

ONE HUNDRED YEARS LATER

UNKNOWNNS OF THE 1918 FLU EPIDEMIC

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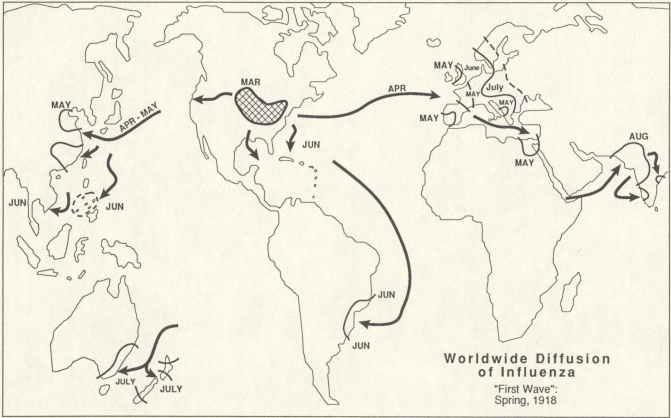
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What Happened?

- One of the greatest natural disasters to hit humans, almost certainly with greater mortality than the Great Plague.
 - Even the number of deaths is unknown (see below), higher bound of 100 million.
- Pandemic first recorded to Kansas, spreads through much of the world in Spring 2018; second wave starts in Europe, spreads throughout the world in Fall 2018; third wave over the next few years.
 - Spread driven by transportation: ships and trains.
 - Not even sure that the third wave is realted.
- Crosby (1989) *America's Forgotten Epidemic*: how the pandemic had evaporated from our collective consciousness.
 - Not just the United States, but globally.

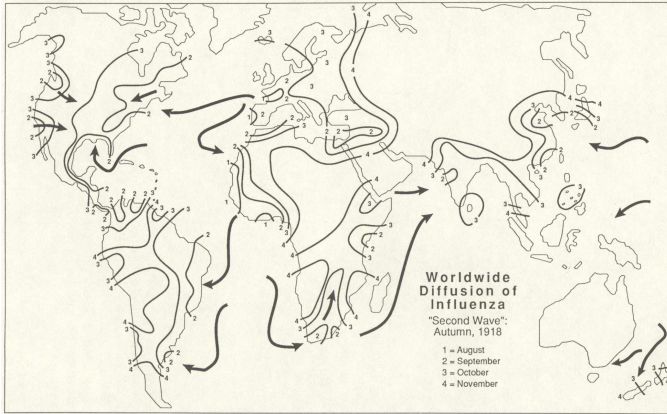
First Wave



From Patterson & Pyle 1991.



Second Wave



From Patterson & Pyle 1991.



Unknown: What Was the Mortality?

- Estimates vary :

Source	Estimate (millions)
Jordan 1927	22
Burnet 1979	50 -100
Beveridge 1978	15 -25
Webster & Lever 1975	20 -50
Schild 1977	15 -50
Patterson & Pyle 1991	25 -39
Johnson & Mueller 2002	50

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Unknown: Why Was the Mortality so High?

- What was the pathogenesis?
- Different pathogens not documented.
- Causes of death similar to other fly pandemics: most deaths due to secondary pneumonia caused by common bacteria.
- High virulence fully not understood.

Unknown: Why Was Mortality Very High among Young and Healthy?

- Answer entirely unknown.

Unknown: Why Was Mortality Low for Elderly?

- Unknown.
- Evidence consistent with previous exposure to the virus that conferred (partial) immunity.

Unknown: Why Were There Three Waves?

- Unknown.
- At least two viruses in the second wave.
- Identity of viruses in first and third wave not established.
- Epidemiology of rapidly recurrent waves not understood through limited mathematical modeling.

Unknown: Where Did the Virus Originate?

- Influenza A virus of the H1N1 subtype.
- All eight gene segments are of avian origin.
- Origin unknown

Lessons

- We do not understand flu.
- Genome sequencing has not solved our puzzles but it has raised new questions that deepen our understanding.
- Lack of understanding of epidemiological dynamics.
- Flu mortality, and probably morbidity, must have multifactorial etiology.