The race for cures: a good immune response to COVID-19

Richard Béliveau

Translated from Le Journal de Montréal, September 5th, 2020

Several recent studies indicate that the immune response to the coronavirus responsible for COVID-19 is in the majority of cases very good and appears to protect against reinfection, as one would expect.

Two features of the current COVID-19 pandemic indicate that the immune response to the coronavirus is mostly adequate.

On the one hand, it is estimated that between 40 and 45% of people infected with the coronavirus are asymptomatic, that is to say that they do not develop any clinical sign of COVID-19 and that they can therefore fight effectively the virus (1).

On the other hand, the vast majority of healthy people do not develop serious complications from the disease.

A high risk of mortality is especially observed in people with compromised immunity, either because they are very old or have pre-existing health problems (obesity, diabetes, cancer, cardiovascular disease).

Overall, and even if it is still a little too early to get a definitive figure (due to the high number of asymptomatic cases, in particular), the estimates of the death rate associated with COVID-19 seem to converge at around 1% (2), which confirms that the immunity manages to contain the virus in the vast majority of cases (99%).

MULTIPLE RESPONSES

Research has revealed two very interesting aspects of the immune response to the coronavirus:

1. **A convergent production of extremely powerful antibodies**. Studies recently published in the prestigious journals *Nature* and *Science* show that many people infected with the coronavirus produce very powerful antibodies, and are able to neutralize the virus even when present in very small quantities. These antibodies are very similar from person to person and are all directed to the region of the virus involved in its binding with the ACE2 membrane protein and which is absolutely essential for its entry into cells (3, 4). It therefore appears that infection with the coronavirus induces a very similar immune response from person to person, suggesting that a vaccine capable of promoting the production of these high-performance antibodies could have strong therapeutic activity in a large segment of the population.

2. **Activation of T lymphocytes.** CD4 (helper) and CD8 (killer) T lymphocytes are also absolutely essential for the establishment of long-term immune memory. It has recently been shown that in individuals affected by COVID-19 who have developed a mild form of the disease, the infection caused a strong activation of T cells (5).

It should also be noted that some people who have not been infected with the SARS-CoV-2 coronavirus nevertheless have T lymphocytes active against the virus, possibly due to previous infections with other coronaviruses, which have certain proteins similar to the current virus. It is likely that this cross-immunity contributes to the absence of symptoms in some people infected with the coronavirus.

PREVENT REINFECTIONS

We do not yet know the degree of protection offered by antibodies generated against the coronavirus or following activation of T cells, but preliminary data are very encouraging.

For example, there was recently a case of a person who, after contracting COVID-19 last winter, tested positive for the coronavirus four months later, but without showing any clinical signs of the disease. It is therefore possible to be infected again, but it appears that the immunity derived from the first infection can significantly reduce the negative impact of the virus.

The antibodies could also help neutralize the virus in the event of future re-exposure. For example, a study recently reported that a COVID-19 outbreak affected the majority of crew members on a commercial fishing vessel, but that three people who had antibodies to SARS-CoV-2 before the departure of the shipment showed no signs of virus infection (6).

OPTIMISTIC SCENARIO

Although the novelty of SARS-CoV-2 means that the duration of the immune response is not yet known, current data indicates that this response appears to be quite long.

A study from Iceland has just shown that neutralizing antibodies to the virus are still present in high amounts four months after infection (7).

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And although these antibodies gradually decline over time, the cells that make them last much longer and can therefore quickly be mobilized in the event of re-exposure to the virus.

Activation of T cells is also very important, as it plays a key role in maintaining longer-term immune memory.

Overall, therefore, we can say that the immune response to the coronavirus is excellent and involves all of the cellular systems necessary to obtain optimal immunity.

We can therefore envisage a scenario where even if the virus still circulates for several years and infects certain people repeatedly (children, in particular), the immune system will learn to adequately manage the virus and prevent the development of the vast majority of cases of serious COVID-19.

If we want to be even more optimistic, we could even say that it is possible that the threat posed by the coronavirus will gradually diminish due to this good immunity and that the SARS-CoV-2 will over time become, like its cousins OC43, 229E, NL63 and HKU1, just another of the coronaviruses responsible for the mild cold.

(1) Oran DP and EJ Topol. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. Ann. Intern. Med 2020; 173(5): 362-367.

(2) Mallapaty S. How deadly is the coronavirus? Scientists are close to an answer. Nature 2020; 582: 467-468.

(3) Robbiani DF et coll. Convergent antibody responses to SARS-CoV-2 in convalescent individuals. Nature 2020; 584: 437-446.

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