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Interpretación de Resultados de exámenes de SARS-Cov-2

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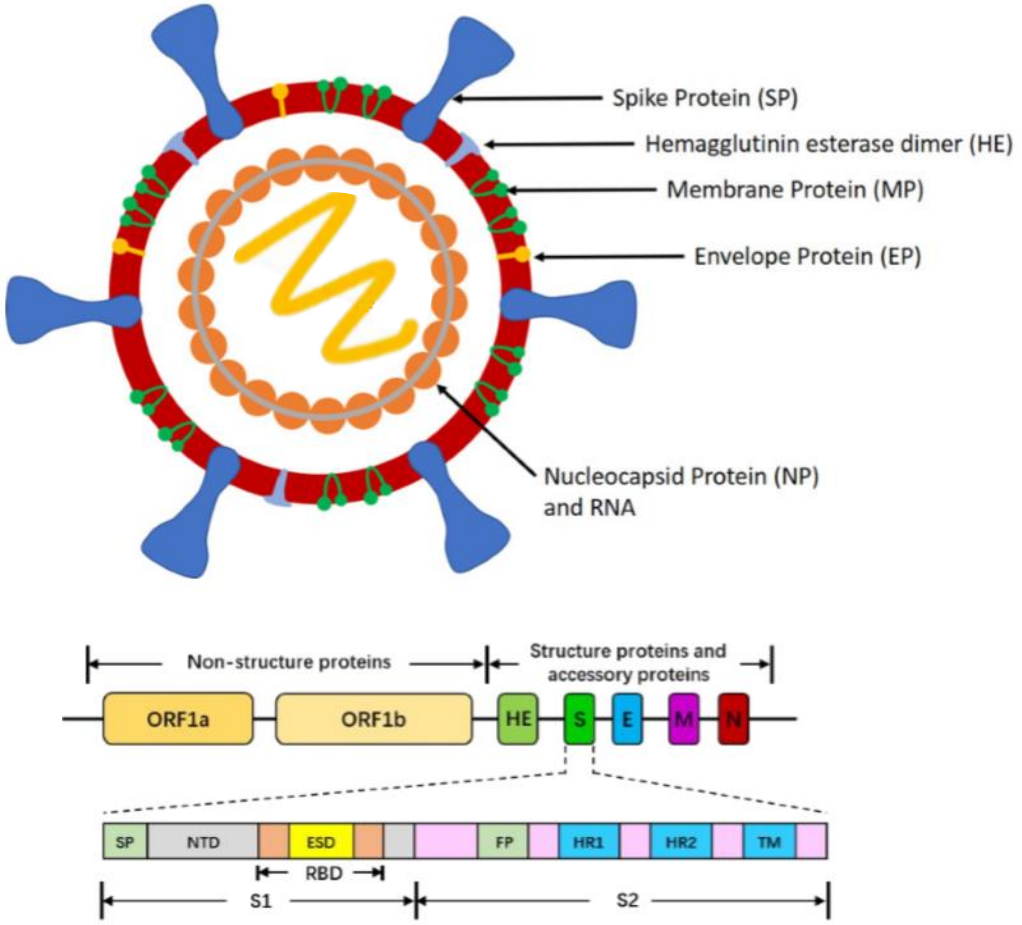
SARS-CoV-2: Estructura

- Varios tipos de Coronavirus la mayoría producen cuadros de resfrío común
- Brote actual es por el SARS-Cov-2 que viene de *severe acute respiratory syndrome*
- Virus RNA, envoltura lipídica, proteínas de membrana, glicoproteínas.



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VIEWPOINT

Interpreting Diagnostic Tests for SARS-CoV-2

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The pandemic of coronavirus disease 2019 (COVID-19) continues to affect much of the world. Knowledge of diagnostic tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is still evolving, and a clear understanding of the nature of the tests and interpretation of their findings is important. This Viewpoint describes how to interpret 2 types of diagnostic tests commonly in use for SARS-CoV-2 infections—reverse transcriptase–polymerase chain reaction (RT-PCR) and IgM and IgG enzyme-linked immunosorbent assay (ELISA)—and how the results may vary over time (Figure).

Detection of Viral RNA by RT-PCR

Thus far, the most commonly used and reliable test for diagnosis of COVID-19 has been the RT-PCR test performed using nasopharyngeal swabs or other upper respiratory tract specimens, including throat swab or, more recently, saliva. A variety of RNA gene targets are used by different manufacturers, with most tests targeting 1 or more of the envelope (*env*), nucleocapsid (*N*), spike (*S*), RNA-dependent RNA polymerase (*RdRp*), and *ORF1* genes. The sensitivities of the tests to individual genes are comparable according to comparison studies except the RdRp-SARSr (Charité) primer probe, which has a slightly lower sensitivity likely due to a mismatch in the reverse primer.[1]

In most individuals with symptomatic COVID-19 infection, viral RNA in the nasopharyngeal swab as measured by the cycle threshold (Ct) becomes detectable as early as day 1 of symptoms and peaks within the first week of symptom onset. The Ct is the number of replication cycles required to produce a fluorescent signal, with lower Ct values representing higher viral RNA loads. A Ct value less than 40 is clinically reported as PCR positive. This positivity starts to decline by week 3 and subsequently becomes undetectable. However, the Ct values obtained in severely ill hospitalized patients are lower than the Ct values of mild cases, and PCR positivity may persist beyond 3 weeks after illness onset when most mild cases will yield a negative result.[2] However, a "positive" PCR result reflects only the detection of viral RNA and does not necessarily indicate presence of viable virus.[3]

In some cases, viral RNA has been detected by RT-PCR even beyond week 6 following the first positive test. A few cases have also been reported positive after 2 consecutive negative PCR tests performed 24 hours apart. It is unclear if this is a testing error, reinfection, or reactivation. In a study of 9 patients, attempts to isolate the virus in culture were not successful beyond day 8 of illness onset, which correlates with the decline of infectivity beyond the first week.[3] That is in part why the "symptom-based strategy" of the Centers for Disease Control and Prevention (CDC) indicates that health care workers can return to work, if "at least 3 days (72 hours) have passed since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath); and, at least 10 days have passed since symptoms first appeared."[4]

The timeline of PCR positivity is different in specimens other than nasopharyngeal swab. PCR positivity declines more slowly in sputum and may still be positive after nasopharyngeal swabs are negative.[3] In one study, PCR positivity in stool was observed in 55 of 96 (57%) infected patients and remained positive in stool beyond nasopharyngeal swab by a median of 4 to 11 days, but was unrelated to clinical severity.[2] Persistence of PCR in sputum and stool was found to be similar as assessed by Wölfel et al.[3]

In a study of 205 patients with confirmed COVID-19 infection, RT-PCR positivity was highest in bronchoalveolar lavage specimens (93%), followed by sputum (72%), nasal swab (63%), and pharyngeal swab (32%).[5] False-negative results mainly occurred due to inappropriate timing of sample collection in relation to illness onset and deficiency in sampling technique, especially of nasopharyngeal swabs. Specificity of most of the RT-PCR tests is 100% because the primer design is specific to the genome sequence of SARS-CoV-2. Occasional false-positive results may occur due to technical errors and reagent contamination.

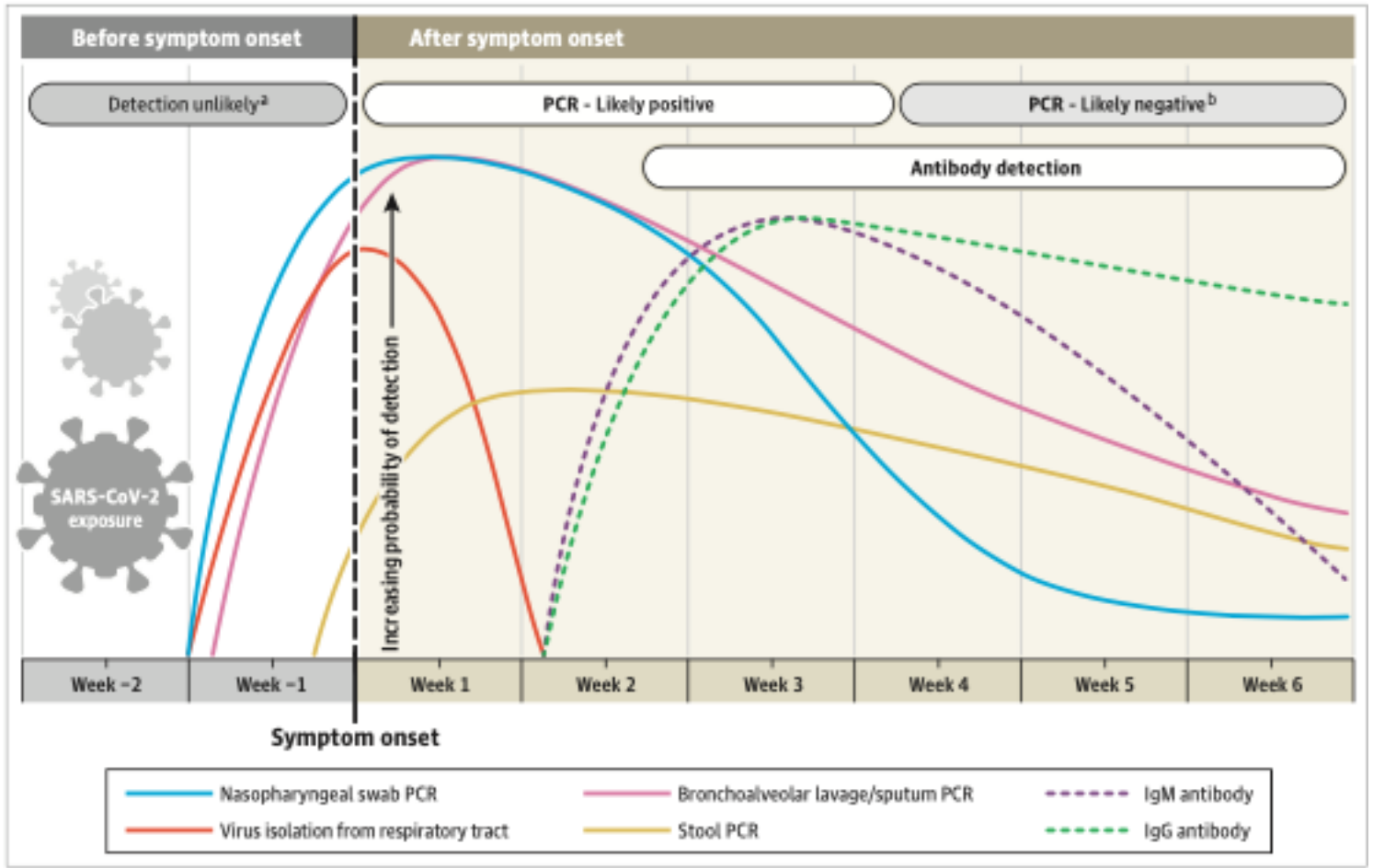
Detection of Antibodies to SARS-CoV-2

COVID-19 infection can also be detected indirectly by measuring the host immune response to SARS-CoV-2 infection. Serological diagnosis is especially important for patients with mild to moderate illness who may present late, beyond the first 2 weeks of illness onset. Serological diagnosis also is becoming an important tool to understand the extent of COVID-19 in the community and to identify individuals who are immune and potentially "protected" from becoming infected.

The most sensitive and earliest serological marker is total antibodies, levels of which begin to increase from the second week of symptom onset.[6] Although IgM and IgG ELISA have been found to be positive even as early as the fourth day after symptom onset, higher levels occur in the second and third week of illness.

For example, IgM and IgG seroconversion occurred in all patients between the third and fourth week of clinical illness onset as measured in 23 patients by To et al[7] and 85 patients by Xiang et al.[8] Thereafter IgM begins to decline and reaches lower levels by week 5 and almost disappears by week 7,

Figure. Estimated Variation Over Time in Diagnostic Tests for Detection of SARS-CoV-2 Infection Relative to Symptom Onset



Estimated time intervals and rates of viral detection are based on data from several published reports. Because of variability in values among studies, estimated time intervals should be considered approximations and the probability of detection of SARS-CoV-2 infection is presented qualitatively. SARS-CoV-2 indicates severe acute respiratory syndrome coronavirus 2; PCR, polymerase chain reaction.

[a] Detection only occurs if patients are followed up proactively from the time of exposure.

[b] More likely to register a negative than a positive result by PCR of a nasopharyngeal swab.

ARTICLE INFORMATION

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Conflict of Interest Disclosures: None reported.

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