

What types of diagnostic tests exist to detect COVID-19?

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with additional sections on antigen testing
and clarification of some concepts.

A critical element for combatting the COVID-19 pandemic is to have suitable diagnostic tests available.

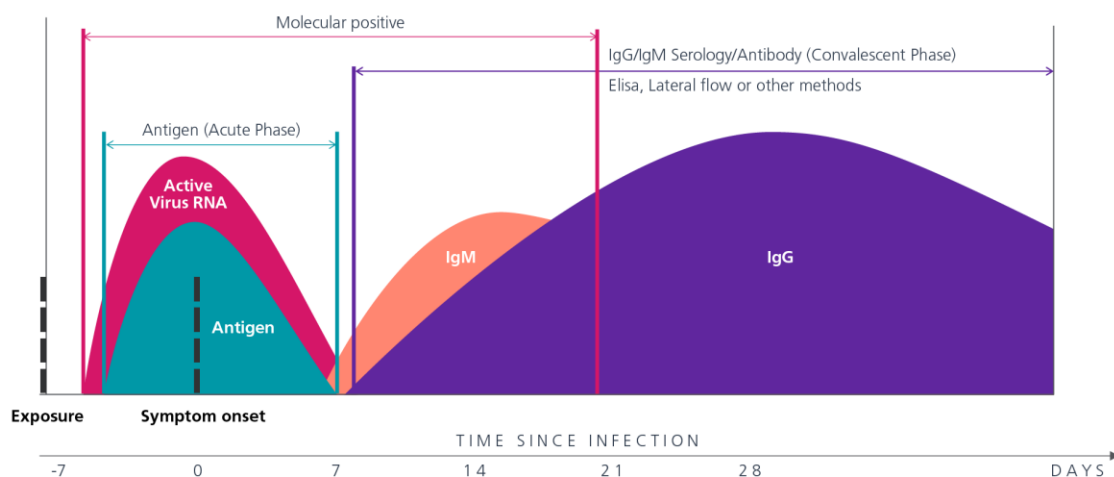
There are generally two different types of tests used to detect the presence of the virus:

- I. **Molecular based COVID-19 tests:** these tests detect the presence of the virus (viral RNA) but do not detect if you have previously been in contact with the virus.
- II. **Antigen detection based COVID-19 tests:** these tests detect the presence of viral antigen (proteins) but do not detect if you have previously been in contact with the virus.

And one type of test used to detect the immune response to the virus:

- III. **Serology tests for COVID-19 (Antibody tests):** these tests detect the immune response against the virus (production of antibodies - IgG and IgM), meaning that the person has previously been in contact with the virus.

The graph below illustrates the evolution of the various markers (viral RNA, Antigens, Antibodies) of COVID-19. This is based on the typical viral load evolution and patient response based on the present knowledge about SARS-CoV2.



COVID-19 timelines are not yet precisely and completely documented, especially for antigens.

Testing of these markers can take place in different settings:

- **Laboratory testing**

Testing that takes place in a specialised laboratory with specific infrastructure, equipment, and trained personnel.

- **Point-of-care (POC) or near-patient testing**

Testing that takes place at the time of the consultation with the results made available in a short time (from few minutes to generally less than one hour). The tests provide immediate information to help make decisions about patient care. Tests can be performed at the bedside or near the patient. In broad terms, POC testing is performed in a healthcare setting that is not the laboratory. These settings can be, for example, in emergency departments, urgent care clinics, general practitioner's offices, or mobile care units. COVID-19 specific locations for POC testing depend on local regulations.

What are rapid tests?

These tests are used singly or in small series and involve simple procedures. Devices validated to run these types of tests have been designed to give a fast result (in less than 1 hour). They may be intended either for use in laboratories or in point-of-care settings.

For laboratory testing and POC testing, all the steps from sampling to interpretation of the result are performed by healthcare professionals.

- **Self-sampling**

Self-sampling implies the possibility for patients to collect the sample themselves. The sample can then be sent to a laboratory for central testing or be tested by the patients themselves, in a case where a test is classified as a self-test.

- **Self-testing**

Self-testing is performed with a device intended to be used by anyone even without formal healthcare or medical experience in their own environment, such as their homes. (e.g. pregnancy test, blood glucose monitoring...). At the time this document was produced, there are very few COVID-19 tests for self-testing and none yet approved for use in Europe.

It is important to mention that the possibility for self-sampling or self-testing depends on local regulations.

I. Molecular based COVID-19 Tests

A. What are molecular based COVID-19 tests?

Molecular based COVID-19 tests work with a sample commonly taken from a person's **nose or back of the throat**.

A molecular test is a highly sensitive and specific technique. The tests allow for testing people at an early stage of the infection. They also allow, when performed in laboratories in larger populations, for assumptions about the spread of the virus in a whole population. These tests provide authorities important information for case confirmation and isolation guidance in order to guide measures to protect the people.

B. How do molecular tests work?

The tests look at a specific viral genetic material showing the presence of the virus in the body.

C. Where are these molecular tests performed?

The first step of taking a sample (usually using a nasopharyngeal swab) can be taken anywhere, if the medical staff is well protected by using 'personal protective equipment' (PPEs).

The preparation and analysis of the swabs is usually happening in specialised and approved laboratories by large, immobile molecular machines.

There are also new 'point-of-care' molecular tests. Those can be performed with mobile devices in clinics, doctors' offices, or even mobile drive-in sites.

One main difference between laboratory and point-of-care molecular-tests is the throughput: laboratory tests allow to process hundreds to thousands of samples per day on automated instruments having a footprint of several square meters; point-of-care tests and the corresponding printer-size instruments are suited for running small batches or individual samples at a time.

D. Components and accessories of COVID-19 molecular tests:

- Nasal, nasopharyngeal (NP) or throat swabs (specific long Q-tip style equipment)
- Personal protective equipment for the medical staff taking and processing the swabs
- Dependent on the platform (laboratory-based or point-of-care), additional external reagent may be needed, as extraction reagents.
- Molecular testing reagents including quality controls
- Molecular testing equipment

Increasing demand for testing implies that in addition to scaling up production capacities for tests, third parties' components and accessories are also needed in larger quantities. A shortage of any of these materials would jeopardise the production capacity.

Furthermore, the laboratory capacity, namely the available amount of staff and molecular equipment in the territories are another determinant for the number of tests that could be performed at a given amount of time.

II. Antigen based COVID-19 Tests

A. What are antigen based COVID-19 tests?

Diagnostic tests detecting the presence or the absence of proteins of the virus, called antigens.

B. How do antigen based tests work?

The tests detect a specific viral protein material showing the presence of the virus in the body. A variety of different sample types (e.g. blood, saliva, faeces) can be used for antigen testing.

C. Where are antigen based tests performed?

These tests are generally performed at near patient or community care testing. Most of the antigen based tests developed so far are point-of-care tests.

The first step of taking a sample can be taken anywhere. The medical staff taking the sample must be well protected with 'personal protective equipment' (PPEs).

The preparation and analysis of the samples depend on local regulations but are usually done by healthcare professionals and can take place on mobile units in emergency wards, clinics and doctors' offices.

Antigen tests could be developed and validated for self-testing.

D. Components and accessories of COVID-19 antigen based tests:

- According to the technology used: swabs, blood samples or other biological fluid collectors.
- Personal protective equipment for the medical staff taking the samples
- According to the platform (laboratory-based or point-of-care), additional external reagent may be needed.
- Antigen testing reagents including quality controls
- Antigen testing equipment

III. Serology tests for COVID-19

A. What are serology tests for COVID-19?

Serology tests for COVID-19 generally are performed on blood samples (venous, capillary or serum). The test detects if a person has developed antibodies against SARS-CoV-2. The presence of antibodies and the correlation with acquired immunity, i.e. if a person is protected against a reinfection, is still subject to medical and scientific research at the time of the publication of this paper.

These tests are useful at a later stage of an infection since antibodies need around 5-14 days (IgM and/or IgG) to develop and be detectable in the blood and hence have little diagnostic value. In a few cases when a molecular assay is negative while clinical presentations suggest a potential COVID-19 infection, then serology tests can be used as complementary diagnostic tools.

When performed in large portions of a population, these tests could also provide important information on the diffusion of the infection in the population and could therefore guide authorities in their efforts to ease social distancing measures appropriately.

B. How do serology tests work?

Serology tests, also called immunoassays or antibody tests, come in many different formats and variants. Some immunoassays consist of multiple steps with various reagents being added and washed away or separated at different time points in the assay.

Serology tests detect the presence of antibodies, called IgG and IgM, in the blood. Presence of IgM only suggests that the person is in the early stage of the infection. Presence of both IgM and IgG (which develop later during the course of infection) suggest that the patient is in a later stage of the disease, whereas IgG only is present during the recovering phase, and should stay positive for months and possibly years depending on the virus.

Some serological tests give a qualitative result only (positive or negative) indicating if the person has developed antibodies against the virus or not; others can quantify the level of antibodies which may be correlated with a “level of immunity”.

Serology tests will also play a major role in vaccine development. Once vaccination will be available, they might also have an important role in monitoring pre and post vaccinal immunity.

For a serology test, the accuracy level is important. It is defined by its sensitivity (ability to detect infected people) and its specificity (limiting false positives). A good sensitivity means no or very few false negative results, a good specificity means no or very few false positive results.

C. Where are these tests performed?

The first step of taking a blood sample can be performed anywhere, if the medical staff is well protected by using 'personal protective equipment' (PPEs).

The preparation and analysis of the blood sample is performed in clinical laboratories on large automated systems.

There are also 'point-of-care' serology tests. Those can be performed with mobile hand-held devices in clinics, doctors' offices or even mobile drive-in sites.

One main difference between laboratory and point-of-care molecular-tests is the throughput: laboratory tests allow to process hundreds to thousands of samples per day on automated instruments having a footprint of several square meters; point-of-care tests and the corresponding printer-size instruments are suited for running small batches or individual samples at a time.

D. Components and accessories of COVID-19 serology tests:

- According to the technology used: lancet or blood sample collectors
- Personal protective equipment for the medical staff taking the blood samples
- According to the platform (laboratory-based or point-of-care), additional external reagent may be needed.
- Serology testing reagents including quality controls
- Serology testing machines

IV. Safety and performance of COVID-19 tests

All COVID-19 tests today must adhere to strict regulatory procedures before they get to the market. These laws establish the essential requirements for safety and performance of diagnostic tests. At the same time, market surveillance mechanisms are set-up to ensure that products are further monitored once they are in the market.

It is crucial, more than ever, that requirements and procedures set by the laws are followed. This ensures that reliable and accurate tests are deployed in the battle against the COVID-19 pandemic.

At the same time, COVID-19 tests must be purchased from reliable diagnostic tests producers. It is recommended that prior to purchasing tests, all safety and performance information must be obtained, analysed, and properly taken into account.

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