Encouraging signs our immune system may be able to fight off Covid-19 reinfection

Opinion by Erin Bromage

CNN

This is an installment in a series of regular columns on emerging science related to Covid-19 by Erin Bromage, an associate professor of biology at the University of Massachusetts Dartmouth. His research focuses on the evolution of the immune system and how animals defend themselves from infection. Follow him on Twitter @ErinBromage. The views expressed are his own. View more opinion articles on CNN.

My son was so excited the day that he had earned enough money to buy his own BB gun. When I brought it home, he immediately went to the shooting range we had built and started shooting. The first pellet went left. The second pellet went right. We never found where the third hit.

"The gun is broken" he said, as he stormed away frustrated that each shot landed differently. After giving him a few minutes to collect his thoughts, we discussed what happened. I told him the gun is new and we don't know how it behaves yet. We shouldn't be surprised that there are some kinks to work through but the more we shoot it the better we will understand how it performs. A day later, and with much patience, every shot was clustering tightly on the target.

Erin Bromage

A similar narrowing in on the target has been playing out as studies have emerged on the body's immune responses to Covid-19. We are still at the stage of sighting-in a new gun; the shots are landing across the target and people are becoming frustrated by the lack of agreement within the scientific community. Countless questions continue to be asked:
Do Covid-19 antibodies protect us from reinfection? Are they persistent long after recovery or do they wane fast? And what does this mean for the development of a vaccine?

These questions resounded in early April as the first antibody data started emerging. After reading an early article on antibody testing, I wrote a note to my undergraduate class in an online forum which I titled "this is terrible news, tell me why." The paper clearly showed that people who had recovered from infection where producing antibodies against the virus, but that was not my concern. It was troubling that the antibodies peaked, but then rapidly diminished in concentration -- so much so that if the reduction followed in a linear fashion, within 120-150 days you would have no protective antibodies left.

This suggested that patients who had recovered from Covid-19 could be reinfected and get sick all over again. Antibody-induced immunity lasting six months to a year is what we often observe with the human coronaviruses which cause the common cold. If this early study was to be trusted in full, this truly would be terrible news.

Another article describing quickly diminishing antibody levels was published in June and followed up with a second report in July showing a similar result. The latter paper showed that, on average, patients' antibody levels tended to fall by half around 36 days after the onset of symptoms, while a small portion of those sampled declined much more slowly.

The science seemed to be confirming my initial fear that antibody immunity would not be enough to protect recovered coronavirus victims from reinfection.

Residents have their blood drawn by a registered nurse for an antibody test for the coronavirus.

But then the science progressed further. A series of publications in recent weeks on antibody responses to vaccines and an elegant serological study -- an examination of antibodies in your blood -- moved the focus of our knowledge.
Both the Oxford and Moderna vaccines generated a robust antibody response, as high or higher than what is generated by a mild or moderate infection with live SARS-CoV-2 virus. These vaccines are like a school for your immune system, they teach your body how to respond to a virus without producing disease. This was good news! If the antibody level starts higher, it will possibly persist for longer than previously reported. The limitation is that we still need time to determine how long the antibodies will persist -- and whether they will be shown to prevent infection with the virus in the real world.

Additionally, the serological study, posted as a pre-print by a research team at Mount Sinai Hospital in New York City, demonstrated quite clearly that after a mild to moderate Covid-19 infection, antibody levels declined from their peak, then maintained a steady level for at least three months.

Infecting volunteers with Covid-19 might speed up the race for a vaccine. But it could be risky

It also showed that this immune response was capable of neutralizing the virus, providing the recovered patient with a strong sign of what could be some level of immune protection. This study differed from the early antibody studies in that the number of patients assessed was much larger -- it included nearly 20,000 patient blood samples (more than 9x the sample size of the larger previous studies) and the methods were designed to specifically measure the concentration of the antibodies against the virus' spike protein that allows it to enter our cells. Though it has not yet been peer reviewed the study's comprehensive methods make it the best example yet of serological research on coronavirus.

It is not that the early studies were wrong, they just hadn't considered how their data related to the battle for immunity. In battle, you aim to overwhelm your opponent with strength of numbers and superior armament. This is also true for the immune system's antibody response.
When a virus invades your body and an antibody response is required for protection, you don't just make enough antibody to match your viral opponent, you overshoot the target significantly to overwhelm the virus and clear it from your system. When the viral threat is cleared, many of the antibody-secreting cells recruited into the fight are allowed to die to free space and resources for your body to respond to new threats, and with that cell death the antibody they are producing also starts to wane. This anti-viral antibody response would be observed as a rapid rise in antibody levels, and then a rapid waning of antibodies in the months after infection. This quick fall in antibodies was what the early studies captured.

But, what those early studies fail to resolve was that some of those antibody secreting cells may live on in the bone marrow, potentially persisting for years, secreting virus-neutralizing antibody. So after the rapid reduction in antibody levels post-infection, the antibody levels would plateau and persist for as long as those long-lived antibody-secreting cells were maintained in the bone marrow. That type of response is well known with many viral infections, and importantly, it has been well documented to occur in people surviving MERS infection.

High antibody concentrations are not necessarily needed to fight off future infections. We only require enough antibody to provide assistance to the innate immune system to stop a new exposure to the virus from establishing infection.

Given the promising results of antibody stimulation from the Covid-19 vaccines in development, my confidence continues to grow that a vaccine that provides at least modest protection from severe disease symptoms is on the horizon.

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However, we must be mindful that each new antibody study may bring different findings, resulting in the need to readjust our understanding -- and we should keep in mind what this might mean for asymptomatic Covid-19 victims. Remember, long, hard fights help to train our immune system for future threats.

So being infected and avoiding developing symptoms of infection may not yield the protective antibodies that you may need in the future to ward off future exposure. It is also likely that we will find differences in antibody responses between children and adults, or between males and females.

In the meantime, conflicting results are usual in science, especially at the beginning of studying a new subject. We should not rush to conclusions, especially in studies with few samples or with headline-grabbing titles. Each new study published helps refine our understanding and we should be mindful that we are all seeking quality results, but negative results or those that do not fit the current narrative all help scientists refine the focus of our understanding.

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