

Multiple sclerosis:

To effectively assist your patients with managing their disease, a thorough understanding of how it affects them is essential.

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The most common cause of nontraumatic disability in adults between the ages of 20 and 50, MS affects people with unpredictability, volatility, and confusion in the prime of their lives. This neurologic disorder is believed to be caused by a combination of immune-mediated processes and genetic and/or infectious factors that damage the central nervous system (CNS), affecting the myelin and nerve fibers of the brain and spinal cord, including the optic nerves. More than 2.3 million people around the world have MS, according to the National Multiple Sclerosis Society, with the disease affecting young women three times more often than men. In recent decades, disease-modifying treatments have made a significant impact on decreasing exacerbations of symptoms.

The etiology of MS is a bit of a riddle, with complex immune, genetic, and possibly infectious involvement. A single causative infectious agent hasn't been identified. Environmental factors, such as increased northern distance from the equator, correlate with increased incidence and prevalence of the disease. MS is thought to be triggered by these factors fitting together in a genetically susceptible individual. Although MS isn't considered a hereditary condition, there's an overall familial recurrence rate of approximately 20%. This genetic susceptibility is associated with a gene complex known as human leukocyte antigen or HLA—a

cell-surface protein that's in charge of immune system regulation. However, a specific variant for MS isn't known, so genetic testing isn't definitive when assessing the risk of developing MS.

In this article, we break down this complex disease to give you the information you need to know.

Pathophysiology

In chronic autoimmune disorders, our own defense mechanisms, such as antibodies and T cells, mistakenly target the body's different structures. In the case of MS, the target is brain tissue. MS is believed to be an autoimmune disorder characterized by CNS inflammation, axonal injury, and loss due to demyelination—the destruction of the myelin sheath that surrounds the nerve fibers (axons) in the white matter of the CNS, resulting in axonal damage. Myelin is produced by a group of cells that support the neurons called oligodendrocytes. The myelin sheath is essentially a fatty material that protects and insulates the nerve fibers, improving the conduction speed of impulses. Once the nerve fibers are damaged or destroyed from the lack of myelin, signals within the CNS will be completely altered or stopped (see *Nerve cell in MS*).

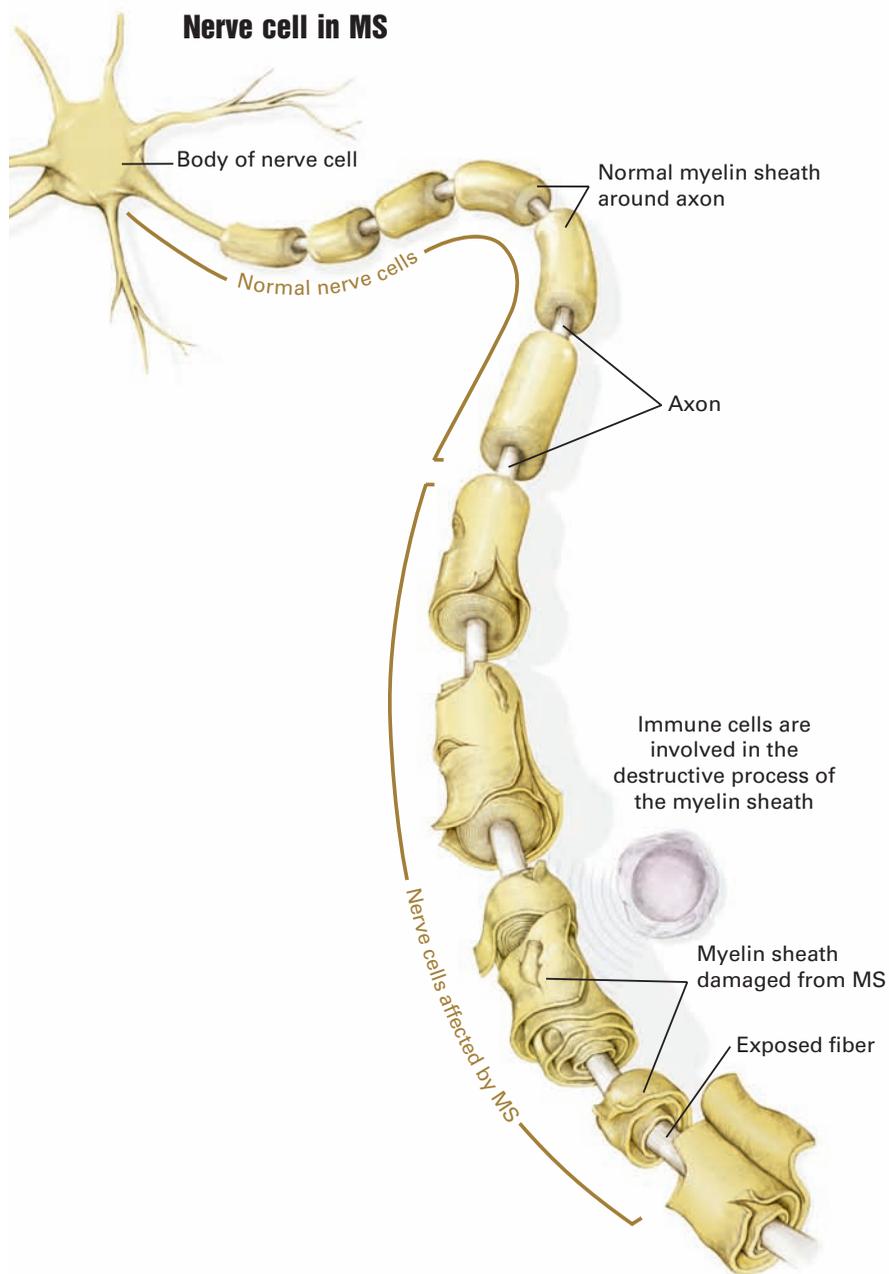
The brain is typically protected from invaders by the blood-brain barrier that only lets specific cells through from the blood. Usually, T cells and B cells are

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Solving the plaque puzzle





Source: Anatomical Chart Company. *Diseases and Disorders*. 3rd ed. Skokie, IL: Wolters Kluwer/Lippincott Williams & Wilkins; 2008.

required to have the right surface molecule to get through the blood-brain barrier. Once a T cell gets through, it becomes activated by whatever it encounters.

In MS, myelin activates the T cells. Once this happens, it signals the blood-brain barrier to put out more receptors, allowing more immune cells to cross and triggering a cell-mediated reaction. In this type of response, the T cells then release cytokines, which causes vasodilation and more immune cells to get in and damage the oligodendrocytes.

The B cells make the antibodies that mark the myelin sheath proteins as being

an outside invader. Once this happens, the macrophages use markers to find the myelin and destroy the oligodendrocytes. This damage causes the affected areas to grow scar tissue known as plaques. Sclerosis means scarring, hence the name of the disease to describe multiple scarring areas.

These lesions result from the immune system causing inflammation that destroys myelin. The damage causes diffuse random or patchy areas of plaque in the white matter of the CNS. Inflammation in the brain is due to inflammatory cell infiltrates and gliosis. Damage to the different areas of the CNS can result in a variety of neurologic symptoms that differ in form and severity.

Types of MS

The four phenotypes of MS are defined by relapses and/or disease progression, and each is characterized by its own clinical course. Relapses or flares happen when the T cells cause damage to the oligodendrocytes in the CNS. Flares are defined as newly appearing neurologic symptoms in the absence of an infection or fever that last longer than 24 hours.

In relapsing-remitting MS (RRMS), patients may recover symptomatically but the damage may leave behind small residual deficits. More frequently diagnosed in women, RRMS is the most common type of MS, affecting about 85% of patients with the disease. The brain accumulates damage from the flares that increase in severity during the relapsing phase. In the remitting stage, the immune system suddenly stops the attacks, leaving the brain some time to repair the myelin (remyelination) to a limited degree. Then the immune system comes back and attacks again, causing another flare.

This cycle of relapses and remissions happens in various lengths of time between days to years. It was once thought that complete stability was happening during the remitting phase. New



research has shown that this may not be true. Continued damage can occur in both the white and gray matter of the CNS, causing cerebral atrophy or shrinking of the brain over time.

Another phenotype of MS is called clinically isolated syndrome (CIS). In CIS, the patient experiences neurologic symptoms that point to possible MS. Caused by inflammation or demyelination, these symptoms last at least 24 hours and are followed by a complete or partial recovery. CIS patients may or may not develop MS.

Secondary progressive MS (SPMS) occurs in approximately 60% of patients with RRMS, with conversion to SPMS within 10 to 15 years of initial disease onset. This type starts with the same relapsing-remitting cycle, but later in life the remitting phase stops and there's a steady progression of the disease due to the continued damage to the myelin over time.

Primary progressive MS (PPMS) is diagnosed in approximately 10% of all cases of MS. PPMS affects men and women equally and starts in the late 30s. It's similar to SPMS, but the relapses and remissions don't happen. The patient progressively gets worse over time from the primary phase of disease because the immune system continues to attack the myelin, making treatment options limited.

Signs and symptoms

The characteristic symptoms of MS develop depending on the area affected by the loss of neurons. The breakdown in communication between neurons in the cerebellar region of the brain causes sensory, motor, and cognitive problems known as Charcot neurologic triad.

The first part of the triad is nystagmus. In MS, nystagmus is an involuntary rapid eye movement caused by plaques in the optic nerves known as optic neuritis. These optic nerve plaques can cause vision loss, changes in peripheral vision, scotomas (blind spots in the center of the

Understanding the myelin sheath

cheat

sheet

The myelin sheath protects and insulates the nerve fibers, improving the conduction speed of the impulses. To visualize:

- Think of an electrical cord as the nerve fiber and the myelin as the protective outer coating.
- Without this protective outer coating, touching the actual electrical wiring inside would cause a shock.
- This coating is needed for the electrical activity to make its way to the source you wish to power.

This same concept can be applied to the CNS. Nerve fibers lacking the myelin sheath won't transmit the proper signals within the CNS to power the brain and spinal cord.

visual field), diplopia (double vision), and severe pain with eye movement.

The second factor in the triad is intention tremor, which is caused by the destruction of myelin along the motor pathways in the CNS. Weakness, spasms, vibratory tremors, ataxia, and, in severe cases, paralysis may develop. Vibratory tremors are challenging to explain and invisible to others, which makes them frustrating for patients with MS. They can be described as feeling like sitting on a cell phone when the ringer is set to vibrate. Stiffness and spasticity can range from mild to severe and cause significant pain.

The third part of the triad is dysarthria stemming from plaques in the brainstem, resulting in awkward or scanning speech. Patients will sometimes substitute incorrect words in their sentences. For example, while baking a cake, the patient asks his or her family member to help with the process. The patient may say, "Please go get the milk out of the oven" when they meant to say, "Please go get the cake out of the oven." Brainstem plaques can also cause problems with unconscious movement, such as swallowing, as well as conscious movement, such as eating or talking.

Other classic symptoms of MS include sensory loss such as skin paresthesia,



MS phenotypes

cheat

sheet

The four phenotypes of MS are defined by relapses and/or disease progression:

- RRMS consists of a cycle of flares or relapses and remissions in various lengths of time from days to years. Patients may recover symptomatically, but the damage may leave behind small residual deficits.
- CIS is characterized by neurologic symptoms that point to possible MS. Caused by inflammation or demyelination, these symptoms last at least 24 hours, followed by a complete or partial recovery. Patients may or may not develop MS.
- SPMS starts with the same relapsing-remitting cycle as RRMS but later in life, patients experience a stoppage of the remitting phase and show a steady disease progression.
- PPMS is similar to SPMS but the relapses and remissions don't happen. Patients progressively get worse over time from the primary disease phase because the immune system continues to attack the myelin.

including numbness, pins-and-needles feeling, tingling, itching, and even burning. Tinnitus, hearing loss, and dizziness or vertigo may also be obstacles due to brainstem plaques. Lhermitte sign—an electric shock type sensation that moves down the spine with neck flexion—isn't specific to MS but is often reported.

Other symptoms stemming from spinal cord involvement can cause motor problems, such as painful cramping from spasticity, as well as autonomic nervous system (ANS) disorders. ANS involvement causes bowel or bladder problems, such as constipation, incontinence, urgency, nocturia, or sexual dysfunction.

Constitutional symptoms include sleep disorders, exertional exhaustion, and fatigue. Unrelenting fatigue or lassitude is the most common complaint in patients with MS, occurring about 80% of the time. Your patient may tell you it's like hitting a wall, interfering with his or her ability to perform activities of daily living. Lassitude

isn't related to activity, often occurs around the same time each day, and may be worsened by heat.

Uhthoff phenomenon is a temporary worsening of MS symptoms caused by an increase in temperature. This temperature sensitivity is caused by a rise in body temperature that slows and even blocks nerve conduction of an impulse due to the demyelinating process. Uhthoff's phenomenon can cause severe lassitude in some MS patients.

Other cognitive difficulties, such as decreased attention span; depression; anxiety; and problems with concentration, memory, and judgment, have been described by patients with MS. Bilateral facial weakness or severe pain often triggered by chewing or speaking, known as trigeminal neuralgia, is also associated with MS.

Is it MS?

MS is diagnosed by MRI with a contrast medium to detect the presence of active plaques on the brain. It will also reveal inactive lesions that may not be associated with the patient's current symptoms. There's no single lab test to definitely diagnose MS; the disease is primarily a clinical diagnosis. With cerebrospinal fluid testing, the presence of elevated protein levels and white blood cells (WBCs) may show an increase in the basic myelin protein and the presence of oligoclonal bands in most patients with MS. This finding together with clinical symptom correlation and MRI results usually forms a collective assessment in the diagnostic process.

Medications and more

One aspect of medication management for MS involves a variety of drugs that are used to reduce the frequency of relapses and slow disease progression. Injectable immunomodulators, such as interferon beta-1a and interferon beta-1b, have antiviral properties and may modify the



disease course. Fingolimod, teriflunomide, and dimethyl fumarate are oral immunomodulators with antioxidant properties that help protect brain cells and the spinal cord while hindering immune cell invasion. Synthetic proteins, such as injectable glatiramer acetate, are used to reduce the frequency of flares; however, randomized controlled trials to date haven't shown a reduction in disease progression. Antineoplastic, anti-inflammatory agents, such as mitoxantrone, may be used to help stop relapses. However, mitoxantrone is cardiotoxic and may increase the risk of leukemia.

The first monoclonal antibody approved for MS is natalizumab. This medication binds to WBCs, preventing more damage to the myelin sheath. It has shown promise, particularly with SPMS and PPMS, in decreasing the level of neurologic disability and frequency of relapses, but it isn't without serious risk. Ocrelizumab, an IV monoclonal antibody, targets B cells and is approved for the treatment of RRMS and early PPMS. Corticosteroids, such as dexamethasone, suppress the immune system by decreasing inflammation. They're given for a short period of time at the onset of or during an acute exacerbation. Despite the use of these FDA-approved medications, many patients with MS continue to experience symptoms, relapses, and disease progression.

Although controversial, evidence suggests that the use of cannabinoids in marijuana can be effective in minimizing spasticity and MS-related pain. Marijuana is a schedule I controlled substance that comes in several formulations. One formulation is from the cannabis sativa plant. These botanicals are legal in many states for medical use, including MS management. Overall, data suggest the use of cannabinoids may decrease the severity of muscle spasticity and neuropathic pain in patients with MS. Other alternative therapies are often used, such as reflexology, Reiki, massage, meditation, and acupuncture. The use of

key points

Nursing Interventions

When caring for a patient with MS, the following nursing interventions should be implemented:

- refer the patient to physical therapy to assist with mobility and balance
- implement fall prevention strategies
- assess for medication adverse reactions
- provide patient and family education, particularly for invisible symptoms like fatigue
- focus on energy conservation techniques and cooling strategies
- assess the patient's mental health and evaluate his or her level of social isolation
- connect the patient with support groups online or in your area
- discuss the benefits of journaling to track symptoms and recognize triggers.

these therapies may increase quality of life in some patients with MS.

Your role

Interdisciplinary treatment is the key to effective management given the wide variety of neurologic symptoms that can arise in MS. Working with patients to manage their symptoms is crucial. These symptoms not only affect them physically, but also psychologically, socially, and professionally.

Visible symptoms such as ataxia require a referral for physical therapy, which may assist the patient with the use of mobility aids, strengthening exercises, balance, and fall prevention. Dalfampridine has been shown to improve walking speed in patients with MS. Tremors and other movement disorders, such as spasticity and restless legs syndrome, can be the most debilitating aspects of MS. Onabotulinum toxin A injected into specific muscles has been shown to improve dystonia. Gamma-aminobutyric acid agonists, such as diazepam and baclofen, work by inhibiting the transmission of nerve cells in the brain to allow for muscle relaxation. Anticholinergic drugs are used to help spasms

by blocking the effect of acetylcholine in the brain. Antiepileptic drugs such as gabapentin can help with the chronic pain associated with dystonia. Understanding these medications and their implications in the management of MS is essential because all of them have adverse reactions; patient education is key.

Fatigue is a major factor for these patients because it affects the ability to perform daily roles, mood, and overall quality of life. It's considered an invisible symptom that's easily misinterpreted as laziness or disinterest. You can help patients with MS by educating them on energy-conservation techniques, the use of mobility aids, and cooling strategies. Lassitude can be exacerbated by excessive heat, so the use of air conditioning or cooling vests may help. Allowing for frequent rest periods is important and enables patients to conserve energy for other activities. Amantadine and modafinil are medications approved for primary MS fatigue.

It's important to understand that fatigue may cause social isolation. One metaphor used for patients with MS is called the spoon theory. Spoons are used to define a unit of energy. The energy in MS may be limited and can depend on how a patient sleeps, his or



did you know?

To get through the blood-brain barrier, the T and B cells need to have the right surface molecule. Essentially, it's like having the correct QR code on your movie ticket. You may have a ticket, but you need the right code to get into the movie you wish to see. B cells are responsible for attacking invaders outside the cells. Once a T cell gets through, it becomes activated by whatever it encounters. In MS, it's myelin that activates the T cells.

Now, imagine opening the side door of the movie theater once you're inside to let all your friends join you. When the T cells become activated, it signals the blood-brain barrier to put out more receptors, allowing more immune cells to cross. In this cell-mediated reaction, the T cells release cytokines, which causes vasodilation that leads to more immune cells getting in and damage to the oligodendrocytes. Once you open the side door of the movie theater, not only are your friends running in, so is the rest of the neighborhood.



on the web

Mayo Clinic: www.mayoclinic.org/diseases-conditions/multiple-sclerosis/symptoms-causes/syc-20350269

Medline Plus: <https://medlineplus.gov/multiplesclerosis.html>

MS International Foundation:
www.msif.org

Multiple Sclerosis Association of America:
www.mymsaa.org

Multiple Sclerosis Foundation:
<https://msfocus.org>

National Multiple Sclerosis Society:
www.nationalmssociety.org

her stress level, and pain. These patients need to worry about the effects of their actions because they start out with a limited amount of spoons each day. Ordinary, simple tasks such as showering or getting dressed utilize spoons. Theoretically, patients may use up multiple spoons within a short period of time, leaving them without the energy they need to make it through the rest of the day.

Teach patients and their families that it's okay to slow down. Both patients and family members need to understand that accomplishing every daily task may not be possible. Conserving their spoons for things they really want to do may help. Surrounding themselves with supportive people as they learn to live with the disease is also beneficial. Connect patients with support groups in your area.

Lastly, help patients with MS understand that their symptoms are unpredictable and may differ. Keeping a journal of how they feel and what their symptoms are can assist with determining triggers and recognizing flares.

Improved quality of life

Although there's no cure for MS, newer treatments may slow disease progression.

Various therapies exist that have been shown to prevent disability, giving patients living with MS a better quality of life. ■

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