

COVID-19 Antibody Total, Serum, Plasma, or Whole Blood (Lab Tests and Diagnostic Procedures)

Comment

The FDA has noted that unauthorized **fraudulent** COVID-19 test kits are being sold online. 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](#)). Consumers and health care professionals can help by reporting suspected fraud to the [FDA's Health Fraud Program](#) or the [Office of Criminal Investigations](#).

Note: In June, 2021 the FDA issued a statement to stop the use of Lepu Medical Technology Leccurate SARS-CoV-2 Antibody Rapid Test Kit (Colloidal Gold Immunochromatography) due to a high risk of false results. Although not FDA-authorized for distribution in the US, these test kits were distributed to pharmacies for at-home testing by consumers, and offered for sale directly to consumers (FDA Lepu 2021).

Note: In May 2021 the FDA released a statement that SARS-CoV-2 antibody testing should be used only for identifying individuals who have developed an adaptive immune response due to exposure to the virus. At this time antibody testing **should not be used to determine immunity or protection against the virus, including vaccine-induced antibody response.**

Related Information

- [COVID-19 Antibody \(IgG\), Quantitative, Serum or Plasma](#)
- [COVID-19 Antibody \(IgG\), Semi-quantitative, Serum or Plasma](#)
- [COVID-19 Antibody \(IgG\), Serum, Plasma, or Whole Blood](#)
- [COVID-19 Antibody \(IgM\), Serum or Plasma](#)
- [COVID-19 Antibody Total, Oral Fluid](#)
- [COVID-19 Antibody, IgG/IgM Rapid Test, Serum, Plasma, or Whole Blood](#)
- [COVID-19 Antigen, Upper Respiratory Specimen](#)
- [COVID-19 Neutralization Antibody, Serum or Plasma](#)
- [COVID-19, PCR, Respiratory Specimen](#)
- [COVID-19, PCR, Saliva](#)
- [Influenza A/B, SARS-CoV-2, Respiratory Syncytial Virus, PCR](#)
- [Influenza and SARS-CoV-2 Antigen, Upper Respiratory Specimen](#)
- [Influenza SARS-CoV-2 Multiplex Assay, PCR, CDC](#)
- [Respiratory Panel, PCR, Nasopharyngeal](#)

- T-Detect COVID Test, Whole Blood

Overview

At the end of 2019, a novel coronavirus was identified as the cause of several cases of pneumonia in Wuhan City, Hubei Province, China. Initially linked to a large seafood and animal market suggesting animal-to-human spread, person-to-person transmission was quickly confirmed (Li Q 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 400 million infections have been confirmed globally in over 200 countries and territories with over 6 million deaths ([WHO situation report 2022](#)).

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, or COVID-19**. The virus spreads by contact with respiratory fluids (droplets or aerosol) produced when an infected person exhales (eg, breathes, speaks, coughs, sneezes, or sings). These droplet/aerosol particles can be

- inhaled directly into lungs
- directly deposited on exposed mucous membranes (eyes, mouth, nose)
- transferred to mucous membranes by hands contaminated with virus-containing respiratory fluids or by indirectly touching surfaces with virus on them ([CDC SARS-CoV-2 Transmission 2021](#))

COVID-19 symptoms typically appear within 2 to 14 days (median of 5 days) of exposure and include **fever, chills, fatigue, cough, shortness of breath, myalgia, recent loss of taste or smell, vomiting or diarrhea, and/or sore throat**. 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 global fatalities around 2 to 3 percent ([WHO situation report 2021](#)). The CDC currently estimates that about 30% of COVID-19 infections are asymptomatic, and 50% of transmission occurs prior to symptom onset ([CDC Pandemic Planning 2021](#)).

Although molecular nucleic acid polymerase chain reaction tests have become the current gold standard method for diagnosis of SARS-CoV-2 infection (see [COVID-19, PCR, Respiratory Specimen](#)), there is also a need for antibody assays to assist in identifying infected patients, asymptomatic carriers, and exposed individuals, thus assuring timely treatment of patients, helping to prevent virus transmission, and determining depth of population exposure. The FDA has issued Emergency Use Authorizations (EUA) for the qualitative detection of total antibodies to SARS-CoV-2. These assays are intended for detecting individuals with an adaptive immune response to SARS-CoV-2.

Use/Indications

Aid in the identification of individuals who have been exposed and/or recovered from SARS-CoV-2 infection by identifying an immune response. Antibody assays should **not** be used to diagnose acute SARS-CoV-2 infection. It is recommended to use a viral (nucleic acid or antigen) test to diagnose acute infection ([CDC 2021 Overview of Testing](#)).

- Support diagnosis of COVID-19 illness for patients who present later in infection (≥ 7 days). Serologic testing should be offered in addition to recommended molecular testing ([CDC Interim](#)

[Guidelines 2021](#)). During this time period, the sensitivity of nucleic acid detection is decreasing, and the sensitivity of serologic testing is increasing.

- A positive antibody test in a symptomatic patient (with negative viral test) at least 7 days post symptom onset. The CDC recommends proof of seroconversion (ie, two antibody tests, a negative result on initial specimen converting to a positive result on second specimen).
- Assessment of multisystem inflammatory syndrome (in both children and adults) ([CDC Interim Guidelines 2021](#); [IDSA \[Hanson\] 2020](#)).
- Serosurveillance studies ([IDSA \[Hanson\] 2020](#)).

IgG and IgM antibodies rise (almost) simultaneously and are detectable 1 to 3 weeks post symptom onset. IgG antibodies persist longer than other antibodies. As the time between infection and antibody testing increases, assays that measure IgG and total antibody may have more sensitivity. When laboratory confirmation is needed for clinical or epidemiological purposes, the [IDSA \[Hanson\] 2020](#) recommends IgG antibody or total antibody 3 to 4 weeks after symptom onset to detect evidence of past SARS-CoV-2 infection.

Test Includes

Qualitative detection of total SARS-CoV-2 antibodies. Depending on manufacturer, this may include total IgG and IgM or total IgG, IgM, and IgA antibodies.

Contraindications

Although some individuals (23% to 63%) will develop antibodies within the first week of symptom onset, the IDSA recommends **against** serologic testing during the first two weeks (14 days) following symptom onset due to variable sensitivities and specificities of available assays ([IDSA \[Hanson\] 2020](#)).

Assessing immunity to COVID-19 following vaccination or assessing the need for vaccination in an unvaccinated person via antibody testing in **not** currently recommend ([CDC Interim Guidelines 2021](#)).

Test should **not** be used for screening of donated blood for the purpose of preventing COVID-19 transmission.

Specimen

Serum, plasma, venous whole blood, or fingerstick whole blood (manufacturer dependent)

Container(s)

- Serum separator tube or red top (no additive) tube

Alternate Container(s)

- Confer with testing laboratory for appropriate alternate container(s).
- Fingerstick whole blood may be acceptable
- Green top (lithium heparin) tube

- Green top (sodium heparin) tube
- Lavender top (EDTA) tube
- Light blue top (sodium citrate) tube

Volume / Minimum Volume

Tube filled to capacity or 1 mL blood (0.5 mL serum or plasma)

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 pre-labeled. Use computer-generated label(s), if available, to avoid transcription errors.

Routine venipuncture, using appropriate personal protective equipment; transport to laboratory immediately.

Processing and Storage

- Allow serum separator tube or red top (no additive) tube to clot completely at room temperature. Centrifuge clotted or anticoagulated specimen within 2 hours of collection and transfer serum or plasma into clean, plastic vial and refrigerate or freeze.
- Refer to manufacturer instructions.
- Whole blood specimen should be tested immediately.

Stability

- Room temperature: 8-72 hours (manufacturer dependent)
- Refrigerated: 2-7 days (manufacturer dependent)
- Frozen for longer storage: Not established to 1 month

Causes for Rejection

Incorrect specimen, follow manufacturer instructions.

Methodology

Microsphere Immunoassay (MIA) measured by fluorescence; Lateral Flow (LF); Enzyme-linked Immunosorbent Assay (ELISA) with chromogenic or electrochemiluminescence detection

Normal Values/Findings

Negative or nonreactive

All positives must be reported to local/state health departments.

Interpretative Information

Results from antibody testing should not be used as the sole basis to diagnose or rule out SARS-CoV-2 infection. Results should be used in conjunction with other data including symptoms, results of other tests, and clinical impression.

- A positive test indicates detection of antibodies to SARS-CoV-2 and is consistent with a recent or previous SARS-CoV-2 infection.
- A negative result suggests absence of detectable antibodies to SARS-CoV-2, however, this does not preclude SARS-CoV-2 infection and should not be the sole basis for patient management decisions. A negative result can occur if antibody level is below the assay limit of detection, or if antibodies are not present during disease stage in which the sample was collected (eg, too early in the infection cycle [prior to IgG seroconversion] or due to a decline in titer over time). For patients who have been in contact with known infected individuals, have been in areas with high prevalence of active infection, or are experiencing symptoms consistent with COVID-19, a molecular diagnostic test is necessary to rule out infection.
- It is important to note, as very little is known about protective immunity of SARS-CoV-2 antibodies, serology results should **not** be used to establish immunity, make staffing decisions or decisions regarding the need for personal protective equipment.

Limitations

- In patients tested too early during infection, antibody levels may be below level of detection despite active infection, thus yielding false-negative results.
- Immunocompromised patients may have a delayed antibody response to COVID-19 and produce levels of antibody below the assay level of detection.
- Viral amino acid mutations in the epitope recognized by the antibody utilized in the test can cause false negative results (Vitros 2020).
- False-positive results due to cross-reactivity may occur with other coronaviruses including common cold coronaviruses (HKU1, NL63, OC43, 229E), and SARS-CoV-1 and MERS-CoV (Platelia 2020; Dimension 2020).
- A positive result may not indicate previous SARS-CoV-2 infection. Clinical history and local disease prevalence should be considered in assessing the need for a second, but different antibody test to confirm immune response.
- The presence of heterophilic antibodies in patient specimen can interfere with immunoassay (Vitros 2020).
- Presence of biotin can interfere with assays that use biotinylated reagents (FDA New York 2020)
- Gross hemolysis (QIArearch 2021)

Diagnostic Role

Current antibody testing can help identify patients who previously had SARS-CoV-2 infection as well as patients with current infection who have had symptoms for several days to weeks. However, due to variability in detectable antibody levels in early stage disease, there is limited utility for diagnosis of acute infection with antibody testing.

Thus far, serologic correlates of protective immunity are not fully understood, but current evidence indicates that production of antibodies following SARS-CoV-2 infection confers some portion of immunity to reinfection for at least three to six months ([CDC Interim Guidelines 2021](#); Lumley 2021; Hall 2020). The robustness and durability of natural-infection immunity, how it compares to vaccine-induced immunity, and the impact of emerging viral variants are currently unknown and under study.

Because SARS-CoV-2 infection can be asymptomatic or minimally symptomatic, the official tally of actual infections is probably substantially underestimated. Large-scale serologic screening with validated tests may be able to provide a better measure of disease activity.

Laboratory/Diagnostic Pearls

- Antibodies to SARS-CoV-2, typically detected 1 to 3 weeks post symptom onset, have been reported in patients with mild and severe disease. The antibody response is more robust (higher titers and longer persistence) in those with severe disease (Rijkers 2020). How long the antibodies persist after infection is unknown but they appear to persist for several months in most (Dan 2021).
- 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). Warmer temperatures and exposure to sunlight reduces viral survival time ([CDC Environment 2020](#)).

Additional Information

The major antigenic targets of SARS-CoV-2 virus that induce antibody response are:

1. Spike glycoprotein (S) which is responsible for receptor binding and membrane fusion for viral entry into the host cell.
2. Nucleocapsid phosphoprotein (N), an immunodominant antigen (or protein) of the CoV family that interacts with RNA.

For more information, interim guidance has been issued by the United States [CDC](#) and the [World Health Organization](#).

See: [Interim Guidelines for COVID-19 Antibody Testing](#)

See: [Guidance for Healthcare Workers about COVID-19 \(SARS-CoV-2\) Testing](#)

See: [Information for Laboratories](#)

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

See: FDA [Emergency Use Authorizations](#)

Index Terms

COVID Antibody Test; COVID-19 Antibodies; COVID-19 Antibody Test; SARS-CoV-2 Antibodies; Total Antibodies, COVID-19

Applies to

ADVIA Centaur SARS-CoV-2 Total (COV2T), Siemens; Atellica IM SARS-CoV-2 Total (COV2T), Siemens; COVID-19 ELISA pan-Ig Antibody Test, University of Arizona; cPass SARS-CoV-2 Neutralization Antibody Detection Kit, Genscript; Dimension EXL SARS-CoV-2 Total antibody assay (CV2T), Siemens; Dimension Vista SARS-CoV-2 Total antibody assay (COV2T), Siemens; Elecsys Anti-SARS-CoV-2 S, Roche; Elecsys Anti-SARS-CoV-2, Roche; FRENDOVID COVID-19 total Ab, NanoEntek America, Inc.; Maverick SARS-CoV-2 Multi-Antigen Serology Panel v2, Genalyte Inc.; MosaiQ COVID-19 Antibody Magazine, Quotient Suisse SA; New York SARS-CoV Microsphere Immunoassay for Antibody Detection, Wadsworth Center; OmniPATH COVID-19 Total Antibody ELISA Test, Thermo Fischer Scientific; Pandemic; Platelia SARS-CoV-2 Total Ab assay, Bio-Rad; Pneumonia of Unknown Etiology; VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack, Ortho; WANTAI SARS-CoV-2 Ab ELISA, Beijing; WANTAI SARS-CoV-2 Ab Rapid Test, Beijing

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