Coronavirus Disease (COVID-19), Respiratory Specimen (Lab Tests and Diagnostic Procedures)

Comment

The FDA has noted that unauthorized **fraudulent** COVID-19 test kits are being sold online. Currently the only way to be tested for COVID-19 is through licensed health care providers. The FDA advises consumers and health professionals to be cautious of websites and stores selling products that claim to prevent, diagnose, treat, or cure COVID-19 (FDA 2020). Any concerns regarding fraudulent products, including tests, should be sent to: FDA-COVID-19-Fraudulent-Products@fda.hhs.gov.

Related Information

- Coronavirus Disease (COVID-19) Antibody, IgG/IgM Rapid Test, Whole Blood, Serum, or Plasma

Overview

At the end of 2019, a novel coronavirus was identified as the cause of several cases of pneumonia in Wuhan City, Huber Province, China. Initially linked to a large seafood and animal market suggesting animal-to-human spread, person-to-person transmission was quickly confirmed (Li 2020). The virus spread rapidly worldwide and in January 2020, the World Health Organization (WHO) declared the outbreak a "public health emergency of international concern." On March 11, 2020, the WHO publicly characterized COVID-19 as a pandemic. Currently, more than 1.9 million infections have been confirmed globally in over 200 countries and territories with over 130,000 deaths (WHO situation rept 2020).

The novel virus has been named **severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)** and the disease it causes has been named **coronavirus disease 2019 (COVID-19)**. The virus is thought to spread mainly by respiratory droplets produced when an infected person coughs or sneezes. The droplets can land in the mouths, noses and eyes of nearby people, or possibly be inhaled into the lungs. Touching a contaminated surface and transferring to eyes, nose or mouth is also thought to be a mode of transmission although not as dominant as by respiratory droplets. Symptoms typically appear within 2 to 14 days (median of 5 days) of exposure and include fever (most common), fatigue, cough, shortness of breath, and myalgia. Sickness ranges from a mild respiratory illness to severe disease including respiratory failure, septic shock, or other organ failure. Most fatalities have occurred in patients with underlying comorbidities with overall fatalities over 6 percent (WHO situation rept 2020). Currently, there is no vaccine or specific treatment; care is supportive.

The Center of Disease Control and Prevention (CDC) has developed a real time Reverse Transcription-Polymerase Chain Reaction (rRT-PCR) assay to diagnose SARS-CoV-2 in respiratory specimens. In the early stages of disease dissemination, the CDC was the only lab conducting

the SARS-CoV-2 testing; however, with the rapid spread of the viral infection in February 2020, the FDA issued an Emergency Use Authorization (EUA) allowing qualified laboratories (as designated by CDC) to perform testing. These facilities include US state and local public health laboratories, Department of Defense (DOD) laboratories, and select reference and international laboratories. Currently, under FDA guidance, there has been local, hospital-based SARS-CoV-2 test development. The developed tests may be based on the CDC, WHO, or manufacturer assays, or created de novo. The laboratories must perform an assay validation and pursue an FDA Emergency Use Authorization (IDSA 2020). Health care providers should contact their local laboratory for testing options including use of the state health department or reference labs that have been approved to conduct testing. State labs may require prior approval (contact directly and receive PUI number). If a case is not approved by a state lab, specimens can be sent to a reference laboratory.

Note: On March 21, 2020, the FDA issued emergency use authorization (EUA) for the first rapid coronavirus diagnostic test, with a detection time of approximately 45 minutes. This is the first COVID-19 test that can be used at the point of care (POC) and should quickly aid with distinguishing presumptive diagnosis from confirmed diagnosis, thus assisting in the decision-making process (isolation, treatment, risk to others, etc.) (Cepheid 2020). Although marketed as POC, most of the testing will be performed in clinical laboratories and not at health provider's office or bedside. Produced by Cepheid, this test is unique in that all steps of the testing process are integrated within one cartridge in which specimen is added. The test is run on Cepheid GeneXpert systems which are located in many health organizations in the US and throughout the world. Currently, supplies are allocated to areas most in need.

On March 27, 2020, under EUA by the FDA, Abbott Laboratories molecular point of care test for the detection of corona virus was approved. This test is run on Abbott's ID NOW™ platform, a small unit that can be used in a variety of locations including health care providers' offices and urgent care clinics. Positive results can be reported in as little as 5 minutes and negative results in 13 minutes (Abbott 2020).

Also, becoming available (via EUA) are molecular respiratory panels that include SARS-CoV-2 and several other well-known respiratory pathogens. These panels are intended for qualitative differentiation of nucleic acid from multiple organisms and can assist health care providers in differentiating various infectious agents that produce similar symptoms to COVID-19. Panel testing can also assist in diagnosing coinfections which have been noted in some COVID-19 patients (Ding 2020; Kim 2020).

Use/Indications
Aid in the diagnosis of coronavirus disease (COVID-19)

Special Instructions

Health care providers should **immediately** contact local or state health department if any patient is determined to be a person under investigation (PUI) for COVID-19. The decision to test these individuals should be based on clinical and local epidemiologic factors. The possibility of COVID-19 should be considered primarily in patients with **fever (subjective or confirmed) and/or symptoms of acute respiratory illness (cough, difficulty breathing).** Testing priorities suggested by the Center of Disease and Prevention (CDC) include:

1. **Priority 1:** Hospitalized patients who have signs/symptoms consistent with COVID-19 and symptomatic health care workers; enables hospital staff to make informed decisions regarding infection control and maintains the integrity of the health care system

2. **Priority 2:** Symptomatic individuals at high risk including patients in long-term facilities, patients over 65 years, patients with underlying conditions, first responders

3. **Priority 3:** Symptomatic individuals in surrounding community of rapidly increasing hospital cases to decrease community spread and ensure health of essential workers. This includes critical infrastructure workers, symptomatic individuals who do not meet any of the previous criteria, health care workers and first responders, individuals with mild symptoms in communities with rapidly expanding COVID-19 hospitalizations.

4. **Nonpriority:** Individuals without symptoms

Testing recommendations by the Infectious Diseases Society of America include (IDSA 2020):

- **Highest priority patients:**
    - Critically ill patients receiving ICU care with unexplained viral pneumonia or respiratory failure
    - Any individual (including health care workers) with fever or features of a lower respiratory tract illness **and** close contact with patients with laboratory-confirmed COVID-19 within 14 days of symptom onset (including all residents of long-term care facilities with a confirmed case)
    - Any individual (including health care workers) with fever or features of lower respiratory tract illness who have traveled with 14 days of symptom onset to geographic regions where sustained community transmission has been identified.
    - Any individual with fever or features of lower respiratory tract illness who is immunosuppressed (including HIV patients), elderly, or have underlying chronic health conditions

- Any individual with fever or features of lower respiratory tract illness who are critical to pandemic response (health care worker, public health official, essential leader)

- **Second-priority** patients include hospitalized, non-intensive care unit (ICU) and long-term care residents with unexplained fever **and** features of lower respiratory tract illness

- **Third-priority** patients for testing are outpatients who meet criteria for influenza testing (eg, common symptoms such as fever, cough and other suggestive respiratory symptoms, myalgia, headache), plus comorbid conditions, such as diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, age >50 years, immunocompromising conditions; testing of outpatient pregnant women and symptomatic children with similar risk factors for complications is also included in this priority level.

- **Fourth-priority** testing includes community surveillance as directed by public health and/or infectious diseases authorities.

Note: Testing for other respiratory pathogens by the provider should be done as part of the initial work-up and should not delay specimen shipping to CDC or qualified laboratory. If a PUI tests positive for another respiratory pathogen, after clinical evaluation and consultation with public health authorities, he/she may no longer be considered a PUI.

Test Includes
Qualitative detection of nucleic acid from SARS-CoV-2

Specimen
Upper Respiratory Tract Specimen

For initial COVID-19 testing, the CDC recommends collecting an upper respiratory specimen. A **nasopharyngeal (NP) specimen is preferred** for swab-based collection. The NP swab can be used for symptomatic, and asymptomatic patients in a healthcare setting, including long term care facilities. Also acceptable (CDC 2020):

- Oropharyngeal (OP) specimen collected by a health care provider. **Or**

- Nasal Mid-turbine (NMT) swab (appropriate **only for symptomatic** patients) collected by a health care provider or onsite self-collection (using flocked or tapered swab). Both nares should be swabbed. **Or**

- Anterior nares (nasal swab; NS) specimen (appropriate **only for symptomatic** patients) collected by a health provider or onsite self-collection (using a flocked or spun polyester swab). Both nares should be swabbed. **Or**

- Nasopharyngeal wash/aspirate or nasal aspirate (NA) specimen collected by health care provider

Lower Respiratory Trace Specimen

- Bronchoalveolar lavage (BAL), tracheal aspirate, pleural fluid, lung biopsy
- Sputum (for patients who develop a productive cough)

Note: SARS-CoV-2 RNA has also been detected in stool and blood.

Container(s)

- Confer with testing laboratory for proper specimen container and collection.
- Sterile NP swab in viral transport media; Note: Some labs accept swabs in 1-3 mL sterile saline
- Sterile NS or NMT swab in viral transport medium, Amies transport medium, or sterile saline
- Sterile, screw-cap plastic container for lower respiratory specimen
- Use only synthetic fiber swab with plastic shaft. Do not use calcium alginate swab or swab with wooden shaft.

Volume / Minimum Volume

- 1 NP swab or 1 OP swab or 1 NS swab or 1 NMT swab
- Fluids: 2-3 mL

Collection
Prior to specimen collection, patient identity should be confirmed using two independent identifiers; use of a patient identification arm band or similar system is recommended. Specimen label(s) should include the two independent identifiers and the date of collection. There should be a method to identify the individual collecting the specimen. The specimen container(s) should be labeled in the presence of the patient after specimen is collected. Container(s) should **not** be prelabeled. Use computer-generated label(s), if available, to avoid transcription errors.

Collect specimen from PUI as soon as possible regardless of time of symptom onset. Specimen should be collected by trained health care professional using proper infection control techniques and wearing personal protective equipment, including an N95 respirator (or facemask if respirator is not available), eye protection, gloves, and a gown.

Upper Respiratory Tract Specimen

- Currently the CDC is recommending collecting only the NP swab. If both swabs are used, NP and OP specimens should be combined at collection into a single vial at the collection site. OP swabs remain an acceptable specimen type.

    - **NP swab:** Insert a mini-tip swab through the nares parallel to the palate (not upwards) until resistance is detected or the distance is equivalent to that from the ear to the nostril of the patient, indicating contact with the nasopharynx. Swab should reach depth equal to distance from nostrils to outer opening of the ear. Gently rub and roll swab. Leave swab in place for several seconds to absorb secretions. Slowly remove swab while rotating it. Place swab immediately into sterile tubes containing 2 to 3 mL of viral transport media (or other *acceptable* media).

    - **OP (throat) swab:** Avoiding the tongue, teeth, and gums, insert swab into the posterior of pharynx and tonsillar areas. Rub swab over both tonsillar pillars and posterior oropharynx. Place swab immediately into sterile tubes containing 2 to 3 mL of viral transport media (or other *acceptable* media). If both are collected, NP and OP specimens should be placed in the same vial at collection site.

- **NP wash/aspirate or nasal aspirate:** Sterile collection by health care provider. Attach catheter to suction apparatus. Have the patient sit with head tilted slightly backward. Instill 1 to 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.

- **NMT swab (deep nasal swab):** Use a flocked tapered swab. Tilt patient's head back 70 degrees. While gently rotating, 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. For more information, see the CDC Influenza Specimen Collection instructions.

- **NS (anterior nares):** Using a flocked or spun polyester swab, insert the swab at least 0.5 inch (1 cm) inside the nares and firmly sample the nasal membrane by rotating the swab and leaving in place for 10 to 15 seconds. Sample both nares with same swab.

Lower Respiratory Tract Specimen

- **BAL, tracheal aspirate, pleural fluid, lung biopsy:** Sterile collection by health care provider. Collect 2 to 3 mL into sterile, leakproof, screw-cap container. Note, collection of lower respiratory specimen other than sputum may be limited to patients presenting with more severe disease (admitted to hospital and/or fatal cases).

- **Sputum:** Patient should be educated on difference between sputum and saliva. Patient should rinse mouth with water then expectorate deep cough sputum directly into sterile, leakproof screw-cap container. **Note:** Sputum induction is **not** indicated.

For more information see: CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19).

See Guidelines for submitting specimens to CDC for laboratory testing for SARS-CoV-2.

Processing and Storage

- For all specimens: Refrigerate at 2°C to 8°C and ship overnight on ice pack to CDC (or qualified laboratory). Specimens are stable 72 hours.
- For longer storage, freeze specimen(s) at -70°C.
- For state labs, follow specific shipping guidelines.

Stability

- Refrigerated: 72 hours
- Frozen (-70°C): Not established

Methodology
Real time Reverse Transcriptase-Polymerase Chain Reaction (rRT-PCR)

Normal Values/Findings
Not detected

Note: If a negative result is obtained from a patient with a high index of suspicion, the World Health Organization (WHO) recommends collection of additional specimens, including the lower respiratory tract if possible, for further testing (WHO March 2020).

Health care providers should report positive results to their local/state health department.

Interpretative Information

- PUI: Any person who is under investigation for having SARS-CoV-2 that causes COVID-19 or who was under investigation but tested negative.
- A Not Detected test result means that SARS-CoV-2 RNA was not present in the specimen above the limit of detection, thus a negative result does not rule out the possibility of COVID-19 and should not be used as the sole basis for patient management decisions.

Limitations
Factors that can lead to a false-negative result include:

- Poor specimen quality; small amount of patient specimen
- Specimen collected very early or very late in the infection process
- Inadequate processing, storage, or shipping of specimen
- Technical reasons inherent in the test (eg, virus mutation, PCR inhibition) (WHO March 2020)

Laboratory/Diagnostic Pearls

- For biosafety reasons it is not recommended to perform viral isolation in cell culture for SARS-CoV-2 or perform initial characterization of viral agents recovered in cultures of specimens from PUI.
- Although 2 to 14 days represents the current official incubation period for COVID-19, one case in China was reported to have a 19-day incubation period (Bai 2020) and another, reported by the Chinese provincial government, had an incubation time of 27 days (World News 2020).
- Studies indicate SARS-CoV-2 may persist on surfaces for a few hours up to several days dependent on conditions (eg, type of surface, temperature or humidity of the environment) (WHO Q&A 2020).
- High SARS-CoV-2 viral loads (more in nose than throat) can be detected soon after symptom onset but prior to diagnosis and can also be found in the asymptomatic patient (Zou 2020). Viral shedding may continue for days after symptom relief and recovery (Lan 2020). Median range of viral shedding among hospitalized patients has been documented as 12 to 20 days (Zhou 2020; Young 2020).

Additional Information

For more information, interim guidance has been issued by the United States CDC and the World Health Organization.

See: Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19).

See: Information for Laboratories

See: Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19)

See: For Healthcare Professionals

See: FDA Emergency Use Authorizations

The CDC is currently working on development of a serologic test for detection of antibodies to SARS-CoV-2. This will assist in determining how much of the US population has been exposed to the virus.

Index Terms
2019 Novel Coronavirus; 2019-nCoV; COVID-19 PCR; COVID-19, Qualitative, PCR; Covid19; nCoV, 2019; Novel Coronavirus, 2019; Qualitative COVID-19; SARS-CoV-2; Severe Acute Respiratory Syndrome Coronavirus 2; Wuhan

Applies to
Pandemic; Person Under Investigation (PUI); Pneumonia of Unknown Etiology

References
Abbott Laboratories. Detect COVID-19 in as little as 5 minutes. Abbott Laboratories website https://www.abbott.com/corpnewsroom/product-and-innovation/detect-covid-19-in-as-little-as-5-minutes.html. Updated March 27, 2020. Accessed March 30, 2020.

Bai Y, Yao L, Wei T, et al. Presumed Asymptomatic Carrier Transmission of COVID-19 [published online February 21, 2020]. *JAMA*. 2020;10.1001/jama.2020.2565.[PubMed 32083643]

Centers for Disease Control and Prevention (CDC). 2019 Novel Coronavirus. Evaluating and reporting persons under investigation (PUI). https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html. Updated March 4, 2020. Accessed March 9, 2020.

Centers for Disease Control and Prevention (CDC). CDC Tests for 2019-nCoV. https://www.cdc.gov/coronavirus/2019-ncov/about/testing.html. Updated February 5, 2020. Accessed February 13, 2020.

Centers for Disease Control and Prevention (CDC). Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for 2019 Novel Coronavirus (2019-nCoV). https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html Accessed April 9, 2020.

Ding Q, Lu P, Fan Y, Xia Y, Liu M. The clinical characteristics of pneumonia patients coinfected with 2019 novel coronavirus and influenza virus in Wuhan, China [published online ahead of print, 2020 Mar 20]. J Med Virol. 2020;10.1002/jmv.25781.[PubMed 32196707]

Infectious Diseases Society of America (IDSA). COVID-19 Prioritization of Diagnostic Testing. https://www.idsociety.org/globalassets/idsa/public-health/covid-19-prioritization-of-dx-testing.pdf. Updated March 17, 2020. Accessed March 24, 2020.

Kim D, Quinn J, Pinsky B, Shah NH, Brown I.Rates of Co-infection Between SARS-CoV-2 and Other Respiratory Pathogens [published online April 15, 2020]. *JAMA*[PubMed 32293646]

Lan L, Xu D, Ye G, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19 [published online February 27, 2020]. *JAMA*. 2020.[PubMed 32105304]

Lippi G, Simundic AM, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19) [published online ahead of print, March 16, 2020]. *Clin Chem Lab Med*.[PubMed 32172228]

Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia [published online January 29, 2020]. *N Engl J Med*.[PubMed 31995857]

Patel A, Jernigan DB; 2019-nCoV CDC Response Team. Initial Public Health Response and Interim Clinical Guidance for the 2019 Novel Coronavirus Outbreak - United States, December 31, 2019-February 4, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(5):140–146. Published February 7, 2020.[PubMed 32027631]

QIAstat-Dx Respiratory SARS-CoV2 Panel Instructions for Use (Handbook). Germantown, MD: QIAGEN; March 2020.

Shen S, Woo R. Coronavirus incubation could be as long as 27 days, Chinese provincial government say. *Reuters [online]* [online]. Published February 22, 2020. Accessed February 27, 2020.

US Food & Drug Administration (FDA). Beware of Fraudulent Coronavirus Tests, vaccines and Treatments. https://www.fda.gov/consumers/consumer-updates/beware-fraudulent-coronavirus-tests-vaccines-and-treatments?utm_campaign=FDA%20MedWatch%20-%20Fraudulent%20Coronavirus%20Tests%2C%20Vaccines%20and%20Treatments&utm_medium=email&utm_source=Eloqua. Published March 24, 2020. Accessed March 26, 2020.

Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern [published online January 24, 2020] [published correction appears in Lancet January 29, 2020]. *Lancet*. 2020 Feb 15;395(10223):470-473.[PubMed 31986257]

World Health Organization (WHO). Coronavirus disease 2019 (COVID-19). Situation reports. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/. Updated April 16, 2020. Accessed April 17, 2020.

World Health Organization (WHO). Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance. Updated February 7, 2020. Accessed February 13, 2020.

World Health Organization (WHO). Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases. https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117. Published March 2, 2020. Accessed March 9, 2020.

World Health Organization (WHO). Q&A on coronavirus (COVID-19). WHO Newsroom. https://www.who.int/news-room/q-a-detail/q-a-coronaviruses. Published February 23, 2020. Accessed March 4, 2020.

Xpert® **Xpress** SARS-CoV-2 Test. Cepheid website. https://www.cepheid.com/coronavirus. Update March 21, 2020. Accessed April 1, 2020.

Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore [published online ahead of print, 2020 Mar 3]. *JAMA*. 2020;e203204. doi:10.1001/jama.2020.3204[PubMed 32125362]

Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study [published correction appears in *Lancet*. 2020 Mar 28;395(10229):1038] [published correction appears in *Lancet*. 2020 Mar 28;395(10229):1038]. *Lancet*. 2020;395(10229):1054–1062.[PubMed 32171076]

Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N Engl J Med*. 2020;382(12):1177-1179.[PubMed 32074444]

Last Updated 4/17/20