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MS study may have treatment implications

By CARLY WEEKS
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Researchers find a connection between a particular protein that regulates immune function and patient response to medication

Multiple sclerosis researchers have found a connection between a particular protein that regulates immune function and patient response to medication, a link they hope may be used to help predict who will benefit from a popular treatment.

The finding, included in a study published online yesterday in the journal *Nature Medicine*, raises the possibility there are two distinct kinds of multiple sclerosis that dictate whether an individual will benefit from taking interferon-beta, one of the most commonly prescribed drugs to treat the disorder.

"It's a pretty big 'aha' moment I think in the field of multiple sclerosis," said Lawrence Steinman, professor of neurology at Stanford University and lead author of the study.

The new research comes at a time when much of the public discussion of multiple sclerosis is fixated on a new theory and experimental procedure from Italian medicine professor Paolo Zamboni. He believes MS is a vascular condition, caused by blocked or malformed veins responsible for draining blood from the brain, and can be treated with surgery.

Although a significant amount of money is being earmarked to study the theory's validity, more conventional research into the cause of MS and potential treatments continues. Doctors have long known that some patients don't respond well to interferon-beta, a front-line MS drug, but the reason has never been clear.

Dr. Steinman and his colleagues, including Canadian post-doctoral fellow Robert Axtell, think they may have found the answer. They discovered that a group of MS patients who didn't respond to the medication all had high levels of Interleukin-17 (IL-17), a cytokine or protein that helps regulate the immune system.

It's an important connection because it opens the door to the possibility MS patients may one day be able to have a simple blood test to determine if interferon-beta will work for them, according to the study.

That would help patients make a rational decision about their course of treatment and be more aware of the potential outcome, Dr. Steinman said.

But it could also represent a significant savings in medication costs. Identifying which patients won't benefit from interferon-beta could help unnecessary prescriptions and the price tag that goes along with them, Dr. Steinman said.

"That [blood] test would have a great impact," he said.

Their research was funded by grants from the U.S. National Institutes of Health and the U.S. National Multiple Sclerosis Society.

However, not everyone is convinced of the significance of this study.

Paul O'Connor, director of the multiple sclerosis clinic at St. Michael's Hospital in Toronto, cautioned against concluding a cause-and-effect relationship between elevated IL-17 levels and a lack of response to medication.

While the theory may have merit, Dr. O'Connor said, the study only looked at 26 patients and shouldn't be considered conclusive.

"It's really a preliminary observation," Dr. O'Connor said. "We would need to do a much larger study to see whether or not this preliminary finding is actually verified."

Yet, most of the new MS research dollars may already be dedicated to getting to the bottom of Dr. Zamboni's novel theory. Some studies are already under way, and the Multiple Sclerosis Society of Canada is expected to announce in coming months who will receive research funding in Canada.

Some Canadian patients excited by the possibility of "curing" their MS or eliminating symptoms have left the country to get the procedure in countries such as the United States and Poland.

But as more researchers investigate Dr. Zamboni's theory, signs are emerging that it may not be as revolutionary as hoped, and could also present significant dangers to patients.

In February, researchers at the University of Buffalo released a study that showed as few as 56 per cent of MS patients they looked at had the blood vessel problem thought to cause the disorder. In addition, researchers found the blood vessel problem in about one-quarter of healthy people involved in the study.

"I certainly would not recommend people get this treatment done ... until we figure out if there's real truth behind it," Dr. O'Connor said.

The Wall Street Journal reported last week that Michael Dake, a vascular specialist at Stanford University, who had been performing the experimental procedure on MS patients, had to stop after one patient died of a brain hemorrhage and another had to have emergency surgery after a problem developed with a stent meant to open up a blood vessel.

Although the report noted there is no proven connection between stents and the patient's death, the program was considered too risky and was shut down. Some patients had reported an improvement after the procedure.

Dr. Steinman said the case illustrates the dangers of embracing an experimental treatment before it has been properly evaluated and the problems that can occur when patients push for a procedure that's not yet adequately backed by evidence. "Those of us that are trying to say 'Slow down, let's prove whether it's right or wrong' are sometimes cast as obstructionists," Dr. Steinman said. "Is Zamboni's breakthrough a big step? It remains to be seen."

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