Lost lessons of the 1918 influenza: the 1920s working hypothesis, the public health paradigm, and the prevention of deadly pandemics.

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ABSTRACT

In standard historical accounts, the hyperlethal 1918 flu pandemic was inevitable once a novel influenza virus appeared. However, in the years following the pandemic, it was obvious to distinguished flu experts from around the world that social/environmental conditions interacted with infectious agents and could enhance the virulence of flu germs. Based on the timing and geographic pattern of the pandemic, they hypothesized that an "essential cause" of the pandemic's extraordinary lethality was the extreme, prolonged, and industrial-scale overcrowding of U.S. soldiers in World War One, particularly on troopships. This literature synthesis considers research from history, public health, military medicine, veterinary science, molecular genetics, virology, immunology, and epidemiology. Arguments against the hypothesis do not provide disconfirming evidence. Overall, the findings are consistent with an immunologically similar virus varying in virulence in response to war-related conditions. The enhancement of virulence hypothesis deserves to be included in the history of the pandemic and the war. These lost lessons of 1918 point to possibilities for blocking the transformation of innocuous infections into deadly disasters and are relevant beyond influenza for diseases like COVID-19.

OBJECTIVES

To determine if the 1920s working hypothesis must be rejected, based on the best evidence available today.

BACKGROUND

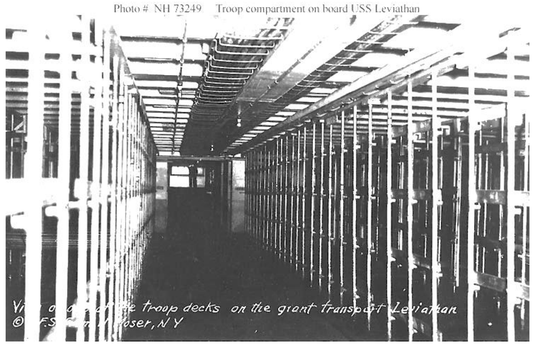
The 1920s working hypothesis on the cause of the 1918 flu pandemic's extraordinary lethality was that war-related conditions, especially industrial-scale, prolonged, extreme overcrowding in the US Army, led to selection for high-virulence influenza. For the last 50 years, this hypothesis has been neglected or actively rejected in the standard histories of the war and the pandemic.

RESULTS

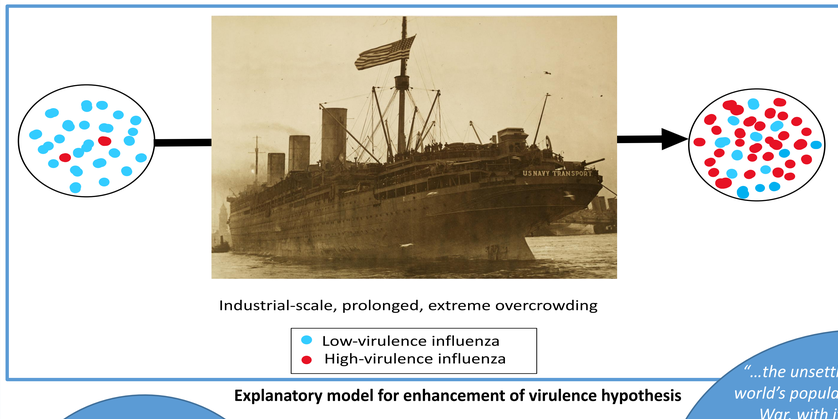
Findings consistent with the 1920s hypothesis

- There was an epidemic of deadly measles (viral) pneumonia in the US Army in early 1918; more pneumonia epidemics were predicted.
- There was a mild 1st (herald) wave before a severe 2nd wave (*suggesting "the novel pandemic virus" was not inherently lethal).*
- People infected in the 1st wave were often immune in 2nd wave (*suggesting an immunologically similar virus in different waves).*
- Between the first and second waves was the main phase of the transoceanic transport of US troops with extreme overcrowding.
- The 2nd wave explodes from Brest, France, where US troops landed.
- The global spread of the 2nd wave frequently involved introduction from (military) ships, with sustained severity related to conditions.
- The 3rd wave corresponds with the return home of guest-workers, demobilized soldiers, liberated POWs.
- The World War created unsanitary living conditions for civilians around the world, including in non-belligerent nations.
- Flu was worse where crowding was worse, e.g. Philadelphia in US
- Soldiers at the front were less vulnerable to flu than those in crowded barracks back home.
- The elderly had negative excess mortality (*suggesting immunity from prior H1N1, arguing against inherent novel H1N1 lethality).*
- Infants and young children were severely affected *(arguing against a biological targeting of "healthy adult" immune systems).*
- Evolutionary biology today provides a model for understanding how overcrowding selects for virulence: host-mobility independence.
- Low-virulence avian influenza virus becomes highly virulent upon introduction into industrial (overcrowded) poultry farms.
- Human activity today is selecting for harmful traits (e.g. antiviral resistance) in human influenza virus.

IMAGES

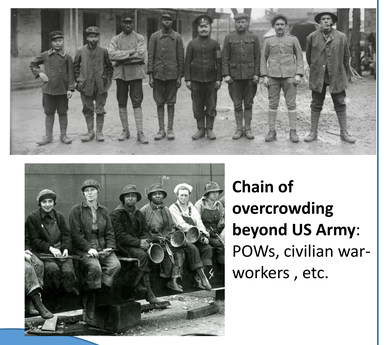


Troopship USS *Leviathan.* Men seeking fresh air on outside decks. Inside troop compartment with 4 berths from floor to ceiling. Below in NY City. Built for 4,000 passengers. Carrying up to 14,000 soldiers. --Images from U.S. Naval History and Heritage Command, and US National Archives.



Industrial-scale, prolonged, extreme overcrowding

Explanatory model for enhancement of virulence hypothesis



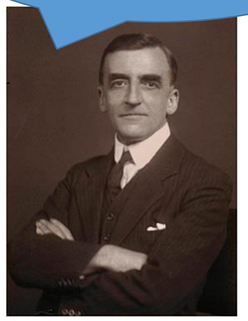
Chain of overcrowding beyond US Army: POWs, civilian war-workers , etc.

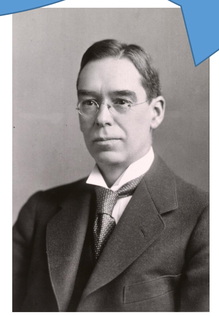
"…the recommendations I have made will tend to correct the existing sanitary errors, but I cannot urge too strongly that they be put into effect at once."
--U.S. Senate testimony Dec. 19, 1917, *NY Times*

"…garrisons, war-time factories, or abnormally over-crowded and ill-ventilated means of transport" constituted "involuntary experimentation in intensive cultivation" and "selection" of a "destructive" microbe, and that this was "essential" in "the chain of causality,"
- - 1920 British Ministry of Health report

"…the unsettled conditions of the world's population due to the Great War, with its numerous close contacts and generally crowded and unhygienic ways of living, led to enhancement of microbic virulence" "…we are forced to accept the hypothesis of a change in the virulence of the infecting microbe as the essential cause of the rise and fall of pandemic influenza."
--*Epidemic Influenza*, 1927

"From the human angle" influenza virus virulence and immunological type are separate characteristics. –Autobiography, 1968.





International experts supported 1920s working hypothesis: William Gorgas (US Army Surgeon General in WWI, controlled yellow fever in Panama to make Canal possible), Major Greenwood (leading medical statistician of early 20th Century) , Edwin Oakes Jordan (Leading microbiologist and public health scientist, founded *Journal of Infectious Diseases*), Frank Macfarlane Burnet (won Nobel Prize, developed method for growing influenza virus in eggs and described how influenza virus genetic reassortment leads to different antigenic types like H1N1).--Images from: UK National Portrait Gallery, National Library of Medicine, Wikimedia

DISCUSSION

Several arguments against the 1920s hypothesis

- "The rich died as readily as the poor."
  - False.
- The pandemic affected women and civilians—not just soldiers.
  - True, and fits with hypothesis.
- The pandemic affected non-belligerent nations.
  - True, and fits with hypothesis.
- The pandemic disproportionately killed soldiers because they were young adults whose healthy immune systems overreacted to the pandemic influenza virus, e.g. with cytokine storms.
  - Maybe, but describes effect—not cause—and doesn't fit with infant deaths or adult immunity from 1st wave.
- The pandemic disproportionately killed soldiers because of conditions at the front unrelated to overcrowding.
  - Does not fit with known pattern of mortality.
- "Once an entirely novel influenza virus had emerged, a pandemic was inevitable; thus, the war did not *per se* cause the pandemic."
  - Does not fit with mild first wave and severe second wave, or with mild H1N1 "pandemics" before and after.
- Overcrowding mattered because it increased transmission.
  - True, but overcrowding could have increased both virulence and transmission.
- Overcrowding didn't matter in WWI because there was not a pandemic in the Second World War (WW2) despite tremendous war-related crowding during the London Blitz .
  - The London Blitz never involved millions of sick people piled on top of each other for ten days like on the WWI troopships. WW2 overcrowding was much less than WWI overcrowding, particularly in the US Army.
- It's all about the virus.
  - In the public health paradigm, pandemics are multifactorial. Causes include multiple infectious agents, as well as host factors and environmental conditions. This is a more complete framework.

CONCLUSIONS & IMPLICATIONS

The hypothesis that industrial-scale prolonged extreme overcrowding of US soldiers constituted a successful "experimentation" in selecting for highly virulent influenza is consistent with available historical and scientific evidence. It has not been replaced by a superior hypothesis for explaining hyperlethality and the other known features of the 1918 flu.

The 1920s working hypothesis deserves to be included in histories of the war and of the pandemic. More importantly, it suggests a possible path forward to prevention of pandemic disasters. These findings are relevant beyond influenza for diseases like COVID-19.

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