# STAT

# The next frontier in coronavirus testing: Identifying the full scope of the pandemic, not just individual infections

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A person (right) who recovered from Covid-19 donates plasma. China OUT (Photo by STR/AFP via Getty Images

Scientists are starting to roll out new blood tests for the coronavirus, a key development that, unlike the current diagnostic tests, will help pinpoint people who are immune and reveal the full scope of the pandemic.

The "serological" tests — which rely on drawn blood, not a nasal or throat swab — can identify people who were infected and have already recovered from Covid-19, including those who were never diagnosed, either because they didn't feel particularly sick or they couldn't get an initial test. Scientists expect those individuals will be safe from another infection for at least some time — so the tests could signal who could be prioritized to return to work or serve as a frontline health worker.

The serological tests, which are being deployed in some countries in Asia and are starting to be used at one New York hospital, could also eventually help scientists answer outstanding epidemiological questions about the spread of the virus and might even steer an inoculation strategy should a vaccine make it to market.

"We need to identify all those people here who not only knew they had the coronavirus but maybe weren't sure because they didn't get tested or because they had minimal symptoms," said <u>Christopher Kirchhoff</u><sup>4</sup>, a former White House aide who wrote a 2016 review of the U.S. government's response to the West African Ebola crisis. "You can imagine asking them to take the key roles in our economy to keep things moving, whether that's manning a checkout aisle at a supermarket or taking the lead for caring for someone else in their family who comes down with the coronavirus."

Serological tests sniff out antibodies in the blood — molecules made by the immune system in response to a pathogen's attack.

Right now, the main diagnostic tests for Covid-19 rely on a technology called PCR and search for evidence of the virus' RNA genome. But as people recover, they vanquish the virus from their system, so PCR isn't helpful much beyond the infection period.

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Antibodies made in response to a virus, however, persist in the blood, acting like sentinels and rallying an immediate response should the virus try to invade again. The antibodies are unique signatures — different protectors modeled after encountering different viruses — so finding them is a signal of past contact with a particular virus.

It's the difference between catching an invader red-handed versus going back to the crime scene and dusting for prints. "It seems very easy to be able to say yes or no, somebody was infected or wasn't infected," said Florian Krammer, a virologist at the Icahn School of Medicine at Mount Sinai.

Earlier this month, Krammer and colleagues posted on a preprint server <u>a paper</u><sup>6</sup> describing the serological assays they had developed to detect previous exposure to SARS-CoV-2, the name of the coronavirus. (Preprints are scientific papers that have not been through the peer-review process yet.) They've also started <u>a</u> website<sup>7</sup> where labs can order the ingredients they need to get tests up and running themselves.

And this week, Mount Sinai announced that antibodies detected in blood from recovered patients would be used<sup>8</sup> to treat current patients. It's hoped that injecting patients with these antibodies — a type of therapy sometimes called convalescent plasma — might provide an initial layer of protection as their own immune system kicks into gear.

Companies and academic researchers are also trying to <u>develop plasma therapies</u><sup>9</sup> and are scrambling to obtain blood from survivors. Serological tests could help expand the supply.

Other tests are being built as well. Researchers in the Netherlands have <u>unveiled</u> <u>assays</u><sup>12</sup>, the United Kingdom is preparing to <u>roll out its own antibody tests</u><sup>13</sup>, and scientists in Singapore have used them to <u>trace chains of transmission</u><sup>14</sup>. Robert Redfield, the director of the Centers for Disease Control and Prevention, told Congress this month<sup>15</sup> that the agency was developing two serological tests; a CDC spokeswoman did not respond to messages asking for more details about the agency's tests or its plans.

Companies have also started to sell antibody tests, though some are being framed as another tool to diagnose acute infections. Some experts are skeptical about this approach because it can take the body <u>a few days</u><sup>16</sup> to ramp up production of the antibodies, meaning a serological test would miss an infection if it was in its early stages.

"It takes you five, seven, 10 days — usually more than one week to develop a

robust antibody response," said Isabella Eckerle, a virologist at Geneva Centre for Emerging Viral Diseases. "And the first week is the week when people <u>shed the</u> <u>virus</u><sup>17</sup> in the highest concentrations."

Serological tests are also critical, experts said, for painting a full picture of the virus's spread, even if not immediately.

In other countries, researchers have started to launch "serosurveys" — testing the blood of a sample of the population to estimate just how widely the virus spread. It's through these types of retrospective initiatives that the full number of cases can be approximated, which can help explain how common asymptomatic infections may be and calculate a better estimate for the mortality rate of a virus.

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A <u>2015 serosurvey</u><sup>19</sup> of the coronavirus MERS, for example, included samples from 10,000 people in Saudi Arabia. Fifteen people were found to have anti-MERS antibodies, which the researchers used to extrapolate that nearly 45,000 people in the country might have been exposed to the virus. That's compared to fewer than <u>2,500 cases</u><sup>20</sup> of MERS that have been verified around the world.

"By doing large sample serology testing, we'll get an idea of what the scale of this pandemic was and what percentage of the population might have immunity," said Stephen Goldstein, a University of Utah virologist.

Because the coronavirus is new, researchers cannot say for certain that an initial infection guarantees lasting protection. But based on the experience with other viruses, including other coronaviruses, they expect that people who recover will be shielded for perhaps at least a year or two, and from there the immunity might start to wane, not disappear. They would also be less likely to pass the virus on to others, so could return to work and normal life.

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At a community level, if a serosurvey points to more people being immune than realized, that could signal that future waves of coronavirus cases might be less intense than some forecasts anticipate. Knowing who has immunity at an individual level could also ensure that people who have not contracted the coronavirus could be first in line for any potential vaccine. If a vaccine is eventually approved, the initial demand will likely far outpace manufacturing capabilities, so researchers expect that doses will have to be allotted in some way.

Already, several countries — including China, where the outbreak started — have begun to serosurvey, though results are not yet available. The World Health Organization has been urging countries to embark on such studies.

"We are pressuring them — not only China, all countries — to carry out these types of investigations and to share their results with us so that we can better understand how transmission is occurring," Maria Van Kerkhove, who is helping lead WHO's pandemic response, said this month.

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