General Information on Covid-19 Infection and Viral and Antibody Testing

Information about Covid-19 and the immune systems response to clearing it and protecting from future infection is evolving as more and more data is gathered. It is this information that helps inform decisions about adequate quarantine and return to work, school and public life. Realize that when the CDC first starting making recommendations about quarantine that very few people were wearing masks but now nearly everyone is wearing them in all indoor public places but the recommendations for quarantine have not taken this into account or been updated.

The primary information about the virus that helped me formulate the recommendations based on symptoms and testing results are summarized.

Covid-19 is a respiratory virus that appears to be spread through the air (contact from contaminated surfaces is less likely but still possible) from person to person. From the day we are infected with the virus it takes 3 to 14 days to incubate (virus rapidly replicates in cells) to the day symptoms develop (average is 5 days). The most common symptoms (which last 3 to 10 days) are fever (101 or more), cough, chest tightness, sore throat and achiness but also loss of taste and smell, headache and GI symptoms have been reported. Spread of the virus to others appears to be more robust early in the infection (48 hours before symptoms develop termed the pre-symptomatic stage) and seems more pronounced in those who eventually become more symptomatic. Studies find that 20 to 80% of patients have no or very minimal symptoms (especially females 10 to 40 years of age) but so far we still think these people can spread the virus through talking, sneezing, singing, yelling and maybe just breathing. This is why masks are so important. They help prevent us from spreading the disease to others even more than they protect us from contracting it. How long we are still infectious to others is not fully known but recent studies reveal infectiousness is gone completely by 10 days after initial onset of symptoms as long as free of fever for at least one day without fever reducing medication and other symptoms are improving.

Fortunately tests are available to help us make good decisions about when to safely stop quarantine measures. Testing for RNA genetic material from the virus can be detected with RT-PCR (reverse transcriptase-polymerase chain reaction) as early as the 2nd day of infection but will miss the infection 100% of the time if tested on the day of exposure. Unfortunately, early in the course of disease the test may still be negative (a false negative test) because not enough of the virus has gotten into the respiratory tract to be in the sample. It is for this reason that recommendations are still for 10 days of self-isolation once people are symptomatic or for 14 days if they have been exposed to someone known to be infected and have a negative test. The new saliva test is more sensitive than the nasal and throat swab tests discussed above as it uses a large sample of saliva spit into cup but it still can produce false negatives very early in an infection. The downside of the PCR is that it can continue to detect viral RNA for 25 to 50 days after onset of infection which is well past when people can infect others.

This is where antibody testing can be very helpful. We use an antibody test that has been approved for accuracy by the FDA (the majority of tests on the market have not so are not recommended for use). Our immune system makes antibodies to try and clear current infections and prevent reinfection in the future. The first antibody we make during an infection is IgM (immunoglobulin M) and it usually develops about 7 days into an infection. We make it to help neutralize and kill an infection. For some reason, the immune system is making IgM more slowly to Covid-19 and it may take up to 14 days to be positive with most positive by 9 to 10 days into infection. It typically remains in the blood for 14 more days and then is gone. IgG is the next antibody made (usually around day 14) and it remains positive for many months and hopefully for years. It helps to neutralize future infections and so can be evidence of protection of future infection. Unfortunately, just like influenza and the common cold, new mutations of the virus can form and cause infection but generally if IgG is present, it still should provide a degree of protection as long as the mutation has not been substantial. The CDC continues to state that we don't know for sure if a positive IgG completely protects from reinfection as there have been cases of reinfection; fortunately though, these cases have been mild and minimally or noninfectious to others. Recent studies are also finding that antibody levels decline about 3 months after the infection (even in those with more severe infections and higher antibody levels) so we really aren't sure how long potential protection can last.

Since antibody tests are so accurate at picking up antibody that is present and we know when levels tend to rise after an infection, we can use this information with or without directly testing for the virus to give us better information about where we are in the course of an infection. This is especially true if the antibody testing is done at least 10 days after exposure and/or 3 to 4 days or more into symptoms or even after they are gone. There are generally very few false positive or negative tests to IgM but false positive tests to IgG are a little more common because of other coronavirus infections that act more like colds that could have occurred previously in our life. In general, if IgM to Covid-19 is present without IgG, then a person is in the latter stages of infection and may still be infectious. If both IgG and IgM are present, then the infection is waning and the person is likely no longer contagious. And if IgG alone is present, then the infection is over and some degree of protection is possible.

The recommendations that are made are the opinion of Rand Malone MD and do not reflect precisely the ever changing recommendations made by the CDC or other agencies. In fact, these organizations have not made formal recommendations about how to employ antibody testing into decision making beyond general screening of past infection or ability to donate plasma to those who are critically ill. Because the degree of infectivity of patient's with Covid-19 cannot be known with any certainty, all people should continue to wear masks in public even after testing is done until definitive long-term guidelines are in place.

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As the new coronavirus spreads across the globe, the chances that you will be exposed and get sick continue to increase. If you've been exposed to someone with COVID-19 or begin to experience symptoms of the disease, you may be asked to self-quarantine or self-isolate. What does that entail, and what can you do to prepare yourself for an extended stay at home? How soon after you're infected will you start to be contagious? And what can you do to prevent others in your household from getting sick?

What are the symptoms of COVID-19?

Some people infected with the virus have no symptoms. When the virus does cause symptoms, common ones include fever, body ache, dry cough, fatigue, chills, headache, sore throat, loss of appetite, and loss of smell. In some people, COVID-19 causes more severe symptoms like high fever, severe cough, and shortness of breath, which often indicates pneumonia.

People with COVID-19 are also experiencing neurological symptoms, gastrointestinal (GI) symptoms, or both. These may occur with or without respiratory symptoms.

For example, COVID-19 affects brain function in some people. Specific neurological symptoms seen in people with COVID-19 include loss of smell, inability to taste, muscle weakness, tingling or numbness in the hands and feet, dizziness, confusion, delirium, seizures, and stroke.

In addition, some people have gastrointestinal (GI) symptoms, such as loss of appetite, nausea, vomiting, diarrhea, and abdominal pain or discomfort associated with COVID-19. These symptoms might start before other symptoms such as fever, body ache, and cough. The virus that causes COVID-19 has also been detected in stool, which reinforces the importance of hand washing after every visit to the bathroom and regularly disinfecting bathroom fixtures.

What should I do if I think I or my child may have a COVID-19 infection?

First call your doctor or pediatrician for advice.

If you do not have a doctor and you are concerned that you or your child may have COVID-19, contact your local board of health. They can direct you to the best place for evaluation and treatment in your area.

It's best to not seek medical care in an emergency department unless you have symptoms of severe illness. Severe symptoms include high or very low body

temperature, shortness of breath, confusion, or feeling you might pass out. Call the emergency department ahead of time to let the staff know that you are coming, so they can be prepared for your arrival.

How do I know if I have COVID-19 or the regular flu?

COVID-19 often causes symptoms similar to those a person with a bad cold or the flu would experience. And like the flu, the symptoms can progress and become life-threatening. Your doctor is more likely to suspect coronavirus if:

- you have respiratory symptoms
- and
- you have been exposed to someone suspected of having COVID-19, or
- there has been community spread of the virus that causes COVID-19 in your area.

How is someone tested for COVID-19?

A specialized test must be done to confirm that a person has been infected with the virus that causes COVID-19. Most often a clinician takes a swab of your nose (or both your nose and throat). New methods of testing that can be done on site will become more available over the next few weeks. These new tests can provide results in as little as 15–45 minutes. Meanwhile, most tests will still be delivered to labs that have been approved to perform the test.

Some people are starting to have a blood test to look for antibodies to the COVID-19 virus. Because the blood test for antibodies doesn't become positive until after an infected person improves, it is not useful as a diagnostic test at this time. Scientists are using this blood antibody test to identify potential plasma donors. The antibodies can be purified from the plasma and may help some very sick people get better.

What are the differences between the nasal swab and saliva tests for COVID-19?

Until recently, most tests for COVID-19 required a clinician to insert a long swab into the nose and sometimes down to the throat. In mid-April, the FDA granted emergency approval for a saliva-based test.

The saliva test is easier to perform — spitting into a cup versus submitting to a swab — and more comfortable. Because a person can independently spit into a cup, the saliva test does not require interaction with a healthcare worker. This cuts down on the need for masks, gowns, gloves, and other protective equipment, which has been in short supply.

Both the saliva and swab tests work by detecting genetic material from the coronavirus. Both tests are very specific, meaning that a positive test almost always means that the person is infected with the virus. However, both tests can be negative, even if a person is proven later to be infected (known as a false negative). This is especially true for people who carry the virus but have no symptoms.

Some early reports suggest that the saliva test may have fewer false negatives than the swab test. If verified, home testing could potentially quickly ramp up the widespread testing we desperately need.

How reliable is the test for COVID-19?

In the US, the most common test for the COVID-19 virus looks for viral RNA in a sample taken with a swab from a person's nose or throat. Tests results may come back in as little as 15–45 minutes for some of the newer on-site tests; with other tests you may wait three to four days for results.

If a test result comes back positive, it is almost certain that the person is infected.

A negative test result is less definite. An infected person could get a so-called "false negative" test result if the swab missed the virus, for example, or because of an inadequacy of the test itself. We also don't yet know at what point during the course of illness a test becomes positive.

If you experience COVID-like symptoms and get a negative test result, there is no reason to repeat the test unless your symptoms get worse. If your symptoms do worsen, call your doctor or local or state healthcare department for guidance on further testing. You should also self-isolate at home. Wear a mask if you have one when interacting with members of your household. And practice social distancing.

What are the chances that a coronavirus test will tell me I am not infected when I actually am?

The chances that a coronavirus test will give you a false negative (indicating that you are not infected when you actually are infected) depend upon the type of test you have and when in the course of your infection the test is performed. There are two main types of tests:

- nasal/throat swab tests and saliva tests, both of which detect the virus itself
- blood tests that detect antibodies that your immune system produces in response to the infection.

If you get the nasal/throat swab or saliva test, you will get a false negative test result:

- 100% of the time on the day you are exposed to the virus. (There are so few viral particles in your nose or saliva so soon after infection that the test cannot detect them.)
- About 40% of the time if you are tested four days after exposure to the virus.
- About 20% of the time if you develop symptoms and are tested three days after those symptoms started.

This possibility of a false negative test result is why anyone who has symptoms that could be due to COVID-19, or has been exposed to someone known to be infected, must isolate even if they test negative for coronavirus.

The blood antibody test does not become positive (or might never be positive in some people) until many days after exposure, and is therefore not the primary test used for diagnosis. It is very useful for research and public health decision making.

I've heard that the immune system produces different types of antibodies when a person is infected with the COVID-19 coronavirus. How do they differ? Why is this important?

When a person gets a viral or bacterial infection, a healthy immune system makes antibodies against one or more components of the virus or bacterium.

The COVID-19 coronavirus contains ribonucleic acid (RNA) surrounded by a protective layer, which has spike proteins on the outer surface that can latch on to certain human cells. Once inside the cells, the viral RNA starts to replicate and also turns on the production of proteins, both of which allow the virus to infect more cells and spread throughout the body, especially to the lungs.

While the immune system could potentially respond to different parts of the virus, it's the spike proteins that get the most attention. Immune cells recognize the spike proteins as a foreign substance and begin producing antibodies in response.

There are two main categories of antibodies:

Binding antibodies. These antibodies can bind to either the spike protein or a different protein known as the nucleocapsid protein. Binding antibodies can be detected with blood tests starting about one week after the initial infection. If antibodies are found, it's extremely likely that the person has been infected with the COVID-19 coronavirus. The antibody level declines over time after an infection, sometimes to an undetectable level.

Binding antibodies help fight the infection, but they might not offer protection against getting reinfected in the future. It depends on whether they are also neutralizing antibodies.

Neutralizing antibodies. The body makes these antibodies specifically against the spike protein. In the laboratory, scientists have observed that neutralizing antibodies block the virus from getting into live cells. The FDA has not yet authorized use of a test for neutralizing antibodies, because it requires handling live COVID-19 coronavirus or a pseudo-virus similar to the real thing. To do the test, a person's blood is mixed with live virus and incubated in a test tube along with living cells to measure the killing action.

In addition to these laboratory observations, human studies have shown that neutralizing antibodies made against other coronaviruses help prevent re-infection.

Scientists are optimistic that the same will be true for the COVID-19 coronavirus, and that neutralizing antibodies will block cell-to-cell transmission of this virus in humans, and offer protection against reinfection, at least for two to three months.

Also, people who have completely recovered from a COVID-19 infection and have neutralizing antibodies in their blood can potentially donate plasma, the component of blood that contains antibodies, to help COVID-19 patients recover from their illness.

Do the antibodies produced by a person who has been infected with coronavirus protect them from becoming infected again?

Most people who are infected with the COVID-19 virus, whether or not they have symptoms, produce antibodies (proteins that fight infections). New research published in *Nature Medicine* looked at how long those antibodies last. Results from this small study suggest that levels of one type of antibody dropped sharply within two to three months. However, the decrease in neutralizing antibodies, which target the spike protein on the coronavirus and can help protect against reinfection, was much smaller.

Whether or not the remaining antibodies protect against reinfection, and for how long, is still unclear. It's possible that even low levels of neutralizing antibodies may be able to protect against reinfection. On the other hand, the presence of antibodies does not guarantee immunity.

Another consideration is that antibodies are only one part of the body's immune response. Memory B cells, for example, can quickly generate a strong antibody response to a virus the body has encountered before.

What is serologic (antibody) testing for COVID-19? What can it be used for?

A serologic test is a blood test that looks for antibodies created by your immune system. There are many reasons you might make antibodies, the most important of which is to help fight infections. The serologic test for COVID-19 specifically looks for antibodies against the COVID-19 virus.

Your body takes at least five to 10 days after you have acquired the infection to develop antibodies to this virus. For this reason, serologic tests are not sensitive enough to accurately diagnose an active COVID-19 infection, even in people with symptoms.

However, serologic tests can help identify anyone who has recovered from coronavirus. This may include people who were not initially identified as having COVID-19 because they had no symptoms, had mild symptoms, chose not to get tested, had a false-negative test, or could not get tested for any reason. Serologic tests will provide a more accurate picture of how many people have been infected with, and recovered from, coronavirus, as well as the true fatality rate.

Serologic tests may also provide information about whether people become immune to coronavirus once they've recovered and, if so, how long that immunity lasts. In time, these tests may be used to determine who can safely go back out into the community.

Scientists can also study coronavirus antibodies to learn which parts of the coronavirus the immune system responds to, in turn giving them clues about which part of the virus to target in vaccines they are developing.

Serological tests are starting to become available and are being developed by many private companies worldwide. However, the accuracy of these tests needs to be validated before widespread use in the US.

How soon after I'm infected with the new coronavirus will I start to be contagious?

The time from exposure to symptom onset (known as the incubation period) is thought to be three to 14 days, though symptoms typically appear within four or five days after exposure.

We know that a person with COVID-19 may be contagious 48 to 72 hours before starting to experience symptoms. Emerging research suggests that people may actually be most likely to spread the virus to others during the 48 hours before they start to experience symptoms.

If true, this strengthens the case for face masks, physical distancing, and contact tracing, all of which can help reduce the risk that someone who is infected but not yet contagious may unknowingly infect others.

For how long after I am infected will I continue to be contagious? At what point in my illness will I be most contagious?

People are thought to be most contagious early in the course of their illness, when they are beginning to experience symptoms, especially if they are coughing and sneezing. But people with no symptoms can also spread the coronavirus to other people if they stand too close to them. In fact, people who are infected may be more likely to spread the illness if they are asymptomatic, or in the days before they develop symptoms, because they are less likely to be isolating or adopting behaviors designed to prevent spread.

Most people with coronavirus who have symptoms will no longer be contagious by 10 days after symptoms resolve. People who test positive for the virus but never develop symptoms over the following 10 days after testing are probably no longer contagious, but again there are documented exceptions. So some experts are still recommending 14 days of isolation.

One of the main problems with general rules regarding contagion and transmission of this coronavirus is the marked differences in how it behaves in different individuals. That's why everyone needs to wear a mask and keep a physical distance of at least six feet.

Here is a more "scientific" way to determine if you are no longer contagious: have two nasal-throat tests or saliva tests 24 hours apart that are both negative for the virus.

If I get sick with COVID-19, how long until I will feel better?

It depends on how sick you get. Those with mild cases appear to recover within one to two weeks. With severe cases, recovery can take six weeks or more.

Some people may experience longer-term physical, cognitive, and psychological problems. They may alternately improve and worsen over time, and can include a variety of difficulties, from fatigue and trouble concentrating to anxiety, muscle weakness, and continuing shortness of breath.

How long after I start to feel better will be it be safe for me to go back out in public again?

We don't know for certain. Based on the most recent research, people may continue to be infected with the virus and be potentially contagious for many days after they are feeling better. But these results need to be verified. Until

then, even after 10 days of complete resolution of your symptoms, you should still take all precautions if you do need to go out in public, including wearing a mask, minimizing touching surfaces, and keeping at least six feet of distance away from other people.