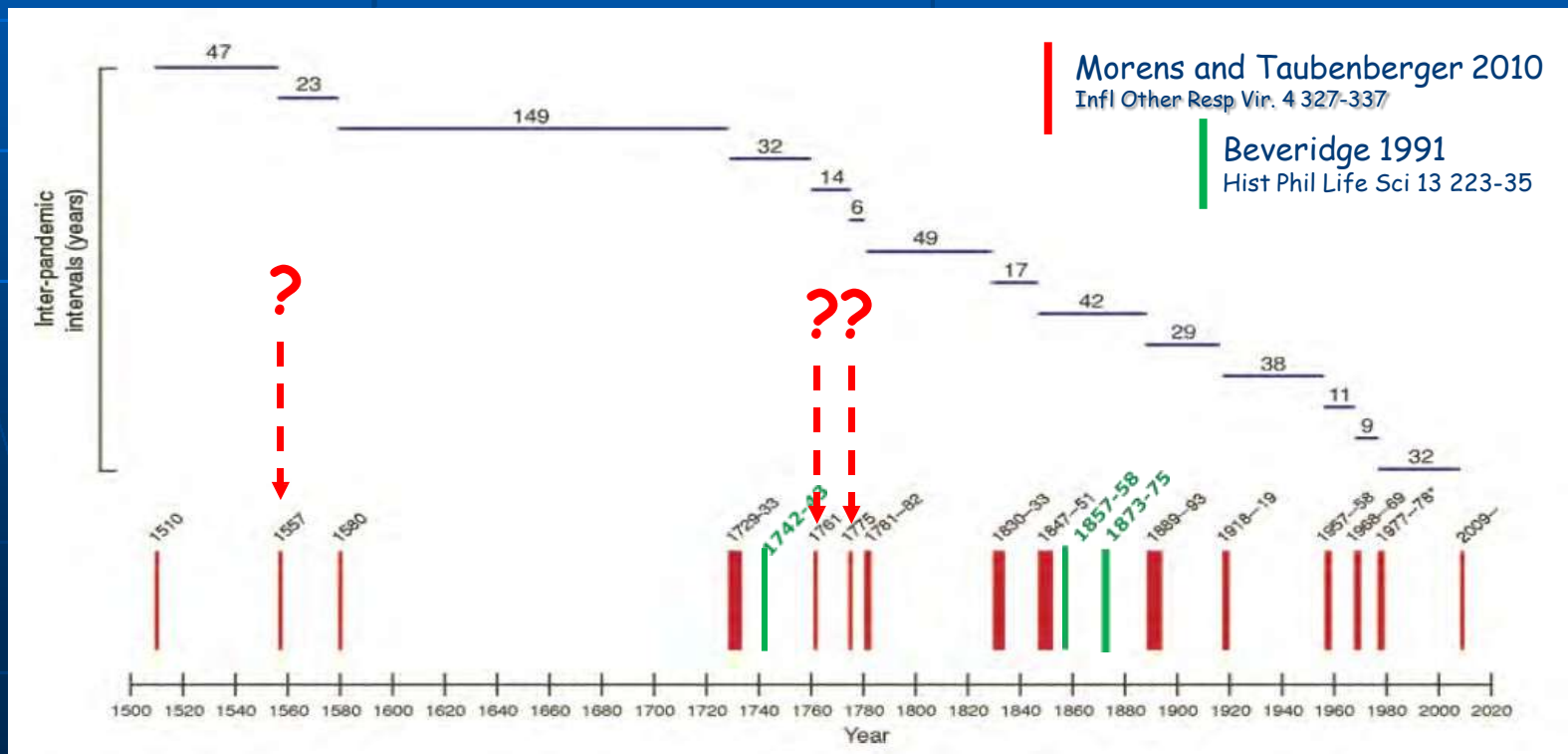
Criteria Used for Selection of Probable Pandemics

- 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

Contemporary Analysis of the Literature

First generally agreed pandemics were those of 1510 or 1580.

Most recent analysis of historical records by Taubenberger and Morens [Rev Sci Tech. 2009 Apr;28(1):187-202] describe 15 pandemics dating back to 1510.



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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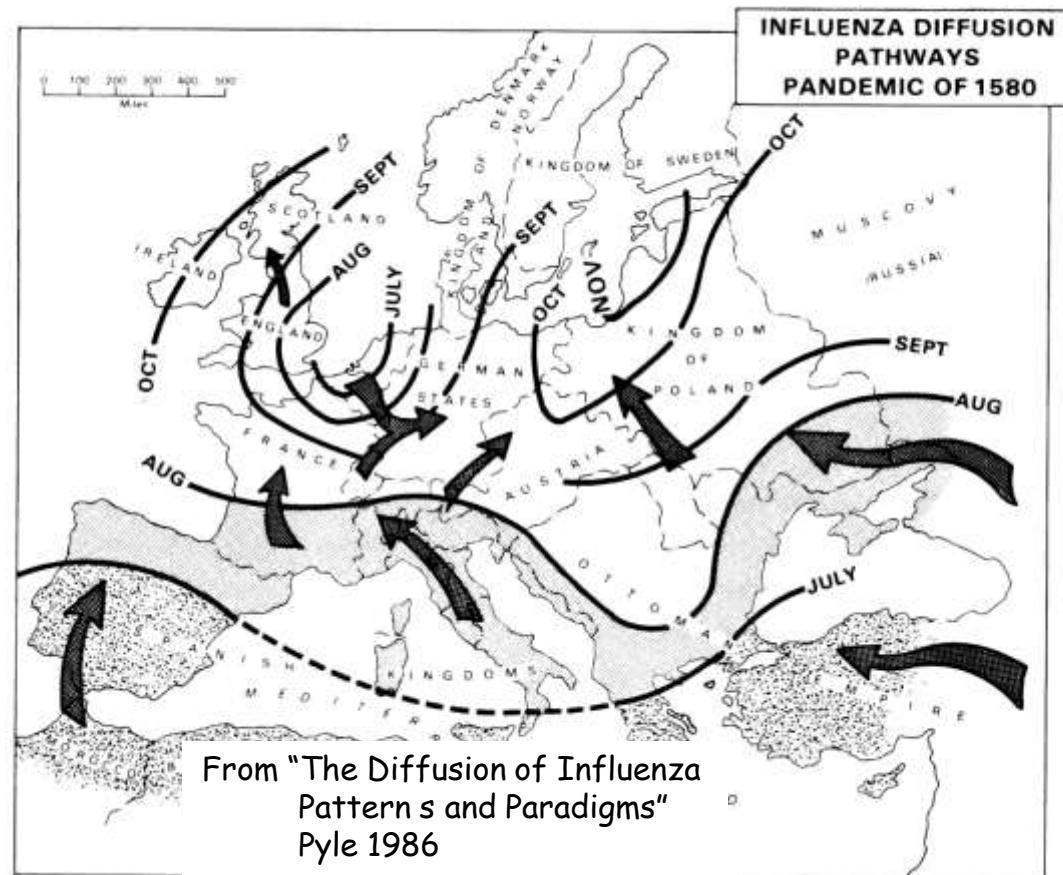
1557-8

- 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



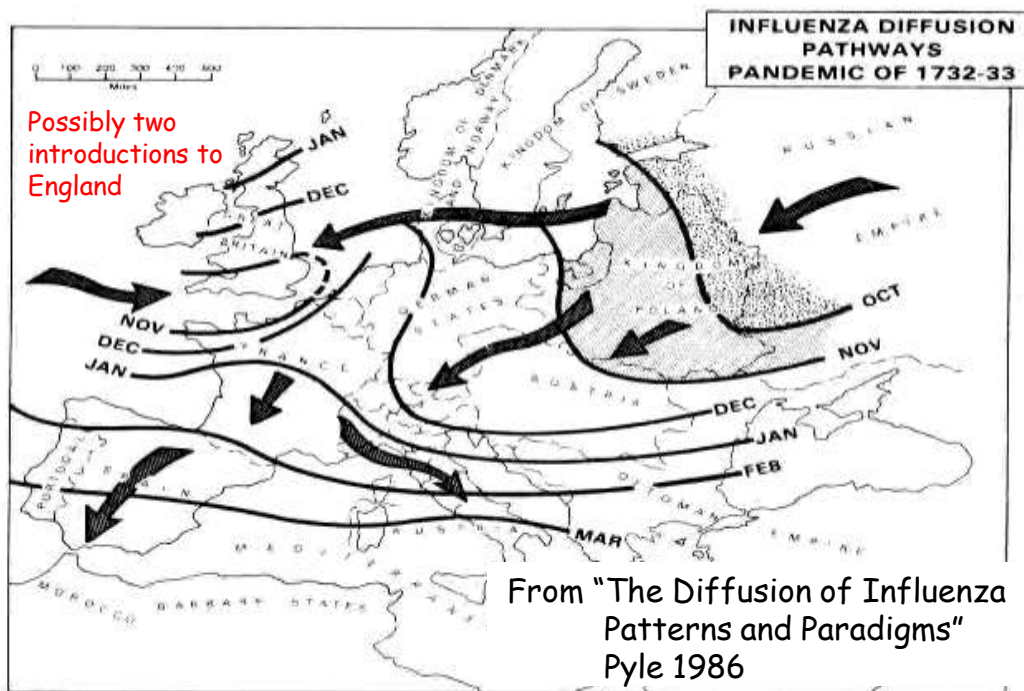
Influenza in the 17th Century

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

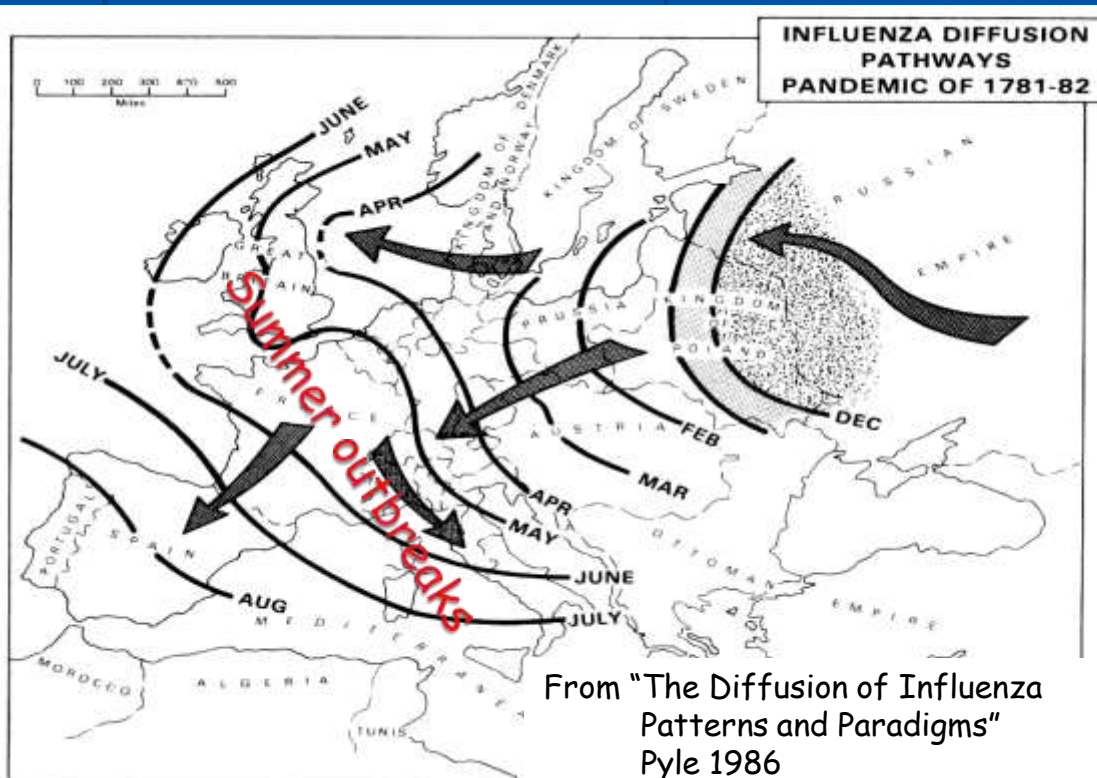
- 1732-3
 - East to West spread
 - May have been a second wave of 1729-30 outbreaks
 - High morbidity and mortality
 - Period of heightened influenza activity
- 1761-2
 - Listed only by Taubenberger & Morens (2009)
 - Possible origin in the Americas



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

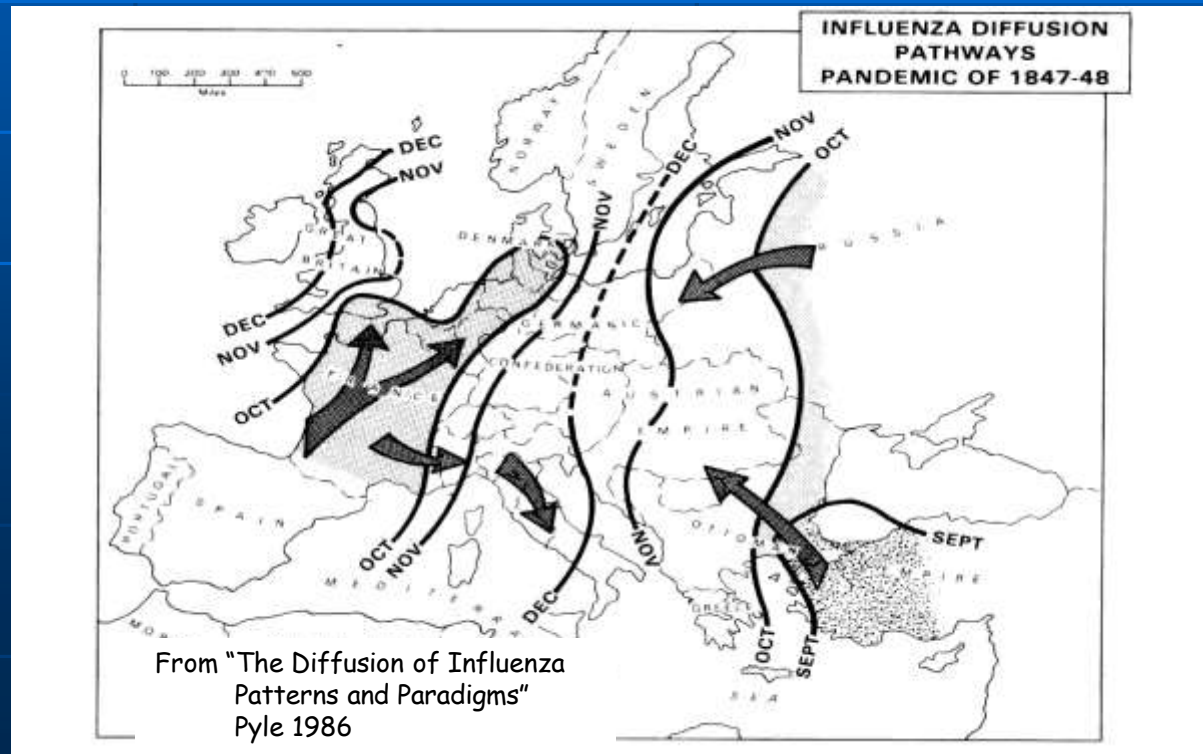
Nineteenth Century Pandemics

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

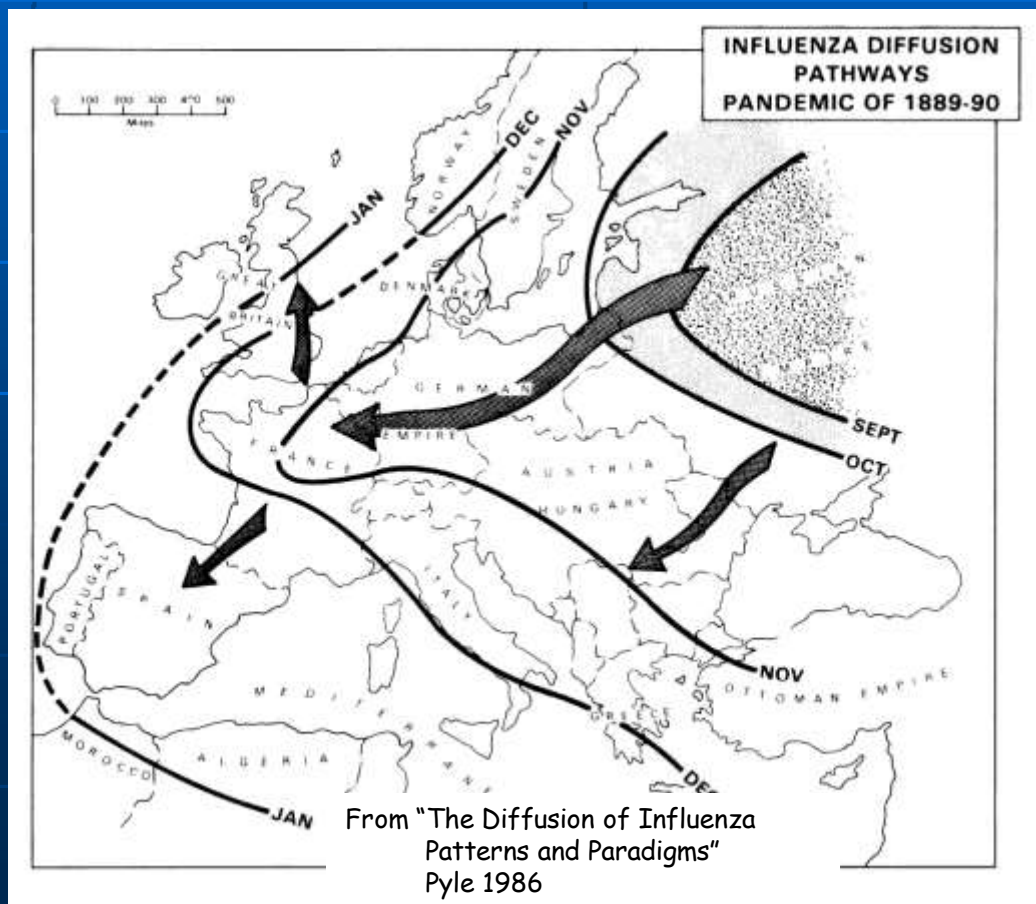
- Pandemic recorded in Europe North America, West Indies & Brazil. Possible origin recorded as Ottoman Empire or Russia.
- High morbidity (25-50% in Paris) high mortality in the UK.
- Suggestions that infection around this time may have been sparing against 1918-19 pandemic.



Nineteenth Century Pandemics

1889-92(93) ('Russian Flu')

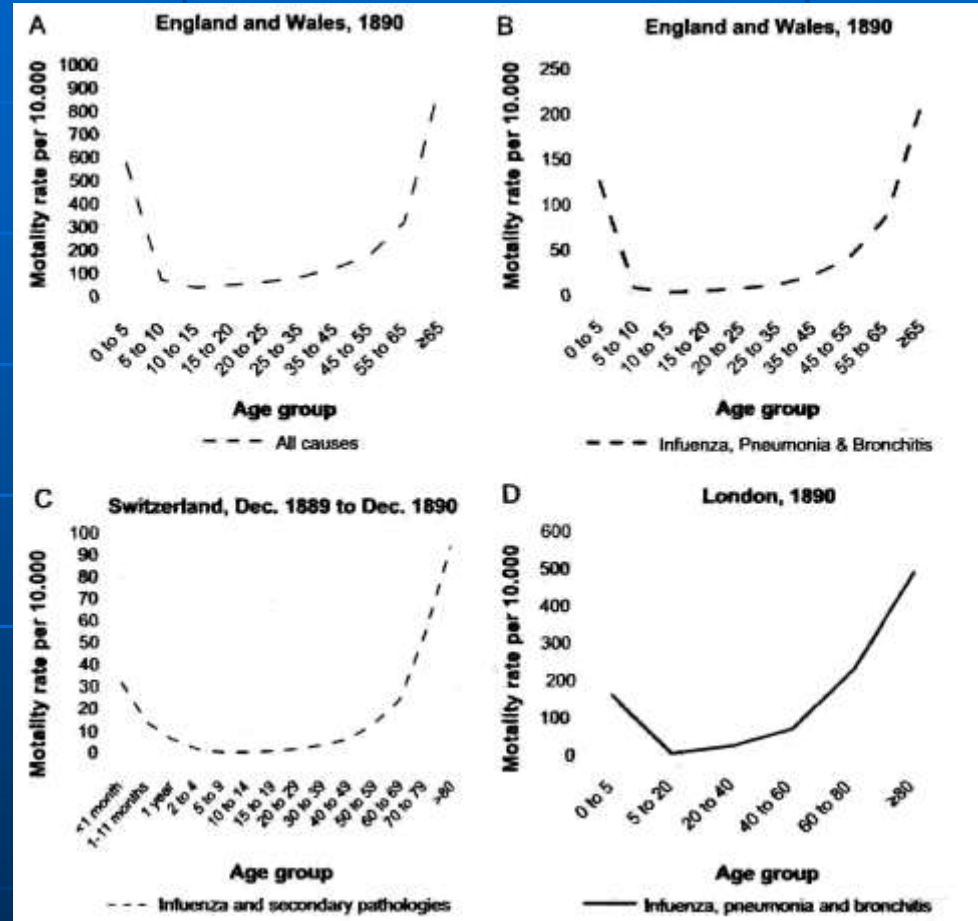
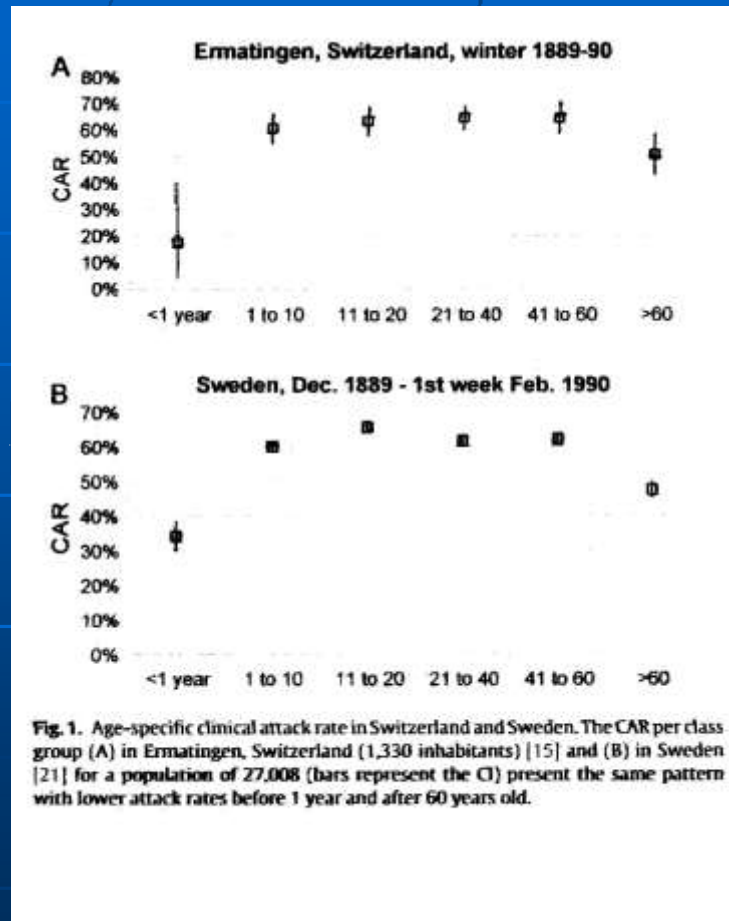
- First reported in Central Asia (Uzbekistan) ~May 1889, summer lull then spread rapidly from Russia along transportation networks (rail).
- Reached the Americas December, Australia in March 1890.
- High morbidity, modest mortality in first wave.
- Two or three subsequent waves, mortality higher in second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



Nineteenth Century Pandemics

1889-92(93) ('Russian Flu')

- Recently (2010) further analysed by Valleron et al.



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'

Twentieth Century Pandemic 1: 1918-19

- 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)



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Twentieth Century Pandemic 1: 1918-19

- Unusual 'W' shaped mortality curve
 - Three waves of differing mortality
 - Sparing of older adults - analysis of excess mortality suggests protection by earlier infection (Luk et al 2001) possibly 1830-33 pandemic (Worobey et al 2014).
- .

Twentieth Century Pandemic 1: 1918-19

- Unusual 'W' shaped mortality curve

Deaths from pneumonia & influenza in USA
in 3 influenza pandemics

