Pathways to cures



New initiative focuses on research to stop, restore and end MS.

By Brandie Johnson

Researchers have gained crucial insights into the causes and drivers of multiple sclerosis. The results of those insights are found in the rapid-fire development of new diseasemodifying therapies (DMTs). But while those therapies have significantly improved outcomes for many people with MS, they're not the end game, says Bruce Bebo, PhD, executive vice president of Research for the National Multiple Sclerosis Society. Instead, they are milestones along pathways to cures for MS.

New insights into the immune system, breakthroughs in remyelination, the potential for a reliable MS biomarker — all these findings and more indicate that research into MS has reached an inflection point, Bebo says. "Now is the time to double down," he says. "We feel like the science is ready. It's time to start talking about cures."

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.

"The Pathways roadmap is about describing areas of research and laying out the questions that still need to be answered to develop cures," Bebo says.

Not a cure. Cures

"It became clear when we started this process that we were talking about more than one

thing, and so we use the plural of 'cure' and 'pathway' intentionally," Bebo says. "This may be obvious to some," he says, particularly to those who have MS, "but what counts as a cure can depend on where you are in your journey with MS."

As such, there are three pathways: "Stop," "Restore" and "End."



For people with MS — particularly relapsing and progressive forms of MS — who haven't accumulated disability, "If you could stop the process in its tracks, and no longer need medication," Bebo says, "that would be a cure."

The "Stop" pathway aims to stop disease activity. It will focus on early detection to catch the disease before it can do significant damage to a person's nervous system and precision medicine to stop the disease in its tracks using a tailored approach.

"There has already been a lot of progress in this area with [disease modifying therapies]," Bebo says. But researchers still need to determine how best to treat each individual. "We need to figure out which therapy works for any given individual."

According to the American Academy of Neurology, there is good evidence that starting early treatment with a disease modifying therapy (DMT) can slow disease progression. But the inverse is also true: "The longer it takes to find the right therapy, the higher likelihood of accumulating disability," Bebo says. "Early detection and precision medicine are the areas of emphasis in the 'Stop' pathway that will get us closer to this cure."

Once a person has accumulated some disability, a cure looks different. The "Restore" pathway focuses on reversing MS disability and returning people to their active lives through various means, including rehabilitation and symptom management. But "Restore" also focuses on regeneration of the nervous system, especially myelin, the nerve fiber insulation that is attacked by an immune system thrown out of whack by this immune-mediated disease.

The idea of regenerating myelin is not at all far-fetched. "There have been tremendous advances in our understanding of the nervous system's ability to repair itself," Bebo says. Clinical trials in people have already shown that boosting myelin repair is possible. There hasn't yet been clear-cut evidence that repairing myelin leads directly to restored clinical benefits (i.e., the reversal of disability) but Bebo thinks it's a matter of time and a concerted research effort, which the Pathways initiative supports. "Being able to measure repair and measure the clinical benefit is one of the milestones in our roadmap," Bebo says. "I am confident that we will see real progress on this pathway in the next few years."

That's just three years from now.



Now imagine you do not have multiple sclerosis, but your sister does. But having a first-degree relative with MS means that, although your risk is still low, it's higher than someone with no family history. So at every annual physical, you take an additional blood test. Your doctors are looking for a biomarker, some telltale sign in your blood that alerts them to the fact that you are, in fact, at risk for developing MS, just like your sister.

"We have a reason to think we can identify people at high risk," Bebo says. He points to similar tests that are either available or undergoing late-stage trials for other related diseases, including Type 1 diabetes and rheumatoid arthritis. Four new biomarkers were identified this year.

The "End" pathway is working toward a future where no one ever hears a doctor say, "You have MS."

"The fact we're even talking about cures indicates the arc of where we are," Bebo says.

His optimism is backed up by a career dedicated to MS research, both academic and private. That background also makes him acutely aware of the elusive nature of this complex disease.

Bebo entered the field because his mother was diagnosed with MS in the early 1980s. At the time, he says, "There was absolutely nothing that you could offer," as far as treatment. As optimistic as he is, he knows there is an urgency to find a cure for people living with MS that the deliberate pace of research struggles to match.

But it's that deliberate nature of Pathways to a Cure that is one of its biggest strengths.

"We are, in a way, trying to engineer a cure," Bebo says. The roadmap provides a clear outline of what research needs to be done and what questions need to be answered to get to the point where researchers have all the missing pieces of the MS puzzle.

The Society has received the endorsement of 15 MS patient and professional organizations around the world to date.

Bebo says the Society has also been clear to leave room — and funding — for the unexpected.

"We're not so short-sighted as to believe we know everything that there is to do," Bebo says. "We're leaving the opportunity for serendipity and happy accidents."

Brandie Jefferson is a writer in St. Louis, Missouri. She was diagnosed with MS in 2005.

Find more information about the research being done in each of the <u>stop, restore and end</u> <u>pathways</u>.