PART 1

How Do You Prepare for a Pandemic of a Virus That Doesn't Exist Yet?

By Polly Shulman

When the COVID-19 pandemic struck in early 2020, the world was caught by surprise. On January 30, 2020, only a few weeks after scientists first learned that people were dying from a new virus in China, the World Health Organization issued its highest level of warning. In many areas, schools, businesses, public venues, and houses of worship shut down overnight. Classrooms sat empty, and parents who could work from home scrambled to supervise their children's lessons, while those whose jobs required their physical presence scrambled to find safe childcare. As infected patients crowded into hospitals, medical workers did what they could to make meager supplies of personal protective equipment last. As morgues filled, refrigerated trucks were pressed into service to hold the grim overflow.

To epidemiologists, the pandemic was not a surprise at all. They had known for years that a novel coronavirus could jump from animals to humans and spread quickly across borders, and they had been preparing for just such a pandemic. How did they know, and how could they prepare for a pandemic of a brand-new virus?

But First, What Is a Virus?

To understand how a viral pandemic happens, it helps to take a closer look at viruses. A virus is just a bit of genetic code wrapped in a protein shell. In fact, scientists don't even agree on whether viruses are living things. A virus can do very little on its own—it needs a host to replicate and survive. When a virus encounters a susceptible host cell, it attaches to the cell's outer membrane and inserts its genetic material into the host. Once inside, the viral genetic material can force the host to use its cellular machinery to make copies of the virus and release them. Then the copies can go on to infect new cells, repeating the cycle.

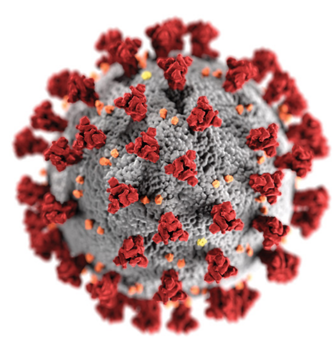

Figure 1. A Model of SARS-CoV-2, the Virus Responsible for COVID-19
The red protrusions are spike proteins that resemble the points on a crown, giving the coronavirus its name. © CDC/Alissa Eckert, MS; Dan Higgins, MAM

Viruses are all around us and in us, and in other living organisms, too. Most aren't harmful to humans. Some, including some parts of our microbiome—the community of microscopic organisms that inhabit our intestinal tract—actually help us. Some have evolved with us and have even contributed important genetic material to our own genomes. But as most of us know from sick days or worse, many viruses are indeed harmful.

COVID-19 is caused by a virus called SARS-CoV-2 (**Fig. 1**), which belongs to a group called coronaviruses. (The "19" comes from 2019, the year it began infecting humans.) Coronaviruses get their name from the protein spikes protruding from their surface, which scientists thought resembled the spikes on a crown. Coronaviruses that infect humans are actually pretty common; four strains of coronavirus are responsible for about 20 percent of the cases of the common cold. Other viruses, such as rhinoviruses and respiratory syncytial virus, called RSV, account for the rest of the common colds that affect humans.

Why Are Novel Viruses Dangerous?

A novel virus is simply a virus that humans have not yet encountered before. Most novel viruses that infect humans are zoonotic: They start out in other animals, then jump to humans. Scientists think SARS-CoV-2 probably began in a bat. Other novel viruses have started in pigs and birds, among other animals. Our immune systems remember viruses they have encountered before, giving us tools with which to resist them when we meet them again. But we haven't built up these defenses against novel viruses. They can spread unimpeded.

Coronaviruses are respiratory pathogens, infecting the cells in our respiratory tract—the nose, throat, larynx, trachea, lungs, and so on—when we take a breath. They can spread easily through the air from person to person. Respiratory pathogens also tend to have short incubation times, which means there's a very brief window of time in which to stop them from spreading. That makes them hard to control. As a novel respiratory virus, then, SARS-CoV-2 was well positioned to cause a pandemic.

What's a Pandemic?

A pandemic is defined not by how deadly or terrifying a disease may be, but by how widely it spreads. The CDC defines a pandemic as "an event in which a disease spreads across several countries and affects a large number of people."

Of course, a pandemic can be deadly and terrifying! The Spanish flu pandemic of 1918, which killed in the range of 50 million to 100 million people around the world, is a classic example. So is the ongoing HIV/AIDS pandemic, which has killed approximately 81 million people so far. By contrast, acute hemorrhagic conjunctivitis, commonly known as pink eye, which became a pandemic in 1981, is mostly just annoying. **Fig. 2** below places many of the infectious diseases that have menaced humans on a timeline.

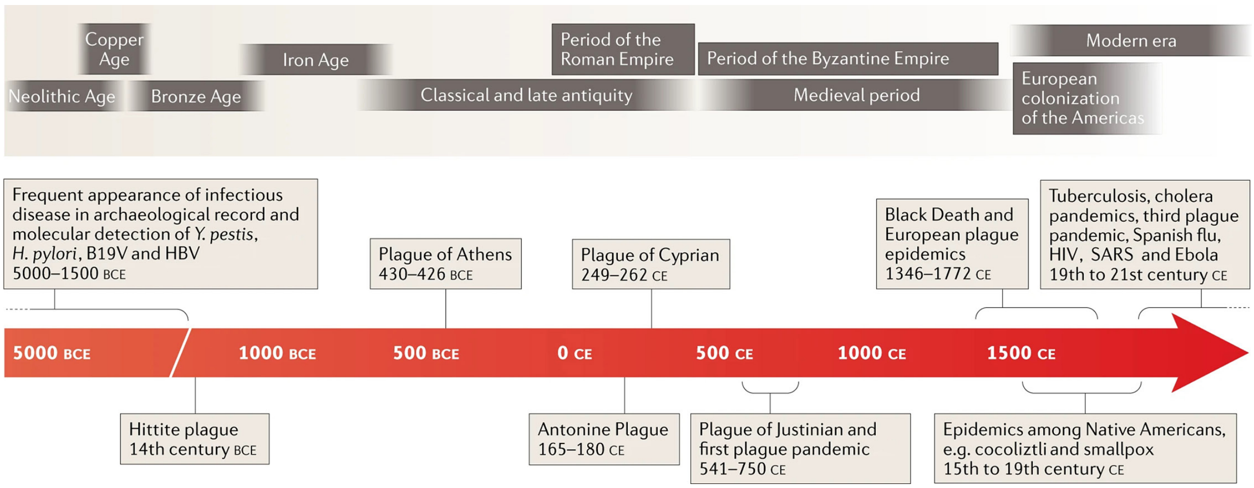

Figure 2. Timeline of Infectious Diseases
Anthropological ages, from the Neolithic to the present, are indicated at the top. Several emerging infectious diseases are pinpointed on the timeline. While this timeline is weighted toward Europe due to differences in the availability of records, it is likely that other regions would show a similar pattern of diseases. (BCE and CE stand for "before the Common Era" and "Common Era.") © Spyrou, M.A., Bos, K.I., Herbig, A., et al./Nat Rev Genet 20, 323–340 (2019)/Springer Nature

Meet the Scientists

Dr. Jennifer Nuzzo, Pandemic Preparedness

Dr. Nuzzo is an associate professor at the Johns Hopkins Bloomberg School of Public Health and a senior scholar at the Johns Hopkins Center for Health Security. She is an epidemiologist who studies whether governments have the tools they need to respond to pandemics.

Nuzzo wrote a report at the end of 2019 about how a coronavirus pandemic was likely. "I'm an epidemiologist, but I spend a lot of time studying policies and practices, and whether governments have all the tools they need to be able to respond to outbreaks, epidemics, or pandemics," she explains. She runs a project

Figure 3. Dr. Jennifer Nuzzo
Dr. Jennifer Nuzzo, an epidemiologist at Johns Hopkins University, focuses on pandemic preparedness and outbreak detection and response. © Johns Hopkins Center for Health Security

called The Outbreak Observatory to study responses to outbreaks, identifying what worked well and what needs to be improved. "It's really important to study outbreaks, because if you can stop outbreaks, you can prevent them from becoming epidemics or growing even larger, into pandemics," she says.

Nuzzo recalls two earlier experiences with novel coronaviruses that concerned epidemiologists. The first was in 2003, when a coronavirus now called SARS-CoV-1 jumped from animals to humans and went on to cause an outbreak of Severe Acute Respiratory Syndrome (SARS) that sickened about 8,000 people worldwide. Then in 2012 another novel coronavirus, MERS-CoV, spread from camels to people in Saudi Arabia, causing Middle East Respiratory Syndrome (MERS). Unlike COVID-19, SARS and MERS did not go on to become pandemics. However, Nuzzo and other scientists were able to learn a great deal about coronaviruses by studying those viruses.

Dr. Lisa Cooper, Health Equity

Dr. Lisa Cooper is a physician and social epidemiologist who has spent her career studying disparities in healthcare. "Health inequities cause a huge burden of human suffering and increased healthcare costs," says Cooper. Health inequities are avoidable differences in health among different groups of people. "They cause reduced productivity. They can even contribute to civil unrest," she says.

Figure 4. Dr. Lisa Cooper
Dr. Cooper is a Bloomberg Distinguished Professor at Johns Hopkins University School of Medicine and Bloomberg School of Public Health and the director of The Johns Hopkins Center for Health Equity. © Johns Hopkins University

Because it's the nature of infectious diseases to spread, pandemics affect everyone, but they don't affect everyone equally, Cooper explains. The COVID-19 pandemic shed an intense light on the long-standing worldwide problem of health inequities. Differences in opportunities have resulted in a greater burden of injury, death, violence, and sickness in different social groups. People who belong to racial or ethnic minority groups and people with lower income levels are more likely to become more ill, at younger ages, than richer people and members of a majority group.

Cooper points to racial and ethnic disparities in cardiovascular disease, one of the most common diseases and the top cause of mortality in the United States, as well as disparities in maternal and infant mortality. African Americans die in childbirth or the period immediately surrounding it at about three to four times the rate of White Americans, and African-American and Native American babies die before their first birthday at much higher rates than White babies.

It's tempting to blame differences in genes for these outcomes, but it would be wrong. "Health disparities are not caused, for the most part, by biological differences between people of different social groups," says Cooper. "They're caused by exposures to things in our environment, and by the way we distribute our resources within our society."

Many of these disparities have deep historical roots. Cooper says, "European settlers in America forced Native people off their land. They spread smallpox, killing a large proportion of the Native population. They brought and enslaved people from Africa and elsewhere and forced them to labor for generations under horrific conditions. In the early 1930s, housing policies and real estate lending practices expanded homeownership opportunities for Whites while confining African Americans to crowded neighborhoods with more pollution, less green space, and less access to healthy food, safe schools, and healthcare."

Preparing to Develop and Distribute a COVID-19 Vaccine

With COVID-19 spreading across the planet, it was vital to develop a vaccine and get it into people's arms as fast as possible. Fortunately, scientists had been working on developing coronavirus vaccines since the SARS epidemic in 2003, and they had also spent decades working on a powerful, flexible new vaccine platform that would allow them to quickly design vaccines for specific viruses. Vaccine researchers developed the first COVID-19 vaccines in record time. But first, they needed to make sure the vaccines were safe and effective. They do this through clinical trials.

Stop and Think

1. If a novel coronavirus emerges, what do you need to know about it in order to take public health measures?

2. What do you need to know about it in order to develop a vaccine?

3. What steps need to be taken to make sure that a new vaccine is effective and safe to use. Make a list of steps, concerns, and variables that need to be considered in designing a clinical trial. Draw a schematic showing your design for a clinical trial.