



masks. Caution should be taken when interpreting test performance characteristics; for a test with 99% specificity used in a population like Nebraska with less than 5% prevalence, 1 in every 6 positive tests will represent a false-positive result.

A positive serology might reflect prior infection with SARS-CoV-2, but might also represent a nonspecific, false-positive reaction to an antigen unrelated to SARS-CoV-2, such as past or present infection with a coronavirus other than SARS-CoV-2.

A negative result from antibody testing does not rule out SARS-CoV-2 infection, particularly for exposed individuals who are still within the estimated incubation period or the window period of illness prior to generating an antibody response.

While the presence of COVID-19 antibodies might imply some level of immunity to the virus, uncertainty remains at this time whether detection (or a certain titer) of SARS-CoV-2 antibodies provides immunity to future COVID-19 infections or prevents carriage/shedding of COVID-19 virus.

Laboratories and providers must be aware of FDA requirements regarding appropriate settings where specific tests can be performed. Many can only be performed in a moderate- or high-complexity CLIA laboratory setting, and should not be deployed as point-of-care tests. The manufacturer's instruction/package insert (available at the link below) must be reviewed to determine if the test is intended for use by a laboratory approved to perform moderate- or high-complexity tests.

Health care providers and clinical laboratories must carefully review the performance characteristics of any SARS-CoV-2 serology test kits considered for patient testing. Some falsely advertise Food and Drug Administration (FDA) approval and sufficient reliability for use in routine clinical practice.

The risks of inaccurate tests are high. A false-positive COVID-19 antibody test might wrongly suggest that individuals have immunity against the virus when in fact they don't. This could result in inappropriate and misguided behavior that would endanger the patient and their close contacts.

### **When to Use Serology Tests**

- 1) Public health authorities may use serology to assess seroprevalence in a population.
- 2) In **rare, selected** patients who present very late in their course of illness where PCR may be negative, serology may help prevent unnecessary workup for other illnesses, and assist with isolation and contact tracing

decisions. Exposure risk and pretest probability must be carefully considered.

- 3) Serology may be used to diagnosis patients with late complications of COVID-19, such as multisystem inflammatory syndrome in children (MIS-C).
- 4) Serology can identify potential donors for convalescent plasma in recovered, previously-confirmed positive patients

### When NOT to Use Serology Tests

- 1) Serologic tests should not be used routinely to establish acute infection.
- 2) Serologic tests should not be used to determine immune status or to guide employment decisions, social distancing, or PPE use.
- 3) Serologic tests should not be performed if the results will not change clinical management decisions (i.e. patient request).

### Additional Recommendations:

- 1) There are no substantial performance differences between assays that measure IgG vs. total antibody. Antibody class should not determine the choice of assay in most circumstances.
- 2) A separate IgM assay to establish a diagnosis of early infection is not recommended at this time.

A second, different serologic assay (i.e. different antigenic target) might improve the positive predictive value for an initial positive test.

### **RESOURCES:**

Review of the COVID serology issues from Johns Hopkins:

<https://www.centerforhealthsecurity.org/our-work/publications/developing-a-national-strategy-for-serology-antibody-testing-in-the-US>

CDC COVID Serology page:

<https://www.cdc.gov/coronavirus/2019-ncov/lab/serology-testing.html>

Currently 16 COVID-19 serology tests with Emergency Use Authorization are listed on the FDA website:

<https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance>

NYC Health Advisory on Role of COVID-19 Serology Tests:

<https://www1.nyc.gov/assets/doh/downloads/pdf/han/alert/2020/covid-19-status-of-serologic-testing.pdf>