Post-COVID-19 conditions alter a person's immune response

April 27 2023

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A new study by investigators from the Smidt Heart Institute at Cedars-Sinai suggests long COVID-19 might be caused by a dysfunction of the immune system.

The study, published in *BMC Infectious Diseases*, found that after people with long COVID-19 received the COVID-19 vaccine, they produced antibodies against the virus that causes COVID-19 for months longer than expected.

When a person has an infection, the immune system typically responds by making antibodies that block germs from entering cells. Vaccines imitate an infection so that the body's immune system knows to release certain antibodies when it comes across a virus. In both cases, the immune system eventually stops creating antibodies when the suspected infection is gone.

"There's general consensus that some level of aberrant immune response happens in long COVID-19, and this study adds to the evidence to suggest this is true," said Catherine Le, MD, co-director of the Cedars-Sinai COVID-19 Recovery Program and a senior author of the study.

Long COVID-19, a condition in which people experience COVID-19-related symptoms three months or more after initial infection with the virus that causes COVID-19, is estimated to affect 65 million people worldwide. Common symptoms include fatigue, shortness of breath, and cognitive dysfunction such as confusion and forgetfulness. Some symptoms can have debilitating effects.

To study the immune response of people with long COVID-19, investigators analyzed blood samples from 245 people diagnosed with long COVID-19 and 86 people who had COVID-19 and fully recovered. All the study participants had received either one or two doses of a COVID-19 vaccine regimen.

"We examined one part of the immune system response, the production of antibodies, which is mediated by immune cells called B-cells," Le explained.

Specifically, the investigators looked at two types of antibodies that attack the virus that causes COVID-19. One of these is called the spike protein antibody, which attacks a protein on the exterior of the virus. The other is the nucleocapsid antibody, which attacks the part of the virus that allows it to replicate.

The investigators found that people who were diagnosed with long COVID-19 produced higher levels of spike protein and nucleocapsid antibodies than people without long COVID-19. Eight weeks after receiving a dose of the COVID-19 vaccine, antibody levels in people without long COVID-19 began to decrease, as was expected. People with long COVID-19, however, continued to have elevated antibody levels, especially of nucleocapsid antibodies.

"What you would expect after getting a COVID-19 vaccination is a jump in your spike protein antibody levels, but you wouldn't expect a significant increase in nucleocapsid antibody levels," said Susan Cheng, MD, MPH, the Erika J. Glazer Chair in Women's Cardiovascular Health and Population Science, director of the Institute for Research on Healthy Aging in the Department of Cardiology at the Smidt Heart Institute, and a senior author of the study. "You would also expect these levels to eventually decrease and not persist for so long after vaccination."

Although this study shows that long COVID-19 affects the immune system, it's too soon to draw firm conclusions from these findings, according to the study's authors.

"Theoretically, the production of these antibodies could mean that people are more protected from infection," Le said. "We also need to investigate if the elevated immune response corresponds with severity or number of long COVID-19 symptoms."

Investigators are continuing to study blood samples from people with

long COVID-19. They are hoping to identify a measurable molecule that could be used to diagnose long COVID-19 and better understand the biological processes that cause it.

More information: Sandy Joung et al, Serological response to vaccination in post-acute sequelae of COVID, *BMC Infectious Diseases* (2023). DOI: 10.1186/s12879-023-08060-y

Provided by Cedars-Sinai Medical Center