COVID-19: Serology - where are we?

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WHO update
Coronavirus disease (COVID-19), Situation Report– 108, 7th May 2020. 3,672,238 cases with 254,045 deaths reported to date (1)

ECDC update

ESCMID e-academy:
COVID-19 diagnostics - Lights and shadows: https://eacademy.escmid.org/escmid/2020/covid-19/293259/doctor.g.greub.doctor.b.lina.doctor.m.sanguinetti.doctor.j.moran-gilad.doctor.html?f=menu%3D8%2Abrowseby%3D8%2Asortby%3D2%2Alabel%3D19858

Serology

Testing for SARS-CoV-2 specific antibodies is a hot topic and can theoretically be used to determine the number of people exposed to the virus in a population and to determine who have had the disease and are currently immune.

However, the methods are still in development and it is too early to know what will be the use of antibody testing in epidemiology for the individual.

A study looking at long-term antibodies in healthcare workers recovering from SARS (infected in 2003) found that anti-SARS-CoV-specific IgG persisted for up to 12 years (3).

Two in-house ELISA assays, using full-length nucleoprotein (N) or trimeric Spike (S) ectodomain antigens were studied in four different assays (4). Overall, the results obtained with the four assays were similar. In hospitalized patients, seroconversion and neutralisation occurred on 5-14 days post symptom onset, confirming previous studies. Seropositivity was detected in 29% of pauci-symptomatic individuals within 15 days post-symptoms (4).

A study used a virus neutralisation test (VNT) and a ELISA with recombinant nucleocapsid protein from SARS-CoV and SARS-CoV-2 expressed in mammalian cell culture and a recombinant receptor binding domain (RBD) of the SARS-CoV-2 spike protein custom-produced by a commercial provider (GenScript, Piscataway, NJ, USA) (5).
Another study looked at the antibody responses to SARS-CoV-2 in 285 patients with COVID-19. Within 19 days after symptom onset, 100% of patients tested positive for antiviral immunoglobulin-G (IgG) (6).

A study found that the RBD and N protein ELISAs were more sensitive than S1 ELISA in detecting antibodies in mildly infected patients and showed stronger correlations with PRNT₅₀ titers. Therefore, detecting antibodies against 2 different antigens might be needed to confirm the findings and avoid false-negative results in surveillance studies. However, the sensitivities of the assays need to be further validated (7). Another study also used the SARS-CoV-2 internal nucleoprotein (NP) and surface spike protein receptor binding domain (RBD) in an ELISA system but did not further evaluate the performance of the serological assay (8).

A study from China used chemiluminescence immunoassay (CLIA) in which the magnetic beads of these CLIA assays are coated with two antigens of SARS-CoV-2 (nucleocapsid protein or N protein, spike protein or S protein). 100% of the patients tested were IgG positive after 3 weeks (9).

A recent study has suggested that saliva is an alternative to nasopharyngeal sampling. However, it still needs further investigation (10).

The different protocols for expression of antigens derived from the spike protein of SARS-CoV-2 that can serve as a substrate for immunological assays, as well as a two-stage serological enzyme-linked immunosorbent assay (ELISA) have been reviewed (11).

**Conclusion**

The assays available at the moment will detect SARS-CoV-2 specific IgG-antibodies 21 days after the onset of the symptoms in symptomatic COVID-19 patients, but may not be positive in patients with a pauci-symptomatic or asymptomatic infection (these may not develop an IgG-response detectable with the current systems).

Two-antigen systems are better than one-antigen systems, but further studies with different constructs are urgently needed.

IgG testing, with previously described limitation, is useful for seroprevalence studies and to definitively assess SARS-CoV-2 etiology in PCR negative but clinically suspect COVID-19 cases.

Molecular test is still the gold standard for acute case investigation.

Few tests are detecting IgM and IgA and most of them are still under evaluation as well as is the dynamics of these Abs in infected patients.

Thus, further development and validation are urgently required.

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References


In the literature

Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study
In this retrospective cohort study of patients with COVID-19 and ARDS managed with non-invasive ventilation outside of the ICU, treatment with high-dose anakinra was safe and associated with clinical improvement in 72% of patients.

Autopsy findings of the first 12 patients who died of COVID-19 in a hospital in Hamburg, Germany, has found that 7 (58%) of them had undiagnosed deep vein thrombosis.
