Long COVID: What is it and what do we know about it?

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Credit: AI-generated image (disclaimer)

With over 139 million COVID-19 cases globally, the latest challenge for medical researchers is a post-COVID-19 syndrome referred to as "long COVID."

Since the COVID-19 global pandemic was declared over a year ago,

medical research has gradually turned its focus on a condition that has been coined 'long COVID' – a term to describe the effects of COVID-19 that can continue for months after the initial acute infection.

Since April 2020, UNSW Sydney medical researchers have been investigating the long-term effects of COVID-19 to develop improved post-COVID-19 clinical care and help guide future health service requirements. This is part of the ADAPT study at the Kirby Institute where researchers have been following patients diagnosed with COVID-19 at regular intervals over a minimum of one year post-diagnosis.

In its most recent report—published on preprint server *medRxiv* and yet to be peer reviewed—the ADAPT team revealed only 80 percent of patients reported full recovery at eight months. Additionally, there was no significant improvement in symptoms or measures of health-related quality of life between the four- and eight-month assessments.

What is 'long COVID'?

Professor Gail Matthews from the Kirby Institute, who is one of the lead investigators of the study, said there was no clear definition for long COVID yet, and it was likely to be several different syndromes with different causes.

"Generally, long COVID refers to people who don't recover from the acute COVID-19 infection and go on to have longer-term symptoms. The acute phase of illness can last up to two weeks, but beyond that, you potentially have a post-acute illness, or what is now called long COVID. Most people are tending to use a period for long COVID at around the two to three months mark," Professor Matthews said.

The most common symptoms long COVID sufferers experience are

fatigue, shortness of breath, chest pain and brain fog. Professor Matthews notes one systematic meta-analysis describes 55 different symptoms of long COVID.

"It's very hard to come down to a clear definition, and there is no accepted global definition. But most accept the common symptoms being fatigue, shortness of breath, tightness in the chest, racing heart, difficulty concentrating and brain fog.

"There are probably several different syndromes that cause long COVID. In other words, long COVID isn't just one thing. There can be many underlying causes for somebody still being persistently symptomatic three months-plus after infection," she explained.

Who are the long COVID sufferers?

"People who've been very sick in intensive care on a ventilator for two to three weeks are most likely not going to be fully recovered, even at three months. This can also happen with other infections and we refer to this as post-intensive care syndrome or post-sepsis syndrome. Certainly, some people who have long COVID fall into that bracket."

However, Professor Matthews said, the most interesting thing about long COVID was the number of people who only suffered mild illness, weren't hospitalized, didn't have pneumonia or go to ICU. Yet a large proportion of these people were still not better at 12 weeks after infection.

"The question is, why aren't these people better? Why wouldn't they have recovered as they should have if they had the flu or another viral illness?

"We know from our ADAPT study, that 30 percent of our group were

not better at 12 weeks. What we're concerned about is, by this stage, more people should have recovered by now because it's now after six months post-infection."

She added the syndrome was not limited to elderly patients. The patients participating in the study range from 18 to 80-year-olds with the average being in the mid-40s.

"We really don't understand why fit, young adults are still unwell. In some cases, they have evidence of myocarditis, which is inflammation of the heart. In other cases, we can't find evidence of specific organ damage, but the patient continues to experience intense fatigue, almost like a chronic fatigue type syndrome," explained Professor Matthews.

Women affected twice as often as men

Professor Matthews said there were several theories about why long COVID affected certain individuals. One theory is the SARS-CoV-2 virus (that causes the COVID-19 disease) is very good at triggering an immune response and in some individuals, the immune response is triggered in the wrong way.

"It's almost as though the immune response has been turned up but doesn't turn itself off. So, you have this chronic, aberrant immune response with the body trying to react against something. And that's why people have this ongoing fatigue and viral-type symptoms."

Another theory relates to an auto-immune phenomenon where the COVID-19 virus triggers the autoimmunity, which may also explain why the virus has a female predominance, as women tend to be affected twice as often as men.

"We know that women have a tendency to suffer from autoimmune

diseases, so maybe that's the reason why it's common in women. It could be an autoimmune process that is stimulated by the virus," Professor Matthews explained.

"There is also the theory that the virus is still in the body, but deep inside—not an active infectious virus—and that's triggering an ongoing reaction in terms of an immune response."

Does the vaccine reduce long COVID symptoms?

Recent cases have suggested that vaccines has helped reduce long COVID symptoms, but Professor Matthews said that at this stage, it was anecdotal.

"It's a very interesting theory. And certainly, we would all agree that people who have had COVID-19 should be vaccinated because although they've got antibodies, they do start to drop off. Biologically, the theory could go that if there was still some virus hiding in the body, and we triggered the immune system with another dose of vaccine, maybe that would help switch off that aberrant immune, but don't believe we have any evidence to suggest that's the case yet."

Professor Matthews said research would continue at the Kirby Institute, looking at the immunological response of COVID-19 patients and what their cells looked like. They will also collaborate with other institutions including The Peter Doherty Institute for Infection and Immunity, ANU and Deakin University to look at aspects of the cohort and to answer questions about specific areas of their ill-health.

More information: DR Darley et al. Limited recovery from post-acute sequelae of SARS-CoV-2 (PASC) at eight months in a prospective cohort, *medRxiv* (2021). DOI: 10.1101/2021.03.29.21254211

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