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# **Omicron Is a Dress Rehearsal for the Next Pandemic**

Emily Anthes Tue., December 14, 2021, 6:46 a.m. 13 min read

When scientists discovered the highly mutated omicron variant of the coronavirus last month, it set off an eerily familiar chain of events.

Health experts held somber news conferences that raised more questions than answers. Officials imposed travel bans that very likely came too late. Virus trackers filled in their maps as the variant was reported in country after country. And the rest of us waited, with increasing unease, to learn more about the threat we were facing.

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The same sequence unfolded nearly two years ago when the novel coronavirus, SARS-CoV-2, was first discovered. In those early weeks of 2020, the United States proved to be woefully unprepared for the challenges ahead, starting with the most fundamental of tasks: detecting the virus.

"We had a delay of one to two months before we were even able to identify the presence of the virus," said Dr. Charles Chiu, an infectious disease specialist and microbiologist at the University of California, San Francisco. "And by that time, it had already circulated widely between multiple states and from coast to coast."

These failures have been well chronicled, and omicron is one more sign that the current pandemic, which has now claimed the lives of nearly 800,000 Americans, is not over.

But omicron is also a dress rehearsal for the next pandemic. The work before us now — detecting, tracking and slowing the spread of a health threat we do not fully understand — is the same work that will be required to stop a future outbreak in its tracks.

The analogy is not perfect. When omicron arrived, scientists had already developed vaccines and treatments for the virus and were on high alert for new variants. The next pandemic may come with less warning.

"We know that there are pathogens worse than SARS-CoV-2 that are emerging and reemerging and waiting for their moment to take off," said Rick Bright, CEO of the Pandemic Prevention Institute at the Rockefeller Foundation.

Omicron's emergence is an opportunity to take stock of both the gains we have made and the ways in which we are still falling short. It is also a call to action: Whatever progress we have made is not enough.

# Seek and You Shall Find

In any other context, it would have been unremarkable: On Nov. 28, a San Francisco resident who had been feeling mildly ill took a COVID test. The next day, it came back positive.

What set off alarm bells, however, was that the resident had recently returned from South Africa, where the newly discovered omicron variant was widespread.

The traveler's test sample was flagged for priority genomic sequencing, which would reveal the precise genetic code of the virus that had infected the traveler and whether it had omicron's telltale mutations.

Chiu, the microbiologist at UCSF, was tapped to do the sequencing. By 6 p.m. Nov. 30, just a few hours after Chiu first learned about the sample, it was hand-delivered to his lab, packed in dry ice.

Chiu and his colleagues quickly got to work. Although generating the full sequence takes hours, the scientists chose to use a technique known as nanopore sequencing, which allowed them to analyze the results in real time, while the process was still underway.

"As the data accumulated, we were able to identify more and more mutations," Chiu recalled.

Before dawn, he was certain: It was omicron, the first case found in the United States. Less than a week had passed since South Africa first publicly announced the existence of the variant.

We cannot fight what we cannot see, and preventing the next pandemic begins with detecting and tracking the pathogens that threaten us. In that regard, at least, "we're extraordinarily better off than we were this time last year," said Joseph Fauver, a genomic epidemiologist at the University of Nebraska Medical Center in Omaha.

# **Testing**, **Testing**, **Testing**

The first link in the disease surveillance chain is testing. Who is infected, and where are they? Without accurate, timely testing, it can become impossible to curb the spread of a pathogen.

Unfortunately, America bungled testing from the beginning. The Centers for Disease Control and Prevention distributed faulty test kits, while supply shortages and regulatory delays created an epic mismatch between supply and demand. In the summer and fall of 2020, waits at testing sites could stretch for hours; the wait for results could take a week or more. There was no coordinated national testing plan.

These missteps allowed the virus to spread, unseen and unchecked, increasing the burden on hospitals and making other mitigation measures more difficult. Without accessible testing, the strategy that helped other countries break the chain of transmission — swiftly identifying people with the virus, isolating them and tracing their contacts — stood little chance.

As time passed, the testing crunch eased. Labs diversified their supply chains, bought new equipment and hired more staff, said Kelly Wroblewski, director of infectious diseases at the Association of Public Health Laboratories.

More and more tests won emergency authorization from the U.S. Food and Drug Administration, including rapid, at-home tests that delivered results on the spot.

"We've moved from hospitals to central labs to your living room," said Mara Aspinall, an expert in biomedical diagnostics at Arizona State University. (Aspinall is on the board of directors of OraSure, which makes COVID tests.)

The CDC, which initially imposed stringent requirements on who could be tested for the virus, began recommending routine screening as a tool to curb transmission. By the time omicron was in the headlines, it was no longer remarkable for a 5-year-old to swab his own nose before school or for an ailing San Francisco resident, recently returned from South Africa, to get PCR results back in 24 hours.

"It's like a night-and-day comparison between where we were at the beginning of the pandemic," Wroblewski said.

But the United States is still doing less daily testing per capita, and it has a higher share of tests come back as positive than many other high-income countries, according to the Johns Hopkins Coronavirus Resource Center.

"We haven't done a great job on making tests available," said Dr. Ezekiel J. Emanuel, a bioethicist at the University of Pennsylvania who was a member of President Joe Biden's COVID-19 Advisory Board during the presidential transition.

PCR processing times still vary widely, while rapid tests can be difficult to find in stores and remain beyond the budget for many Americans, especially because they are designed to be used frequently. (The Biden administration's new plan to have health insurers reimburse members for at-home tests may help but has its limitations.)

Many of these problems can be traced to the nation's failure to invest in testing early in the pandemic. The Trump administration created Operation Warp Speed to turbocharge vaccine development. The country needed a similar effort for diagnostic tests, experts said. Diagnostic testing may not be as tantalizing as vaccines, but in any future pandemic, they said, it should be a priority from the start.

# Surveillance

The next vital link in the surveillance chain is routine, widespread genomic sequencing. This kind of surveillance helps experts keep tabs on how a pathogen is mutating and how new variants are spreading.

In the United States, this effort got off to a very slow start. "Many of the public health labs were, frankly, just overwhelmed by the initial testing volume and competing obligations," said Duncan MacCannell, chief science officer at the CDC's office of advanced molecular detection.

Although some research laboratories established their own independent sequencing programs, there was little funding or coordination.

In the spring of 2020, the CDC created a consortium of academic, commercial and public health labs to "start bootstrapping" a more focused national effort, MacCannell said. But progress was slowed by a lack of resources and a fragmented health care system that had no organized pipeline for getting patient samples from testing sites to sequencing labs.

"A lot of sequencing machines were idle in 2020," said Bronwyn MacInnis, who directs pathogen genomic surveillance at the Broad Institute in Cambridge, Massachusetts.

But in late 2020 and early 2021, the emergence of the highly contagious alpha variant and an influx of federal funding finally kicked genomic surveillance into a higher gear. Since January, the country has gone from sequencing fewer than 3,000 samples a week to 50,000 to 60,000, on average, according to the CDC.

And when news of omicron broke, on Nov. 25, some labs redoubled their efforts, adding weekend hours and night shifts to search for the variant. Although Chiu's lab was the first to detect it, researchers in other states — Minnesota, Colorado, New York and Hawaii — soon followed suit.

"Omicron has really shown that we have expanded our capacity significantly to be able to identify these variants as they emerge," Chiu said.

Some research teams began looking for the variant in sewage. Because the virus is shed in feces, analyzing wastewater can provide a snapshot of whether the virus, or a particular variant, is present in a community and how prevalent it is.

Although wastewater epidemiology is not new, the pandemic has turned it from a niche pursuit into a mainstream strategy. The need to monitor the virus prompted the CDC, in partnership with other federal agencies, to create the National Wastewater Surveillance System, which could eventually be used to monitor antibiotic-resistant bacteria, food-borne pathogens and other microbes.

Omicron was a test of the approach. In early December, researchers found the variant at eight wastewater treatment plants in Houston, days before the city reported its first cases.

"This is the kind of thing that really allows us to get out in front of SARS-CoV-2," said Samuel Scarpino, managing director of pathogen surveillance at the Pandemic Prevention Institute.

#### **Room for Improvement**

And yet, if omicron is a test of our preparedness for the unexpected, some experts are not convinced that we have passed. The United States was days behind many other countries in detecting the variant.

"That's not a good sign," said Dr. Eric Topol, founder and director of Scripps Research Translational Institute in San Diego.

Despite recent improvements, the country has sequenced a smaller share of cases since the beginning of the pandemic than many other nations, according to GISAID, an international database of viral genomes.

There are still delays in the system, and the omicron news broke on Thanksgiving, when processing times were most likely even longer than usual, experts said. (CDC data show a dip in the number of virus sequences added to public databases during the week of and the week after the holiday.)

The national effort is also uneven — with some states sequencing more than 20% of their COVID cases and others sequencing less than 3% — and may be missing certain regions or communities even within states, experts said.

"That is not an effective infrastructure for genetic surveillance of viral infections," Emanuel said. "It's got to be nationwide, and it's got to be uniform."

And the country needs to do a better job identifying people who are especially likely to be harboring new variants, scientists said. Rather than restrict travelers from abroad, officials could make a more concerted effort to test them for the virus and sequence positive samples.

People with breakthrough infections and those with compromised immune systems — who may have more trouble fighting off the virus, giving it more chances to mutate — should also be priorities for sequencing, experts said.

"Not only do we have to sequence, but we have to make sure we're sequencing in the right communities and the right people," said Janet Robishaw, senior associate dean for research at Florida Atlantic University's College of Medicine in Boca Raton.

And while countries with centralized or nationalized health care systems, like Britain, can link the viral sequences to clinical data about patients relatively easily, in the United States that is much more difficult. Did the sample come from someone who was in the ICU or just home with a sniffle? Were they vaccinated and, if so, with which vaccine and when?

"We can do a lot with sequences in terms of looking at how fast omicron or delta or whatever is spreading," said Trevor Bedford, an expert on viral evolution and surveillance at the Fred Hutchinson Cancer Research Center in Seattle. "But it makes it hard to address really important scientific questions like, is delta more severe?"

#### For the Next Time

Some of the progress the country has made could leave us better positioned for the next pandemic. For instance, public health laboratories have new equipment and expertise, which they can now use to track the flu, food-borne illnesses and whatever the next great global health threat turns out to be.

But solidifying these gains will require a continuing commitment and funding after the immediate crisis has passed. "The historical pattern is, we surge, and then we forget, and we neglect," Bright said.

Many exhausted health officials have already left their jobs, and legislators have passed more than 100 laws limiting the public health powers of state and local authorities, a New York Times review found.

Some of the problems that the pandemic has highlighted are deeply rooted. For example, a highly coordinated genomic surveillance program like Britain's, which is frequently held up as an exemplar, was always going to be a heavy lift in the United States.

"We have this Balkanized health care system, and the system is a giant mess," said Jeremy Kamil, a virus expert at Louisiana State University Health Sciences Center Shreveport.

And pandemic preparedness does not happen in a vacuum. Just as a more equitable distribution of vaccines might help squelch the next variant of concern, preventing the next big global outbreak will require ensuring that every country has the resources to detect and respond to emerging pathogens.

The United States is a large and fractured country — politically polarized and burdened with glaring inequities, rampant misinformation and disinformation, and a considerable distrust of public officials. These are enormous, thorny problems and are much harder to address than ensuring that labs have the capacity to detect omicron or any new pathogen.

"I'm confident in our ability to detect the variant," Fauver said. "What I'm not confident in is our ability to do anything about it. We're detecting the delta variant every single day, every time we sequence."

Even before the omicron news broke, another delta-driven surge had already begun. Scientists are finding more omicron cases every day, and the variant could soon overtake delta. What comes next — what we should aim for, even — is less clear. Should we spend the winter trying to stop every infection? Protecting the highest risk people from severe disease and death? Ensuring that hospitals are not overrun?

"One thing that we've lacked continuously through the pandemic is a goal," said Emily Gurley, an epidemiologist at the Johns Hopkins Bloomberg School of Public Health. "We still don't have that. Certainly, we don't have that for omicron."

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