



## Diagnosics and Serology

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### Diagnosics

Shortly after reports of the SARS-CoV-2 virus spreading in human populations, [scientists](#) sequenced its RNA genome, identified the human receptor for the virus, and developed both PCR- and antibody-based tests for viral infection and the human immune response.

Rapid, [widespread](#), and [easily accessible testing](#) is [necessary](#) to limit the spread of COVID-19 after an initial peak of viral spread has been contained. To minimize viral spread, various models for contact tracing of positive cases and government-supported quarantine have been developed in [Germany](#), [South Korea](#), [China](#), [Taiwan](#), [Singapore](#), and elsewhere.

All of these measures require a state-supported scaling of testing capacity to ensure individuals positive for COVID-19 can be [rapidly isolated to prevent viral spread](#). [Two types of test \(acute/diagnostic and serological\)](#) offer different information about infection and immunity, and both should be deployed at population scale before social distancing is significantly reduced.

The standard diagnostic test for SARS-CoV-2 infection requires in-laboratory amplification of genetic material from the virus. More recently, rapid and inexpensive point-of-care tests, both for viral protein/antigen and viral RNA fragments, have been [granted Emergency Use Authorizations \(EUA\)](#) by the FDA.

### COVID-19 qPCR test (RT-PCR; qRT-PCR)

[PCR-based COVID-19 tests](#) use amplification of the viral RNA genome to determine whether a patient is currently infected with SARS-CoV-2. PCR – [Polymerase Chain Reaction](#) – is a widely used molecular technique that uses short sequences of DNA and heating and cooling of a chemical reaction to detect even miniscule amounts of DNA or RNA in a sample. Clinical labs [use primers against three regions](#) of the viral RNA genome to determine a positive test. [National labs, public health departments, and even individual](#)

[clinical labs](#) have developed their own PCR-based tests using unique primer sequences optimized for their particular lab setup.

Many individuals who have recently recovered and who are no longer shedding infectious virus [may also test positive for COVID-19 based on a PCR-based test](#). Some PCR-tests have been reported to have a high [false-negative rate](#) – up to [30% or more](#) later in acute infection – making a single negative result by PCR an [imperfect tool alone to identify COVID-19 infections](#).

Widespread qPCR-based remains an essential tool to identify current COVID-19 infections in order to quarantine the individual and isolate close contacts.

### **COVID-19 serology test (antibody test, ELISA test)**

Serology tests (also called antibody tests, ELISA-based tests, and lateral flow assays) determine whether an individual has [seroconverted during or following an infection with SARS-CoV-2](#). [ELISA and lateral flow assays](#) use various biochemical methods to detect the presence or absence of a protein in the blood, serum, or urine, such as an antibody in the case of infectious disease or [human chorionic gonadotropin](#) in the case of pregnancy tests.

During an active [viral infection](#), the patient's [adaptive immune system](#) rapidly mounts a humoral response [specific to the infectious agent](#). As a part of this response, [highly specific antibodies](#) become detectable in a patient's serum. These antibodies are [both a marker that someone has been infected](#) and a primary mechanism of [recognizing and eliminating the virus](#) upon attempted reinfection.

While infected [patients can seroconvert for IgM within days of a new COVID-19 infection](#), serology tests are not a good tool to detect an active COVID-19 infection. IgG, a class of antibody that B-cells secrete later in infection, [can both be maintained and provide at least some immunity for the life of an individual](#). Therefore, serology based tests may accurately determine whether an individual has ever been infected by a viral pathogen such as SARS-CoV-2.

Scientists do not yet know the [duration, quality, and population dynamics of protective immunity against SARS-CoV-2](#) (whether an infected individual can be re-infected and whether a vaccine will provide no, short term, or long term protection against COVID-19). Serology assays, done on a subset of COVID-19 patients during and long after infection, will clarify this critical question.

Serology tests are an essential component in our understanding of the COVID-19 pathology and immune response, both short and long term. These tests may also be a

crucial tool in determining which individuals can more safely return to work, including in higher-risk professions such as hospital intensive care units.

### **Point of Care COVID-19 Testing**

Both COVID-19 serology test and RT-PCR tests typically require experimentation (ELISA and RNA extraction follow by qPCR respectively) and analysis by clinical laboratories. The disadvantage of these tests is that, as demand increases, the [turnaround time for testing](#) in the United States has at times [been a week or more](#). Because the typical course of COVID-19 infection is [seven to fourteen days](#), delays in testing negate the usefulness of the test. Furthermore, individuals typically have to return to a patient portal to receive their results, and positive individuals may be disconnected from further care and support.

To address these shortcomings, several companies have developed rapid tests that can be given directly in a healthcare setting, with the results available within minutes and able to be interpreted directly by a clinician.

**Antigen tests** detect viral proteins (antigens) directly. Currently, Becton, Dickinson and Company ([BD Veritor](#)) and the Quidel Corporation ([Sofia SARS Antigen FIA](#)) have EUAs from the FDA. These tests use [lateral flow assay strips](#), similar to those used in at-home pregnancy tests, to identify viral proteins by binding them to antibody-conjugated lines on the test strip. Both of these tests report [high specificity](#) but a [lower sensitivity](#) than the laboratory based qPCR tests described above.

Point of care tests to amplify and identify **viral RNA** are also both currently in use and at various stages of product development. These tests use various methods of RNA amplification and detection, most typically LAMP to amplify RNA and then a color-based or CRISPR/Cas9 based method to detect amplified DNA. Currently, [Cue Health](#) and [Accula](#) have received EUAs from the FDA for rapid, point of care COVID-19 RNA tests. The [manufacturers' data](#) show [lower sensitivity](#) than the laboratory-based RNA detection assays, but a high specificity.