

Rapid Review of Literature

Review Title:	At what time in the disease timeline of COVID-19 do antibodies develop?
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Key Findings

- The majority of patients (>50%) appear to seroconvert between 8-14 days following the onset of symptoms.
- Nearly all patients (>80%) seroconvert >15 days following the onset of symptoms.
- The IgM response is detected earlier (median 12 days) than the IgG response (median 14 days).
- Seroconversion appears to follow clinical recovery in most cases.

Limitations

- Only 2 studies were well designed with large patient cohorts [2, 7].
- Some of the references are available as preprints and are pending peer review.

GRADE of Evidence: B - Moderate

A grade of "B" is assigned when further research is likely to have an important impact on confidence in the estimate of effect and may

change the estimate. The review may include one high quality study and/or several studies with some limitations.

For more information about how this rating was determined, visit https://www.essentialevidenceplus.com/product/ebm_loe.cfm?show=grade

Background

The EOC has requested more information regarding whether serology have a role in the clinical care of COVID-19 patients. One component of this larger question is to understand what the time course of antibody development is in the clinical course of the disease.

Research Question(s)

- At what time in the disease timeline of COVID-19 do antibodies develop?

Method

A rapid review of the literature was performed to answer this question. This method entails a brief scan of the relevant literature to gather publications with potentially relevant information to the question at hand. These publications are reviewed by a team of experts (library, research, and clinical staff) to determine the quality of the data and provide recommendations based on the question and available data. The rapid review is performed over a period of several days to provide a quick response, based in evidence, to a policy question. Note: this is not the same as a systematic review which has much more stringent criteria for analysis and requires a longer turnaround time for results.

PICO Statement

P – Patients/Population	N/A
I – Intervention/Indication	N/A
C – Comparator/Control	N/A
O – Outcome	N/A

Search Strategy

PubMed strategy: ((((((coronavirus OR “corona virus” OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR “covid 19” OR nCoV OR “CoV 2” OR CoV2 OR sarscov2 OR 2019nCoV OR “novel CoV” OR “wuhan virus”) OR ((wuhan OR hubei OR huanan) AND (“severe acute respiratory” OR pneumonia) AND (outbreak)) OR “Coronavirus”[Mesh] OR “Coronavirus Infections”[Mesh] OR “COVID-19” [Supplementary Concept] OR “severe acute respiratory syndrome coronavirus 2” [Supplementary Concept] OR “Betacoronavirus”[Mesh]) AND (((detect* OR develop*)) AND (((((((antibody[Title/Abstract] OR antibodies[Title/Abstract])) AND ((antibody[Text Word] OR antibodies[Text Word])) OR (“Antibodies”[Mesh] AND (((“Immune System”[Mesh] OR (“immune system”

The searcher employed a broad search strategy and asked the researcher to identify relevant articles. Articles citing a very relevant article were identified and reviewed.

Inclusion Criteria

Articles were searched from 2019 to the present. No exclusions were employed.

Sources

The following sources were searched: PubMed, Embase, CDC database, WHO database, PHAC database.

Findings

Antibodies (IgG/IgM) against SARS-CoV-2 viral proteins appear to be detectable in the majority of patients (>50%) by about 8-14 days following the onset of symptoms, while nearly all patients (>80%) are seroconverted beyond 15 days following symptom onset. The IgM response is detected earlier (median 12 days) than the IgG response (median 14 days) [7]. Only 2 studies of high quality provided evidence [2, 7], however, data from the remaining lower quality studies corroborated this timeline. Most authors agreed that serology testing in conjunction with RNA testing (rt-PCR) is the most accurate method to diagnose SARS-CoV-2 infection at any stage, with RNA testing becoming unnecessary beyond 2 weeks following onset of symptoms. In some patients, viral RNA was detected despite high antibody titres, indicating that in some patients antibody production may be insufficient to clear the virus [7]. Only viral culture or epidemiological follow-up will clarify whether such RNA detection indicates the presence of active virus or only inactive viral remnants.

It is unclear at this time if seropositive patients are indeed immune to re-infection.

Conclusions

According to the evidence reviewed, the majority of COVID-19 patients produce antibodies to the virus by the intermediate stage of infection (8-14 days after onset of symptoms) and nearly all are seropositive in the late stage of infection (>15 days after onset of symptoms).

References Included in Summary

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6. To K, Tsang O, Leung W-S, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *The Lancet Infectious Diseases*. 2020. DOI: 10.1016/S1473-3099(20)30196-1
7. Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis*. 2020. DOI: 10.1093/cid/ciaa344