DIAGNOSTIC LABORATORY OF OKLAHOMA

Frequently Asked Questions

SARS-CoV-2 Serology (COVID-19) Antibody (IgG), Immunoassay

Test Code 39504

Question 1.

What types of immunoassays are available for SARS-CoV-2 (COVID-19)?

Currently, 2 types of serological assays are available in the marketplace for SARS-CoV-2 testing:

1. Laboratory-based immunoassays: There are various types of immunoassays in this category, such as enzyme-linked immunosorbent assays (ELISAs), chemiluminescent microparticle immunoassays (CMIAs), and immunometric assays. These tests can be qualitative or quantitative and are generally performed using serum. All of these immunoassays use a solid phase coated with viral antigen to bind SARS-CoV-2 antibodies, but different tests may use different solid phases. For example, ELISAs use a plate and CMIAs use paramagnetic microparticles. Diagnostic Laboratory of Oklahoma (DLO) and Quest Diagnostics currently offer a high-complexity laboratory-based qualitative immunoglobulin G (IgG) SARS-CoV-2 immunoassay and not a rapid diagnostic test (RDT). Our IgG testing is also amenable to high-throughput testing commensurate with national pandemic testing needs.
2. RDT: These are typically lateral flow assays that can be used for point-of-care (POC) testing. RDTs most frequently test for SARS-CoV-2 IgG, immunoglobulin M (IgM), or viral antigen. These tests usually use blood samples from a finger stick, and some can use saliva or other specimen types.[1,2] DLO and Quest do not offer RDTs for SAR-CoV-2 antibody or antigen testing in its regional laboratories.

Question 2.

What is the US Food and Drug Administration (FDA) policy for commercial manufacturers and laboratory development/use of serology tests for SARS-CoV-2?

The FDA does not intend to object to the development and distribution by commercial manufacturers, or development and use by laboratories, of serology tests to identify antibodies to SARS-CoV-2, where the test has been validated, notification is provided to FDA, and information along the lines of the following is included in the test reports[2]:

- This test has not been reviewed by the FDA.
- Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Follow-up testing with a molecular diagnostic should be considered to rule out infection in these individuals.
- Results from antibody testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
- Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.

The FDA issued a letter for healthcare providers on the use of serological (antibody) tests for COVID-19 on April 17, recommending continued use of serological tests, as appropriate, with awareness of their limitations.[3] Refer to Question 9 for more information about the cross-reactivity due to past or present infection with other coronaviruses.

Frequently Asked Questions

Question 3.
How does DLO and Quest Diagnostics ensure that the serologic assays are accurate?

DLO and Quest Diagnostics ensure that tests offered for SARS-CoV-2 IgG are highly specific and have validated accuracy:

1. We use laboratory-based immunoassays from manufacturers who have demonstrated robust validationof their kits. Highlights of the manufacturers' validation include:
    a. Clinical performance of approximately 90% to 100% (assessed as percent agreement of serology results on known COVID-19 PCR positive cases).
    b. Specificity of approximately 99% to 100%. This was assessed by performing cross-reactivity studies utilizing serum samples positive for antibodies to other respiratory viruses, as well as panels of samples from pre-COVID times (2010, 2017, and 2019).[4,5]
2. We verify the performance characteristics of the kits by doing CLIA/CAP-required in-laboratoryvalidations using stringent acceptability criteria for precision, reproducibility, accuracy, method comparison, cross-reactivity, and clinical performance before starting patient testing.

Question 4.
How soon do IgG antibodies to SARS-CoV-2 appear in a patient who has been exposed to the virus?

The antibody response to SARS-CoV-2 usually starts with IgM and/or IgA being detected first, followed by the longer-lasting and more-specific IgG. Data suggest that IgG antibodies can be detected from 10 days after SARS-CoV-2 exposure or post symptom onset. However, some people do not generate detectable IgG antibodies after infection, because of an underlying immune disorder, immunosuppression, or other reasons. Additionally, an individual immune response can vary in the speed and strength of IgG production based on infective dose or viral burden upon exposure to SARS-CoV-2.

Question 5.
Can antibody tests be used to diagnose SARS-CoV-2 infection?

No. At present, no antibody tests have an intended use that includes definitive diagnosis of, or ruling out, current SARS-CoV-2 infection. Serological IgG assay provides information about whether a person has been exposed to SARS-CoV-2. A molecular diagnostic test should be considered to diagnose or rule out current infection.[2]

Question 6.
How do I interpret SARS-CoV-2 Serology (COVID-19) Antibody (IgG), Immunoassay results?

Results from this qualitative test for SARS CoV-2 IgG can be positive (reactive), negative (non-reactive), or, occasionally, equivocal (borderline).

A positive (reactive) result indicates detection of SARS-CoV-2 IgG, which may suggest exposure to SARS-CoV-2. It usually takes at least 10 days after symptom onset for IgG to reach detectable levels. Although the relationship between IgG positivity and immunity to SARS-CoV-2 has not yet been established, the detection of IgG antibodies may suggest an immune response to SARS-CoV-2 (COVID-19) after resolution of infection with SARS-CoV-2. Antibody tests should not be used to diagnose SARS-CoV-2 infection. Patients with symptoms should be evaluated with a molecular assay instead.

A negative (non-reactive) result indicates that SARS-CoV-2 IgG is not present at a level that is detectable by the SARS-CoV-2 Serology (COVID-19) Antibody (IgG) Immunoassay. It usually takes at least 10 days after symptom onset for IgG to reach detectable levels. However, the rate of IgG development can vary between individuals, and it is currently not known for how long IgG remains detectable after exposure to SARS-CoV-2. Negative results do not rule out COVID-19 infection, particularly in those who have been in contact with the SARS-CoV-2 virus. Follow-up testing with a molecular diagnostic assay should be considered to rule out infection if clinical condition is indicated.

Frequently Asked Questions

An equivocal (borderline) result indicates that IgG was detected at a level or close to the threshold of the limit of detection for the test. Equivocal results may represent an early infection, detection of an IgG generated from a past infection (refer to Question 9 for cross-reactivity with non-SARS CoV-2 coronavirus strains), or, in some cases, an underlying immune disorder, immunosuppression or other reasons.

In populations with a high prevalence of non-SARS-CoV-2 coronavirus strains, a positive result could also be due to past or present infection with one of these strains (refer to Question 9).

Question 7.

Does a positive result for IgG to SARS-CoV-2 mean that the patient is immune?

Presence of IgG to SARS-CoV-2 indicates that the patient has mounted an immune response to the virus. Although the immune response may protect against reinfection, this has yet to be established. It is also not known how long antibodies to the virus will protect someone, if at all. Scientists are conducting research to answer these questions. Therefore, patients with positive IgG results should continue to take steps to protect themselves and others.

Question 8.

What are the indications for use of the SARS-CoV-2 Serology (COVID-19) Antibody (IgG), Immunoassay?

Testing for SARS-CoV-2 IgG, including for individuals who may be asymptomatic or are ≥10 days after SARS-CoV-2 exposure or post-symptom onset, can play a critical role in the fight against COVID-19. SARS-CoV-2 IgG testing can be used to[2,6]:

1. Identification of SARS-CoV-2 exposed persons with PCR-negative results, especially for patients who present late with a very low viral load below the detection limit of RT-PCR assays, or when lower respiratory tract sampling is not possible.
2. Identify whether people have been exposed to SARS-CoV-2 and have mounted an immune response
3. Assess how many people have been exposed to SARS-CoV-2 in a population, by identifying individuals who have developed antibodies to the virus.
4. Possibly help identify individuals who may be able to donate convalescent plasma as a possible treatmentfor those who are seriously ill from COVID-19.

In the future, this test, along with other clinical data, may help identify individuals who may be less susceptible to infection and can return to work.

Question 9.

Is there cross-reactivity between SARS-CoV-2 antibodies and any of the human coronaviruses or SARS-CoV?

Cross-reactions with antibodies against the closely related SARS-CoV and other known human coronaviruses (HKU1, NL63, OC43, or 229E) cannot be completely excluded. However, specificity of the SARS-CoV-2 IgG immunoassays (ELISA and CMIA) is approximately 99%. Manufacturers[4,5] tested panels of samples from pre-COVID times (2010, 2017, and 2019), with less than 1% samples showing positive results. These findings suggest that antibodies against SARS-CoV and other coronaviruses are not commonly found in the general public.

Frequently Asked Questions

Question 10.

What is the role of neutralization assays, and are they available to assess immunity to SARS-CoV-2?

Neutralization assays are done to help assess the ability of neutralizing antibodies (NAbs) in patient serum to neutralize virus infectivity. These tests are useful to assess whether past infection (or vaccination, if available) has provided protection against infection. In these tests, serial dilutions of patient serum are spiked with known virus concentrations and then added to cell lines. After incubation, infected cells are quantified to determine the effectiveness of patient antibodies in neutralizing the virus.[1] The presence of NAbs may suggest immunity, and convalescent serum with NAbs is being studied as a treatment for COVID-19. Testing for NAbs is only available at some public health laboratories and research facilities. It is not performed at DLO or Quest Diagnostics.

References

1. Center for Health Security. Serology based tests for COVID-19. Accessed April 12, 2020. https://www.centerforhealthsecurity.org/resources/COVID-19/serology/Serology-based-tests-for-COVID-19.html
2. US Food and Drug Administration. FAQs on diagnostic testing for SARS CoV-2. Accessed April 12, 2020. https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic-testing-sars-cov-2
3. US Food and Drug Administration. Important information on the use of serological (antibody) tests for COVID-19– letter to health care providers. Accessed April 23, 2020. https://www.fda.gov/medical-devices/letters-health-care- providers/important-information-use-serological-antibody-tests-covid-19-letter-health-care-providers
4. Anti-SARS-CoV-2 ELISA (IgG). Instructions for use. Euroimmun; March 2020.
5. Abbott Architect SARS-CoV-2 IgG [package insert]. Abbot; April 2020.
6. International Society for Infectious Diseases. COVID-19 antibody testing primer. Updated April 22, 2020. https://www.idsociety.org/globalassets/idsa/public-health/covid-19/idsa-covid-19-antibody-testing-primer.pdf

This FAQ is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the individual.

Document FAQS.219 Version: 0
Version 0: Effective 04/24/2020 to present