



# Prior pandemics. looking to the past for insight into the COVID-19 pandemic

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#### **ABSTRACT**

COVID-19 is not the world's first pandemic, not its worst, or likely to be its last. In fact, there have been many pandemics throughout history with lessons for the current one. The most destructive pandemic of all time, at least in terms of the number of people killed in the shortest time, was the "Spanish flu" pandemic of 1918/1919. Why did it happen? What lessons did it teach us? And could it happen again? These questions are addressed in the context of the current COVID-19 pandemic and several other nearly equally devastating pandemics of earlier times

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# 1. Plague of Athens

One of the earliest and most mysterious pandemics for which we have information, was one that occurred in the 5<sup>th</sup> century B.C.E., and became known as the 'Plague of Athens.' The painting by Michiel Sweerts shown in Figure 1 gives artistic expression to the devastating effects of the disorder on the people of Athens. The pandemic erupted during the early months of the Peloponnesian War, a war that pitted Sparta against Athens in a struggle for leadership of the league of Greek city states joined together as a defense against Persian aggression. The war began in the summer of 431 B.C.E., when Sparta marched north and besieged Athens. Almost immediately a strange illness began raging among the Athenians huddled for safety within their walled city, killing an estimated quarter of the population, contributing to both their eventual capitulation and the end of their golden age. The cause of the epidemic has never been determined. However, according to Thucydides, who described the disorder for posterity, victims of the plague exhibited a blistering rash, which if true, makes smallpox a likely cause of the pandemic. A careful review of the limited information available on the pandemic suggests that like several later pandemics, the infection responsible for the Plague of Athens arose in Africa before sweeping throughout what was then the known world [1]. Fortunately for mankind, smallpox was eliminated from the list of human diseases as of 1977, thanks to the use of a highly effective vaccine in a global eradication program.

### 2. The Black Death

In his famous painting, *The Triumph of Death* (Figure 2), Pieter Bruegel depicts the indiscriminate destruction of human life and the social disruption caused by pandemics like the Spanish flu pandemic of 1918/1919, and in Bruegel's case, the Black Death. The latter plague, the Black Death, was a world-wide epidemic (or pandemic) that killed an estimated 1/3 of the population of Europe, Asia and Africa during the second half of the 14<sup>th</sup> Century C.E. and persisted in sporadic outbreaks for another 200 years. Its cause, the bacterium Yersinia pestis, continues to cycle quietly among several animal species, occasionally re-emerging to cause limited outbreaks to this day - most recently in Madagascar. The infection spreads to humans from rats and other small animals by fleas that have fed on infected animals. The 14<sup>th</sup> century pandemic likely originated in Mongolia and spread west along the Silk Road among crusaders returning from fighting in the Holy Land. As reflected in Bruegel's painting, the large number of deaths caused by the infection generated a sense of inevitable doom that led to waves of warfare, crime, popular revolt, flagellation and persecution. Although the 14<sup>th</sup> century pandemic of bubonic plague is the best known example of the Black Death, the Justinian Plague of the 6<sup>th</sup> century C.E. had an equally devastating effect on Rome's Byzantine Empire, killing an estimated 25-50 million people and contributing to the eastern empire's eventual decline [2].

# 3. The White Plague

An even deadly disorder, known as 'the white plague' for draining the color from its victims, has raged continuously in pandemic form since the very dawn of mankind. It too is an infection that came out of Africa ....70,000 years ago with the migration of modern humans northward [3]. In the past 2 centuries alone, the infection, now known as tuberculosis, killed roughly a billion people. Ancient physicians were well aware of the existence of the disorder, though ignorant



Figure 1. Plague in an Ancient City, oil on canvas, c. 1652–1654, by Michiel Sweerts.



Figure 2. The Triumph of Death, oil on panel, c. 1562 by Pieter Bruegel the elder.

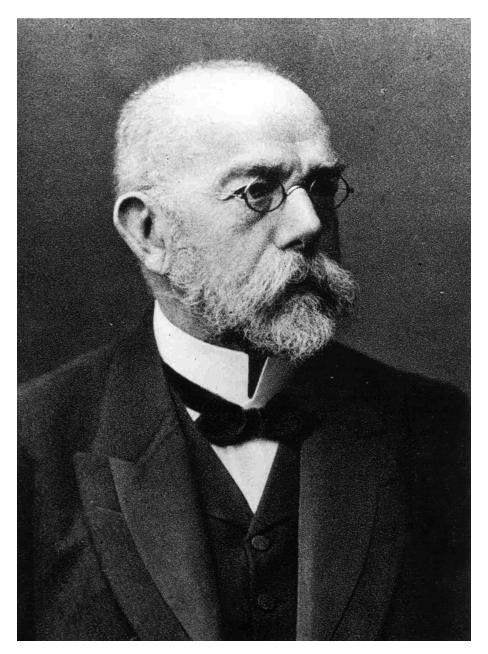


Figure 3. Robert Koch (1843–1910), German physician/microbiologist.

of its cause. Early theories attributed tuberculosis to a variety of factors, including heredity, nutrition, the environment and contagion. Robert Koch (Figure 3) ended speculation as to its cause on 24 March 1882, when he announced to the Berlin Physiological Society that he had isolated the bacterium responsible for tuberculosis – Mycobacterium tuberculosis [2].

## 4. Lues (Latin for plague)

Following the arrival of Europeans in the Americas, one major infection only, as far as I know, traveled from the New World to the Old, that is from the native American population to the Europeans. All others - measles, smallpox, varicella, etc. - traveled in the opposite direction. Syphilis was the exception. We are reasonably confident that this was the case for three reasons. First, five centuries ago syphilis was a spectacularly destructive disorder (of skin, bones and internal organs), the likes of which had never before been seen in the Old World. Second, the native women encountered by Columbus' men on reaching the New World after months at sea were comely, naked and submissive - in short, a recipe for the kind of promiscuity designed to spread a sexuallytransmitted disease like syphilis. And finally, immediately after the return of Columbus and his crews to Spain from their first voyage to the New World, a great plague of this new and highly destructive infection swept across Europe and then to Asia and beyond [4].

### 5. AIDS

The AIDS pandemic contains some grim statistics that call to mind a modern corollary of these past



Figure 4. Thomas – Galveston Hospital. 'My family didn't want me for Christmas. They gave me paper plates and cups to eat off.' Dry point, sheet (irregular), 1994 by Sue Coe.

plagues. Like the Plague of Athens, AIDS is a pestilence that came out of Africa - one caused by a virus (the human immunodeficiency virus) believed to have originated among the chimpanzees of the Congo and having spread to humans in the 1920s. Early on, cases were nearly uniformly fatal, and as indicated in the caption in Figure 4, were shunned by both health professionals and the general public. Happily, treatment of the infection is now one of modern medicine's great success stories. Newly developed anti-retroviral drugs have converted what was a uniformly fatal infection to one with which patients are now able to live a nearly normal lifespan. Nevertheless, the AIDS epidemic is far from over. As of 2019, there were nearly 38 million people infected with the AIDS virus worldwide, 1.7 million of whom were newly infected that year, and 690,000 who died as a result of the infection [5].

## 6. Spanish Flu

The pandemic with the most relevance for the current COVID-19 pandemic, and the one that has been singularly responsible for determining the public health efforts directed against the current pandemic, is, of course, the 1918/1919 Spanish flu pandemic.

No one knows for certain where the pandemic began. If the past is prologue, E. Asia, in particular China, would have been its origin, as it is for most new strains of influenza today. However, according to John Barry [5], 6 the author of an authoritative book on the pandemic titled The Great Influenza, the 1st report of unusual flu

activity in 1918 came not from China, but from Haskell, Co., Kansas, (the location of which is shown in Figure 5) – a county noted for its hog farms and its location in the major flyway for 17 migratory bird species (the significance of which I'll address shortly). According to Barry, the virus made its way from Haskell Co. to nearby Camp Funston in Ft. Riley, KS, to other U.S. mobilization centers and then to France and beyond.

The pandemic was unique in a number of ways. First, as seen in Figure 6, its epidemic curve was odd. It contained 3 distinct waves of cases, with the initial wave occurring in June and July, not during the winter as is typical of seasonal influenza. The second wave extended from October to the end of December, with a third wave peaking in March. Each wave ended as

mysteriously as it had begun. Cases in the first wave were typical of seasonal flu, except for their timing. Cases in the second and third waves were of a severity never before seen, suggesting that the virus had undergone a major mutation.

The pandemic took the lives of an estimated 20 million people worldwide. Some say 50 million. In either case, this was more deaths than the military deaths of World War I and World War II combined. Over half a million people in the U.S. died during the epidemic, with certain villages in Alaska literally wiped out. The overall case-fatality rate was 2–3%, although as in the current COVID-19 pandemic, the number of fatal cases varied depending on the presence of comorbidities such as old age, heart disease, etc. Today, with

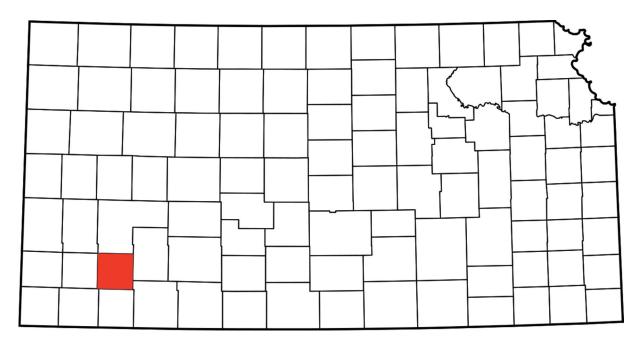


Figure 5. Location of Haskell county within the state of Kansas.

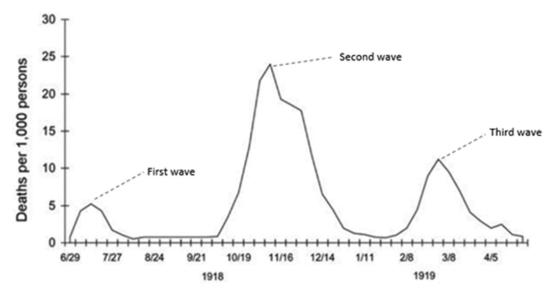


Figure 6. Epidemic curve of the 1918/1919 Spanish flu pandemic.

a global population of 7.6 billion people (vs 1.6 billion in 1918), a pandemic of similar severity would cause between 100 million and 500 million deaths. This is compared to 300,000 to 600,000 influenza deaths occurring during a typical influenza season today.

The illness seen during the 1918 pandemic differed from typical (seasonal) influenza in several ways. For one thing, during the 2<sup>nd</sup> and 3<sup>rd</sup> waves of the pandemic, the illness began as typical flu, but in 2-3% of cases accelerated at an astonishing pace. Shortly after the onset of classic flu symptoms (fever, sore throat, headache and myalgia), an alarming number of cases progressed to respiratory collapse, during which they turned blue, struggled to breath due to congested lungs, began hemorrhaging and died. The cause of such rapid deterioration is thought to have been a combination of bacterial superinfection and a hyper-active immune response to the infection.

Healthcare workers - that is those not involved in the fighting in Europe - became too sick themselves to care for victims of the pandemic. In fact, everyone was either sick or afraid to go near those who were.

The mortality curve of the Spanish flu pandemic was no less odd than its epidemic curve (Figure 7). It had a 'w'-shape, reflecting a substantial increase in mortality among 20-40 year-olds, as opposed to the increased mortality typically seen only among the very young and very old during seasonal influenza. The increased mortality among 20-40 year-olds, of course was also different from what we're seeing in the current COVID-19 pandemic, where the elderly, particularly those with underlying chronic diseases are, by far, the ones most likely to die of the infection.

Several elements came together to create the 'perfect storm' that allowed the 1918 pandemic to materialize. For one thing, the virus was both new and highly virulent. How it arose is not known, but likely it came into existence via the process depicted in Figure 8. According to a theory first envisioned by Robert Webster [7] in 1972, new human strains of influenza are derivatives of viruses that originate in birds (especially water fowl). These bird stains reassort (i.e., mix) with other stains that have found their way into pigs before gaining the capacity to infect humans ... hence, the importance of the Haskell Co. pig farms and their location in the migratory bird flyway.

The strain of influenza virus responsible for the Spanish flu pandemic, now known as the H1N1 strain, has persisted in birds and pigs since 1918, and occasionally spills over into humans. Interestingly, the H1N1 stain currently circulating among humans is now much less aggressive than it was in 1918 .... again, for reasons we still don't understand. Most often, the strains responsible for new influenza epidemics originate in East Asia, particularly China, where pigs and water fowl are caged in close proximity in numerous live markets.

World War I was another factor involved in creating the 'perfect storm' responsible for the catastrophe that became the Spanish flu pandemic. Figure 9 gives you a sense of how great a factor crowding during military operations is in spreading infections such as the H1N1 influenza virus. This was certainly a factor during WWI in fueling the pandemic, just as it was during the Plague of Athens, the Black Death and the White Plague. Crowding, privation, malnourishment, chemical

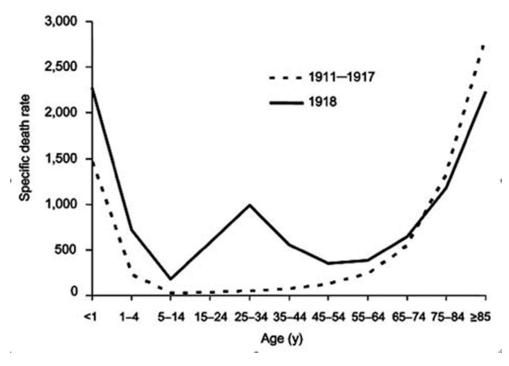


Figure 7. Mortality curve of the 1918/1919 Spanish flu pandemic.

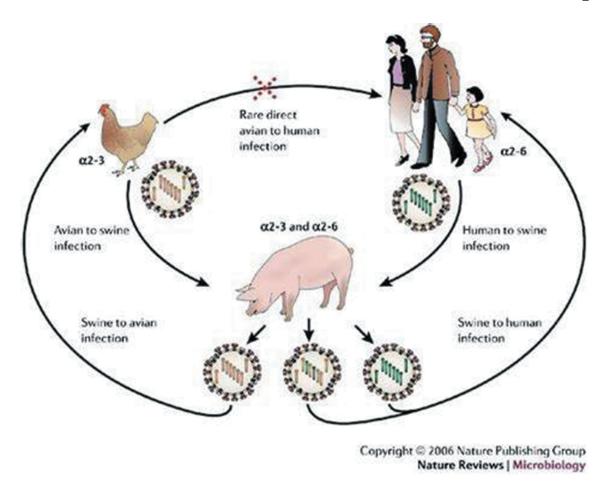


Figure 8. Diagram illustrating Robert Webster's theory as to how bird strains of influenza virus reassort with pig strains to develop into ones capable of infecting humans.

exposure and absence of care givers are just a few of the ways in which World War I stoked the pandemic. However, propaganda could have had the war's most important potentiating effect on the pandemic. During the war, governments' policies toward truth vanished. In the interest of the war effort, the existence of the pandemic was denied by all of the countries engaged in the conflict ....hence the name 'Spanish flu,' reflecting the fact that the only western nation giving an accurate

report of the pandemic was Spain, a non-participant in WWI.

In the U.S., Congress passed the Sedition Act at Wilson's urging, making it a crime punishable by 20 years in prison to 'utter, print, write or publish any disloyal, profane, scurrilous or abusive language . . . .[that would adversely affect] the prosecution of the war.' Government posters urged people to report to the Justice Department anyone spreading pessimistic stories that might impair our effort to win the war. As



Figure 9. World War I trench packed with allied troops.

a result, news of the influenza pandemic, of which Wilson was a victim, was suppressed and control measures delayed until too late [8].

And, of course, the pandemic flourished because there was no flu vaccine, no Tamiflu, no antibiotics and no ICUs. However, there was aspirin. Unfortunately, aspirin had only recently become generally available and its toxicity, one of which is bleeding, was not yet known. The standard practice in 1918 called for administration of huge doses of the drug, which some believe was at least in part responsible for the massive hemorrhaging seen during the pandemic [9].

Well, all this being said, could we have another influenza pandemic like the one that occurred in 1918? A reasonable person would say, 'not likely,' given the fact that we now have flu vaccines, Tamiflu, antibiotics, ICUs and the CDC. Why then do experts like Dr. Anthony Fauci claim that even with all these modern innovations, the appearance of an influenza virus like the 1918 H1N1 strain would likely kill >100 million people today?

For one thing, currently available flu vaccines are only modestly effective. In fact, during the 2017/2018 flu season in Australia, the H3N2 vaccine was just 10% effective. And protection afforded by influenza vaccines wanes rapidly, so rapidly that consideration is being given to immunizing people twice during each season [10]. For another thing, vaccine production is delayed, usually by at least 6 months after the identification of a new strain of influenza.

We don't know why flu vaccines are not as effective as other vaccines. However, we do know that when the virus is cultivated in eggs during the vaccine production process, changes take place in its antigenic composition which favor growth in eggs while simultaneously decreasing the immunogenicity of influenza vaccines in humans [11].

With some strains, repeated annual immunization actually causes a decrease in vaccine effectiveness, for reasons not yet understood [12]. And a substantial portion of the population refuses to be vaccinated or lacks access to vaccines. Moreover, in 1918, fatal cases of flu progressed so rapidly that Tamiflu, antibiotics and ICU care could not have been initiated early enough to have made a difference.

Bottom line ... .Yes a return of a pandemic of the magnitude of the 1918 Spanish flu pandemic is possible, whether due to an influenza virus, coronavirus or some other aggressive respiratory pathogen.

However, in my opinion, a pandemic of the magnitude of the 1918/1919 pandemic would require the sudden emergence not just of a new and highly aggressive strain of pathogen, but also a time of worldwide social disruption, most likely in the form of another world war.

#### **Disclosure statement**

No potential conflict of interest was reported by the author.

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