



Interim Guidance: Interpretation of COVID-19 PCR Diagnostic Test Results Frequently Asked Questions

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The following FAQ was developed by the San Francisco Department of Public Health for local use, and will be posted at <http://www.sfcdcp.org>. This interim guidance may change as knowledge, community transmission, and availability of testing change.

AUDIENCE: Health care providers

BACKGROUND: COVID-19 is a new disease caused by an RNA virus (SARS-CoV-2). Patients typically have fever, dry cough, and may develop respiratory distress. Other symptoms that may occur are sore throat, sinus congestion, runny nose, fatigue, myalgia, headache, loss of taste or smell, or diarrhea. Currently, diagnosis relies on real-time polymerase chain reaction (PCR) testing in conjunction with symptoms, other laboratory tests, and radiological findings. FDA approval for tests in use are under an [Emergency Use Authorization only](#).¹ Studies are underway to evaluate their accuracy.

INTERPRETING PCR TESTING FOR COVID-19

Q. What does a positive PCR test for COVID-19 mean?

- PCR tests for COVID-19 have very few false positives. As an initial diagnostic test, if a patient tests positive, they should be told they have COVID-19 infection and to take steps to care for themselves and prevent the spread of infection.²
- If a person who previously tested positive, or had symptoms consistent with COVID-19, has a positive PCR test after symptoms are resolved, it is unclear if they remain infectious and a symptom-based strategy (10 days since symptom onset, improvement in symptoms, and no fever for 3 days) is advised for return to work decisions.³

Q. What does a negative PCR test for COVID-19 mean?

- PCR tests for COVID-19 have variable sensitivities, somewhere in the 56-83% range. There may be false negatives depending on timing of the test related to when symptoms began, the type of specimen, and the technique of collection.
- If a patient tests negative, they should be told that the result only means that virus was not detected at the time of testing and to still take measures to protect themselves and others.⁴
- For symptomatic patients who test negative:
 - They may leave isolation/return to work once it has been 72 hours from their last fever and 72 hours since they have had improvement in their symptoms with the following caveats and considerations:
 - If the patient is in close contact with persons who are vulnerable for severe disease from COVID-19,⁵ they can consider remaining isolated for a longer period of time (10 days).



- For asymptomatic patients who test negative:
 - It is not necessary to repeat the test unless symptoms develop or they have a new exposure to a person with COVID 2019.
 - Repeat testing may be warranted for patients who test negative for COVID 2019 depending on the degree of clinical suspicion and whether the result will affect management, infection control measures, or return to work. This decision needs to be made on a case-by-case basis.

Q. Can serological (antibody) testing diagnose COVID-19?

- No, serologic tests may indicate that a patient has had COVID-19 in the recent past but cannot be used for diagnosis of COVID-19. SFDPH does not recommend the use of serologic tests to diagnose or exclude COVID-19 infection, and results from these tests should not be used as the sole basis for treatment or patient management decisions.⁶

Q. What type of specimen should be collected for COVID-19 PCR testing? NP, OP, or other?

- SFDPH recommends nasopharyngeal (NP) specimens for testing in settings of high risk for complications or rapid spread (e.g., outbreaks in skilled nursing facilities). Alternate upper respiratory specimens, including oropharyngeal (OP), nasal mid-turbinate, anterior nares, and nasopharyngeal wash are acceptable when a patient is at lower risk or if there are limited supplies.

BACKGROUND AND SUPPORTING EVIDENCE

What does a positive PCR test for COVID-19 mean?

PCR detects one or more of the genes associated with the virus. Because PCR detects RNA specific to the SARS-CoV-2 genome, the specificity of most of the PCR tests is 100%. Occasional false-positive results occur due to technical errors and reagent contamination.⁷ That said, a positive result on a PCR generally confirms the diagnosis of COVID-19 infection.

However, the detection of viral RNA does not necessarily equate to live virus. Non-infectious RNA particles will produce positive results on PCR. Studies have detected SARS-CoV-2 RNA up to 20 days or longer after onset of symptoms by PCR, but culture viable virus could not be isolated after day 9 in spite of high viral loads.^{7,8,9} This makes it difficult to use the test for decision making about removal from isolation or return to work. As a result, the CDC changed its guidance to prefer the use of a “symptom-based strategy” rather than testing-based strategy for these decisions (i.e., 3 days since resolution of symptoms and at least 10 days since their onset).³

What does a negative PCR test for COVID-19 mean?

The sensitivity of the PCR tests appears to be between 56% and 83% for nasopharyngeal (NP) swabs, although the quality of evidence is variable.⁷⁻¹³ False negative results can arise from the source of the specimen, the quality of the sample, degree and types of symptoms, patient characteristics, and the timing of the test. Available data suggest that detection of COVID-19 varies by time since symptom onset due to changes over time in viral load.⁷ COVID-19 can be detected by nasopharyngeal (NP) swab as early as day 1 of symptoms, and



detection peaks in the first week of symptom onset. Positivity starts to decline by the third week after symptom onset. One study using PCR and an IgM serologic test suggested that PCR positivity rates were >90% on days 1 to 3 of illness, <80% at day 6, and <50% after day 14.¹¹ Patients who have been exposed to COVID-19, but do not yet have symptoms, may not have sufficient virus to turn the test positive. In 15 of 51 patients (29%) in China¹² and 8 of 71 patients (11%) in Singapore,¹³ the PCR test was initially negative but became positive with repeat testing between 1 and 8 days later. A study in Germany found that the highest viral loads occur in the first 4 days of symptoms.⁹ PCR positivity declines more slowly in sputum and may still be positive when NP swabs are negative; stool may be positive for a median of 4 to 11 days.⁷ Taken together, the evidence suggests patients who are infected but not yet symptomatic may have false-negative test results, as may those whose symptoms are waning.

When interpreting a negative test, clinicians should bear in mind that a false negative result is less likely when prevalence of COVID-19 is high in the population or when the patient has symptoms that are highly suspicious for COVID-19. If an initial test is negative but the suspicion for COVID-19 remains and determining the presence of infection is important for patient management or infection control, the test should be repeated, but no sooner than 24 hours later.¹³

Can serological (antibody) testing diagnose COVID-19?

Serological tests rely on the production of antibodies by a patient exposed to disease, and do not generally develop until 2-3 weeks after the onset of symptoms.⁷ Moreover, the current state of evidence on the accuracy and interpretation of COVID-19 antibody test results is limited. The SFDPH does not recommend the use of serologic tests to diagnose or exclude COVID-19 infection, and results from these tests should not be used as the sole basis for treatment or patient management decisions.⁶ At present, the use of serological tests in San Francisco is for research and surveillance purposes only. See SFDPH's [Statement on Serologic Testing of SARS-CoV-2](https://www.sfdcp.org/wp-content/uploads/2020/05/COVID19-Statement-Serology-FINAL-05.06.2020.pdf) (posted at <https://www.sfdcp.org/wp-content/uploads/2020/05/COVID19-Statement-Serology-FINAL-05.06.2020.pdf>) for more information.

What type of specimen should be collected for COVID-19 PCR testing?

The anatomical site from which the specimen is taken may affect the sensitivity of the PCR test. One study from China comparing 1,070 specimens from multiple sites in 205 hospitalized patients with COVID-19 found the highest rates of positive viral RNA tests were from bronchoalveolar lavage (95%, 14 of 15 specimens) and sputum (72%, 72 of 104), compared with an oropharyngeal (OP) swab (32%, 126 of 398).¹⁴ Viral RNA levels were higher and more frequently detected in nasal compared with oral specimens, although only eight nasal swabs were tested. Three studies not yet peer reviewed had conflicting findings regarding the yield of upper respiratory tract specimens. One study of 213 patients reported NP swabs detected COVID-19 more frequently than OP swabs at all stages of illness, with the difference in yield between the two sites being most notable after 8 days.¹⁵ A second study with nine cases found no discernible differences in detection rates between NP and OP specimens.⁹ The third study included approximately 500 patients who self-tested in an ambulatory clinic and found 96% sensitivity of nasal mid-turbinate (NMT) swabs and 94% sensitivity of anterior nares (nasal) swabs when compared to NP swabs taken by health care workers.¹⁶

According to the FDA, a health care professional swabbing the back of the nasal cavity through the nostril (i.e., NP) is the preferred choice of specimen collection.¹ If an NP specimen is not available, the health care professional may swab the back of the throat, or for patients with symptoms of COVID-19, the inside of the front of the nose. Depending on the type of swab used, a health care professional may collect the sample, or the patient may collect the sample at a collection site under health care provider supervision.

In their 5 May 2020 update, the CDC removed the preference for an NP specimen from [their guidance on](#)



[collecting, handling, and testing of clinical specimens for COVID-19](#).¹⁷ For initial diagnostic testing for COVID-19, the CDC recommends collecting an upper respiratory specimen; the following are acceptable:

- A nasopharyngeal (NP) specimen collected by a healthcare professional; or
- An oropharyngeal (OP) specimen collected by a healthcare professional; or
- A nasal mid-turbinate (NMT) swab collected by a healthcare professional or by a supervised onsite self-collection (using a flocked tapered swab); or
- An anterior nares (nasal swab) specimen collected by a healthcare professional or by onsite or home self-collection (using a flocked or spun polyester swab); or
- Nasopharyngeal wash/aspirate or nasal wash/aspirate (NW) specimen collected by a healthcare professional. NW specimen collection is risky; SFDPH advises only for certain circumstances by trained professionals.

While collection of sputum or and bronchoalveolar lavage fluid is thought to provide the highest sensitivity, collection of these types of specimens increases the biosafety risk to healthcare workers through the production of aerosol droplets.¹⁸ Expecterated sputum should be collected from patients with productive cough; induction of sputum is not recommended. A lower respiratory tract aspirate or bronchoalveolar lavage should be collected from patients who are intubated.

Can collection and handling of specimens affect COVID-19 PCR test results?

A specimen collected with the wrong materials, with inadequate technique, or improper handling may lead to a false-negative result. NP specimens are particularly challenging to obtain. The CDC provides guidelines for collecting and handling NP, OP, NMT, nasal, and NW specimens of the upper respiratory track, and bronchoalveolar lavage, tracheal aspirate, pleural fluid, lung biopsy, and sputum specimens for the lower respiratory track.¹⁷ The FDA provides a list of test kits and approved swabs by brand and manufacturer.¹

Summary of upper respiratory specimen type, collection, and handling¹⁷

Specimen Type	Swab	Media	Comments
Nasopharyngeal (NP)	Synthetic fiber swabs with plastic or wire shafts (no calcium alginate swabs or swabs with wooden tips).	Viral transport media (VTM), Amies transport medium, or sterile saline, unless using a test designed to analyze a specimen directly, (i.e., without placement in VTM)	If both NP and OP swabs are collected, combine in single tube
Oropharyngeal (OP)			
Nasal Mid-turbinate (MT)	Flocked tapered swab		Swab both nares; supervised self-swab OK.
Anterior nares (nasal)	Flocked or spun polyester swab		Swab both nares; supervised self-swab OK

What other factors affect the results of the COVID-19 PCR test?

One peer-reviewed study of 23 patients in Hong Kong found older age correlated with a higher viral load.¹⁹ Another study suggested that non-respiratory symptoms (headache, muscle ache, malaise, tiredness, fever, anosmia, and ocular pain) may be associated with increased PCR test positivity compared to respiratory symptoms (cough, cold-like symptoms, sneezing, sore throat, runny nose, and shortness of breath).²⁰



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