*Question: Rapid lit review and international scan of practices on the topic of "Immunity Post-Infection".*

2020-04-06

## Key points

- Distinguishing people in the population that are immune to SARS-COV-2 is being considered as a part of risk-based de-escalation plans in several countries according to the recent news and there are some predictive models looking at this as a strategy.
- Post exposure immunity has not been demonstrated in humans. Several studies provide evidence of antibody response and immune response in COVID-19 cases during infection and in convalescent phases. The assumption that the antibodies developed during infection may provide protection is reasonable based on current early evidence. This will need to be confirmed with evolving state of knowledge on this particular topic.
    - SARS-COV-2 was used in a non-human primate challenge trial that demonstrated the reinfection challenge, 2 weeks after symptoms resolved, was unsuccessful (Bao et al., 2020).
    - Sera from convalescent COVID cases were able to neutralize SARS-CoV-2 in an in vitro plaque assay, suggesting a possible successful mounting of the humoral responses (Zhou et al., 2020).
    - Studies of SARS cases detected IgG antibodies for approximately 3 years (Wu LP, 2007).
- Currently, most nations are initiating serological surveys to start evaluating and understanding who in the population has been exposed.
- There is a lot of work being done on developing serological tests, however validation of these tests is lagging behind as it takes time to develop serological panels for validation of the serological tests.

## In the news

"Immunity passports" are being considered in Europe (Germany, Italy and UK as of last week, the UK ordered 3.5 million tests). This would be a way of getting recovered, immune individuals back into the workforce faster. Preparation to study immunity is currently being set up in Germany where they are going to do repeated sampling on 100 000 people.
https://www.theguardian.com/world/2020/mar/30/immunity-passports-could-speed-up-return-to-work-after-covid-19

CDC is collecting and testing for SARS-COV-2 antibodies and the idea of immunity allowing a person to re-enter society has been discussed in the news, but CDC is only quoted as stating it will help them understand what the true amount of infection in the community is. They are using a rapid test (15 min) produced by Cellex. https://www.vox.com/science-and-health/2020/4/5/21208630/coronavirus-cdc-blood-test-immunity-serological-cellex

## In Canada

Large targeted sero-surveys to understand who has been exposed to COVID-19 and further define high risk of exposure situations and eventually also understand potential immunity are being initiated in Canada. (personal comm OCSO) They are following the WHO protocols so results are comparable across provinces and countries.

## NML special pathogens and diagnostics

Their focus is trying to secure a good serological panel that you can evaluate these serological tests on as well as develop some that perform well. The three serological approaches that the NML is looking into is establishment of neutralisation assays (which have limited commercial platforms), followed by evaluation of commercial ELISAs and finally looking at front-line point of care assays. Many of these are being developed and evaluating their performance is a big priority. (personal comm R. Lindsay)

## In research articles:

**Animal models:** Rhesus Macaques in a non-human primate model demonstrated resistance to reinfection with SARS-COV-2. Initial infection was undetectable by 14 dpi, during infection virus was identified widely in tissues. Specific antibodies were elevated 14-21 dpi and 28 dpi. Re-challenge occurred at 28dpi. There was no evidence of re-infection in any monkeys or in select tissues tested. "Table 1, the titers of 1:16 (M2, M4) and 1:8 (M3) exhibited the neutralizing effect at 21 dpi and 28 dpi. After the re-exposure, the titers for M4 elevated 1:40 at 5 dpr and 14 dpr, while M3 maintained the same titer as 1:8 at 5 dpr. They indicate that the monkeys produced neutralizing antibodies at an early stage of infection similar to recovering COVID-19 cases, which protected them from developing a new infection when challenged and there was evidence that the virus had been cleared from the sampled tissues.

**Human immune response to SARS-COV-2 infection:** In humans, there is only evidence of mounting an immune reaction, but no evidence of whether an individual has protection against re-infection (Jiang et al., 2020). An antibody response for total antibodies, IgM, IgA and IgG were shown to occur around 2-3 weeks post exposure (Long et al., 2020; Lou et al., 2020; OKBA et al., 2020; To et al., 2020; Zhao et al., 2020). Immunological changes in patients with mild to moderate COVID-19 show increased antibody-secreting cells, follicular T-helper cells, activated CD4+ and CD8+ T-cells and IgM/IgG SARS-CoV-2-binding antibodies detection in blood prior to resolution of symptoms, thus a substantial anti-viral immunity in non-severe COVID-19 case (Thevarajan et al., 2020).

***In vitro* study:** Sera from convalescent COVID cases were able to neutralize SARS-CoV-2 in an in vitro plaque assay, suggesting a possible successful mounting of the humoral responses (Zhou et al., 2020).

**Predictive Models on Looking at Using Recovered cases strategically** Describes a public health intervention "shield immunity" where recovered cases with immunity are identified and used around high risk populations to reduce the risk of exposure (Weitz et al., 2020)

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