Immunity Post-COVID-19 Infection: Literature Review as of September 3, 2020
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Methods

A rapid search of LitCovid supplemented with full Pubmed, plus a scan of popular media via a web search was conducted using terms such as COVID-19 and SARS combined with reinfection, immunity, antibodies, and immune response. Findings of studies targeting the topic were selected and summarized.

Duration and Strength of Immunity

Knowledge about the duration and strength of the immune response in patients who have recovered from COVID-19 is evolving quickly. More severe illness has been shown to elicit a strong immune response, however, even mild illness has produced lasting immune responses. Although, there are significantly lower in mean titers of neutralizing antibodies when compared to those with mild to severe pneumonia. In contrast, Wu et al. found 30% of recovered mild COVID-19 patients from China had low levels of neutralizing antibodies at the time of discharge (median 16 days in hospital; 22 days of illness duration), with 10/175 having them below the limits of detection. Others have looked at more specific antibodies over a longer follow-up time and found that antibodies to the receptor binding domain and the S2 region of the spike protein of SARS CoV-2 were still high at 2-3 months post-infection, but those against the nucleocapsid varied and rapidly declined in many. Their work also demonstrated stronger responses in more severe illness. Another analysis of 15 patients who had recovered from mild cases of COVID-19 found maintenance of anti-RBD IgG levels above negative threshold. 71% and 36% of patients maintained anti-RBD IgM and IgA, respectively, at a median of 86 days post-symptom onset.

While most vaccine development utilizes neutralizing antibody responses as a key measure, T and B cells are also of interest for long term immunity. Sekine et al. found that T cell activation was a hallmark of COVID-19 infection and memory T cell responses were robust in recovered patients even when circulating antibodies were not detected. Rodda et al. also found enhanced both memory B and T cell activity. Additionally, two studies have shown development of immune responses in rhesus macaques when they were challenged at 28-35 days post initial infection.

Reports of Reinfection and Re-positives

Two recent reports of reinfection have gained attention. Both appear to be considered true reinfections since the strains they were infected with were found to be genetically different and both men had negative tests in between infections. One report, a 33 year old Hong Kong man, experienced his second positive 4.5 months after his first. His second infection was asymptomatic. His viral load was high despite being asymptomatic. There was a difference of 24 nucleotides between the 2 strains of SARS CoV-2 in this case. Another very recent report is that of a 25 year old man from Reno, NV. According to news reports, his second bout of COVID-19 was worse than the first, which would not generally be
Tomasini et al. present 6 potential reinfection cases in a recent paper, two of which they feel very confident are reinfections due to 84 and 87 days passing in between the infections. Patients in this report did have negative test in between their infections.

Countries such as China and South Korea had protocols whereby all positive patients (regardless of symptom levels) were hospitalized and not discharged until negative tests were recorded. These patients were also followed and re-tested after discharge. Post discharge monitoring uncovered several re-positive results. Contact tracing protocols in these reports indicate that these patients most likely did not have a new contact with a positive case, thus, these authors believe these patients had reactivated virus. The time to repositive in these reports (from initial positive diagnosis, through negative discharge, and then repositive) is generally under 40 days.11-13

**Historical Immunity and Reinfection with MERS, SARS CoV, and Seasonal Coronaviruses**

Reinfection with seasonal coronaviruses is common. A recent study of viral data from Manhattan between October 2016 and April 2018 found 86 out of 214 tested positive for one of the common seasonal coronaviruses once, while 12 were positive for the same virus multiple times (3 positive 3 times, 6 positive 2 times).14 The range of time for recurrence was 4 to 48 weeks. Many of the reinfections (75%) were in children between 1 and 9 years old.

Immune responses to seasonable coronaviruses as well as MERS and SARS CoV have also been studied. A recent publication found 43/200 participants had a seasonal coronavirus during the study. In this population, binding antibodies were increased more than neutralizing antibodies, which they suggest increases risk for infection.15 A recent review by Kellam et al. describes immune responses in patients who had MERS or SARS CoV.16 With MERS, severe infection or those with prolonged viral shedding had robust functional antibody response for greater than 1 year with one study finding continued immune response nearly 3 years post infection, though the response did decline over time. Mild or asymptomatic MERS infections have more limited antibody responses or rapid decline in that response. SARS CoV was a largely symptomatic coronavirus, and lasting antibody response up to 30 months post-infection was found. However, there is a subset where that response declines significantly.