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Commentary

Diagnostic Tests for SARS-CoV-2 and Not for COVID-19: Trying to Uncomplicate

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Dear reader, this informative article aims to spread the science of COVID-19 in a more accessible way for those who are not used to its jargons. Despite the colloquial vocabulary in this manuscript, many of the technical terms already widely seen in the media will be used here in order to further clarify. We understand that knowledge is the light that allows people to choose the most coherent path to follow, including with regard to individual and collective security measures in the battle against COVID-19.

- What are the diagnostic tests for SARS-CoV-2 for?
- To inform whether the individual has COVID-19.

The seemingly correct answer above is fragile for two reasons. First, because not every individual infected with SARS-CoV-2 has or will have COVID-19, which is a disease caused by that virus (COVID-19 = Corona Virus Disease 2019). So, already at this point, we have the opportunity to address something important, the infection by SARS-CoV-2 does not necessarily lead to the disease, COVID-19. So, we can establish now the famous concept of the asymptomatic individual, the one who has the virus, but no symptoms. They are not sick but they can get sick and also transmit the virus to other people. It is believed that there is a strong and direct relationship between the viral load (the amount of virus) and the destination of the infection, ranging from asymptomatic, mild, and moderate to severe. It is also believed that the viral load is closely related to the potential of transmission.

The other reason refers to the fact that the available tests can show the presence of the virus (antigens or genetic material) or specific antibodies against the virus but not the presence of the disease, what is a clinical condition mostly characterized by signs and symptoms. The symptoms, if respiratory, are mainly identified by imaging resources (chest X-ray and chest computed tomography) and also by the patient's loss of smell and taste complaints, which are the most specific symptoms. It is then appropriate to discuss the terms presented before addressing the function of the tests.

Regarding the term antibodies, also called immunoglobulins, they are proteins produced by a type of cell in our immune system, the plasmocytes. These antibodies have the property of interacting with specific particles called antigens. Therefore, antibodies interact with viral antigens and help us defend against the virus.

There are different types of antibodies, but the most important ones for our understanding are the immunoglobulins A (IgA), immunoglobulins M (IgM) and immunoglobulins G (IgG). They are present in different amounts according to the time of the infection, being markers of the time of infection, not informing about the existence or not existence of disease though. In this sense, it is important to know that IgA and IgM are found in greater concentration in the mucous membranes and in the blood, respectively. IgA and IgM in the initial phase of the infection while IgG in the chronic or late phase. The detection of these antibodies is carried out by means of a serological test using the ELISA technique (Enzyme-Linked ImmunoSorbent Assay) or other immunoenzymatic techniques, which use the patient's serum

extracted from his blood and a specific kit of chemical solutions. When positive, the technique does not inform whether the individual has the virus or not, at some point he/she has had the virus instead but somehow managed to build an immune response against it. That does not mean he/ she is not infected any longer or is that defense capable of solving the high inflammatory response generated by COVID-19, which has been the main cause of its complications.

Interestingly, it is known that some individuals do not show the formation of these proteins, even if they were exposed to infection or positive results were obtained in the search for antigens or the genetic material of the virus through specific tests. It all demonstrates that we are still learning about this viral infection and its consequences.

After being given the possibility of verifying the presence of the virus in situ, it is the perfect time to address the concept of RT-PCR, or Reverse Transcriptase - Polymerase Chain Reaction, a method that detects the presence of the virus genetic material by expanding the number copies of that genetic material to facilitate its detection.

The genetic material of this virus is formed by the simple strand of positive RNA, which means that it has the ability to be translated / used in our cells to produce structural and non-structural viral proteins directly, forming new viruses.

In this context, it is worth mentioning that viral genetic metabolism does not use the host cell's DNA, that is, it does not promote any changes in our cells, so it is not worth saying that vaccines that use this technology can trigger mutations in our genetic material.

During the RT-PCR operation there is an amplification of the genetic material that is sought, therefore, if there is no genetic material available, the result will be negative for SARS-CoV-2. False negative results can be obtained in this method due to the low concentration of genetic material obtained in a sample collected by the nasal swab. When the number copies of the genetic material is below the limit of sensitivity of the technique, the result is negative but the patient is infected. That is what we call false negative. In this sense, we can highlight that there are kits with high capacity of detecting only 2 strands of viral RNA in a nasal swab sample. Thus, the values of sensitivity and specificities of laboratory tests, not only for RT-PCR, but also for antigen or antibody research, should be informed to customers for a better choice and interpretation of the effectiveness of the method used by the laboratory.

Another available technique is the antigen research, which like RT-PCR, investigates the presence of viral structures in the patient's sample (nasal swab). It is based on the use of standardized and labeled antibodies. They have high specificity, but the sensitivity tends to be lower than in RT-PCR, especially in the early stages of the infection.

There are also rapid tests to detect antibodies in high concentration in the blood circulation, although they are tests with low sensitivity.

Getting back to the question:

- What are the diagnostic tests for SARS-CoV-2 for?

We believe that it is now possible to answer the question in a more appropriate way:

1. The Antigen Test or the RT-PCR Test can identify whether the individual has SARS-CoV-2

2. Rapid tests found in pharmacies or serological investigation using the ELISA method can inform that the individual has had contact with the virus or still has it, and also the stage of the immune response: acute (initial - IgA and IgM) or chronic (late - IgG).

We hope to have been able to clarify some of the obscure points about the available tests used during the Pandemic for those who are not closely related to the daily life of health technologies.

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