Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Disease-a-Month 66 (2020) 101067

Contents lists available at ScienceDirect

Disease-a-Month

journal homepage: www.elsevier.com/locate/disamonth

COVID-19 Testing

COVID-19 Laboratory Testing/CDC Guidelines

Dr. R.B. McFee

Ellis Medical, Dept. of Emergency and Family Medicine, LMU-DCOM, United States

****** CDC's 24-hour Emergency Operations Center at 770–488–7100.******

What follows is abstracted from the Centers for Disease Control and Prevention (CDC) COVID-19 resources and guidelines section for health care professionals. Comments by Disease A Month are preceded by **.

The following are the most recent guidelines on testing by the Centers for Disease Control and Prevention (CDC), and most up to date information available RE: CDC COVID-19 Laboratory Guidelines as of 06/20. The reader is encouraged to regularly check the CDC COVID-19 site for updates. https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

Revisions made on August 24, 2020

Diagnostic testing categories have been edited to focus on testing considerations and actions to be taken by individuals undergoing testing –

Please refer to https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html

Revisions made on July 17, 2020

Except for rare situations, a test-based strategy is no longer recommended to determine when an individual with a COVID-19 infection is no longer infectious (i.e., to discontinue Transmission-Based Precautions or home isolation)

Revisions made on July 2, 2020

Added = screening to possible testing types

Removed = examples – please refer to setting specific guidance.

See https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/testing.html

CDC Testing:

Two kinds of tests are available for COVID-19:

- A viral test tells you if you have a current infection.
- An antibody test tells you if you had a previous infection.

E-mail address: drmcfee2020@gmail.com

https://doi.org/10.1016/j.disamonth.2020.101067

An antibody test may not be able to show if you have a current infection, because it can take 1–3 weeks after infection to make antibodies. We do not know yet if having antibodies to the virus can protect someone from getting infected with the virus again, or how long that protection might last.

As of 08/24/20 the CDC recommends testing the following:

Considerations for who should get tested

- People who have symptoms of COVID-19
- People who have had close contact (within 6 feet of an infected person for at least 15 minutes) with someone with confirmed COVID-19
- People who have been asked or referred to get testing by their healthcare provider, local or state health department

Not everyone needs to be tested. If you do get tested, you should self-quarantine/isolate at home pending test results and follow the advice of your healthcare provider or a public health professional.

Viral Testing

Authorized assays for viral testing include those that detect COVID-19 nucleic acid or antigen. Viral (nucleic acid or antigen) tests check samples from the respiratory system (such as nasal or oral swabs) or saliva to determine whether COVID-19 is present. Viral tests are recommended to diagnose infection. Some tests are point-of-care tests, often used in emergency rooms, doctor's offices, and outpatient clinics. These tests can produce results at the testing site in less than an hour. Other tests must be performed in a laboratory. If there is not a Point-of-Care (POC) device or laboratory at the collection point, samples must be sent (deliver or shipped) to a laboratory for analysis, a process that can take at least 1-2 days.

For more information on testing for COVID-19 see the Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens and Biosafety FAQs for handling and processing specimens from possible cases.

CDC Guidance on who should be tested and various methods.

***For further guidance the reader is also referred to their local, or state health department for region specific testing guidelines, and your health care facility laboratorian for information on best protocols.

CDC Recommendations for Antibody Testing

CDC does not currently recommend using antibody testing as the sole basis for diagnosis of acute infection, and antibody tests are not authorized by FDA for such diagnostic purposes. In certain situations, serologic assays may be used to support clinical assessment of persons who present late in their illnesses when used in conjunction with viral detection tests. In addition, if a person is suspected to have post-infectious syndrome (e.g., Multisystem Inflammatory Syndrome in Children) caused by SARS-CoV-2 infection, serologic assays may be used.

Serologic assays for SARS-CoV-2, now broadly available, can play an important role in understanding the transmission dynamic of the virus in the general population and identifying groups at higher risk for infection. Unlike viral direct detection methods, such as nucleic acid amplification or antigen detection tests that can detect acutely infected persons, antibody tests help determine whether the individual being tested was previously infected—even if that person never showed symptoms.

It is currently not clear whether a positive serologic test indicates immunity against SARS-CoV-2; serologic tests should not be used at this time to determine if an individual is immune. As additional data are collected to understand the significance of the presence or level of antibodies and their correlation with immunity, serologic tests may have utility in infection control decisions, but for now this evidence is not available.

These tests can help determine the proportion of a population previously infected with SARS-CoV-2. Thus, demographic and geographic patterns of serologic test results can help determine which communities may have experienced a higher infection rate.

Categories for COVID −19 (SARS-CoV-2) Testing

This document describes five categories of people for SARS-CoV-2 testing with viral tests (i.e., nucleic acid or antigen tests) [the following are hot links to CDC resources]:

- Testing individuals with signs or symptoms consistent with COVID-19
- Testing asymptomatic individuals with recent known or suspected exposure to SARS-CoV-2 to control transmission
- Testing asymptomatic individuals without known or suspected exposure to SARS-CoV-2 for early identification in special settings
- Testing to determine resolution of infection (i.e., test-based strategy for Discontinuation of Transmission-based Precautions, HCP Return to Work, and Discontinuation of Home Isolation)
- Public health surveillance for SARS-CoV-2

Generally, viral testing for SARS-CoV-2 is considered to be diagnostic when conducted among individuals with symptoms consistent with COVID-19 or among asymptomatic individuals with known or suspected recent exposure to SARS-CoV-2 to control transmission, or to determine resolution of infection. Testing is considered to be surveillance when conducted among asymptomatic individuals without known or suspected exposure to SARS-CoV-2 for early identification, or to detect transmission hot spots or characterize disease trends.

Recommended testing for individuals with signs or symptoms consistent with COVID-19

CDC recommends using authorized nucleic acid or antigen detection assays that have received an FDA EUA to test persons **with** symptoms when there is a concern of potential COVID-19. Tests should be used in accordance with the authorized labeling; providers should be familiar with the tests' performance characteristics and limitations.

According to the CDC *"Clinicians should use their judgment to determine if a patient has signs or symptoms compatible with COVID-19 and whether the patient should be tested. Most patients with confirmed COVID-19 have developed fever and/or symptoms of acute respiratory illness (*e.g.*, cough) but some infected patients may present with other symptoms as well. Clinicians are encouraged to consider testing for other causes of respiratory illness, for example influenza, in addition to testing for SARS-CoV-2 depending on patient age, season, or clinical setting; detection of one respiratory pathogen (*e.g.*, influenza) does not exclude the potential for co-infection with SARS-CoV-2. Because symptoms and presentations may be different in children, consider referencing the CDC guidelines for COVID in neonates and for multisystem inflammatory syndrome in children."*

***CDC rightly notes that the severity of symptomatic illness due to infection with may vary. Among persons with extensive and close contact to vulnerable populations (e.g., healthcare personnel [HCP]), even mild signs and symptoms (e.g., sore throat) of possible COVID-19 should prompt consideration for testing. Additional information is available in CDC's. The reader is referred to the CDC Interim U.S. Guidance for Risk Assessment and Public Health Management of Healthcare Personnel with Potential Exposure in a Healthcare Setting to Patients with Coronavirus Disease 2019 (COVID-19).

Recommended testing for asymptomatic individuals with known or suspected exposure to SARS-CoV-2 to control transmission

Testing is recommended for all close contacts of persons with SARS-CoV-2 infection, especially initial testing during an outbreak or pandemic due to the high likelihood of exposure. Because of the potential for asymptomatic and pre-symptomatic transmission, it is important that contacts of individuals with SARS-CoV-2 infection be quickly identified and tested.

CDC further adds:

- In areas where testing is limited, CDC has established a testing hierarchy; refer to the Interim Guidance on Developing a COVID-19 Case Investigation and Contact Tracing Plan for more information.
- CDC specifically recommends testing for all neonates born to women with COVID-19, regardless of whether there are signs of infection in the neonate.

Their guidance towards COVID – 19 includes:

In some settings, broader testing, beyond close contacts, is recommended as a part of a strategy to control transmission of SARS-CoV-2. This includes high-risk settings that have potential for rapid and widespread dissemination of SARS-CoV-2 (e.g., meat processing plant) or in which populations at risk for severe disease (e.g., long-term care facilities, including nursing homes, intermediate care facilities for individuals with intellectual disabilities, and psychiatric residential treatment facilities) could become exposed. Expanded testing might include testing of all contacts in proximity to someone with SARS-CoV-2 infection, or even testing all individuals within a shared setting (e.g., facility-wide testing). Currently CDC recommends expanded contact testing in the following guidance documents:

- Testing guidance for nursing homes.
- Following identification of SARS-CoV-2 infection in a worker in a high-density critical infrastructure workplace

Recommended testing for asymptomatic individuals without known or suspected SARS-CoV-2 exposure for early identification in special settings

Certain settings can experience rapid spread of SARS-CoV-2, resulting in substantial adverse effects. This is particularly true for settings that house vulnerable populations in close quarters for extended periods of time (e.g., long-term care facilities, correctional and detention facilities) and/or settings where critical infrastructure workers (e.g., healthcare personnel, first responders) may be disproportionately affected.

A strategy aimed at reducing introduction of SARS-CoV-2 into the setting through early identification could reduce the risk of widespread transmission in these situations.

Facilities are encouraged to work with local, territorial, and state health departments to help inform decision-making about broad-based testing. Before testing large numbers of asymptomatic individuals without known or suspected exposure, the facility should have a plan in place for how it will modify operations based on test results.

Approaches for early identification of asymptomatic individuals include:

- Initial testing of everyone residing and/or working in the setting,
- Regular (e.g., weekly) testing of everyone residing and/or working in the setting, and
- Testing of new entrants into the setting and/or those re-entering after a prolonged absence (e.g., one or more days)

Settings for which these approaches could be considered include:

- Long-term care facilities
- Correctional and detention facilities
- Homeless shelters
- Other congregate work or living settings including mass care, temporary shelters, assisted living facilities, and group homes for individuals with intellectual disabilities and developmental disabilities
- High-density critical infrastructure workplaces where continuity of operations is a high priority

CDC guidance currently addressing such testing includes:

- Pre-admission or pre-procedure testing as part of the evaluation of patients could be considered to inform decisions about deferring elective care (e.g., certain dental procedures) or procedures and the use of personal protective equipment.
- Testing guidance for nursing homes

Recommended testing to determine resolution of infection with SARS-CoV-2

A test-based strategy, which requires serial tests, can be used as an alternative to a symptom-based or time-based strategy, to determine when a person with SARS-CoV-2 infection no longer requires isolation or work exclusion. This strategy could be considered in three situations:

- Discontinuation of Transmission-Based Precautions and Disposition of Patients with COVID-19 in Healthcare Settings

- Discontinuation of Isolation for Persons with COVID −19 Not in Healthcare Settings
- Determining Criteria for Return to Work for Healthcare Personnel with Suspected or Confirmed COVID-19

Public health surveillance for SARS-CoV-2

Testing is a fundamental part of the United States SARS-CoV-2 Surveillance Plan, which uses multiple surveillance systems and epidemiology networks, in collaboration with state, local, and academic partners, to monitor the progression and impact of SARS-CoV-2 spread in the United States.

Viral tests are used in community, outpatient, and hospital-based surveillance systems to identify cases of SARS-CoV-2 infection. These data help identify areas of ongoing circulation (hot spots), determine trends in disease by location, provide insight into the impact of the disease over time and by location, and inform disease forecasts.

Antibody tests are increasingly used to monitor disease burden by location and over time. Use of serologic assays in populations can help determine the proportion of a population previously infected with SARS-CoV-2. Thus, demographic and geographic patterns of serologic test results provide data that can be used in forecasts of disease spread that can support resource allocation decisions and planning by local, territorial and state officials.

Additional Resources:

- Nasal (Anterior Nasal) Specimen Collection for SARS-CoV-2 Diagnostic Testing
- Guidance – Proposed Use of Point-of-Care (POC) Testing Platforms for SARS-CoV-2 (COVID-19)
- State health department

TESTING (CDC Recommendations)

For initial diagnostic testing for SARS-CoV-2, CDC recommends collecting and testing an upper respiratory specimen. The following are acceptable specimens:

- A nasopharyngeal (NP) specimen collected by a healthcare provider; or
- An oropharyngeal (OP) specimen collected by a healthcare provider; or
- A nasal mid-turbinate swab collected by a healthcare provider or by a supervised onsite self-collection (using a flocked tapered swab); or
- An anterior nares (nasal swab) specimen collected by a healthcare provider 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 provider.

Swabs should be placed immediately into a sterile transport tube containing 2–3 mL of either viral transport medium (VTM), Amies transport medium, or sterile saline, unless using a test designed to analyze a specimen directly, (i.e., without placement in VTM), such as some point-of-care tests. If VTM is not available, see the standard operating procedure for public health labs to create viral transport medium in accordance with CDC's protocol.

The NW specimen and the non-bacteriostatic saline used to collect the specimen should be placed immediately into a sterile transport tube.

Lower Respiratory Tract (LRT)

Testing lower respiratory tract specimens is also an option. For patients who develop a productive cough, sputum should be collected and tested for SARS-CoV-2. The induction of sputum is not recommended. When under certain clinical circumstances (e.g., those receiving invasive mechanical ventilation), a lower respiratory tract aspirate or bronchoalveolar lavage sample should be collected and tested as a lower respiratory tract specimen.

Collecting and Handling Specimens Safely

For providers collecting specimens or within 6 feet of patients suspected to be infected with SARS-CoV-2, maintain proper infection control and use recommended personal protective equipment (PPE), which includes an N95 or higher-level respirator (or facemask if a respirator is not available), eye protection, gloves, and a gown, when collecting specimens.

For providers who are handling specimens, but are not directly involved in collection (e.g. self-collection) and not working within 6 feet of the patient, follow Standard Precautions; gloves are recommended. Healthcare personnel are recommended to wear a form of source control (facemask or cloth face covering) at all times while in the healthcare facility.

PPE use can be minimized through patient self-collection while the healthcare provider maintains at least 6 feet of separation.

Handling Bulk-Packaged Sterile Swabs Properly for Upper Respiratory Sample Collection

Sterile swabs for upper respiratory specimen collection may be packaged in one of two ways:

- Individually wrapped (preferred when possible)
- Bulk packaged

Bulk-packaged swabs may be used for sample collection; however, care must be exercised to avoid SARS-CoV-2 contamination of any of the swabs in the bulk-packaged container.

- Before engaging with patients and while wearing a clean set of protective gloves, distribute individual swabs from the bulk container into individual disposable plastic bags.
- If bulk-packaged swabs cannot be individually packaged:
  - Use only fresh, clean gloves to retrieve a single new swab from the bulk container.
  - Close the bulk swab container after each swab removal and leave it closed when not in use to avoid inadvertent contamination.
  - Store opened packages in a closed, airtight container to minimize contamination.
  - Keep all used swabs away from the bulk swab container to avoid contamination.
- As with all swabs, only grasp the swab by the distal end of the handle, using gloved hands only.
- When patients are self-collecting their swabs under clinical supervision:
  - Hand a swab to the patient only while wearing a clean set of protective gloves.
  - The patient can then self-swab and place the swab in transport media or sterile transport device and seal.
  - If the patient needs assistance, you can help the patient place the swab into transport media or a transport device and seal it.

General Guidelines

Proper collection of specimens is the most important step in the laboratory diagnosis of infectious diseases. A specimen that is not collected correctly may lead to false negative test results. The following specimen collection guidelines follow standard recommended procedures.

For more information, including illustrations and step-by-step guidance, see the CDC Influenza Specimen Collection instructions. Note that these instructions are applicable for respiratory viruses in general, and not specific for only influenza virus.

I. Respiratory Specimens

A. Upper respiratory tract

Nasopharyngeal swab/Oropharyngeal (Throat) swab

Use only synthetic fiber swabs with plastic or wire shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing. CDC is now recommending collecting only the NP swab (Fig. 1), although OP swabs remain an acceptable specimen type. If both NP and OP swabs are collected, they should be combined in a single tube to maximize test sensitivity and limit use of testing resources.

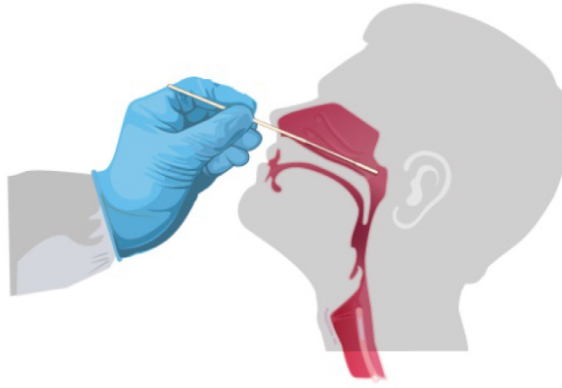

Fig. 1. Proper placement of nasal swab (from www.cdc.gov).

NP swab: Insert mini tip swab with a flexible shaft (wire or plastic) through the nostril parallel to the palate (not upwards) until resistance is encountered or the distance is equivalent to that from the ear to the nostril of the patient, indicating contact with the nasopharynx (Fig. 1). Swab should reach depth equal to distance from nostrils to outer opening of the ear. Gently rub and roll the swab. Leave swab in place for several seconds to absorb secretions. Slowly remove swab while rotating it. Specimens can be collected from both sides using the same swab, but it is not necessary to collect specimens from both sides if the minitip is saturated with fluid from the first collection. If a deviated septum or blockage create difficulty in obtaining the specimen from one nostril, use the same swab to obtain the specimen from the other nostril.

OP swab: Insert swab into the posterior pharynx and tonsillar areas. Rub swab over both tonsillar pillars and posterior oropharynx and avoid touching the tongue, teeth, and gums.

Nasal mid-turbinate (NMT) swab, also called Deep Nasal Swab

Use a flocked tapered swab. Tilt patient's head back 70°. While gently rotating the swab, insert swab less than one inch (about 2 cm) into nostril (until resistance is met at turbinates). Rotate the swab several times against nasal wall and repeat in other nostril using the same swab.

Anterior nares specimen

Using a flocked or spun polyester swab, insert the swab at least 1 cm (0.5 inch) inside the nostril (naris) and firmly sample the nasal membrane by rotating the swab and leaving in place for 10 to 15 s. Sample both nostrils with same swab.

Nasopharyngeal wash/aspirate or nasal wash/aspirate

Attach catheter to suction apparatus. Have the patient sit with head tilted slightly backward. Instill 1 mL-1.5 mL of non-bacteriostatic saline (pH 7.0) into one nostril. Insert the tubing into the nostril parallel to the palate (not upwards). Catheter should reach depth equal to distance from nostrils to outer opening of ear. Begin gentle suction/aspiration and remove catheter while rotating it gently. Place specimen in a sterile viral transport media tube.

B. Lower respiratory tract

Bronchoalveolar lavage, tracheal aspirate, pleural fluid, lung biopsy

Collect 2–3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container.

Due to the increased technical skill and equipment needs, collection of specimens other than sputum from the lower respiratory tract may be limited to patients presenting with more severe disease, including people admitted to the hospital and/or fatal cases.

Sputum

Educate the patient about the difference between sputum and oral secretions (saliva). Have the patient rinse the mouth with water and then expectorate deep cough sputum directly into a sterile, leak-proof, screw-cap collection cup or sterile dry container.

II. Storage

Store specimens at 2–8 °C for up to 72 h after collection. If a delay in testing or shipping is expected, store specimens at −70 °C or below.

III. Shipping

If local laboratory capacity is unavailable, samples may be shipped to CDC if repeated testing results remain inconclusive or if other unusual results are obtained.

Please contact **CDC at** respvirus@cdc.gov prior to submitting samples and other information.

****** CDC's 24-hour Emergency Operations Center at 770–488–7100.******