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U.S. NEWS

## More Evidence Found of Biological Basis to Chronic Fatigue Syndrome

Discovery may help identify and treat patients earlier

By **AMY DOCKSER MARCUS**

Feb. 27, 2015 2:00 p.m. ET

In what is perhaps the most significant evidence yet that chronic fatigue syndrome has a biological basis, researchers said they found an immune system signature that is present in newly diagnosed patients but not in healthy people.

The pattern, published on Friday in a paper in *Science Advances*, wasn't seen in people who had been ill for more than three years, but the discovery may help identify and treat patients earlier.

The researchers, led by Columbia University's Mailman School of Public Health, looked at 51 proteins, also known as cytokines, released by cells involved in the immune system. Among 646 patients studied, including CFS patients and healthy controls, people who were ill for three years or less had higher protein levels than the others, the researchers found.

Researchers have been looking for years for a signature in the blood or cerebrospinal fluid to help diagnose CFS, a debilitating condition that can involve profound physical and cognitive impairment, unrefreshing sleep and other symptoms, but have largely been unsuccessful. As a result, diagnosis can take years, as doctors run tests and rule out other possible causes.

The immune signature must be replicated by other labs, but "I think it is convincing," said Benjamin Natelson, director of the Pain and Fatigue Study Center at Mount Sinai Beth Israel in Manhattan. Dr. Natelson, who wasn't involved in the paper, is working to identify proteins in cerebrospinal fluid that might differentiate patients with CFS from those with other health problems.

The *Science Advances* study, funded by the private Chronic Fatigue Initiative of the

Hutchins Family Foundation and the National Institutes of Health, comes as new attention is focused on the condition, also known as myalgic encephalomyelitis/chronic fatigue syndrome. The Institute of Medicine recently studied the biological evidence for the disease, which they estimate affects up to 2.5 million Americans. The IOM also proposed a new name for the condition, systemic exertion intolerance disease.

The IOM report, issued earlier this month, concluded that misconceptions by some doctors that ME/CFS isn't a serious illness, is a mental-health issue, or is even imagined by patients, have made it difficult to diagnose patients early.

One of the strengths of the Science Advances study is that researchers identified 52 people who had the illness less than three years. Previous studies have looked at fewer patients, making it harder to detect patterns or differences between various groups.

Mady Hornig, the study's lead author and director of translational research at the Center for Infection and Immunity at Columbia's Mailman School, said that in the early phase of the disease, there is evidence of proteins that are usually found in blood when someone is fighting an infection. Those proteins should return to normal levels after the acute illness has faded.

But in the newly diagnosed ME/CFS patients, "the immune system doesn't quiet down," she said. This finding fits in with reports by many, but not all, patients, that they were sick with an infection and never completely recovered.

Dr. Hornig said the reason why the same immune signature cannot be found after patients have been ill for more than three years is "the immune system shows evidence of exhaustion."

There are existing monoclonal antibodies that target some of the elevated proteins and might eventually be tested with newly diagnosed ME/CFS patients, Dr. Hornig said. The hope is that immune-modifying drugs used early enough might help stave off the decline experienced by patients who have been ill for longer.

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