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New Theory Suggests that Autoimmunity May be Causing Long COVID in Some People
WASHINGTON, D.C.— More than four years and billions of research dollars after the start of the COVID-19 pandemic, long COVID remains a poorly understood public health crisis, and there is a lack of clarity on its impact on patients with autoimmune conditions. One researcher presenting on Nov. 16 at ACR Convergence 2024 suggests that a dysregulated immune system is a possible driver for long COVID-19. He also suggests that rheumatologists can offer relevant insight into treating patients experiencing both conditions.

Long COVID causes often-debilitating symptoms for millions of people worldwide – 17 million in the United States alone – yet little is known about what causes it or how to treat it. This complex disease, associated with more than 200 wide-ranging symptoms, likely has more than one cause for different symptoms in a person. This is partly why Leonard Calabrese's, DO, hypothesis is gaining attention. Dr. Calabrese is a rheumatologist, immunologist and researcher at the Cleveland Clinic.

“This hypothesis has profound clinical implications, suggesting that treatments often used by rheumatologists could potentially have a role in treating or preventing post-infectious consequences of COVID-19, including long COVID,” says Dr. Calabrese.
Dr. Calabrese will discuss the case for and against immune dysfunction as a causative factor in long COVID on Nov.16 during the American College of Rheumatology’s annual meeting in Washington, D.C.
“Given that the scientific research in this field changes on a daily basis, it is important for clinicians to be aware of data that might affect treatment for patients with autoimmune disorders,” he says.

In June 2024, the National Academies of Sciences, Engineering and Medicine issued a broad, new definition of long COVID stating that any unexplained symptom lasting for more than three months after COVID-19 infection can be diagnosed as long COVID. It also suggests that many common conditions can fall under this definition, including autoimmune disorders such as lupus, Sjogren’s disease and rheumatoid arthritis (RA).

Calabrese expressed significant concerns over the wording and interpretation of the new case definition, especially its inclusion of immune mediated rheumatic disorders as qualifying conditions for its diagnosis. He believes it will take more time and critical appraisal of additional data to more accurately assess its utility in both clinical care and research.

But as Calabrese notes, “As of August 2024, the data are far from clear as to whether autoimmunity is a driver of all or even part of the long COVID clinical spectrum.”
It is clear COVID-19 infection generates autoantibodies – that is, antibodies against a person’s own tissue like those seen in autoimmune diseases. But it is less clear what role these antibodies play in long COVID, in part because they are different in different people. Normally, in

an autoimmune disorder like RA, antibodies all have the same target. Healthy people can also have autoantibodies, or they can appear when there is an infection and then disappear without causing harm.
Recent animal studies make a stronger case for autoimmunity as a driver of long COVID. In these studies, researchers transferred antibodies from the blood of human patients with long COVID to mice. Most of the mice subsequently developed symptoms similar to those of the human donors, especially an increased sensitivity to pain.

However, more work needs to be done. Some researchers think there is a trigger before autoantibodies are activated, such as lingering bits of virus – another common explanation for long COVID.

“The establishment of a small animal model of long COVID could potentially be a breakthrough for both understanding the cause of the disorder and testing new therapies,” he says. “The role of autoimmunity in COVID-19 and long COVID is clearly a work in progress, and the rheumatology community has much to add based on their vast experience with immune-mediated inflammatory diseases and autoimmunity.”

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About ACR Convergence
ACR Convergence, the annual meeting of the American College of Rheumatology, is where rheumatology meets to collaborate, celebrate, congregate, and learn. With hundreds of sessions and thousands of abstracts, it offers a superior combination of basic science, clinical science, business education and interactive discussions to improve patient care. For more information about the meeting, visit the ACR Convergence page, or join the conversation on X by following the official hashtag (#ACR24).

About the American College of Rheumatology
Founded in 1934, the American College of Rheumatology (ACR) is a not-for-profit, professional association committed to advancing the specialty of rheumatology that serves nearly 9,600 physicians, health professionals, researchers and scientists worldwide. In doing so, the ACR offers education, research, advocacy and practice management support to help its members continue their innovative work and provide quality patient care. Rheumatology professionals are experts in the diagnosis, management and treatment of more than 100 different types of arthritis and rheumatic diseases. For more information, visit rheumatology.org.