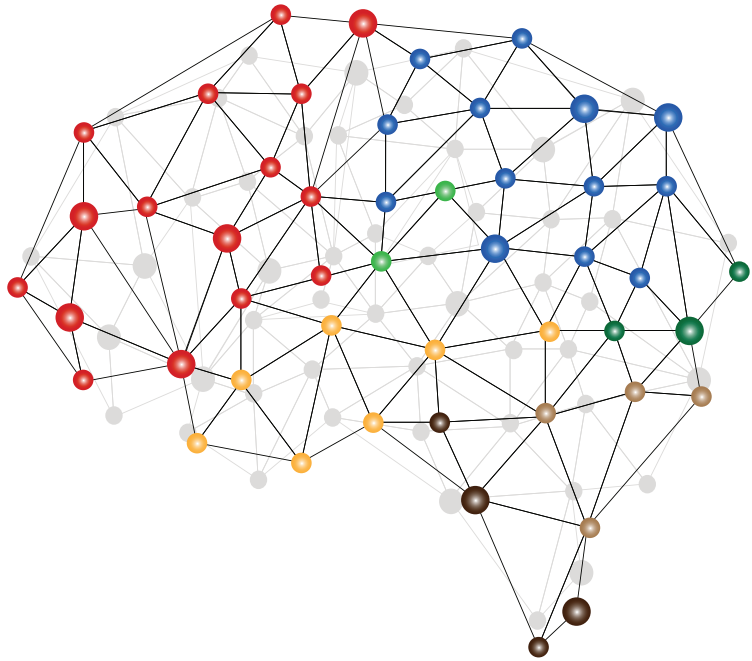
A Resource for Healthcare Professionals:

Overview of Multiple Sclerosis



Multiple Sclerosis Society of Canada

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A Resource for Healthcare Professionals: Overview of Multiple Sclerosis

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS). It is thought to be an immune-mediated disease in which the immune system recognizes self cells and tissues within the CNS and orchestrates an inflammatory response that damages and/or destroys:

- myelin – the insulating substance wrapped around the nerve fibers (axons) in the white matter of the CNS
- axons
- oligodendrocytes - the CNS myelin-making cells [1]

Damaged myelin (demyelination) forms scar tissue (sclerosis), giving the disease its name. When the myelin sheath and/or nerve fiber is damaged or destroyed, nerve impulses transmitted to and from the brain and spinal cord are distorted or interrupted, producing a variety of symptoms. Inflammation, demyelination, and degeneration occur in both the white and gray matter of the CNS beginning early in the disease course.[2–4]

Canada has one of the highest rates of MS in the world, with an estimated 1 in every 385 Canadians living with the disease.[5] While it is most often diagnosed in adults aged 20 to 49, younger children and older adults are also diagnosed with the disease. MS is three times more likely to occur in women than in men and is more common in people of northern European background.

Etiology

The etiology of MS is unknown, but decades of research indicate that MS may be the result of an abnormal immune response to some infectious or environmental trigger in a genetically susceptible individual. Each of these factors—immunologic, environmental, infectious, and genetic—is the subject of intensive ongoing research.

- Since viruses are well recognized as causes of demyelination and inflammation, it is possible that a virus or other infectious agent is the trigger in MS. More than a dozen viruses and bacteria – including measles, canine distemper, human herpes virus-6, Chlamydia pneumoniae, and Epstein-Barr – have been or are being investigated but none have been positively identified as the trigger in MS. Currently, attention is focused on the Epstein-Barr virus.[6,7]
- Other risk factors have been identified, including smoking, low levels of vitamin D [8], and adolescent obesity.[9]
- MS is not directly inherited, but genetics play an important role in a person's risk of developing MS. While the risk in the general population is 1/750, the risk rises to 1/40 in anyone who has a close relative (parent, sibling, child) with the disease. Even though identical twins share the same genetic makeup, the risk for an identical twin is only 1/4— which means that some factor(s) including genetics are involved.[10,11]

Epidemiology

- Historically, it has been observed that the risk of MS is greater farther from the equator (with reduced vitamin D exposure from the sun). However, some recent studies have not indicated the same geographic gradient, which could suggest either a change in regional risk determinants for MS or a broadening recognition of MS around the world.[12,13]
- Migration data suggest that exposure to an environmental agent or agents occurring before puberty may predispose

a person to develop MS. Studies of migration patterns have shown that people born in areas with a high risk of MS who move to an area with a lower risk before the age of 15, acquire the risk of their new area.[14]

- MS occurs in most ethnic groups but is more common in Caucasians of northern European ancestry. Some ethnic groups, such as Indigenous peoples, have few documented cases of MS. One American study reported that Black women have a higher than previously reported risk of developing MS [15] and several studies have suggested that Black people may have a more active, rapidly progressive disease course.[16,17] These variations in prevalence and disease progression suggest that geography, ethnicity, and other factors interact in some complex way [18,19] to impact a person's risk of developing MS and of disease progression.

Disease Courses

Four clinical courses (phenotypes) of MS have been identified [20].

- **Clinically isolated syndrome** (CIS) is a first episode of neurologic symptoms caused by inflammation and demyelination in the central nervous system. The episode, must last for at least 24 hours, is characteristic of multiple sclerosis, but does not yet meet the criteria for a diagnosis of MS. Not all people who experience a CIS will go on to develop MS.
- **Relapsing-remitting MS** (RRMS) is the most common disease course (approximately 85 percent at the time of diagnosis) and is characterized by clearly defined attacks of new or increasing neurologic symptoms. These attacks – also called relapses or exacerbations – are followed by periods of partial or complete recovery (remissions). During remissions, all symptoms may disappear, or some symptoms may continue and become permanent. Research suggests that disease activity continues in most patients during the remission period. At different points in time, RRMS can be further characterized as either **active** (with relapses and/or evidence of new MRI activity) or **not active**,

as well as **worsening** (a confirmed increase in disability over a specified period of time following a relapse) or **not worsening**.

- **Secondary progressive MS** (SPMS) follows an initial relapsing-remitting course. Most people who are diagnosed with RRMS will eventually transition to a secondary progressive course in which there are fewer inflammatory changes (clinical relapses and/or new inflammatory CNS activity seen on the MRI) and a progressive worsening of neurologic function (accumulation of disability) over time. SPMS can be further characterized at different points in time as either **active** (with relapses and/or evidence of new MRI activity) or **not active**, as well as **with progression** (evidence of disease worsening on an objective measure of change over time, with or without relapses) or **without progression**.
- **Primary progressive MS** (PPMS) is characterized by worsening neurologic function (accumulation of disability) from the onset of symptoms, without early relapses or remissions. PPMS can be further characterized at different points in time as either **active** (with an occasional relapse and/or evidence of new MRI activity) or **not active**, as well as **with progression** (evidence of disease worsening on an objective measure of change over time, with or without relapse or new MRI activity) or **without progression**. Approximately 15 percent of people with MS are diagnosed with PPMS, of those about 5 percent have active PPMS.

Diagnostic criteria

The long-standing criteria[21] for diagnosing MS requires:

- Evidence of damage in at least two separate areas of the CNS (dissemination in space).
- Evidence that the damage occurred at distinct time points at least one month apart (dissemination in time).

- Ruling out other possible causes. When MS is suspected, other potential causes for the symptoms a patient is experiencing must be ruled out. Many symptoms suggestive of MS are also seen in other conditions such as, lyme disease, chronic fatigue syndrome (CFS) and lupus (systemic lupus erythematosus).

At the present time, there are no symptoms, physical findings, or laboratory tests that can, by themselves, determine if a person has MS. The diagnostic process includes a thorough medical history, neurologic exam, and tests including magnetic resonance imaging (MRI), evoked potential (EP) testing, and spinal fluid analysis.

- Recent proposed revisions to the McDonald diagnostic criteria [22] allow for an earlier diagnosis in many people.
- In a patient with a typical clinically isolated syndrome (CIS) and fulfilment of clinical or MRI criteria for "dissemination in space" and no better explanation for the clinical presentation, demonstration of CSF-specific oligoclonal bands allows an MS diagnosis to be made without the previously required "dissemination in time."
- Both symptomatic and asymptomatic MRI lesions can be used for fulfilling MRI criteria for dissemination in space or dissemination in time. Previously, only asymptomatic MRI lesions could fulfill these criteria (not including MRI lesions in the optic nerve in a person presenting with optic neuritis).
- In addition to juxtacortical lesions, cortical lesions can also be used to demonstrate dissemination in space requirements.
- The requirements for the diagnosis of primary progressive MS have not changed.

The main aims of these revisions are to clarify components of the 2010 McDonald criteria in order to facilitate earlier diagnosis and reduce misdiagnosis.

Treatment strategies

Comprehensive MS care includes the treatment of acute exacerbations (also called relapses or attacks), disease management, symptom management, rehabilitation, psychosocial support, and wellness strategies.

- **Treatment of acute exacerbations**: Exacerbations (or relapses) of MS are caused by inflammation in the CNS that damages the myelin and slows or blocks transmission of nerve impulses. Most relapses last from a few days to several weeks or even months. Relapses can be mild or severe enough to interfere with a person's ability to function at home and at work. Symptoms associated with a MS exacerbation are variable, and can include a change in energy level, sensation, motor function, cognitive function, and/or mood. Exacerbations that interfere with function are typically treated with intravenous, high dose corticosteroids to reduce the inflammation and accelerate recovery. Comparably high doses of oral steroids may be used instead of IV steroids.[23] Steroids may decrease acute inflammation in the CNS but have no long-term benefits.
- **Symptom management**: A wide variety of medications help ease MS-related symptoms such as fatigue, mobility impairment, spasticity, and pain, among others.
- **Disease-modifying therapies (DMTs)**: At the present time, there are more than a dozen disease-modifying therapies that have been approved by Health Canada to treat relapsing forms of MS (including RRMS, active SPMS, and early PPMS). These medications have different mechanisms of action and modes of delivery (injectable, oral, infusion).

When should MS be treated:

Initiation of treatment with a Health Canada approved disease-modifying therapy is recommended:

- As soon as possible following a diagnosis of relapsing or early primary progressive multiple sclerosis.
- For individuals with a first clinical event and MRI features consistent with MS in whom other possible causes have been excluded.
- For individuals with progressive MS who continue to demonstrate clinical relapses and/or demonstrate inflammatory activity.
- Treatment with a given disease-modifying medication should be continued indefinitely unless any of the following occur (in which case an alternative disease-modifying therapy should be considered):
  - > Sub-optimal treatment response as determined by the individual and his or her treating clinician
  - > Intolerable side effects
  - > Inadequate adherence to the treatment regimen
  - > Availability of a more appropriate treatment option
- Movement from one disease-modifying therapy to another should occur only for medically appropriate reasons as determined by the treating clinician and patient.
- When evidence of additional clinical or MRI activity while on treatment suggests a sub-optimal response, an alternative regimen (e.g., different mechanism of action) should be considered to optimize therapeutic benefit.
- The factors affecting choice of therapy at any point in the disease course are complex and most appropriately analyzed and addressed collaboratively by the individual and his or her treating clinician.

Early, adequate control of disease activity – including the reduction of clinical and sub-clinical attacks and the delay of the progressive phase of the disease—appears to play a key role in preventing accumulation of disability, prolonging the ability of people with MS to remain active, and enhancing quality of life.[24] In considering disease activity and progression in MS, it is important to remember that cognitive as well as physical impairments are common in all types of MS[25] and throughout the disease course, beginning prior to initial clinical symptoms.[26,27]

MS Symptoms and Management:

The inflammation, demyelination, and neurodegeneration that comprise the MS disease process result in a number of possible symptoms that vary from one individual to another and over time for any given individual. Primary symptoms, which are the direct result of damage to the myelin and nerve fibers in the CNS, include the following:

- **Fatigue**: One of the most common symptoms, occurring in about 80% of people.[28] People living with MS can experience fatigue from many sources such as sleep disturbance, overactivity, or metabolic disorders. A type of fatigue that is unique to MS – often described as lassitude – is characterized by abrupt exhaustion occurring at a similar time each day. It is unrelated to sleep, activity, or MS disease course and is worsened by heat. MS fatigue interferes with usual daily activities.
- **Vision problems**: A common first symptom of MS. Symptoms may include optic neuritis, typically unilateral, which causes temporary blurring or loss of vision, often accompanied by pain on eye movement. It may also cause a "blind spot" (scotoma) in the center of vision. Other common visual symptoms include diplopia (double vision) and nystagmus, a rhythmic jerkiness or bounce in one or both eyes.
- **Mobility problems**: Impaired walking, gait disturbance, lack of balance or coordination.

- **Spasticity**: Feelings of stiffness and a wide range of involuntary muscle spasms. Spasticity can range from relatively mild to quite severe, and treatment is approached in a step-wise fashion. Note: Some degree of spasticity may be required to support weakened limbs. [29]
- **Bladder dysfunction**: Occurs in at least 80% of people with MS. Most commonly a neurogenic overactive bladder characterized by urgency, frequency and possibly incontinence. Less frequent may be difficulty emptying the bladder, characterized by urgency, frequency, double voiding, and infection.
- **Bowel dysfunction**: Constipation and less frequent, involuntary loss of bowel control.
- **Sensory problems/pain**: Including numbness, tingling, and neuropathic pain in the face, body, or extremities.
- **Cognitive dysfunction**: Approximately 65% of people with MS will develop problems with high-level functions including processing speed, new learning, memory, and executive functions. [30]
- **Depression**: More than 50% of people with MS will experience a major depressive episode which is more common in MS than in the general population or those with other equally disabling chronic illnesses. [31]
- **Sexual dysfunction**: May include impaired arousal, sensory changes, reduced vaginal lubrication, or erectile dysfunction. [32]
- **Dizziness and Vertigo**: A sensation that the individual or his/her surroundings are in motion and may be accompanied by nausea. [33]
- **Dysarthria**: A speech disorder caused by muscle weakness and characterized by slow, slurred, or low volume speech.
- **Tremor**: Uncontrollable shaking of the limbs, trunk, voice, eyes, or head with movement and/or against gravity. [34]

Secondary symptoms are the complications that can arise as a result of the primary symptoms. Secondary symptoms such as infection from bladder symptoms, pressure sores caused by immobility, or decreased bone density due to inactivity, can be addressed and treated, but the goal is to prevent them from happening in the first place.

MS and Other Health Conditions

Having MS doesn't stop people from developing other conditions, and vice versa. Recent research suggests that the five most common conditions that exist alongside MS are depression, anxiety, high blood pressure, high cholesterol, and chronic lung disease. Regular health checks such as pap tests, mammograms, testicular exams, vitamin D levels, and appropriate vaccinations should be considered as needed. Please see the MS Society of Canada website for information related to immunization and vitamin D recommendations.

Role of Primary Care Physicians

Generally, the role of a primary care physician is to monitor the overall health and wellness of the person with MS and his or her family members. In addition to screening for common comorbidities— which can easily be overshadowed by the symptoms of MS — the primary care physician also helps to coordinate care provided by all specialists. Additionally, primary care physicians might be responsible for filling out disability assistance forms such as provincial and territorial income support and drug coverage programs. For information related to government forms or other information about MS, please contact an MS Navigator through the MS Society's Knowledge Network. MS Navigators are available to all Canadians affected by MS and healthcare professionals. Connect with an MS Navigator by calling 1-844-859-6789 or send an email to: msnavigators@mssociety.ca.

Rehabilitation

Although there are disease-modifying therapies available to help slow the progression of multiple sclerosis, most people with MS will continue to have limitations. Rehabilitation in MS involves the intermittent or ongoing use of multidisciplinary strategies to promote functional independence, prevent complications, and enhance overall quality of life. It is an active process directed toward helping the person recover and/or maintain the highest possible level of functioning and realize his or her optimal physical, mental, and social potential given any limitations that exist.

Rehabilitation specialists (including physiatrists, physical therapists, occupational therapists, and speech/language pathologists) target the following impairments in their work with individuals with MS: fatigue, weakness, spasticity, cognitive impairments, mobility, imbalance, sensory loss, ataxia/tremor, pain, paraparesis, speech and swallowing problems, visual disturbances, and bowel and bladder problems.

Although rehabilitation interventions cannot reverse the neurologic damage caused by MS, they can reduce disablement by:

- Minimizing the impact of existing impairment(s) on day-to-day functioning.
- Enhancing the person's ability to carry out daily activities and participate to the fullest extent possible, in all of his or her life roles.

Initiating rehabilitation early in the disease course is essential for education, fatigue management, exercise recommendations, and prevention of unnecessary complications.

Psychosocial support: Psychosocial support is a major category of treatment in MS, encompassing:

- Disease-related education (psychoeducation)– a supportive educational process designed to enhance people's understanding of the disease, adaptive coping strategies, and available resources.

- Diagnosis/treatment of emotional and/or cognitive problems.
- Family interventions designed to support family members' efforts to cope with the effects of MS in the household.
- Support for people's efforts to remain productively employed as long as they are able and interested, and to transition out of the workforce when, and if, it is necessary to do so.
- Helping individuals with MS and their families to access available resources.

Health and wellness: In addition, wellness – and the strategies needed to achieve it – is a high priority for people living with MS. Wellness encompasses many dimensions: physical well-being (diet, exercise and healthy behaviors); emotional well-being; spiritual well-being; cognitive health; participation in work, home and leisure activities; and healthy relationships.

Living a healthy lifestyle is one of the most important ways people living with MS can start taking charge of their disease. There are important strategies that may help improve quality of life, including exercise and a healthy diet, in addition to physiotherapy, rehabilitation, massage, getting enough sleep, stress reduction techniques, planning an appropriate work—life schedule, and other wellness approaches. These non-medicinal strategies play a key role in managing all types of MS. Overall, balance in the many aspects of one's life is key to managing MS.

Summary

MS is a complex disease that impacts each individual and family in varied and unpredictable ways. People affected by MS benefit from ongoing partnerships with caring, knowledgeable healthcare professionals in a wide range of disciplines to enhance health and wellbeing, mobility, safety, independence, participation in meaningful activities, and quality of life.

How the MS Society of Canada can help a patient living with MS

The MS Society offers a variety of programs and services to help people affected by multiple sclerosis effectively manage and cope with the disease. Programs and services listed in this resource may vary from province-to-province.

- Information and referral
- Support and self-help groups
- Recreation, social and wellness programs
- Conferences, and education programs
- Quality of Life Grants
- Government relations and advocacy

MS Knowledge Network

The MS Knowledge Network is the MS Society of Canada's hub of knowledge, lead by a team of MS navigators, who provide trusted, consistent, quality MS information and support. MS Navigators are available to assist anyone in Canada, from 8am to 8pm ET, Monday to Friday.

Phone: 1-844-859-6789
Email: msnavigators@mssociety.ca
Live Web Chat is available by visiting www.mssociety.ca

Additional resources

- Multiple Sclerosis and How We Can Help
- Newly Diagnosed with Multiple Sclerosis
- My MS Healthcare Team Discussion Guide
- MS: Its effects on you and those you love
- Women's Health and MS

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