“THE GREAT INFLUENZA”, BY JOHN M. BARRY (2004)

Ultimately, the virus mutated into a less lethal form before a cure was found.

Virus spread worldwide with troop movements.

Virus came in three waves: early 1918; late 1918; and 1919. Second wave was most deadly and most explosive. Last case was in March 1920.

The waves were due to “passage”, a phenomenon whereby a virus can become more deadly as adapts to its hosts.

> Influenza is an RNA virus and mutates much faster than DNA viruses but less accurately. As a result, a “swarm” of different but related strains can be in circulation.
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> “’Passage’ reflects an organism’s ability to adapt to its environment. When an organism of weak pathogenicity passes from living animal to living animal, it reproduces more proficiently, growing and spreading more efficiently. This often increases virulence.”
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> These mutations allow a virus to adapt rapidly and become resistant to drugs, but also tend to make it less lethal over time.
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> “But the phenomenon is complex. The increase in killing efficiency does not continue indefinitely. If a pathogen kills too efficiently, it will run out of hosts and destroy itself. Eventually its virulence stabilizes and even recedes. Especially when jumping species, it can become less dangerous instead of more dangerous. This happens with the Ebola virus, which does not normally infect humans. Initially Ebola has extremely high mortality rates, but after it goes through several generations of human passages, it becomes far milder and not particularly threatening.”

Two thirds of deaths occurred in a period of 24 weeks from mid-September 1918 to December 1918.

> “During the course of the epidemic, 47 percent of all deaths in the United States, nearly half of all those who died from all causes combined—from cancer, from heart disease, from stroke, from tuberculosis, from accidents, from suicide, from murder, and from all other causes—resulted from influenza and its complications. And it killed enough to depress the average life expectancy in the United States by more than ten years.”
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> “Some of those who died from influenza and pneumonia would have died if no epidemic had occurred. Pneumonia was after all the leading cause of death. So the key figure is actually the “excess death” toll. Investigators today believe that in the United States the 1918–19 epidemic caused an excess death toll of about 675,000 people. The nation then had a population between 105 and 110 million, while it was approaching 300 million in 2006. So a comparable figure today would be approximately 1,750,000 deaths.”
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> “Chiefly because antibiotics would slash the toll from secondary bacterial infections, if a virus caused a 1918-like pandemic today, modern medicine could likely prevent significantly more than half of those deaths—assuming adequate supplies of antibiotics, which is quite an assumption—but tens of millions would still die. And a severe influenza pandemic would hit like a tsunami, inundating intensive-care units even as doctors and nurses fall ill themselves and generally pushing the health care system to the point of collapse and possibly beyond it.

> Hospitals, like every other industry, have gotten more efficient by cutting costs, which means virtually no excess capacity—on a per capita basis the United States has far fewer hospital beds than a few decades ago. Indeed, during a routine influenza season, usage of respirators rises to nearly 100 percent; in a pandemic, most people who needed a mechanical respirator probably would not get one. This and similar problems—such as if a particular secondary bacterial invader is resistant to antibiotics, or shortages of such seemingly trivial items as hypodermic needles or bags to hold IV fluids (a severe shortage of these bags is a major problem as I write this)—could easily moot many medical advances since 1918."

Initial response in the US was poor for a variety of reasons, including poor municipal governance and public sanitation (Philadelphia), as well as a desire to maintain morale for the war effort. Vital information which should have been communicated to the public was not.

The scientific response to the epidemic was rapid but much energy was wasted in the belief that the (airborne, filterable) virus was in fact a bacterial infection.

The young and able made up a large proportion of the dead

> Possibly because army camps were frequent sites of outbreak; and
>
> Possibly too because older people had already been exposed to a related strain of the virus in an earlier epidemic).

The spread was accelerated by poor and cramped living quarters in army bases and big cities.

There were two forces which allayed the virus' impact (see the full discussion below):

i. People developed a natural immunity after surviving an earlier wave; and

ii. The virus continued to mutate but mutated into a less lethal strain (following a reversion to the mean of all influenza viruses).

<u>Population centres hit later in the second wave of the epidemic saw a lower rate of mortality as the virus mutated into a less lethal (but still very lethal) strain.</u>

> "NOTHING COULD HAVE STOPPED the sweep of influenza through either the United States or the rest of the world—but ruthless intervention and quarantines might have interrupted its progress and created occasional firebreaks. Action as ruthless as that taken in 2003 to contain the outbreak of a new disease called severe acute respiratory syndrome, SARS, could well have had effect.* Influenza could not have been contained as SARS was—influenza is far more contagious. But any interruption in influenza's spread could have had significant impact. For the virus was growing weaker over time. Simply delaying its arrival in a community or slowing its spread once there—just such minor successes—would have saved many, many thousands of lives."

However, immunity to one strain of the virus was not enough to guarantee immunity to subsequent strains and the third wave was still very deadly.

Direct quote from the book:

With the influenza virus, natural processes began to work as well.

At first those processes had made the virus more lethal. Whether it first jumped from an animal host to man in Kansas or in some other place, as it passed from person to person it adapted to its new host, became increasingly efficient in its ability to infect, and changed from the virus that caused a generally mild first wave of disease in the spring of 1918 to the lethal and explosive killer of the second wave in the fall.

But once this happened, once it achieved near-maximum efficiency, two other natural processes came into play.

One process involved immunity. Once the virus passed through a population, that population developed at least some immunity to it. Victims were not likely to be reinfected by the same virus, not until it had undergone antigen drift. In a city or town, the cycle from first case to the end of a local epidemic in 1918 generally ran six to eight weeks. In the army camps, with the men packed so densely, the cycle took usually three to four weeks.

Individual cases continued to occur after that, but the explosion of disease ended, and it ended abruptly. A graph of cases would look like a bell curve—but one chopped off almost like a cliff just after the peak, with new cases suddenly dropping to next to nothing. In Philadelphia, for example, in the week ending October 16 the disease killed 4,597 people. It was ripping the city apart, emptying the streets, sparking rumors of the Black Death. But new cases dropped so precipitously that only ten days later, on October 26, the order closing public places was lifted. By the armistice on November 11, influenza had almost entirely disappeared from that city. The virus burned through available fuel. Then it quickly faded away.

The second process occurred within the virus. It was only influenza. By nature the influenza virus is dangerous, considerably more dangerous than the common aches and fever lead people to believe, but it does not kill routinely as it did in 1918. The 1918 pandemic reached an extreme of virulence unknown in any other widespread influenza outbreak in history.

But the 1918 virus, like all influenza viruses, like all viruses that form mutant swarms, mutated rapidly. There is a mathematical concept called “reversion to the mean”; this states simply that an extreme event is likely to be followed by a less extreme event. This is not a law, only a probability. The 1918 virus stood at an extreme; any mutations were more likely to make it less lethal than more lethal. In general, that is what happened. So just as it seemed that the virus would bring civilization to its knees, would do what the plagues of the Middle Ages had done, would remake the world, the virus mutated toward its mean, toward the behavior of most influenza viruses. As time went on, it became less lethal.

This first became apparent in army cantonments in the United States. Of the army’s twenty largest cantonments, the first five attacked saw roughly 20 percent of all soldiers who caught influenza develop pneumonia. And 37.3 percent of the soldiers who developed pneumonia died. The worst numbers came from Camp Sherman in Ohio, which suffered the highest percentage of soldiers killed and was one of the first camps hit: 35.7 percent of influenza cases at Sherman developed pneumonia. And 61.3 percent of those pneumonia victims died. Sherman doctors carried a stigma for this, and the army investigated but found them as competent as elsewhere. They did all that was being done elsewhere. They were simply struck by a particularly lethal strain of the virus.

Prepared by Graham F. Rhodes, CFA

In the last five camps attacked, hit on average three weeks later, only 7.1 percent of influenza victims developed pneumonia. And only 17.8 percent of the soldiers who developed pneumonia died.

One alternative explanation to this improvement is that army doctors simply got better at preventing and treating pneumonia. But people of scientific and epidemiological accomplishment looked hard for any evidence of that. They found none. The army's chief investigator was George Soper, later handpicked by Welch to oversee the nation's first effort to coordinate a comprehensive program of cancer research. Soper reviewed all written reports and interviewed many medical officers. He concluded that the only effective measure used against influenza in any of the camps had been to isolate both individual influenza victims and, if necessary, entire commands that became infected: these efforts "failed when and where they were carelessly applied" but "did some good. . . . when and where they were rigidly carried out." He found no evidence that anything else worked, that anything else affected the course of the disease, that anything else changed except the virus itself. The later the disease attacked, the less vicious the blow.

Inside each camp the same thing held true. Soldiers struck down in the first ten days or two weeks died at much higher rates than soldiers in the same camp struck down late in the epidemic or after the epidemic actually ended.

Similarly, the first cities invaded by the virus—Boston, Baltimore, Pittsburgh, Philadelphia, Louisville, New York, New Orleans, and smaller cities hit at the same time—all suffered grievously. And in those same places, the people infected later in the epidemic were not becoming as ill, were not dying at the same rate, as those infected in the first two to three weeks.

Cities struck later in the epidemic also usually had lower mortality rates. In one of the most careful epidemiological studies of the epidemic in one state, the investigator noted that, in Connecticut, "one factor that appeared to affect the mortality rate was proximity in time to the original outbreak at New London, the point at which the disease was first introduced into Connecticut. . . . The virus was most virulent or most readily communicable when it first reached the state, and thereafter became generally attenuated."

The same pattern held true throughout the country and, for that matter, the world. It was not a rigid predictor. The virus was never completely consistent. But places hit later tended to be hit more easily. San Antonio suffered one of the highest attack rates but lowest death rates in the country; the virus there infected 53.5 percent of the population, and 98 percent of all homes in the city had at least one person sick with influenza. But there the virus had mutated toward mildness; only 0.8 percent of those who got influenza died. (This death rate was still double that of normal influenza.) The virus itself, more than any treatment provided, determined who lived and who died.

A decade after the pandemic, a careful and comprehensive scientific review of findings and statistics not only in the United States but around the world confirmed, "In the later stages of the epidemic the supposedly characteristic influenza lesions were less frequently found, the share of secondary invaders was more plainly recognizable, and the differences of locality were sharply marked. . . . [I]n 1919 the 'water-logged' lungs"—those in which death came quickly from ARDS—"were relatively rarely encountered."

Despite aberrations, then, in general in youth the virus was violent and lethal; in maturity it mellowed. The later the epidemic struck a locality, and the later within that local epidemic someone got sick, the less lethal the influenza. The correlations are not perfect. Louisville suffered a violent

attack in both spring and fall. The virus was unstable and always different. But a correlation does exist between the timing of the outbreak in a region and lethality. Even as the virus mellowed, it still killed. It still killed often enough that in maturity it would have been, except for its own younger self, the most lethal influenza virus ever known. But timing mattered.

The East and South, hit earliest, were hit the hardest. The West Coast was hit less hard. And the middle of the country suffered the least. In Seattle, in Portland, in Los Angeles, in San Diego, the dead did not pile up as in the East. In St. Louis, in Chicago, in Indianapolis, the dead did not pile up as in the West. But if the dead did not pile up there as they had in Philadelphia and New Orleans, they still did pile up.

Barry, John M.. The Great Influenza (pp. 370-373). Penguin Publishing Group. Kindle Edition.