New Mexico Medical Advisory Team (MAT) Assessment

RECOMMENDATIONS TO CLINICIANS REGARDING SARS-CoV-2 ANTIBODY TESTING

MAT Workgroup Name: MAT Testing Group **Date:** April 21, 2020

Question or request:

1. What are the indications for SARS-CoV-2 antibody testing in the diagnosis and management of patients?
2. How should SARS-CoV-2 antibody testing be used as an epidemiologic tool and as a guide to inform public policy?
3. What specific SARS-CoV-2 antibody tests should be used?

Recommendations in bullet form:

- MAT recommends that SARS-CoV-2 antibody testing should be considered: 1) in a subset of patients with acute respiratory tract disease as a complement to nucleic acid amplification testing (NAAT), especially in patients in whom COVID-19 disease is suspected and NAAT results are negative; 2) in patients with resolved serious upper respiratory tract infection that occurred during the timeframe of the COVID-19 pandemic in whom the cause is suspected to have been SARS-CoV-2 infection; 3) as an epidemiologic tool to estimate seroprevalence of infection in the general population and select sub-groups; 4) as an epidemiologic tool to help determine whether individuals with SARS-CoV-2 antibodies are protected from subsequent SARS-CoV-2 infection; and, 5) as an epidemiologic tool to study long-term outcomes among people who have had both symptomatic and asymptomatic SARS-CoV-2 infection.

- The MAT recommends that testing should be performed using assays from reputable established biotechnology companies that have undergone rigorous independent assessment of performance characteristics and that have received, minimally, an Emergency Use Authorization from the Food & Drug Administration. The MAT recommends that clinicians avoid the use of rapid point-of-care SARS-CoV-2 antibody tests whose performance characteristics have not been independently assessed even if that device has received an Emergency Use Authorization from FDA.

- MAT recommends that, until the natural history of SARS-CoV-2 infection is better understood, positive tests for SARS-CoV-2 antibody should not be used as an indication of resolved infection or protection from future infection.

- The MAT recommends that clinicians who obtain SARS-CoV-2 antibody testing on patients should fully inform the patient of the significant issues inherent in these assays, i.e. false negative results in early infection and false positive test results (together with a discussion of positive predictive value).

Assessment:

SARS-CoV-2 infection is usually detected first by obtaining a swab sample of secretions from the nasopharynx and testing the sample for the presence of viral RNA by nucleic acid amplification tests (NAAT). The NAAT assays usually amplify three distinct nucleic acid segments of the viral genome and therefore have a very high specificity. The sensitivity of SARS-CoV-2 NAAT assays is dependent upon the viral load in pharyngeal secretions, the quality of the sampling, and the performance characteristics of the specific assay used. NAAT assays have been the mainstay of SARS-CoV-2 diagnosis because 1) they are usually positive early in infection, including in asymptomatic and pre-symptomatic people; 2) they are an indication of infectiousness; and, 3) they are widely available through reference laboratories. It has been observed that the presence of viral RNA in the pharynx by NAAT decreases to undetectable levels in some people as COVID-19 disease progresses to the lower respiratory tract. NAAT testing of the pharynx in more advanced disease is more likely to give a false negative test result.

Among patients with COVID-19 disease who have been studied, a detectable antibody response generally begins a few to several days following infection. Serum antibodies are often undetectable during the first few days of infection when pharyngeal virus is detectable at high viral loads and the patient is infectious to others. As COVID-19 disease progresses, the detection of virus-specific antibodies (IgM and IgG) increases. Completely asymptomatic patients in whom persistent virus is detectable in the pharynx may not develop a detectable antibody response. Detectable serum antibodies can appear while the patient is still infected and before the disease is resolved. It is not yet known

whether, or the degree to which, the presence of detectable SARS-CoV-2 antibodies in the blood confers protection against subsequent infection with SARS-CoV-2.

Evidence:
SARS-CoV-2 RNA is detected at high viral loads from pharyngeal secretion samples at the time of symptom onset and often days before symptom onset. Virus is actively replicating within mucosal cells of the pharynx during early infection. Viral RNA is readily detected from pharyngeal secretion samples using nucleic acid amplification tests (NAAT) through reference laboratories and as rapid NAAT tests (Cepheid SARS-CoV-2 Xpert Xpress assay; Abbott ID NOW COVID-19 assay) from many regional laboratories.

SARS-CoV-2 specific IgG and IgM antibodies appear in the blood a few to several days after infection. Detection of antibody is not a reliable diagnostic test when used alone in people with early infection, the people who are at greatest risk of transmitting infection. There is evidence that supports the use of antibody testing in individuals with suspected COVID-19 disease in whom SARS-CoV-2 RNA testing from respiratory tract secretions is negative.

Performance characteristics of many commercially available SARS-CoV-2 serologic tests have not been independently evaluated, and many commercially available tests have not yet received an Emergency Use Authorization by FDA.

Serologic assays can give false positive results at a non-trivial rate that produces a significant reduction in positive predictive value when used in populations with low prevalence of infection and in individuals with a low prior likelihood of infection. These considerations must be kept in mind when applying these tests and when counseling patients regarding their test results.

Contributors: There was consensus on these recommendations among the following contributors.
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Resources/Reference:

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