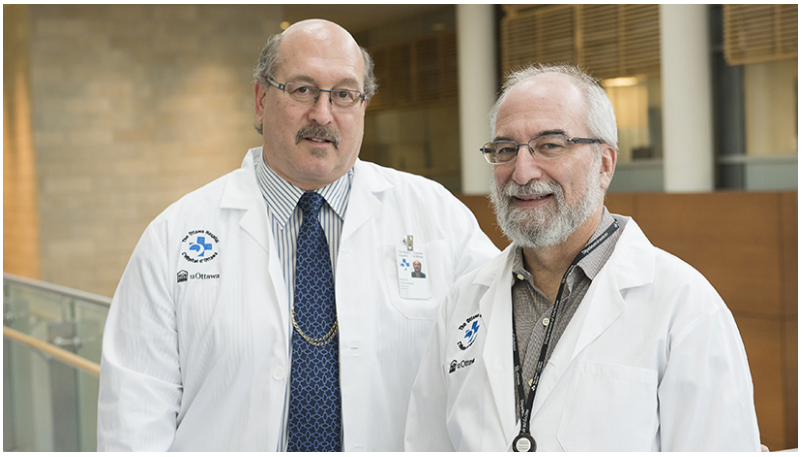
HEALTH

A new ‘cure’ for MS? Not so fast.

The stem cell treatment for MS greeted as a “cure” is a breakthrough for five per cent of people with MS. What about the other 95 per cent?

by Anne Kingston Jun 17, 2016



Harold Atkins, a haematologist, and Mark Freedman, a neurologist, worked on the breakthrough Canadian study published in The Lancet (Trevor Lush/Ottaw

Last week the respected British medical journal *The Lancet* published a Canadian study that landed with a bang: it revealed that a sma segment of people diagnosed with multiple sclerosis (MS) experienced remarkable results after undergoing autologous hematopoietic transplant (aHSCT). In the 13-year study, Ottawa-based doctors Harold Atkins, a haematologist, and Mark Freedman, a neurologist, treated 24 patients. They administered a drug that caused the stem cells in their bone marrow to move into their bloodstream, then e stem cells, and processed them in a lab to purify them. Patients were given a chemotherapy drug that wiped out their immune system immune system was rebuilt, with the purified stem cells re-injected into their bloodstream. This group was tracked between four and saw a return of function taken away by the disease, such as vision, balance or ability to walk, and eight saw disease progression halted; experienced worsening disease progression. One person died after liver failure.

Both the MS Society of Canada, which funded the research, and the Ottawa Hospital, where the research took place, spoke in terms o “breakthrough.” Medical professionals used the words “miracle” and “cure” to describe the results of the phase II study. “Everyone is h the ‘c word,’ but these patients are cured,” Michael Rudnicki, director of the Regenerative Medicine Program and the Sprott Centre fo Research at the Ottawa Health Research Institute, who was not involved in the research, told Vox.

It’s not surprising then that headlines suggested a cure for MS itself was at hand: “An aggressive Canadian treatment offers stunning r patients,” claimed the Toronto Star. “This isn’t hype: Canadian doctors just reversed severe MS using stem cells,” Vox proclaimed. “Ne can ‘halt’ multiple sclerosis, says study,” reported the BBC. Many news reports led with the heart-warming story of the study’s most su participant: 41-year-old Jennifer Molson, diagnosed with MS in 1996 at age 21; when Molson underwent the procedure in 2002, she w assisted care. In another nice twist, she now works at the Ottawa Hospital, where she was treated. Not only can she walk independent also ski and kayak. She’d marry, and dance at her wedding. There are lasting effects of the year of horrible sickness, of course; Molson bear children and is on constant watch against infection. But those lingering effects and the risks, which included a 10 percent chance death, were worth it, Molson told the *Star*: “I have been given a second chance at life.”

Anyone familiar with MS, an unpredictable mysterious degenerative condition that can rob people of their ability to touch, to see, to v will be inspired by Molson's tale of recovery and that of several of the study's participants. They will also understand why the patients were willing to take such a risk to forestall degeneration. But to see this as an MS "cure" is mistaken; if anything, the study's results pro of how heterogeneous the population living with an MS diagnosis can be. Only a small subset fit the study's criteria: those with an ear inflammatory, relapsing-remitting form of the disease who do not respond to drug therapies. Study participants ranged in age from 21 been diagnosed within the previous 10 years; all were ranked between 3 and 6 on an MS disability scale ranging between 0 and 10 (6 is needs a walking aid to walk 100 metres). Atkins estimated five percent of the MS population could potentially benefit. That is a not in number given that 2.3 million people are estimated to be living with MS worldwide, more than 100,000 of them in Canada where the declared the condition "Canada's disease." And it is undeniably a breakthrough, but there's a danger in forgetting it's not a potential cu cent of people living with MS. Hematopoietic stem cell transplantation (HSCT), which has shown considerable success treating paed not a new treatment for MS; Richard Burt of Northwestern University pioneered its use in the mid-'90s; over the past two decades, th cases have been treated. Results from Burt's 2015 study, published in the *Journal of the American Medical Association*, were promising— dramatic. The Ottawa study is the most aggressive and high-risk in carpet bombing (rather than suppressing) immune cells; it was als in harvesting immature stem cells. Other studies are in the works. An innovative FDA-approved stem cell treatment trial that does no chemotherapy is under way at the Tisch MS Research Centre in New York City. Phase I results, presented at the American Academy of meeting in April, are promising: it was found to be safe and well-tolerated with no serious adverse events reported. An aHSCT study c underway at Sheffield University in the U.K. uses lower intensity, and thus less dangerous chemotherapy to target the immune system a flurry of similarly jubilant headlines earlier this year: the BBC reported "patients who were paralysed have been able to walk again."

Such uplifting stories are staples of medical news; media coverage of the Ottawa study highlighted the most dramatic recovery; we did name of the person who died, per clinical trial protocols which protect anonymity. As promising as the Ottawa study is, it's far from d Freedman himself notes in *The Lancet* press release: "The sample size of 24 patients is very small, and no control group was used for co the treatment group. Larger clinical trials will be important to confirm these results." Nor has aHSCT been tested in a randomized, do placebo-controlled trial— the "gold standard" in medical research. "A blinded trial would not be feasible in this case," Freedman and A told *Maclean's* in an email, "because the effects of the chemotherapy (e.g. hair loss, nausea, infections) would be very obvious and the p researchers) would easily know which group they were in." The research community has talked about randomized, controlled (but no trials but questions remain, Freedman and Atkins say: "For example, it is unclear if patients who would be eligible for this trial would part of it, knowing that if they were assigned to the control arm, they would not have access to this procedure." There are still kinks to A quarter of participants developed infections and all but one had a toxic response to the treatment; one landed in intensive care.

Risks associated with procedure remain high, Jan Dörr, of NeuroCure Clinical Research Center, Charité-Universitätsmedizin, Berlin, *Lancet*. "These results are impressive and seem to outbalance any other available treatment for multiple sclerosis," he says, adding it's t "show complete suppression of any inflammatory disease activity in every patient for a long period…However, aHSCT has a poor safe especially with regards to treatment-related mortality." Dörr doubts the study will change MS treatment in the short term, "mainly be mortality rate will still be considered unacceptably high." Stem cell specialist Paolo Muraro called for caution in interview posted on t Society website: "High-intensity chemotherapy, as used in this study, is associated with higher toxicity. Additionally, the benefit of pu cells is currently unclear, and needs more investigation."

Other questions remain. Studies show chemotherapy itself affects neurological function and stem cells affect brain atrophy. Freedman author of a study published last month that indicated MS patients showed accelerated whole-brain atrophy after treatment "likely ass treatment-related toxicity and degeneration of "committed" tissues." It also noted "atrophy eventually slowed to that expected from n suggesting that stopping inflammatory activity in MS can reduce secondary degeneration and atrophy." Freedman was also a co-autho study that found aHSTC didn't work: "it fails to halt the demyelination and inflammation of MS," it concluded. Two factors made it d interpret that study's results, he tells *Maclean's*: "The study examined five patients who received different forms of chemotherapy and stem cell therapy (one was from our trial at the Ottawa Hospital, but the others were from different trials that used different procedu the patients died fairly soon after the therapy due to treatment-related complications."

Stem cell specialist Rudnicki remains optimistic about the aggressive Ottawa protocol which is now being performed at the Ottawa H that fit the criteria: "I think this is going to be the new standard of care for progressive MS," he told *Vox*. Muraro is more circumspect: study] confirms previous thinking that aHSCT is not suitable for people with progressive forms of MS who have accumulated long-sta no longer related to ongoing inflammatory damage. For these people, the risks of treatment outweigh any potential benefit."

Fifteen people have received treatment, covered by OHIP, at the Ottawa Hospital; their progress is being tracked for study. Freedman contend the benefits outweigh the risks: "The evidence from this study clearly shows that our treatment can produce a long lasting re select patient population…who have already failed other therapies," they write. "While further research is aimed at refining the techni minimize toxicity, we feel that the treatment should be made available for similar poor prognostic patients as long as it is offered by ce comparable transplantation expertise."

The new Ottawa study puts a lens on MS, a complex condition that remains little understood. Some media coverage would lead one t wiping out and replacing the immune system addresses the root cause of MS, when what it does, according to researchers themselves inflammation. The cause, or even causes, of MS remain a mystery. The dominant theory that MS is an autoimmune condition caused attacking its own immune system, repeated like gospel, remains unproven. Other news coverage suggests that those ineligible for the well-served by other therapies. "Latest MS 'miracle treatment' overshadows the real news: Multiple sclerosis was once considered a ho Today, drug treatments are highly effective," the CBC reported. The accompanying story states "one of the major reasons why today's transplant story is not relevant to 95 per cent of MS patients is that they won't need it." Yet people diagnosed with the most debilitatin who do not experience relapses and are not eligible for the Ottawa stem cell treatment, more than 10 per cent of the MS population, h therapies available to them. Exactly how effective MS "disease modifying-drugs" are for a condition characterized by unpredictable rel remissions is unclear. A spate of studies indicate that a major class of these drugs do not stop disability; all come with serious side effe include cancer and death. Frustration with MS drugs, in fact, is driving stem cell research, as Burt's January 2015 study states: "No curr relapsing-remitting multiple sclerosis results in significant reversal of disability."

The promise of stem cell therapy has given rise to understandable optimism but also hope ripe for exploitation. A British doctor lost h 2010 after offering MS patients a treatment that turned out to use bovine stem cells. Last month, the International Society for Stem C issued new guidelines instructing scientists to be circumspect when talking about their research. It's a useful instruction when discuss MS "cures." The news that five percent of the MS population could potentially see disease reversal as the result of a new therapy is goo a most welcome development. To call it an MS "cure" is to forget the remaining 95 percent.