

NERVTAG: View on SARS-CoV-2 protective immunity

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Background

1. NERVTAG have been asked to provide advice on what is currently known about protective immunity following infection with SARS-CoV-2 infection.

If someone is SARS-CoV-2 antibody positive, what do we know about duration and strength of immunity?

2. This is currently unknown for COVID-19. The virus has only been circulating in humans for about 5 months, and there has not been enough time for those previously infected to be exposed to the virus a second time and for re-infection to be a possibility.
3. Antibody is one part of the immune response that is relatively readily measured. We can see antibody responses in most but not all people who have been infected by SARS CoV2 after 10 days and continuing to rise for around 28 days after first symptoms. In animal models the presence of antibody protected animals against infection when re-challenged with the virus.
4. The persistence of antibody represents only part of the immune response and it is not clear how the presence of an immune response will alter the type and severity of any subsequent disease (preventing it completely or preventing only the lung complications, for example).
5. In terms of how long the antibody will last, we can speculate from what we know about other related coronaviruses, MERS, SARS and the well-adapted human common cold coronaviruses. However it is important to emphasise that SARS CoV-2 is a novel virus and information from past viruses is only an approximate guide.
6. The antibody response to other coronaviruses
 - a. Is higher in people who were severely infected and rather low or even absent in people who got mild infections
 - b. Diminishes over time, in a way that correlates with an individual becoming susceptible to reinfection. The exact time varies: estimates include becoming susceptible after 44 weeks for seasonal coronaviruses, human challenge studies showed volunteers were not protected from reinfection on challenge

at one year, mild infection with MERS showed antibody waning within months, camels, the intermediate animal host for MERS, show evidence of reinfections.

What needs to be done to improve understanding?

7. We need longitudinal studies to understand the duration of the antibody response. That means taking samples from the same individuals at regular intervals and measuring the antibodies in their blood over time.
8. In the short term the best cohort is those who were infected at the beginning of the outbreak, who had mild symptoms (and were in hospital for isolation rather than management). Some care needs to be given over the type of antibody test used. The gold standard would be a neutralization test but these are not high throughput. Most high throughput kits measure antibodies that bind and we don't yet know whether they correlate with protection, although emerging data suggest they might.
9. We also need a wider view of the immune response (not just antibodies) and to evaluate the effect of immunity in the mucosal surfaces. There is also a gap in knowledge of the part played by innate and cellular immunity.

Could you be antibody positive and still transmit the virus?

10. Viral RNA has been detected for several weeks after recovery in some people. By this time they are also antibody positive. We do not know if they can still transmit virus at this late time, the presence of the viral RNA in a swab does not necessarily mean the virus is still replicating and infectious, but it might do. More studies are needed to measure infectious virus (not just RNA) at these late time points and to estimate infectivity inferred from studies of community or hospital transmission (which demonstrates directly the ability of a person to infect another).
11. Other studies that could help are animal transmission studies to understand the duration of contagiousness; dynamic contact tracing and analysis of chains of transmission in those with archived samples from saliva, crevicular swabs, blood spots etc. to determine the transmission events and the status of the person transmitting.

Do individuals with confirmed (high-confidence) personal immunity, pose a significant risk of transmission to other people as carriers i.e. through the surfaces they touch.

12. It is not clear that any current test can confirm personal immunity. But a person with high antibody levels who has recovered and is not currently shedding virus is unlikely to transmit infection. However, immune individuals could still act as a passive 'vehicle' for transmission e.g. spreading virus from a contaminated surface via their contaminated hands.