

Understanding and Treating Multiple Sclerosis



It is still unknown what causes this nerve disorder, but research is uncovering some interesting information that could lead to prevention and better treatment.

By Annaben Kazemi

In 2004, Mabelle, a successful young chef working in the Chicago area, woke up with an excruciating headache that went from the back of her neck up to the top of her head. The pain was so intense, she felt nauseous. She made it in to see her primary care physician, who immediately sent her for a CT scan. The doctor delivered the stunning news that Mabelle, an otherwise healthy and active 32-year-old, was suffering from either a possible stroke or multiple sclerosis (MS). Mabelle took some time off from work, and after numerous tests, she saw a neurologist who conducted a spinal tap and said it was most likely MS.

As her symptoms progressed, Mabelle moved to Washington, D.C., where she could be closer to family. Then, in 2005, she experienced numbness in her right leg and had trouble walking. After more testing and another neurologist referral, she was finally diagnosed late in 2006 with MS. "Managing MS is an ongoing process, beginning with the very first symptoms and then continuing," explains Mabelle. "I don't think my story is unique; the journey to diagnosis is typically long and complicated."

Having a support network of professionals, family and friends helped during the most trying times of her journey. But, "there were times when it was a struggle, and I felt very frustrated," says Mabelle. The hardest time was when high-dose corticosteroid treatment failed, and her symptoms progressed. She spent two weeks in the hospital while her doctors tried short-term high doses of corticosteroids (methylprednisolone and then dexamethasone) given intravenously. She then began both physical therapy and counseling to adjust to all the changes her body was going through.

Nonetheless, she says, "Having MS doesn't mean going from a great future to no future. There's a way to balance your health concerns with your goals. My life was going in one direction, then this thing [MS] came along and made me reassess what's really important. Time is much more precious. I don't want to waste time doing things that don't fulfill and serve my purpose."

More than 2.1 million people are affected by MS worldwide. In the U.S., it is estimated that more than 350,000 people have MS. But, because symptoms can be completely invisible, the actual prevalence of MS is not completely certain.¹

What Is MS?

MS is a chronic, unpredictable disease that attacks the central nervous system (the brain, spinal cord and optic nerves). It is an inflammatory nerve disorder in which myelin sheaths around axons of the brain and spinal cord are damaged, leading to loss of myelin and scarring. The

damage is caused due to the destruction of the insulating layer surrounding neurons in the brain and spinal cord. This insulation, called myelin, helps electrical signals pass quickly and smoothly between the brain and the rest of the body. When the myelin is destroyed, nerve messages are sent more slowly and less efficiently. Patches of scar tissue, called plaques, form over the affected areas, further disrupting nerve communication. The symptoms of MS occur when the brain and spinal cord nerves no longer communicate properly with other parts of the body.²

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There are four basic types of MS. Relapsing-remitting MS (RRMS) is the most common form of the disease. Approximately 85 percent of people with MS begin with a RRMS course. RRMS is characterized by clearly defined acute attacks with full recovery or with a residual deficit upon recovery. Periods between relapses are characterized by a lack of disease progression. Some people with RRMS go a year or more between relapses; others have them more frequently.

RRMS patients often develop secondary-progressive MS (SPMS) somewhere between 10 years and 15 years after their initial diagnosis of RRMS. When this happens, patients notice a change in the pattern of their disease. While some acute attacks (exacerbations) and periods of remission may still occur, they happen less frequently, recovery is less complete, and symptoms become chronic, gradually worsening over time.

Primary-progressive MS (PPMS) is diagnosed in approximately 10 percent of MS patients. With this form, exacerbations, or attacks, are rare, if they occur at all. Instead, MS symptoms worsen over time, gradually leading to disability.

Progressive-relapsing MS (PRMS) is the least common type of MS. Like PPMS, this form is characterized by a gradual worsening of symptoms over time, but patients also experience exacerbations and remissions. Unlike RRMS, however, people with PRMS do not typically regain complete functioning after a symptom relapse. Disability is caused by the combination of disease progression and incomplete recovery after an attack.³

Symptoms of MS

MS is considered an autoimmune disorder because the immune system incorrectly attacks healthy tissue. It causes a wide variety of symptoms and can affect vision, balance, strength, sensation, coordination and bodily functions. In severe cases, patients can become paralyzed and/or blind, while in milder cases, there may be only numbness in the limbs.

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Symptoms present differently among patients. Some may have a single symptom and then go months or years without any others. It's even possible for a symptom to occur just one time, go away and never return. However, most patients with MS, particularly in the beginning stages of the disease, experience relapses of symptoms that are followed by periods of complete or partial remission. Partial remission can last weeks or even months.⁴

Early symptoms of MS may include blurred or double vision, lack of clarity in thinking or trouble concentrating, clumsiness or a lack of coordination, a loss of balance, numbness and/or tingling, and weakness in an arm or leg.

While no two people have exactly the same symptoms, there are some common indicators:

- About half of patients say they feel a “pins and needles” sensation. They may also have numbness, itching, burning, stabbing or tearing pains.
- About eight in 10 patients have bladder problems. They may need to urinate more frequently and urgently, need to go at night or have trouble emptying the bladder fully. Bowel problems, especially constipation, are also common.
- Patients may have difficulty walking because MS can cause muscle weakness or spasms. Balance problems, numb feet and fatigue can also make walking difficult.
- It's common for patients to feel dizzy or lightheaded.
- About eight in 10 people feel very tired or fatigued and complain about weak muscles, slowed thinking or sleepiness. Some feel tired even after a good night's sleep.

- Muscle spasms are another common symptom, usually affecting the leg muscles. For about 40 percent of patients, spasms are an early symptom. In PPMS and PRMS, muscle spasms affect about six in 10 people.⁵

Causes of MS

What causes MS is not clear, but the underlying mechanism is thought to be either destruction by the immune system or failure of the myelin-producing cells.⁶

Some studies suggest that genetic factors make certain individuals more susceptible to MS than others. Yet, while MS is not directly inherited (a great deal of evidence suggests that most people who are genetically susceptible must still be exposed to some other factor or factors in their environment or life experience for MS to develop), genes play an important role in who gets the disease. The risk of developing MS in the general population is one in 750, yet the risk rises to one in 40 in anyone who has a close relative (parent, sibling, child) with the disease. In families in which several people have been diagnosed with MS, the risk may be even higher. And, even though identical twins share the same genetic makeup, the risk for a person whose identical twin has MS is only a one in four chance of contracting it — which again suggests that some factors other than genetics are also involved.⁷

More than twice as many women as men have MS. Dr. Brian Weinschenker of the Mayo Clinic and recipient of the 2011 John Dystel Prize for MS Research examined the genetic underpinnings of MS and found that more women had variations in the gene that instructs interferon gamma, a molecule that ratchets up the immune attack in MS. The genetic variations were associated with different levels of production of interferon gamma by immune cells.⁸

In all parts of the world, MS is more common at northern latitudes that are farther from the equator and less common in areas closer to the equator. Researchers are now investigating whether increased exposure to sunlight and the vitamin D it provides may have a protective effect on those living nearer the equator. While MS occurs in most ethnic groups, including African-Americans, Asians and Hispanics/Latinos, it is more common in Caucasians of northern European ancestry. However, some ethnic groups, such as the Inuit, Aborigines and Maoris, have few if any documented cases of MS regardless of where they live.⁹

Infectious agents are most often proposed as the triggering factors of MS, yet evidence suggests that geography, ethnicity, genes and other factors interact in some complex way to cause MS. Researchers have examined

environmental and industrial toxins, diet, trace metal exposures and certain climatic elements such as sunlight. But, none has been shown to be causally linked to MS, and exactly what factors are the cause remains an open question.¹⁰

Diagnosing MS

The diagnosis of MS is notoriously tricky. There is no single test,¹¹ and confirming a diagnosis can become a waiting game because the doctor must find evidence of two episodes of disease activity in the central nervous system that have occurred at different points in time.¹² Most often, a diagnosis can take years because doctors must rule out all other possible explanations.

Dr. Weinschenker's most important lesson for clinicians: "Make sure the diagnosis is right. We see a lot of people who are put on MS treatments but who do not have MS." In fact, Dr. Weinschenker conducted a landmark study that tracked the course of MS, which helped develop ways to distinguish MS from look-alikes. His research resulted in a clarification of an MS diagnosis by defining no fewer than 79 "red flags" that point away from MS.¹³

Most people are diagnosed between the ages of 20 and 50, although MS has been detected in patients as young as 2 and as old as 75. It is unclear why the disease appears so early in some children.¹⁴

While more people are being diagnosed with MS today than in the past, epidemiologists have found no evidence to suggest that the disease is on the increase. More likely explanations include a greater awareness of the disease, improved medical care and more effective tools for making a diagnosis. In addition, the availability of effective treatments makes physicians more likely to communicate the diagnosis to their patients.¹

MS Treatment Options

Although there is no cure for MS, effective treatments are available to modify the disease course, treat attacks and relapses, manage symptoms and improve function and safety. In combination, these treatments enhance the quality of life for people living with MS.¹⁵

Permanent damage to nerve fibers (called axons) occurs early in MS in

association with the destruction of myelin. In addition, overall brain atrophy can occur early in the disease, and damage can be ongoing even when patients have no symptoms of an attack and feel well. Therefore, MS specialists advise the early use of a medication such as Gilenya (fingolimod), a once-daily oral capsule,¹⁶ that effectively limits lesion formation and brain atrophy. In the opinion of the National MS Society's Medical Advisory Committee, limiting lesions may be a key to reducing future permanent disability for many people with MS.¹⁷

The vast majority of people who experience acute attacks respond well to the standard high-dose corticosteroid treatment.¹⁸ For those unresponsive to steroids, plasma exchange therapy (also known as plasmapheresis, a blood-cleansing procedure) may be a possible alternative treatment.¹⁹ However, plasma exchange should be considered a treatment alternative for only the few who do not respond to treatment, and only for a short time. And, in people with relapsing forms of MS, it may be effective as a secondary therapy for exacerbations that have not responded to treatment with corticosteroids. Plasma exchange has not been found to be effective for SPMS or PPMS.²⁰

Intravenous immune globulin (IVIG) remains a controversial treatment option. In the late 1990s, there were a few studies that showed patients with RRMS had reduced exacerbations of their MS when treated with IVIG.²¹ Since that time, pharmaceutical companies have developed more disease-modifying therapies more specifically targeted



to MS (Avonex, Copaxone, Rebif, Tysabri, Gilenya, etc.), and additional studies have shown no statistical significance when IVIG is added to these treatment regimens.²²

Some physicians treat MS patients with IVIG postpartum. MS patients seem to develop a natural disease-modifying effect when they are pregnant, so most go off of their therapy during pregnancy and do fairly well. After they deliver, however, the protective effect of the pregnancy is gone, and these patients may be at a higher risk of exacerbating soon after delivery. In addition, if patients are planning to breast-feed, they usually remain off of their current therapy.²³

Some studies suggest that genetic factors make certain individuals more susceptible to MS than others.

Managing Day to Day

While MS is not considered a fatal disease since the vast majority of patients live a normal life-span, patients may struggle to live as productively as they desire, often facing increasing limitations.²⁴

Medication can help manage disease symptoms, yet there also needs to be a focus on function — improving or maintaining the ability to perform effectively and safely at home and at work. Rehabilitation is an important component of comprehensive, quality healthcare for patients with MS at all stages of the disease. Rehabilitation programs include physical therapy, occupational therapy, cognitive rehabilitation and vocational rehabilitation. Rehabilitation professionals focus on overall fitness and energy management, while addressing problems with accessibility and mobility, speech and swallowing, and memory and other cognitive functions.²⁵

Future Outlook

Many advances have been made in the fight against MS. And, each advance interacts with the others, adding greater depth and meaning to each new discovery. The National MS Society supports and funds research activities

spanning all research stages. This research provides information about relationships among factors so that the disease can be better understood and helps explain who gets MS and why.²⁶

Finding the underlying causes of MS brings researchers closer to developing a cure. Because MS is significantly more common (at least two to three times) in women than men, the gender difference has stimulated important research initiatives looking at the role of hormones in MS. How hormones influence inflammation and neuron and glial function is being slowly unraveled. There is increasing evidence that estrogen, progesterone and testosterone contain immune responses and influence damage repair in the nervous system. Hormones such as prolactin and vitamin D are being explored as immunomodulators and how they may influence MS or may be used therapeutically to modulate the immune response. More recently, hormones such as leptin and ghrelin have been found to possibly influence the course of disease.²⁷

Alberto Ascherio, MD, DrPH, professor of nutrition and epidemiology and associate professor of medicine at the Harvard School of Public Health, is conducting research to identify causes and risk factors for MS and other neurodegenerative diseases, as well as biomarkers that may provide information about susceptibility, and that may lead to earlier diagnosis. One infectious factor that Dr. Ascherio's team and others continue to pursue is Epstein-Barr virus (EBV), which causes several disorders, including infectious mononucleosis. Most people in the U.S. show signs of having been exposed to EBV. In one study, the team reported that individuals with signs of significant exposure to EBV were twice as likely to develop MS up to 20 years later.²⁸

Research also continues to be conducted to find new therapies to treat MS. U.S. and German researchers have developed a therapy that stops the autoimmune attack against myelin in its tracks without impairing the normal function of the immune system. The experimental treatment targets T cells in the brain that are responsible for the disease. According to Stephen Miller, a microbiologist and immunologist at Northwestern University in Evanston, Ill., the therapy has a different mode of action from current MS treatments, which suppress the immune system. The current treatments “will not only try to down-regulate the autoimmune response that’s actually causing the disease, but will also make patients, in the long run, susceptible to everyday infections and increased rates of cancer,” states Miller. In effect, they sweep away the dead T cells. The

experimental treatment resets the patients' immune systems, halting the leukocytes' attack on the nerve sheaths and reducing the assault on the myelin by 50 percent to 75 percent. While not a cure for MS, Miller believes it's a step in the right direction.²⁹

The Hope for a Cure

As research continues, determining the cause of MS, as well as ways to prevent it, becomes more likely. But, that will require a greater understanding of the genetics that make people susceptible to developing the disease, and an identification of the environmental triggers that should be avoided or otherwise derailed. In the meantime, new therapies are being developed to help patients live healthier lives.

"Having MS has helped me learn to balance and cherish the things that are important in life," says Mabelle. But, "I'm hoping the researchers find something that not only stops the progression of MS from happening, but also reverses the damage that has already been done ... because I still have to live every day with the symptoms that were caused by previous attacks."

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