

Multiple Sclerosis

Course Goals & Objectives

Course Description

Multiple Sclerosis is an asynchronous online continuing education program for physical therapists and physical therapist assistants. The course presents contemporary information about multiple sclerosis including sections on epidemiology, etiology, symptomology, diagnosis, and treatment.

Course Rationale

The purpose of this course is to present current information about Multiple Sclerosis to physical therapists and physical therapist assistants. Physical therapists and physical therapist assistants will find this information pertinent and useful when developing and implementing rehabilitation programs that address the challenges and needs specific to individuals with MS.

Course Goals & Objectives

At the end of this course, the participants will be able to:

1. identify the possible etiological factors that cause multiple sclerosis
2. recognize the epidemiology and risk factors of multiple sclerosis
3. identify the clinical signs of multiple sclerosis
4. differentiate the pharmacological treatment options available to treat multiple sclerosis
5. define the systemic effects of multiple sclerosis
6. identify adaptive/assistive equipment that can individuals with MS
7. define the parameters of safe and effective exercise for individuals with MS
8. define disability determination for individuals with MS
9. identify challenges faced by the caregivers

Course Provider – Innovative Educational Services

Course Instructor - Michael Niss, DPT

Target Audience – physical therapists and physical therapist assistants.

Course Educational Level – Introductory / intermediate

Course Prerequisites – None

Method of Instruction/Availability – Online text-based course available continuously.

Criteria for Issuance of CE Credits - A score of 70% or greater on the course post-test

Continuing Education Credits – 4 hours

Fees - \$39.95

Conflict of Interest – No conflict of interest exists for the presenter or provider of this course.

Refund Policy - Unrestricted 100% refund upon request. The request for a refund by the learner shall be honored in full without penalty or other consideration of any kind. The request for a refund may be made by the learner at any time without limitations before, during, or after course participation.

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Course Outline

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Overview

Multiple Sclerosis (MS) is an immune-mediated demyelinating and axonal degenerative disease of the central nervous system (the brain, spinal cord, and optic nerves). It is the most common disabling neurological disease of young adults.

The course of MS is unpredictable. A small number of those with MS will have a mild course with little to no disability, while another smaller group will have a steadily worsening disease that leads to increased disability over time. Most people with MS, however, will have short periods of symptoms followed by long stretches of relative relief, with partial or full recovery. There is no way to predict, at the beginning, how an individual person's disease will progress.

While MS sometimes causes severe disability, it is only rarely fatal and most people with MS have a normal life expectancy.

The term multiple sclerosis refers to the distinctive areas of scar tissue (sclerosis or plaques) that are visible in the white matter of people who have MS. Plaques can be as small as a pinhead or as large as the size of a golf ball. Plaques are the result of an inflammatory process in the brain that causes immune system cells to attack myelin. The myelin sheath helps to speed nerve impulses traveling within the nervous system. Axons are also damaged in MS, although not as extensively, or as early in the disease, as myelin.

Under normal circumstances, cells of the immune system travel in and out of the brain patrolling for infectious agents (viruses, for example) or unhealthy cells. This is called the "surveillance" function of the immune system. Surveillance cells usually won't spring into action unless they recognize an infectious agent or unhealthy cells. When they do, they produce substances to stop the infectious agent. If they encounter unhealthy cells, they either kill them directly or clean out the dying area and produce substances that promote healing and repair among the cells that are left.

Immune cells behave differently in the brains of people with MS. They become active and attack what appears to be healthy myelin. It is unclear what triggers this attack. MS is one of many autoimmune disorders, such as rheumatoid arthritis and lupus, in which the immune system mistakenly attacks a person's healthy tissue as opposed to performing its normal role of attacking foreign invaders like viruses and bacteria. Whatever the reason, during these periods of immune system activity, most of the myelin within the affected area is damaged or destroyed. The axons also may be damaged. The symptoms of MS depend on the severity of the immune reaction as well as the location and extent of the plaques, which primarily appear in the brain stem, cerebellum, spinal cord, optic nerves, and the white matter of the brain around the brain ventricles.

Epidemiology

Multiple Sclerosis is the most common progressive neurologic disorder of young adults (the median age of onset is 30 years), affecting 350,000 to 400,000 people in the United States and 2.5 million people around the world. Studies of the prevalence (the proportion of individuals in a population having a particular disease) of MS indicate that the rate of the disease increased steadily during the twentieth century.

As with most autoimmune disorders, twice as many women are affected by MS as men. MS is more common in colder climates. People of Northern European descent appear to be at the highest risk for the disease, regardless of where they live. Native Americans of North and South America, as well as Asian American populations, have relatively low rates of MS.

Etiology

The ultimate cause of MS is damage to myelin, nerve fibers, and neurons in the brain and spinal cord. But how that happens, and why, are questions that challenge researchers. Evidence appears to show that MS is a disease caused by genetic vulnerabilities combined with environmental factors.

Although there is little doubt that the immune system contributes to the brain and spinal cord tissue destruction of MS, the exact target of the immune system attacks and which immune system cells cause the destruction isn't fully understood.

Researchers have several possible explanations for what might be going on. The immune system could be:

- fighting some kind of infectious agent (for example, a virus) that has components which mimic components of the brain (molecular mimicry)
- destroying brain cells because they are unhealthy
- mistakenly identifying normal brain cells as foreign.

The last possibility has been the favored explanation for many years. Research now suggests that the first two activities might also play a role in the development of MS. There is a special barrier, called the blood-brain barrier, which separates the brain and spinal cord from the immune system. If there is a break in the barrier, it exposes the brain to the immune system for the first time. When this happens, the immune system may misinterpret the brain as “foreign.”

Genetic Susceptibility

Susceptibility to MS may be inherited. Studies of families indicate that relatives of an individual with MS have an increased risk for developing the disease. Experts estimate that about 15 percent of individuals with MS have one or more family members or

relatives who also have MS. But even identical twins, whose DNA is exactly the same, have only a 1 in 3 chance of both having the disease. This suggests that MS is not entirely controlled by genes. Other factors must come into play.

Current research suggests that dozens of genes and possibly hundreds of variations in the genetic code (called gene variants) combine to create vulnerability to MS. Some of these genes have been identified. Most of the genes identified so far are associated with functions of the immune system. Additionally, many of the known genes are similar to those that have been identified in people with other autoimmune diseases as type 1 diabetes, rheumatoid arthritis or lupus. Researchers continue to look for additional genes and to study how they interact with each other to make an individual vulnerable to developing MS.

Sunlight and Vitamin D

A number of studies have suggested that people who spend more time in the sun and those with relatively high levels of vitamin D are less likely to develop MS. Bright sunlight helps human skin produce vitamin D. Researchers believe that vitamin D may help regulate the immune system in ways that reduce the risk of MS. People from regions near the equator, where there is a great deal of bright sunlight, generally have a much lower risk of MS than people from temperate areas such as the United States and Canada. Other studies suggest that people with higher levels of vitamin D generally have less severe MS and fewer relapses.

Smoking

A number of studies have found that people who smoke are more likely to develop MS. People who smoke also tend to have more brain lesions and brain shrinkage than non-smokers. The reasons for this are currently unclear.

Infectious Factors and Viruses

A number of viruses have been found in people with MS, but the virus most consistently linked to the development of MS is Epstein Barr virus (EBV), the virus that causes mononucleosis. Only about 5 percent of the population has not been infected by EBV. These individuals are at a lower risk for developing MS than those who have been infected. People who were infected with EBV in adolescence or adulthood and who therefore develop an exaggerated immune response to EBV are at a significantly higher risk for developing MS than those who were infected in early childhood. This suggests that it may be the type of immune response to EBV that predisposes to MS, rather than EBV infection itself. However, there is still no proof that EBV causes MS.

Autoimmune and Inflammatory processes

Tissue inflammation and antibodies in the blood that fight normal components of the

body and tissue in people with MS are similar to those found in other autoimmune diseases. Along with overlapping evidence from genetic studies, these findings suggest that MS results from some kind of disturbed regulation of the immune system.

Symptomology

Common MS symptoms include fatigue, cognitive impairment, mood disorders, visual difficulties, motor and sensory deficits, incoordination, gait dysfunction, speech and swallowing deficits and impairments of bowel and bladder control as well as sexual functioning.

The symptoms of MS usually begin over one to several days, but in some forms, they may develop more slowly. They may be mild or severe and may go away quickly or last for months. Sometimes the initial symptoms of MS are overlooked because they disappear in a day or so and normal function returns. Because symptoms come and go in the majority of people with MS, the presence of symptoms is called an exacerbation. Recovery from symptoms is referred to as remission, while a return of symptoms is called a relapse. This form of MS is therefore called relapsing-remitting MS, in contrast to a more slowly developing form called primary progressive MS. Progressive MS can also be a second stage of the illness that follows years of relapsing-remitting symptoms.

The first symptoms of MS often include:

- vision problems such as blurred or double vision or optic neuritis, which causes pain in the eye and a rapid loss of vision.
- weak, stiff muscles, often with painful muscle spasms
- tingling or numbness in the arms, legs, trunk of the body, or face
- clumsiness, particularly difficulty staying balanced when walking
- bladder control problems, either inability to control the bladder or urgency
- dizziness that doesn't go away

MS may also cause later symptoms such as:

- mental or physical fatigue which accompanies the above symptoms during an attack
- mood changes such as depression or euphoria
- changes in the ability to concentrate or to multitask effectively
- difficulty making decisions, planning, or prioritizing at work or in private life.

Most individuals with MS have muscle weakness, often in their hands and legs. Muscle stiffness and spasms can also be a problem. These symptoms may be severe enough to affect walking or standing. In some cases, MS leads to partial or complete paralysis. Many people with MS find that weakness and fatigue are worse when they have a fever or when they are exposed to heat. MS exacerbations may occur following common infections.

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Tingling and burning sensations are common, as well as the opposite, numbness and loss of sensation. Moving the neck from side to side or flexing it back and forth may cause "Lhermitte's sign," a characteristic sensation of MS that feels like a sharp spike of electricity coursing down the spine.

While it is rare for pain to be the first sign of MS, pain often occurs with optic neuritis and trigeminal neuralgia, a neurological disorder that affects one of the nerves that runs across the jaw, cheek, and face. Painful spasms of the limbs and sharp pain shooting down the legs or around the abdomen can also be symptoms of MS.

Most individuals with MS experience difficulties with coordination and balance at some time during the course of the disease. Some may have a continuous trembling of the head, limbs, and body, especially during movement, although such trembling is more common with other disorders such as Parkinson's disease.

Fatigue is common, especially during exacerbations of MS. A person with MS may be tired all the time or may be easily fatigued from mental or physical exertion.

Urinary symptoms, including loss of bladder control and sudden attacks of urgency, are common as MS progresses. People with MS sometimes also develop constipation or sexual problems.

Depression is a common feature of MS. A small number of individuals with MS may develop more severe psychiatric disorders such as bipolar disorder and paranoia, or experience inappropriate episodes of high spirits, known as euphoria.

People with MS, especially those who have had the disease for a long time, can experience difficulty with thinking, learning, memory, and judgment. The first signs of what doctors call cognitive dysfunction may be subtle. The person may have problems finding the right word to say, or trouble remembering how to do routine tasks on the job or at home. Day-to-day decisions that once came easily may now be made more slowly and show poor judgment. Changes may be so small or happen so slowly that it takes a family member or friend to point them out.

Diagnosis

There is no single test used to diagnose MS. Doctors use a number of tests to rule out or confirm the diagnosis. A diagnosis of MS is often delayed because MS shares symptoms with other neurological conditions and diseases.

McDonald Criteria

The best and most current set of criteria for diagnosing MS is the McDonald Criteria. The McDonald Criteria were developed in April 2001 by an international panel in association with the National MS Society of America, modified in 2005, and revised in 2010.

The primary goal of the McDonald Criteria is to enable the diagnosis of MS sooner and to permit earlier treatment of MS. There have to be 2 attacks in time and at 2 locations. You can get the locations in time either by clinical attacks or by MRI changes over time. You can get the 2 locations in the nervous system either by clinical attacks or by MRI criteria.

The requirement for at least 2 attacks in time is needed to assure that the condition is not due to a one-time event such as a viral infection. This requirement can be met by having 2 clinical attacks (for example, two different episodes of optic neuritis). If there is only one clinical attack, then changes on serial MRIs can be used to document the second event. MRI changes could be a new T2/FLAIR lesion or a newly enhancing lesion. A new enhancing lesion must be ≥ 3 months after the onset of the initial clinical event and at a site different from the initial event. A new T2/FLAIR lesion must be ≥ 30 days after the event.

The requirement for lesions in at least 2 locations within the central nervous system assures that single-site pathologies are not misdiagnosed (for example, recurrent spinal cord events due to a disc). This requirement can be met by having 2 clinical locations (for example, optic neuritis and transverse myelitis). If there are not two clinical locations, then changes on the MRI can be used instead.

Finally, the criteria require that no better explanation be present. This is often the most difficult portion of the criteria. It assures that patients are not misdiagnosed due to other diseases (for example, a patient with ocular migraine and cervical myelopathy due to disc disease).

The diagnosis of MS is based on the history and neurological examination. To make a definitive diagnosis of MS, one must demonstrate neurological episodes separated in space and time.

Supporting paraclinical evidence may include cerebrospinal fluid oligoclonal bands, visual-evoked potential studies, magnetic resonance imaging (MRI), and laboratory data to rule out diseases that mimic MS or are autoimmune in nature. Major conditions on the differential diagnosis include age-related white matter changes, central nervous system bacterial or viral infections, cervical spondylosis or stenosis, neoplasms, migraine, sarcoidosis, stroke, collagen vascular disease, vasculitis, and vitamin B12 deficiency.

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Laboratory studies need to be tailored to the patient and may include: complete blood count; chemistry panel; liver enzymes; thyroid-stimulating hormone (TSH), prothrombin time (PT) and partial thromboplastin time (PTT); serum B12 level; sedimentation rate; C-reactive protein; rheumatoid factor; anti-nuclear antibodies; Sjogren's antibodies; antiphospholipid antibodies; serum Venereal Disease Research Laboratory (VDRL) test; angiotensin converting enzyme; Human T-lymphocyte Virus I and II (HTLV I/II); Human Immunodeficiency Virus (HIV); and Lyme disease serology.

Doctors may also order evoked potential tests, which use electrodes on the skin and painless electric signals to measure how quickly and accurately the nervous system responds to stimulation. In addition, they may request a lumbar puncture to obtain a sample of cerebrospinal fluid. This allows them to look for proteins and inflammatory cells associated with the disease and to rule out other diseases that may look similar to MS, including some infections and other illnesses. MS is confirmed when positive signs of the disease are found in different parts of the nervous system at more than one-time interval and there is no alternative diagnosis.

Clinical Course

MS typically presents with intermittent neurological relapses and remissions. A relapse or exacerbation is a sudden worsening of MS symptoms, or the appearance of new symptoms that lasts for at least 24 hours. MS relapses are thought to be associated with the development of new areas of damage in the brain.

An attack may be mild or its symptoms may be severe enough to significantly interfere with life's daily activities. Most exacerbations last from several days to several weeks, although some have been known to last for months.

When the symptoms of the attack subside, an individual with MS is said to be in remission. However, MRI data have shown that this is somewhat misleading because MS lesions continue to appear during these remission periods. Patients do not experience symptoms during remission because the inflammation may not be severe or it may occur in areas of the brain that do not produce obvious symptoms. Research suggests that only about 1 out of every 10 MS lesions is perceived by a person with MS.

Most patients with MS develop permanent neurological deficits and enter a progressive phase of the disease after the initial relapsing phase. There are four major subtypes of MS:

1. **Relapsing-remitting MS (RR MS).** This is the most common subtype of MS (85 percent at onset) and is characterized by clearly defined relapses. Relapses are followed by periods of partial or complete recovery (remissions) that are free of disease related progression.

2. **Secondary Progressive MS (SP MS).** Patients with this subtype start with RR MS and then begin progressing with or without occasional relapses.
3. **Progressive Relapsing MS (PR MS).** Patients with this subtype have a slow progression of disability from onset with periods of stability and occasional relapses (about 5 percent of patients from onset).
4. **Primary Progressive MS (PP MS).** Patients with this subtype have progressive worsening in disability from onset without exacerbations. There may be changes in the rate of progression or periods of stability during the course of disease (about 10 percent of patients from onset).

The course of MS is different for each individual, which makes it difficult to predict. For most people, it starts with a first attack, usually (but not always) followed by a full to almost-full recovery. Weeks, months, or even years may pass before another attack occurs, followed again by a period of relief from symptoms. This characteristic pattern is called relapsing-remitting MS.

Primary-progressive MS is characterized by a gradual physical decline with no noticeable remissions, although there may be temporary or minor relief from symptoms. This type of MS has a later onset, usually after age 40, and is just as common in men as in women.

Secondary-progressive MS begins with a relapsing-remitting course, followed by a later primary-progressive course. The majority of individuals with severe relapsing-remitting MS will develop secondary progressive MS if they are untreated.

Finally, there are some rare and unusual variants of MS. One of these is Marburg variant MS (also called malignant MS), which causes a swift and relentless decline resulting in significant disability or even death shortly after disease onset. Balo's concentric sclerosis, which causes concentric rings of demyelination that can be seen on an MRI, is another variant type of MS that can progress rapidly.

Determining the particular type of MS is important because the current disease modifying drugs have been proven beneficial only for the relapsing-remitting types of MS.

Prognosis

Multiple sclerosis is characterized by considerable interpatient variability in prognosis. Less than 5% of patients have very severe disability within the first 5 years after onset and 10–20% of patients remain unimpaired without therapy over 20 years. Although the disorder is chronic and incurable, life expectancy can be normal or nearly so.

Factors associated with a better prognosis:

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- female gender
- age of disease onset earlier than 40 years
- a first attack consisting of optic neuritis or other sensory symptoms
- lack of significant disability 5 years after onset
- minor abnormalities on brain MRI scan at the time of diagnosis.

Factors associated with a less favorable prognosis:

- male gender
- age of onset at age 40 or later
- a first attack consisting only of motor symptoms
- difficulty walking or sustained impairment in coordination after resolution of first attack
- large number of MRI lesions

Pharmacological Treatment

Initial Attack

The usual treatment for an initial MS attack is to inject high doses of a steroid drug, such as methylprednisolone, intravenously over the course of 3 to 5 days. It may sometimes be followed by a tapered dose of oral steroids. Intravenous steroids quickly and potently suppress the immune system, and reduce inflammation. Clinical trials have shown that these drugs hasten recovery.

There is debate among doctors about whether to start disease modulating drugs at the first signs of MS or to wait until the course of the disease is better defined before beginning treatment. On one hand, U.S. Food and Drug Administration (FDA)-approved medications to treat MS work best early in the course of the disease and work poorly, if at all, later in the progressive phase of the illness. Clinical trials have shown convincingly that delaying treatment, even for the 1 to-2 years that it may take for patients with MS to develop a second clinical attack, may lead to an irreversible increase in disability. In addition, people who begin treatment after their first attack have fewer brain lesions and fewer relapses over time.

On the other hand, initiating treatment in patients with a single attack and no signs of previous MS lesions, before MS is diagnosed, poses risks because all FDA-approved medications to treat MS are associated with some side effects. Therefore, the best strategy is to have a thorough diagnostic work-up at the time of first attack of MS. The work-up should exclude all other diseases that can mimic MS so that the diagnosis can be determined with a high probability. The diagnostic tests may include an evaluation of the cerebrospinal fluid and repeated MRI examinations. If such a thorough work-up cannot confirm the diagnosis of MS with certainty, it may be prudent to wait before starting treatment. However, each patient should have a scheduled follow-up evaluation by his or her neurologist 6 to 12 months after the initial diagnostic evaluation, even in

the absence of any new attacks of the disease. Ideally, this evaluation should include an MRI examination to see if any new MS lesions have developed without causing symptoms.

Until recently, it appeared that a minority of people with MS had very mild disease or “benign MS” and would never get worse or become disabled. This group makes up 10 to 20 percent of those with MS. Doctors were concerned about exposing such benign MS patients to the side effects of MS drugs. However, recent data from the long-term follow-up of these patients indicate that after 10 to 20 years, some of these patients become disabled. Therefore, current evidence supports discussing the start of therapy early with all people who have MS, as long as the MS diagnosis has been thoroughly investigated and confirmed. There is an additional small group of individuals (approximately 1 percent) whose course will progress so rapidly that they will require aggressive and perhaps even experimental treatment.

Disease-Modifying Therapy (DMT)

Most patients with MS are treated with a disease-modifying therapy. Fortunately, there are several medications that slow the course of MS. These medications have all been proven to benefit MS patients in well-designed large studies. Based on the results of these studies, the National Multiple Sclerosis Society states: “Initiation of therapy is advised as soon as possible following a definite diagnosis of MS and determination of a relapsing course.” Patients must decide for themselves, with the help of their doctor, whether they wish to use one of these medications.

Reasons patients choose to use DMTs:

- These are the only medications proven to slow the disease. After 20 years, 15-20% of untreated patients are in wheelchairs and another 50% need aids to walk. Use of these medications should improve these odds and lessen the disability that develops over time.
- Some patients believe they do not have enough attacks to warrant use of DMT’s. However, patients are not aware of most MS attacks. A very conservative estimate is that patients have ten silent attacks for every attack they are aware of. These “silent” attacks can eventually affect memory, cognition, and other important areas.
- We now know that one of the effects of MS can be in thinking or memory loss. This can be a serious symptom and decreasing this loss should be a high priority.
- Some patients wait to see if they will become more disabled before using DMT’s. However, these drugs do not reverse damage; they decrease future damage. Our advice is to start DMT’s before more damage occurs.
- There is some evidence that patients using DMT’s early in the disease leads to a better response than those treated later in the disease. There

are even studies indicating benefit in patients using these drugs after their first attack, before the diagnosis of MS can technically be made (the diagnosis of MS requires at least two attacks). This first attack is called Clinically Isolated Syndrome (CIS), and several of the medications are FDA approved for use in CIS.

- Although there are side effects, none of the side effects are medically serious.

Reasons patients hesitate or wait to use DMT medications:

- On average, DMTs decrease disease activity by about 1/3. Each patient must balance the 1/3 slowing of the disease with the inconvenience of using these treatments.
- Though the majority of patients develop some impairment with time, about 15% have very little or no disability even after 20 years. Some patients do not use these medications, hoping they will be one of the fortunate ones. However, there is no way to predict which patients will remain without disability.
- The medications are expensive. They are generally covered by insurance, but some insurance plans have high medication co-payments. Also, insurance plans may refuse to cover the cost for some types of MS (such as primary progressive).
- Some of these medications are given by injection. The needles are small and usually cause little pain. The greatest barrier to using them is the inconvenience of injections rather than the pain.

Choosing a Disease Modifying Therapy (DMT)

There are presently five injectable disease modifying therapies (DMTs), two infusion therapies, and one oral therapy that are FDA approved for the treatment of relapsing MS.

The injectables include four forms of human recombinant interferon-beta (Avonex®, Betaseron®, Extavia® and Rebif®) and a polypeptide, glatiramer acetate (Copaxone®).

Two forms of infusion therapies include natalizumab (Tysabri®) and a chemotherapy drug, mitoxantrone (Novantrone®) which is also registered to treat relapsing and secondary progressive MS. In general, Tysabri® and Novantrone® are second line therapies for most patients because of their potential for serious side effects.

The first oral medication is called fingolimod (Gilenya®).

All DMTs have been shown to decrease MS disease activity in comparison with placebo. There are no well-designed, long term (≥ 2 years) randomized, double-blind

comparison trials to help decide which, if any, of these drugs is the "best" treatment. There also is no consensus among MS experts about which agent is the "best," although many physicians who treat MS patients preferentially use one or two of the medications.

- **Glatiramer acetate (Copaxone®)** is given at a dose of 20 mg once a day. It is not an interferon and does not have the "flu-like" side-effects that occur with the interferons. The most common side-effects are injection site reactions. These consist of erythema and induration. Some patients will develop lipoatrophy at injection sites. About 15% of patients will have an idiosyncratic immediate post-injection reaction characterized by flushing, chest pain, shortness of breath and anxiety. These spells generally occur only once but occasionally will occur more than once. They are self-limited and do not require specific treatment. No laboratory abnormalities occur with glatiramer acetate so laboratory monitoring is not necessary.
- **Interferon beta-1b (Betaseron®, Extavia®)** is given at a dose of 250 µg every other day. The most common side-effects are "flu-like" symptoms (fever, muscle aches, malaise) that typically last about 24 hours after the injection. These symptoms usually can be controlled with pre- and post-injection treatment with acetaminophen (1000 mg 4-6 hours) and/or naproxen (220-440mg bid). Patients typically stop having these side-effects after they have been on the medication for several weeks to months. Injection site reactions are common. These usually consist of mild erythema. Skin necrosis at some injection sites rarely occurs. Leukopenia and elevations in liver function tests occur in some patients. Patients should undergo a CBC with differential and liver function tests before starting therapy, within one to two months afterwards and then, periodically as needed. After the first year of therapy laboratory testing should be repeated every 6 months. Betaseron® and Extavia® may occasionally increase depression. Women planning to become pregnant should not be taking Betaseron® or Extavia® as it can increase the risk of spontaneous abortions. There are no known drug interactions.
- **Interferon beta-1a (Rebif®)** is given at a dose of 44 µg three times a week on alternate days (e.g. Monday, Wednesday, Friday). The most common side-effects are "flu-like" symptoms (fever, muscle aches, malaise) that typically last about 24 hours after the injection. These symptoms usually can be controlled with pre- and post-injection treatment with acetaminophen (1000 mg 4-6 hours) and/or naproxen (220-440mg bid). Patients typically stop having these side-effects after they have been on the medication for several weeks to months. Injection site reactions are also common. These usually consist of mild erythema. Skin necrosis at some injection sites rarely occurs. Leukopenia and elevations in liver function tests occur in some patients. Patients should undergo a CBC with differential and liver function tests before starting therapy, within one to two months afterwards and then, periodically as needed. After the first year of therapy laboratory testing should be repeated every 6 months. Rebif® may

occasionally increase depression. Women planning to become pregnant should not be taking Rebif® as it can increase the risk of spontaneous abortions. There are no known drug interactions.

- **Interferon beta-1a (Avonex®)** is given at a dose of 30 µg once a week. The most common side-effects are "flu-like" symptoms (fever, muscle aches, malaise) that typically last about 24 hours after the injection. These symptoms usually can be controlled with pre- and post-injection treatment with acetaminophen (1000 mg 4-6 hours) and/or naproxen (220-440mg bid). Patients typically stop having these side-effects after they have been on the medication for several weeks to months. Mild leukopenia and mild elevations in liver function tests occur in some patients. Patients should undergo a CBC with differential and liver function tests before starting therapy, one month afterwards and then every three months for the first year. After the first year of therapy laboratory testing should be repeated every 6 months. Avonex® may occasionally increase depression. Women planning to become pregnant should not be taking Avonex® as it can increase the risk of spontaneous abortions. There are no known drug interactions.
- **Natalizumab (Tysabri®)** is only available for prescribers that are registered in the TOUCH™ Prescribing Program. The recommended dose is 300 mg IV infusion every four weeks, with each dose being infused over approximately one hour. It is a recombinant humanized monoclonal antibody and is indicated for the treatment of patients with relapsing forms of MS to reduce the frequency of clinical exacerbations. It is known to be associated with hypersensitivity reactions including serious systemic reactions like anaphylaxis (less than 1%) and flu-like symptoms and urticaria generally occurring two hours after the infusion. Natalizumab increases the chance of getting a rare brain disorder that usually causes death or severe disability, called progressive multifocal leukoencephalopathy (PML). There is no known treatment or cure for PML.
- **Mitoxantrone (Novantrone®)** is given at a dose of 12 mg/M² intravenously over 15-30 minutes every 3 months. This is generally done in an infusion center. It is a chemotherapy treatment that decreased the activity of the immune system. Side effects include damage to the heart muscle (requiring measurement of heart function before each dose) and rare cases of leukemia. More minor side effects include an increased risk of infection for several days after each infusion, and mild nausea, hair thinning, cessation of menstruation, and blue discoloration. A total lifetime dose of 140mg/M² should not be exceeded.
- **Fingolimod (Gilenya®)** is the first oral agent approved by the FDA as a disease modifying treatment for MS. It is given at a dose of .5mg capsule taken once per day by mouth with or without food. It is a new class of MS medication called a sphingosine 1-phosphate receptor modulator. The medication mechanism of action can reduce neurodegeneration by reducing inflammatory damage to nerve cells. Side effects patients may develop include bradycardia, atrioventricular block, hypotension and other cardiac manifestations.

Spasticity

Spasticity is defined as a velocity-dependent increase in muscle tone, which is usually associated with hyperactive deep tendon reflexes. It is one of the more common symptoms of multiple sclerosis, affecting approximately 80 percent of patients. In MS, spasticity is usually the result of relaxation and contraction in opposition muscles at the same time, caused by upper motor neuron damage that disrupts the normal coordination of muscle movement. Therefore, muscles are held in a constant state of contraction, causing increased stiffness and tone that can lead to decreased range of motion of major joints. This constant state of contracting muscles can eventually, shorten the connective tissue around the joints causing contractures. The stiffness people experience can range from a minimal level of stiffness to an extreme level. The stiffness can also be very painful and often times, interferes with performing activities of daily living.

Clinical Signs and Symptoms

Spasticity occurs most frequently in the antigravity or postural muscles, including the muscles of the calf (gastrocnemius), thigh (quadriceps), buttock (gluteus maximus), groin (adductor), and occasionally the back (erector spinae). Clinical signs and symptoms of spasticity are variable and may include the following:

- an increase in deep tendon reflexes;
- clonus, a repetitive rhythmic beating movement of a foot or wrist;
- difficulty initiating movements;
- impaired voluntary movements;
- difficulty relaxing muscles once a movement has ceased (needs to be distinguished from myotonia—however, myotonia is not linked to hyperactive or pathological reflexes and is not typically part of MS);
- sensation of muscle tightening or pain;
- flexion or extension synergy patterns;
- decreased range of motion.

Various factors increase spasticity. For some people, spasticity increases with fatigue, heat, humidity, infection, and sudden movements or position changes, especially lying in extension for long periods. Stimulation causes inappropriate activation of the muscle group, and infection, stress, and pain can worsen it. Spasticity can increase fatigue, as a result, of the excessive energy expenditures required to overcome tone during voluntary movement.

Screening

Every MS patient should be screened for spasticity at every appointment. Screening involves assessing range of motion and functional ability, such as mobility, transfers, self-care, assistive devices, braces, strength, and balance. It is important to consider functional ability in addition to increased tone because some patients may require some tone increase to maintain posture, ambulation, and overall functional ability. Eliminating spasticity is not always a goal, as some individuals with muscle weakness use their increased tone to stand and transfer.

Grading Spasticity

The Modified Ashworth Scale is used to grade spasticity. This scale measures the presence of velocity dependent resistance from 0 to 4, with “0” representing normal muscle tone and “4” representing a limb that is fixed in flexion or extension.

Modified Ashworth Scale

Grade	Description
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone passive movement difficult
4	Affected part(s) rigid in flexion or extension

Spasticity Management

Management of spasticity involves five key strategies, not just pharmacologic options.

1. **Treat problems that increase the spasticity.** Evaluate for infections, fatigue, stress, and pain and address those that are modifiable. Develop a specific exercise program for patients. Referral to physiatrists and physical and occupational therapists not only can benefit spasticity management but also can address conserving energy that will lessen fatigue.
2. **Stretching.** The most effective and simplest way to reduce spasticity is passive stretching. This is accomplished by stretching the affected joint slowly and moving it into a position that stretches the spastic muscles. After each muscle reaches its stretched position, it is held there for approximately one minute to allow it to slowly relax and release the undesired tension. This stretching program should begin at the ankle to stretch the calf muscle and then proceed upward to the muscles in the back of the thigh, the buttocks, the groin, and, after turning from the back to the stomach, the muscles in the front of the thigh.

Although range of motion is important, holding the stretch is very important and patience is essential when doing the stretches. Exercising in a pool may also be extremely beneficial because the buoyancy of the water allows body movements with less energy expenditure and more efficient use of many muscles. The optimal pool temperature should be 85 degrees. Warmer temperatures will produce muscle fatigue and colder temperatures can actually cause spasticity.

3. **Mechanical devices.** These should be used to counteract spasticity and prevent contractures. Specific devices, such as finger or toe spreaders, are used to relax tightness in the feet and hands and aid immobility. Orthoses for the wrist, foot, and hand are used to maintain a natural position and to prevent limitations on movement and the development of spasticity.

4. **Pharmacologic approaches.**

Baclofen is the most commonly used antispasmodic medication used in MS treatment. While a common medication, dosing is very patient-specific due to the narrow therapeutic window between effectiveness and inability to maintain functional ability.

Tizandine is effective in decreasing stiffness and muscle spasms with less effect on strength than many other drugs. Because it can cause drowsiness, it is especially useful for nighttime stiffness and spasticity and can be used with baclofen for greater effectiveness.

Dantrolene is a direct-acting muscle relaxant; however, it also has a narrow window between effectiveness and weakness, much like baclofen.

Diazepam is often useful for spasms that occur at night. Because of its sedative effect, it also helps to induce sleep, but, as a barbiturate, it also has addictive potential, which may make it inappropriate for some patients.

Clonazepam also can be used to promote significant relaxation but must be used with caution for the same reasons as diazepam.

Cyproheptadine is an antihistamine that has antispasmodic properties and can be a good add-on. It can cause sedation, but at a dose of 4 mg daily, it is useful for MS patients.

Cyclobenzaprine is commonly used for back spasms. This drug can relieve limb spasms and works well in combination with other antispasmodics.

Gabapentin is approved for seizures but also has antispasmodic properties. When taken in doses of more than 1g per day, it can ease problematic spasms. It can also be effective for pain caused by spasticity.

5. **Surgical interventions.** Patients with MS that have intractable spasticity and do not respond to oral medication, surgical intervention may be necessary. A motor point block, done by injecting phenol into specific groups of muscles, is useful for severe spasms that do not respond to drug therapy. This older surgical procedure may produce flaccidity in muscles. However, does not usually

increase functional mobility and is not commonly used because newer techniques are available.

At present, Botulinum toxin is more commonly used to cause a temporary blockade of neuromuscular transmission. It is practical for treating small group muscle spasms, especially the muscles of the eye or face, but can also be useful for larger muscle groups depending on the dosage necessary to control spasticity.

A more invasive approach to controlling spasticity is the use of a baclofen pump that delivers baclofen directly into the spinal canal. Programming can require sometime, but this method is very effective for severe spasticity. This procedure requires test dosing before actual pump implantation.

Finally, there are several more invasive, nonreversible procedures, such as tenotomy, neurectomy, and rhizotomy, which can be considered. In some circumstances, these may be effective strategies.

Walking and Balance

Many people with MS experience difficulty walking. In fact, half of those with relapsing-remitting MS will need some kind of help walking within 15 years of their diagnosis if they remain untreated. The most common walking problem in people with MS experience is ataxia due to damage with the areas of the brain that coordinate movement of muscles.

Because MS can affect all areas of the central nervous system it can cause different problems for each person but, more than half of the people with MS have problems with their balance and walking and are at high risk for falls.

By 15 years from first symptom onset, 20 percent require a cane to walk. This percentage increases to 69 percent by 40 years after onset

Imbalance

Imbalance is one of the most common, and often the first symptom of MS. People with MS often say they feel off balance or dizzy. Researchers have found three main problems with balance in MS.

- First, most people with MS sway more than they should when they are trying to stand still. This swaying worsens more than expected with eyes closed or with reduced support, such as standing on one leg or with feet together.
- Second, when leaning, reaching or starting to walk, people with MS cannot go as far or move as quickly. This is not only leaning, reaching and stepping forwards but also upwards, such as getting something off a tall shelf or walking up stairs.

- Third, they have difficulty maintaining balance and controlling how much their body sways when pushed or pulled.

Walking Problems

The three identified balance problems are related to a very important function that is often impaired in people with MS - walking. Walking problems are common in people with MS. They tend to walk more slowly than healthy people, take shorter and slower steps, and their joints move less when they walk. They also use more energy to walk. Their walking gets even slower when performing a mental task like walking through a store while looking at things on the shelves, talking, or trying to remember a grocery list. Walking problems in people with MS are related to problems with balance. Walking involves standing on one leg, leaning forward, and then using the other leg to catch oneself and maintain balance. Because people with MS often have trouble standing, leaning, and maintaining balance when their body moves, it's not surprising that they also have trouble walking.

Risk of Falling

Problems with balance and walking also put people with MS at risk for falling. People with MS fall frequently and often fall badly enough to be injured. Many people with MS are also afraid of falling and stop being active to avoid falling. Trying to do mental tasks while walking increases the risk of falling and many people with MS say they fall more when fatigued or hot.

Imbalance in MS is caused by slowed conduction, from the legs along the spinal cord, of the sensation of where one's body parts are. This sensation is known as proprioception. Stepping forwards and landing where you want to, without looking down, requires you to be able to feel where your legs and feet are. When proprioception is slowed you don't know where your feet are quickly enough to put them in the right place, and this can make you unsteady and more likely to fall. Difficulty with thinking about many things at once can also contribute to problems with balance and walking and make people with MS fall.

Preventing Falls

Understanding why people with MS fall and studies on preventing falls in older people have yielded good ideas for helping people with MS. Some of these ideas include exercising in a standing position while gradually increasing balance challenges. This type of posture and slow moving body movements are similar to the martial art form of Tai Chi. There are various programs that use this milder form of yoga to improve balance.

Another way to prevent falls is to walk with a purpose by minimizing distractions and taking note of possible floor hazards like rugs or cracks in the sidewalk. Removing “throw rugs” in the home, tying up drapery/shade cords off of the floor and/or securing rugs to the floor are other examples of ways to prevent falls. As mentioned earlier, with MS, sensory nerves can have slowed conduction that interferes with the body’s sense of position.

Fatigue

One of the most common and disabling symptoms of MS is fatigue. MS fatigue, also called MS lassitude, can significantly interfere with a person's ability to function at home and at work, and it is a major reason why people with MS have to leave the workforce early.

Fatigue in MS patients is defined as an overwhelming sense of tiredness, lack of energy, or a feeling of exhaustion. It is distinct from weakness, and it is different from depression.

Assessment

There is a variety of different scales for measuring MS fatigue. The most commonly used scale is the Fatigue Severity Scale. Other scales are the Fatigue Impact Scale, the Fatigue Scale, the Profile of Mood States, and the Visual Analogue Measure. There are also scales for home use so patients (or their caregivers) can easily track and report changes. The home scales do have some drawbacks in that they are very subjective, and require a fair amount of insight on the part of the patient.

Fatigue Severity Scale (FSS)

The Fatigue Severity Scale (FSS) was developed by Lauren Krupp, MD, a neurologist who specializes in MS, to address this overwhelming MS symptom. She and her colleagues designed a self-report survey that patients could complete and bring to appointments that would help providers in recognizing and diagnosing fatigue related symptoms of MS.

The self-report questionnaire is a 9 question survey that takes approximately 5 minutes to complete and score. This short survey can provide a wealth of clinical information on the severity of fatigue symptoms. The questionnaire addresses fatigue symptoms as they relate to physical functioning, exercise and work, and family or social life. The scoring is based on a scale ranging from 1 (strongly disagree with the statement) to 7 (strongly agree with the statement). The results are easy to score. The score is based upon an average of the responses to the questions (add up the circled number from each question and then divide by nine). The final number can then be compared to other diseases that are associated with fatigue. The final score is a good indicator of

how each person rates their level of fatigue. This information should be shared with healthcare providers so appropriate interventions can be made.

Fatigue Severity Scale Questionnaire

Instructions: Circle the number that best represents your response to each question.								
Scoring Range: 1 = strongly disagree with the statement to 7 = strongly agree with the statement.								
								Score
During the past week, I have found that:								
1.	My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2.	Exercise brings on my fatigue.	1	2	3	4	5	6	7
3.	I am easily fatigued.	1	2	3	4	5	6	7
4.	Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5.	Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6.	My fatigue prevents sustained physical conditioning.	1	2	3	4	5	6	7
7.	Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8.	Fatigue is among my three most disabling symptoms.	1	2	3	4	5	6	7
9.	Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7
FSS Scoring: Add up the circled numbers and divide by 9.								
Compare results with the following scores:								
People who do not experience fatigue - score about 2.8.								
People with Lupus - score about 4.6.								
People with Lyme Disease - score about 4.8.								
People with fatigue related to Multiple Sclerosis – score about 5.1.								
People with Chronic Fatigue Syndrome – score about 6.1.								

An alternative and easier way of assessing fatigue is to take a more objective look at assessing fatigue by describing changes in function. This method focuses on changes in sustained functioning, sustained motor grip, or problems with sustained cognitive functioning and/or cognitive performance.

An accurate measurement of fatigue is needed when deciding on the best treatment. The reason for this is what was found when studies were done looking at tests of attention and vigilance. When people with MS do these tests, they tend to deteriorate over a period in contrast to people without MS. When we look at studies of memory, the same thing happens. A person with MS cannot continue doing their memory tasks as well as somebody without MS. For example, someone without MS gets a chance to improve and learn from practice, and that does not seem to help the person with MS.

Assessment of fatigue should also include a review of medicines and comorbid conditions that can produce fatigue. Primary or secondary sleep impairments, anemia, thyroid disease, and mental health conditions may be responsible for fatigue.

Appropriate evaluations need to include a complete blood count, thyroid stimulating hormone, and referral to a sleep disorders clinic.

Cause for Fatigue

PET scans show areas of glucose utilization are diminished in people with MS fatigue and MR spectroscopy reveals areas of axonal injury that seem to correlate with severe fatigue; however, no association has been found between where lesions lay, the number of lesions, and the severity of fatigue.

There are many other causes, including neuroendocrine and hypothalamic causes, motor system fatigue, and problems with the immune system. In terms of the motor causes, impaired drive from the motor cortex, decreased motor unit firing, inadequate motor unit recruitment, as well as impaired muscle metabolism all are important. In terms of the immune factors, we know that in MS (as well as in other diseases) when we use medications that are cytokines (like the interferons), many people report they have transient fatigue (or short-lived fatigue). Animal studies have shown that different cytokines when administered to animals can cause fatigue. There has been a range of different reasons to think cytokines are important in fatigue because other autoimmune diseases that are based on immune dysfunction also have fatigue as a component.

In terms of axonal injury, we know that atrophy, low NAA, changes in the normal-appearing white matter, all contribute. Among the neuroendocrine reasons for fatigue, we think of thyroid dysfunction. There have been varieties of abnormalities in the HPA axis in patients with MS that have been linked to fatigue. It's also likely that the effects of cytokines in MS on the HPA axis are contributing to impairments in cortisol and ACTH release.

There are medications that can make fatigue worse. People with MS have many different symptoms that require medications. Some of these medications can interfere with fatigue, for example, antispasticity medications for stiffness or spasms.

Anticonvulsants can cause fatigue, and they're used frequently for neurologic pain. Antidepressants, benzodiazepines (used in treating periodic leg movement disorder or spasms), and medications used to improve bladder control can also have fatigue as a side effect. Interferon therapy (used with some patients) can also cause transient fatigue.

Treatment

The first step in treating fatigue is developing specific treatment goals. The overarching goals are to reduce fatigue severity, reduce its impact, help patients reach their goals, develop an improved sense of control, and improve their quality of life. This is done by addressing those things that are cofactors for fatigue such as depression. If someone is depressed, that must be dealt with before addressing fatigue. If someone is in pain all

the time, that will make the person tired; the pain must be treated first. If someone is inactive, deconditioned, or taking medications that are responsible for fatigue, each must be addressed to lessen the fatigue.

Non-pharmacological Treatment

There are varieties of non-pharmacological strategies that can be used.

- Education regarding sleep hygiene (e.g., relaxing pre-sleep routine, avoid caffeine in evening);
- Exercise and activity endurance training
- Physical/occupational therapy
- Energy efficiency techniques;
- Schedule reorganization: perform demanding tasks early in day, maintain regular exercise and balanced nutrition; and
- Temperature regulation: maintain a cool environment or cooling therapy (e.g., cooling vests).

Fatigue may be reduced if the person receives occupational therapy to simplify tasks and/or physical therapy to learn how to walk in a way that saves physical energy or that takes advantage of an assistive device. Some people benefit from stress management programs, relaxation training, membership in an MS support group, or individual psychotherapy. Treating sleep problems and MS symptoms that interfere with sleep (such as spastic muscles) may also help.

Pharmacological Treatment

There are a number of different medications that have been used successfully when fatigue. One of the first was amantadine, which is actually an antifu agent. A very frequently used medication is modafinil, which was originally developed for narcolepsy but has been shown to be helpful. It has not been universally effective for all patients. Most recently, there has been some exciting work looking at aspirin, and that seems to have been providing some benefit.

Pain

Nagging, burning, aching, sharp, stabbing or squeezing are words that are used to describe pain experienced by people with multiple sclerosis. About two thirds of people with MS experience some level of pain at some time in their life. Pain should always be addressed as it impacts function and is often associated with depression, anxiety and fatigue.

Up to 50 percent of people with MS suffer from chronic pain. Individuals with MS who present with pain need proper assessment and management. Not all pain is attributable to MS, and as with other signs and symptoms, other causes, from radiculopathies to arthritis among them, need be considered. Pain in MS takes on many forms and has many causes. Some of these include neurological pain from central nervous system

dysfunction, muscle pain from cramps and spasms, musculoskeletal pain from maladaptive joint positions due to weakness, and pain due to over-exertion and exhaustion in an effort to cope with weakness. Pain may be secondary to neuromuscular or musculoskeletal impairments such as carpal tunnel syndrome, osteoarthritis, or radiculopathies. Depression and anxiety often enhance pain perception.

Causes of MS Pain

Pain in MS is directly related to either an MS lesion or plaque in the nervous system (nerve pain), or the effects of disability. When MS makes moving about difficult, stress on muscles, bones and joints can cause pain (musculoskeletal pain). Pain in MS can be caused or worsened by infection, or pressure ulcers

Nerve pain can be continuous and steady or sudden and irregular. Nerve pain is reported in varying degrees of severity. Fifty percent of those who report MS pain say their pain is constant and severe. Intermittent, sudden pain is described as shooting, stabbing, electric shock-like, or searing and is often caused by sensations that normally do not cause pain like the weight of bed covers, chewing, or a cold breeze. Other examples of intermittent pain include the feelings of tightness, cramping, clawing, and sudden spasms of a limb.

Tightness or band-like feelings, nagging, numbness, tingling in legs or arms, burning, aching, and throbbing pain is termed constant or steady nerve pain. Steady nerve pain is often worse at night or during changes in temperature, and can be worsened with exercise. The most common pain syndromes experienced by people with MS include: headache (seen more in MS than the general population), continuous burning pain in the legs and/or arms, back pain, and painful spasms.

Treatment of MS Pain

Treatment of pain in MS requires consideration of the whole person- the body, mind and spirit. This is called a biopsychosocial approach to pain management. Pain is both a physical sensation, a psychological experience having impact on emotions and emotions having an impact on pain, as well as, influenced by individuals who interact with the persons suffering pain. Addressing the biopsychosocial nature of pain is important to the effective management of MS pain. Pain is complex and often requires a team approach and the skills of pain management experts.

Biological Management (Medication and Surgical Approaches)

There are many proven medications used to manage pain in MS. The use of medications to manage pain in MS is always a balance of risk versus benefit. In other words, medication side effects vs. the effects of pain are considered and continually evaluated in terms of their impact on quality of life. Pain character that is, sharp and

intermittent or burning and constant, determines the medication or combination of medications to best manage pain.

Opioids are used for moderate to severe pain with great caution for three reasons: The side effects of opioids contribute to severe constipation, sleepiness, and lethargy; tolerance develops to opioids and higher doses are often required to achieve pain relief; opioids are only about 30% effective for MS nerve pain. Opioid use can exaggerate pain sensations and decrease activity levels. In other words, opioids used for MS pain may cause more harm than good and when considered, management of opioid side effects is very important.

Massage and acupuncture modulate the experience of pain by expressing the body's natural opiates, endorphins.

Surgical pain management is sought when medical, physical and behavioral options fail to impact pain outcomes. The sharp, stabbing facial pain of trigeminal neuralgia or painful contractures may require more aggressive management. Surgical procedures for trigeminal neuralgia may be short lived and carry risks of having worse pain or nerve damage that result in facial numbness and tingling. Surgical treatments include non-invasive Gamma-knife stereotactic radiosurgery, or invasive percutaneous rhizotomy, nerve block, or microvascular decompression. Painful contractures are relieved by permanent tendonotomy. These options are used specifically to manage pain and enhance quality of life.

Managing Psychological and Social Factors

Individuals having stress, anxiety or depression report more severe pain. Identifying stressors, causes for anxiety and recognizing depression is important to MS pain management. Relaxation techniques minimize stress. Talk therapy or cognitive-behavioral therapy is one solution for managing psychological factors. Identifying social factors or social support is critical to managing MS pain. Joining a support group, engaging with others, becoming more physically active (joining an exercise group, yoga, tai chi) and mentally active (engaging in discussions with others, taking a class) is important to MS pain management.

Self-Management

Self-management is a willingness to experience pain and at the same time, engage with life. The experience of pain may be consuming or the focus of every action. Finding meaning in life beyond pain is the goal of pain self-management. Recognizing maladaptive thinking, that MS pain is insurmountable, awful, horrible, unbearable is important to pain self-management. Shifting maladaptive thinking to adaptive thinking and behavior is key. Initiating self-management skills that increase pain coping and pain acceptance is important. Use of coping self-talk, "I have the tools to handle this pain"; "I can have a meaningful life" is helpful.

The aim of self-management is to increase mastery and control over pain. Self-management starts with acceptance of pain, that is, allowing some pain, some of the time. Meditation, relaxation exercises, hypnosis and guided imagery are ways of pain self-management. Mindfulness meditation promotes a non-judgmental awareness of pain and includes acting with intention. Mindfulness is attention to, or focus on, pain, accepting pain, considering the specific pain sensation and adjusting thinking about pain sensation to positive, adaptive thinking. Attention to burning pain, and experiencing warmth is an example of mindfulness meditation. Self-management consists of both thinking and doing. Behavioral activation includes increasing physical activities that are enjoyable, meaningful, or pleasurable. Setting realizable goals for increasing activity is a recipe for success. These techniques and therapies are often overlooked but should be considered from the start of pain symptoms.

Bowel and Bladder Dysfunction

Bowel and bladder dysfunction can present early in MS and lead not only to impaired quality of life but also to medical complications if not assessed and treated.

Bladder Dysfunction

Urinary control is a very common concern among persons with multiple sclerosis, and the prevalence of bladder dysfunction is high in MS. The innervation to the bladder and urinary sphincters emanates primarily from the sacral spinal cord (with some contributions from the lumbar cord), and thus the long CNS pathways that regulate the micturition reflex are more “exposed” to the demyelinating process. The exact prevalence of urinary problems is not known because the onset is insidious, and if the symptoms are mild, they are often disregarded.

The physiological effects on demyelination on bladder control are usually one or more of the following:

- loss of sensation of bladder fullness
- loss of cortical inhibition of the micturition reflex, resulting in frequency, urgency and urge incontinence
- loss of bladder contractility
- loss of coordination between the urinary sphincters and bladder contraction.

Functionally, patients experience problems containing urine, problems emptying urine, or a combination of both.

Assessment of bladder function needs to include the following: history of bladder urgency, frequency, hesitancy, incontinence, and nocturnal voiding; post void residual (PVR) volume via bladder ultrasound or catheterization; urinary tract infection history, urinalysis, and urine culture.

Post Void Residual Volume

One of the most important determinants of bladder management is the post void residual volume. This can be measured with an ultrasound or with bladder catheterization after voiding. How efficiently a bladder empties (i.e., how much urine is left behind after a void) helps the practitioner decide on treatment and management.

Several common scenarios exist:

- A person with a large (>275-300 cc) post void residual on two separate occasions should perform clean intermittent catheterization, or have a chronic, indwelling catheter.
- A patient with frequency and urgency likely has detrusor hyperreflexia, that is, bladder contractions without full cortical regulation. If the post void residual is small, then a trial of anticholinergic medications is indicated. Common side effects are dry mouth, constipation, and urinary hesitancy/retention, which are already problematic in persons with MS. Thus, careful medication titration (avoid long-acting anticholinergic medications) and aggressive bowel care (including fiber supplements, stool softeners, suppositories, mini-enemas) are necessary to avoid exacerbating one problem to treat another.
- If a person with the same symptoms has a large post void residual (>150-200 cc), one would not prescribe anticholinergic medication unless the patient were to begin CIC.

A person with tolerable urinary symptoms, who is not in urinary retention or having UTIs, does not have to be treated.

Bladder Management

The objectives of bladder management are the same in multiple sclerosis as they are for any person with bladder dysfunction. The primary objective is to do what is necessary to preserve renal function, since problems of the bladder can result in renal deterioration. This can be achieved by emptying the bladder efficiently (completely) and regularly, whether by spontaneous voiding, clean intermittent catheterization or chronic catheterization. Fortunately, renal failure due to bladder dysfunction is not common in MS, in part because most of the patients are women, and the short (and generally, non-obstructive) female urethra allows for a “pop-off” valve in bladders with poor compliance.

The secondary objectives for bladder management are the maintenance of social continence and the avoidance of complications such as cystitis and stone formation. Additionally, a patient should not be committed to a bladder management regimen that makes them dependent on someone else for bladder emptying. For example, a tetraplegic patient should not be started on self-catheterization. The mode of bladder management should be consistent with the patient’s physical and mental capacities.

Bowel Dysfunction

The symptoms of multiple sclerosis (MS) are unpredictable and vary from person to person. A common symptom that affects approximately 68% of people with MS is bowel dysfunction. People can experience bowel dysfunction when demyelination in the central nervous system (CNS) interferes with nerve transmission needed for normal bowel function. This demyelination can affect muscle groups, which are needed to produce normal bowel function. Other factors like slowed transit time of the intestines, muscle weakness, fatigue and lack of exercise can also contribute to the problem.

Medications like sedatives/tranquilizers, diuretics, narcotics/analgesics, antidepressants, anticholinergics, antacids, iron supplements, and antihypertensives that are used to manage symptoms of urinary problems or depression might also alter bowel functions. In addition, many people with multiple sclerosis want to decrease their bladder incontinence by inappropriately limiting their fluid intake, which in turn increases their risk for constipation.

Common Bowel Problems

The reasons for bowel dysfunction vary, but the usual bowel problems reported by people with MS are constipation, diarrhea and fecal incontinence.

- **Constipation** is the most frequently reported problem. The definition of constipation is infrequent (two bowel movements or less per week) or difficult elimination of stool. Slowed transit time, altered fecal composition, decreased ability to expel feces and altered ability to acknowledge the urge to defecate may all cause constipation.
- **Diarrhea** is less common than constipation and may even be a result of constipation. The definition of diarrhea is abnormal fluid stools. If hardened stool is retained, diarrhea may occur around the mass.
- **Fecal incontinence** is the involuntary passage of stool. Contributing factors include sphincter dysfunction, sensory loss in the rectum, medications and dietary problems.

Bowel Dysfunction Treatments

The treatment for bowel dysfunction includes patient assessment, interventions, medications, and bowel reflexes. Following these four steps can aid in helping the patient experience a more normal bowel program.

Step 1: Assessment of the person's history is the beginning of the treatment for bowel dysfunction, which includes:

- Frequency and type of bowel movements
- Usual time of day pattern
- Reliance on laxatives or enemas
- Current medications
- Comorbid medical conditions that may affect medications

- If assistance is needed for toileting, consider when help is available.

Step 2: Interventions should be designed to develop and maintain consistent emptying of the bowel. Use the following guide for dietary and fluid changes:

- A consistent habit and time of emptying (usually 1 to 3 days)
- Predictable bowel emptying
- Maintain a balance of stool that is easy to pass
- Provide for sufficient hydration with 1.5 to 2 liters per day of non-caffeinated, non-alcoholic fluids.
- Include 25 to 30 grams per day of dietary fiber.
- An exercise program shortens transit time through the gastrointestinal (GI) tract. Walking and active exercise are best, but when that is not possible, encourage as much activity as the person can do.
- A dietary supplement that can aid in bowel emptying is a combination of several food products high in dietary fiber blended together.

Dietary Fiber is an important component of bowel management to encourage consistent bowel emptying. Dietary fiber is beneficial in the management of both constipation and diarrhea. Its bulking action helps alleviate diarrhea and its softening action helps to prevent constipation. Fiber functions by binding water in the intestines in the form of a gel to prevent over absorption by the large intestines. This ensures that feces are bulky, soft and does not have delayed transit time. Delayed transit time generally results in constipation.

Chief dietary sources of fiber: whole grain breads and cereals, leafy vegetables, legumes, nuts and fruits. Increased fiber intake needs to be gradually introduced to allow the GI tract time to adapt. Too rapid an increase may result in flatulence, distention and diarrhea.

Step 3: Medications may be necessary if dietary and fluid changes are not adequate.

- *Suppositories* – act on colonic mucosa to produce peristalsis to initiate reflex emptying of the bowel (e.g. Glycerin, Dulcolax, and mini-enemas).
- *Stool softeners* – adjust stool consistency; usually the effects of stool softeners take several days after initial use (e.g. Dialose, Colace, and Surfak).
- *Softeners with a laxative component* may be used when additional softening or peristaltic stimulus is needed. They need to be given approximately 12 hours before the desired results (e.g. Dialose Plus, Pericolace, and Senokot).
- *Bulking formers* – these agents add substance to the stool by increasing its bulk and water content (e.g. Metamucil, Fibercon, and Citrucel, etc.).
- *Osmotic laxatives* such as Sorbitol, Milk of Magnesia and Lactulose act in both the small and large intestines to attract and retain water in the intestinal lumen increasing intraluminal pressure. These drugs may be an option for bowels that do not respond to other drugs.
- *Enemas*

Medication Cautions - Laxatives are oral stimulants that provide a chemical irritant to the bowel. Laxatives can become habit forming so should be used cautiously (e.g. Pericolace, Milk of Magnesia, Senna, and Dulcolax). In addition, routine use of large-volume enemas can result in overdistended bowel.

Changes in the bowel program may be needed, but changes should be one change at a time. Allow a 5 to 7 day trial period for each bowel program intervention.

Step 4: Routine reflexes can aid in managing bowel function. There are several methods to stimulate a routine reflex to empty the bowel. Stimulation techniques include mini-enemas and/or digital stimulation. After using one of these stimulation techniques the reflex to empty takes approximately 30 to 45 minutes. It is important that these stimulation techniques be used at the same time of day to help the body develop routine reflexes. It is most common to initiate this protocol after breakfast. Generally, the gastrocolic and duodenocolic reflexes occur between 30 to 45 minutes after ingestion of a meal or drinking a hot beverage. The natural timing of reflexes needs to be considered when developing a bowel toileting routine.

- *Mini-enemas*
- *Digital stimulation* is used to induce reflex contraction of the colon and relaxation of the anal sphincter muscle to facilitate defecation. A gentle clockwise rotation of the index finger against the anal sphincter wall for several minutes at a time can promote stool expulsion. This type of stimulation might need to be repeated until the bowel evacuation is completed.

Step 5: Colostomy is considered after the above interventions are ineffective in developing normal bowel function. A colostomy is a surgical operation that creates an opening from the colon to the surface of the body to function as an anus. The fecal matter is deposited in a bag that is on the outside of the body. This is not an uncommon medical procedure for some people with severe disease and/or slowed transit time. A colostomy can actually provide the much needed relief for patients and simplify care by caregivers.

Additional Bowel Intervention Tips include:

- Maintain regular mealtimes.
- Positioning aids help with elimination. An upright position allows gravity to assist in peristalsis and stool expulsion. In addition, having knees higher than the hips and feet flat on a surface (e.g. a small step-stool might work well) helps increase abdominal pressure to facilitate defecation. It also straightens the angle between the rectum and the anal canal to promote rectal emptying.
- Abdominal massage can also stimulate peristalsis. Massage the right groin upward, across and down to left groin.
- Breathing techniques can increase intra-abdominal pressure. By taking slow, deep breaths combined with abdominal muscle contractions (or leaning forward) help perform a Valsalva maneuver increasing rectal emptying.

Sexual Dysfunction

Sexual dysfunction is a common symptom in MS and affects more than 75% of people living with the disease; a frequency greater than that reported in other chronic diseases.

Sexual dysfunction in MS has many causes. Primary causes may be the direct result of demyelinating lesions in the CNS (central nervous system) that can affect sexual response and sexual feelings. Primary sexual dysfunction includes decreased or loss in libido, painful or uncomfortable genital sensations (burning, tingling, numbness), and /or altered orgasmic response in both women and men. Women may experience decreased vaginal lubrication and dryness, inorgasmia, and low sex drive. Men may experience difficulty achieving and/or maintaining an erection, and diminished frequency of ejaculation.

Secondary sexual dysfunction problems arise as a consequence of disability caused by MS. Examples of secondary symptoms include poor bladder and bowel control, fatigue, muscle weakness, spasticity, immobility, tremor, cognitive impairment, and sensory problems. In addition, medications that are used for MS (spasticity, urinary frequency, sensory pain) and non-MS diseases (hypertension, diabetes, depression) can further contribute to secondary sexual dysfunction.

Tertiary sexual dysfunction in MS occurs as a result of disability related psychological, social and cultural issues that affect sexual response. These variables can include anxiety, low self-esteem, altered marital and family roles, changes in body image, and fear of rejection by one's partner.

Although sexual dysfunction is a prevalent problem, in the MS population, and can be caused by a host of variables, for both men and women, it is a topic that is frequently overlooked, rarely discussed, and often left untreated.

Importance of Sexual Dysfunction in MS

Sexual function is a vital element to a person's health and well-being. People living with MS are sexual beings, yet health care providers often ignore or forget this part of a patient's identity. This avoidance to address and treat sexual dysfunction profoundly impacts the quality of life for all people living with MS; not only the patient but also their partner.

It is important to address and treat sexual dysfunction, in the MS population, because sexual dysfunction is a prevalent problem. In reports of men with MS, sexual dysfunction may range from 23% up to 91%. Women may report SD up to 85% of the time. Eighty percent of the sexual dysfunction problems in men consist of erectile dysfunction. In women, up to 72% report decreased libido and hyposexuality.

Health care providers often omit the assessment of sexual function when taking a patient history because of several reasons. Limitations to dialogue between MS health care providers and their patients can occur because clinicians:

- feel embarrassed and/or awkward about bringing up the issue;
- may not have the knowledge/training to comfortably talk about sexual dysfunction;
- may be biased in thinking the patient is too disabled or too old to engage in sex;
- may have time constraints and believe other issues take precedence over sexual dysfunction concerns;
- may believe the issue is outside their scope of practice or role;
- may believe the topic is too intrusive a subject to discuss; and
- may believe the patients have limited medical coverage and therefore could not afford treatment.

Patients, on the other hand, may be reluctant to initiate sexual dysfunction dialogue because of embarrassment, and beliefs the problem is untreatable, it is a normal part of aging, the provider does not want to hear about the problem, the provider is too busy, or the provider may not think the subject is important.

As a consequence of poor communication and misconceptions, in most MS clinical settings, the topic of sexual dysfunction is rarely addressed by the health care team despite its prevalence in the MS population.

Management

The first step in management of sexual dysfunction is to acknowledge that sexual dysfunction is a significant health care problem that most MS patients face at some point in their lives. It is also important to realize that sexual dysfunction is a subject that often goes under recognized and under treated.

The second step is to educate and train all members of the MS health care team about sexual dysfunction and teach them how to discuss the subject with patients. For instance, physical therapists can address positioning techniques that enhance sexual comfort. Clinical psychologists can work with individuals or couples in promoting sexually sensitive communication to enhance sexual performance.

Because patients are reluctant to reveal they are having sexual difficulty, it is the responsibility of all health care team members to routinely ask about sexual functioning. Asking about the problem acknowledges that the topic is important and it opens the door to therapeutic communication and problem resolution.

Discussion of sexual function can begin at a patient's initial clinic visit during the review of medical and surgical history which can also include sexual, personal, social, and medication history. The subject might also be incorporated into future visits, as appropriate. For example, if a patient presents with bowel, bladder, fatigue, or spasticity

problems, the provider can mention these problems may contribute to sexual dysfunction and if a problem occurred now or in the future, treatments are available to enhance sexual function. The goal is to normalize the subject and let the patient know that sexual function/dysfunction is a topic worthy of discussion.

Depression

Approximately 50 percent of persons with MS experience depression and 10-15 percent experience emotional variability. Psychological challenges arise from the unpredictable nature of relapses, the uncertainty of disease progression, difficulties with coping with relationships, and professional stress.

Clinical depression is more frequent among people with MS than it is in the general population or in persons with many other chronic, disabling conditions. MS may cause depression as part of the disease process, since it damages myelin and nerve fibers inside the brain. If the plaques are in parts of the brain that are involved in emotional expression and control, a variety of behavioral changes can result, including depression. Depression can intensify symptoms of fatigue, pain, and sexual dysfunction. It is most often treated with selective serotonin reuptake inhibitor (SSRI) antidepressant medications, which are less likely than other antidepressant medications to cause fatigue.

MS is sometimes associated with a condition called pseudobulbar affect that causes inappropriate and involuntary expressions of laughter, crying, or anger. These expressions are often unrelated to mood; for example, the person may cry when they are actually very happy, or laugh when they are not especially happy. In 2010 the FDA approved the first treatment specifically for pseudobulbar affect, a combination of the drugs dextromethorphan and quinidine. The condition can also be treated with other drugs such as amitriptyline or citalopram.

Cognitive Effects

Half to three-quarters of people with MS experience cognitive impairment. These cognitive changes may appear at the same time as the physical symptoms or they may develop gradually over time. Some individuals with MS may feel as if they are thinking more slowly, are easily distracted, have trouble remembering, or are losing their way with words. The right word may often seem to be on the tip of their tongue. Some experts believe that it is more likely to be cognitive decline, rather than physical impairment, that causes people with MS to eventually withdraw from the workforce.

Cognitive changes can occur at any time, and their severity doesn't appear to correlate with either length of time since diagnosis or the level of a person's physical disability. For example, a person with significant physical limitations, who has had MS for some

time, can be totally free of cognitive symptoms, while a person with a recent diagnosis and few physical symptoms can have significant cognitive impairment.

Even relatively mild symptoms can have a pretty big impact on various activities of daily living. For instance, people with MS are more likely to leave the workforce because of cognitive symptoms and fatigue than because of mobility problems. Early departure from the workforce is a critical issue for people with MS, but it can often be avoided with adequate symptom management.

Cognitive fatigue can interfere with the ability to get things done. Research has shown that people with MS who are concentrating very hard on a cognitively strenuous task can experience a kind of mental fatigue that feels like acute "brain drain." Fortunately, a brief rest from the task will generally help get them back on track.

Cognitive changes tend to progress slowly over time. Even though MS relapses can include a sudden worsening of cognitive symptoms as well as physical ones, which tend to improve as a relapse ends, problems with thinking and memory don't generally disappear completely. The sooner these kinds of cognitive problems are identified, the easier it is to develop effective strategies to manage them.

Like the physical symptoms that can occur in MS, the cognitive changes are highly variable from one person to another. One person may experience a lot of problems while another person experiences none or very few. In other words, no two people experience the same changes in exactly the same way. However, the following types of problems are the most common in MS.

Memory

Until fairly recently, experts believed that the primary memory problem for people with MS was with the retrieval of information that had been stored in memory. In other words, these experts believed that a person could learn new information and tuck it away in memory, but then be unable to recall or retrieve it from storage when needed. More recent evidence suggests that the problem may involve the initial learning phase. People with MS may need longer time or a few more repetitions to learn and store new information successfully. After it has been stored, however, it can generally be recalled without difficulty. For example, if you have memory problems, it may take you longer than someone without memory problems to memorize a list of words. But once you have the words memorized, you'll remember them just as well as the other person does.

Information processing

Slowed processing is important because it may be the primary reason why a person with MS needs more time or repetitions to learn new information. When processing is impaired, the person has trouble keeping up with incoming information, whether it's from conversations, TV shows, or books. People describe this slowing by saying, "I can still

do everything I used to be able to do, but it all seems much slower — like my brain needs to be oiled."

Attention and concentration

Attention and concentration, which form the basis for many other cognitive functions, can also be impaired by MS. For example, people who are used to being able to focus on many complex and competing tasks at the same time may notice some frustrating changes, such as being easily distracted by interruptions or competing stimuli, having difficulty moving smoothly from one task to another, or finding it more difficult to multi-task (an essential skill in any occupation, particularly parenthood).

Executive functions

Executive functions include the high-level processes of planning, prioritizing, and problem-solving. Research has shown that people with MS may find thinking through complex problems or projects more difficult because they lose the mental agility to shift from concept to concept along the way. People often describe this impairment as "feeling stuck" or "lost in a maze."

Visual perceptual skills

Visual perceptual skills, which include simple perception or recognition of objects, as well as sense of direction and orientation in space, can be affected in MS. These problems can interfere with activities ranging from reading a map or driving, to programming electronics or dealing with those pesky "some assembly required" projects.

Verbal fluency

Verbal fluency includes the ability to find the word you're looking for quickly and easily. "It's on the tip of my tongue" is a particularly common complaint from those who have MS, as is "I'm talking to someone and all of a sudden I'm stuck without the word I need." People who experience these kinds of problems may feel less confident about their ability to talk smoothly and comfortably with others.

General intelligence

People with MS sometimes say they feel "dumber." The good news is that general intelligence is usually not affected in MS. However, individual functions that make up general intelligence, such as memory, reasoning, or perceptual skills, can be affected or slowed temporarily during a relapse or more permanently over the course of the disease. So, a person's intelligence quotient (IQ), which is a composite score made up of individual subtest scores on all these functions, can become lower over time.

Vision

Patients with multiple sclerosis (MS) can have many different kinds of vision problems, including optic neuritis, diplopia, and nystagmus.

Optic Neuritis

Optic neuritis is blurry vision or hazy vision affecting one eye. It is usually associated with some eye pain or discomfort, especially with eye movements. Often the center of vision is most affected, making it difficult to see people's faces or creating a "line" in the center of their vision. More than half of all MS patients will experience optic neuritis at one point in their lives. In fact, for 15% to 20% of patients, optic neuritis will be the first presentation of their MS. On examination, a patient with optic neuritis often has an afferent pupillary defect (APD), which is an asymmetry in the two pupils' reaction to light. Initially, the optic nerve head may look normal or mildly swollen. Later on, the optic nerve may develop pallor (paleness).

The good news is that optic neuritis usually gets better, though the vision in the affected eye may not return 100%. Vision in the affected eye might not be as clear as before, and colors may seem faded or "washed out". Depth perception is often not as good after an episode of optic neuritis.

MS patients are often given intravenous methylprednisolone (also known as Solu-Medrol®) for optic neuritis. The steroids do not appear to improve visual outcome in the end, but they do seem to speed up the recovery of vision.

Double Vision

Double vision, or diplopia, occurs when the eyes are not moving together so that the brain is getting two slightly different pictures simultaneously. This typically occurs when MS affects the brainstem, where the coordination of eye movements is controlled. One common cause of double vision in MS is an internuclear ophthalmoplegia (also known as an INO). Rarely, MS patients may develop double vision from a sixth nerve palsy or other neuro-ophthalmologic disorder.

Sometimes the patient does not see two completely separate images. MS patients may report a "shadow" or a "blur" instead of frank double vision. An important question to ask is whether the visual problem goes away if either eye is closed. Because diplopia is caused by the brain receiving two different images, one from each eye, as soon as *either* eye is closed, this type of visual problem will go away. On examination, there may be an obvious problem with the movement of the eyes, but sometimes the misalignment is not easy to see without special equipment.

Diplopia often resolves on its own. As with optic neuritis, intravenous corticosteroids are often prescribed, in the hopes of speeding up the recovery. Patients may need to wear

an eye patch temporarily. The eye patch is guaranteed to “cure” the diplopia, since only one eye will be sending an image to the brain, but some patients may feel self-conscious while wearing the patch. Sometimes, if recovery is incomplete, eyeglasses with prisms can be used to bring the eyes back into alignment. Prism eyeglasses are similar to prescription eyeglasses for reading. The prism prescription can be added to an already existing eyeglass prescription. In rare cases, strabismus surgery may be recommended to realign the eyes.

Nystagmus

Nystagmus is an involuntary, rhythmic movement of the eyes that can be associated with vertigo, oscillopsia (the illusion that the world is “jumping” or “swinging back and forth”), blurry vision, or diplopia. Nystagmus can occur in the setting of an internuclear ophthalmoplegia (INO), or due to a MS attack in the vestibular part of the brainstem or cerebellum.

The nystagmus may be visible when the patient is looking straight ahead, but sometimes is only present when the patient is looking off to the side, up, or down. If the nystagmus is very mild, it may only be perceptible while using an ophthalmoscope.

Nystagmus can be difficult to treat if it does not resolve on its own. Various medications may help dampen down the nystagmus, including clonazepam (Klonopin®), baclofen (Lioresal®), gabapentin (Neurontin®), and memantine (Namenda®). In rare instances, surgery or botulinum toxin (Botox®) may help.

Dysphagia

Swallowing problems (dysphagia) are often seen in people with multiple sclerosis. Swallowing problems can occur in the mouth, back of the throat or esophagus. Available research has varying estimates of how often swallowing problems happen in people with multiple sclerosis. The range is from 3% to 51%. Common symptoms include the following:

- coughing,
- choking,
- a sticking sensation,
- difficulty starting to swallow
- difficulty chewing.

People with multiple sclerosis are more likely to develop dysphagia as their multiple sclerosis progresses.

Swallowing problems can lead to complications including poor nutrition, dehydration and lung infections caused by swallowing “down the wrong pipe” (aspiration pneumonia). In

addition, it can interfere with enjoyment of meals, a major source of social interaction and pleasure for many individuals.

Aspiration pneumonia is a potentially life-threatening lung infection caused by breathing in a foreign material like food, liquid, or bacteria-infused saliva. In the past scientists thought that aspiration pneumonia occurred after breathing in food or liquid alone. Current thought suggests, however, that three steps must occur.

- First, bacteria must breed in the mouth or the back of the throat.
- Second, the material must be breathed in.
- Finally, the patient must not be able to cough out the material either immediately or after breathing it in.

Diagnosing Swallowing Problems

The goal of treating swallowing problems is to maximize the safety and efficiency of eating. In order to meet that goal, it is important to thoroughly review the patient's history and to evaluate the swallowing mechanism. This might include a clinical or bedside evaluation, using a tube called a fiber optic scope to watch a person swallow from the inside and/or an x-ray test called a modified barium swallow. The completion and interpretation of these studies provide information about how to manage swallowing problems. It is important to note, however, that silent aspiration (aspiration with no overt signs of swallowing problems) can be an issue in multiple sclerosis, sometimes limiting the value of a clinical exam.

During the examinations, compensatory techniques may be attempted to reduce the symptoms of swallowing problems. Postural adjustments, therapeutic techniques and/or diet changes can be assessed during the actual exam to determine if they are, indeed, effective. Specific treatment recommendations can be made once the evaluation process is complete.

Treating Swallowing Problems

Treatment techniques for swallowing problems may include direct treatment (aimed at increasing the strength or movement of the swallowing structures) or compensations (designed to improve the swallow without directly treating a deficit). There are many treatment techniques available for persons who have swallowing problems secondary to multiple sclerosis. The research supporting these treatments is, however, quite limited. Texture adjustments of the diet, most often thickened liquids, are often recommended to manage swallowing problems. Current scientific studies suggest that when geriatric stroke patients are put on thickened liquids (a common strategy for managing swallowing problems) they are at higher risk of becoming dehydrated. It is important to consider this risk in patients with other neurological problems like multiple sclerosis. For that reason, this option should be considered as a last resort.

Respiratory Dysfunction

Motor deficits in MS can involve the respiratory muscles. Both strength and endurance can be affected with decrements in maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP). Non-ambulatory patients with MS with Expanded Disability Status Scale levels greater than 6.5 have MIPs of 27-74 percent of predicted values. Acute respiratory failure can occur in MS and must be promptly diagnosed and appropriately treated. Patients, especially if non-ambulatory, may be unaware of this condition. Simple measures, such as ability to blow out a match or candle, counting from 1-20 without pause, and timed breath-holding are of value in alerting the clinician to potential problems in this area.

Assessment of respiratory muscle strength by MIP and MEP and respirator muscle endurance (by maximal voluntary ventilation) needs to be performed every 1 to 3 years depending on the severity of pulmonary impairment. These tests can be performed with the assistance of the pulmonary function lab or via portable hand-held devices. Referral to pulmonary services for evaluation and discussion of treatment options is appropriate for patients with significant respiratory weakness or dysfunction. Rehabilitation of respiratory muscle weakness includes the use of Threshold EMT (expiratory) trainer for expiratory muscle weakness; and Threshold IMT (inspiratory) trainer for inspiratory muscle weakness.

Heat Sensitivity

Often after someone develops multiple sclerosis (MS), it is not unusual to develop heat intolerance. Small increases – as little as $\frac{1}{2}^{\circ}\text{F}$ – in core body temperature can increase MS symptoms. The cause of this is that nerves that have lost their conductive coating (myelin sheath) become more sensitive to heat, and the nerve signal slows down or is blocked resulting in an increase in symptoms. Depending on the location of the nerve damage in the body, symptoms may include increased heart rate, sweating, dizziness, muscle weakness, slowed reaction times, reduced energy, and difficulties with attention and concentration.

Causes of Increased Body Heat

Many things can cause body temperature to rise – some we usually think of, and some are a little harder to see. Obvious causes of increased body temperature are things such as being in a warm environment, increasing physical activity, or wearing too many clothes. All these can easily lead to increased body temperature and for some an increase in MS symptoms. A not so obvious cause of increased body heat is having a fever.

Warm environments may include things such as being in the kitchen during meal preparation, working hard around the home (whether cleaning the house or working

outdoors), taking a hot shower, swimming in a warm pool, or being out in the sun. Core body temperature may also rise with increased physical activity, such as when walking, propelling a wheelchair, exercising or doing other leisure activities. Causes that are not too obvious would be things such as wearing clothing that keeps the person too warm, or being in rooms that are too warm. Medical illnesses such as bladder infections, colds, and/or the flu might cause an individual to experience a low to medium grade fever, which in turn increases the core body temperature.

There are a number of ways to help the body to stay cool. These include:

Adjust the temperature in the environment.

- Use an air conditioner or fan in the room or in vehicle
- Rest in rooms that are out of direct sunlight or have adequate shading over windows that have a West or Southern exposure
- When showering or bathing, turn the fan on in the bathroom and/or open a window if possible to help circulate the room air;
- Make sure the water temperature in the shower or bathtub is significantly lower than body temperature;
- Take a cool bath
- Wear layered clothing that can be removed as necessary to adjust body temperature
- Avoid traveling to warm parts of the country or world during their hot and/or humid seasons
- Use a spray bottle to mist with water at regular intervals during activity (or even when sitting) – as many people with MS lose the ability to perspire and release body heat

Drink plenty of fluids.

During periods of increased activity, the body can generate several times the amount of heat it does at rest. The body releases excess heat by sweating and evaporation. Adequate water intake is important to be able to perspire during exercise and still remain hydrated. Here are some tips for better hydration:

- Place a plastic bottle of water in the freezer until frozen. Place this by the bedside at night to have cold water available to drink without having to get out of bed.
- Drink chilled water, juices, ices, and popsicles throughout the day to help keep body temperature down.
- Avoid drinks with caffeine (e.g. Sodas, colas, coffee, tea, chocolate, and some energy drinks) are diuretics, so fluid loss is increased by urination. This leaves less fluid in the body to sweat (one of our natural ways of cooling down).

Use cooling equipment

- Layer up with lightweight, breathable clothes. Remove the layers as necessary to keep cool. Look for clothing that is designed to have more air flow through it, making it cooler to wear.

Multiple Sclerosis

- Use an umbrella while out in the sun.
- Wear a vented hat, sunglasses, and use sunblock while outdoors. (The sunblock won't reflect heat, but will help prevent you from skin cancer.)
- Use a cooling vest.
- Use cooling packs on your wrists, neck, and on your head (under a hat). Another strategy is to wear cloth-type hats and dip them in water, then allow the sun to evaporate the water, cooling your head.

Cooling Vests

A cooling vest is designed to keep the body's core temperature (around the heart and spinal cord) within safe levels to reduce symptoms of heat intolerance. The vest absorbs body heat, evaporates perspiration, and conducts cooler temperatures to the body through the skin. Cold packs for the neck, wrists and head conduct cold through to the arteries, cooling the blood circulating in the body.

The cooling vest should be worn in warm-to-hot conditions or when physical activity is planned. The vest can help keep a person cool up to 3 hours when worn correctly, although this can depend on things such as environmental temperature, humidity, and your level of activity.

It is beneficial to wear the cooling vest at least 30 minutes prior to physical activity. The cooling vest is more effective when worn over thin clothing and, when needed, when breathable fabrics are worn over the vest.

Mattresses

Because of the problems with sensation and movement that are often a component of multiple sclerosis, people with the disease often require special mattresses to keep them safe from developing bed sores and other skin problems. Another problem that people with MS suffer from is heat intolerance. In the presence of a high ambient temperature (temperature of the inside or outside environment), the nerves damaged by MS cease to function. So that when people with MS become overheated, their ability to move and sense the environment is diminished. Choosing a mattress that will protect the individual from becoming overheated and that will provide skin protection is very important for the health of the person with MS.

Types of Mattresses

When choosing a mattress, it is important to consider the effects of that mattress on skin protection and heat intolerance. Mattresses may be either static or dynamic. In general, a static mattress refers to a mattress that doesn't move when a person lies on it. A dynamic mattress is powered by electricity to change the surface under a person to

allow for a variety of medical needs. Dynamic mattresses involve at least one of the following technologies: fluidized air, alternating pressure or side-to-side turning.

Dynamic Mattresses

- **Fluidized air therapy** involves blowing warmed air through a bed of tiny silicone beads creating a surface that is like a “waterbed” but with warm air blowing up through it continuously. This type of surface is used mostly in health care institutions for patients either with very severe pressure ulcers (bedsores) or after surgery to close these wounds.
- **Alternating pressure:** Air is pumped into cylinders that are placed parallel to each other inside a mattress. As one set of cylinders inflates, the other set deflates. This way the pressure under any part of the body is relieved on a regular basis. This type of mattress can reduce the number of times a person needs to be turned while in bed.
- **Side-to-side turning:** One side of the mattress deflates and the other side inflates, alternating over time, turning the person in the bed gently from side to side. This is normally used for patients with lung problems, but can be used for people with MS as another way to reduce the number of times an attendant must turn a person while in bed.

Of these mattresses, only fluidized air is heated. The heat can be adjusted so that people with MS can use these surfaces, but they carry some risk of overheating. Alternating pressure and side-to-side turning are not heated. Therefore, heat intolerance is not as much of an issue with these mattresses.

Static Mattresses

- **Viscoelastic or memory foam:** One kind of static mattress that gets a lot of attention on TV is made of viscoelastic or memory foam (the Tempur-pedic™). People with disabilities often find these mattresses difficult to use because they get “stuck” in a hole in the mattress and cannot move themselves out of it. Some medical mattresses are made of this substance but they do not really work out very well for people with MS.
- **Low air loss:** This involves an air sack where a small amount of air leaks through the cover on a continuous basis. It helps to control moisture (like sweating). It provides some pressure reduction but the surface doesn't change over time and people need to be turned more frequently on this kind of surface. The air in a low air loss mattress may be heated and so this could pose problems with heat intolerance for people with MS.
- **Air covered by foam:** Another kind of static mattress is filled with air covered by foam. The air is in interwoven but not interconnected air cells that have certain stretchiness (distensibility). That way when a person lies on the bed, the air cells

move and adjust to small changes in position. This kind of mattress is a good basic surface for a person who does not have a high-risk of developing bedsores.

Mattress Covers

All of these mattresses (except fluidized air) have Gortex™ covers. This is a slippery fabric that is often used to make rain gear for hiking. It allows moisture to travel in one direction (which is to say, not into the mattress) so that the mattress is protected from moisture, and bowel and bladder accidents. It is customary to cover these mattresses with only one sheet. The goal is to minimize the number of layers between the skin and the surface of the mattress. Too many layers will increase the risk of bedsores and negate the advantages of the mattress.

Gortex™ fabric reduces the friction and shear from the mattress that could also injure the skin when a person is repositioned (especially pulled up in the bed). Lying on these mattresses may feel "sweaty" and warm to the person in the bed and this can be a problem for a person with MS. The only real alternative is to control the temperature in the room where the person is sleeping by using air conditioning or fans.

Exercise and MS

Regular exercise is essential to maintaining a healthy lifestyle and is recommended for everyone, including individuals with multiple sclerosis (MS). People with MS often ask about the risks and benefits of exercise.

Some questions commonly asked about exercise are:

- Will exercise make my symptoms (like fatigue, pain and weakness) worse?
- Could exercise cause a relapse of my MS symptoms?
- Will my sensitivity to heat make it difficult or impossible for me to exercise?

Despite these concerns, current research shows:

- Exercise is a popular way to improve health, physical functioning and overall well-being for people with MS.
- There are safe ways to exercise for people with MS.
- Exercise, if done properly, DOES NOT make MS worse or cause a relapse of MS symptoms

Benefits

Exercise may have a number of benefits for individuals with MS, including:

- Improved mood (less depression and/or anxiety)
- Increased strength and mobility
- Decreased overall fatigue (even if you experience more fatigue immediately after exercise)

- Improved social interactions/self-esteem
- Improved bowel and bladder functioning
- Increased clarity of thinking
- Improved sleep
- Preventing weight gain

Some people with MS report feeling worse when they first start exercising, or feel more fatigued after exercise instead of energized. Generally, these symptoms get better as you become more accustomed to exercise and get in better physical shape.

Setting exercise goals

People with MS have a wide range of physical abilities so it is important for them to consult their health care provider to develop the best exercise program.

Individuals with MS should:

- Talk with their health care provider before starting an exercise program to get advice on where to start.
- Keep their health care provider informed about exercise progress
- Talk with a physical therapist to identify specific exercises to help achieve fitness goals safely.
- Keep track of progress:
 - Start with realistic and attainable exercise goals. Write down what exercises are performed, when, where and for how long.
 - Track exercise progress to help set new goals. Some people find that tracking their exercise activities helps them stay motivated.
- Document barriers to exercise, and bring notes to the health care provider to help brainstorm ways to overcome them.

About exercise

Exercise programs should include stretching, aerobic exercise (for increasing endurance), and strength-training.

Stretching

Improving flexibility in muscles is important for maintaining the ability to perform everyday activities and prevent injuries.

- Stretch for at least 10 minutes per day
- Stretch after a 5-10 minute warm-up to prevent injuries caused by stretching cold muscles.
- Stretch once again after the workout.
- Stretch slowly, holding each stretch for 30-60 seconds. Be sure to stretch all the body's major muscle groups.
- Yoga and tai chi include a variety of stretching exercises.

Aerobic activity

Any activity that causes the heart rate to increase for an extended period of time can be considered an aerobic activity. Some popular choices for people with MS are walking, swimming, cycling, and water aerobics.

- Experts recommend a goal of at least 150 minutes total of moderate-intensity (heavier than usual breathing and sweating) aerobic activity per week.
- When getting started, aerobic activity should increase slowly. Beginning with a shorter time period and working up to a 150-minute total over many weeks or as comfortable.
- If time is limited, several 10 minute periods of exercise in a day is recommended.

Strength training

Any kind of activity that causes the muscles to work against an applied force or weight. This helps maintain and improve the strength of the muscles. You can do strength training exercises can be performed with weights (such as small hand weights, wrist cuff weights, or even a soup can) elastic resistance bands.

- Strength training exercises should be done at least twice a week.
- Strength training exercises should vary so that they target all major muscle groups (legs, hips, back, abdomen, chest, shoulders, and arms).
- Core strength exercises should be included to strengthen the muscles in the stomach, back and around the pelvis. (Pilates and yoga include many core strength exercises.)

Preventing Problems

To prevent problems, individuals with MS should:

- Start slowly by not pushing themselves to do too much at once, especially if they have been inactive for a long time.
- Keep hydrated. Water is the best hydration-- drink more water before, during, and after exercise.
- Make sure to stay cool. This can mean exercising in front of a fan, in a cool room, or after the peak heat of the day. Or, by using a cooling device (vest, wrist bands, etc.).
- Take time to recuperate after exercise. Rest and replenish the body with protein and water.
- Do not continue to exercise during times when their MS symptoms are exacerbated. While exercise doesn't cause exacerbations of MS, it's better to conserve energy and rest during these periods.
- Use appropriate footwear.
- Be safe when they exercise by preventing falls and injuries that can happen when their body is tired or they have MS symptoms that affect their balance.

Determining Disability

Quantifying the Level of Disability

The Kurtzke Disability Status Scale (DSS) was developed by Dr. John Kurtzke in the 1950s to measure the disability status of people with multiple sclerosis. The purpose was to create an objective approach to quantify the level of functioning that could be widely used by health care providers diagnosing MS. The scale was modified several times to more accurately reflect the levels of disabilities clinically observed. The scale was renamed the Kurtzke Expanded Disability Status Scale (EDSS).

EDSS Scoring

The EDSS provides a total score on a scale that ranges from 0 to 10. The first levels 1.0 to 4.5 refer to people with a high degree of ambulatory ability and the subsequent levels 5.0 to 9.5 refer to the loss of ambulatory ability. The range of main categories include (0) = *normal neurologic exam*; to (5) = *ambulatory without aid or rest for 200 meters; disability severe enough to impair full daily activities*; to (10) = *death due to MS*. In addition, it also provides eight subscale measurements called Functional System (FS) scores. These subscale categories are listed below. The levels of function within each category refer to the eight functional systems affected by MS.

Functional Systems

The eight Functional Systems (FS) and their abbreviations are as follows:

1. Pyramidal (motor function) (P)
2. Cerebellar (C11)
3. Brainstem (BS)
4. Sensory (S)
5. Bowel and Bladder (BB)
6. Visual (V)
7. Cerebral or Mental (Cb)
8. Other (O)

Functional System Score

The Functional Systems (FS) are scored on a scale of 0 (low level of problems) to 5 (high level of problems) to best reflect the level of disability observed clinically. The "Other" category is not rated numerically, but measures disability related to a particular issue, like motor loss.

In contrast, the total EDSS score is determined by two factors: gait and FS scores. EDSS scores below 4.0 are determined by the FS scores alone. People with EDSS scores of 4.0 and above have some degree of gait impairment. Scores between 4.0 and 9.5 are determined by both gait abilities and the FS scores. For simplicity, many experts gauge the EDSS scores between 4.0 and 9.5 entirely by gait, without considering the FS scores.

The Scale

The EDSS is widely used and accepted as a valid tool to clinically measure and evaluate MS patients' level of functioning. Below is the EDSS:

Kurtzke Expanded Disability Status Scale

0	Normal neurological exam (all grade 0 in Functional Systems (FS); cerebral grade 1 acceptable).
1	No disability, minimal signs in one FS (i.e., one grade 1 excluding cerebral grade 1).
1.5	No disability, minimal signs in more than one FS (more than one grade 1 excluding cerebral grade 1).
2.0	Minimal disability in one FS (one FS grade 2, others 0 or 1).
2.5	Minimal disability in two FS (two FS grade 2, others 0 or 1).
3.0	Moderate disability in one FS (one FS grade 3, others 0 or 1), or mild disability in three or four FS (three-four FS grade 2, others 0 or 1).
3.5	Fully ambulatory but with moderate disability in one FS (one grade 3 and one or two FS grade 2) or two FS grade 3, others 0 or 1, or five FS grade 2, others 0 or 1.
4.0	Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability consisting of one FS grade 4 (others 0 or 1), or combinations of lesser grades exceeding limits of previous steps. Able to walk without aid or rest some 500 meters (0.3 miles).
4.5	Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability. (Usually consisting of one FS grade 4 (others 0 or 1) or combinations of lesser grades exceeding limits of previous steps. Able to walk without aid or rest for some 300 meters (975 ft.).)
5.0	Ambulatory without aid or rest for about 200 meters (650 ft.); disability severe enough to impair full daily activities (e.g., to work full day without special provisions). (Usual FS equivalents are one grade 5 alone (others 0 or 1); or combinations of lesser grades usually exceeding specifications for step 4.0.)
5.5	Ambulatory without aid or rest for about 100 meters (325 ft); disability severe enough to impair full daily activities. (Usual FS equivalents are one grade 5 alone (others 0 or 1); or combinations of lesser grades usually exceeding specifications for step 4.0.)
6.0	Intermittent or constant unilateral assistance (cane, crutch, or brace) required to walk about 100 meters (325 ft.) with or without resting. (Usual FS equivalents are combinations with more than two FS grade 3+.)
6.5	Constant bilateral assistance (canes, crutches, or braces) required to walk about 20 meters (65 ft.). (Usual FS equivalents are combinations with more than two FS grade 3+.)
7.0	Unable to walk beyond about 5 meters (16 ft.) event with aid, essentially restricted to wheelchair, wheels self in standard wheelchair a full day and

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	transfers alone; up and about in wheelchair some 12 hours a day. (Usual FS equivalents are combinations with more than one FS grade 4+; very rarely pyramidal grade 5 alone.)
7.5	Unable to take more than a few steps; restricted to wheelchair; may need aid in transfers, wheels self but cannot carry on in standard wheelchair a full day; may require motorized wheelchair. (Usual FS equivalents are combinations with more than one FS grade 4+.)
8.0	Essentially restricted to bed or chair or perambulated in wheelchair; but may be out of bed much of the day; retains may self-care functions; generally has effective use of arms. (Usual FS equivalents are combinations, generally grade 4+ in several systems.)
8.5	Essentially restricted to bed for much of the day; has some effective use of arm(s); retains some self-care functions. (Usual FS equivalents are combinations, generally grade 4+ in several systems.)
9.0	Helpless bed patient; can communicate and eat. (Usual FS equivalents are combinations, mostly grade 4.)
9.5	Totally helpless bed patient; unable to communicate or effectively eat/swallow. (Usual FS equivalents are combinations, almost all grade 4+.)
10	Death due to MS.

Caregiving and MS

Caregiver wellness and burden is something that doesn't get acknowledged very often. Approximately 25% of people in the United States who have MS need help with their daily activities or personal care. Most of this care comes from spouses. Care giving can affect couples' relationships in a variety of ways. A couple's partnership may shift gradually into a caregiver/patient relationship, making it very difficult on both people. There may be a gradual erosion of communication which can cause anxiety, guilt, frustration, resentment, and even cognitive impairment. Changes can occur in the sexual relationship whereby sexual intimacy is gradually replaced by the unwanted intimacy of care giving activities. Partners may engage in a contest over who "has it worse," the person with MS or the caregiver who is living with a disease that isn't even theirs.

Some caregivers become confused when thrust into a caregiver role and find it difficult to separate their role as a caregiver from their role as a spouse, lover, or friend. They expect their involvement to have a positive effect on the health and happiness of their loved one and this may be unrealistic for individuals who suffer from progressive diseases such as MS. Many caregivers experience significant stress and burnout that seems to have little to do with the partner's degree of physical impairment or length of time that they've had MS, and more to do with the feeling of feeling trapped.

Caregiver Burnout

Caregiver burnout is a state of physical, emotional, and mental exhaustion that may be accompanied by a change in attitude from positive and caring--to negative and unconcerned. Burnout can occur when caregivers don't get enough needed help or they try to do more than what they are able to do – physically, mentally, or financially.

Most caregivers are unable to recognize when they are suffering burnout and eventually get to the point where they cannot function effectively. This may lead to abuse and neglect in even the most loving couples. Burnout doesn't happen all at once, it happens in stages, or so-called "phases."

Phase I: The caregiver goes through a "honeymoon" period. They enter the caregiver relationship with idealism and have an eagerness to do well and make changes. But, after 16-18 months the situation becomes more routine and unexpected disappointments can and do occur.

Phase II: Caregivers may have decreased motivation and become less efficient, putting in more hours, but with poor effort and outcome. They may even voice complaints about care giving efforts and their role as a caregiver.

Phase III: Caregivers experience more serious problems, including chronic physical, mental, and behavioral symptoms. Physical signs can include changes in sleep patterns or appetite, illness, physical exhaustion, and loss of interest in activities previously enjoyed. Mental signs can include depression, emotional exhaustion, withdrawal, anxiety, frustration, and resentment. The physical and mental signs can manifest in one's behavior through unpleasant communication and interactions, wishing to get away, drinking, abuse and neglect, and becoming lost in the caregiver role. If these symptoms develop, help should be sought.

Supplemental Information

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Multiple Sclerosis
Post-Test

1. Which of the following statements regarding multiple sclerosis is TRUE? (p. 4)
 - A. The median age of onset is 19 years of age.
 - B. Twice as many men are affected by MS than women.
 - C. MS is more common in colder climates.
 - D. Native Americans have a relatively high rate of MS.
2. People who smoke are more likely to develop MS. (p. 5) A. True B. False
3. The first symptoms of MS often include _____. (p. 6)
 - A. Hearing loss, diminished sense of smell, and heart palpitations
 - B. Vision problems, weakness, and dizziness
 - C. Forgetfulness, tremor, and joint pain
 - D. Hair loss, dysphagia, and shortness of breath
4. "Lhermitte's sign," is a characteristic sensation of MS that feels like a sharp spike of electricity coursing down the spine. (p. 7) A. True B. False
5. The best and most current set of criteria for diagnosing MS is the _____. A positive diagnosis for MS requires _____. (p. 8)
 - A. McDonald Criteria; 2 attacks in time and at 2 locations
 - B. Sanford Assay; the presence of MS antibodies in the cerebral spinal fluid and neurological involvement
 - C. SMN Assessment; proof of cognitive deficits and muscle weakness
 - D. Sidney Criteria; at least one documented neurological deficit and positive MRI results
6. The most common subtype of multiple sclerosis is _____. (p. 9-10)
 - A. Relapsing-remitting MS
 - B. Secondary progressive MS
 - C. Progressive relapsing MS
 - D. Primary progressive MS
7. Which of the following is associated with a less favorable prognosis? (p. 10-11)
 - A. Female
 - B. Age of disease onset before 40
 - C. First attack consisting only of motor symptoms
 - D. Minor abnormalities on brain MRI scan at time of diagnosis
8. DMT should begin as soon as possible following a definite diagnosis of MS and determination of a relapsing course. (p. 12) A. True B. False
9. Fingolimod is a second line injectable DMT. (p. 13) A. True B. False
10. Approximately eighty percent of individuals with MS experience spasticity. (p. 16) A. True B. False
11. A score of ____ on the Modified Ashworth Scale indicates the effected part is rigid. (p. 17)
 - A. 1
 - B. 2
 - C. 3
 - D. 4

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12. What is the most common walking problem for people with MS? (p. 19)
- A. Foot drop
 - B. Trendelenburg
 - C. Ataxia
 - D. Festination
13. Which assessment tool is most commonly used to measure fatigue of MS patients? (p. 21)
- A. Fatigue Severity Scale
 - B. Profile of Mood States
 - C. Visual Analog measure
 - D. Fatigue Digital Inventory
14. Renal failure due to bladder dysfunction is common in MS. (p. 28) a. True B. False
15. Sexual dysfunction is a common symptom in MS and affects more than 75% of people living with the disease. (p. 32) A. True B. False
16. MS is sometimes associated with a condition called _____ that causes inappropriate and involuntary expressions of laughter, crying, or anger. (p. 34)
- A. pseudobulbar affect
 - B. transient affective disorder
 - C. emotional transitional disturbance
 - D. behavioral incongruence
17. Which cognitive function is usually NOT affected by MS? (p. 34-36)
- A. Attention and concentration
 - B. Executive functions
 - C. Visual perceptual skills
 - D. General intelligence
18. _____ is NOT a problem typically associated with MS? (p. 37-40)
- A. Nystagmus
 - B. Dysphagia
 - C. Pulmonary sarcoidosis
 - D. Heat intolerance
19. Exercise is beneficial for individuals with MS because it _____. (p. 44-46)
- A. Improves mood
 - B. Decreases overall fatigue
 - C. Improves bowel and bladder function
 - D. All of the above
20. An EDSS score of _____ indicates that the individual has some degree of gait impairment. (p. 47)
- A. less than zero
 - B. zero
 - C. zero to four
 - D. four or higher

C122823G122823R10223T31517