

Multiple Sclerosis Association of America

All About Multiple Sclerosis

Third Edition



MSAA

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THIRD EDITION

What is Multiple Sclerosis?

Multiple sclerosis (MS) is the most common neurological disorder diagnosed in young adults. Its causes are not yet fully understood and researchers continue to search for answers. Although the disease may not be cured or prevented at this time, treatments are available to reduce severity and delay progression.

MS is not contagious and does not shorten the life expectancy of those who are diagnosed with the disease. The most dangerous complication relating to MS is usually infection, which may occur when someone has had MS for a long time and is not as strong or physically active as an individual without the disease. Infection may often be successfully treated if recognized early.

MS is a disease of the central nervous system (CNS). The CNS consists of the brain and spinal cord. This disorder damages the protective insulation (known as “**myelin**”) surrounding the nerves (known as “**axons**”), and may also damage the nerves as well within the CNS. As a result, messages from the brain and spinal cord may short circuit, causing reduced or lost bodily function.

The effects of MS differ with each individual. Some people experience symptoms for a short period of time and afterward may remain symptom-free for years, while others may experience a more steady progression of the disease.

Most researchers believe MS is an “autoimmune disease” -- one in which white blood cells, meant to fight infection or disease, are misguided to target and attack the body’s own cells. This attack causes inflammation in the CNS, which may damage the myelin and ultimately injure the nerves.

Areas of inflammation are known as “**active lesions**.” Areas of thick scar tissue, known as “**plaques**,” form along the damaged myelin. The changes in size, number, and location of the lesions and plaques may determine the type and severity of symptoms. The term “multiple sclerosis” originates from the discovery of the plaques. Multiple refers to many; sclerosis refers to scars.

Researchers have studied a variety of possible causes for MS.

The most popular theory at this time involves a commonly known **slow-acting virus** (one that could remain dormant for many years) such as measles, herpes, human T-cell lymphoma, and Epstein-Barr. After being exposed to one of these viruses, some researchers theorize that MS may develop in genetically susceptible people, and genetic research is ongoing. Some scientists are also looking for a connection between MS and nutritional factors, including deficiencies in vitamin D and fish oil.

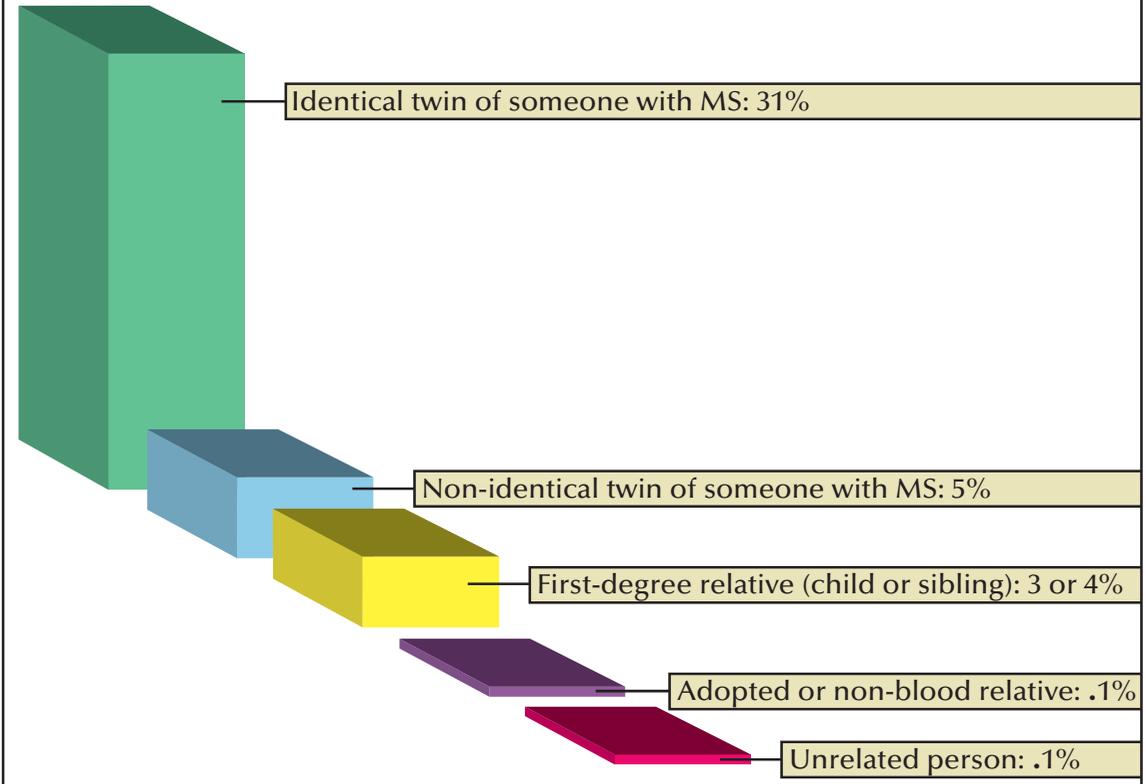
Who Gets MS?

Approximately 350,000 individuals have been diagnosed with MS in the United States and one million worldwide, with an estimated 10,000 new cases diagnosed in the United States annually. Most people with MS experience their first symptoms and are diagnosed between the ages of 15 and 50.

The distribution of this disease is not totally random. On average, women are three times as likely than men to develop MS. Additionally, the occurrence of this disorder is positively correlated with **latitude**. People living beyond the 40-degree mark north or south of the equator are far more likely to develop MS than those living in the warmer climates near the equator. This is especially true for people in North America, Europe, and southern Australia, while Asia continues to have a low incidence of MS. More prevalent among those of northern European or Scandinavian ancestry, Caucasians are far more likely than those of African heritage to develop this disease.

While MS is not contagious or hereditary, MS susceptibility is increased if a family member has MS. The average risk of developing MS in the United States is one in 1,000, or one tenth of one percent. For first-degree relatives (such as a child or sibling), the risk increases to three or four percent. This is not true for adopted children or half siblings (who do not share the same parent who has MS), whose risk is the same as unrelated individuals. In instances where one identical twin has been diagnosed with MS, the other twin has a 31 percent risk of developing the disease. The risk for twins who are not identical is five percent – similar to that of other siblings.

The Risk of Developing MS



Another factor linked to MS is cigarette smoking. Women who smoke are 1.6 times more likely to develop MS than women who are non-smokers. Additionally, individuals with MS who smoke appear to be at a much greater risk of experiencing a quicker progression of their disease.

What are the Symptoms of MS?

Commonly seen symptoms include:

- fatigue
- weakness
- swallowing disorders
- visual disorders
- tremor
- chronic aching pain
- numbness
- impaired mobility
- depression
- dizziness/vertigo
- sexual dysfunction
- mild cognitive and memory difficulties
- bladder and bowel dysfunction
- slurred speech
- spasticity (leg stiffness)

While MS has the potential to cause several different symptoms, the specific symptoms each person experiences vary greatly. Many with MS only experience a few of these symptoms.

When experiencing one or more of these symptoms, an individual should consult his or her physician. Medications are available to treat nearly all MS symptoms. These may include over-the-counter drugs as well as prescribed medications. Diet and exercise may also be helpful with managing certain symptoms. All treatments or changes in diet or exercise should only be done under the guidance of a qualified physician.

MS symptoms are often compounded by extreme fatigue, which may be worse in the afternoon, sometimes relating to a rise in body temperature. Most symptoms may be temporarily increased by **heat intolerance** – a classic MS tendency, where a rise in temperature (internally or externally) causes a person to feel much worse. Keeping cool through air-conditioning or various cooling devices (such as those offered by MSAA's Cooling Equipment Distribution Program), may be helpful for people with heat-sensitive MS.

When recovering from a symptom flare-up or learning to cope with a change in mobility, **rehabilitation through physical therapy and occupational therapy can be of great value. Speech therapy, therapeutic exercise, and certain medical devices may also be useful** in dealing with the symptoms of MS. Some of those who have a physically demanding or highly stressful job may choose to make a career change, in which case **vocational training** is helpful.

When a family member is diagnosed with MS, participating in some type of **counseling program** is often of benefit to everyone involved. Individuals may be affected in different ways, both physically and emotionally. Seeking professional assistance helps to ensure that MS does not disrupt one's family and happiness.

For more information on symptom management and handling the challenges of MS, MSAA offers several helpful publications, as well as an extensive collection of MS-related books from MSAA's Lending Library. Additionally, MSAA's staff of qualified consultants is available to discuss a caller's needs and questions personally.

To contact MSAA, interested individuals may call **(800) 532-7667** or visit the MSAA website at **www.msaa.com**. Other sources for information are listed on page 14 of this booklet.

Common Types of MS

On average, **80 percent of people with MS begin with the relapsing-remitting form of MS (RRMS)**. What distinguishes this type of MS from other types are the temporary symptom flare-ups or “**exacerbations**” (also referred to as relapses, attacks, or bouts), which typically last for one to three months. These are followed by a complete or partial recovery (“**remission**”).

Between relapses, many people may go into remission for a year or more. During this time, they may remain symptom free, or only experience mild changes with symptoms that did not fully remit following the exacerbation. While symptoms may not appear or worsen between MS attacks, changes do continue within the CNS. New treatments are now available to help slow the damage caused by MS. Information about these treatments begins on page 9 of this booklet.

Initially, people with RRMS often experience:

- sensory disturbances (such as numbness or tingling)
- optic neuritis (inflammation of the optic nerve causing visual changes or loss; usually occurring in one eye)
- diplopia (double vision; objects may also appear to jump as a result of the eyes not properly coordinating together)

Fortunately, **visual changes are often temporary**. Other initial symptoms with RRMS may include limb weakness, clumsiness, fatigue, cognitive changes, bladder and bowel problems, sexual difficulties, and **Lhermitte’s sign**. The latter is a tingling sensation that radiates down the spine and into the limbs when the neck is flexed.

If untreated, more than 90 percent of individuals with RRMS may eventually enter a second phase of RRMS, known as **secondary-progressive MS (SPMS)**, within 25 years. This phase is reached when the person experiences a progressive worsening of symptoms. SPMS may occur with or without superimposed relapses.

While the majority of individuals with MS (80 percent) are diagnosed with RRMS, most of the other **20 percent fall under the heading of primary-progressive MS (PPMS)**. This form of MS presents a gradual but steady accumulation of neurological problems from the onset, without the presence of relapses and remissions. Unlike RRMS, where women are three times as likely to be diagnosed than men, PPMS is equally divided between the genders.

Other types of MS exist, but these are not as common. These include **benign** (little or no change after 20 years), **progressive-relapsing MS (PRMS)** (progressive course from the onset with acute relapses), and **malignant or fulminant MS** (rapidly progressive disease course).

| TYPES OF MULTIPLE SCLEROSIS | |
|---|--|
| Name | Characteristics |
| Relapsing-Remitting Multiple Sclerosis (RRMS) | Symptom flare-ups followed by recovery; stable between attacks |
| Secondary-Progressive Multiple Sclerosis (SPMS) | Second phase of RRMS; progressive worsening of symptoms with or without superimposed relapses; treatments may delay this phase |
| Primary-Progressive Multiple Sclerosis (PPMS) | Gradual but steady accumulation of neurological problems from onset |
| Benign | Few attacks and little or no disability after 20 years |
| Progressive-Relapsing Multiple Sclerosis (PRMS) | Progressive course from the onset, sometimes combined with occasional acute symptom flare-ups |
| Malignant or Fulminant Multiple Sclerosis | Rapidly progressive disease course |

MS Diagnosis

MS diagnosis is based upon an individual's history of clinical symptoms and neurological examinations. A qualified physician – often a neurologist – must thoroughly review all symptoms experienced by an individual to suspect MS. Other conditions with similar symptoms must be ruled out, often requiring various lab tests.

Magnetic resonance imaging (MRI) of the brain has been used to assist in the diagnosis of MS for more than 20 years. The MRI consists of a computer, radiofrequency stimulator, and large electromagnet. An MRI picture looks like an x-ray, but rather than x-rays, a magnet and radio waves are used to produce a picture of the brain. For those with MS, the MRI is used to show the size and location of active lesions and plaques. Sometimes dye is given to the person with MS to better illuminate areas of inflammation.

Cerebrospinal fluid (CSF) analysis is occasionally recommended to determine disease activity or to provide further evidence for diagnosis. CSF is the fluid that surrounds the spinal cord and brain. When someone has MS, this procedure frequently shows evidence of abnormal antibody production. Since the introduction of the MRI, CSF analysis is used less often.

When performing a CSF analysis, a local anesthetic is given to reduce any discomfort. A needle is inserted in the lower back to collect a small amount of CSF fluid. Anyone planning to have a CSF analysis performed is encouraged to ask his or her physician to provide an explanation of the procedure.

Treating Exacerbations with Steroids

Most people with MS experience exacerbations (or MS attacks) which often last from one to three months. Acute physical symptoms and neurological signs must be present for at least 24 to 48 hours – without any signs of infection or fever – before the treating physician may consider it to be a true relapse.

A **pseudoexacerbation** is a temporary worsening of symptoms, without actual myelin inflammation or damage, which is brought on

by external influences – such as infection, exhaustion, heat, depression, or stress. **Checking for a fever is important**, since even a minor infection can cause old symptoms to reappear. **Urinary tract infection (UTI)** is the most common illness to cause a pseudoexacerbation. People with “heat-sensitive” MS should avoid hot tubs, saunas, or other situations that can raise the body’s temperature. These too can cause a temporary increase in symptoms.

Exacerbations are usually treated with a high-dose, short-term course of powerful steroids (corticosteroids). The goals are to (1) reduce the severity and duration of the relapse by decreasing inflammation, and (2) potentially minimize any permanent damage resulting from the attack. Steroid treatments are often given by **IV injection** (intravenously), which injects the drug directly into the bloodstream for quick action. In the past, this could only be done in a hospital setting, but now this treatment may be performed in the comfort of one’s home.

Long-term use of steroids is not generally recommended. They can cause many side effects when given over a long period of time and may have no effect on the long-term progression of MS.

Approved Long-Term Treatments

The first three long-term MS treatments to be approved were dubbed the “A-B-C” drugs because of their brand names: Avonex[®], Betaseron[®], and Copaxone[®]. These are interferon beta-1a, interferon beta-1b, and glatiramer acetate, respectively. All were approved by the Food and Drug Administration (FDA) for treating RRMS. These drugs have been used for several years and research shows that people are doing well on these medications for long periods of time (up to 20 years to date).

The fourth drug to be approved by the FDA was Novantrone[®] (mitoxantrone), and this was the first drug indicated for both worsening RRMS and SPMS. News then arrived of a **fifth FDA-approved drug** for RRMS: **Rebif[®]** (interferon beta-1a). This is the same drug as Avonex, but is injected differently and in more frequent and higher doses.

Several large clinical trials have been conducted to study each of these drugs separately for their effects on MS. Although differences exist in study design and specific findings, trials generally showed these common results:

- Reduced the number of relapses
- Reduced the severity of relapses
- Reduced the development of new areas of inflammation as seen on MRI
- Showed some evidence of delaying short-term disease progression

Each of the approved treatments has side effects which are usually manageable. Novantrone is the only drug that has a set limit of doses, which is necessary to avoid **cardiotoxicity** (heart damage). The other drugs appear safe provided the person taking the drug is not experiencing any adverse effects and blood tests continue to be normal.

While no damage to the reproductive system or the fetus has been observed, these drugs are not recommended if a woman is pregnant or considering pregnancy during her treatment period. Male patients considering long-term treatment should discuss options for family planning with their doctor.

Other treatments are sometimes used to try to slow MS disease progression when other therapies have been ineffective.

Such treatments are approved by the FDA for other illnesses, but not specifically for the treatment of MS. These include intravenous immunoglobulin (IVIg) therapy, methotrexate, azathioprine (Imuran[®]), and cyclophosphamide (Cytoxan[®]).

Treating Early

Many experts now recommend treatment as early as possible with one of the five approved agents. Studies show that treating after the first attack can significantly delay time to the second attack. Early treatment is also thought to possibly limit axonal (nerve) injury, which may be irreversible, and later lead to progressive disease.

Administration and Side Effects

Four of the five approved long-term treatments for MS are easily administered. Betaseron, Copaxone, and Rebif are injected just under the skin (subcutaneously), while Avonex is injected into the muscle (intramuscularly). The frequency ranges from once per week to once per day, depending on which medication is used. Although this means some changes to one's normal routine, most people quickly adapt to these changes.

Additionally, these types of injections may be self-administered, or given by a family member or other care partner, in the comfort of one's home. Pharmaceutical companies have made injections even easier by offering **pre-filled syringes** (Avonex, Copaxone, and Rebif) and "**auto-injectors**," which give a quick, pre-measured injection under the skin with the touch of a button (Betaseron, Copaxone, and Rebif). Auto-injectors also reduce injection-site reactions (redness, soreness, and swelling).

The fifth drug, Novantrone, is given via intravenous injection once every three months for two to three years. This may only be performed at an IV infusion facility.

Each of the approved treatments has side effects that are usually manageable. With the interferons (Avonex, Betaseron, and Rebif), these may include temporary flu-like symptoms, headache, injection-site reactions, and blood count or liver test abnormalities -- depending on the drug. A few individuals taking Copaxone may experience injection-site reactions and a brief systemic reaction (such as anxiety, flushing, chest tightness, dizziness, palpitations, and/or shortness of breath), that quickly subsides without the need for any treatment.

Although Novantrone is usually well tolerated, side effects may include nausea, thinning hair, loss of menstrual periods, bladder infections, and mouth sores. Individuals using this treatment should not be alarmed if their urine and whites of the eyes turn a bluish color -- this is just a temporary side effect of the drug. As mentioned earlier, Novantrone carries the risk of cardiotoxicity and may not be given beyond the two-to-three year limit.

Five Approved Long-Term

| DRUG | TYPE | SIDE EFFECTS |
|------------|---|--|
| Betaseron | Interferon beta-1b* (immune system modulator with antiviral properties) | Flu-like symptoms, injection-site skin reaction, blood count and liver test abnormalities |
| Avonex | Interferon beta-1a* (immune system modulator with antiviral properties) | Flu-like symptoms and headache |
| Rebif | Interferon beta-1a* (immune system modulator with antiviral properties) | Flu-like symptoms, injection-site skin reaction, blood count and liver test abnormalities |
| Copaxone | Synthetic chain of four amino acids found in myelin (immune system modulator that blocks attacks on myelin) | Injection-site skin reaction as well as an occasional systemic reaction - occurring at least once in approximately 10 percent of those tested |
| Novantrone | Antineoplastic agent (immune system modulator and suppressor) | Usually well tolerated; side effects include nausea, thinning hair, loss of menstrual periods, bladder infections, and mouth sores; additionally, urine and whites of the eyes may turn a bluish color temporarily |

***Additional information about interferons:** Some individuals develop neutralizing antibodies (NABs) to the interferons (Avonex, Betaseron, and Rebif), but their impact on the effectiveness of these medications has not been established. Many continue to do well on these drugs despite the presence of NABs. Others may have sub-optimal results even without NABs present.

Treatments for MS

| HOW ADMINISTERED | NOTES |
|--|---|
| 250 micrograms taken via subcutaneous injections every other day | Side effects may be prevented and/or managed effectively through various treatment strategies; side effect problems are usually temporary. |
| 30 micrograms taken via weekly intermuscular injections | Side effects may be prevented and/or managed effectively through various treatment strategies; side effect problems are usually temporary. |
| 44 micrograms taken via subcutaneous injections three times weekly | Side effects may be prevented and/or managed effectively through various treatment strategies; side effect problems are usually temporary. |
| 20 milligrams taken via daily subcutaneous injections | Systemic reactions occur about five to 15 minutes following an injection and may include anxiety, flushing, chest tightness, dizziness, palpitations, and/or shortness of breath. Usually lasting for only a few minutes, these symptoms typically do not require specific treatment and have no long-term negative effects. |
| IV infusion once every 3 months (for two to three years maximum) | Novantrone carries the risk of cardiotoxicity (heart damage) and may not be given beyond two or three years. People undergoing treatment must have regular testing for cardiotoxicity, white blood cell counts, and liver function. Novantrone was studied in combination with large IV doses of steroids. Concurrently, many physicians often use it in combination with one of the interferons or Copaxone. |

The MS Council and the American Academy of Neurology have concluded that the higher-dosed interferons are likely to be more effective than lower-dosed interferons. Several factors, however, must be considered when selecting one of these drugs, and this decision must be made on an individual basis under the guidance of a qualified physician.

Looking Ahead

This is a promising time for individuals who have been diagnosed with MS. Since the early 1990s, treatment options have gone from zero to five and more therapeutic agents are on their way. Among others, MS drugs under investigation include cancer-fighting drugs, antiviral medications, vaccines, bone marrow transplants, pregnancy-related hormones, cholesterol-fighting drugs, stem cells, and agents such as growth factors that may repair myelin. Regeneration, neuroprotection, and gene therapy are also being explored. At the time of this writing, Tysabri® (natalizumab) had been approved as a sixth drug treatment for MS, but was suspended due to adverse events.

For more information about MS research and treatments, please contact MSAA, which offers several other informative publications and a quarterly magazine, *The Motivator*, as well as the MSAA Lending Library.

MSAA may be contacted by calling (800) 532-7667, or by visiting MSAA's website at www.msaa.com.

Sources for more information include:

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| | (Avonex) MS ActiveSource (800) 456-2255 www.avonex.com |
| Consortium of Multiple Sclerosis Centers (CMSC) CMSC/NARCOMS patient registry: (800) 253-7884 www.mscares.org www.narcoms.org | (Betaseron) MS Pathways (800) 788-1467 www.mspathways.com |
| Multiple Sclerosis Foundation (888) 673-6287 www.msfacts.org | (Copaxone) Shared Solutions (800) 887-8100 www.sharedsolutions.com |
| National Multiple Sclerosis Society (800) 344-4867 www.nmss.org | (Novantrone) MS LifeLines (877) 447-3243 www.novantrone.com |
| | (Rebif) MS LifeLines (877) 447-3243 www.MSLifeLines.com |

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The Multiple Sclerosis Association of America (MSAA) is a national nonprofit organization dedicated to enriching the quality of life for individuals with multiple sclerosis. MSAA provides ongoing support and direct services to individuals with MS and the people close to them. MSAA also serves to promote greater understanding of the needs and challenges of those with MS.

MSAA provides a variety of programs and services, including:

- *Toll-free Helpline (800) 532-7667*
- *Support groups*
- *Equipment Distribution Program*
- *Home Modification Program*
- *MRI Diagnostic Fund*
- *MRI Institute (follow-up MRI assistance and advocacy)*
- *Educational literature*
- *Quarterly magazine, The Motivator*
- *Lending Library*
- *Cooling Equipment Distribution Program
(to provide relief for heat-sensitive individuals)*
- *Barrier-free Housing Program*
- *Networking Program (linking clients through letters and email)*
- *Informative regional events (helping to promote awareness)*

*If you would like additional information about multiple sclerosis, the Multiple Sclerosis Association of America, or its programs and services, please call **(800) 532-7667**. You may also visit MSAA's website at **www.msaa.com**.*

*MSAA programs and services listed above are supported by individual and corporate contributions. If you would like to offer support to MSAA, please call **(800) 532-7667, extension 159** or visit MSAA's website at **www.msaa.com** and select "how to give." Your donations are greatly appreciated.*



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