

Blood tests for long COVID could lead to better treatments

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People who develop long COVID have distinct abnormalities in their



immune and hormonal function that can be picked up with blood tests, researchers have found.

In a new study of 268 patients with and without long COVID, those with the condition showed a number of biological "markers" in their <u>blood</u> <u>samples</u>.

People with long COVID often showed signs of compromised <u>immune</u> <u>function</u>, including abnormal T cell activity and a reactivation of "sleeping" viruses that their immune system had previously kept in check—including Epstein-Barr and other herpesviruses.

They also had markers of hormonal dysfunction, like reduced morningtime levels of cortisol. That hormone, which normally peaks in the morning, plays an essential role in many <u>bodily functions</u>—from the sleep/wake cycle and metabolism to controlling inflammation and responding to stress.

Researchers hope the discovery will lead to a deeper understanding of what causes long COVID, and ultimately, ways to treat it.

"This study does start to give us some clues," said study author David Putrino, a physical therapist and professor at Mount Sinai in New York City. "We're seeing signs of an <u>immune system</u> in trouble, a reactivation of viruses you'd conquered, evidence of hormonal dysfunction."

More immediately, the findings offer yet more proof that long COVID is real.

"Hopefully, we can move away from the narratives that long COVID is a psychosocial condition," Putrino said. "There should be no more questions about that."



Nearly four years since the start of the pandemic, long COVID remains a puzzle. Its symptoms are complex and wide-ranging—including <u>chronic</u> <u>fatigue</u>, breathing problems, heart palpitations, neurological issues like headaches, dizziness and "brain fog," digestive problems, muscle and <u>joint pain</u>, and more.

Complicating matters, those symptoms vary from one person to another—as does the duration. Some people have persistent symptoms for weeks to months after their initial bout of COVID; others are still waiting for a resolution years out.

But researchers are starting to make sense of the noise and see patterns.

One <u>recent study</u> applied a machine-learning algorithm to nearly 35,000 patients' electronic health records to distinguish four major subtypes of long COVID.

One type involved a cluster of heart and kidney symptoms, and the affected patients were often older and had been hospitalized with COVID. Another subtype was dominated by respiratory symptoms, sleep problems, anxiety and headaches; those patients were a bit younger and only a minority had been hospitalized. A third subtype largely involved joint and muscle pain, and neurological symptoms like brain fog. The fourth, and least common, mainly involved digestive and respiratory symptoms.

Fei Wang, the researcher on that study, said that given the broad spectrum of long COVID symptoms, it's important to nail down whether they arise randomly or tend to occur in definable clusters.

That could help point toward potential mechanisms behind long COVID, according to Wang, an associate professor at Weill Cornell Medicine in New York City.



The new findings—published in the Sept. 25 issue of <u>Nature</u>—go further down the mechanism path—linking long COVID to specific biological markers in the blood.

The study cannot prove those markers—the reactivated viruses, the low cortisol, the abnormal T cell activity—are causes of long COVID, Wang said. But, he added, they raise the possibility.

The patients in the new study came from Mount Sinai and Yale New Haven hospitals: Some had long COVID, others had fully recovered from a COVID bout, and others had never been infected.

Putrino's team analyzed all participants' blood samples—which, on average, were taken one year after COVID patients' initial infection. They detected a number of differences in the study groups' blood biomarkers. Based on those biomarkers, a <u>machine-learning algorithm</u> was able to distinguish patients with and without long COVID with 96% accuracy.

That does not mean researchers will come up with a single blood test—or single treatment—for long COVID, according to Putrino.

Just as long COVID symptoms vary from one person to another, so do the blood biomarkers, the study found.

But in the future, Putrino said, it might be possible to use <u>blood</u> tests to better define what's going on for an individual patient with long COVID symptoms. The goal then would be individualized therapies, when possible.

"We have to accept that there will be no silver bullet," Putrino said.

For people dealing with long COVID, the wait for answers can be



frustrating. Wang noted that clinical trials are testing potential treatments. They include a longer course of <u>Paxlovid</u>, the antiviral used to treat acute COVID, and brain "training" and noninvasive brain simulation for memory and thinking problems.

For everyone else, Putrino said, the best way to prevent long COVID is to minimize your chances of contracting the virus.

More information: Jon Klein et al, Distinguishing features of Long COVID identified through immune profiling, *Nature* (2023). DOI: 10.1038/s41586-023-06651-y

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