About MS
An Overview of Multiple Sclerosis (MS), Including Symptoms, Treatments, and Research
Introduction

Multiple sclerosis (MS) is an unpredictable disorder that can cause a variety of symptoms, which for many, can flare-up and then subside over the course of days, months, or even years. While MS is not contagious, its causes are not yet fully understood and researchers continue to search for answers.

MS is most frequently diagnosed in young adults, although individuals of any age may be diagnosed with this neurological condition. People who are not familiar with MS can easily be confused by its name and its unique symptoms. Particularly with today’s approved treatments and wellness strategies, most individuals with MS are able to live a full and productive life, with much hope for the future.

History

The fact that MS symptoms flare-up and subside, combined with the unpredictability of symptoms, has made MS a difficult disease to recognize, define, and treat. Since the late 1300s, individuals with a progressive illness suggestive of MS have been observed. Not until 1868 did the famous neurologist, Jean-Martin Charcot, lecture on the features of MS and give it a name.

Throughout the 1800s and 1900s, hundreds of therapies were tried, without success, in the treatment of multiple sclerosis. In 1951, cortisone (a steroid) was first used to treat MS relapses (also known as exacerbations, attacks, or symptom flare-ups). Cortisone was found to reduce the severity of the relapse and to shorten its duration, but it had no long-term effects on the disease.

The first drug proving to be effective in the long-term treatment of MS received approval in 1993. As of early 2014, 10 long-term treatments have been approved for relapsing forms of MS, with many more on the way. These are also referred to as disease-modifying therapies (DMTs). While these medications do not cure MS, they do work to slow disease activity as well as reduce the severity and frequency of flare-ups. Additionally, these DMTs may delay disease progression, delay disability, and increase longevity.
The MS Process and Symptoms

Multiple sclerosis (MS) is a disease of the central nervous system (CNS). The CNS consists of the brain, optic nerves, and spinal cord. With MS, areas of the CNS become inflamed, damaging the protective covering (known as “myelin”) that surrounds and insulates the nerves (known as “axons”). In addition to the myelin, over time, the axons and nerve cells (neurons) within the CNS may also become damaged.

The damage to the protective covering and also to the nerves disrupts the smooth flow of nerve impulses. As a result, messages from the brain and spinal cord going to other parts of the body may be delayed and have trouble reaching their destination – causing the symptoms of MS.

Although each person with MS experiences different types and severity of symptoms, the range of symptoms includes:

- anxiety
- balance issues
- bladder dysfunction
- bowel problems
- cognitive changes
- depression
- dizziness/vertigo
- fatigue
- mobility and walking issues
- numbness
- pain
- pseudobulbar affect (PBA)
- sexual dysfunction
- sleep issues
- spasticity (stiffness)
- speech difficulties
- swallowing disorders
- tremor
- Uhthoff’s syndrome (when heat worsens visual symptoms)
- visual disorders
- weakness

Illustration of MS damage to the myelin of a nerve cell
Areas of inflammation and damage in the CNS are known as "lesions." The changes in size, number, and location of these lesions may determine the type and severity of symptoms. Disease activity may also be evaluated from these changes in the size or number of lesions. Frequently, MS may be "clinically silent," showing no increase in symptoms, yet continuing to show signs of disease activity within the CNS.

For individuals with relapsing forms of MS, early and continued treatment with a disease-modifying therapy (DMT) can often slow the "clinically silent" disease activity in the brain, reducing the size and number of active lesions. This is why most neurologists, as well as the American Academy of Neurology, recommend that individuals with relapsing forms of MS begin treatment as soon as possible after the diagnosis is established. However, treatment cannot be effective unless it is taken exactly as prescribed and without missing doses, so adherence is critical.

In addition to the lesions, areas of thick scar tissue may eventually form along the areas of permanently damaged myelin. These areas of scar tissue are referred to as "plaques." The term "multiple sclerosis" originates from the discovery of these hardened plaques. Multiple refers to "many;" sclerosis refers to "scars."

Lesions and plaques are viewed on a magnetic resonance imaging (MRI) scanner. This technology is used to help diagnose MS and evaluate its progress at various intervals. The MRI and other tools are described in the section titled, "Diagnosing MS and Evaluating Disease Activity," beginning on page 10 of this booklet.
Many experts estimate that **2.5 million people worldwide have MS**. The number of people diagnosed with MS in the United States was previously estimated more than a decade ago at 400,000. However, without a comprehensive, national registry, this figure cannot be confirmed and more research is needed. Most people with MS experience their first symptoms and are diagnosed between the ages of 15 and 50, although individuals of any age may be diagnosed with MS.

**MS in childhood and adolescence is now being diagnosed more frequently,** due in part to an increased awareness that children can get MS. Known as **pediatric MS**, diagnosis in children is still extremely involved, as experts have identified more than 40 common diseases that may initially behave similarly to early MS. In the United States, estimates range from **7,000 to 10,000 children and teens** who have MS.

**The distribution of this disease is not totally random.** On average, with relapsing forms of MS, women are three times more likely than men to develop this disorder. With the primary-progressive form, genders are more equally divided.

**Geographically, people who live farther from the equator** (in more temperate climates) **have a higher risk of developing MS** than people living in hotter areas near the equator, or in very cold areas near the north or south poles. Individuals living beyond the 40-degree mark north or south of the equator are far more likely to develop MS, and this is especially true for people in North America, Europe, and southern Australia. The degree of risk associated with where someone lives as a child will remain throughout his or her life.

MS is very rare in Inuit populations (sometimes referred to as Eskimos) living in the far north. Asia continues to have a lower incidence of MS. **More prevalent among those of northern European or Scandinavian ancestry, Caucasians have a higher incidence than those of African heritage to develop MS.**
A recent study may show that African Americans are at a higher risk of MS than originally thought, but more research is needed. **African-Americans tend to have more symptoms at the time of diagnosis,** which are usually limited to the optic nerves and spinal cord, and this is termed “opticospinal MS.” This means that African-Americans may experience more problems with vision and mobility, versus other common MS symptoms. The disease course tends to be more progressive and responds less to disease-modifying therapies.

Research also reveals that **Latinos are usually diagnosed at a younger age** than both African-American as well as Caucasian Americans of non-Latino descent. Latinos tend to have fewer mobility and bladder/bowel problems, but may experience more depression.

**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 situations where one identical twin has been diagnosed with MS, the other twin has a 31-percent risk of developing the disease. (If MS was strictly hereditary, when one identical twin has MS, the other identical twin would have a 100-percent risk of getting MS.) The risk for twins who are not identical is five percent – similar to that of other siblings. Other groups of individuals who appear to have an increased risk of developing MS include those who smoke cigarettes, individuals with less exposure to sunlight and with lower amounts of Vitamin D, as well as people living in cleaner environments with fewer parasites. These findings are explained later on page 8, under “Possible Causes of MS.”
Types of MS

Multiple sclerosis (MS) affects each person differently. The most common types of MS are:

- Relapsing-Remitting MS (RRMS)
- Secondary-Progressive MS (SPMS)
- Primary-Progressive MS (PPMS)
- Progressive-Relapsing MS (PRMS)

Initially, most people with MS experience symptom flare-ups, which are also known as relapses, exacerbations, or attacks. When someone experiences a relapse, he or she may be having new symptoms or an increase in existing symptoms. These usually persist for a short period of time (from a few days to a few months) and afterward may remain symptom-free for periods of months or years. This type of MS is referred to as relapsing-remitting MS (RRMS). Approximately 80 to 85 percent of MS patients are initially diagnosed with this form of the disease.

Over time, RRMS may advance to secondary-progressive MS (SPMS). This form of MS does not have the dramatic variations in symptoms that RRMS does, but rather has a slow, steady progression – with or without relapses. If relapses do occur, they usually do not fully remit. Without treatment, approximately half of individuals with RRMS convert to SPMS within 10 years. However, with the introduction of long-term disease-modifying therapies (DMTs), fewer individuals advance to this latter form of the disease.

Individuals who are not initially diagnosed with RRMS may be experiencing a more steady progression of the disease from the onset. Approximately 10 percent of the MS population is diagnosed with primary-progressive MS (PPMS), where individuals experience a steady worsening of symptoms from the start, and do not have periodic relapses and remissions.
Approximately 5 percent of patients are initially diagnosed with progressive-relapsing MS (PRMS). This type of MS steadily worsens from the onset, but symptom flare-ups – with or without remissions – are also present.

Other types of MS exist, but these are uncommon. These include:

- **benign MS** (with little or no change after 15 years; however, progression may occur at a later time)
- **fulminate MS** (a rapidly progressive disease course with severe relapses within five years after diagnosis; also known as “malignant MS” or “Marburg MS”)
- **burned-out MS** (controversial term used to describe MS patients whose MS progression slows dramatically later in life)

Prior to an MS diagnosis, individuals with “possible MS” may often fall under the parameters of one of two syndromes. The first is **clinically isolated syndrome (CIS)**, where someone may have experienced symptoms of MS for the first time, and an MRI may show evidence of MS, but a diagnosis cannot be confirmed at that time. The second syndrome is **radiologically isolated syndrome (RIS)**, which is the term used when someone has an MRI performed for an unrelated reason, and shows evidence of MS on the MRI scan, but does not have any signs of MS symptoms. As with CIS, more evidence will be needed in the future to determine if someone with RIS may be diagnosed with MS.
Possible Causes of MS

Researchers have studied a variety of possible causes for multiple sclerosis (MS), and a combination of factors appears to be involved. A popular theory looks at commonly known slow-acting viruses (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.

In the absence of a solid understanding of the mechanisms that underlie MS, no compelling candidate genes for MS have been identified. Genes have some role in susceptibility to MS, but the exact mechanisms remain unclear.

The list of genes that have been investigated for MS susceptibility is long and continually expanding. Linkage studies show that the major histocompatibility complex (MHC), which is a cluster of genes on chromosome 6, has the strongest genetic effect in MS. Additionally, other genes must make considerably weaker contributions to MS disease risk.

Some scientists are looking for a connection between MS and nutritional factors, including fat intake, as well as deficiencies in fish oil and Vitamin D. The idea that a diet rich in saturated fat may increase one’s risk of getting MS, as well as worsen his or her disease course, has been a popular theory for several decades. In addition to food and supplements, Vitamin D is also derived from sunlight. Reduced sunlight may be involved in the development of MS.
As noted earlier, populations living closer to the equator have a lower incidence of MS. A popular theory is that those living closer to the equator are exposed to more sunlight and therefore are less likely to experience a Vitamin D deficiency. Studies suggest that low levels of Vitamin D may increase one’s risk of MS. Conversely, the Nurses’ Health Studies (I & II) found that women who were taking 400 IU or more of Vitamin D daily had a lower risk of developing MS.

**Parasites** are another possible risk factor in the development of MS. Research has found that parasites can modulate the immune system and dampen its responses. **People who have parasites are less likely to be diagnosed with MS,** and as conditions in different countries become cleaner – with fewer parasites – the number of individuals being diagnosed is increasing in these parts of the world. Parasites are less common in the United States, which may contribute to the higher incidence of MS in this country.

**Salt is also under investigation with MS.** One study showed that high dietary salt was found to increase autoimmune neuro-inflammation in animal models. A separate study revealed that higher salt consumption was associated with increased clinical and MRI disease activity in people with MS.

**Another factor linked to MS is cigarette smoking.** One study shows that women who smoke are 1.6 times more likely to develop MS than women who are non-smokers. Individuals with MS who smoke also appear to be at a much greater risk of experiencing a more rapid progression of their disease.
Diagnosing MS and Evaluating Disease Activity

Diagnosing and evaluating MS disease activity is most reliably done by neurologists through a neurological history and examination. Tests that can indicate MS and rule out “MS mimickers” (other diseases that resemble MS but have other causes) are also performed.

Lesions (areas of inflammation and myelin damage in the brain and/or spine) may be viewed on a magnetic resonance imaging (MRI) scan. The MRI uses a computer, radiofrequency stimulator, and a large electromagnet to provide a picture of the brain and/or spine. While the picture looks a bit like an x-ray, it uses a different technology to show other details, and the MRI does not expose the patient to any radiation.

For people with multiple sclerosis, the MRI is used to evaluate the size and location of lesions. Inflammation can be better evaluated with gadolinium (or contrast) enhancement – a type of dye given to the patient via injection prior to the procedure. The MRI, particularly with gadolinium enhancement, allows doctors to measure disease activity within the central nervous system (brain, optic nerves, and spinal cord). Test results can help determine the effectiveness of a disease-modifying therapy (DMT), or to get an “inside view” of a patient’s disease status.

Another tool that is sometimes used in the diagnosis of MS is a lumbar puncture (also known as a spinal tap). This is a procedure where a very thin needle is inserted at the base of the spine and a small amount of cerebrospinal fluid (CSF) is collected. CSF is the liquid that surrounds the brain and spinal cord. By collecting a small amount of this fluid, laboratory testing may be performed to evaluate cellular and chemical abnormalities. However, even if no evidence of MS is found in the CSF, this does not rule out MS as a possible diagnosis.
Evoked potential (EP) tests may also be used to help diagnose MS, if further support is needed. These measure the speed of the brain’s response to visual, auditory (sound), or sensory (feeling) stimuli, using electrodes taped to the patient’s head. Delayed responses can indicate possible damage to the nerve pathways.

Additional tools are available to measure disease activity. These are used mainly in clinical trials to help evaluate disease progression as well as changes in specific symptoms, such as fatigue, strength, mobility, vision, cognition, and others. The most widely known scale among the MS community is the Kurtzke Expanded Disability Status Scale (EDSS). It uses whole and half numbers from one to 10 to measure degree of disability, largely in terms of mobility.

Another measurement system is the MS Functional Composite (MSFC) scale. This measures lower-extremity function with a Timed 25-Foot Walk, upper-extremity function through the 9-Hole Peg Test (9-HPT), and cognitive function, using the Paced Auditory Serial Additions Test (PASAT).
Relapse Management

Relapses, also referred to as exacerbations, attacks, flare-ups, episodes, or bouts, are initially experienced by most people diagnosed with multiple sclerosis (MS). Relapses occur with relapsing-remitting, progressive-relapsing, and sometimes secondary-progressive forms of MS. Relapses do not occur with primary-progressive MS, although patients may experience day-to-day fluctuations in how they feel.

During a relapse, inflammation is occurring along the nerves and the myelin, causing patients to have a temporary worsening or recurrence of existing symptoms and/or the appearance of new symptoms. This can range from a few days in duration to a few months, followed by a complete or partial recovery (remission). 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 this type of flare-up to be a true relapse.

A pseudoexacerbation is a temporary worsening of symptoms without actual myelin inflammation or damage, brought on by other influences. Examples include other illnesses or infection, exercise, a warm environment, depression, exhaustion, and stress. When symptoms flare, checking for a fever is important, since even a minor infection and slight increase in temperature can cause symptoms to appear.

Relapses are usually treated with a high-dose course of powerful corticosteroids (a type of steroid) over a period of three to five days. These are given by intravenous (IV) infusion, administering the drug directly into the bloodstream for a quicker response. Some doctors prescribe oral steroids after the high-dose treatment, to ease the patient off of the medication. These are usually tapered over one to two weeks. Another FDA-approved option is Acthar® Gel, which contains a highly purified form of the hormone adrenocorticotropic (ACTH). It is given once daily for two to three weeks and is injected either into the muscle or under the skin.

For more information on relapse management, please visit MSAA’s MS Relapse Resource Center, found at relapses.mysaa.org.
The Importance of Long-Term Treatment

Presently, the 10 FDA-approved disease-modifying therapies (DMTs) are only available for individuals with relapsing forms of multiple sclerosis – largely for those with RRMS. Research (including many clinical trials) is ongoing at a rigorous pace to find treatments that will also be effective for the progressive forms of MS. Fortunately, symptom-management strategies and comprehensive care plans with teams of doctors, nurses, and therapists, help to greatly improve the quality of life for all individuals with MS – both with relapsing and progressive forms of MS.

Treatment with a long-term DMT is crucial for most patients with relapsing forms of MS, since disease activity and damage usually continue within the CNS even when no new symptoms are present. When a patient begins a treatment regimen early in his or her disease course, disease activity is slowed for most individuals. This not only reduces the number and severity of symptom flare-ups, as well as delays the progression of the disease (and possibly delays any related disability), but also reduces the number of active lesions that appear on an MRI.

Additionally, a 21-year prospective study of individuals (with RRMS) who began therapy early in the disease found that they experienced a longer lifespan than those who did not begin treatment as early. This study was conducted with a specific DMT; more studies are needed to see if the same is true for all DMTs.

Getting early treatment and staying on one of the DMTs for MS may also delay the rate of conversion from RRMS to secondary-progressive MS (SPMS). This latter form of MS that follows RRMS exhibits a steady worsening, with or without relapses. If flare-ups do occur, they usually do not remit fully. As mentioned earlier, without treatment, about half of individuals with RRMS convert to SPMS within 10 years. However, since the introduction of the first treatment in 1993, those taking a DMT have reduced or delayed the conversion to SPMS.
The 10 FDA-Approved Long-Term Treatments for MS

The following list includes the 10 disease-modifying therapies (DMTs) that are FDA-approved (at the time of this booklet’s printing) for the long-term treatment of MS.

**Given via self-injection:**
- **Avonex®** (interferon beta-1a), given weekly
- **Betaseron®** (interferon beta-1b), given every other day
- **Copaxone®** (glatiramer acetate), given daily or three-times weekly
- **Extavia®** (interferon beta-1b), given every other day
- **Rebif®** (interferon beta-1a), given three-times weekly

**Given via intravenous (IV) infusion:**
- **Novantrone®** (mitoxantrone), given every three months, although seldom prescribed due to serious health risks
- **Tysabri®** (natalizumab), given every four weeks

**Taken orally:**
- **Aubagio®** (teriflunomide), taken daily
- **Gilenya®** (fingolimod), taken daily
- **Tecfidera™** (dimethyl fumarate or DMF), taken twice daily

At the time of printing, the 10 drugs listed above were the only ones approved by the FDA for the long-term treatment of MS. However, **several other drugs are under FDA review.** These include: **Plegridy™** (PEGylated interferon beta-1a), which is self-injected every two weeks; one or more **generic versions of Copaxone®** (listed above); and **Lemtrada®** (alemtuzumab), given via IV in annual courses.

For more information on long-term treatments for MS and how to select the treatment that is right for you, please see MSAA’s **S.E.A.R.C.H.™ program** at mymsaa.org/manage-your-ms/search.
How MSAA Can Help

INFORMATION AND EDUCATION
MSAA’s website provides a wealth of information at mymsaa.org. This includes written information, online videos, event listings, and more.

Multiple Sclerosis Information (MSi) is MSAA’s growing library of award-winning, on-demand video programming and archived webcasts. These feature healthcare professionals who provide valuable insights and updated information on the latest advances in MS research, disease and symptom management, wellness strategies, and more. Please visit mymsaa.org/manage-your-ms/videos for more information.

All of MSAA’s award-winning publications are designed to be easy to read, informative, and inspiring. These include MSAA’s magazine, The Motivator, published twice yearly, and the widely acclaimed MS Research Update, published annually. Other publications include children’s books on MS, as well as booklets on such topics as how to S.E.A.R.C.H.™ for the best disease-modifying therapy, understanding depression in MS, and treating relapses, among others. Please visit mymsaa.org/publications or call (800) 532-7667 for more information.

MSAA’s educational programs provide an excellent opportunity to connect clients with many of the country’s leading MS healthcare professionals. These events provide information in an easy-to-understand conversational format that strongly encourages open dialog between clients and presenters. Please visit MSAA’s homepage (at mymsaa.org) and select “Calendar of Events” at the center of the top menu bar to view events happening in your area, or call MSAA at (800) 532-7667 for more information.

At SwimForMS.org, individuals may also visit MSAA’s online Aquatic Center. Given the fact that water offers an ideal exercise environment for individuals with MS, this comprehensive online Aquatic Center features key information about aquatic exercise, helpful tips, and inspirational stories from people with MS.
TOLL-FREE HELPLINE
MSAA’s Helpline allows individuals with MS, family members, care partners, and friends, to speak directly with one of MSAA’s experienced consultants by calling (800) 532-7667. Individuals may also email questions to MSquestions@mymsaa.org or have a live Chat while visiting MSAA’s website.

MSAA’s Helpline consultants can offer encouragement to clients and their care partners to identify obstacles and discover ways to overcome them. Helpline consultants may also recommend the program(s) offered by MSAA and other resources that would be of help to the caller, and assist him or her with the application process. Members of the MS community are also encouraged to connect through our online blog, “MS Conversations,” and through other social media.

SHAREd-MANAGEMENT TOOLS TO MANAGE MS
“Shared Management” is a new philosophy supported by MSAA, where both the patient and healthcare providers work together to achieve the best possible health outcomes for the patient. To date, MSAA has developed three programs as part of its Shared-Management philosophy:

- **My MS Resource Locator®** – an MS-specific, online database offering targeted information and unique support services, including detailed guides, found at resources.mymsaa.org

- **My MS Manager™** – a mobile-phone application to track disease activity, store medical information, generate reports, and assist individuals with their treatment plan, accessed through mymsaa.org/manage-your-ms/mobile

- **MSAA’s S.E.A.R.C.H.™ Program** – tools to help individuals with learning about the approved long-term treatments for MS, along with questions to discuss with the patient’s medical team, located at mymsaa.org/manage-your-ms/search
COOLING AND ASSISTIVE EQUIPMENT
Many people with multiple sclerosis are heat sensitive, experiencing increased symptoms when in warm temperatures. MSAA’s Cooling Program offers cooling vests and accessories for adults with multiple sclerosis as well as children diagnosed with pediatric MS.

MSAA’s Equipment Distribution Program offers products designed to improve safety, dignity, mobility, and independence. MSAA provides items such as shower chairs, grab bars, hand rails, and mobility devices.

MSAA provides equipment through both programs at no charge (certain restrictions may apply) and ships directly to clients. Please visit mymsaa.org/msaa-help/cooling for more information on either of these programs.

MRI ASSISTANCE
Magnetic resonance imaging (MRI) is a vital tool for diagnosing multiple sclerosis and tracking its progression. MSAA has created two separate MRI programs: the MRI Diagnostic Fund helps individuals who are suspected of having MS obtain an initial diagnostic MRI exam; and the MRI Institute, which provides advocacy and financial assistance to those already diagnosed and in need of a follow-up MRI scan. Please visit mymsaa.org/msaa-help/mri for more information.

OTHER MSAA PROGRAMS
Additional programs and services include MSAA’s free Lending Library, Networking Program, and more. For more information, please visit MSAA’s website at mymsaa.org or call the Helpline at (800) 532-7667.

MSAA strives to provide useful, up-to-date information on matters of concern to MS patients and their families. This material is intended for general informational purposes only, and it does not constitute medical advice. You should not use the information presented as a means of diagnosis or for determining treatment. For diagnosis and treatment options, you are urged to consult your physician.

Those affiliated with this booklet and MSAA cannot be held responsible for any unintentional errors in the writing of this booklet, or changes in information that may occur, possibly affecting certain details of an explanation, assumption, or treatment.
MSAA’s Mission:
The Multiple Sclerosis Association of America (MSAA) is a
leading resource for the entire MS community, improving lives today
through vital services and support.

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please visit support.mymsaa.org/donate or call (800) 532-7667.

To learn more about MSAA’s Swim for MS fundraising initiative,
please visit SwimForMS.org or call (800) 532-7667, extension 157.

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