Etiological confirmation of COVID-19 virus (SARS-CoV-2) infection can only be made by laboratory tests. In general, the currently available assays for COVID-19 can be classified into two groups:

- The first group (virological tests) includes tests that can detect the presence of the components of the virus (genetic material or antigens). These tests can confirm the diagnosis of patients with symptoms compatible with COVID-19, detect infections in populations with high-risk of infection (such as health workers) or severity (hypertension, diabetes, obesity, cardiovascular history, chronic respiratory, immunosuppression, cancer, etc.), and assess whether an individual recovered from COVID-19 may still be infectious.
- The second group of tests (serological) detect antibodies (IgM or IgG) generated as part of the individual's immune response against the SARS-CoV-2 virus, that is, they indicate previous or ongoing contact. The immunity (protection) conferred by the antibodies is still under investigation. Once sufficient evidence is available, serological tests would be, together with direct virus detection, an essential tool in the development of strategies that allow relaxation of current public health measures.

The appropriate interpretation of the results obtained in any type of assay must be carried out carefully and considering the dynamics of the infection (when is the sample collected and the quality of this sample) and the objective for which a sample is taken (diagnosis, seroprevalence, etc.).

1. Interpretation of results in COVID-19 symptomatic cases

Molecular detection:

The diagnostic confirmation of COVID-19 is based on the molecular detection of the viral genome (RNA detection by PCR) or of its proteins (antigens). Although the dynamics of the infection including viral secretion in different fluids is still under study, to date it has been possible to establish that the virus can be detected from at least 48 hours before the onset of symptoms (pre-symptomatic cases) and up to 12-14 days (at least 6-7 days) after, in samples from the upper respiratory tract (naso/oropharyngeal swabs) and up to 20 days (or more) in samples from the lower respiratory tract including sputum, tracheal aspirate, bronchioalveolar lavage, etc. (Figure1).
Serological detection:

Since antibodies (IgM / IgG) against the virus are detectable around day 7 from the onset of symptoms (in approximately 50% of cases), a negative serology result during the first 7 days of illness cannot be used as a rule out criterion. Although the sensitivity of antibody detection increases after day 7, a negative serology result after day 7 should be carefully interpreted before ruling out a case (Figure 2).

On the other hand, a positive result between days 7 to 14 indicates a previous contact and does not rule out the presence of the virus. For this reason, serology alone should not be used as a criterion to rule out a case or to consider the patient as non-infectious. Likewise, a patient who has had previous contact with the virus but who later becomes infected with another circulating pathogen that generates respiratory symptoms (influenza or another pathogen), may present to a clinical consult and a positive result for COVID-19 antibodies would lead to a wrong diagnosis; for this reason, the use of serology (by itself) to confirm a case must be carefully evaluated.
2. Interpretation of results in contacts of COVID-19 symptomatic cases

In an individual identified as a contact of a confirmed case, the added value of conducting laboratory testing should be evaluated, keeping in mind that regardless of the result, the recommendation for the contact is at least 14 days of quarantine (from the day of last contact with the case).

If a molecular assay (PCR) is performed, a negative result does not rule out previous contact, nor the possibility that the contact is in the incubation period. Regardless of the test result, the contact would have to be quarantined. Likewise, if a positive result is obtained by molecular diagnosis (PCR), the case is an asymptomatic or pre-symptomatic case, and must be isolated regardless.

On the other hand, a positive antibody result only indicates previous contact with the virus but does not rule out nor it confirms an active infection; that is, it does not allow to rule out or confirm the presence of the virus (Figure 3).
3. Interpretation of results in asymptomatic individuals

In an asymptomatic individual, since there is no date that can be used as a reference, a negative molecular assay (PCR) result can occur because the amount of virus is not sufficient to be detected, because the individual is in the post-infection period, or simply because the individual has never been infected. Thus, a negative result does not rule out a possible infection (Figure 4). If as part of an active surveillance (health workers, caregivers in nursing homes, etc.) a positive result is obtained by molecular detection, the result constitutes an asymptomatic case and the individual should be isolated.

An asymptomatic individual may have a small amount of virus and antibodies will most likely be generated from contact with the virus. For this reason, although a positive serological test in healthy individuals indicates previous contact, it does not allow inferring the moment of contact. Some individuals develop IgM antibodies very late after contact and it is not yet clear for how long these antibodies can be detected. Likewise, IgG levels may increase at the same time as IgM levels, so detection of both antibodies at the same time or detection of only one of them (IgM or IgG) is not an adequate criterion to define the time of possible contact. Furthermore, there is insufficient evidence to ensure that the detected antibodies are actually protective or for how long they could be. The use of serology in these cases will be for research purposes or to determine seroprevalence in a given population, but they should not be used as the sole diagnostic criterion.
Figure 4

Asymptomatic

IgM

IgG

Fading of the IgM (??)

Days of contact...???
References