# Using Proficiency Testing to Ensure Accurate Serologic Testing of SARS-CoV-2

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**Julie McDowell:**

As we move into the next phase of this pandemic, laboratories are ramping up efforts to implement SARS-CoV-2 antibody testing to identify individuals who may have been infected with SARS-CoV-2 in the past. In this CAPcast, Dr. Daniel Rhoads, Section Head of Microbiology at the Cleveland Clinic, and Dr. Elitza Theel, Director of Infectious Disease Serology from Mayo Clinic, explain the clinical use of antibody testing for SARS-CoV-2 and describe the work of the CAP's Microbiology and Diagnostic Immunology and Flow Cytometry Committees to support the development of the CAP's statement on the current role of serologic testing for SARS-CoV-2 and the new proficiency testing program, SARS-CoV-2 Serology.

Dr. Theel, let's start with you. Can we begin with an explanation from you about why testing for antibodies is important? Specifically, how is the clinical impact of an antibody test result different from a molecular test result for SARS-CoV-2?

**Dr. Elitza Theel:**

Sure. As the audience is well aware, detection of antibodies developed against SARS-CoV-2 indicate that an individual has been infected at some point in time, either potentially recently or sometime in the past, but it's really hard to pinpoint when that occurred exactly. Many infected patients start to develop antibodies about 8 to 12 days or so post-symptom onset or exposure and then over 95% of individuals are seropositive after about two weeks or so.

After that time point, IgM antibodies start to taper off between weeks five and seven, whereas IgG antibodies persist for quite a bit longer. Because of these antibody kinetics, including the delayed seroconversion and then the persistent seropositivity after infection, we really can't rely on antibody testing to make a diagnosis of acute COVID-19. On the flip side, molecular tests are really the preferred method to make that diagnosis of acute or recent infection as they're the ones that are detecting the nucleic acid from the virus rather than our immune response to it.

That then brings up the question of when and for what should serologic tests be used. We now have a number of organizations, including ASM and IDSA amongst others, that have put forth really excellent guidelines to address this important question. There's generally four scenarios at this point for when antibody testing can be useful, including as part of epidemiologic or seroprevalence studies, also to identify potential convalescent plasma donors. Then in the future, as vaccine candidates enter clinical trials, serologic tests will obviously play an important role to evaluate a recipient's immune response to those vaccines.

Then finally, antibody tests may be helpful as an aid to detect COVID-19 in individuals who present later on in their disease course and who test negative by PCR or for whom a lower respiratory tract sample for PCR testing can't be collected. At this point, those are the four general situations for which antibody testing is most useful. I think as we continue to learn about our immune response to this virus, the utility of antibody testing will likely increase.

**Julie McDowell:**

Dr. Rhoads, why is the CAP offering the COVS program and how will this benefit the laboratory?

**Dr. Daniel Rhoads:**

As we know, clinical labs are required to assess proficiency using blinded samples, and the best way to do this is through a formal proficiency testing program like what is offered by the CAP. Typically, creating a new proficiency testing product by the CAP can take months or years, but the CAP put a lot of effort into expediting the development and production of this material for the survey so labs can use the material as part of their quality assurance program. Laboratory testing for COVID-19 has been very busy these past few months, as you know, and I know Dr. Theel knows, and not needing to find an alternative way to assess proficiency, but being able to rely on the CAP for this proficiency material makes life just a tiny bit easier for labs.

**Julie McDowell:**

Also, Dr. Rhoads, can you discuss your involvement in the development of this program?

**Dr. Daniel Rhoads:**

Sure. The CAP tried to work quickly, as I mentioned, because we recognized that a significant number of labs would be bringing up a SARS-CoV-2 serology this year and they would need a way to assess the proficiency. The CAP has a number of scientific committees comprised primarily of laboratory directors, like myself and Dr. Theel, and these committees help to develop and oversee the CAP's proficiency testing program.

In this case for the serology program, the Diagnostic Immunology and Flow Cytometry Committee and the Microbiology Committee worked together to clearly define what labs would require from a proficiency testing program for SARS-CoV-2 serology. The staff at the CAP then quickly worked to find a source of the material that would meet these requirements. The CAP then pilot-tested the material on multiple platforms to make sure that the samples would perform as expected.

**Julie McDowell:**

Finally, Dr. Theel, do you have any advice for laboratories who are starting up this type of testing?

**Dr. Elitza Theel:**

Sure. As clinical laboratory directors, supervisors, technologists, we're all trained to routinely perform well-thought-out and thorough validations and verifications prior to implementing any new clinical test. I'd say that this situation is no different. In fact, given the large influx of commercially available serologic tests for SARS-CoV-2 and given the reports that not all of these assays perform equally well, I think it's essential that we continue to perform really careful evaluations of any possible serologic tests that we're considering prior to implementing, and possibly even with a higher or a greater level of scrutiny.

For sensitivity studies, I think collecting serial serum or plasma samples from PCR-confirmed patients is important and a good gold standard to compare against. Then for specificity, I think evaluating any samples selected prior to the outbreak is highly recommended. Given how these tests will be used, I think having a highly specific test is really important, and so would also recommend testing any samples with antibodies to other respiratory viruses or to other infectious agents that may present similarly to COVID-19. Then in general, I'd also recommend that listeners visit the CAP website, which provides additional resources and information on this topic.

**Julie McDowell:**

Thank you, Drs. Rhoads and Theel. You can order the new SARS-CoV-2 Serology PT program today. The program code is COVS and the first shipment is scheduled for June 22nd, 2020. Visit the COVID-19 page on the CAP's website for the latest news and resources, including those for proficiency testing customers and CAP-accredited laboratories. The CAP's COVID-19 page offers useful links to helpful tools and resources to clarify rules of compliance as you implement COVID-19 testing in your laboratory. Thank you for listening to this CAPcast. Be sure to listen to our other CAPcasts from the CAP on our SoundCloud channel by downloading the SoundCloud app on your mobile device. We're also on Apple Podcasts and the Stitcher app. To find this podcast, search for the word CAPcast on these apps. Once you find our podcast, be sure to click the subscribe button so you don't miss new CAPcast episodes.