# A COMBINED TEST APPROACH IS ESSENTIAL

## A more complete picture requires both diagnostic and antibody testing.

Given extensive coverage of COVID-19 testing in the media, it is not surprising that some confusion exists. There are essentially two types of tests for determining if a person has or had COVID-19: a diagnostic test, and an antibody test. Table 2, summarized from the FDA[1], highlights the primary use cases.

A diagnostic test looks for signs of an active virus in the body. One way to do this is through the polymerase chain reaction (PCR), a molecular test that detects the virus's genetic material through a mucus sample. As noted in a recent article in the *Journal of the American Medical Association (JAMA)*[2], the PCR swab test is the "most commonly used and reliable test for the diagnosis of COVID-19." It is typically used when someone presents with symptoms, and it indicates whether that the person is infected with the SARS-CoV-2 virus.

The other type is the antibody test. This requires a blood sample, either from an intravenous draw in a lab or a finger-prick that can be taken anywhere. Instead of looking for the disease virus, this test looks for evidence that the body has fought the disease by way of specific antibodies. Two antibodies that exist in the body after a COVID-19 are IgM and IgG. They can take a few days to build up as the body fights the disease, and once in the body they can remain for a long time. Current studies are determining the duration of IgG forSARS-CoV-2, but studies have shown the IgG antibody in patients up to two years after recovery from the previous pandemic of severe acute respiratory distress syndrome (SARS)[3].

In addition to the FDA summary, a recent serodiagnostics for coronavirus report[4] underlined several other possible uses cases for antibody tests (summarized in Table 3). Most notably, in addition to "identifying persons who were previously infected," antibody testing "may also serve as an adjunct to molecular methods for COVID-19 diagnosis in certain clinical scenarios."[5] And while antibody testing should not be used as the sole basis for diagnosis, there is a strong overlap between the virus being active and

*Table 2 Potential antibody test use cases.*

| Use Cases | Advantages | Current Limitations |
|---|---|---|
| **Diagnosis of suspect cases when PCR is not available** | Could enable decentralized testing where PCR is limited<br>Diagnosis of patients presenting late (low viral load)<br>Diagnosis when low respiratory tract sample not available | Unlikely to catch early-stage infection (<7 d)<br>May not detect asymptomatic<br>Negative test cannot rule out infection<br>IgM appears early, but less specific |
| **Identify plasma donors** | Treatment of critically ill patients | Ideal timing unknown |
| **Individual assessment of exposure** | Could enable individuals to understand their exposure and potentially their risk | May be infectious even with antibodies<br>Antibody protection unknown<br>Protection duration unknown |
| **Public health response and planning** | Estimation of number of people previously infected | May require volume testing<br>Need to avoid biased sample |
| **Community-based contact tracing** | Objective marker to connect case clusters | May have lower sensitivity if asymptomatic<br>Negative test cannot rule out past infection |
| **Management of exposed individuals** | Potential to expedite return to work if antibodies present | Immunity still pending clinical studies |
| **Monitoring essential workers** | Decentralized testing<br>Rapid results | Antibody-positive individuals can be infectious |
| **Assessment of vaccine** | Aid vaccine development | May need to be antigen specific |
| **What it can't do…** | Show if you were infected with the coronavirus in the past. | Diagnose active coronavirus infection at the time of the test |
| **Combined value…** | Symptomatic testing and confirmation of active COVID-19 | Asymptomatic screening and confirmation of previous COVID-19 infection |



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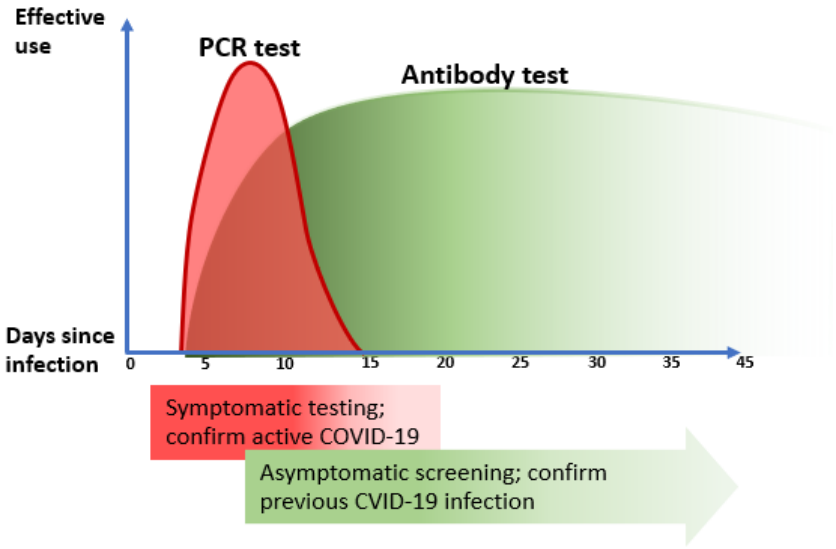
the initial antibody response. The table also mentions convalescent plasma donors, individual understanding of previous disease, public health planning, as well as potential use in monitoring workers and response to a vaccine as potential use cases as we learn more about the virus and the body's response to it.

Figure 3 shows this overlap and the complementary nature of the two tests. PCR testing is used early in the disease progression to confirm diagnosis (red curve) and the antibody test is used after the body's immune response has kicked in as one is fighting the disease (green curve). This immune response begins with IgM soon after the disease onset and continues with IgG, which is more persistent in the body. A test that measures both IgM and IgG will provide the greatest coverage.

*Figure 1 Combined value of PCR + antibody testing.*




Osterholm et al., in their recent viewpoint, *Smart Testing for COVID-19 Virus and Antibodies*[6], encourage the use of a "smart testing" framework where both PCR and antibody tests are used when and where appropriate. PCR testing is useful when a patient presents as symptomatic or is in an at-risk population, and antibody testing is useful when looking to confirm potential previous exposure. Each has an important role to play, and without a combined effort, singular testing amounts to flying blind.

## Antibody testing is a powerful complement to symptomatic PCR testing.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3. Wu L-P, Wang N-C, Chang Y-H, Tian X-Y, Na D-Y, Zhang L-Y, et al. Duration of Antibody Responses after Severe Acute Respiratory Syndrome. Emerging Infectious Diseases. 2007 Oct;13(10):1562–4.
4. Cheng MP, Yansouni CP, Basta NE, Desjardins M, Kanjilal S, Paquette K, et al. Serodiagnostics for Severe Acute Respiratory Syndrome–Related Coronavirus-2. Annals of Internal Medicine [Internet]. 2020 Jun 4 [cited 2020 Jul 11]; Available from: https://www.acpjournals.org/doi/full/10.7326/M20-2854
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6. Kristine A. Moore, Marc Lipsitch, John M. Barry, Michael T. Osterholm. Part 3: Smart Testing for COVID-19 Virus and Antibodies. [Internet]. 2020. Available from: https://www.cidrap.umn.edu/sites/default/files/public/downloads/cidrap-covid19-viewpoint-part3_0.pdf




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