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SEROLOGICAL TESTING FOR SARS-CoV-2 ANTIBODIES

Background

Unlike molecular tests used to detect the SARS-CoV-2 viral RNA from nasopharyngeal and other respiratory specimens, serological tests are blood tests that are used to detect the presence of antibodies produced by the immune system in response to the infection. Serological tests are designed to detect either a specific antibody class, such as IgM or IgG, or "total antibodies" that detect both IgM and IgG but do not differentiate between them.

Current evidence indicates that antibodies to SARS-CoV-2 begin to develop approximately six to 10 days after infection.[1] IgM appears to peak approximately 12 days after infection and persists in sufficient quantities for as long as 35 days, after which the quantity declines rapidly.[2] IgG has been observed to peak approximately 17 days after infection and persist for at least 49 days (at which time the study was concluded).[2] Further, IgG has been observed in patients two weeks after symptom onset.[3]

As of April 26, 2020, there is no evidence that the presence of antibodies to SARS-CoV-2 confers immunity to subsequent infection by the virus. Until it is known if antibodies provide protective immunity, serological test results should not be used to make decisions regarding decreased social distancing, return to work policies, or a decreased need for personal protective equipment.

Indications For Testing

Currently, the clinical value of SARS-CoV-2 antibody testing remains limited to specific indications:

1. As a potential indicator of infection following a negative SARS-CoV-2 nucleic acid amplification test result in patients with symptoms of COVID-19 who present later in their illness.
2. To identify individuals who have been previously infected with SARS-CoV-2 and who may now be considered as potential convalescent plasma donors.

Antibody testing will be useful as public health surveillance tools to estimate the relative proportions of different populations that have been exposed to SARS-CoV-2 but they have little utility as diagnostic tools for individual patient assessment.

Concerns About Quality

In its March 6, 2020 guidance document to help accelerate the availability of novel coronavirus diagnostic tests, the US Food and Drug Administration (FDA) authorized four pathways for tests to come to market.[4] One of those pathways (IV.D), permits the distribution of commercial serological tests without review by FDA. As a result there are now over 100 different antibody tests, many

NOTES

1. Okba NMA, Müller MA, Li W, et al. Severe acute respiratory syndrome coronavirus 2-specific antibody responses in coronavirus disease 2019 patients. Emerg Infect Dis 2020;26(7).

2. Tan W, Lu Y, Zhang J, et al. Viral kinetics and antibody responses in patients with COVID-19. medRxiv March 26, 2020.

3. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020 Mar 23. doi:10.1016/S1473-3099(20)30196-1

4. Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency. Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff. US Food and Drug Adminstration. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-diagnostic-tests-coronavirus-disease-2019-during-public-health-emergency doi:10.1101/2020.03.24.20042382

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of with questionable performance, being marketed by manufacturers and distributors. Most of these are "rapid" tests that use a fingerstick blood sample and produce results in a few minutes. While these may appear to be simple tests that can be performed at the point-of-care, the absence of FDA approval means that these tests must validated prior to use and can only be performed in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), to perform high complexity tests.

Serological Testing At TriCore

Serological testing for SARS-CoV-2 antibodies is expected to be available at TriCore on May 4, 2020. This is a qualitative IgG antibody test manufactured by DiaSorin, Inc. that received Emergency Use Authorization (EUA) by FDA on April 24, 2020. Results will be reported as "negative" or "positive" for recent or prior infection with SARS-CoV-2. According to the manufacturer, test sensitivity is 97.6% at 15 or more days after COVID-19 diagnosis. Test specificity is 99.3%. Accordingly, assuming a 1% prevalence rate in the population tested, the positive and negative predictive values for recent or prior infection with SARS-CoV-2 would be 50 and 99.9%, respectively. At a prevalence of 5%, the positive predictive value increases to 84% and negative predictive value remains unchanged.

Due to limited test availability, TriCore will only be able to perform 300 serological tests each day. Capacity is expected to increase in the weeks ahead.

Remember

- Molecular testing is the current test of choice for the diagnosis of acute SARS-CoV-2 infection.
- Serological tests for SARS-CoV-2 infection have no role to play in the acute diagnosis of COVID-19.
- Serological tests will miss patients in the early stages of disease when they are infectious to other people.
- It is not definitively known if the antibodies detected by serological tests confer immunity.
- Serological tests have little utility as diagnostic tools for individual patient assessment.