Guidance for Healthcare Providers Ordering COVID-19 Testing

COVID-19 Testing: PCR, Antigen, and Antibody Tests Explained

The medical/technical team of the Unified Health Command (UHC), which is made up of Billings Clinic, St. Vincent Healthcare, RiverStone Health and Yellowstone County Disaster and Emergency Services, offers this guidance on COVID-19 testing.

When to Consider Testing:
At this time, the Unified Health Command is not recommending broad population testing with either PCR or serology. Consider the information below when making a decision about ordering a test, keeping in mind clinical symptoms and history, exposure history, and the prevalence of disease in the population. If someone has tested positive for Covid-19 in the previous 90 days, repeat testing is not indicated if they remain asymptomatic. For persons with new onset of symptoms during the 90 days, if an alternative diagnosis cannot be identified, consultation with infectious diseases, infection control, or RiverStone Health Public Health Services is recommended prior to considering repeat Covid-19 testing. For more information, https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html and https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

There are three types of tests available for COVID-19: polymerase chain reaction (PCR), antigen, and antibody (serology) testing. PCR and antigen tests detect whether a person is currently infected, and serology detects whether a person had an infection in the past. This document is designed to explain the differences between PCR, antigen, and serology testing, and when one test might be used over another. *Source: Adapted from the Texas Department of State Health Services, version 2.1 – Released 8/31/2020.*

Topic	PCR Test	Antigen Test	Antibody (Serology) Test
Why is the test used?	PCR tests detect segments of RNA specific to SARS-CoV-2, the virus that causes COVID-19, in the nose, throat, or other areas in the respiratory tract.	Antigen tests look for pieces of proteins that make up the surface of SARS-CoV-2 virus to determine if the person has an active infection.	Serology looks for antibodies[1] against SARS-CoV-2 in the blood to determine if there was a past infection.
How is the test performed?	In most cases, a nasal or throat swab is taken by a healthcare provider and tested. Sometimes the test can be run while you wait, and sometimes the swab needs to be sent to a lab for testing.	In most cases, a nasal or throat swab is taken by a healthcare provider and tested. Sometimes the test can be run while you wait, and sometimes the swab needs to be sent to a lab for testing.	In most cases, a blood sample is taken and sent to a lab for testing.

[1] Antibodies are formed by the body to fight off infections. Immunoglobulin M (IgM) is the first antibody that is formed against a germ, so it appears on tests first, usually within 1-2 weeks. The body then forms immunoglobulin G (IgG), which appears on tests about 2 weeks after the illness starts. IgM usually disappears from the blood within a few months, but IgG can last for years. Some antibody tests test for IgM and IgG, and some only test for IgG.

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What does a positive test result mean?	A positive PCR test means that the person being tested is likely to have active COVID-19 if the person has not been infected or tested before. Individuals who recovered from COVID-19 may continue to have positive PCR test for several weeks after the initial positive test result.	A positive antigen test means that the person being tested is likely to have active COVID-19.	A positive antibody test means that the person being tested was infected with COVID-19 in the past and that their immune system developed antibodies to try to fight it off.
What does a negative test result mean?	A negative PCR test means that person was likely not infected at the time their sample was collected. However, recently exposed persons who are in the early stage of their illness may not have detectable RNA level. Repeat testing is advised if there is high clinical suspicion, e.g. contact with known COVID-19 cases or pertinent recent travel.	A negative antigen test means that SARS-CoV-2 viral proteins were not detected. However, a negative test does not rule out COVID-19. If there is still concern that a person has COVID-19 after a negative antigen test, then that person should be tested again with a PCR test.	A negative antibody test means that the person may not have had COVID- 19 in the past. However, they could still have a current infection, and the antibody test was collected too soon to give a positive result.
When is it helpful?	• It can be used to determine who has an active infection. • It can help identify people who are contagious to others. • It may be used to confirm the results of the antigen-based tests when there are concerns about the accuracy of the results, especially in high risk persons.	• It can be used to quickly determine who has an active infection. • It can help identify people who are contagious to others. • It is a less expensive test than PCR.	• It can identify people who had an infection in the past, even if they had no symptoms of the illness. • It can help determine who qualifies to donate convalescent plasma (a blood product that contains antibodies against COVID-19 and can be used as a COVID- 19 treatment). • If lots of people take the test in a community, it can help public health leaders and researchers know what percentage of the population has already had COVID-19.

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When is it not as helpful?	• It does not help determine if persons without symptoms (asymptomatic or pre-symptomatic) who were exposed to cases of COVID- 19 will develop active infection during the two weeks after exposure. • It should not be used as a "test of cure" as detection of SARS-CoV-2 RNA may persist weeks after the infection. • Depending on local test availability, send out tests may have longer turnaround times which may affect decision making regarding infection control and medical treatment. • This test requires certain kinds of swabs that may be in short supply.	• Antigen tests are less sensitive (accuracy) than PCR tests, meaning there may be false negative results. Therefore, it may not accurately identify those who are infected. • Negative tests should be treated as presumptive. If a healthcare provider is concerned that the person has COVID-19, even after a negative antigen test, then the test result should be confirmed with PCR testing.	• It may be negative in the first week of infection, which is why it should not be used to detect active COVID-19 infection. • We do not know yet if having antibodies to the virus that causes COVID-19 can protect someone from getting infected again or, if they do, how long this protection might last. Until scientists get more information about whether antibodies protect against reinfection with this virus, everyone should continue to take steps to protect themselves and others, including staying at least 6 feet away from other people outside of their home (social distancing), even if they have had a positive antibody test.
What public health activities will be conducted?[2]	• If positive, the health department will conduct a case investigation. Contact tracing will be performed to identify individuals who might have been exposed to the PCR-positive person when they could have spread COVID-19. • If negative, no public health activities will be performed.	• If positive, the health department will interview the antigen-positive person about symptoms and if they were around someone who had COVID-19. Contact tracing will be performed. • If negative, no public health activities will be performed.	• None

[2] Case investigations and contact tracing are conducted in accordance with local jurisdictional capacity. Public health departments may prioritize PCR positive cases in the event of capacity limitations

SARS-CoV-2 RT-PCR Test Result Interpretation:

With many COVID-19 tests available, it can be a challenge for clinicians to determine which is the best test to order and how to interpret the results. The first step is to determine the reason for testing. For most clinicians, it is to diagnose COVID-19 in persons who have symptoms consistent with the disease. However, there may be situations where you may be asked to order a test for a patient who is asymptomatic, whether this may be part of a contact investigation, fulfilling a requirement for work, school, or anticipated travel, or surveillance of disease. In general, the reported sensitivity and specificity of most RT-PCR assays are high, thus, they are the preferred tests for most situations. Often the case, clinicians typically choose an assay based on availability and test result turnaround time.

There are many factors that should be considered in interpreting the results of any of the above-mentioned tests. They include, but not limited to, the following:

- Sensitivity and specificity of the test that was performed. Because all commercially available SARS-CoV-2 RT-PCR assays received the Emergency Use Authorization through the Food and Drug Administration, the sensitivities reported by the test developers are typically determined by running known samples on their platforms, i.e., analytical sensitivities. There are, however, very limited published data on the clinical sensitivities and specificities, i.e., real life performance, of most platforms as well as comparative data of various platforms.
- Specimen collection technique and location. Upper respiratory sample (nasal, oral, nasopharyngeal) preferred in early disease and lower respiratory sample (tracheal aspirate or BAL) preferred in late disease.
- Time of disease process when the specimen was collected. SARS-CoV-2 viral load in the upper respiratory tract is highest from two days prior to onset of symptoms to 5 days after onset of symptoms.
- The pretest probability, or likelihood, of the tested patient to have the disease. This may be determined by local prevalence of the disease and exposure history of the patient.

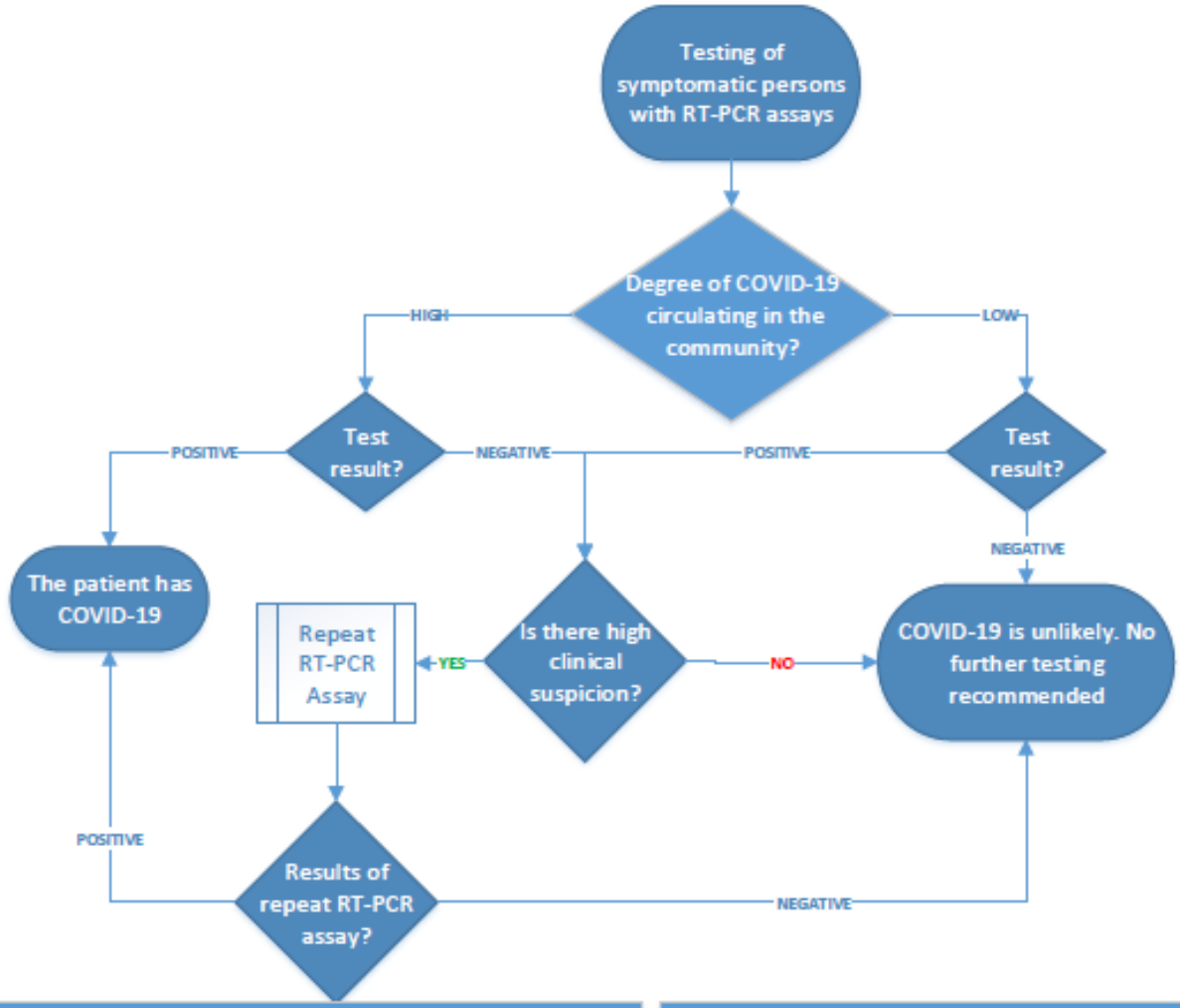
Although many test developers report very high analytical sensitivities of their assays to the FDA, there are anecdotal reports that some SARS-CoV-2 RNA RT-PCR assay do not perform as well clinically. Presently, the assay (Hologic Panther Fusion) that is performed at the Montana Public Health Laboratory is considered the gold standard for our state. Other reference laboratories, such as Quest, LabCorp, Mayo Clinic, and National Jewish, have longer test result turnaround because of sample transport time and more complicated sample processing. Most local clinic and hospital laboratories utilize systems, such as Cepheid GeneXpert Xpress and Abbott ID NOW, which allow easy sample processing and short test result turnaround time. The trade-off of utilizing local SARS-CoV-2 test platform for faster test result turnaround time is that these assays seem to have less sensitive clinically in detecting SARS-CoV-2 RNA when compared those assays used by reference laboratories.

It is important to recognize that all the available SARS-CoV-2 RNA RT-PCR assay results often require clinical correlation in their interpretation. Typically, a single test result is sufficient to determine if a patient has COVID-19, especially if the clinical correlation supports that conclusion. Thus, the interpretation should always be done in conjunction with the pre-test probability of the patient of having COVID-19, i.e., the likelihood of a patient of being infected with SARS-CoV-2. For example, the disease is more likely in a symptomatic person from a community where there is moderate to high incidence of SARS-CoV-2 circulating or if there is prolonged direct contact with another person who is known to have COVID-19. Although a positive result in a patient with high pre-test probability is indicative of COVID-19, a negative assay result in this patient does not necessary rule out disease as it may be a false-negative result. Thus, patients who are deemed to have high suspicion of COVID-19, such as the patient in this scenario, should undergo

repeat testing, typically using a different assay, e.g., Hologic Panther Fusion at the Montana Public Health Laboratory, as an appropriate next step to help confirm the diagnosis. If the repeat assay result is negative, other causes of the patient's symptoms should be pursued as COVID-19 would be unlikely. Conversely, a positive SARS-CoV-2 RNA RT-PCR assay result on an asymptomatic patient from a region or community with low incidence of SARS-CoV-2 circulating or no significant contact history, is likely to be a false-positive result. In this scenario, however, repeat testing is typically not recommended. Additionally, retesting may be considered if there are concerns surrounding other variables, such as poor sample collection techniques, testing upper instead of lower respiratory samples in late disease, etc. The use of other tests, such as antigen-based assays or serological antibody detection, is not recommended as a follow-up test.

Please refer to the following flow map on the next page for interpreting SARS-CoV-2 RT-PCR Results.

Interpretation of SARS-CoV-2 RT-PCR Results | October 1,2020



Clinical suspicion may be determined by the following factors:
1. Presence of: fever, respiratory (cough or dyspnea), GI (diarrhea), other (anosmia, dysgeusia)
2. History of travel to area with community transmission of SARS-CoV-2
3. Prolonged exposure (≥ 15 minutes) to known case of COVID-19

Consider using a different platform, preferably with the Montana State Public Laboratory (Hologic Panther Fusion System) when performing repeat SARS-CoV-2 RT-PCR testing