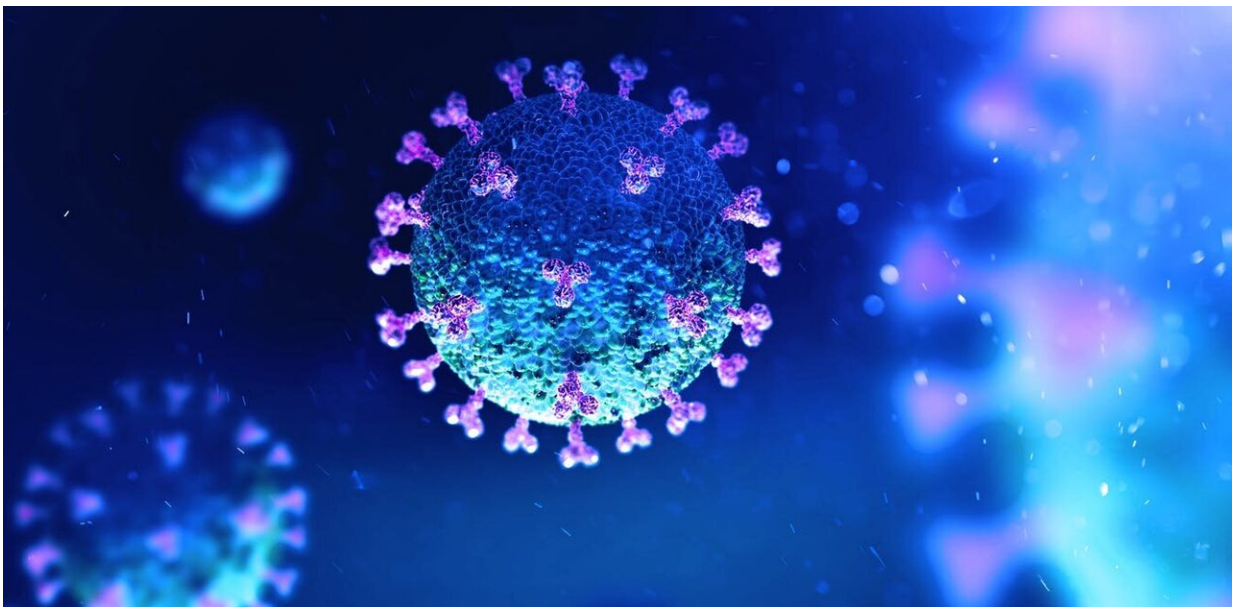


Coronavirus: We must step up research to harness immense power of the immune system

May 12 2020, by Daniel M Davis and Sheena Cruickshank



Credit: Andrii Vodolazhskyi/Shutterstock

Many countries are moving to exit a lockdown triggered by COVID-19, but the virus has not gone away and there are real concerns that a second wave of infection could happen. We urgently need to understand more about how the body deals with this infection and what we can do to tackle it. Immunology has taken center stage here in revealing what happens when our body fights this virus, and brings us the possibility of

treatments and vaccines.

One of the most amazing things about our [immune system](#) is that it can fight germs it has never encountered before. We understand much about how this works, and this detailed knowledge seeds ideas about how COVID-19 could be tackled with a vaccine or other types of drugs, such as those that have made AIDS a disease that can be controlled. But we must be under no illusion—it will take time. There are seven known types of [coronavirus](#) that infect humans and we don't have a vaccine against any of them.

Scientific understanding of COVID-19 is moving fast. We already know that the [virus](#) enters the body's cells through a protein on cells called ACE2. ACE2 is highly prevalent in cells that line the airway.

Once inside the cells, the virus can exploit their machinery to create a viral production factory. A [chain reaction](#) builds up where new virus particles are released, which either infect more cells or can be expelled from the body to infect others.

The virus mainly moves from one person to another in respiratory droplets, sent out as we cough, sneeze or talk. This can happen before a patient has symptoms, which is one reason this particular virus has spread so effectively throughout the world. ACE2 is also present in gut cells and there are reports of viral shedding occurring in [fecal](#) samples, suggesting a need for good personal hygiene, although for the moment this is only a potential route of transmission.

The process of infection causes signals which alert the immune system that there is a threat to deal with. Immune cells that live in the lung airways, such as macrophages, natural-killer cells and others, deal with the infection early on. Macrophages can also help repair the damage the infection causes and recruit other immune cells to the airways too. How

macrophages are [activated](#) and how they [respond](#) may be important in what happens to each of us overall. The most severe cases of COVID-19 have been associated with macrophages that produce high levels of inflammatory protein molecules called cytokines, such as interleukin-6.

This early immune response probably can't wholly eliminate the infection; we need other [white blood cells](#) to get involved. An enormous reservoir of immune cells is available, but only a few of these will be a good match to tackling this specific virus. Once the best match is established, these specific immune cells multiply. B cells make large quantities of antibody which can neutralize the virus directly and mark infected cells for attack. T [cells](#) also destroy the [infected cells](#) directly. This process of generating large numbers of the right [immune cells](#) happens in the lymph nodes, sometimes felt as "glands" which get swollen when this is happening.

There are many questions about whether or not people who have had the infection are immune afterwards and how we can detect this. Tests for our exposure to the virus rely on detecting this specific activity of our immune response, in the presence of antibodies. These antibodies can reveal if someone has been infected in the past but we do not yet know if this indicates that they have full or partial protection against future infections and so an "antibody passport" may not be useful.



The virus spreads to others through respiratory droplets. Credit: Elizaveta Galitckaia/Shutterstock

Also, reports suggest that around 10%-20% of patients who have been infected have little or no detectable antibody in their blood and there are concerns about the reliability and validity of the antibody tests currently available. We urgently need to understand the role of antibodies, as well as other components of the immune response, and whether these can provide, or correlate with, protection against this [infection](#).

It is not yet clearly understood why disease severity varies between people. Age is an important factor, which may partly be because the immune system changes as we age. Older people are more likely to have a background low level of inflammation and are less able to mount

effective immune responses to new infections.

There is also evidence that an overly exuberant immune system can cause problems by directly contributing to lung damage. If the immune system gets out of control, this in itself can be dangerous and even fatal. This is why one type of therapy being tested for COVID-19 patients are drugs that dampen excessive [immune responses](#), normally used to treat autoimmune diseases. They act by blocking the action of inflammatory protein molecules such as interleukin 6 and [tumour necrosis factor](#).

Best way out

A vaccine is the best way out. For a vaccine to really work, the critical issue is whether it can trigger the immune system enough to keep us protected for a good length of time. Nobody knows yet if this is possible.

You'll already know that some vaccines induce immunity which lasts a lifetime, others need boosters, and some are needed annually. A lot plays into this; the rate the virus changes, whether antibodies are good at neutralizing it, and so on.

For the SARS epidemic in 2002-03, also caused by a coronavirus, we think that protection lasted about a year. Other coronavirus infections tend to induce immunity for around only three months. Also, because every person's immune system is configured slightly differently—from a combination of our genetic inheritance, the diseases we've previously had and any number of lifestyle factors—each person's immunity to COVID-19 will almost certainly vary.

So much depends on our immune system: we must appreciate it more, we must step up the research, and every idea for harnessing its power must now be explored.

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