

**UPDATED 5/19/2020 - PAGES 1, 2 and top of 3 New Content.**

### Primer: Diagnostic Testing for COVID-19

There are several ways to diagnose COVID-19. It is important to understand that tests are usually used for people who have symptoms that could be related to COVID-19 (e.g. fever, cough, shortness of breath, body aches, loss of smell or taste). Some tests are more accurate when symptoms are present. People who don't have symptoms may have higher rates of false positive tests. However, some people who don't have symptoms may be encouraged or required to have testing done, including nursing home patients in the setting of an outbreak, people with weakened immune systems, and those undergoing certain surgical procedures. In some cases, public health authorities may perform community-based testing, even among asymptomatic persons, to better understand community spread. Listed below are some of the currently available tests and some of their characteristics.

#### RTPCR (Reverse Transcriptase Polymerase Chain Reaction) Tests

- Also called NAAT (nucleic acid amplification tests).
- Test for the presence of RNA (genetic material) of SARS-CoV-2, the virus that causes COVID-19.
- Preferred way to confirm infection.
- RTPCR test can be positive right before symptoms begin and may stay positive even after symptoms resolve. Can also be positive in someone without symptoms.
- Several different specimens can be used:
  - Nasopharyngeal swabs - taken from the back of the nasal passages by a healthcare provider.
  - Anterior nares swabs - taken from the front of the nostrils.
  - Occasionally, in patients with severe nasal problems, oropharyngeal swabs may be used, but these are less accurate.
  - Saliva - obtained by spitting into a test tube (easiest specimens to obtain but are also the least accurate; persons should not eat, drink, smoke or chew gum before giving a saliva sample). Please note saliva is not an acceptable sample for the ChristianaCare tests,
- RTPCR tests and testing supplies remain in short supply and may not be readily available in some locations.
- Many large commercial laboratories perform these tests, but there may be a wait time of several days for results.
- Abbott ID NOW Real Time SARS-CoV 2 Assay is less sensitive (80% or less) than other NAAT tests. The FDA is now requiring negative tests on the Abbott ID NOW to be reported as presumptive negative. Patients with significant COVID-19 symptoms should be retested with another more sensitive NAAT test.

#### Antibody Tests

- Test for the presence of proteins (antibodies) that the immune system makes in response to infection with SARS-CoV-2, so are an indirect way of making the diagnosis.
- Usually don't become positive for 1-2 weeks after infection.
- Can be used to diagnose COVID-19 but have limitations:
  - Antibodies are not present in initial phase of symptoms,

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| <b>Date</b>   | 5/19/2020  | <b>Time</b> | 7 pm |

- Accuracy is not as good for the type of antibody called IgM (can be false positive).
  - All rapid (point of care) tests are less reliable than those done in laboratories.
- It is not known at the present time whether the presence of antibodies means that a person is immune to SARS-CoV-2 or for how long.

### **Antigen Tests**

- Newly authorized by FDA on May 9, 2020.
- New category of diagnostic tests that detect fragments of virus using nasopharyngeal swabs.
- Results may be rapidly available, but less accurate than PCR testing.
- Currently not widely available.

### **Caregiver FAQs: Should I Get Antibody Testing?**

Some caregivers may have access to serology/antibody testing via state or county health departments. The information below is intended to help caregivers make an informed decision about testing.

#### **Shouldn't I be tested to make sure that I'm not an asymptomatic carrier?**

Serology testing cannot tell you if you are an asymptomatic carrier. PCR nasal swab testing is required to rule out carrier status. The tests being used by different state/local health departments are variable, and not all have been FDA-approved. IgM antibodies, in particular, are unreliable, and false positives are common. If you have a positive IgM result, you will not be allowed to work until it can be confirmed with PCR testing (2 negative tests will be required to return to work).

#### **Shouldn't I be tested to make sure that I'm immune?**

The tests being used by different state/local health departments are variable, and not all have been FDA-approved. Even FDA-approved SARS-CoV 2 serology tests do not yet tell us if you are immune. A positive test may be due to exposure to other human coronaviruses that circulate every winter, causing the common cold, and thus may give a person a false sense of security that they are immune to COVID-19. We do not want anyone to let their guard down related to masking, social distancing, frequent hand hygiene or any other measure and then put themselves at increased risk.

#### **If I'm having symptoms that could be COVID-19, can't I get a blood test instead of the nasal swab?**

For people with symptoms, the nasal PCR is clearly superior to antibody testing. IgM antibodies may be positive in only 40% of patients in the first week of illness. On the other hand, people tend to have the highest viral loads in the nose/sinuses around the time of illness onset.

#### **What happens if I get a blood test and I'm positive?**

If your test is IgM positive (with or without positive IgG), you will need to be restricted from working until the test can be confirmed. You will need confirmatory nasal PCR testing. If this test is positive, you will need to stay out of work until you can be cleared to return. If this test is negative, you will

need a 2<sup>nd</sup> negative test at least 24 hours later to confirm that you are truly negative and can return to work.

If your test is IgM negative but IgG-positive, you will not be restricted from work. This probably means that you have been exposed to COVID-19 (or possibly another human coronavirus) at some point in the past but does not necessarily mean that you are immune.

### **What should managers do if their direct reports have a positive IgM antibody?**

As above, any positive IgM serology will need to be confirmed by nasal PCR testing. The person cannot work until they either are confirmed positive (in which case the usual return to work policy will apply) or have 2 negative tests. No other coworkers should be sent home, furloughed, tested or have any other work restrictions (assuming they are asymptomatic) until the initial caregiver's status is confirmed.

## **COVID 19 FAQs: Antibody Testing**

### **What is the role of serologic (antibody) testing in the diagnosis of COVID-19?**

Serologic tests may be able to identify some patients with current infection (particularly those who present late in the course of illness), but they are less likely to be reactive in the first several days to weeks of infection, and thus may have less utility for diagnosis in the acute setting. In general, antibody test results should NOT be used as the sole basis to diagnose someone with an active SARS-CoV-2 infection.

### **Can serologic testing be used to confirm immunity to SARS-CoV-2?**

High-quality antibody tests can help us understand a person's and a population's exposure to COVID-19. A person who has been exposed to and recovered from COVID-19 will likely have antibodies to the SARS-CoV-2 virus in their blood. These tests may be important for guiding our next steps in the fight against this pandemic, such as by providing information on disease prevalence and the frequency of asymptomatic infection, and also by identifying potential donors of "convalescent plasma." However, it is unclear whether the presence of antibodies confers immunity, and, if so, for how long.

### **Why do I keep hearing conflicting information about the accuracy of serologic tests for SARS-CoV-2?**

In mid-March, the FDA cleared the way for commercial development of antibody tests to be used for helping to understand the spread of COVID-19 and for other public health purposes. Commercially available serologic assays are highly variable, differing in their format, the antibody class detected, the targeted antigen and the acceptable specimen types. The following statement was published by FDA in early May: "We unfortunately see unscrupulous actors marketing fraudulent test kits and using the pandemic as an opportunity to take advantage of Americans' anxiety. Some test developers have falsely claimed their serological tests are FDA approved or authorized. Others have falsely claimed that their tests can diagnose COVID-19 or that they are for at-home testing, which would fall outside of the policies outlined in our March 16 guidance, as well as the updated guidance. Also, since that time, the FDA has become aware that a concerning number of commercial serology tests are being promoted inappropriately, including for diagnostic use, or are performing poorly

based on an independent evaluation by the NIH." FDA has recently updated its guidance on serologic testing.

### **What are the characteristics of available antibody tests?**

ChristianaCare currently sends specimens to Mayo Clinical Labs, which performs ELISA for SARS-CoV-2 IgG antibodies, orderable via the "Serology COVID antibody test" care set. ELISA IgG serologic tests approach 100% sensitivity by 14 days after the onset of COVID-19 symptoms. IgM tests, by their very nature, are less specific than IgG tests. Other commercial labs (e.g. LabCorp and Quest) offer reliable tests for outpatients. Rapid point of care "lateral flow" tests (including the State of Delaware rapid test) are not as sensitive or specific as enzyme linked immunosorbent assay (ELISA) or other laboratory performed serology tests. Remember that test performance (especially specificity and positive predictive value) are influenced by pre-test probability of disease (and overall low prevalence of disease), meaning that false positives may occur when antibody tests are run on patients who have not had COVID-19 exposure or symptoms.

### **My patient was tested with a point-of-care serology test and came back IgM positive. What should I do?**

The Delaware Division of Public Health is utilizing some point-of-care IgM/IgG tests in high-risk areas, such as long-term care centers and local "hotspots." In general, IgM testing is less specific than IgG and positive results may indicate a false positive, particularly if pre-test probability is low. However, DPH is interpreting these as positive COVID cases without further testing, and appropriate isolation and other measures should be taken.

### **Can serologic testing be used to ease restrictions related to masking and social distancing in someone who tests positive for antibodies against the virus?**

There are two problems with this strategy. First, we still are not sure how protective the antibodies are and for how long. The second is that some serologic tests suffer from low specificity (as low as 85%), in part because they may cross-react with antibodies against the seasonal (common cold) coronaviruses that many people have. In other words, a positive test may be a false positive. This could lead to a false sense of security in someone who is not immune, thereby placing them at risk.

### **Can serologic testing be used to get a healthcare provider who has previously had COVID-19 back to work?**

No, for the same reasons listed above.

### **What about antigen testing? Is that useful for acute diagnosis?**

While in theory, antigen testing can be more useful for diagnosis of acute disease than antibody testing, available COVID-19 antigen tests have not been shown to be more specific or sensitive than PCR testing but are being aggressively marketed. We continue to recommend nasal PCR testing for diagnosis of acute COVID-19.

### **What is the future of serologic testing?**

CDC is evaluating the performance of commercially available tests in collaboration with various regulatory agencies. Results from the initial federal evaluation are expected sometime in May and will be updated as more tests are evaluated. Eventually, these tests will be an important part of our response to the COVID-19 pandemic. Vaccine trials will rely heavily on the use of antibody testing.