

What If MS Could Be Prevented?



MS



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INFOCORNER



What is NARCOMS?

NARCOMS is a registry for people who have multiple sclerosis (MS). Registry participants complete two surveys each year to provide information about themselves and their experience living with MS. Data from these surveys are used in research studies and to help further our understanding of MS. Participation in the registry is voluntary, and responders' identity and privacy are carefully secured.



What is the Goal of NARCOMS?

The NARCOMS Global MS Patient Registry helps to facilitate research about multiple sclerosis in North America and around the world. Collaboration between MS centers of excellence throughout the world helps to increase knowledge, improve clinical care, and enhance the quality of life for persons with MS.



How Private Is My Information?

We will keep the information that you provide us private and confidential by storing your data in a secure database. All information will be used for research purposes only. We do not share any personally identifying information with any person or research institution. We follow all Federal (HIPAA) laws regarding confidentiality.



Not Yet a NARCOMS Participant?

Please contact us at www.NARCOMS.org to enroll online, or call toll free at 1-800-253-7884.



Tell Us Your Thoughts!

Have an idea? We would love to hear from you!
Send us your questions, comments, and suggestions.

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www.mscares.org.

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DIRECTOR'S LETTER

Dear NARCOMS Now Readers:

In this issue of NARCOMS Now, we focus on preventative strategies for MS that may slow onset and reveal underlying causes of MS or the initial triggers that start the disease process. We examine diabetes as a model of disease prevention and the use of mesenchymal stem cells as a possible therapy for progressive MS.



Robert Fox, MD

In the Feature Focus, Dr. Alberto Ascherio (Professor of Epidemiology and Nutrition at Harvard T.H. Chan School of Public Health) outlines key risk factors for MS, including those that are “modifiable” or preventable. While seemingly insignificant for those people that already have MS, this information may offer some peace of mind concerning MS onset in others in their family.

In the SnapShot, we examine the diet and physical activity of NARCOMS participants as important factors to prevent or reduce MS symptoms. We also ask that NARCOMS participants complete a short survey to improve NARCOMS Now to suggest topics of interest in future issues.

In the MS News sections, we examine approaches to delay or prevent diabetes and their possible application to the prevention or delay of MS onset. In addition, we discuss the application of mesenchymal stem cell therapy to treat people with progressive MS. Further information on the exciting possibilities of stem cell therapy is provided in a sidebar and infographic defining types of stem cells and their potential application in treatment.

We thank you for your continued participation in the NARCOMS registry! Your involvement in this registry is critical in advancing our knowledge of MS.

Sincerely,

Robert Fox, MD

Managing Director, NARCOMS



What If MS Could Be Prevented?

A Look at Risk Factors, Viruses, and Vitamins

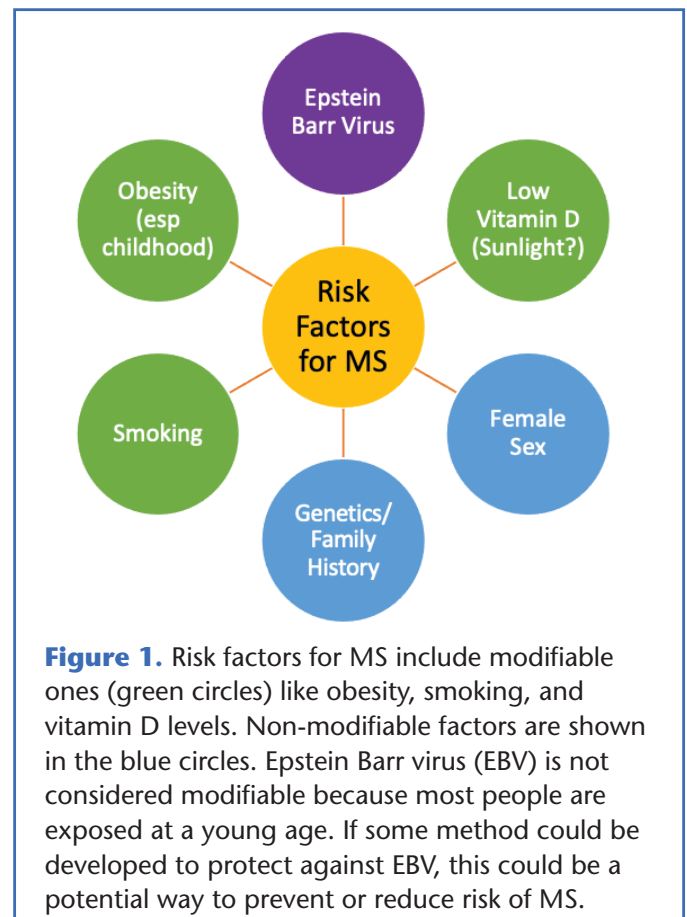
Multiple sclerosis (MS) currently affects about 1 million people in the United States (US), with an estimated 15,700 people newly diagnosed each year. If the onset of MS could somehow be stopped, or even slowed, the impact would be profound. Can MS be prevented? If so, how? These are questions that some MS researchers are pursuing. Finding answers would mean getting down the root causes of MS, or the initial triggers that start the disease process.

“It is still not entirely clear what causes some people to develop MS and others to be spared,” explains MS expert Alberto Ascherio, MD, PhD, of Harvard University. Dr. Ascherio is an epidemiologist at Harvard’s T.H. Chan School of Public Health, where he studies patterns and possible causes of neurologic diseases like MS. “We now know much more about the conditions and factors that increase MS risk,” he told *NARCOMS Now*.

MS Risk Factors

In several papers Dr. Ascherio has written on MS prevention, he outlines the key risk factors that occur more often in people with MS (Figure 1). The greatest known risk factor is having a family history of MS. Risk of developing MS is about 30 times higher among siblings of affected individuals than in the general population. Of course, family

history and biologic sex are beyond one’s control. Other risk factors are considered “modifiable” or *preventable*. These include excess body weight, cigarette smoking, and intake of vitamin D. A key risk factor that may be critical for the development of MS is infection with the Epstein Barr virus (EBV). EBV infection is not currently preventable, but this concept may be an important path toward future MS prevention.



About Epstein Barr virus

EBV is a member of the human herpesvirus family, like the viruses that cause chicken pox or shingles. EBV is easily spread through saliva. When the initial infection occurs in young children, it often causes minimal or no symptoms. EBV is the virus that causes infectious mononucleosis, or “mono,” which can be a more serious or prolonged illness in adolescents and adults. After the initial infection, EBV takes up permanent residence in the body, usually in a dormant state. It’s hard to avoid EBV. Up to 90% of U.S. adults carry the virus in their bodies by the time they are in their mid-thirties.

What does EBV have to do with MS?

Similarities between the epidemiology of MS and that of infectious mononucleosis (mono)

are “striking,” Dr. Ascherio noted. MS is much more common in people who are positive for EBV and have a history of being sick with mono (Figure 2).

- Among all people who carry EBV, the risk of developing MS is 15 times higher in people who have had mono compared with EBV carriers who did not become ill from EBV.
- In people who test negative for EBV, MS is very rare. EBV-negative individuals have a ten-fold lower risk of developing MS versus EBV-positive people of the same age (with no history of mono).

Interestingly, about 90% of children in developing countries have already been exposed to EBV by age 4 years. Infectious mono rates are much lower in these areas

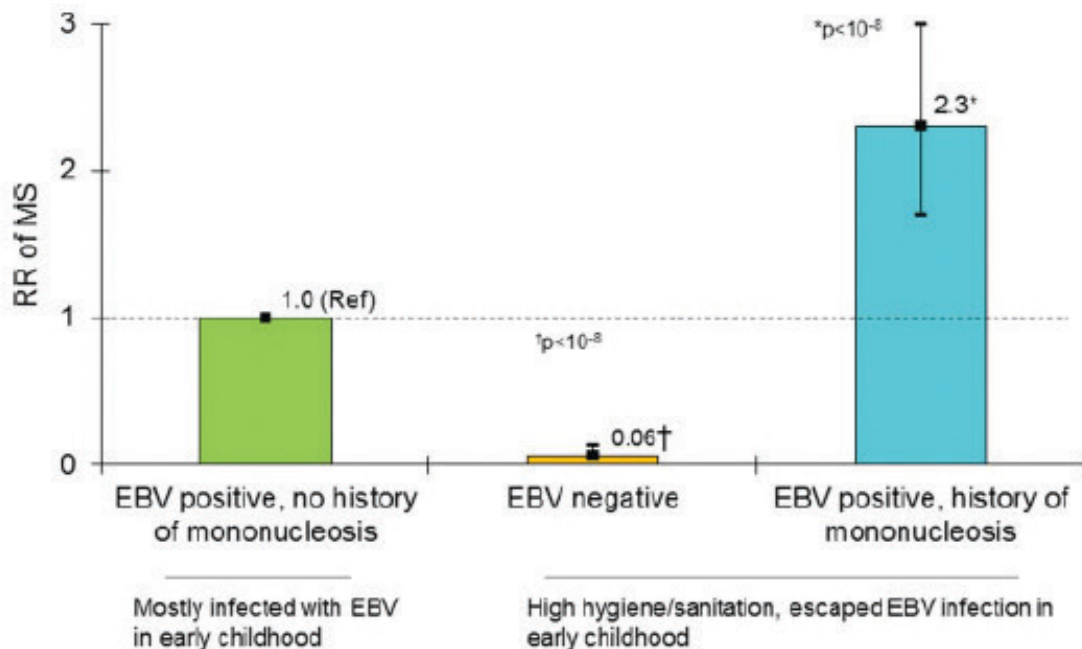


Figure 2. Risk of MS in people with EBV who have never had mono (green bar) was used as a reference point, or value of 1. By comparison, people who were EBV negative (yellow bar) had a very low chance of developing MS. Those with EBV and history of mono (blue bar) had more than double the risk of developing MS. RR = relative risk.

Reprinted with permission from Ascherio A, et al. Epidemiology of multiple sclerosis: from risk factors to prevention—an update. *Semin Neurol.* 2016;36:103-114.

compared to rates in North America and Europe. Likewise, MS prevalence is lowest in developing countries. This observation suggests that the timing of exposure to EBV may trigger a protective process in the immune system that could help to prevent MS later in life. It also suggests that preventing EBV with a vaccine might be helpful in preventing MS (see **Sidebar, page 7**).

Sunlight and vitamin D

Vitamin D behaves like a hormone in the body, regulating the function of many bodily systems. These include bone development, cardiovascular health, and immune system function. We get most of our vitamin D from exposure to sunlight. The rest comes from our diet (oily fish, eggs, vegetables, meat) or supplements. However, in some areas of the world, sunlight is minimal during the cooler months of the year. This provides too little of the ultraviolet B rays needed for our bodies to make enough vitamin D. With more time spent indoors in recent years, much of the population has lower blood levels of vitamin D than in the past.

Vitamin D is thought to play a role in MS development. People with low blood levels of the vitamin have a higher risk of developing MS. A large study of MS risk and vitamin D was based on a database with over 50 million blood samples drawn from U.S. military personnel, some of whom later developed MS. Those with the highest vitamin D levels had a greater than 60% reduced risk of developing MS. The associations between vitamin D and MS risk were stronger for people under age 20 years. In people who already have MS, adequate levels of vitamin D have been

associated with lower relapse rates and lower risk of MS progression.

According to Dr. Ascherio, most people can achieve a healthy vitamin D level by taking an oral D3 supplement (suggested 1,000 IU to 2,000 IU per day or as recommended by a healthcare provider). Although the USDA recommended daily dose is currently 600 IU, studies have shown that higher doses are safe and may help to reduce health problems associated with MS and other autoimmune diseases. In fact, vitamin D may help interfere with the effects of EBV. “Awareness of the importance of vitamin D has markedly increased over the past 10 to 15 years,” Dr. Ascherio told *NARCOMS Now*. “We have seen higher vitamin D levels across some populations, and I expect there will be a benefit on several conditions related to vitamin D insufficiency.”

Body weight and obesity

Obesity is another modifiable condition shown to increase the risk of developing MS. Obesity is associated with low-grade, persistent, systemic (whole-body) inflammation. This inflammatory state can be particularly harmful in women. Fat or “adipose tissue” may attract the inflammatory changes seen in MS. Being overweight could also affect the blood-brain barrier to enhance access of inflammatory cells into the brain.

In a large study following over 200,000 nurses over many years, having a body mass index (BMI) higher than 30 was associated with more than double the risk of having MS. Larger body size during young adulthood is associated with a higher risk of later developing MS, especially for children who are moderately or extremely

obese. A 2019 study from Germany showed that both boys and girls who are overweight or obese have twice the risk of developing MS, compared with non-overweight children or adolescents.

Smoking

A history of smoking may be another factor that predisposes a person to MS. Several large studies have shown that smokers have a higher risk of developing MS than nonsmokers. One large study in women found that the risk of having MS was 70% higher among those who had smoked 25 or more pack-years, compared with same-aged women who never smoked. (A pack-year refers to smoking 1 pack per day for 1 year). As with obesity, smoking can shift the body's immune system toward

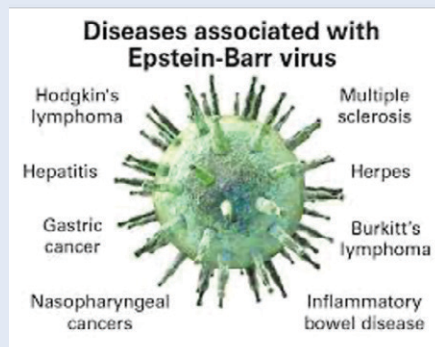
a pro-inflammatory state. Nicotine or other components of cigarette smoke may affect the blood-brain barrier as well.

The Importance of Prevention

Why does prevention matter to someone who already has MS? Some feel that preventing the disease may provide some peace of mind for loved ones, along with lifting the burden for society as a whole. "I know that MS has a genetic component. I would love to think that my grandchildren or future great-grandchildren could be spared this disease," said Sandra, a 62-year-old woman who was diagnosed with MS in her early forties. Better understanding of the immune system triggers that "switch on" the disease process may also help on the quest to find novel ways to stop ongoing damage in people who have MS.

Could An Epstein Barr Vaccine Help Prevent MS and Other Diseases?

The Epstein Barr virus (EBV) might remind us of the now-infamous SARS-Cov-2, due to its protruding spikes that enable it to bind to receptors on human cells. Preventing infection with EBV could affect multiple sclerosis (MS), and other conditions associated with chronic EBV infection, as shown in the box below. So far, small trials of vaccines to prevent EBV have yielded disappointing or limited results. However, as we know from the COVID-19 pandemic, vaccine science is evolving very rapidly. Some of this advancement is in genomic vaccines. Genomic vaccines take the form of DNA or RNA that encodes desired proteins. When injected, these genes enter cells and instruct them to make specific proteins that guard against



a particular type of viral infection. In addition to vaccines under ongoing study for coronaviruses, genomic vaccines are being studied to prevent hepatitis C and even some cancers.

Can a preventive vaccine be developed to block or prevent EBV infection? If so, would it also succeed in preventing MS?

This idea is "appealing, but also fraught with major challenges," said Gavin Giovannoni, MD, an MS expert and researcher based in London, England. Providing immunity against any herpesvirus is "almost an improbable endpoint," he said. However, he suggested that a vaccine to reduce the risk of developing infectious mononucleosis in a person exposed to EBV may be sufficient to have an impact on MS risk. "Challenges exist in development of an EBV vaccine, but efforts have begun and may yield surprising results," Dr. Giovannoni wrote in a recent article on EBV. In addition to vaccines, other treatment approaches being explored to fight the virus include antiviral drugs and cell-based immunotherapies.



SNAPSHOT

WHAT WE CAN LEARN FROM NARCOMS SURVEYS

Survey: Lifestyle, Physical Activity, and Diet

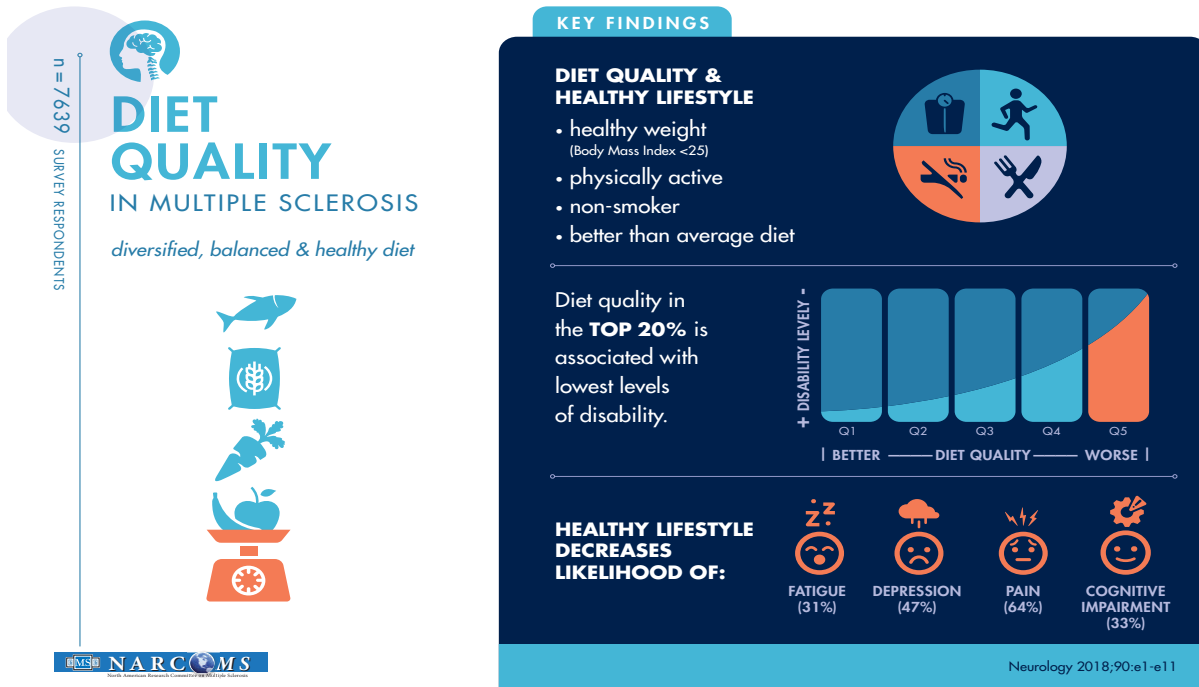
As described in this Issue’s Feature Focus, some risk factors for the onset and progression of MS may be modifiable through lifestyle changes. One thing that is important to many people is the prevention of MS for future generations of their families. Practices can be implemented early and can minimize the risk, delay onset, or reduce relapses for participants and their loved ones. One risk factor for MS, obesity, may be controlled through diet and exercise.

While beneficial for many reasons, a high quality diet with frequent exercise can reduce the chance of being obese, which also may delay MS onset or reduce MS symptoms. Thus, promoting a healthy diet and exercise in families with a history of MS may improve the

lives of all members of the family. NARCOMS participants were asked whether they followed any specific diets after their diagnosis. Results from past surveys suggest that many NARCOMS participants pursue dietary changes to support their health. In fact, a healthy diet was associated with lower levels of disability in people with MS, as well as a lower frequency of fatigue, depression, pain, and cognitive impairment (Figure 1).¹ According to the Fall 2020 survey, very few participants had met with a Nutritionist/Dietician in the past 6 months. Less than 5% of NARCOMS participants had discussed their meals and nutrition with a Nutritionist/Dietician. This was similar across all age groups.

In most NARCOMS surveys, we ask questions

Figure 1.



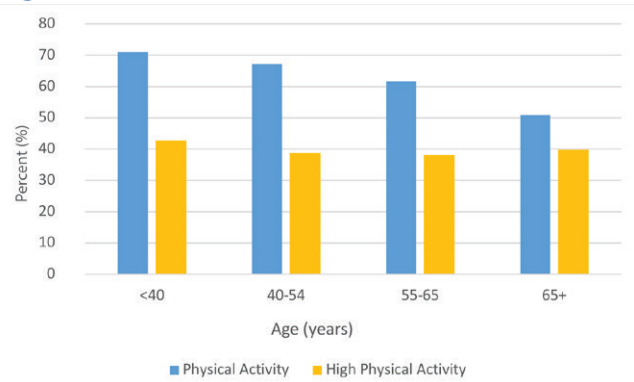
about general lifestyle characteristics, such as frequency of smoking and alcohol consumption.

- In the Fall 2020 Survey, ~93% of NARCOMS participants reported that they did not smoke currently. Findings were similar between men and women. Participants ≥ 65 years old reported less smoking. The Centers for Disease Control reported that, in 2019, 14% of U.S. adults aged 18 years or older smoked cigarettes.²
- Alcohol consumption data show that ~62% of NARCOMS participants don't consume alcohol or consume up to 1 drink per month, while ~13% have ≥ 4 alcoholic drinks each week.
- Women tended to consume less alcohol than men.
- Participants < 40 years old tended to consume more alcohol than older participants. The frequency of heavier alcohol consumption (≥ 4 alcoholic drinks/week) was similar across age groups.
- The rates of alcohol consumption by NARCOMS participants are lower than that reported by the CDC (20.6% of adults 18 years or older consume ≥ 4 alcoholic drinks/week).³

Two survey questions from Fall 2020 examined light physical activity (1 event/month), as well as moderate or high exercise activity (30 min sessions, 5 times/week).

- For light physical activity, ~60% of NARCOMS participants reported walking, running, biking, and other similar exercise at least once each month.
- For moderate or high exercise activity, ~40% of participants reported engaging in moderate or high levels of exercise (30 min sessions, 5 times/week), which is a lower rate of exercise than reported by CDC for adults aged 18 years and over across the US (53.3% engaged in at least

Figure 2.



150 minutes/week of moderate-intensity aerobic physical activity, 75 minutes/week of vigorous-intensity aerobic physical activity).⁴

- More women tended to report engaging in light physical activity, while more men tended to report moderate to high exercise activity.
- Participants < 40 years old reported a higher rate of light physical activity than other age groups, while participation in moderate or high exercise activity was similar across all age groups (**Figure 2**).

The survey data suggest that NARCOMS participants smoke less and consume less alcohol after their MS diagnosis compared to the general US population. In addition, relatively few NARCOMS participants consult a Nutritionist/Dietician to discuss eating habits and diet goals.

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MSMESSENGER

WHAT TO EXPECT ON THE NEXT NARCOMS SURVEY

The NARCOMS Registry Data Coordinating Center has moved from Washington University in St. Louis, MO, to the University of Texas Southwestern Medical Center in Dallas, TX. While Dr. Amber Salter continues as Director, we must say goodbye and thank you to Michele Curran as the NARCOMS Project Manager. If you call or email, you will likely end up speaking to Ms. Brenda Lewis.



The fall 2021 survey is going on now! Please be sure to check your emails or postal mailboxes and return your surveys. We had over 70% of the surveys returned last spring, which is fantastic! This fall survey includes some new questions on attitudes towards brain donation, and we are repeating the MSIS-29 (Multiple Sclerosis Impact Survey) and the METER. You may also notice revisions to the immunotherapy questions. Instead of asking for *how long you have taken* the therapy, we ask when you first began taking the therapy and the infusion questions have been changed to better reflect the administration of the therapies.

As a refresher for those who complete your surveys online: you no longer need to go to the NARCOMS website to access your surveys, and you do not need a login username or password. A link to your individual survey is emailed to you. You can just click on that link to access your survey. If you need to take a break, you can use the “save and return” function and a return code will be emailed to you.



As always, you can update your contact information with us by calling us at (800) 253-7884 or by email at msregistry@narcoms.org.



We welcome your comments or suggestions about the *NARCOMS Now* magazine and semi-annual survey. If there is a topic you would like to see discussed in *NARCOMS Now* please let us know by completing the short survey in this issue.



We understand that the past year has been difficult for many of you. If you are experiencing any new or troubling symptoms, physically or mentally, please contact your medical provider. Stay healthy and well. We care about you!



Breakthrough Study Delays or Prevents Autoimmune Form of Diabetes

Could a Similar Approach Work for Preventing MS?

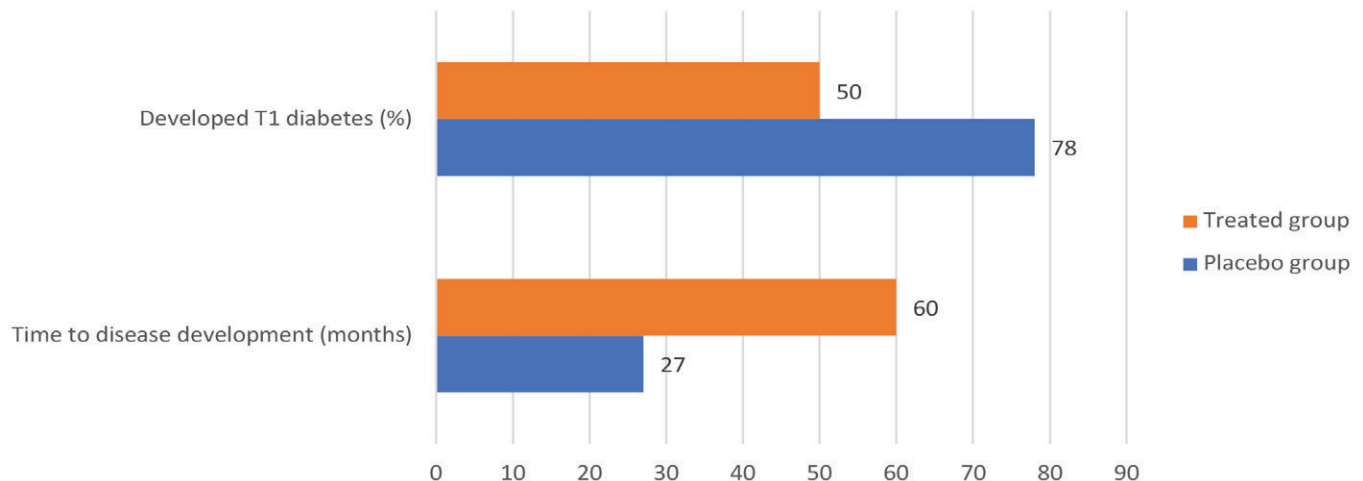
Type 1 diabetes is a severe form of diabetes that usually starts in childhood and can be passed down within families. It is sometimes called “juvenile diabetes.” This type of diabetes is caused by the loss of beta cells in the pancreas, which make insulin. This differs from the underlying cause of type 2 diabetes, which is due to insulin resistance (when the cells in the body do not respond well to insulin). Type 1 diabetes can be a devastating disease that can cause damage throughout the body despite treatment. Even delaying its onset could give affected children and teens an improved quality of life.

In two recent studies, Herold et al. and Sim et al. showed that modifying the immune

system might prevent or slow down the onset of type 1 diabetes in people who are at high risk for developing the disease.^{1,2} The results suggest that a similar approach of modifying the immune system in at-risk individuals might work to delay or prevent other autoimmune diseases, too. Some researchers believe this could have future implications for multiple sclerosis (MS).

The study enrolled 76 young people aged 8 years and over (median age, 13 to 14 years) who were at risk for type 1 diabetes. Trial participants had a family member with type 1 diabetes plus at least two antibodies in their blood indicating they are very likely to be diagnosed with diabetes in the future (see box). Half of the participants received one 14-day course of an injectable monoclonal antibody called teplizumab. This drug blocks the activity of a type of immune cell, CD3,

Figure 1. Results of 14-Day Course of Immune Therapy in Young People at Risk for Developing Type 1 Diabetes



known to be involved in autoimmune diseases. The other half received a placebo.

After an extended follow-up period, 50% of the treated group developed type 1 diabetes, compared with 78% of the placebo group (Figure 1). Among trial participants who developed diabetes, the time to onset in the treated group was delayed substantially—an average of about 5 years, versus a little over 2 years for the placebo group. The lead investigator, Kevan Herold of Yale University, described the importance of such a delay. “If you are in early elementary school and now you are not going to get diabetes for 5 years, that is a big deal. Or delaying diagnosis from high school to college.”

Teplizumab is not approved by the U.S. Food & Drug Administration (FDA) as of fall 2021. The FDA declined to approve the drug in July 2021 and requested more safety data. Other experimental anti-CD3 drugs have been studied in MS. One such drug, foralumab, is in early trial stages in people who have non-active progressive forms of MS. Thus far, there are no preventive studies for MS under way using anti-CD3 drugs.

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Study Finds Mesenchymal Stem Cell Treatment Safe and Possibly Beneficial in People With Progressive Multiple Sclerosis

There are two main types of stem cell therapies being explored to treat diseases like cancer or multiple sclerosis (MS) (see Sidebar). One is an intensive procedure that seeks to “reboot” the immune system. Hematopoietic stem cells are collected from the patient’s bone marrow. Subsequently, the individual is exposed to chemotherapy to deplete the immune system. The stems cells are infused back into the body and develop into new immune cells. A comparatively simpler form involves the injection of mesenchymal (mee-sen-KYE-mal) stem cells, which are also found in bone marrow, fat, and many other tissues. These cells are intended to go to areas of tissue injury and replace injured or sick cells.

A recent study conducted at research centers in Israel and Germany used mesenchymal stem cells to treat people with progressive MS (41 people with secondary progressive and 7 with primary progressive disease).¹ The stem cells were “autologous,” meaning they were obtained from the person’s own body rather than from a donor. Two different methods were tested for administering the stem cells— intravenously (IV; into the vein) or intrathecally (into the fluid around the spinal cord). These methods were compared with a placebo group which received a sham injection. Some of the patients were retreated with a second injection

The average age of diagnosis of type 1 diabetes is 13 years.

People with two antibodies associated with type 1 diabetes have a:

- 44% risk of developing the disease within 5 years
- 70% risk in 10 years
- 100% risk within their lifetime

of stem cells after 6 months. The overall follow-up period was 14 months.

Safety is an important concern with the more complex form of bone marrow transplant, hematopoietic stem cell therapy (HSCT). This is because patients must receive strong immune-suppressing drugs. The mesenchymal type of stem cell treatment may be safer because it usually doesn't involve those strong immune-suppressing drugs. In this study, there were no serious safety events that were considered related to the procedure. Two patients had an MS relapse, and one had an upper respiratory infection.

The main benefit examined in this study was "no evidence of disease activity," or NEDA. This means that the person with MS has no relapses, disease activity on MRI, or new or worsening clinical signs of MS. In this study:

Intrathecal stem cell therapy	59% exhibited NEDA
IV stem cell therapy	42% exhibited NEDA
Placebo group	10% exhibited NEDA

Intrathecal administration appeared to have several benefits over IV. Participants receiving intrathecal stem cells had improvements in terms of lower relapse rates, new MS lesions on MRI, walking tests, and other functional or radiologic tests. While this study was designed to be a short-term study, the results indicate that larger, long-term studies should be done to evaluate the longer term effects of this treatment. "Our results provide clear signals of short-term clinical efficacy and possible indications of neuroprotection, induced by the administration of autologous [mesenchymal stem cells] in patients with progressive multiple sclerosis," the researchers noted. This treatment is not available outside of clinical trials and needs to undergo further testing before it might be made available for routine clinical use.

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NARCOMS NOW SURVEY

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Stem Cell Treatments for MS: What are the Benefits and Risks?

Stem cell treatments for multiple sclerosis (MS) are often surrounded by confusion and controversy. The benefits and risks of this procedures depend partly on whether it is done at a legitimate medical center with expertise in the treatment. Many “fake” or highly questionable stem cell centers have cropped up around the world and target people with MS and other diseases.

The two main types of stem cell treatments used in MS are outlined below.

Autologous hematopoietic stem cell therapy (AHSCT)

This procedure involves use of immature cells (also called “progenitor cells”) taken from the person’s own blood or bone marrow. These can develop into any other type of blood cell. AHSCT is a bone marrow transplant. Strong chemotherapy drugs are used to wipe out almost all of the existing immune system. The infused stem cells are the source of the newly populating bone marrow, allowing the immune system to reboot. The benefits and safety depend on the expertise of the center, the patient’s health, and the type of chemotherapy used prior to infusing the stem cells.


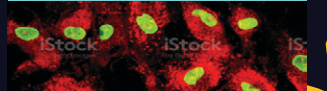
Mark S. Freedman, MD, of the University of Ottawa in Ontario, Canada, has led studies of AHSCT in patients with aggressive MS. “AHSCT is not appropriate for all MS patients,” Dr. Freedman noted. “It is mainly for those with a very aggressive course that cannot be managed with current therapies. It is not for someone with longstanding disease, advanced disability, and no evidence of recent inflammation.” There is a risk of serious side effects or death from the procedure. Among its benefits include reduced relapse activity, MRI lesions, and brain atrophy levels among patients who did not achieve results with other MS therapies.

Mesenchymal stem cell therapy (MSCT)

MSCT is considered an experimental therapeutic approach at present. Mesenchymal stem cells can be isolated from many types of adult tissues, including fat cells or bone marrow. The cells are multiplied in a laboratory and then re-introduced in greater numbers to the patient without the need for significant destruction of large populations of immune cells. MSCT differs from AHSCT because no chemotherapy is needed. However, mesenchymal cells must be

STEM CELL THERAPIES IN MS

HEMATOPOIETIC (AHSCT)	VS	MESENCHYMAL (MSCT)
WHAT ARE THE KEY DIFFERENCES?		
<ul style="list-style-type: none"> Uses patient’s own cells (autologous) Uses precursor cells (stem cells) usually taken from bone marrow (hematopoietic) More complex, high-risk procedure Similar to a bone marrow transplant Involves chemotherapy to ablate immune system 		<ul style="list-style-type: none"> Usually uses patient’s own stem cells (autologous) Uses mesenchymal cells (in many tissues including fat) Does not involve chemotherapy Requires cells to be duplicated with specialized equipment Infused via IV or into area around spinal cord
PROS AND CONS		
<ul style="list-style-type: none"> More widely studied, thus far, in patients with MS Higher-risk procedure Involves prolonged hospital stay and recovery period Must be done at highly specialized center Mainly for very aggressive cases (not those with advanced disability) 		<ul style="list-style-type: none"> Larger studies need to be done in MS Has been studied in patients with progressive MS (including secondary progressive) Lower risks associated with procedure versus HSCT Beware of bogus “stem cell clinics” that charge large sums and may be dangerous and/or ineffective

cultured in large quantities in an ultra-specialized cell growth facility. The process must be carefully controlled to prevent contamination. Once the cells have grown, they are infused into the patient, usually via a vein (intravenous) or the space between the bones of the spinal column (intrathecal).

Current guideline statements in MS, including European stem cell guidelines, state that “[stem cell therapy] should only be considered where potential risks are justified.”

The non-legitimate “stem cell clinics” that are widely advertised do not perform an immune system reboot like AHSCT. They use mesenchymal cells but most likely infuse too few cells, impure cells, or the wrong kind of cells, Dr. Freedman warned. “There is no evidence that such a procedure serves to reset the immune system,” he commented. There is also no evidence that they offer any form of sustained benefit.

Play WORDSEARCH

Find the following hidden words relating to MS Treatment.

DIET
EBV
GENETIC
MODIFIABLE

MONO
OBESITY
PREVALENCE
PREVENTION

RISK
SMOKING
SUNLIGHT
SUPPLEMENT

VACCINATION
VIRUS

U R X S X K J Y Z R E L X Q V
P R E V A L E N C E V E M D F
G P R E V E N T I O N B O S K
M E L I V B K Q X V N V N U S
F B N N C A S R W I S Z O P M
S X S E B Z C V K R F K A P O
U R W J T E L C H U G H W L K
N O K W P I P N I S Z I U E I
L N B Y E X C R M N T P A M N
I T P E M O D I F I A B L E G
G D R C S E R S U Y D T B N S
H I J U C I Z K B D C J I T K
T E L C H C T Z P L J U L O V
W T A S B N F Y J S A Y N D N
C P H S Q Q E M Q V L P C W F

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