Centers for Disease Control and Prevention

Coronavirus Disease 2019 (COVID-19)

Serology Testing for COVID-19 at CDC

CDC has developed a laboratory test to help estimate how many people in the United States have been infected with SARS-CoV-2, the virus that causes COVID-19. Clinicians and researchers refer to this as a **serology test**, and many commercial laboratories call it an **antibody test**. CDC is using this serologic (antibody) test to evaluate the performance of commercial antibody tests. CDC will develop guidance for the use of antibody tests in clinical and public health settings.

An antibody test looks for the presence of antibodies, which are specific proteins made in response to infections. Antibodies are detected in the blood of people who are tested after infection; they show an immune response to the infection. Antibody test results are especially important for detecting previous infections in people who had few or no symptoms.

We do not know if the antibodies that result from SARS-CoV-2 infection will provide someone with protection (immunity) from getting infected again. If antibodies do provide immunity, we don't know how much antibody is protective or how long protection might last. CDC scientists are currently conducting studies to answer these questions.

CDC's serologic test has been designed and validated for surveillance and research purposes. It is designed to estimate the percentage of the U.S. population previously infected with the virus – information needed to guide the response to the pandemic and protect the public's health.

The CDC test is not currently designed to test individuals who want to know if they have been previously infected with SARS-CoV-2. Commercial tests are available to provide test results to individuals.

CDC is evaluating the performance of commercial antibody tests

Commercially manufactured antibody tests check for SARS-CoV-2 antibodies in individuals and are available through healthcare providers and commercial laboratories. CDC is evaluating the performance of these tests in collaboration with the following federal organizations:

- Biomedical Advanced Research and Development Authority
- U.S. Food and Drug Administration (FDA)
- National Institutes of Health
- Department of Defense
- White House Office of Science and Technology Policy

Results from the initial federal evaluation are included in FDA's EUA Authorized Serology Test Performance and will be updated as more tests are evaluated.

Limitations of antibody tests

Antibody test results should not be used to diagnose someone with an active SARS-CoV-2 infection. It typically takes 1 to 3 weeks after infection with SARS-CoV-2 for antibodies to be made; some people may take even longer to develop antibodies. Depending on when someone was infected and the timing of the test, antibody tests may not find antibodies in someone with an active infection. Rather, a test that detects the SARS-CoV-2 virus targets from respiratory samples is used to diagnose active infections.

Commercial antibody tests designed to provide results to individuals or healthcare providers can show whether someone was previously infected with SARS-CoV-2. However, these tests have limitations and vary in their **specificity** (do they detect **only** antibodies to SARS-CoV-2 and not to other coronaviruses) and their **sensitivity** (do they detect SARS-CoV-2 antibodies in **all** positive blood samples tested).

The predictive values of a test should also be considered:

- **Positive predictive value (PPV)** is the probability that people with positive test results are truly antibody positive. A high PPV means if they test positive, they probably have antibodies to SARS-CoV-2 and were infected in the past.
- **Negative predictive value (NPV)** is the probability that people with negative test results are truly antibody negative. A high NPV means if they test negative, they probably do not have antibodies to SARS-CoV-2 and were not infected in the past.

Positive and negative predictive values are determined by the percentage of truly antibody positive individuals in the tested population (prevalence, or pre-test probability) and the sensitivity and specificity of the test. For example, in settings with a high percentage of people previously infected, it is more likely that people who test positive are truly antibody positive than if the test were performed in a population with a low percentage of people previously infected.

Guidance for clinicians on optimizing testing outcomes

Clinicians need to consider ways to optimize serology test results. Currently, the overall prevalence of SARS-CoV-2 antibodies in most populations is likely low. Therefore, in most instances it is best to select a test with the highest specificity and PPV. For example:

- In a population where 5% of people were previously infected and have antibodies, a test with 90% sensitivity and 95% specificity will yield a positive predictive value of 49%. In other words, less than half of those testing positive will truly have antibodies.
- Alternatively, use of the same test in a population in which more than 50% of people were previously infected and have antibodies will yield positive predictive values of 95-98%, meaning that fewer than 1 in 20 people testing positive will have a false positive test result.

Three strategies can be used to improve PPV:

- Choose a test with a very high specificity, perhaps 99.5% or greater, to yield a higher positive predictive value in nearly all populations tested.
- Focus testing on people with a high pre-test probability of having SARS-CoV-2 antibodies, such as those with a history of COVID-19-like illness.
- Use an orthogonal testing algorithm in which people who initially test positive are tested again with a different test.
    - Effective orthogonal algorithms are generally based on testing a patient sample with two tests, each with unique design characteristics (e.g., antigens or formats).
    - Algorithms can be designed to maximize overall specificity while retaining maximum sensitivity. For example, in the example above with a population prevalence of 5%, the same test (90% sensitivity, 95% specificity) will yield a positive predictive value of 95% if the initial test's positive sample is tested again with a different test, also with 90% sensitivity and 95% specificity.

FDA has developed a calculator that allows users to see the estimated performance of a single test or two independent tests based on their performance characteristics and the estimated prevalence of SARS-CoV-2 antibodies in the target population.

- Insight into FDA's Revised Policy on Antibody Tests: Prioritizing Access and Accuracy
- Check FDA's website for EUA Authorized Serology Test Performance , including information on specificity and sensitivity.
- FDA Calculator for Positive Predictive Value and Negative Predictive Value for Individual Tests and Combined
- Read FDA's letter to healthcare providers: Important Information on the Use of Serological (Antibody) Tests for COVID-19

About CDC's serologic test

CDC's serologic test is an ELISA-based test to detect SARS-CoV-2 antibodies in serum or plasma components of blood. It uses purified SARS-CoV-2 S protein (no live virus) as antigen (designed by the Vaccine Research Center at the National Institutes of Health).

CDC's serologic test is designed to detect antibodies produced in response to SARS-CoV-2 and minimize cross-reactivity to antibodies generated to other common coronaviruses that cause less severe illnesses, such as colds. However, potential cross-reactivity cannot be completely ruled out.

CDC's serologic test has a specificity of greater than 99% and a sensitivity of 96% based on initial performance evaluations. It can be used to identify past SARS-CoV-2 infection in people who were infected at least 1 to 3 weeks previously.

CDC serology surveillance strategy

CDC has a strategy for using antibody testing as part of surveillance efforts to better understand how much of the U.S. population has been infected with SARS-CoV-2 and how the virus is spreading through the population over time.

Learn more about CDC's COVID-19 serology surveillance strategy.

Additional Resources

FAQs for Laboratories: Serology

How to Get CDC's COVID-19 Diagnostic Test and Supplies

Testing for COVID-19

FDA: Serology/Antibody Test FAQs

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