CLINICAL LABS OF HAWAII

SARS-CoV-2 IgG Serologic Test: Frequently Asked Questions May 1, 2020

Background:

- On February 29, 2020, the U.S. Food and Drug Administration (FDA) issued a policy to enable the development of diagnostic testing under an "emergency use authorization" (EUA), in an effort to accelerate testing during the COVID-19 public health emergency. Tests with an EUA undergo an expedited review of the test's characteristics by the FDA.
- On April 30, 2020, Clinical Labs of Hawaii (CLH) offered serologic testing for SARS-CoV-2, the virus that causes COVID-19.
- CLH also offers SARS-Cov-2 rRT-PCR molecular testing for active COVID-19 detection.

Q: What is this serology test called?

A: SARS-CoV-2 IgG. This test has FDA EUA and is conducted on the Abbott Architect instrument. The test detects IgG antibodies to SARS-CoV-2. (IgG is formed by the immune system when the virus is encountered).

Q: What is the purpose of this serology test?

A: There are several potential reasons why this test might be ordered.

1) To see who was infected by SARS-CoV-2
2) To see who might be immune to SARS-CoV-2. At this writing, this must be confirmed by additional research.
3) To see who might be potential donors for convalescent plasma

Prior to testing, these above reasons and any others should be discussed with your healthcare provider.

Q: What is the difference with the other tests for COVID-19?

A: There are two laboratory-based tests for COVID-19. This SARS-CoV-2 IgG serology test is a venipuncture blood test that looks for antibodies (not the actual virus). The other test (real time reverse transcriptase polymerase chain reaction or rRT-PCR) is a molecular test that detects the actual virus, done usually via nasopharyngeal swabbing.

Additionally, there are point-of-care (POC), handheld, "rapid" tests (resembles home pregnancy tests) that use blood from finger sticks to detect antibodies to SARS-CoV-2. These POC tests use a different methodology, and only one brand among the multiple POC tests has an FDA EUA at this writing. CLH does not have plans to use, distribute, or guarantee the validity of these POC tests.

Q: Can I use this test to see if I am infected by SARS-CoV-2?

A: No. This test does NOT indicate whether you have an ACTIVE infection. Negative serology results do not rule out SARS-CoV-2 infection. The rRT-PCR test should be used to diagnose active infection.

Q: What type of specimen is required for the serology test?

A: Blood obtained by venipuncture. The test is not conducted on other specimen types, such as saliva or nasopharyngeal and oropharyngeal swabbing.

Q: What are the test characteristics?

A: The manufacturer of this serologic test conducted studies to determine clinical performance. The following data is taken from the Abbott SARS-CoV-2 IgG product insert* and interpretations of these studies are provided by CLH.

1) *Positive Percent Agreement (PPA, analogous to "sensitivity")*: 100% for patients ≥14 days post-symptom onset.
   Study: 88 patients who were ≥14 days post-symptom onset were tested.
   Results: 88 patients had detectable IgG, indicating 100% PPA for patients who were ≥14 days post-symptom onset. The PPA (or sensitivity) decreases as the days post-symptom onset shortens (PPA: 8-13 days post-symptom onset=86.36%, 3-7 days post-symptom onset=25%, <3 days post-symptom onset=0%).
   Interpretation: This suggests a low false negative rate for patients tested two weeks after symptoms start and suggests an optimal time period for when serologic testing could occur.
2) *Negative percent agreement (NPA, analogous to "specificity")*: 99.6%.
   Study: 997 patient specimens taken before September 2019 (pre-COVID-19 outbreak) were tested.
   Results: There were 993 negative (99.6%) results, and 4 positive (0.4%) results.
   Interpretation: This suggests a low false positive rate.

Caveat: Additional future studies to confirm the test manufacturer's studies are not available at this writing.

Q: What are potential limitations of this testing?

A: 1) Patients who are immunosuppressed (i.e., on immunosuppressant drugs, HIV) may not produce detectable antibodies or may have a delayed response.
2) The Abbott SARS-CoV-2 IgG product insert suggests that patients who may have heterophilic antibodies (i.e., patients exposed to animals/animal sera), patients who received human anti-mouse antibodies (HAMA) as treatment, and patients with rheumatoid factor (RF) may have anomalous results.* However, it should also be noted that limited studies (5 patients with HAMA, 5 patients with RF) presented in the manufacturer's product insert demonstrated no cross reactivity / false positivity.

Caveat: Additional future studies to confirm the test manufacturer's studies are not available at this writing.

Q: Will this serologic test give false positive results by detecting non-SARS-CoV-2 coronaviruses (i.e., HKU1, NL63, OC43, 229E)?

A: The test manufacturer's product insert indicates "pedigreed specimens with direct evidence of antibodies to nonSARS-CoV-2 coronavirus (common cold) strains such as HKU1, NL63, OC43, or 229E have not been evaluated with this assay." However, it should be noted that their study addressing NPA (see earlier) indirectly addresses this question and suggests low false positivity.

Caveat: Additional future studies to confirm false positive cross reactivity to non-SARS-CoV-2 coronaviruses are not available at this writing.

Q: How are results reported?
A: The results are reported as an index value with an interpretation. Index values of ≥1.40 are interpreted as being "positive" for IgG to SARS-CoV-2. Index values of <1.40 are interpreted as being "negative" for IgG to SARS-CoV-2. The actual protein amount of IgG or antibody titers are not reported. Also, it should be noted that the manufacturer indicates that this test is *qualitative*, and the manufacturer does not guarantee that this index can be used in a quantitative manner.

Q: Where is the blood analyzed?
A: The testing is conducted at the main laboratory of CLH in Aiea, HI.

Q: Who can be tested?
A: Requests require an order from healthcare providers.

Q: How many tests can CLH do?
A: As of this writing, 1000 tests per day with plans to increase capacity in the near future.

Q: How soon can I get results?
A: Tests are run 24 hours a day, 7 days a week, and results are usually available within 24 hours. If the demand is great, results may require additional time.

Q: Is this antibody test covered by insurance?
A: Most insurance payers have indicated that the tests will only be covered if *"medically necessary"*. Please contact your insurance company to determine coverage benefits.

Q: How can I be tested?
A: You may visit any CLH location with a lab order from your healthcare provider to get tested. Please visit www.clinicallabs.com to find a location nearest to you and for up-to-date hours of service. You may also call 1-833-920-2559 to schedule an appointment at select locations.

Please know that, per state mandate, a mask is required in all public areas; and CLH is practicing social distancing for the safety and welfare of all. All patients should be asymptomatic and not have an active COVID-19 infection when presenting for a blood draw.

Visit us at www.clinicallabs.com for more information or contact CLH Client Services at (808)677-7998.

*https://www.fda.gov/media/137383/download