Coronavirus Disease (COVID-19) Antibody Total Serum or Plasma (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) Serum or Plasma
- Coronavirus Disease (COVID-19) Antibody, IgG/IgM Rapid Test, Whole Blood, Serum, or Plasma
- Coronavirus Disease (COVID-19) Antigen, Upper Respiratory Specimen
- Coronavirus Disease (COVID-19), PCR, Respiratory Specimen
- Coronavirus Disease (COVID-19), PCR, Saliva
- Influenza SARS-CoV-2 Multiplex Assay, CDC

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 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 42 million infections have been confirmed globally in over 200 countries and territories with over 1.1 million 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, 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 3 percent (WHO situation rept 2020). The CDC currently estimates that about 40% of COVID-19 infections are asymptomatic, and 50% of transmission occurs prior to symptom onset (CDC Pandemic Planning 2020). Currently, there is no vaccine or specific treatment; care is supportive.

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 recently 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 2020 Overview of Testing).

- Support diagnosis of acute COVID-19 illness for patients who present later in infection (9 to 14 days post symptom onset). Serologic testing should be offered in addition to recommended molecular testing (CDC Interim Guidelines 2020). During this time period, the sensitivity of nucleic acid detection is decreasing, and the sensitivity of serologic testing is increasing.
- Assessment of multisystem inflammatory syndrome in children (CDC Interim Guidelines 2020; IDSA 2020).
- Serosurveillance studies (IDSA 2020).

Currently, there is no identified advantage of assays whether they test for IgG, IgM and IgG, or total antibody (CDC 2020 Antibody Testing), however; when laboratory confirmation is needed for clinical or epidemiological purposes, the IDSA 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

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

Specimen

Serum or plasma

Container(s)

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

Alternate Container(s)

- Confer with testing laboratory for appropriate alternate container(s).

- 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 prelabeled. 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.

Stability

- Room temperature: 8-72 hours (manufacturer dependent)
- Refrigerated: 2-7 days (manufacturer dependent)
- Frozen: Not established

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 patient has been exposed to the virus.
- A negative result may indicate absence of antibodies to SARS-CoV-2, or antibody level is below the assay limit of detection. 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).
- The presence of heterophilic antibodies in patient specimen can interfere with immunoassay (Vitros 2020).

Diagnostic Role

Understanding the antibody response to SARS-CoV-2 is still in the early stages and clinical utility is not completely established. When more information is acquired, the potential of serology testing may include:

- Testing of PCR-negative cases when patient presents late and the viral load has decreased; or when lower respiratory tract sampling is not possible
- Identification of convalescent plasma donors
- Studies of community disease prevalence
- Possible verification of vaccine response (IDSA 2020 Ab Testing Primer)

Note: At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

Laboratory/Diagnostic Pearls

- Severe Acute Respiratory Syndrome (SARS) was identified in 2003 and Middle East Respiratory Syndrome (MERS) was identified in 2012. As these syndromes are also caused by viruses in the coronavirus family, researchers are incorporating information learned from these previous infections to aid in understanding SARS-CoV-2.
- Although more information is needed to determine a definite seroconversion window, in a study of 173 Chinese patients, the median seroconversion time for IgM and IgG antibodies, after symptom onset, was 12 days and 14 days respectively (Zhao 2020). In the first week after symptom onset, fewer than 40 percent had detectable antibodies; by day 15, IgM and IgG were detectable in 94 and 80 percent, respectively. **Note:** The CDC is currently reporting 1 to 3 weeks after symptoms appear for detection of SARS-CoV-2 antibodies (CDC, Serology 2020). Further information/studies are needed for a firm seroconversion window.
- Antibodies to SARS-CoV-2 are unusual in that IgM and IgG antibodies rise almost simultaneously within 2 to 3 weeks after symptom onset. The detection of IgM without IgG is uncommon (CDC 2020 Antibody Testing).
- 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).

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: Information for Laboratories

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

See: COVID-19 Testing and Reporting by Laboratories: Q & A

See: For Healthcare Professionals

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

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

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