

Commentary

The site of origin of the 1918 influenza pandemic and its public health implications

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The 1918–1919 influenza pandemic killed more people than any other outbreak of disease in human history. The lowest estimate of the death toll is 21 million, while recent scholarship estimates from 50 to 100 million dead. World population was then only 28% what is today, and most deaths occurred in a sixteen week period, from mid-September to mid-December of 1918.

It has never been clear, however, where this pandemic began. Since influenza is an endemic disease, not simply an epidemic one, it is impossible to answer this question with absolute certainty. Nonetheless, in seven years of work on a history of the pandemic, this author conducted an extensive survey of contemporary medical and lay literature searching for epidemiological evidence – the only evidence available. That review suggests that the most likely site of origin was Haskell County, Kansas, an isolated and sparsely populated county in the southwest corner of the state, in January 1918 [1]. If this hypothesis is correct, it has public policy implications.

But before presenting the evidence for Haskell County it is useful to review other hypotheses of the site of origin. Some medical historians and epidemiologists have theorized that the 1918 pandemic began in Asia, citing a lethal outbreak of pulmonary disease in China as the forerunner of the pandemic. Others have speculated the virus was spread by Chinese or Vietnamese laborers either crossing the United States or working in France.

More recently, British scientist J.S. Oxford has hypothesized that the 1918 pandemic originated in a British Army post in France, where a disease British physicians called "purulent bronchitis" erupted in 1916. Autopsy reports of

soldiers killed by this outbreak – today we would classify the cause of death as ARDS – bear a striking resemblance to those killed by influenza in 1918 [2].

But these alternative hypotheses have problems. After the 1918–1919 pandemic, many investigators searched for the source of the disease. The American Medical Association sponsored what is generally considered the best of several comprehensive international studies of the pandemic conducted by Dr. Edwin Jordan, editor of *The Journal of Infectious Disease*. He spent years reviewing evidence from all over the world; the AMA published his work in 1927.

Since several influenza pandemics in preceding centuries were already well-known and had come from the orient, Jordan first considered Asia as the source. But he found no evidence. Influenza did surface in early 1918 in China, but the outbreaks were minor, did not spread, and contemporary Chinese scientists, trained by Rockefeller Institute for Medical Research (now Rockefeller University) investigators, stated they believed these outbreaks were endemic disease unrelated to the pandemic [3]. Jordan also looked at the lethal pulmonary disease cited by some historians as influenza, but this was diagnosed by contemporary scientists as pneumonic plague. By 1918 the plague bacillus could be easily and conclusively identified in the laboratory [3]. So after tracing all known outbreaks of respiratory disease in China, Jordan concluded that none of them "could be reasonably regarded as the true forerunner" of the pandemic [3].

Jordan also considered Oxford's theory that the "purulent bronchitis" in British Army camps in 1916 and 1917 was

the source. He rejected it for several reasons. The disease had flared up, true, but had not spread rapidly or widely outside the affected bases; instead, it seemed to disappear [3]. As we now know a mutation in an existing influenza virus can account for a virulent flare-up. In the summer of 2002, for example, an influenza epidemic erupted in parts of Madagascar with an extremely high mortality and morbidity; in some towns it sickened an outright majority – in one instance sixty-seven percent – of the population. But the virus causing this epidemic was an H3N2 virus that normally caused mild disease. In fact, the epidemic affected only thirteen of 111 health districts in Madagascar before fading away [4]. Something similar may have happened in the British base.

Jordan considered other possible origins of the pandemic in early 1918 in France and India. He concluded that it was highly unlikely that the pandemic began in any of them [3].

That left the United States. Jordan looked at a series of spring outbreaks there. The evidence seemed far stronger. One could see influenza jumping from Army camp to camp, then into cities, and traveling with troops to Europe. His conclusion: the United States was the site of origin.

A later equally comprehensive, multi-volume British study of the pandemic agreed with Jordan. It too found no evidence for the influenza's origin in the Orient, it too rejected the 1916 outbreak among British troops, and it too concluded, "The disease was probably carried from the United States to Europe [5]."

Australian Nobel laureate MacFarlane Burnet spent most of his scientific career working on influenza and studied the pandemic closely. He too concluded that the evidence was "strongly suggestive" that the disease started in the United States and spread with "the arrival of American troops in France [6]."

Before dismissing the conclusions of these contemporary investigators who lived through and studied the pandemic, one must remember how good many of them were. They were very good indeed.

The Rockefeller Institute, whose investigators were intimately involved in the problem, alone included extraordinary people. By 1912 its head Simon Flexner – his brother wrote the "Flexner report" that revolutionized American medical education – used immune serum to bring the mortality rate for meningococcal meningitis down from over 80% to 18%; by contrast, in the 1990s at Massachusetts General Hospital a study found a 25% mortality rate for bacterial meningitis. Peyton Rous won the Nobel Prize

in 1966 for work he did at the institute in 1911; he was that far ahead of the scientific consensus. By 1918 Oswald Avery and others at Rockefeller Institute had already produced both an effective curative serum and a vaccine for the most common pneumococcal pneumonias. At least partly because of the pandemic, Avery would spend the rest of his career studying pneumonia. That work led directly to his discovery of the "transforming principle" – his discovery that DNA carries the genetic code.

The observations of investigators of this quality cannot be dismissed lightly. Jordan was of this quality.

More evidence against Oxford's hypothesis comes from Dr. Jeffrey Taubenberger, well-known for his work extracting samples of the 1918 virus from preserved tissue and sequencing its genome. He initially believed, based on statistical analysis of the rate of mutation of the virus that it existed for two or three years prior to the pandemic. But further work convinced him that the virus emerged only a few months prior to the pandemic (personal communication with the author from J Taubenberger, June 5th 2003).

So if the contemporary observers were correct, if American troops carried the virus to Europe, where in the United States did it begin?

Both contemporary epidemiological studies and lay histories of the pandemic have identified the first known outbreak of epidemic influenza as occurring at Camp Funston, now Ft. Riley, in Kansas. But there was one place where a previously unknown – and remarkable – epidemic of influenza occurred.

Haskell County, Kansas, lay three hundred miles to the west of Funston. There the smell of manure meant civilization. People raised grains, poultry, cattle, and hogs. Sod-houses were so common that even one of the county's few post offices was located in a dug-out sod home. In 1918 the population was just 1,720, spread over 578 square miles. But primitive and raw as life could be there, science had penetrated the county in the form of Dr. Loring Miner. Enamored of ancient Greece – he periodically reread the classics in Greek – he epitomized William Welch's comment that "the results [of medical education] were better than the system." His son was also a doctor, trained in fully scientific ways, serving in the Navy in Boston.

In late January and early February 1918 Miner was suddenly faced with an epidemic of influenza, but an influenza unlike any he had ever seen before. Soon dozens of his patients – the strongest, the healthiest, the most robust people in the county – were being struck down as suddenly as if they had been shot. Then one patient pro-

gressed to pneumonia. Then another. And they began to die. The local paper *Santa Fe Monitor*, apparently worried about hurting morale in wartime, initially said little about the deaths but on inside pages in February reported, "Mrs. Eva Van Alstine is sick with pneumonia. Her little son Roy is now able to get up... Ralph Lindeman is still quite sick... Goldie Wolgehagen is working at the Beeman store during her sister Eva's sickness... Homer Moody has been reported quite sick... Mertin, the young son of Ernest Elliot, is sick with pneumonia... Pete Hesser's children are recovering nicely... Ralph McConnell has been quite sick this week (Santa Fe Monitor, February 14th, 1918)."

The epidemic got worse. Then, as abruptly as it came, it disappeared. Men and women returned to work. Children returned to school. And the war regained its hold on people's thoughts.

The disease did not, however, slip from Miner's thoughts. Influenza was neither a reportable disease, nor a disease that any state or federal public health agency tracked. Yet Miner considered this incarnation of the disease so dangerous that he warned national public health officials about it. *Public Health Reports* (now *Morbidity and Mortality Weekly Report*), a weekly journal produced by the U.S. Public Health Service to alert health officials to outbreaks of communicable diseases throughout the world, published his warning. In the first six months of 1918, this would be the only reference in that journal to influenza anywhere in the world.

Historians and epidemiologists have previously ignored Haskell most likely because his report was not published until April and it referred to deaths on March 30, after influenza outbreaks elsewhere. In actuality, by then the county was free of influenza. Haskell County, Kansas, is the first recorded instance anywhere in the world of an outbreak of influenza so unusual that a physician warned public health officials. It remains the first recorded instance suggesting that a new virus was adapting, violently, to man.

If the virus did not originate in Haskell, there is no good explanation for how it arrived there. There were no other known outbreaks anywhere in the United States from which someone could have carried the disease to Haskell, and no suggestions of influenza outbreaks in either newspapers or reflected in vital statistics anywhere else in the region. And unlike the 1916 outbreak in France, one can trace with perfect definiteness the route of the virus from Haskell to the outside world.

All Army personnel from the county reported to Funston for training. Friends and family visited them at Funston. Soldiers came home on leave, then returned to Funston.

The Monitor reported in late February, "Most everybody over the country is having lagrippe or pneumonia (Santa Fe Monitor, February 21st 1918)." It also noted, "Dean Nilson surprised his friends by arriving at home from Camp Funston on a five days furlough. Dean looks like soldier life agrees with him." He soon returned to the camp. Ernest Elliot left to visit his brother at Funston as his child fell ill. On February 28, John Bottom left for Funston. "We predict John will make an ideal soldier," said the paper (Santa Fe Monitor February 28th, 1918).

These men, and probably others unnamed by the paper, were exposed to influenza and would have arrived in Funston between February 26 and March 2. On March 4 the first soldier at the camp reported ill with influenza at sick call. The camp held an average of 56,222 troops. Within three weeks more than eleven hundred others were sick enough to require hospitalization, and thousands more – the precise number was not recorded – needed treatment at infirmaries scattered around the base.

Whether or not the Haskell virus did spread across the world, the timing of the Funston explosion strongly suggests that the influenza outbreak there did come from Haskell. Meanwhile Funston fed a constant stream of men to other American locations and to Europe, men whose business was killing. They would be more proficient at it than they knew.

Soldiers moved uninterrupted between Funston and the outside world, especially to other Army bases and France. On March 18, Camps Forrest and Greenleaf in Georgia saw their first cases of influenza and by the end of April twenty-four of the thirty-six main Army camps suffered an influenza epidemic [3]. Thirty of the fifty largest cities in the country also had an April spike in excess mortality from influenza and pneumonia [7]. Although this spring wave was generally mild – the killing second wave struck in the fall – there were still some disturbing findings. A subsequent Army study said, "At this time the fulminating pneumonia, with wet hemorrhagic lungs, fatal in from 24 to 48 hours, was first observed [8]." (Pathology reports suggest what we now call ARDS.) The first recorded autopsy in Chicago of an influenza victim was conducted in early April. The pathologist noted, "The lungs were full of hemorrhages." He found this unusual enough to ask the then-editor of *The Journal of Infectious Diseases* "to look over it as a new disease" [3].

By then, influenza was erupting in France, first at Brest, the single largest port of disembarkation for American troops. By then, as MacFarlane Burnet later said, "It is convenient to follow the story of influenza at this period mainly in regard to the army experiences in America and Europe [6]."

The fact that the 1918 pandemic likely began in the United States matters because it tells investigators where to look for a new virus. They must look everywhere.

In recent years the World Health Organization and local public health authorities have intervened several times when new influenza viruses have infected man. These interventions have prevented the viruses from adapting to man and igniting a new pandemic. But only 83 countries in the world – less than half – participate in WHO's surveillance system (WHO's flunet website <http://rhone.b3e.jussieu.fr/flunet/www/docs.html>). While some monitoring occurs even in those countries not formally affiliated with WHO's surveillance system, it is hardly adequate. If the virus did cross into man in a sparsely populated region of Kansas, and not in a densely populated region of Asia, then such an animal-to-man cross-over can happen anywhere. And unless WHO gets more resources and political leaders move aggressively on the diplomatic front, then a new pandemic really is all too inevitable.

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