A Centenary Tale of Two Pandemics: The 1918 Influenza Pandemic and COVID-19, Part II

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Both the 1918 influenza pandemic and the 2019–2021 COVID-19 pandemic are among the most disastrous infectious disease emergences of modern times. In addition to similarities in their clinical, pathological, and epidemiological features, the two pandemics, separated by more than a century, were each met with essentially the same, or very similar, public health responses, and elicited research efforts to control them with vaccines, therapeutics, and other medical approaches. Both pandemics had lasting, if at times invisible, psychosocial effects related to loss and hardship. In considering these two deadly pandemics, we ask: what lessons have we learned over the span of a century, and how are we applying those lessons to the challenges of COVID-19? (*Am J Public Health*. 2021;111(7):1267–1272. https://doi.org/10.2105/AJPH.2021.306326)

There are many similarities, and some differences, between the influenza pandemic of 1918–1919 and the COVID-19 pandemic of 2019–2021. Epidemiological and clinical similarities, including viral origin, transmission, and disease morbidity and mortality, were discussed in Part I of this article.¹

PUBLIC HEALTH RESPONSES

In 1918, fundamental knowledge of sanitation, hygiene, and principles of disease transmission were almost as well understood as they are today.² Mechanisms of respiratory spread and means of preventing respiratory transmission were particularly well understood (Figure 1). The dangerous effects of crowding in public places and closed airflow in buildings and the need to socially distance were likewise fully appreciated. This knowledge had been accumulating since the beginning of the sanitary movement in the 1840s, was greatly advanced by acceptance of a "germ theory" in the 1870s, and had been publicly visible since the 1880s in international public health efforts to control the spread of tuberculosis, then a major killer.

Masks, coughing etiquette, use of clean handkerchiefs, proscription of spitting, placement of spittoons in saloons, isolation of the ill, avoidance of congregation, and closing of sports events, theaters, schools, and churches were all employed in 1918 (Figure 1). In the pandemics of both 1918 and 2019–2021, public health officials recommended wearing face masks. As neither N95 nor modern surgical masks were available in 1918, newspapers printed illustrated instructions on making homemade masks using cloth handkerchiefs and string. Both pandemics prompted fanciful improvisations, including morbid art that seemed to mock death; others made masks for domestic pets (Figure 1). In 1918, some

professional, collegiate, and other sports events were closed,³ but in other cases athletes went on playing with or without masks (Figure 1). Public refusal to wear masks was nearly as common as it is today, even though in 1918 scofflaws often faced stiff fines.

Church gatherings and even court proceedings in 1918 were held outdoors, even in the streets. Forced and self-isolation were common. Just as Boccaccio and friends had done more than five centuries earlier, during the 1348 pandemic of bubonic and pneumonic plague, in 1918 citizens took their own public health actions, such as isolating themselves away from crowds, work, and school. After he was rejected for US military service, future novelist William Faulkner fled to Canada for air force training; the Royal Canadian Air Force locked down (i.e., isolated) Faulkner and the other trainees for a period of time during the pandemic, preventing them from being infected. In the



FIGURE 1— Wearing of Face Masks, 1918 and 2020

Note. In the pandemics of both 1918 (influenza) and 2019–2021 (COVID-19), public health officials recommended wearing face masks for both casual outings and at sports events, and at other large gatherings. Parts a and b: Masked pet owners and pets, circa 1918 (a) and 2020 (b). Parts c and d: Fanciful masks seem to mock the pandemic's "grim reaper" circa 1918 (c) and 2020 (d). Parts e and f: In 1918, some sports events were canceled but others went on, often with masked players or spectators, or both (e). In 2019–2021, many live sports events have been canceled or played without live spectators (f; Photo by Mike Kireev/NurPhoto via Getty images; published with permission).

COVID-19 pandemic, many more people are able to self-isolate at home because of teleworking and betterorganized food-delivery services.

Public health programs in the United States in 1918 were largely state- and city-based. The key pandemic decisionmakers were governors, mayors, local health departments, businessmen, and community leaders, and sometimes nurses and volunteers. Because the pandemic spread so rapidly across the United States,⁴ there was little time for planning or coordination. In smaller towns, the pandemic abruptly emerged, peaked, and was often receding or gone within three or four weeks. Different public health response plans were improvised on the spot. Some were more effective than others; mortality varied greatly from one place to

the next. Many citizens defied public health recommendations.

Associations between strictness of public health measures and low mortality were immediately noted and much discussed in 1918, especially in cities such as Pittsburgh and Philadelphia, Pennsylvania, where overcrowding, lockdown resistance, and tolerance of social gatherings were associated with increased mortality. Modern analyses are consistent with the beneficial effects of stricter measures.² Inactivated bacterial vaccines, intended to prevent death from influenza-associated secondary bacterial pneumonia, which caused the vast majority of pandemic deaths, were often used in 1918, and seem to have been moderately effective in preventing death.^{5,6}

Similarities between the public health responses in 1918–1919 and 2019–2021 are many. National and international public health approaches to both pandemics varied widely, with predictable and unpredictable successes and failures. COVID-19 public health responses rely on the basic strategies of 1918: public "lock down," social distancing, hygiene, and self-isolation. During the COVID-19 pandemic, we have also had polymerase chain reaction and serologic testing to identify the virus and its immune fingerprints, as well as contact tracing, well understood in 1918 but not widely used, probably in part because pandemic explosivity led guickly to an overwhelming number of unmanaged cases. In 2019-2021, we have had bacterial vaccines for two of the bacteria (Streptococcus pneumoniae and Haemophilus

influenzae type b) associated with fatal secondary pneumonias in 1918.⁷ Deployment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines (ongoing as of May 1, 2021) is expected to offer the most realistic hope of ending or at least slowing down the pandemic in the immediate future, although many months of scale-up and vaccine distribution and uptake, prioritizing who gets vaccinated, overcoming vaccine hesitancy, and conceivably dealing with vaccine complications, remain as challenges, especially in countries such as India.

An ominous turn of events now unfolding (as of May 2021) is the emergence of multiple SARS-CoV-2 genetic variants apparently associated with increased transmissibility and possible immune escape, potentially affecting vaccine efficacy and diagnostic test sensitivity.⁸ Though some of these variants have been suspected of causing more severe disease, this has not been scientifically established at the time of this writing. In 1918–1919, high influenza mortality was associated with viral genetic stability, but over the decade of the 1920s, as population immunity rose, mortality and case-fatality declined. Because viruses have not been recovered from the period of 1920–1932, it is unclear whether and when viral attenuation occurred and what were its genetic determinants. In contrast to early suspicions about SARS-CoV-2, there are no data to support that the 1918 influenza virus became more transmissible or more deadly after its emergence.

DIAGNOSIS AND TREATMENT

As the viral cause of the 1918 pandemic was unknown, diagnosis was clinical and

treatment largely supportive. This was the first major disease emergence in which the new technique of diagnostic radiology was used, particularly in the US military.⁹ Although most physicians did not have access to diagnostic x-rays, they were often remarkably skilled at using auscultation, percussion, elicitation of tactile fremitus, and observation of respiration, among other diagnostic skills. Oxygen was often available and used. Appearance of so-called "heliotrope cyanosis" of the prominent facial parts,^{4,10} although not unique to the 1918 pandemic, was recognized as a terminal event associated with profound hypoxia attributable to loss of gas exchange together with metabolic acidosis.

Those who survived bacterial pneumonias often developed life-threatening empyemas, requiring difficult clinical and surgical management.¹¹ In an era when therapeutic successes for various other diseases had been achieved with immune plasmas obtained from hyperimmunized horses, goats, or other animals, some influenza patients were treated, with apparent success, by using human convalescent plasmas,¹² as is now the case with COVID-19.¹³ Then, as now, the pandemics brought out wishfully repurposed drugs that had little chance of success (e.g., quinine in 1918, hydroxychloroquine in 2020). Then, as now, irrational and often harmful remedies enticed the hopeful (enemas and laxatives in 1918; bleach, disinfectants, and colloidal silver in 2020), in addition to known therapeutics such as immune plasmas and monoclonal antibodies, dexamethasone, and the antiviral remdesivir (used in the United States under Food and Drug Administration emergency use authorization), but the efficacy and appropriate therapeutic indications of the latter remain uncertain. Early data, for example, suggest

that in certain patients remdesivir may be of some benefit in shortening illness, although reduction in overall mortality has yet to be fully established.¹⁴

Lacking antivirals and antibiotics in 1918, supportive care was the mainstay of treatment, with an emphasis on attentive nursing care, and was considered the most effective way to save lives. Nurses from the Red Cross and other agencies, as well as volunteer nurses, mostly women with little or no previous nursing training, went into homes, especially in poorer neighborhoods, to tend to the sick; they were widely regarded as pandemic heroes, as are frontline health care workers in 2019–2021. It is of note that deployment of physicians in the war opened leadership positions for women physicians and scientists on the home front at a time when the women's suffrage movement was at its peak.

The COVID-19 pandemic arrives at a time when remarkable medical advances create a diagnostic and therapeutic world unimagined in 1918: rapid viral diagnostics, x-rays and magnetic resonance imaging, blood gasses and chemistries, antibiotics, antivirals, intensive care units with ventilators and monitors, and extracorporeal membrane oxygenation. However, even with the very best care, many patients who survive the period of SARS-CoV-2 replication and cellular damage still do not survive, or survive with serious longterm complications. Lack of complete understanding of the natural history and pathogenesis of COVID-19 stands in counterpoint to the high level of understanding of the mechanisms of secondary bacterial pneumonia in 1918, even though, ironically, treatment options were far fewer in that era. COVID-19 causes pneumonia; however, unlike influenza, it also damages a wide



FIGURE 2— The 1918 Pandemic Inspired Many Artists

Source. Part b used with permission of the artist, Pete Ryan (https://www.peterthomasryan.com). Note. Part a: Dying in his Vienna, Austria, apartment of influenza pneumonia (1918), painter Egon Schiele produced his last artistic work, a drawing of his wife, Edith Harms, 6 months pregnant and suffering from the same disease. She died hours after the drawing. Part b: A 2020 illustration captures the anxieties of COVID-19 spread; design by Pete Ryan for Vox, printed with permission.

range of organ systems, causing vascular¹⁵ and neurologic symptoms,¹⁶ and may be associated with aberrant immune responses¹⁷ that may differ from those of influenza, often complicated by microthrombi in lungs and other organs associated with thromboembolic phenomena.¹⁸ Our understanding of the natural history and pathogenesis of COVID-19 is just beginning.

RESEARCH

The 1918 pandemic occurred at the dawn of the era of virology. Viruses as we know them today had been characterized only as "filter-passing agents," submicroscopic entities of some sort

that were able to cause diseases after passage through porcelain filters that trapped bacteria.¹⁹ Although a descendant of the 1918 human influenza virus was not officially isolated until 15 years after the pandemic, it seems likely that in 1918 two research groups, one in Tunisia and the other in Japan, actually did isolate the virus, but had no way to maintain the agent via continuous passage in humans or animals, or via freezing.^{20,21} Human challenge studies were conducted with human secretions: however, results were problematic. The 1918 pandemic came and went so quickly that comprehensive research programs could not be set up in time, and isolates of virus-containing

infectious material could not be easily propagated or maintained.

In contrast, complete genome sequences of SARS-CoV-2 were made public in early January 2020, and, as of May 2021, many tens of thousands of genome sequences have already been published in online databases. In vitro culture and initiation of in vivo experimental animal modeling have occurred rapidly, followed by extensive basic and clinical testing of diagnostic assays, therapeutics, and vaccines leading to studies on natural history and pathogenesis. The rapidity with which important scientific knowledge about COVID-19 has accrued in just a few months would have astonished scientists in 1918.

RESPONSES TO PSYCHOLOGICAL AND PSYCHOSOCIAL EFFECTS

Then, as now, contemporary photographs show images of horror: stacked bodies, rows of grave markers, and open pits into which bodies are thrown (see Figure 1 in Part I¹). People were dying alone, in their own homes, with no one to comfort them in their final hours. Mercifully, the horrors of the 1918 pandemic were brief, as the pandemic passed through most towns and cities like lightening and was suddenly gone. In 2019–2021, many months of ever-climbing COVID-19 deaths, lockdown, dread, and uncertainty, have added to the tragedy and led to outbreaks of depression, suicide, anger, hopelessness, and even anomie.

It has often been said that the 1918 pandemic was quickly forgotten, reflecting a global exercise in intentional amnesia; however, a closer look at the legacy of 1918 suggests otherwise. For example, the pandemic inspired many artists. In a Vienna, Austria, apartment, a brilliant painter who always aimed to shock and infuriate, Egon Schiele (1890–1918), lay dying of influenza pneumonia in late October 1918. Schiele's last work was a drawing of his wife, Edith Harms (1893–1918), six months pregnant and dying beside him, also of influenza pneumonia (Figure 2). She died hours after the drawing; Schiele survived another two days. Before dying, he arranged with friend Marta Fein-Spraider (1894-c. 1941) to take a photograph at the moment of his death.²² There are also the self-portraits of painter Edvard Munch suffering from influenza in his own bedroom; Thomas Wolfe's wrenching account of the death of his beloved brother Benjamin, written down in

exacting autobiographical detail (Look Homeward, Angel and O Lost: A Story of the Buried Life); Katherine Anne Porter's haunting tale of her own survival (Pale Horse, Pale Rider), unfolding dream-like to its tragic ending; the surge in the Dada art movement in response to the horrors of the war and the pandemic; the hedonistic escapism of the Roaring Twenties; and the exhaustingly comprehensive files of millions of photos, letters, diaries, and recollections that still survive today, and that still speak to us. The 1918 pandemic was never really forgotten. We just forgot that we had never forgotten it.

It will probably be a long time until we can fairly look back to compare and contrast all of the effects of these centenary pandemics. Both came at times of upheaval, periods in which dramatic changes seemed inevitable, but in what direction could not be predicted. In 1918, the world had been stunned by the carnage of the Great War (around 40 million deaths), including the senseless deaths of a whole generation of young men, leaving widows, orphans, and broken, grieving families. Shock, disbelief, anhedonia, and dark cynicism prevailed. Then, just at the war's end, the pandemic came, lightening-like, killing tens of millions more.

The year 1918 marked the last year of the deadliest war, and the first year of the deadliest pandemic in human history, up to that time. Looking back across the last century, we can see that the "War to End All Wars" did not, in fact, end wars, and that the deadliest pandemic did not end deadly pandemics. A century later, tragic wars and tragic pandemics are still occurring, and we are still struggling to deal with them. We retain a hope that we can one day end wars, pandemic diseases, and many other human ills, but, in May 2021, as the COVID-19 pandemic still spreads, it is hard for many to be optimistic.

Like global wars, pandemics are clearly existential threats. Even in the midst of fear and loss, such deadly challenges can bring out the best in us. If 2021 seems the worst of times, we can still look back, as did centenarian Marilee Shapiro Asher,¹ down a path that is dark and long, but still seeded with hope. Asher, the artist who survived both the 1918 and the 2020 pandemics, died at home on September 11, 2020. Through two pandemics, four major wars, a Great Depression, and a Great Recession, Asher saw more than a century of progress and struggle and was able to find a life-long joy and fulfillment. Near the end, she confronted humankind's latest existential challenge, COVID-19, and survived it. If we can remember the best in Asher and in humankind, so will most of the rest of us. **AIPH**

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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