Prudent use of SARS-CoV-2 antibody testing: Avoiding false assumptions

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Tests for SARS-CoV-2
Over the past few months, testing for SARS-CoV-2 and its use in managing the COVID-19 pandemic have generated much discussion. As of April 13, 2020, FDA has granted Emergency Use Authorization (EUA) to 33 in-vitro diagnostic tests intended to help diagnose COVID-19 infections. One such test, qSARS-CoV-2 IgG/IgM Rapid Test (Cellex, Inc., Research Triangle Park, NC, USA, and Guangdong, China) is the first, and to date only, serology test authorized to detect SARS-CoV-2 antibodies (immunoglobulin M and immunoglobulin G) in blood samples from patients with suspected COVID-19 infections. This serology test has garnered a lot of attention and excitement. Many people may think this test will be the answer to safely getting people back to work, reducing the need for social distancing, and resuming activities that involve large gatherings, such as sports and weddings. ECRI wants to sound a loud alarm to help people understand the risks and how to avoid making wrong assumptions regarding testing. The great majority of the other in-vitro diagnostic tests that FDA has authorized for diagnosing COVID-19 are polymerase chain reaction (PCR)-based nucleic acid tests that can identify the viral genetic material obtained from nasopharyngeal swabs of individuals suspected of SARS-CoV-2 infection. ECRI recommends using a cautious approach and avoiding over-interpreting what these tests can show and how to apply information obtained from these tests.

Immunoassays are less accurate
Serology and PCR-based tests have tradeoffs. Both the serology and PCR-based tests can provide some useful information to help make informed, evidence-based decisions during a pandemic with an unknown trajectory. PCR-based tests can only inform whether an individual harbors the virus during the time of testing and can be used in conjunction with patient medical history and physical examination to aid in COVID-19 diagnosis. A serology test that identifies antibodies can inform on who has the disease, who has been infected (whether asymptomatic or not), and who may have potentially acquired immunity. However, immunoassays are less accurate and more difficult to develop than the PCR-based tests but can be performed at the point of care and produce faster results (typically within one hour), allowing physicians to accelerate clinical decision making. PCR-based tests are considered more accurate and reproducible; however, they are more technically involved and challenging to perform, and test results are not available for several days after testing (mainly due to logistics associated with shipping samples to laboratories). Both test types are qualitative, and results cannot predict viral load or antibody titer.

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Testing is critical

The importance of testing for COVID-19 cannot be understated. The information testing provides is critical to understand, stem, and control the spread of SARS CoV-2. Timely testing can provide evidence to inform patient management and identify carriers and allows those on the front lines to understand how wide-spread the virus is and the effects of mild or asymptomatic infections on disease transmission, as well as define risk factors associated with severe disease and characteristics of those who are asymptomatic or exhibit mild symptoms. Through testing, understanding SARS CoV-2’s natural history in these different populations provides the basis for identifying effective, evidence-based strategies to appropriately allocate resources.

EUA’s clinical care limitations

Usually, clinical studies provide diagnostic accuracy and clinical utility evidence for making evidence-based decisions for a test’s efficacy. Under the EUA, only analytic validity is assured. Analytic validity is a test’s ability to accurately and reliably measure the properties it is intended to measure—for example, does the test accurately identify antibodies specific to SARS-CoV-2 and not those against other coronaviruses? Analytic validity is a reasonable expectation given the urgency of the situation and considering that better-quality evidence requires time and large clinical studies to acquire. However, analytic validity does not provide information on patient outcomes, which is the ultimate endpoint to measure. This type of information comes from clinical studies that provide evidence to address important questions regarding a diagnostic test’s accuracy and impact on patient-orientated outcomes (i.e., clinical utility). EUA-based tests do not yet permit evidence-based conclusions to how well a test correctly identifies those who have and those who do not have the disease, whether one test is better than another to aid in COVID-19 diagnosis, and how testing affects patient management and patient outcomes.

Antibody test results may be helpful but cannot form the basis for policy decisions at this time.

ECRI recommends using a cautious approach and avoiding over-interpreting what these tests can show and how to apply information obtained from these tests. A serology test that can identify antibodies to SARS-CoV-2 may be tempting to use to indicate who has immunity to the virus and to form the basis for decisions regarding who can go back to work, who requires personal protective equipment, who no longer needs to practice social distancing, or who can attend activities that involve large gatherings, such as weddings and sporting events. Although the presence of antibodies against a specific virus typically suggests an individual has protection from that virus, it is still unknown whether the presence of antibodies specific to SARS-CoV-2 means that someone cannot be reinfected. Whether mild or asymptomatic cases confer the same level of immune response and immunity as more severe cases has yet to be determined. It is also unknown how long any potential immunity from these antibodies could last. For example, it has been reported that immunity to other seasonal coronaviruses lasts only a few months, whereas immunity to the SARS CoV-1 virus outbreak in the early 2000s lasted an average of approximately three to six years. Early indications suggest the SARS-CoV-2’s mutation rate is relatively slow, meaning that mutations that may allow reinfection in individuals deemed “safe” because they have antibodies to the virus are unlikely; however, this needs further confirmation.

Nonevidence-based decisions can have dire societal effects.

Additional evidence is needed to address the questions mentioned above and to evaluate the accuracy of available tests. Although these tests are proving useful, their accuracy needs validation given the potential for disease spread with each false-negative test result. What must be avoided is overestimating the type of information that available tests can provide and extrapolating findings beyond what the evidence supports, which may lead to nonevidence-based decisions that can have dire long-term societal effects.

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