

Module 5

MS Symptoms, Causes, Risk Factors, Diagnosis, & Treatments

Learning Objectives

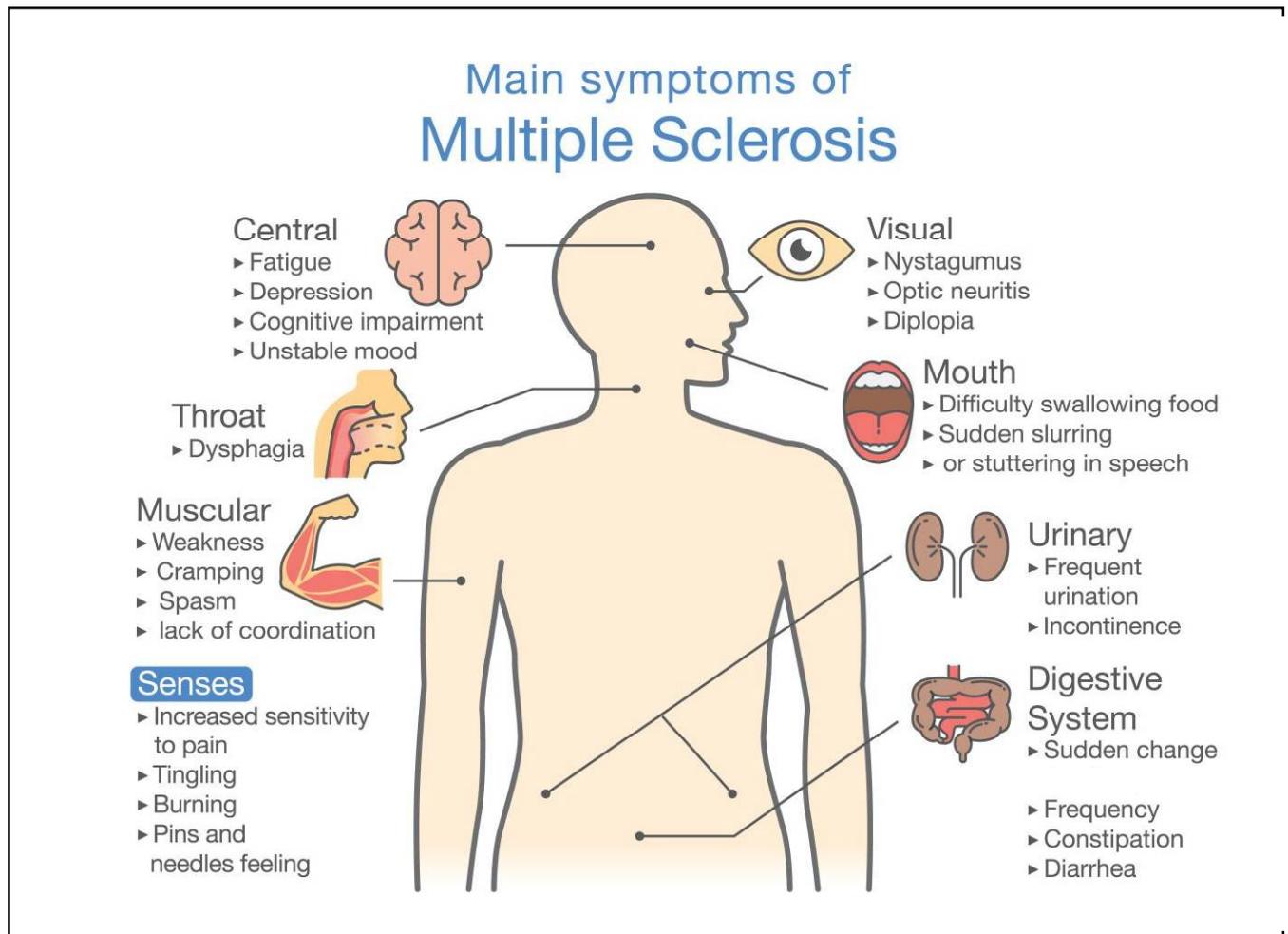
1. Be able to identify the symptoms of MS
2. Be able to identify the possible causes & risk factors of MS
3. Obtain a working knowledge of the diagnosis process of MS and identify the treatments of MS

Chapter Five

MS: Symptoms, Causes, Risk Factors, Diagnosis, and Treatments

Symptoms

Multiple sclerosis causes many different symptoms. The symptoms, severity, and duration can vary from person to person. Some people may be symptom free most of their lives, while others can have severe chronic symptoms that never go away. Signs and symptoms of MS vary widely and depend on the amount of nerve damage and which nerves are affected. Some people with severe MS may lose the ability to walk independently or at all, while others may experience long periods of remission without any new symptoms. There's no cure for multiple sclerosis. However, treatments can help speed recovery from attacks, modify the course of the disease and manage symptoms.



Symptoms of MS can be divided into two categories, Common Symptoms and Less Common Symptoms.

Common Symptoms

- **Fatigue:** Occurs in about 80% of people, can significantly interfere with the ability to function at home and work, and may be the most prominent symptom in a person who otherwise has minimal activity limitations.
- **Walking (Gait) Difficulties:** Related to several factors including weakness, spasticity, loss of balance, sensory deficit and fatigue, and can be helped by physical therapy, assistive therapy and medications.
- **Numbness or Tingling:** Numbness of the face, body, or extremities (arms and legs) is often the first symptom experienced by those eventually diagnosed as having MS.
- **Spasticity:** Refers to feelings of stiffness and a wide range of involuntary muscle spasms; can occur in any limb, but it is much more common in the legs.
- **Weakness:** Weakness in MS, which results from deconditioning of unused muscles or damage to nerves that stimulate muscles, can be managed with rehabilitation strategies and the use of mobility aids and other assistive devices.
- **Depression:** Studies have suggested that clinical depression — the severest form of depression — is among the most common symptoms of MS. It is more common among people with MS than it is in the general population or in persons with many other chronic, disabling conditions.
- **Other Common Symptoms:** Other common symptoms include vision problems, dizziness, vertigo, bladder problems, bowel problems, sexual problems, pain, itching, cognitive changes, and emotional changes.

Less Common Symptoms

Less common symptoms include speech problems, swallowing problems, tremors, seizures, breathing problems, respiration problems and hearing loss.

Causes and Risk Factors

The cause of MS is not known. Scientists believe MS is triggered by a combination of factors. To identify the cause, research is ongoing in areas of:

Immunology (the study of the body's immune system): In MS, an abnormal immune response causes inflammation and damage in the CNS. Many different cells are involved in the abnormal immune response. Two important types of immune cells are T cells and B cells.

- In MS, T cells become activated in the lymph system and enter the CNS through blood vessels. Once in the CNS, T cells release chemicals that cause inflammation and damage. This results in damage to myelin, nerve fibers, and the cells that make myelin. T cells are also important to help activate B cells and call on other immune system cells to participate in the immune attack.
- T regulatory cells, a type of T cell, dampen or turn off inflammation. In MS, T regulatory cells do not function correctly and do not effectively turn off inflammation.
- Cytotoxic or “killer” T cells directly attack and destroy cells bearing certain characteristics
- B cells become activated with the help of T cells. B cells produce antibodies and stimulate other proteins and in MS, these cause damage in the CNS.

Environment: Although the cause of MS is not known, more is being learned about environmental factors that contribute to the risk of developing MS. There is no single risk factor that provokes MS, but

several environmental factors are believed to contribute to the overall risk.

- **Geographic:** MS is known to occur more frequently in areas that are farther from the equator. Epidemiologists — scientists who study disease patterns in large groups of people— are looking at variations in geography, demographics (age, gender and ethnic background), genetics, infectious causes and migration patterns in an effort to understand why.
- **Vitamin D:** Growing evidence suggests that vitamin D plays an important role in MS. Low vitamin D levels in the blood have been identified as a risk factor for the development of MS. Some researchers believe that sun exposure (the natural source of Vitamin D) may help to explain the north-south distribution of MS.
- **Smoking:** The evidence is also growing that smoking plays an important role in MS. Studies have shown that smoking increases a person's risk of developing MS and is associated with more severe disease and more rapid disease progression. Also, cessation of smoking slows the progression of MS.
- **Obesity:** Several studies have shown that obesity in childhood and adolescence, particularly in girls, increased the risk of later developing MS.

Genetics (understanding the genes that may not be functioning correctly in people who develop MS): MS is not an inherited disease, meaning it is not a disease that is passed down from generation to generation. However, in MS there is genetic risk that may be inherited. Research is ongoing to better understand genetic risk and other factors that contribute to the development of MS.

- In the general population, the risk of developing MS is about 1 in 750 – 1000 (.01%)
- In identical twins, if one twin has MS the risk that the other twin will develop MS is about 1 in 4.
- The risk of developing MS is also increased when other first degree relative (parents, siblings and children) have MS, but far less than in identical twins.
- The risk for a child with one parent who has MS is approximately 2%.
- The risk for a child with two parents who have MS is approximately 12.2%
- About 200 genes have been identified that each contribute a small amount to the overall risk of developing MS.

Infectious Agents (such as viruses): Researchers are considering the possibility that bacteria and viruses may cause MS. Viruses are known to cause inflammation and a breakdown of myelin. Therefore, it's possible that a virus could trigger MS. It's also possible that the bacteria or virus that have similar components to brain cells trigger the immune system to mistakenly identify normal brain cells as foreign and destroy them. Several bacteria and viruses are being investigated to determine if they contribute to the development of MS.

These include:

- measles,
- canine distemper,
- human herpes virus-6,
- Epstein-Barr virus (EBV)

Other risk factors for MS:

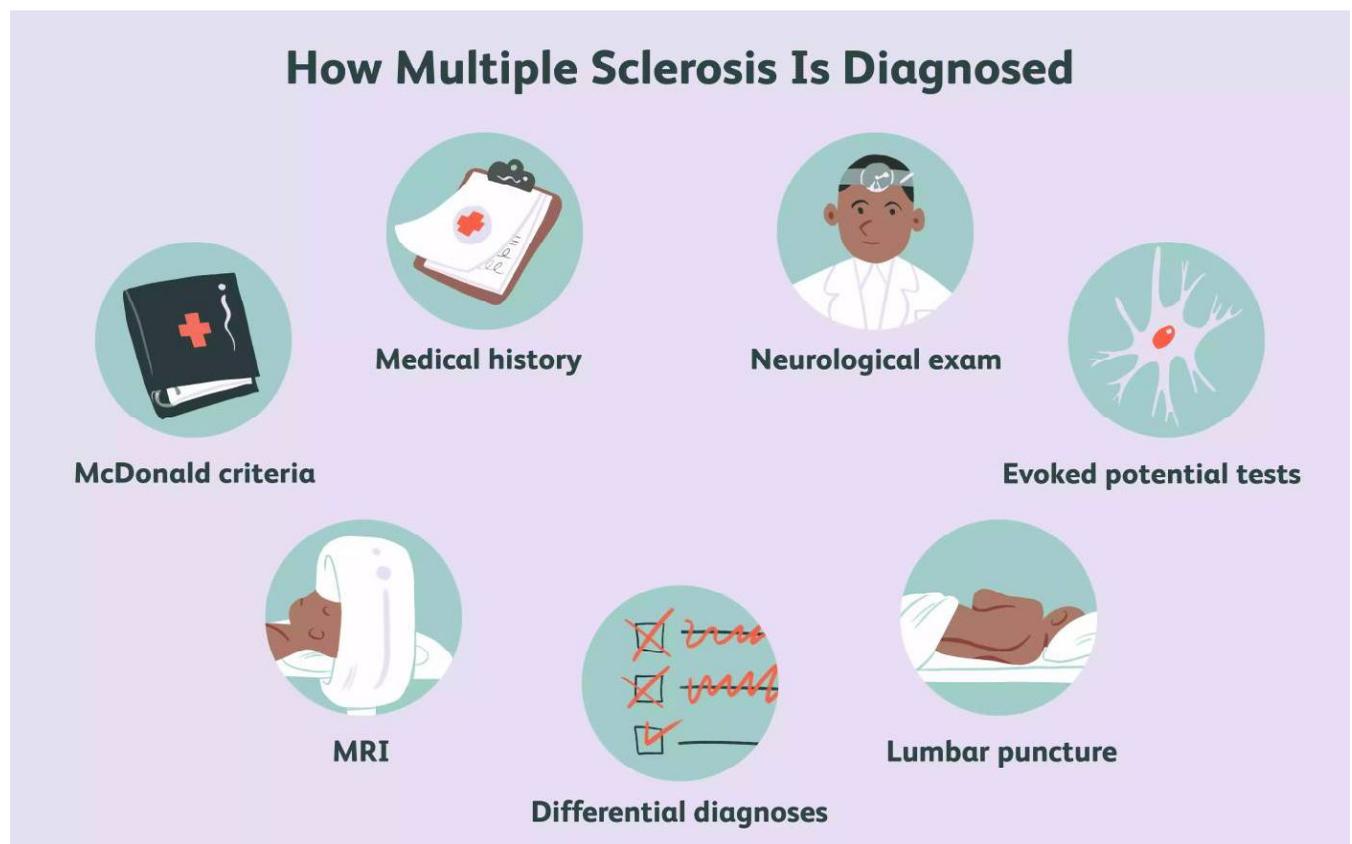
- **Age:** MS can occur at any age, but usually affects people somewhere between the ages of 16 and 55.
- **Gender:** Women are more than two to three times as likely as men are to have relapsing-remitting MS.
- **Race:** White people, particularly those of Northern European descent, are at highest risk of developing MS. People of Asian, African or Native American descent have the lowest risk.

- Climate: MS is far more common in countries with temperate climates, including Canada, the northern United States, New Zealand, southeastern Australia and Europe.
- Certain autoimmune diseases: You have a slightly higher risk of developing MS if you have thyroid disease, type 1 diabetes or inflammatory bowel disease.

Diagnosis

Diagnosing MS is complex and requires a complete review of one's medical history, and will include a physical exam and various tests. At this time, there are no symptoms, physical findings or laboratory tests that can, by themselves, determine if one has MS. Several strategies are used to determine if one meets the criteria for a diagnosis of MS, and to rule out other possible causes of whatever symptoms one is experiencing. These strategies include a medical history, a neurologic exam and various tests including magnetic resonance imaging (MRI), spinal fluid analysis, and blood tests to rule out other conditions. (National Multiple Sclerosis Society, 2006)

Regardless, it is imperative that the diagnosis of MS is timely and accurate since permanent neurologic damage can occur even in the earliest stages of MS. Having a quick and accurate diagnosis of MS will enable one to start the appropriate treatment(s) as early in the disease process as possible.



Criteria for a diagnosis of MS: The Revised McDonald Criteria, published in 2017 by the International Panel on the Diagnosis of Multiple Sclerosis, include specific guidelines for using MRI and cerebrospinal fluid analysis to speed the diagnostic process. MRI is used to demonstrate lesion dissemination in time (DIT) and space (DIS). The MRI can be used to look for a second area of damage in a person who has experienced only one attack (also called a relapse or an exacerbation) of MS-like symptoms — referred to as clinically-isolated syndrome (CIS). The MRI can also be used to confirm that damage has occurred at two different points in time. In some circumstances, the presence of

oligoclonal bands in a person's cerebrospinal fluid analysis can be used instead of dissemination in time to confirm the MS diagnosis. (Mantero, V., et al. 2018)

- Find evidence of damage in at least two separate areas of the central nervous system (CNS), which includes the brain, spinal cord and optic nerves AND
- Find evidence that the damage occurred at different points in time AND
- Rule out all other possible diagnoses

Medical History: A medical history, including past and present symptoms, will provide the physician with important information when diagnosing MS. A physician may also ask about past treatments and ongoing medical conditions in addition to gathering information about birthplace, family history, environmental exposures, history of other illnesses and places traveled that might provide further clues.

Physical and Neurological Examination: One's healthcare provider will perform a comprehensive neurologic exam, which includes tests of cranial nerves (vision, hearing, facial sensation, strength, swallowing), sensation, reflexes, coordination, walking and balance. A physical examination may reveal MS signs including:

- Irregular eye movement
- Changes in the way one talks
- Lack of coordination
- Sensory disturbances
- Changes in reflexes
- Weakness/spasticity in arms or legs

In many instances, medical history and neurologic exam provide enough evidence to meet the diagnostic criteria. Other tests are used to confirm the diagnosis or to identify other possible causes of the symptoms or neurological exam findings.

MRI Test: A common test in MS diagnosis is the magnetic resonance imaging test (MRI). An MRI can detect the distinctive lesions or scars in the central nervous system (brain, spine and optic nerve) that give multiple sclerosis its name. MRI is used to demonstrate lesion dissemination in time (DIT) and space (DIS). As MRI technology improves, the diagnosis of MS will be made more quickly and easily.

The 2017 diagnostic criteria for MS make it possible to diagnose MS in a person with CIS who also has specific findings on brain MRI that provide evidence of an earlier episode of damage in a different location and indicate active inflammation in a region other than the one causing the current symptoms. After reviewing one's medical history, doing a physical exam, and performing an MRI, healthcare teams sometimes have enough information to make a diagnosis of MS. In some cases, one may need additional tests to make a confirming diagnosis (spinal tap, blood tests, etc.).

Blood tests: While there is no definitive blood test for MS, blood tests can rule out other conditions that cause symptoms similar to those of MS, including lupus erythematosus, Sjogren's, vitamin and mineral deficiencies, some infections, and rare hereditary diseases.

Spinal tap (lumbar puncture): A sample of cerebrospinal fluid is removed and analyzed. The protein content of the fluid may be higher than normal. The concentration of antibodies may be high, and a specific pattern of antibodies (called oligoclonal banding) is detected in most people with multiple sclerosis.

Evoked responses: For this test, sensory stimuli, such as flashing lights, are used to activate certain areas of the brain, and the brain's electrical responses are recorded. In people with multiple sclerosis, the brain's response to stimuli may be slow because the demyelinated nerve fibers cannot conduct nerve signals normally. This test can also detect slight damage to the optic nerve.

Treatments

If one is diagnosed with MS or experiences a first-time MS event, he/she should consider talking about starting treatment as soon as possible with a healthcare team. Researchers have found that MS often causes more damage in the first year than in later years.

There are various MS treatment options available today that have been shown to decrease the frequency of relapses and to delay disease progression. There are several ways that these treatment options can be taken. Some treatments use an injection—either subcutaneous (under the skin) or intramuscular (into the muscle)—while others are given intravenously (via an infusion) or orally (by mouth).

When working with those who are taking medications for MS, it would be prudent to adjust the exercise routines in response to the side effects that one may experience. Side effects from infusions may include fatigue, nausea, headaches, and fever. Whereas one may experience tender spots from injections. Clients will usually know how they feel after treatment, but timing and programming of sessions relative to the treatment days should be taken into consideration. Communication with the client is key to providing the best exercise programming possible.

All of the medications listed below are disease modifying agents and are listed for educational purposes:

- **Beta interferons (Avonex, Betaferon, Extavia, Plegridy, Rebif)** are injectable medications used for the treatment of relapsing-remitting MS. Certain beta interferon products also may be used for a first clinical episode with MRI findings consistent with MS. Depending on the medication, injections for beta interferons can be either subcutaneous or intramuscular and dosing can vary from every other day to once a week.
- **Glatiramer acetate (Copaxone)** is given by subcutaneous injection every day for the treatment of relapsing-remitting MS. It is also used for patients who have experienced a first clinical episode and have MRI findings consistent with MS.
- **Fingolimod (Gilenya)** is a once-daily oral capsule indicated for the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.
- **Teriflunomide (Aubagio)** is a once-daily oral tablet used for the treatment of patients with relapsing forms of multiple sclerosis.
- **Dimethyl fumarate** is an oral capsule taken twice a day that is used to treat people with relapsing forms of MS.
- **Mitoxantrone (Novantrone)** is a chemotherapeutic agent for the treatment of worsening relapsing-remitting MS, progressive-relapsing MS or secondary-progressive MS, and is used to reduce neurologic disability and/or the frequency of clinical exacerbations. It is administered intravenously by an infusion once every three months.
- **Natalizumab (Tysabri)** is an intravenous medication reserved for patients with rapidly progressing MS or with high disease activity despite the use of an alternate MS therapy. It is administered once every four weeks.