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Ask the Expert: What is the role of antibody testing for SARS-CoV-2?

by H. Cody Meissner M.D., FAAP

Editor's note:*Ask the Expert is a weekly columnaimed at providing pediatricians information on pressing topics related to COVID-19. Email your questions to*ahegland@aap.org.

Laboratory assays can be helpful in providing support for a diagnosis of SARS-CoV-2 infection. Assays using one of three molecular methods are available.

1. Polymerase chain reaction (PCR) assays detect RNA genetic material of the virus in secretions obtained by a nasopharyngeal or oropharyngeal swab.
2. Antigen assays detect fragments of viral proteins found in the nasal cavity using a swab.
3. Serologic assays detect the antibody response to infection in serum.

SARS-CoV-2 has been isolated in cell culture from several anatomic sites using one of several human or primate cell lines. However, isolation of SARS-CoV-2 by cell culture requires a certified Class II biological safety cabinet as well as personal protective equipment precautions and is not recommended in most circumstances.

PCR assays are nucleic acid amplification tests that are likely to be highly accurate, meaning a positive or negative result from this molecular test is likely to be true based on current understanding (such as the existence of only one viral strain).

Antigen detection assays often are faster and simpler to perform than PCR assays. A positive antigen detection assay is highly accurate, but the risk of a false-negative result is more problematic because of lower sensitivity than a PCR assay result. A negative antigen detection assay result does not rule out infection and may require confirmation with a PCR assay.

A serologic assay detects IgG and/or IgM antibodies to the SARS-CoV-2 virus. Because antibodies are part of the body's immune response to infection (and not a part of the virus), **antibody testing is not as reliable a means of diagnosing acute infection as PCR or antigen detection**. Antibodies to SARS-CoV-2 generally are detectable in blood several days after initial infection, although the types and duration of antibodies that are present post-infection are not well-understood. Individuals may have detectable virus present in the nasopharynx for several weeks (based on PCR results) following the development of detectable antibodies. However, if the viral load is low, a positive PCR result may not correlate with infectivity.

The presence of IgG antibodies does not exclude actively infected patients who are still contagious. It is not known how soon after an infection has begun and how long after an infection has cleared that IgM or IgG antibodies to SARS-CoV-2 remain detectable.

In addition, the four conventional coronaviruses are the second most common cause of the common cold (behind rhinoviruses). Recurrent infection by each of these viruses is common because long-term protection following infection by these four coronaviruses is not sustained. It will be important that an antibody assay for SARS-CoV-2 has sufficient specificity to differentiate between the antibody response to conventional coronaviruses (which circulate annually, particularly in winter and spring months) and the antibody response to the antigenically-related SARS-CoV-2.

Antibody tests should not be used to definitively diagnose or exclude COVID-19 infection. When more fully understood, SARS-CoV-2 antibody tests may be helpful for identifying individuals who have developed an antibody response to SARS-CoV-2, suggesting either acute or previous infection. However, a negative antibody assay result does not rule out acute SARS-CoV-2 infection. Also, every person who experiences SARS-CoV-2

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infection may not have a detectable antibody response to the virus, depending on the characteristics of the assay and the stage of the illness at the time of testing. Direct testing for SARS-CoV-2 using a PCR assay is necessary to rule out or confirm an existing SARS-CoV-2 infection.

In time, interpretation of antibody assays in conjunction with clinical follow-up information will provide a better understanding of whether a person who has recovered from infection is at lower risk of infection when re-exposed to the virus. At the present time, **the clinical value of antibody testing for an individual patient has not been demonstrated**. Eventually, antibody testing may be useful for identification of people who are interested in convalescent plasma donation or for verification of a serologic response to a vaccine after a marker of protection is identified. Generally, antibody testing is not recommended because of limited information regarding the reliability of testing. **At this time, antibody testing is not recommended for use in a pediatrician's office.**

A greater understanding of the immune response will be essential for the development of vaccines. The association of multisystem inflammatory syndrome in children (MIS-C) to SARS-CoV-2 infection is not clear at this time. If MIS-C represents an antibody mediated reaction to coronavirus proteins in certain genetically predisposed children, it will be important to avoid those proteins in a vaccine.

Once reliable antibody assays are available, seroprevalence studies will enable a better understanding of how many people have been asymptomatically infected and how many remain susceptible. Results will provide a better understanding of community protection, or herd immunity, and how far the pandemic has progressed.

Dr. Meissner is professor of pediatrics at Floating Hospital for Children, Tufts Medical Center. He also is an ex officio member of the AAP Committee on Infectious Diseases and associate editor of the AAP Visual Red Book.

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