We Are Not Prepared

SUNGSIL MOON
MICROBIOLOGIST

(Illustration by Min-jeong Kim)

September 2 (Off the western coast of Africa)

"Fine day and sea like glass. Quite a gloom was cast round the cabin as soon as we were up when three deaths were reported on board. The burials took place at 11am and there were 4 burials. The Colonel read the service and it was quite a touching scene. This afternoon two more burials took place and there is another death. The other ships are also busy with burials. One of the deaths is our Clarionette player in the band and a beautiful player he was too. The strange thing about this sickness is that the big strong men seem to get it the worst and are the ones that die. One of the deaths is namesake of myself I hear. Today was mess orderly again. Was also able to eat a bit today and feel much better."[1]

The above is an excerpt from a journal kept by a soldier who left New Zealand by boat in 1918 to fight with the Allies in World War I. He lived with other soldiers on the ship, "packed in like sardines." Right before the massive outbreak of influenza in the fall of 1918, his boat suffered from many deaths. The war itself ended on November 11, 1918, before the soldiers on the ship ever saw battle, yet over 90 percent of the 1,117 on board came down with influenza and 77 died. The journal writer caught the disease but later recovered. The soldier's journal provides an account of epidemiological significance on densely packed spaces and demonstrates that the fear of infectious disease was more acute than that of the war itself.

Influenza and the human race share a long history together. Doctors in the Middle Ages believed that people were infected with diseases due to influence from the position of the stars and the cold. The Italians coined a term for this "influenced illness": influenza. The word was then brought to English in the 18th century during a European pandemic. The Middle Ages had the Black Death, but 20th century world faced the threat of influenza.

The first case of the 20th century's influenza pandemic was reported at an American military camp in Kansas, USA, in the spring of 1918. Soldiers at the camp were dispatched to Europe to fight in World War I, and when they returned home, the influenza they brought back was even more virulent than before.

How was this frightening infectious disease discovered one hundred years ago?

[1] https://wwwnc.cdc.gov/eid/article/18/11/ad-1811_article

Richard Pfeiffer, a student of the "father of bacteriology," Robert Koch, isolated bacteria he found in the lungs and mucous of patients who were infected by influenza during an outbreak in 1892. Pfeiffer believed that the bacteria was the cause of the influenza, and people called the bacteria "Pfeiffer's bacillus." When an influenza pandemic broke out in 1918 and patients exhibited similar symptoms to the outbreak in 1892, many in the world's scientific and medical communities accepted Pfeiffer's theory even though there was not much evidence for it. There were, of course, those who disagreed with Pfeiffer's theory. Some believed that pneumococcus or streptococcus were to blame, while others argued that not all influenza patients had influenza bacillus. A paper published in the *Journal of the American Medical Association* (JAMA) in 1919 reported on test results that found that influenza bacillus created a toxin and that this toxin could seep through filters and was strong enough to kill rabbits within hours.

Despite the controversy over Pfeiffer's bacillus, Dr. William H. Park of New York City Board of Health, Division of Pathology, Bacteriology, and Disinfection was sure that Pfeiffer had pinpointed the cause of the influenza pandemic and he tried to develop a vaccine. Dr. Paul Louis in Philadelphia, who was developing a vaccine for pneumococcus, also tried to develop a new vaccine by adding influenza bacillus to his pneumococcus vaccine. On October 19, 1918, he produced a vaccine that could treat pneumococcus, streptococcus, and influenza bacillus. Clinical trials were conducted in several areas with around 100,000 participants, but Dr. Louis was unable to prove that his vaccine had any effect.

This was because the influenza pandemic was caused by a virus, not the bacteria called influenza bacillus. Everyone knows about this virus today, but the fact that the influenza was caused by a virus—not bacteria—was discovered in the 1930s. That was ten years after the 1918 pandemic had ended, killing around 50 million people worldwide. It turns out that Pfeiffer's bacillus was actually *H. influenzae* type b (Hib), the cause of cerebromeningitis.

How were the genes of the virus thought to have been bacteria in 1918 eventually discovered?

In 1951, Johan Hultin, a doctoral student at the University of Iowa, traveled to a small village in Alaska called Brevig Mission to find the cause of the 1918 influenza virus. He went to Alaska because a large number of Alaskan Inuit had died from the 1918 influenza outbreak and their bodies had been buried in Alaska's permafrost. Hultin believed that the 1918 influenza virus could still be inside the bodies because they had not decomposed, due to the cold. Hultin received permission from the village elders to collect a lung tissue sample from a young woman who had been buried in the permafrost. He took that lung tissue sample back to Iowa and injected it into chicken eggs to try to isolate the virus. Unfortunately, he failed in this endeavor.

By the late 1970s, scientists in the life sciences had developed the technology to analyze gene hierarchies. Hultin set out again to find the influenza virus in 1997, 46 years after his first endeavor. At the time, a team led by Dr. Jeffery Taubenberger at the Armed Forces Institute of Pathology succeeded in isolating the RNA of the influenza virus from a stored sample of lung tissue of an American soldier who had died of the disease in 1918. The team was able to analyze three short hierarchies of the eight fragments of the virus's genome from the 1918 influenza virus. Using the lung tissue from the Inuit woman named "Lucy," and the lung tissues taken from dead American soldiers, which had been stored for research purposes, Taubenberger's team and Hultin successfully analyzed the genome of the influenza virus that had caused the 1918 pandemic.

The team found, surprisingly, that the 1918 influenza virus had not spilled over from birds to humans; rather, it was similar to an influenza virus that infected pigs. It took a great deal of effort by a lot of scientists over a period of 10 years to identify the whole genome sequencing of the eight fragments of the virus.

Since 1918, humankind has faced three different strains of influenza. The 1957 avian influenza outbreak (H2N2) and the 1968 (H3N2) outbreak in Hong Kong each killed around one million people. The swine flu (H1N1) outbreak in 2009 killed around 250,000 people. While these influenza strains are genetically different from each other, the outbreaks have forced humans to interact with viruses and to even cultivate the ability to fight back and defeat them.

We know who the enemy is. With the knowledge that the enemy is a viruses, not bacteria, scientists have been able to develop vaccines and medical treatments. Scientists have also been able to quickly analyze the genomes of viruses within days of an outbreak, and this knowledge is shared across the globe. The World Health Organiza-

tion (WHO) has a Global Influenza Surveillance and Response System (GISRS) that monitors changes in influenza viruses and has worked to establish a defense mechanism to protect the world economy and international society.

Why, then, are we being pummeled by COVID-19?

Dr. Donald Burke, a virologist at the University of Pittsburgh, has long warned about viruses that can cause pandemics. He has explained that there are three types of viruses we must be aware of: 1) viruses that have already caused worldwide pandemics such as Orthomyxoviridae viruses (influenza) and retroviruses (HIV); 2) viruses that have the proven ability to cause pandemics among animals, not human beings (such as Orthomyxoviridae viruses, Paramyxoviridae viruses—also called Hendra and Nipah viruses—and coronaviruses, which include SARS and MERS); and, 3) viruses that have the innate ability to evolve through mutation such as those that may be able to infect human beings through rapid evolution (retroviruses, Orthomyxoviridae viruses, and coronaviruses). Accordingly, it is not a coincidence that Dr. Burke was able to predict something like COVID-19.

In 1918, as World War I was still being fought, the movement and mobilization of militaries across the world meant that many soldiers had to live in extremely densely populated areas. That soldiers were packed in like sardines on the military ship mentioned at the beginning of this article provides a hint at the conditions of closely packed hosts that allow viruses to quickly spread. Humans today live in enclosed spaces and densely populated cities. That New York City, America's most populated city, can suffer more COVID-19 cases than the entire country of China shows how a densely populated area of hosts can serve as the optimal environment for the spread of a virus.

During World War I, soldiers from Europe, America, South America, and different parts of Asia took part in the war. They traveled the globe by land and sea accompanied at all times by viruses. In a globalized world, COVID-19 got its start in China but has spread throughout the world through land and sea routes.

The world's medical system in 1918 failed to respond to the influenza pandemic properly. Over 30 percent of American doctors had gone to war, and there was a shortage of civilian doctors and nurses. This forced the country's medical authorities to set up makeshift hospitals staffed by medical students. Modern health systems, which are focused on treating chronic health problems rather than infectious diseases, are less capable of defending against such diseases. Research funds handed out to the medical and science communities have also shifted from infectious diseases to supporting the study of chronic diseases and ailments associated with old age.

Over the past one hundred years, technology and the environment have undergone major advances; however, ironically, as humankind and its society became more improved and sophisticated, the belief that humankind can overcome viruses has collapsed. The defense mechanisms in place to protect against infectious disease were really just a mirage. The world's response to the novel coronavirus has been a loose collection of individual battles rather than a unified response, due to the economic, political, and cultural characteristics of each country. Viruses never weaken. The way humanity has developed and the way we live our lives have created the perfect environment for viruses to survive.

Nancy Messonnier, the director of the National Center for Immunization and Respiratory Diseases at the Centers for Disease Control and Prevention, said the following as the US just started to face COVID-19: "It's not so much a question of 'if' this will happen anymore, but rather more a question of exactly 'when' this will happen …" Messonnier's statement is applicable to really any of the viruses that Dr. Burke mentioned. In short, while "no one knows the day or hour" when virus pandemics will strike, we should know that they will at some point.

And that is the reason why the entire world, from the medical and scientific communities to politicians and businesspeople, needs to prepare for another pandemic —whenever it comes. Humankind will have to continue fighting this unseen enemy even one hundred years from now. We are still not prepared.

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