

Nebraska Department of Health and Human Services HEALTH ALERT NETWORK Advisory



TO: Healthcare Providers, Infection Control, Hospitals, Labs, and Public

Health

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RE: COVID-19 Serology Testing

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Serologic tests to detect antibodies resulting from COVID-19 infection are increasingly available. This Health Advisory addresses various aspects of these tests including their role in patient care and public health. The information contained herein underscores the fact that **serologic assays have not yet been demonstrated to be useful in making clinical decisions for most individual patients, and should not be routinely ordered for this purpose**.

These tests determine the presence of antibodies against SARS-CoV-2: some confirm overall presence or absence of COVID-19 antibodies, while others specifically detect IgM or IgG COVID-19 antibodies.

COVID-19 antibodies begin to develop approximately 6 to 10 days after infection with SARS-CoV-2. IgM appears to peak approximately 12 days post- infection and persists for as long as 35 days, after which the quantity declines rapidly. IgG has been observed in patients two weeks after symptom onset, peaks approximately 17 days after infection, and persists for at least 49 days. IgG has been found in patients infected with **SARS-CoV-1** (**SARS**) up to 2 years after recovery.

Although the levels of infection are unknown at this time, Nebraska most likely has a low prevalence of persons who have actually had COVID-19 infection. This prevalence undoubtedly varies across different segments of the state's population, but overall is most likely less than 5 %.

Given current limitations, serologic tests should not be used at this point to routinely diagnose acute or prior SARS-CoV-2 infection, nor should they be used in an attempt to establish immune status to SARS-CoV-2. Depending on the sensitivity and specificity of a particular test, they may produce false-negative or false-positive results that would mislead individuals and incline them to abandon useful practices such as physical distancing or protective equipment such as face

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:

 $\frac{https://www.centerforhealthsecurity.org/our-work/publications/developing-a-national-strategy-for-serology-antibody-testing-in-the-US$

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:

 $\underline{https://www.fda.gov/medical-devices/emergency-situations-medical-devices/eua-authorized-serology-test-performance}$

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

 $\frac{https://www1.nyc.gov/assets/doh/downloads/pdf/han/alert/2020/covid-19-status-of-serologic-testing.pdf}{}$