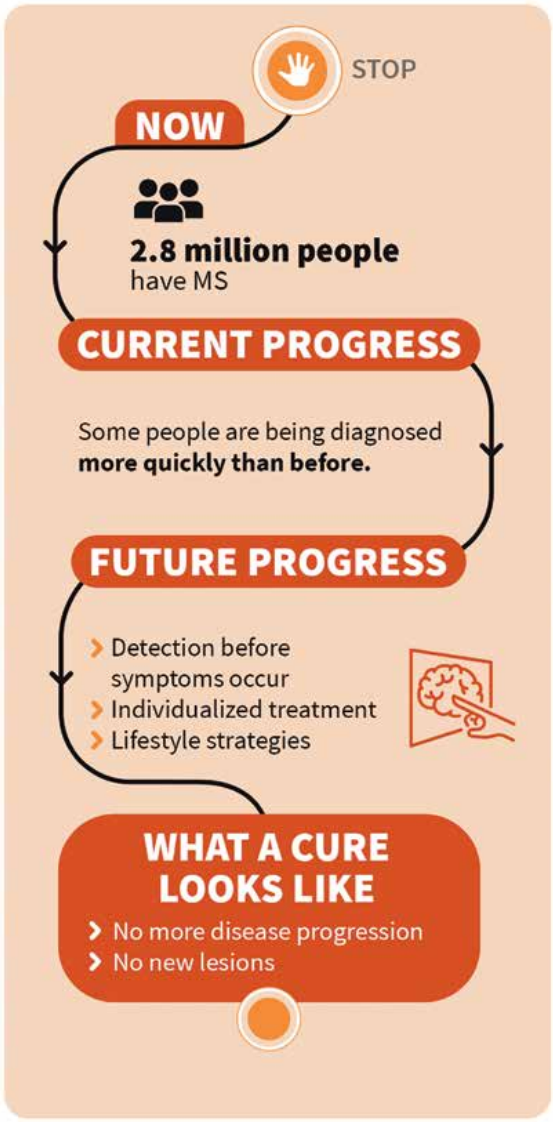
Stop, restore and end MS

Learn more about the researchers working to stop MS, restore function and end the disease.

By Brandie Jefferson

The Pathways to Multiple Sclerosis Cures initiative brings together experts from various research disciplines to identify areas of research where breakthroughs have the potential for the most payoff to develop cures. The initiative has three pathways: stop, restore and end. Here is a look at each one.

Stop: Researchers study earlier stages of MS before symptoms occur
Most people with multiple sclerosis can remember a few key periods related to their condition.



“People I’ve talked to are very aware of the date they were diagnosed,” says Helen Tremlett, PhD.

Ask them to think back further, and they may say something like, “It may have started with optic neuritis a few years ago.” That’s symptom onset.

“The problem is, no one knows when MS starts,” Tremlett says.

Tremlett is the Canada Research Chair in Neuroepidemiology and Multiple Sclerosis at the Djavad Mowafaghian Centre for Brain Health at the University of British Columbia. She is one of 13 new grant recipients from the first round of targeted research funding to support the National Multiple Sclerosis Society’s Pathways to Cures initiative to study an earlier stage of the disease. Her grant is being co-funded with the MS Society of Canada.

As part of the “Stop” pathway, Tremlett’s research will contribute to understanding the impact of MS before symptoms occur.

“My group is going to investigate the time before symptom onset,” Tremlett says. It’s a period of potential disease activity known as the prodrome.

Prodrome markers exist for other diseases — a loss of sense of smell is thought to be a marker in Parkinson's. But, Tremlett says, researchers didn't think MS had a prodrome early on, so the idea hadn't gotten much attention.

With secure access to Canada and Sweden's national healthcare systems, she has an incredible dataset to facilitate this work: two decades' worth of medical records of people in two Canadian provinces and a population in Sweden.

The data connect anonymous doctors' visits with their prescriptions, hospital admissions, and any diagnoses they receive, including MS.

Tremlett's group wants to discern patterns that can help them identify the earliest evidence of MS. They have good reason to think they'll find success.

Several years ago, with funding from the National MS Society, they found that in the five years leading up to MS symptom onset, people were more likely to access the health system for a range of signs and symptoms.

The preliminary study was proof of principle — these commonalities could be measured. But much still remains unknown.

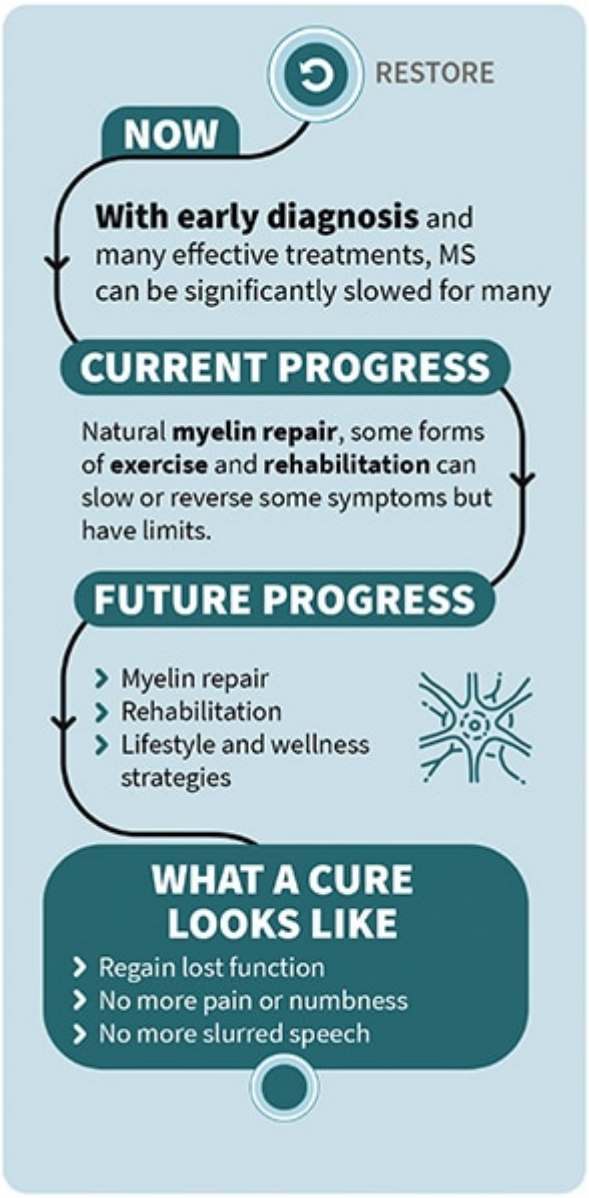
"Now, we're trying a more sophisticated method," Tremlett says. They'll use machine learning to search for clusters of early warning signs and symptoms that might differ for men, women, and people of different ages or those born in different parts of the world.

They'll also look for indicators that someone might be prone to more severe disease progression.

"We hope to be able to identify someone in the prodromal (or early) phase of MS," Tremlett says. "If successful, we might, in the future, be able to offer someone with a high probability of having prodromal MS enrollment in a clinical trial, with a view of testing a promising therapy that might alter the long-term course of MS."

Understanding this early phase of MS can also inform the search for a cause of MS. If, for instance, research determines the prodromal phase of MS is five to 10 years, researchers might be looking further back for an exposure event before it has set the wheels of MS in motion.

Restore: Researchers work to repair damaged myelin in the brain
In a healthy brain, damaged myelin — the tissue that insulates nerve fibers — can repair itself.



Stephen Crocker, PhD, associate professor of neuroscience at the University of Connecticut Health Center, is working to restore that ability in people with multiple sclerosis. He now has the support of the National Multiple Sclerosis Society, which has awarded him a grant so that he and his research team can come up with an answer.

The grant is one of many in the Society's research portfolio focusing on restoring function for people living with MS.

That people can restore myelin after it has been damaged wasn't always a given.

"When I was a grad student, the whole notion was that myelination happened during development, and that's it," Crocker says. "Once it's damaged, we learned, it's done."

Subsequent research has shown remyelination is possible, not just in healthy brains but in the brains of people with MS and other conditions which result in demyelination, or loss of myelin.

But why does demyelination happen in the first place? To find out, Crocker has taken skin

cells from people with progressive MS and transformed them first into stem cells, then into oligodendrocyte progenitor cells — cells that are ultimately responsible for producing myelin.

What he found was striking. Based on the length of telomeres — caps on the end of chromosomes which shorten over time — the brain cells of the people with MS appeared to be much older than the participants' biological age.

"It's the MS paradox," he calls it. "A disease of the young affected by aging."

The promising news is that Crocker and his team have made headway in determining why, exactly, "older" brain cells stop producing more myelin. "The cells don't do what they're supposed to because of a protein in the brain that tells them not to produce myelin," he says.

"Blocking that protein seems to release the brakes," Crocker says, allowing these cells to do what they're meant to do: remyelinate.

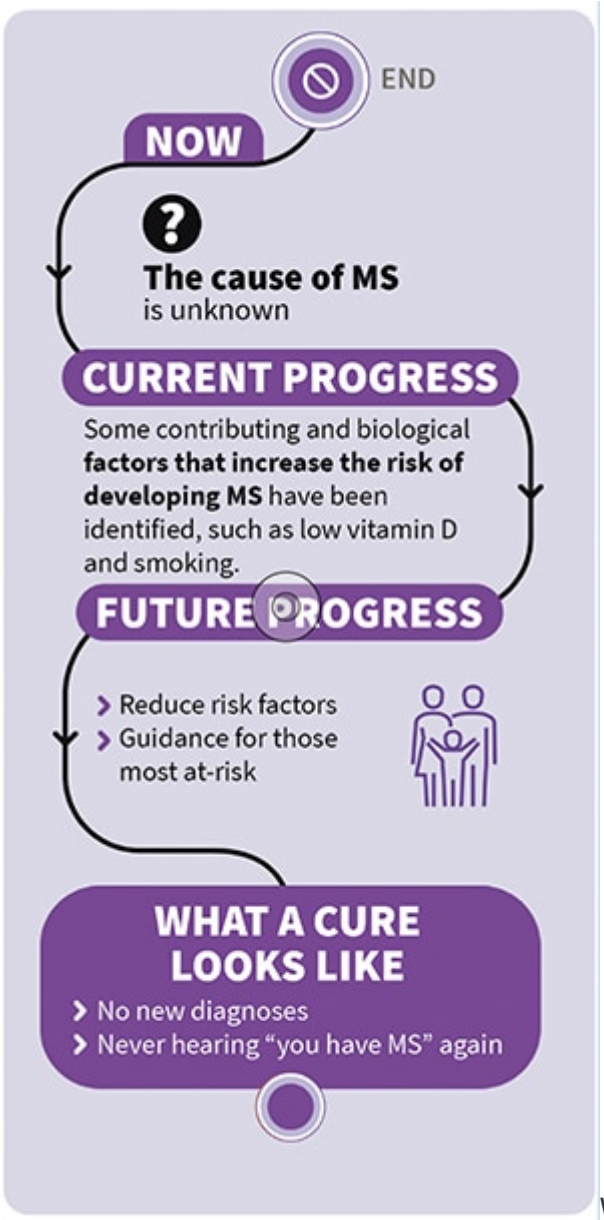
Crocker is hopeful, not only that his research may lead to therapies for everyone with demyelinating diseases, but particularly for those with progressive forms of MS.

"The idea of repairing and restoring is so insightful," he says. "We have so many drugs for MS, and they all work well. But if you have progressive disease, those drugs aren't much help.

"If I could summarize the state of the field in one word, it would be 'hope.' Recent innovations in regenerative medicine are moving at a rapid pace."

End: Research aims to help predict who is at risk for getting MS

With the global pandemic, many people have become more familiar with the idea of antibodies — proteins that target foreign substances, such as viruses and bacteria. That makes it easier for Michael Wilson, MD, to explain his research to the general public.



Wilson, associate professor of neurology at the University of California, San Francisco's Weill Institute for Neurosciences, has received a grant from the National Multiple Sclerosis Society stemming from a recent Pathways to Cures targeted funding initiative. As a part of the "End" pathway, he's looking for a special class of antibodies that may indicate a person's predisposition to multiple sclerosis.

"The goal is to try to identify biomarkers in the blood to help predict who's at risk for getting MS," Wilson says. It's a continuation of the work he's been doing with MS and other diseases.

As a clinician scientist, Wilson sees patients and also researches neuroinflammatory diseases. About half of his patients have multiple sclerosis. The rest have an assortment of disorders with brain inflammation, including infections of the central nervous system. Many times, Wilson says, the root cause of the inflammation is unknown.

To find out, Wilson and his lab have been developing tools to look broadly for antibodies, markers that would indicate a possible cause of a person's inflammation.

"We also look for 'autoantibodies,' " Wilson says. These are the antibodies that get off track

in autoimmune and immune-mediated diseases. They attack a person's body instead of an invading virus.

The tools in Wilson's lab were developed to look for a broad swath of infections all at once and for autoantibodies to help clarify what was causing these rare instances of brain inflammation.

"More and more, we've been applying the same technique to better understand what might be triggers for MS," Wilson says.

Michael Wilson, MD

He'll use these tools on a unique data set provided by his study collaborator, Mitchell Wallin, MD: blood samples from 500 U.S. veterans submitted yearly. Half of these veterans have MS. The other half do not. Wilson will have samples from before and after those with MS were diagnosed.

With one tool, his team can determine the presence of thousands of antibodies. "If we look across every virus, are the profiles in people with MS different from those who do not have MS?"

With the other tool, Wilson can narrow in on MS-specific autoantibodies to determine if those, too, are different in people with MS. And if so, are they different years before clinical presentation?

The discovery of a unique antibody or autoantibody signature would end the search for an MS biomarker. And maybe, coupled with preemptive intervention, could mark the end of MS for some people at high risk for developing this disease.

Brandie Jefferson is a writer in St. Louis, Missouri.

Read about how the Pathways to Multiple Sclerosis Cures initiative was developed.