Autoimmune Response Found in Many With COVID-19

About half of people hospitalized with COVID-19 had antibodies that could mistakenly attack the body's own proteins and tissues.

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More than a year and a half into the COVID-19 pandemic, much about how the human body responds to SARS-CoV-2, the virus that causes COVID-19, remains unclear. Some people have a severe or fatal reaction to infection, while others show no obvious symptoms. Some people bounce back quickly. Others experience so-called "long COVID," symptoms that persist long past recovery from the initial stages of illness.

Researchers are beginning to understand how the human immune system contributes to the varied responses to COVID-19. Autoantibodies—immune system proteins that mistakenly target the body's own tissues—may underlie some of this variation. Autoantibodies are found in a wide range of autoimmune diseases, such as lupus and rheumatoid arthritis. Many people with low levels of autoantibodies in their blood have no obvious symptoms.

A recent study found that autoantibodies that existed before infection with SARS-CoV-2 may account for 20% or more of serious or fatal COVID-19 cases. Scientists have wondered if infection with SARS-CoV-2 could also result in the production of autoantibodies in people who didn't have them before they got sick.

To look at this question, researchers screened for a range of autoantibodies in blood samples from almost 150 people hospitalized with COVID-19 and 41 healthy volunteers. The team was led by Drs. PJ Utz at Stanford University, Chrysanthi Skevaki at Philipps University Marburg in Germany, and Eline Luning Prak at the University of Pennsylvania.

The study was funded by several NIH components, primarily the National Institute of Allergy and Infectious Diseases (NIAID). Results were published on September 14, 2021, in Nature Communications.

The researchers found that about half of the people hospitalized with severe COVID-19 had at least one type of autoantibody circulating in their bloodstream. In contrast, only 15% of healthy controls had such antibodies.

About 50 of the people with COVID-19 had blood samples drawn on more than one day, including

the day they were first hospitalized. The scientists found that about 20% of these didn't have any autoantibodies when they were first admitted but developed them over the course of their illness.

In some people, the levels of autoantibodies were very high, close to the levels seen in autoimmune diseases. Common targets of these misdirected antibodies included immune system proteins such as cytokines, which normally help coordinate the immune response.

The mechanisms behind the production of such autoantibodies aren't yet clear. Widespread and long-term inflammation during severe COVID-19 may cause the immune system to produce antibodies to pieces of the virus it wouldn't normally recognize. Some of those pieces might resemble human proteins enough to trigger the production of autoantibodies.

Excessive inflammation could also boost production of autoantibodies that had previously only existed in the body at very low levels. Vaccination against COVID-19 is much less inflammatory than infection with the virus. In a separate study that looked at COVID vaccination, none of the healthy volunteers developed autoantibodies.

"Patients who, in response to vaccination, quickly mount appropriate antibody responses to the viral spike protein should be less likely to develop autoantibodies," Utz says.

The team is beginning to look at whether autoantibodies produced during COVID-19 could lead to autoimmune diseases later in life. More work is also needed to understand how autoantibodies contribute to COVID symptoms.

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