Guidelines for SARS-CoV-2 Antibody Testing (Serology) in Cancer Patients

The pandemic virus, SARS-CoV-2 – the cause of COVID-19 disease, is thought to have been in our community in Seattle and surrounding metro area for weeks, if not months. It is expected that some patients seen at SCCA may have been exposed to the virus and had symptoms consistent with COVID-19 but were never officially diagnosed with the disease. A new serologic assay (COVID-19 Antibody, IgG [lab code: NCVIGG]) is now available through UW Virology.

Although anyone can order this test, it is important to know that the assay was developed using normal hosts, and therefore the test's utility in cancer patients and those with underlying immunodeficiency has not been characterized. In addition, it is unknown whether detection of antibodies indicates protection from COVID-19. Currently, we do not routinely recommend COVID-19 serologic testing in cancer patients until additional data become available.

FAQs about COVID-19 antibody testing (serology testing):

1. **What are the general indications for serological testing for SARS-CoV-2 (COVID-19)?**

   Serologic testing may be considered among patients who have had a prior illness consistent with COVID-19 or exposure to SARS-CoV-2 more than 21 days ago.

   For patients who have previously tested by positive by SARS-CoV-2 PCR, consider whether serologic testing would change medical management.

2. **Are there any concerns with testing that providers should consider when ordering the test?**

   The major concerns/cautions to this assay:

   - **Serologic testing is NOT indicated for diagnosis of acute infection** and should not be ordered while a patient is being investigated for active SARS-CoV-2 infection.
   - Patients with new or persistent COVID-19 symptoms, or if there is concern for active infection, should undergo molecular testing (PCR) with a nasopharyngeal swab prior to serologic testing.
   - It is unknown if a positive antibody test indicates any level of short- or long-term protection against SARS-CoV-2; antibody testing should not be used to guide decisions about return to work.
   - Immunocompromised patients who have COVID-19 may have a delayed antibody response and/or produce levels of antibody that may not be detected as positive by the assay.

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3. What COVID-19 serology test is currently available through the laboratory?

UW Virology is performing the Abbott SARS-CoV-2 IgG immunoassay on the ARCHITECT instrument. This is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibodies to SARS-CoV-2 nucleocapsid protein in human serum and plasma. This is a high-throughput automated system allowing for the testing of many samples each day.

4. What is the target antigen used in the Abbott immunoassay?

The Abbott SARS-CoV-2 IgG immunoassay detects antibodies to the viral nucleocapsid protein (NP).

5. How are the results reported, and what is the clinical significance?

The results are either "positive" or "negative" based on the manufacturer-indicated cutoffs for antibody levels.

- A NEGATIVE result indicates that either a person has not been infected with SARS-CoV-2 or antibody is not present at levels detectable by this assay. Patients who have had SARS-CoV-2 may have negative antibody responses. Explanations for this may include a very recent exposure such that not enough time has elapsed to generate an immune response, or the immune response has decreased below the detectable level. Patients with cancer or other immune deficits may also not produce antibody at levels detectable by this assay. A negative result therefore does not rule out current or past infection with SARS-CoV-2.

- A POSITIVE result likely indicates previous or current infection. Recent studies examining serial plasma samples in hospitalized patients with SARS-CoV-2 infection suggest that the median time to seroconversion is about 10 days in moderately ill patients, and 14 days in severely ill patients.[1,2] It is important to note that a positive serology test cannot distinguish between active or past COVID-19. If there is concern for active infection, molecular testing (PCR) with a nasopharyngeal swab is recommended.

6. Does a positive result mean that a patient has been previously infected?

Probably YES, but not always. Due to an expected overall low absolute prevalence of SARS-CoV-2 infection locally, false positives may occur.

7. Do antibodies confer protection from COVID-19 if they are detected?

At this time, it is not known whether the presence of antibodies confers protection from reinfection with SARS-CoV-2, how long the antibody response lasts, or the association between antibody response and clinical outcomes of individuals with COVID-19. The value of antibodies in cancer and transplant patients is even less clear and requires further study.

8. What can cause false positives or negatives?

The following can lead to possible false positive or false negative serologic testing:

- Immunocompromised patients who have COVID-19 may have a delayed antibody response and produce levels of antibody that may not be detected as positive by the assay
- Potentially interfering disease states and other cross reactants have been evaluated and are represented in the SPECIFIC PERFORMANCE CHARACTERISTICS section of the package insert.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may develop human anti-mouse antibodies (HAMA). Such patients may show either falsely elevated or depressed values when tested with assay kits such as SARS-CoV-2 IgG that employ mouse monoclonal antibodies.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed.
- Rheumatoid factor (RF) in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays.

9. How do I order the test in ORCA?

The ORCA lab order for COVID-19 serology is “COVID-19 Antibody, IgG”. The laboratory code is “NCVIGG”.

10. What sample types are accepted?

Serum or plasma can be tested for SARS-CoV-2 antibodies.

11. How sensitive is this test?

This depends on the time after infection and on the host who produces antibodies. At approximately 25 days after symptomatic infection in hospitalized patients, the sensitivity approaches 100%. The Abbott product insert reports higher sensitivity, with 91% sensitivity by 14 days after symptom onset. The sensitivity of the test among subjects with asymptomatic infection is unclear, and the duration of positive results (seropositivity) is unknown.

Importantly, the sensitivity of the assay is unknown among cancer, transplant or immunosuppressed patient populations, and so if ordered should be interpreted cautiously.

12. How specific is the UW test? Does it cross react with other human coronaviruses?

The assay does not appear to cross-react with other human coronaviruses, but this type of cross-reactivity cannot be completely ruled out. The product insert of the assay reports a specificity of 99.6% in normal hosts, but the specificity among cancer and immunosuppressed patients is unknown.

13. What are the limitations of this test?

This is not intended for acute diagnosis early in the course of disease. As stated above, negative results do not rule out a SARS-CoV-2 infection. For patients in which there is a high clinical suspicion for COVID-19 is high, PCR-based testing is recommended to evaluate infection. Antibody testing should NOT be used alone to diagnose COVID-19**.** False-positive results rarely may occur as the result of infection with non-COVID-19 human coronaviruses.

Cancer and other immunocompromised populations with COVID-19 may not have detectable levels of antibodies or have a delayed antibody response.

14. What is the turnaround time?

Test results are usually available within 24 hours of the test being ordered.

15. My patient has a positive serology result and is interested in being a potential plasma donor. Where can I refer this patient for more information?

This assay is not meant for the screening of donated blood. However, if a patient is interested in being a potential convalescent plasma donor, please refer them to the following website where they can learn more: https://newsroom.uw.edu/news/plasma-donors-sought-among-those-recovered-covid-19. At the bottom of this website is the contact information patients can use to get more information about participating. Cancer and immunosuppressed patients are often excluded from most plasma donation programs.

16. My patient had a positive (or negative) test at another site using another assay. How does this assay differ from other tests?

There are an emerging number of serologic assays which are becoming increasingly available. A number of these assays are developed using different methods of collection (e.g. fingerstick vs. blood draw), systems for analysis (e.g. lateral-flow assays vs. ELISA), and to date most have not been compared. Recent data suggests a wide range of sensitivity and specificity of these assays[6], so patients with testing from other sites (particularly those that rely on local or non-FDA approved assays) should be interpreted with caution. Repeat testing to confirm results can be considered depending on the clinical utility of such results.

References

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