**IMMUNIZATIONS NEWSLETTER**

**PROVIDING GSA MEMBERS WITH UPDATES ON ADULT IMMUNIZATIONS**

**JANUARY 2018**

Developed by The Gerontological Society of America

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**FEATURES**

**News**

- “To achieve the ultimate objective of a universal influenza vaccine, a broad range of expertise and substantial resources will be required to fill gaps in our knowledge and develop a transformative approach to influenza-vaccine design,” authors wrote in a Perspective article in the *New England Journal of Medicine*. Making the case for a 21st century influenza vaccine, Anthony S. Fauci and other public health officials point to potential problems with the current influenza vaccine based on poor vaccine effectiveness seen in the Southern Hemisphere during the just-completed winter season. Antigenic drift was evident for the A/H3N2 strain, and vaccine produced through egg-based cultures seemed to be less effective than cell-based cultures. The writers advocate for a universal vaccine—one that targets viral antigens that do not mutate frequently—and use of newer technologies in the production process.

- **Global influenza-associated respiratory mortality** is greater than previously estimated, according to an article published online last month in *Lancet*. Using data from a larger and diverse group of countries, researchers found the greatest influenza mortality burden in the world’s poorest regions and among older adults. People aged 75 years and older and people living in sub-Saharan African countries experienced the highest rates of influenza-associated respiratory deaths. Eastern Mediterranean and Southeast Asian countries had slightly lower but still high rates of influenza-associated respiratory deaths.

**Resources**

- Influenza vaccination resources are available from the National Adult and Influenza Immunization Summit.
Influenza vaccine effectiveness presents a real communication challenge. For the 2017–18 influenza season, there are already reports coming from the Southern Hemisphere of a disappointingly low vaccine effectiveness figure against the A/H3N2 strain. How might a health professional express that we can and should do better, while also encouraging patients to still get this year’s vaccine?

It is important to acknowledge that vaccine effectiveness against A/H3N2 strains is generally lower than for other strains. The A/H3N2 strains often have more antigenic drift throughout the season, but they also seem to shift more than other strains when the virus is grown in eggs as part of vaccine production (see above summary of article from the *New England Journal of Medicine*). Also, remember that older adults generally have a lower immune response to influenza vaccines compared with younger, healthier adults.

Despite these limitations, there is good news that patients need to know. While vaccine effectiveness is not as high as most would like, it does still prevent serious illness, hospitalization, and death. Several vaccines have been shown to better protect older adults, including Sanofi Pasteur’s Fluzone High-Dose and Flublok vaccines as well as Seqirus’s adjuvanted Fluad vaccine. For older adults, getting an influenza vaccine each year is the best way to prevent the flu. And hearing a recommendation from a health professional is the top reason that patients get the vaccine.

**IT’S BEEN 100 YEARS SINCE THE LAST HIGHLY VIRULENT INFLUENZA PANDEMIC. WHY?**

Many questions can be asked about one of the most important yet overlooked events of the 20th century. Why did a pandemic influenza spread so easily across the world in 1918? Why was the virus so virulent? Why did the pandemic occur in three waves? And perhaps the most important question of all: why hasn’t another similarly deadly influenza pandemic occurred since then?

With all the research on the influenza disease and virus over the past century, the pandemic known best by the misnomer “Spanish flu” remains in many ways a tragic, frightening enigma. A recently published book, *Pale Rider* by Laura Spinney, summarizes what is known about the influenza pandemic of 1918. Here are some highlights of what she found.
In any narrative about an event like the 1918 influenza pandemic, a writer needs to set the scene. When the story is told 100 years after the fact, an accurate sense of the setting is especially important to fill in important details in the rough outline provided by history books.

First, there’s World War I, which officially ended on November 11, 1918. Despite its name, this conflict was fought primarily in central Europe and directly involved a limited number of countries. Troop movements and tears in the social fabric resulting from the conflict in general certainly contributed to spread of the virus and an inadequate response to it, but this exceptionally virulent flu did not likely originate in Spain nor spread globally because of a “world” war.

Important also to remember is the state of scientific and medical knowledge in the second decade of the 20th century. People had known about microorganisms for a couple centuries before Koch established germ theory as a cause of disease in the 1880s. Even though this theory quickly became accepted in scientific circles and applied by the public health community, many people continued to believe earlier Galenic ideas about miasma (“bad air”) as a primary cause of disease.

The role of public health in society was still being refined when the influenza pandemic occurred. Quarantines and forced institutionalizations were used by public health authorities to prevent spread of pathogens by establishing a cordon sanitaire but were viewed by many in the general public as depriving people of their rights. As now, people were resistant to compulsory vaccination—even when it came to stopping smallpox, the disease successfully prevented by Jenner’s vaccine in late 1700s.

The first virus was isolated in the 1890s, but the influenza virus had not been identified in 1918. The etiology of the “flu” was thus unclear. During the pandemic, the bacterium Haemophilus influenzae (first known as Pfeiffer’s bacillus) was identified and characterized as the cause of influenza based on its presence in respiratory isolates of patients with the disease. Those were secondary infections, with that pathogen as well as staphylococci, streptococci, and pneumococci taking advantage of the damage in the respiratory lining brought on by the primary influenza virus and the body’s reaction to it.

The influenza virus is now known to undergo antigenic shifts during passage through birds and pigs, but whether that happened with the 1918 pandemic virus is unclear. Based on all evidence now available, the virus—an A virus with H1 and N1 antigens—probably emerged as a human pathogen in the waning months of the 1917–18 influenza season (Figure 1) in either northern China, on the Western Front of the European war theater, or at Camp Funston, an American army base in Kansas. The virus circulated widely in this first wave but produced relatively mild illness—just your garden-variety influenza, for the most part. Troops in Europe were packed into trenches, facilitating human-to-human transfer. Illness and deaths wrought by the virus altered the trajectory of the war by affecting the Central Powers more than the Allies.
Recent research indicates that the pandemic influenza virus likely mutated over the summer of 1918. It became highly contagious, with greater capacity to spread among people, and more virulent. The second wave of disease began erupting in early fall. Millions died before the pandemic seemed to subside in December. A maritime quarantine kept the virus out of Australia, but morbidity affected as many as one third of all people on the planet, and millions died in countries on the other five inhabited continents.

The respite was not to last. A third wave began in January 1919. The Australian quarantine was lifted too soon, and this continent recorded 12,000 deaths during its summer of 1918–19. New York City had its peak activity in January 1919, and illness in Paris affected the pace and outcomes of the peace negotiations. U.S. President Woodrow Wilson, who had pre-existing neurologic damage from ministrokes, had a case of influenza that likely contributed to his death from a massive stroke in October of that year. Wilson’s case of influenza reduced his effectiveness in Paris when sanctions on Germany were debated. His death took him out of the debate when the U.S. Congress considered the treaty and participation in the League of Nations. Thus, one could argue that the 1918 influenza sowed the seeds of German discord that led to World War II.

Other waves may have followed the third, with cases reported as late as spring 1920. Since the cause of influenza was unknown at the time and recordkeeping was inconsistent, the number of deaths attributed to the 1918 pandemic influenza virus can only be estimated in the 50 million to 100 million range—3% to 6% of the world's 1.8 billion people. Thus, the pandemic killed more people than World War I; if the latter figure is correct, it killed more than the two world wars combined. Biological and sociological effects would continue for decades as a result of the stress of viral infection in utero or during infancy, loss of parents to the disease, and long-term effects such as slightly shorter height at adulthood and increased risk of heart disease after 60 years of age. In addition to the symptoms that would be expected in any case of influenza—fever, systemic pain, sore throat, coughing—people who acquired the 1918 pandemic influenza virus became gravely ill, sometimes in just a few hours. When the second wave of the pandemic began, flu symptoms were worse, and people were more likely to develop bacterial pneumonia, have trouble breathing, and have a progressive cyanosis that began in the extremities and moved across the body.

As shared by Spinney, the clinical presentation in patients with pandemic influenza was profound: "Two mahogany spots appeared over their cheekbones, and within a few hours that colour had flushed their faces from ear to ear—'until it is hard,' wrote one U.S. Army doctor, 'to distinguish the [black] men from the white.'" Such effects resulted from the dramatic destruction of the lining of the respiratory tract by the influenza virus and the body's initial generalized interferon response to it.

The 1918 influenza pandemic affected people outside the usual U-shaped mortality curve that indicates deaths in the very young and the very old. Instead, available data show a W-shaped mortality curve with the extra peak affecting young adults (Figure 2). Given the state of the world at the time of the pandemic, malnutrition was exceedingly common, as were other infectious diseases such as tuberculosis, anthrax, typhoid, cholera, malaria, and rabies. Host factors could have been in play, as older adults might have had some immunity from the “Russian flu” of the 1890s.
When the pandemic influenza struck, the status of medicine was not elevated much beyond that of other professions people turned to when they were sick: homeopaths, naturopaths, osteopaths, or faith healers. Even for those infected with the virus, physicians had little to offer beyond aspirin for fever and pain—and some evidence shows that morbidity and mortality during the pandemic may have been worsened by excessive doses of this drug, especially in America and other wealthy countries.

The pandemic overwhelmed the health care system as well as much of the rest of society. Gyms and other large buildings were converted into hospitals or morgues. Bodies sometimes stacked up in the streets. One of the hardest hit countries, India, had insufficient firewood for the ritual cremations, leading to people filling the rivers with intact bodies. As a result, more people were exposed to the pandemic influenza virus as well as other pathogens that caused people to die, and a very bad situation was made even worse. Until 1679, Europeans believed that black swans did not exist, Spinney wrote.

BEHAVIORAL/SOCIAL SCIENCES

The reason? They had never seen one. As soon as a Dutch explorer discovered black swans in Australia, “all Europeans realized that black swans had to exist, since other animals came in different colours.”

So it is with an influenza pandemic. Will a pandemic as virulent and transmissible as the one in 1918 ever happen again? Of course it will—the relevant questions are when, what will the disease be like, what preparations will have been made, and how will people react to widespread disease?

While the inherent virulence of a pandemic virus could be as severe as 1918, modern medicine has vaccines to prevent disease, antivirals to treat the virus, antibiotics to treat secondary bacterial infections, and intensive care units to take care of seriously ill patients. Thus, we might expect a better outcome. But supplies of vaccines and drugs could be limited and intensive care units overwhelmed. Vaccines are our best hope to ameliorate the outcome—but there is the issue of making vaccine rapidly enough and in sufficient quantity. One thing is certain, though, the world will be changed by the next influenza pandemic that causes widespread morbidity and mortality, just as it was by the tragic strain that wiped out families and communities 100 years ago.

SOURCES AND RESOURCES

FIGURE 1. Three waves of 1918 pandemic influenza in the United Kingdom.


FIGURE 2. W-shaped influenza/pneumonia mortality curve during 1918 pandemic and U-shaped curve observed during prior 7 influenza seasons.


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R. Gordon Douglas, MD, NAVP Workgroup Chair, is Professor Emeritus of Medicine at Weill Cornell Medical College and Director of biotech companies: Vical, Inc. (Chairman) and Novadigm (Chairman).

L. Michael Posey, BSPharm, MA, Editor, is President, Pharmacy Editorial & News Services.

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