Multiple Sclerosis

Hope Through Research

National Institute of Neurological Disorders
and Stroke
National Institutes of Health

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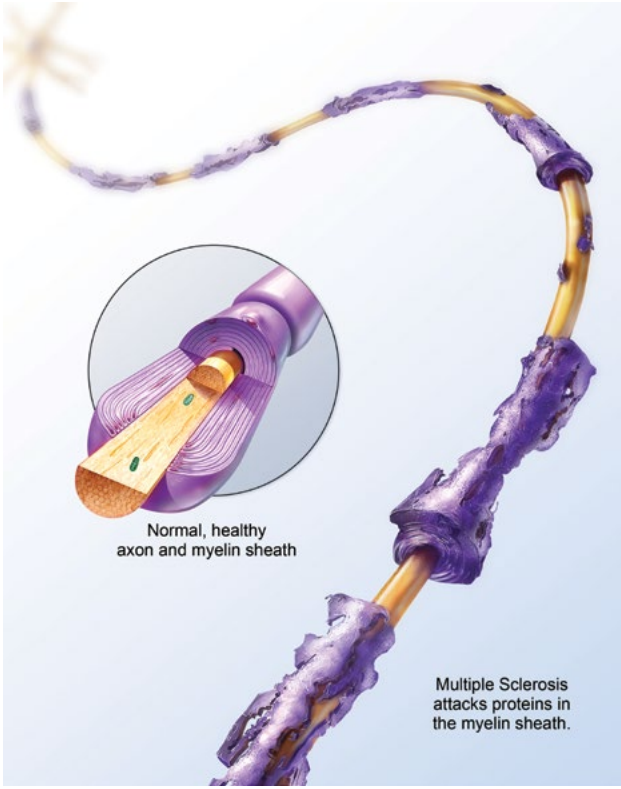
What is Multiple Sclerosis?

Multiple Sclerosis (MS) is the most common disabling neurological disease of young adults with symptom onset generally occurring between the ages of 20 to 40 years. In MS, the immune system cells that normally protect us from viruses, bacteria, and unhealthy cells mistakenly attack myelin in the central nervous system (brain, optic nerves, and spinal cord), a substance that makes up the protective sheath (called the myelin sheath) that coats nerve fibers (axons).

MS is a chronic disease that affects people differently. A small number of those with MS will have a mild course with little to no disability, whereas others will have a steadily worsening disease that leads to increased disability over time. Most people with MS, however, will have short periods of symptoms followed by long stretches of relative quiescence (inactivity or dormancy), with partial or full recovery. Women are affected more frequently with MS compared to men. The disease is rarely fatal and most people with MS have a normal life expectancy. New treatments can reduce long-term disability for many people with MS. Currently there are still no cures and no clear ways to prevent the disease from developing.

Myelin and the immune system

MS attacks axons in the central nervous system protected by myelin, which are commonly called **white matter**. MS also damages the nerve cell bodies, which are found in the brain's **gray matter**, as well as the axons themselves in the brain, spinal cord, and optic nerves that transmit visual information from the eye to the brain. As the disease progresses, the outermost layer of the brain, called the cerebral cortex, shrinks (what is known as cortical atrophy).



Myelin is a substance that makes up the protective sheath that insulates nerve fibers. In MS, myelin is damaged. The illustration above shows a normal, healthy myelin sheath, and one damaged by MS.

The term *multiple sclerosis* refers to the distinctive areas of scar tissue (sclerosis—also called plaques or lesions) that result from the attack on myelin by the immune system. These plaques are visible using magnetic resonance imaging in the white and/or gray matter of people who have MS. Plaques can be as small as a pinhead or as large as a golf ball.

During an MS exacerbation, most of the myelin, and to a lesser extent the axons within the affected area, is damaged or destroyed by different types of immune cells (also known as inflammation). The symptoms of MS depend on the severity of the inflammatory reaction as well as the location and extent of the plaques, which primarily appear in the brain stem, cerebellum (involved with balance and coordination of movement, among other functions), spinal cord, optic nerves, and the white matter around the brain ventricles (fluid-filled spaces).

What are the signs and symptoms of MS?

The natural course of MS is different for each person, which makes it difficult to predict. The onset and duration of MS symptoms usually depends on the specific type but may begin over a few days and go away quickly or develop more slowly and gradually over many years.

There are four main types of MS, named according to the progression of symptoms over time:

- **Relapsing-remitting MS.** Symptoms in this type come in attacks and, in-between attacks, people recover or return to their usual level of disability. The occurrence of symptoms in this form of MS is called an attack, or in medical terms, a relapse or exacerbation. The periods of disease inactivity or quiescence between MS attacks is referred to as remission. Weeks, months, or even years may pass before another attack occurs, followed again by a period of inactivity. Most people with MS (approximately 80%) are initially diagnosed with this form of the disease.
- **Secondary-progressive MS.** People with this form of MS usually have had a previous history of MS attacks, but then start to develop gradual and steady symptoms and deterioration in their function over time. Most individuals with severe relapsing-remitting MS may go on to develop secondary progressive MS if they are untreated.
- **Primary-progressive MS.** This type of MS is less common and is characterized by progressively worsening symptoms from the beginning with no noticeable relapses or exacerbations of the disease, although there may be temporary or minor relief from symptoms.

- **Progressive-relapsing MS.** This rarest form of MS is characterized by a steady worsening of symptoms from the beginning, with acute relapses that can occur over time during the disease course.

There are some rare and unusual variants of MS. One of these is **Marburg variant MS** (also called malignant MS), which causes swift and relentless symptoms and decline in function, which can result in significant disability or even death shortly after disease onset. **Balo's concentric sclerosis**, which causes concentric rings of myelin destruction that can be seen on an MRI, is another variant type of MS that can progress rapidly.

Early MS symptoms often include:

- Vision problems such as blurred or double vision, or optic neuritis, which causes pain with eye movement and a rapid loss of vision
- Muscle weakness, often in the hands and legs, and muscle stiffness accompanied by painful muscle spasms
- Tingling, numbness, or pain in the arms, legs, trunk, or face
- Clumsiness, particularly difficulty staying balanced when walking
- Bladder control problems
- Intermittent or more constant dizziness

MS may also cause later symptoms such as:

- Mental or physical fatigue which accompanies the early symptoms during an attack
- Mood changes such as depression or difficulty with emotional expression or control
- Cognitive dysfunction—problems concentrating, multitasking, thinking, learning, or difficulties with memory or judgment

Vision problems, such as blurred or double vision or optic neuritis, are among the early symptoms of MS.

Muscle weakness, stiffness, and spasms may be severe enough to affect walking or standing. In some cases, MS leads to partial or complete paralysis and the use of a wheelchair is not uncommon, particularly in individuals who are untreated or have advanced disease. Many people with MS find that weakness and fatigue are worse when they have a fever or when they are exposed to heat. MS exacerbations may occur following common infections.

Pain is rarely the first sign of MS, but pain often occurs with optic neuritis and trigeminal neuralgia, a disorder that affects one of the nerves that provides sensation to different parts of the face (see Conditions associated with MS section below). Painful limb spasms and sharp pain shooting down the legs or around the abdomen can also be symptoms of MS.

Many individuals with MS may experience difficulties with coordination and balance. Some may have a continuous trembling of the head, limbs, and body, especially during movement.

MS exacerbation

An exacerbation—which is also called a relapse, flare-up, or attack—is a sudden worsening of MS symptoms, or the appearance of new symptoms that lasts for at least 24 hours. MS relapses are thought to be associated with the development of new areas of damage in the brain. Exacerbations are characteristic of relapsing-remitting MS.

An exacerbation may be mild, or severe enough to significantly interfere with life's daily activities. Most exacerbations last from several days to several weeks, although some have lasted for as long as a few months. When the symptoms of the attack subside, an individual with MS is said to be in remission, characterized by disease quiescence.

Conditions associated with MS

Transverse myelitis (an inflammation of the spinal cord) may develop in those with MS. Transverse myelitis can affect spinal cord function over several hours to several weeks before partial or complete recovery. It usually begins as a sudden onset of lower back pain, muscle weakness, abnormal sensations in the toes and feet, or difficulties with bladder control or bowel movements. This can rapidly progress to more severe symptoms, including arm and/or leg paralysis. In most cases, people recover at least some function within the first 12 weeks after an attack begins.

Neuromyelitis optica is a disorder associated with transverse myelitis as well as optic nerve inflammation (also known as optic neuritis). People with this disorder usually have abnormal antibodies (proteins that normally target viruses and bacteria) against a specific channel in optic nerves, the brain stem, or spinal cord, called the aquaporin-4 channel. These individuals

respond to certain treatments, which are different than those commonly used to treat MS.

Trigeminal neuralgia is a chronic pain condition that causes sporadic, sudden burning or shock-like facial pain. The condition is more common in young adults with MS and is caused by lesions in the brain stem, the part of the brain that controls facial sensation.

What causes MS?

Researchers are looking at several possible explanations for why the immune system attacks central nervous system myelin, including:

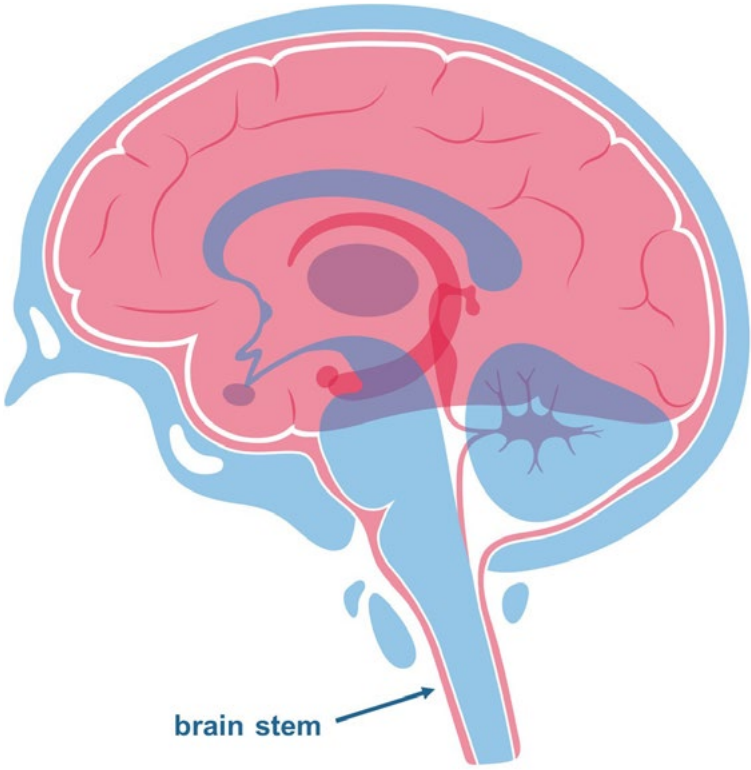
- Fighting an infectious agent (for example, a virus) that has components that mimic components of the brain (called molecular mimicry)
- Destroying brain cells because they are unhealthy
- Mistakenly identifying normal brain cells as foreign

There is also something known as the **blood-brain barrier**, which separates the brain and spinal cord from the immune system. If there is a break in this barrier, it exposes the brain to the immune system. When this happens, the immune system may misinterpret structures in the brain, such as myelin, as "foreign."

Research shows that genetic vulnerabilities combined with environmental factors may cause MS.

Genetic susceptibility

MS itself is not inherited, but susceptibility to MS may be inherited. Studies show that some individuals with MS have one or more family member or relative who also have MS.



Trigeminal neuralgia is caused by lesions in the brain stem which controls facial sensation.

Current research suggests that dozens of genes and possibly hundreds of variations in the genetic code (called gene variants) combine to create vulnerability to MS. Some of these genes have been identified, and most are associated with functions of the immune system. Many of the known genes are similar to those that have been identified in people with other autoimmune diseases as type 1 diabetes, rheumatoid arthritis, or lupus.

Infectious factors and viruses

Several viruses have been found in people with MS, but the virus most consistently linked to the development of MS is the Epstein-Barr virus (EBV) which causes infectious mononucleosis.

Only about 5 percent of the population has not been infected by EBV. These individuals are at a lower risk for developing MS than those who have been infected. People who were infected with EBV in adolescence or adulthood and who therefore develop an exaggerated immune response to EBV are at a significantly higher risk for developing MS than those who were infected in early childhood. This suggests that it may be the type of immune response to EBV that may lead to MS, rather than EBV infection itself. However, there is still no proof that EBV causes MS and the mechanisms that underlie this process are poorly understood.

Environmental factors

Several studies indicate that people who spend more time in the sun and those with relatively higher levels of vitamin D are less likely to develop MS or have a less severe course of disease and fewer relapses. Bright sunlight helps human skin produce vitamin D. Researchers believe that vitamin D may help regulate the immune system in ways that reduce the risk of MS or autoimmunity in general. People from regions near the equator, where there is a great deal of bright sunlight, generally have a much lower risk of MS than people from temperate areas such as the United States and Canada.

Studies have found that people who smoke are more likely to develop MS and have a more aggressive disease course. People who smoke tend to have more brain lesions and brain shrinkage than non-smokers. The reasons for this are currently unclear.

How is MS diagnosed?

There is no single test used to diagnose MS. The disease is confirmed when symptoms and signs develop and are related to different parts of the nervous system at more than one interval in time and after other alternative diagnoses have been excluded.

Doctors use different tests to rule out or confirm the diagnosis. In addition to a complete medical history, physical examination, and a detailed neurological examination, a doctor may recommend:

- **MRI scans** of the brain and spinal cord to look for the characteristic lesions of MS. A special dye or contrast agent may be injected into a vein to enhance brain images of the active MS lesions.
- **Lumbar puncture** (sometimes called a spinal tap) to obtain a sample of cerebrospinal fluid and examine it for proteins and inflammatory cells associated with the disease. Spinal tap analysis also can rule out diseases that may look like MS.
- **Evoked potential tests**, which use electrodes placed on the skin and painless electric signals to measure how quickly and accurately the nervous system responds to stimulation.

Research suggests that people who spend more time in the sun—which helps the skin to produce vitamin D—are less likely to develop MS.

How is MS treated?

There is no cure for MS, but there are treatments that can reduce the number and severity of relapses and delay the long-term disability progression of the disease.

Treatments for attacks

- **Corticosteroids**, such as intravenous (infused into a vein) methylprednisolone, are prescribed over the course of 3 to 5 days. Intravenous steroids quickly and potently suppress the immune system and reduce inflammation. They may be followed by a tapered dose of oral corticosteroids. Clinical trials have shown that these drugs hasten recovery from MS attacks, but do not alter the long-term outcome of the disease.
- **Plasma exchange (plasmapheresis)** can treat severe flare-ups in people with relapsing forms of MS who do not have a good response to methylprednisolone. Plasma exchange involves taking blood out of the body and removing components in the blood's plasma that are thought to be harmful. The rest of the blood, plus replacement plasma, is then transfused back into the body. This treatment has not been shown to be effective for secondary progressive or chronic progressive MS.

Disease-modifying treatments

Current therapies approved by the U.S. Food and Drug Administration (FDA) for MS are designed to modulate or suppress the inflammatory reactions of the disease. They are most effective for relapsing-remitting MS at early stages of the disease.

Injectable medications include:

- **Beta interferon drugs** are among the most common medications to treat MS. Interferons are signaling molecules that regulate immune cells. Potential side effects of these drugs include flu-like symptoms (which usually fade with continued therapy), depression, or elevation of liver enzymes. Some individuals will notice a decrease in the effectiveness of the drugs after 18 to 24 months of treatment. If flare-ups occur or symptoms worsen, doctors may switch treatment to alternative drugs.
- **Glatiramer acetate** changes the balance of immune cells in the body, but how it works is not entirely clear. Side effects are usually mild and consist of local injection site reactions or swelling.

Brand Name	Chemical Name
Avonex Rebif	Interferon beta-1a
Betaseron Extavia	Interferon beta-1b
Plegridy	Peginterferon beta-1a
Copaxone Glatopa	Glatiramer acetate

Infusion treatments include:

- **Natalizumab** is administered intravenously once a month. It works by preventing cells of the immune system from entering the brain and spinal cord. It is very effective but is associated with an increased risk of a serious and potentially fatal viral infection of the brain called progressive multifocal leukoencephalopathy (PML). Natalizumab is generally recommended only for individuals who have not responded well to or who are unable to tolerate other first-line therapies.

- **Ocrelizumab** is administered intravenously every six months and treats adults with relapsing or primary progressive forms of MS. It is the only FDA-approved disease-modifying therapy for primary-progressive MS. The drug targets the circulating immune cells that produce antibodies, which also play a role in the formation of MS lesions. Side effects include infusion-related reactions and increased risk of infections. Ocrelizumab may increase the risk of cancer as well.
- **Alemtuzumab** is administered for 5 consecutive days followed by 3 days of infusions one year later. It targets proteins on the surface of immune cells. Because this drug increases the risk of autoimmune disorders it is recommended for those who have had inadequate responses to two or more MS therapies.

- **Mitoxantrone**, which is administered intravenously four times a year, has been approved for especially severe forms of relapsing-remitting and secondary progressive MS. Side effects include the development of certain types of blood cancers in up to one percent of those with MS, as well as with heart damage. This drug should be considered as a last resort to treat people with a form of MS that leads to rapid loss of function and for whom other treatments did not work.

Brand Name	Chemical Name
Novantrone	Mitoxantrone
Tysabri	Natalizumab
Ocrevus	Ocrelizumab
Lemtrada	Alemtuzumab

Oral treatments include:

- **Fingolimod** is a once-daily medication that reduces the MS relapse rate in adults and children. It is the first FDA-approved drug to treat MS in adolescents and children ages 10 years and older. The drug prevents white blood cells called lymphocytes from leaving the lymph nodes and entering the blood, brain, and spinal cord. Fingolimod may result in a slow heart rate and eye problems when first taken. Fingolimod can also increase the risk of infections, such as herpes virus infections, or in rare cases be associated with PML.
- **Dimethyl fumarate** is a twice-daily medication used to treat relapsing forms of MS. Its exact mechanism of action is not currently known. Side effects of dimethyl fumarate are flushing, diarrhea, nausea, and lowered white blood cell count.

- **Teriflunomide** is a once-daily medication that reduces the rate of proliferation of activated immune cells. Teriflunomide side effects can include nausea, diarrhea, liver damage, and hair loss.
- **Cladribine** is administered as two courses of tablets about one year apart. Cladribine targets certain types of white blood cells that drive immune attacks in MS. The drug may increase the risk of developing cancer and should be considered for individuals who have not responded well to other MS treatments.
- **Diroximel fumarate** is a twice-daily drug similar to **dimethyl fumarate** (brand name Tecfidera) but with fewer gastrointestinal side effects. Scientists suspect these drugs, which have been approved to treat secondary progressive MS, reduce damage to the brain and spinal cord by making the immune response less inflammatory, although their exact mechanism of action is poorly understood.

- **Siponimod tablets (Mayzent)** is taken orally and has a similar mechanism of action to fingolimod. Siponimod has been approved by the FDA to treat secondary-progressive MS.

Clinical trials have shown that cladribine, diroximel fumarate, and dimethyl fumarate decrease the number of relapses, delay the progress of physical disability, and slow the development of brain lesions.

Brand Name	Chemical Name
Gilenya	Fingolimod
Tecfidera	Dimethyl fumarate
Aubagio	Teriflunomide
Mayzent	Siponimod
Mavenclad	Cladribine
Vumerity	Diroximel fumarate

Managing MS symptoms

MS causes a variety of symptoms that can interfere with daily activities but can usually be treated or managed. Many of these issues are best treated by neurologists who have advanced training in the treatment of MS and who can prescribe specific medications to treat these problems.

Eye and vision problems are common in people with MS but rarely result in permanent blindness. Inflammation of the optic nerve (optic neuritis) or damage to the myelin that covers the nerve fibers in the visual system can cause blurred or grayed vision, temporary blindness in one eye, loss of normal color vision, depth perception, or loss of vision in parts of the visual field. Uncontrolled horizontal or vertical eye movements (nystagmus), “jumping vision” (opsoclonus), and double vision (diplopia) are common in people with MS. Intravenous steroid medications, special eyeglasses, and periodically resting the eyes may be helpful.

Muscle weakness and spasticity is common in MS. Mild spasticity can be managed by stretching and exercising muscles using water therapy, yoga, or physical therapy. Medications such as gabapentin or baclofen can reduce spasticity. It is very important that people with MS stay physically active because physical inactivity can contribute to worsening stiffness, weakness, pain, fatigue, and other symptoms.

Tremor, or uncontrollable shaking, develops in some people with MS. Assistive devices and weights attached to utensils or even limbs are sometimes helpful for people with tremor. Deep brain stimulation and drugs, such as clonazepam, also may be useful.

Problems with walking and balance occur in many people with MS. The most common walking problem is ataxia—unsteady, uncoordinated movements—due to damage to the areas of the brain that coordinate muscle balance. People with severe ataxia generally benefit from the use of a cane, walker, or other assistive device. Physical therapy also can reduce walking problems. The FDA has approved the drug dalfampridine to improve walking speed in people with MS.

Physical therapy may help improve balance and walking problems.

Fatigue is a common symptom of MS and may be both physical (for example, tiredness in the arms or legs) and cognitive (slowed processing speed or mental exhaustion). Daily physical activity programs of mild to moderate intensity can significantly reduce fatigue, although people should avoid excessive physical activity and minimize exposure to hot weather conditions or ambient temperature. Other drugs that may reduce fatigue include amantadine, methylphenidate, and modafinil. Occupational therapy can help people learn how to walk using an assistive device or in a way that saves physical energy. Stress management programs, relaxation training, membership in an MS support group, or individual psychotherapy may help some people.

Pain from MS can be felt in different parts of the body. Trigeminal neuralgia (facial pain) is treated with anticonvulsant or antispasmodic drugs, or less commonly painkillers. Central pain, a syndrome caused by damage to the brain and/or spinal cord, can be treated with gabapentin and nortriptyline. Treatments for chronic back or other musculoskeletal pain may include heat, massage, ultrasound, and physical therapy.

Problems with bladder control and constipation may include urinary frequency, urgency, or the loss of bladder control. A small number of individuals retain large amounts of urine. Medical treatments are available for bladder-related problems. Constipation is also common and can be treated with a high-fiber diet, laxatives, and stool softeners.

Sexual dysfunction can result from damage to nerves running through the spinal cord. Sexual problems may also stem from MS symptoms such as fatigue, cramped or spastic muscles, and psychological factors. Some of these problems can be corrected with medications. Psychological counseling also may be helpful.

Clinical depression is frequent among people with MS. MS may cause depression as part of the disease process and chemical imbalance in the brain. Depression can intensify symptoms of fatigue, pain, and sexual dysfunction. It is most often treated with cognitive behavioral therapy, and selective serotonin reuptake inhibitor (SSRI) antidepressant medications, which are less likely than other antidepressant medications to cause fatigue.

Inappropriate and involuntary expressions of laughter, crying, or anger—symptoms of a condition called pseudobulbar affect—sometimes are associated with MS. These expressions are often incongruent with mood; for example, people with MS may cry when they are actually happy or laugh when they are not especially happy. The combination treatment of the drugs dextromethorphan and quinidine can treat pseudobulbar affect, as can other drugs such as amitriptyline or citalopram.

Cognitive impairment—a decline in the ability to think quickly and clearly and to remember easily—affects up to three-quarters of people with MS. These cognitive changes may appear at the same time as the physical symptoms or they may develop gradually over time. Drugs such as donepezil may be helpful in some cases.

Complementary and alternative therapies

Many people with MS benefit from complementary or alternative approaches such as acupuncture, aromatherapy, ayurvedic medicine, touch and energy therapies, physical movement disciplines such as yoga and tai chi, herbal supplements, and biofeedback.

Because of the risk of interactions between alternative and conventional therapies, people with MS should discuss all the therapies they are using with their

Some people with MS use complementary or alternative therapies like yoga and tai chi.

doctor, especially herbal supplements. Herbal supplements have biologically active ingredients that could have harmful effects on their own or interact harmfully with other medications.

What research is being done?

The National Institute of Neurological Disorders and Stroke (NINDS), a component of the National Institutes of Health (NIH), is the leading federal funder of research on the brain and nervous system, including research on MS.

In addition to NINDS, other NIH Institutes—including the National Institute of Allergy and Infectious Diseases (NIAID)—fund research on multiple sclerosis. More information on NIH efforts on multiple sclerosis research and on other disorders can be found using NIH RePORTER (http://projectreporter.nih.gov), a searchable database of current and past research projects supported by NIH and other federal agencies. RePORTER also includes links to publications and patents citing support from these projects.

Although researchers have not been able to identify the cause of MS with any certainty, there has been excellent progress in other areas of MS research—especially in the development of new treatments to prevent exacerbations of the disease. New discoveries are constantly changing MS treatment options and helping to reduce MS-related disability.

Research projects being conducted by NINDS scientists or through NIH grants to universities and other sites throughout the United States cover a wide range of topics such as comorbidities, mechanisms of cognitive impairment, blood-brain barrier breakdown in MS, the role of sleep and circadian rhythms, rehabilitation strategies, and telehealth. Other topics include:

- Biomarkers to accurately diagnose MS and monitor disease progression, including blood and imaging tests (such as MRI)
- Genetic and environmental risk factors for MS such as low Vitamin D or the Epstein-Barr virus
- The role of the gut microbiome and diet in MS
- Mechanisms that underlie gender differences in the incidence and presentation of MS
- MS risk factors and disease course in African American and Hispanic populations and disparities in care
- The role of the immune system in MS, including its function in the central nervous system (CNS)
- The role and crosstalk of various cell types in the CNS with relation to MS
- Basic functions of myelination, demyelination, and axonal degeneration, and strategies to overcome axonal and myelin loss

Scientists sponsored by NIH's NIAID are testing an **experimental stem cell treatment** (called autologous hematopoietic stem cell transplantation, or AHSCT) against the best available biologic therapies for severe forms of relapsing MS. Investigators in the **BEAT-MS** (BEst Available Therapy versus autologous hematopoietic stem cell transplant for Multiple Sclerosis) trial are removing some of the person's immune cells and then infusing some of the person's own blood-forming stem cells to reset the immune system so it no longer attacks the central nervous system. For more information about BEAT-MS and how to apply to participate in this study or other clinical studies, visit www.clinicaltrials.gov.

Genetic research funded by NINDS is exploring the roles of "susceptibility genes"—genes that are associated with an increased risk for MS. Several candidate genes have been identified and researchers are studying their function in the nervous system to discover how they may lead to the development of MS.

Other studies aim to develop better **neuroimaging tools**, such as more powerful MRI methods, to diagnose MS, track disease progression, and assess treatments. NINDS scientists are collecting magnetic resonance imaging of the brain and spinal cord and scans of the retina, along with other clinical and biological data, from more than 100 individuals with MS and 50 individuals without the disease over a period of years to observe changes in the course of MS over time. Investigators also are using MRI to study the natural history of MS and to help define the mechanism of action and cause of side effects of disease modifying therapies.

Intramural research programs on MS

NINDS and other NIH Institutes have a very active MS intramural research program (scientists working at NIH). NINDS Intramural scientists have:

- Established and continue to develop magnetic resonance imaging as a critical tool for examining the natural course of the disease in humans, monitoring disease progression, assessing effects of treatments in clinical trials, and understanding MS biology
- Played an important role in understanding why some patients develop a rare and potentially fatal brain infection (progressive multifocal leukoencephalopathy) when taking potent MS drugs, and they are developing new treatments for this infection.
- Unraveled mechanisms by which viruses, especially the Epstein-Barr virus, contribute to the development of MS
- Conducted next-generation treatment trials targeting specific mechanisms of disease progression, using advanced MRI and fluid biomarkers as outcome measures
- Developed the first MRI method to visualize the lymph vessels surrounding the brain, which play a critical role in neuro-immune communication

Translational research

NIH supports translational studies to develop therapies that will stop or reverse the course of the disease, focusing on pathways that modify immune system function, repair damaged myelin, or protect neurons from damage. Researchers are also developing animal models of MS to more accurately predict drug response in human disease. Currently available animal models share some of the disease mechanisms and symptoms of MS but do not fully mimic the disease, especially in its clinically progressive phase.

Scientists are developing better animal models that closely resemble MS in humans. Testing potential therapies in more accurate models may lead to successful treatments in humans with the disease.

Focus on progressive MS therapies

Scientists continue to study the biology and mechanisms of relapsing-remitting MS while increasing efforts to stop or prevent the steady decline in function that occurs in progressive MS. In the MS-SPRINT trial, the NINDS NeuroNEXT clinical trials network tested the drug ibudilast as a potential neuroprotective drug for progressive MS and showed that the drug slowed the rate of brain shrinkage as compared to a placebo. NINDS Intramural scientists are conducting proof-of-concept clinical trials to address a key driver of clinical progression called the "slowly expanding lesion."

Focus on biomarkers

As part of a larger effort to develop and validate effective biomarkers (signs that may indicate risk of a disease or be used to monitor its progression) for neurological disease, NINDS is supporting two definitive multicenter MS studies:

- The Central Vein Sign in MS (CAVS-MS) study, which is testing whether a rapid MRI approach designed by NINDS Intramural scientists, can use the detection of a central vein passing through brain plaques to differentiate MS from other common neurological disorders that can mimic MS. The goal is to develop a reliable imaging test for MS in order to achieve a rapid but accurate diagnosis and reduce misdiagnosis, which may affect up to 20 percent of people currently diagnosed with MS.
- A study to test whether a simple new blood test, which measures small amounts of neuron-derived proteins (called neurofilaments), can be used to predict the severity of disease and help determine whether MS drugs are working to protect the brain tissues.

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's **Brain Resources and Information Network (BRAIN)** at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
800-352-9424
www.ninds.nih.gov

Information also is available from the following organizations:

Multiple Sclerosis Association of America
856-488-4500
800-532-7667
https://mymsaa.org/

Multiple Sclerosis Foundation
954-776-6805
888 673-6287
https://msfocus.org/

National Multiple Sclerosis Society
800-344-4867
https://www.nationalmssociety.org

Accelerated Cure Project for Multiple Sclerosis
781-487-0008
https://www.acceleratedcure.org/

American Autoimmune Related Diseases Association
586-776-3900
800-598-4668
https://www.aarda.org/

Myelin Repair Foundation
408-871-2410
http://myelinrepair.org/

National Ataxia Foundation
763-553-0020
https://ataxia.org/

National Organization for Rare Disorders (NORD)
203-744-0100
https://rarediseases.org/

National Rehabilitation Information Center
301-459-5900
800-346-2742
301-459-5984 (TTY)
https://www.naric.com

Paralyzed Veterans of America
202-872-1300
800-555-9140
https://www.pva.org/

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