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Understanding Influenza Backward

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The novel 2009 influenza A(H1N1) pandemic virus has been an unexpected trigger for pandemic preparedness plans in the United States and elsewhere.[1] It is appropriate to ask how the novel virus might behave epidemiologically in coming months, including the possibility of multiple recurrences or "waves." Spring circulation of the novel virus in the Northern Hemisphere at the end of the 2008–2009 influenza season inevitably has led to comparisons with events in 1918–1919, which in some settings were preceded and followed by outbreaks of respiratory illnesses. Some also believe that the 1918 pandemic began with a premonitory "herald wave," a term related to an old hypothesis, which influenza and dengue fever appeared to have supported, that as new viruses begin to circulate in human populations they inevitably acquire mutations that increase transmissibility and virulence.[2]

Evidence for unusual influenza activity in the years before 1918 is inconclusive. Occasional outbreaks of severe and fatal bacterial pneumonia possibly related to influenza or other respiratory viruses, detected in the European war theater in 1916–1918, are difficult to interpret in the absence of pathological or other diagnostic material.[3,4]

In spring 1918 there were widespread but distinct outbreaks and epidemics of probable influenza in many different parts of Europe, most featuring low to negligible mortality and a scattershot pattern that differed from the undoubted epidemic waves seen later in the year.[5] Outbreaks of mostly nonfatal acute respiratory diseases were also described in the United States in late 1917 and early 1918, especially in military camps but also in cities. Whether the same or different viruses caused any of these outbreaks is speculative. The first documented wave of 1918,[3] often confusingly referred to as the spring wave, was actually a summer surge of influenza fatalities concentrated in some but not all northern European countries between late June and August 1918.[5,6] Despite enormous wartime traffic, it is curious that many English cities had a summer wave but France did not.

The term "wave" entered into common use after a highly fatal global influenza pandemic that spread from Asia in 1889. The term originally was applied to as many as 4 annual and largely seasonal postpandemic influenza mortality peaks recognized in many large cities between 1890 and 1894.[7] What happened in 1918 was quite different. A recent tendency to refer to any influenza-like illness in the first 8 months of 1918 as "the spring wave" has altered the use of this term. Importantly, no viruses from the 1918 spring outbreaks or the summer wave have

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yet been identified. Many investigators working in and since 1918 have cited evidence for or against "spring waves" and their protection against later pandemic waves. However, such data are potentially confounded by inability to discern whether protection, or lack thereof, was associated with spring or summer infectious agents, which could have been different, and by the possibility of nonspecific short-term influenza cross-protection elicited by a different spring virus (had 1 or more circulated).

What is most puzzling is that during the 1918 pandemic, different countries had anywhere from 0 to 3 waves or occurrences, the course and timing of which varied greatly. Most of the world had 2 occurrences, one around October–November 1918 and a second around February–March 1919. Some countries had no activity until as late as 1920 or later, but other locales, such as Hawaii and Australia, had major influenza epidemics in July–October 1918 associated with very low mortality; ie, no significant waves. Hawaii had a modest outbreak with low mortality in 1919, but in 1920 a highly fatal epidemic suddenly appeared, by which time wavelike behavior and high mortality had both nearly disappeared globally.

With so many confusing aspects of 1918 pandemic behavior, it is of interest to compare patterns of the 14 or so other global, transregional, and interregional pandemics since 1510.[7] In doing so, it is difficult to find evidence of 1918-like waves (ie, to pandemic recurrences within a 9-month time frame, as distinguished from the expected annual recurrences typical of early postpandemic and seasonal influenza), herald waves, or other such phenomena. The pandemics of 1957 and 1968 generally exhibited no more than 1 (mostly seasonal) recurrence, typically affecting populations not involved in the first pandemic appearance, and quickly became seasonal endemics.

The 1889 pandemic recurred annually for up to 4 years, but the recurrence intervals were all about 1 year or more apart; in the Northern Hemisphere they usually occurred between October–April (ie, seasonally). Going back further in time, the transregional pandemic of 1847–1848, which did not spread globally, generally lacked distinctive wavelike patterns. Examining 3 previous ostensible pandemics of 1830–1831, 1833–1834, and 1836–1837 fosters the possibility that there may have been only a single pandemic, presumably caused by 1 new pandemic virus whose recurrences could have been at 2-year intervals, as opposed to the 1-year intervals observed nearly 60 years later (1889), because of lower population density, slower travel, or both.

With little consistent evidence of wavelike behavior in the major influenza epidemics and pandemics of the past, there is a general tendency of pandemics to quickly assume annual seasonality in temperate zones. The distinction between seasonal postpandemic recurrences and seasonal endemic recurrences seems to blur as herd immunity increases over time and viruses drift antigenically. Also, examination of past pandemics reveals a great diversity of severity (ie, ability to produce fatality). Occasional evidence of increased severity associated with recurrences is difficult to interpret in view of much greater evidence of unchanged or lessening severity over time[7] and with some newer evidence casting doubt on original herald wave theories.[8]

What should be made of all this? In the last 200 years, at least, pandemic influenza, a respiratory infection of intermediate transmissibility, has never been able to infect the entire population at once. It has generally recurred 1 or more times before settling into the familiar pattern of annual or seasonal endemicity. Why this is so remains unclear, but a key to understanding this phenomenon may partly lie in the strong modern-day tendency for influenza viruses, along with most other respiratory viruses, to favor cold-weather circulation in human populations, at least in temperate zones.[9] Investigators in 1918 believed that 1918 epidemic patterns were related in part to unfavorable influences on the infectious agent of such climatic factors as

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summer temperature and humidity and on a greater tendency for indoor crowding with inadequate ventilation in the winter.[5] Among other poorly understood factors, pandemic influenza recurrence patterns may well be influenced by place and seasonality of appearance.

Considering the long and confusing track record of pandemic influenza, it is difficult to predict the future course of the present H1N1 pandemic. The virus' modest transmission efficiency, the possibility of a degree of preexisting population immunity due to prior cross-reactive viruses and vaccines,[10] and its arrival in the Northern Hemisphere as summer approaches all give reason to hope for a more indolent pandemic course and fewer deaths than in many past pandemics. If summer weather in the Northern Hemisphere slows viral spread, transmission may well resurge again in the fall or winter to create a seasonal wave, but pandemic history suggests that changes neither in transmissibility nor in pathogenicity are inevitable. It will be critical to assess the effect of large-scale pandemic outbreaks in the Southern Hemisphere in the current and coming (winter) months. Once again, influenza is showing its latest tricks and must be watched closely to understand what is happening. It is well to remember that, as Kierkegaard said about life, influenza epidemics are lived forward and understood backward.

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