Did coronaviruses cause “influenza epidemics” prior to 1918?

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Abstract:

There were epidemics of influenza-like illness during the winters of 1915-6 and 1916-7 when mortality was low among infants and children but high among older adults (like SARS-CoV-2 but not influenza). Records suggest that "influenza" epidemics preceding the 1918-9 pandemic were caused by multiple respiratory viruses possibly an undocumented coronavirus.

The SARS-CoV-2 (COVID-19) pandemic is often referred to as "unprecedented." However, coronaviruses likely coexisted as commensals with various animal hosts for millennia. They were first isolated from animals in the 1930s and are well known pathogens of the respiratory and gastrointestinal tracts of various domestic animals. Coronaviruses were first isolated from humans in 1967. Since then, they have been recognized as common causes of mild upper respiratory illnesses. Coronaviruses were not considered serious threats to human health until 2002 when a coronavirus strain (SARS-CoV-1) that transferred from bats to humans caused acute life-threatening respiratory illnesses among those infected.

SARS-CoV-2 is the seventh coronavirus that is known to infect humans; however, it is only the third that has the potential to cause severe human disease. Interestingly, all three coronaviruses that have caused severe clinicopathologic effects in humans have emerged from animal host precursors in the past 18 years: SARS-CoV-1, MERS-CoV, and SARS-CoV-2. Transmissions of SARS-CoV-1 and MERS-CoV among humans were limited; however, in less than four months, SARS-CoV-2 spread worldwide. The origins of the three recently emerged highly pathogenic coronaviruses were similar. Each was transmitted from a reservoir host (likely bats or pangolins for SARS-CoV and dromedary camels for MERS-CoV) to intermediate animal hosts (perhaps) and then to humans. The initial infections of humans likely occurred in crowded markets where masses of people intermingled with live animals. Because coronaviruses are pervasive, and since for centuries humans have had close contacts with animals that potentially harbor coronaviruses (e.g., wet markets), there have been abundant opportunities for crossovers of various coronavirus strains from their animal hosts to humans. It seems likely, therefore, that more such events have occurred than those detected and characterized in the past 18 years and there are genomic suggestions of cross-over events from cattle.[1] If such events had occurred prior to the time when human

coronavirus infections could be identified in laboratories, the resulting epidemics or pandemics likely would have been labelled "influenza" based on their clinical and epidemiologic manifestations.

For this report, we reviewed characteristics of "influenza epidemics" that occurred before coronaviruses were discovered to identify any that may have been caused by a coronavirus. To distinguish possible coronavirus epidemics from influenza epidemics, we used three characteristics of the ongoing SARS-CoV-2 pandemic as epidemiologic indicators of coronavirus epidemics in general. First, we assumed that during coronavirus epidemics, mortality rates are low among infants and young children. In contrast, consider that during influenza epidemics, age-mortality relationships are typically "U-shaped" with the highest mortality rates among the youngest and oldest.[2-4] Second, we assumed that during coronavirus epidemics, mortality rates increase slowly with increasing age after childhood through approximately 60 years. In contrast, consider that a hallmark of the 1918-9 influenza pandemic was the spike in mortality rates among young adults in their late 20s ("W-shaped" age mortality curve).[5] Third, we assumed that during coronavirus epidemics, mortality rates increase sharply after approximately 60 years of age. In contrast, consider that during the highly lethal second wave of the 1918-9 influenza pandemic, mortality rates among the elderly were lower than during corresponding months of recent prior years.[2,3,6-8]

Vital statistics reports from 35 large USA cities documented sharp peaks of "pneumonia and influenza" mortality during the successive winters of 1915-6 and 1916-7. In some locations, the epidemics were severe; overall, they accounted for estimated 22.8 and 14.0 excess deaths / 100,000 population, respectively.[4] Figure 1A and B shows pneumonia and influenza mortality rates by month between January 1910 and the main pandemic wave in the fall 1918 as well as the periods with excess pneumonia/influenza mortality during 1915-7.

It is noteworthy that in late 1916-early 1917, epidemics of influenza-like illnesses attacked cities throughout the United States nearly simultaneously. The illnesses that characterized the far-flung epidemics ranged from mild coryza to debilitating, life threatening pneumonias, particularly among the elderly. At the same time, epidemics of much more lethal acute respiratory illnesses were attacking soldiers of several nations serving in England and in western Europe. During the winter of 1916–7, British military physicians reported outbreaks of a virulent, life threatening, and distinctive clinical entity, referred to as "purulent bronchitis," among British soldiers at bases in northern France and southern England.[9] During the same period, there were spikes in influenza/pneumonia-related deaths in members of the Australian and Canadian Expeditionary forces serving in England and France.

The wide differences in the clinical expressions of contemporaneous epidemics in 1916-7 suggest that multiple respiratory infectious agents, including but not exclusively influenza viruses -- were co-circulating in the United States and Europe during the period.
Influenza viruses (including seasonal and pandemic strains) and SARS-CoV-2 coronaviruses are the only respiratory infectious agents that are so efficiently transmitted that, in short periods of time, they can cause massive outbreaks of febrile respiratory illnesses with diverse

clinical manifestations in widely dispersed populations across countries and between continents. As such, the widespread epidemics of "influenza-like illnesses" and of purulent bronchitis during the winters of 1915-6 and 1916-7 were likely caused by one or more influenza viruses and/or by a SARS-like coronavirus.

Influenza-related illnesses are generally self-limited and short-lived. However, influenza can be life threatening, particularly among the youngest and oldest of those affected; in turn, the typical age-mortality relationships during influenza epidemics are U-shaped. In contrast, SARS-CoV-2 infections are remarkably benign in infants and children and generally unthreatening in otherwise healthy young and middle-aged adults. However, SARS-CoV-2 infections are life threatening among the very elderly and in those with chronic conditions such as obesity, diabetes, immune deficiencies, and heart, lung, and kidney diseases. In turn, the age-mortality relationships during SARS-CoV-2 epidemics are "reverse ski slope" shaped. Figure 1 shows the composite age mortality figures for both the USA (1C) and England/Wales (1D) emphasizing elderly pneumonia/influenza mortality in 1916 and 1915 respectively even though there is little to differentiate infant mortality at this country-wide level of resolution.

In a review of monthly age-stratified mortality rates in New York City between 1910 and 1920, Olsen and colleagues documented that, during the 1915-6 and 1916-7 winter seasons, the U-shaped age-mortality relationship that typifies influenza epidemics was distorted because mortality rates were unusually low among the youngest (<5 years) and markedly elevated among the oldest (>65 years) aged residents; that is, the age-mortality relationship was SARS-CoV-2-like.[10]

Similarly, official vital statistics of England and Wales between 1890 and 1919 documented that among females (males were not included due to war time commitments) older than 75, influenza-related mortality rates were higher in 1916 than in any year since 1890, while among those younger than 15 and between 15 and 35, influenza-related mortality rates were lower in 1916 than in any of the previous 25 years.[11] Thus, in 1916 and 1917, influenza-related mortality rates among females in England and Wales were low among the youngest and unusually high among the oldest aged. See Figure 2B.

In summary, during 1915-6 and 1916-7, age-mortality relationships, at least in some affected populations, were more SARS- than influenza-like. In the U.S., "influenza and pneumonia" mortality rates among the elderly were higher in 1916-7 than during the 1918 pandemic year. The findings suggest that a SARS-like coronavirus, perhaps with one or more influenza viruses, caused epidemics of influenza-like illnesses during the winters of 1915-6 and 1916-7.

Coronaviruses prior to 1918?

Coronavirus is not a new human viral pathogen; at least four distinct types were known to circulate prior to any knowledge of SARS-CoV 1 (2003) or 2 (2019).[12] Counting the Middle East version MERS, there have been three recognized coronavirus cross-over events in the last 18 years; as such, it seems likely that there were other such events in the not-too distant past. It has been difficult to reconstruct the events that led to the appearance of SARS-CoV-2 in the human population in 2019 (e.g., timing, animal host[s]). It would be even more difficult to discern such details if they occurred in the early 20th century. Using the limited civilian mortality records supplemented with military morbidity records of the First World War, it appears that one or more respiratory viruses caused distinct epidemics just prior to the great mortality of the 1918-9 influenza pandemic. It seems possible that what occurred in early 1918 had been presaged by earlier events in 1916-7 indicating that wartime disruptions and mass population movements had spread this agent(s) globally

Epidemics of mixed viral etiologies seem more likely than single agents given the vast virus universe we now know exists. COVID-19 shows increased mortality in the elderly, spares children and has increased mortality in some racial / ethnic groups for as yet uncertain reasons. The pathogen(s) that caused the winter epidemics of 1915-6 and 1916-7 relatively spared infants and increased in lethality with increasing old age; hence, the age-mortality relationships during the 1915-6 and 1916-7 epidemics were more coronavirus- ("accelerating upward curves") than influenza-like (U-shaped curve). The correspondences prove nothing but do suggest that a coronavirus may have caused pandemic disease prior to the influenza pandemic of 1918-9.

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Legend:

Figure 1:

A. Both pneumonia and influenza mortality per 100,000 population in the registration area of the USA 1910-1918.[2]

B. All-cause mortality and pneumonia/influenza mortality per 100,000 population in the registration area of the USA 1910-1918.[2,3]

C. Age-specific pneumonia/influenza mortality per 100,000 population in the registration area of the USA 1914-1918.[2,3]

D. Age-specific pneumonia/influenza mortality per 1000 (women only) in England and Wales 1914-1918.[11]