SARS-CoV-2 Antibodies Can Protect from Reinfection, NCI Study Suggests

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As the first shipments of COVID-19 vaccines begin to arrive in the United States, some interesting and timely data have emerged from NCI-led research about the coronavirus and immunity. Using real-world data from more than 3 million people, NCI researchers and our collaborators have found that people who have had evidence of a prior infection with SARS-CoV-2, the virus that causes COVID-19, appear to have some degree of protection against being reinfected with the virus.

This finding may explain why reinfection appears to be relatively rare and helps to confirm what many have hoped would be the case since the emergence of the virus.

Some may wonder why NCI is conducting research on COVID-19. Earlier this year, Congress appropriated $306 million to NCI in emergency funding to study the immune response to SARS-CoV-2. This project is one of many in this area that NCI has taken on at the request of Congress.

The NCI research team, which I was a part of, was led by Lynne Penberthy, MD, MPH, associate director of NCI's Surveillance Research Program. Working with two health care data analytics companies (HealthVerity and Aetion) and commercial labs (Quest and LabCorp), we obtained serology (antibody) testing results for more than 3 million people, representing more than 50% of the commercial SARS-CoV-2 antibody tests conducted in the United States. Nearly 12% of these tests were antibody positive; most of the remaining tests were negative (less than 1% were inconclusive).

The research team then looked at what fraction of individuals in each group went on to later develop a positive result on a nucleic acid (PCR) test for SARS-CoV-2, which may indicate a new infection. We found that, 90 or more days after the initial antibody test, people who had been antibody-negative had evidence of infection (a positive PCR test) at about 10 times the rate of people who had been antibody-positive.

This protective effect is strong and comparable to the protection afforded by effective SARS-CoV-2 vaccines, although developing protection from vaccination is much safer than from natural infection. This finding suggests that people who have a positive antibody test result using widely

available assays have substantial immunity to SARS-CoV-2 and are at lower risk for future infection.

Implications for Public Health

Because of the public health significance of these data, we have posted the results of the study on a preprint server (medRxiv), even while the study is undergoing peer review. Our goal is to get the information to the public as quickly as possible so that public health agencies and others can review it and consider using the information, in combination with other studies, in setting policy.

The finding that a positive antibody test is a predictor of a relatively low risk for reinfection could have important implications, influencing decisions about returning to physical workplaces, school attendance, and other activities.

These results might also be used to prioritize individuals for vaccination against the coronavirus at a time when supply is limited, although the results should not deter anyone from seeking vaccination.

Policy recommendations around how individuals should use the results of serology testing come from the Centers for Disease Control and Prevention (CDC) or state public health agencies. Currently, CDC does not recommend that serology status be used to make decisions about personal behavior, work status, or vaccine allocation.

A complication in interpreting the results of this work is that people who have recovered from a SARS-CoV-2 infection can still shed viral material (RNA) for up to 3 months. These individuals are generally thought to have low risk for passing the virus on to others, even though they may continue to test positive for the virus on a PCR test.

To address this concern, our study focused on evidence of new infections more than 90 days (and up to 120 days) after the initial antibody test, to maximize the chance that positive nucleic acids tests represent new infections as opposed to persistent RNA shedding.

We have known for some time that, at the population level, antibody testing is useful for looking at prior rates of infection in large groups of people, known as a seroprevalence survey. But it has not been known whether antibody testing is useful for a given individual.

That is, can a person’s antibody status predict their risk for future infection?

Additionally, there are many different antibody tests available, and many of the assays studied to date have been research-grade assays used only for seroprevalence surveys.

So another important question has been whether the widely available assays, such as those used by major reference labs such as Quest and LabCorp, can be used to assess an individual’s risk for future infection. Our results suggest that they can.

Using Real-World Data

To comprehensively address the question of whether, and to what degree, detectable antibodies protect from infection, NCI is supporting clinical trials that monitor infection rates in large populations of people whose antibody status is known. Such “seroprotection” trials, however, take a relatively long time to complete and may not provide clear answers for several more months.

That’s why we decided to use real-world data for this study. Real-world data approaches are not as powerful or compelling as carefully designed prospective trials for providing clinical evidence, but they have major advantages, including size (they can include many more people) and speed (they can be completed more quickly). They can also be more representative of the broader population, in contrast to clinical trials, which typically include only a subset of individuals who may not represent all population groups.

Using real-world data involves inferring the answers to clinical questions by aggregating and analyzing patient information collected from multiple sources, including commercial labs, electronic medical records, and private insurers. Importantly, this is done in a way that completely protects the privacy of individual people’s health information and is compliant with relevant patient privacy laws, including HIPAA.

The use of real-world data is also subject to biases that may confound a study’s results.

For example, some people, upon learning they had a positive antibody test, might have behaved differently from people who were antibody-negative. If antibody-positive people believed they were protected during the period of study, they could have engaged in behaviors that could increase their likelihood of exposure to the virus, such as poor social distancing or failure to wear a mask in public places. If this occurred, the degree of protection inferred from this study might be an underestimate of the actual protection.

There also may be biases that could have worked in the other direction. Resolving this issue will require further studies.

How Long Does Immunity Last?

As interesting as these data are, the work leaves several important questions unanswered. One of the most important is how long immunity lasts.

We were only able to follow individuals for less than 120 days. Also, we don’t know if the antibodies detected in these assays provide protection directly or are just a marker for immunity. This question is important for the modest fraction of individuals who have recovered from COVID but who do not have detectable antibodies after recovery.

Nevertheless, we believe these data, together with results of several other studies, suggest that SARS-CoV-2 infection provides strong immunity to reinfection that lasts for at least several months. And we believe that immunity can be identified in most patients using antibody tests available to all Americans.

Future studies by NCI researchers, working with other parts of the federal government—including CDC and the National Institute of Allergy and Infectious Diseases—as well as our academic and industry partners, will build on these findings, so that individuals can best understand their risk of subsequent SARS-CoV-2 infection.

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