Your Client Has Multiple Sclerosis

Understanding the Challenge

Beatrice Turkoski

Multiple sclerosis (MS) is an autoimmune inflammatory disease that causes muscle weakness or spasticity, balance incoordination, sensory deficit, and fatigue. Any of these effects of MS can increase the risk for orthopaedic injury that places individuals with MS in an orthopaedic care setting. Nurses with an understanding of MS and the effect of MS on the body will be better prepared to educate peers about MS, act as advocates for individuals with MS in the orthopaedic setting, and offer optimum care that addresses the patient's MS as well as the orthopaedic problem. The following discussion addresses MS, its effect on the body, and various approaches to managing the disease, including a brief look at the current disease-modifying agents available to reduce or slow the neurologic damage caused by MS.

Multiple sclerosis (MS) is an incurable disease of the central nervous system that affects an estimated 350–400 thousand people with unpredictable disabling effects in the United States. Most of those individuals with MS will experience varying severity of muscle weakness, spasticity, loss of balance, sensory deficit, and fatigue. Any of these effects can put people with MS at risk of orthopaedic injury. Orthopaedic nurses who are knowledgeable about MS will be better prepared to provide optimum care and education for those individuals with this challenging disease.

The first section of the following discussion offers a brief overview of MS and the challenges it presents for both patients and professionals (National Multiple Sclerosis Society, 2012). In the second section, a look at some general strategies for addressing the effects of MS is followed by a review of agents currently available to modify the course of the disease. Resources for current information about MS are also identified (see Table 1).

Multiple Sclerosis—What Is It and Who Gets It?

Multiple sclerosis is an incurable inflammatory disease that affects neuronal transmission in the central nervous system. The inflammation acts to indiscriminately damage the protective myelin sheath covering long axon fibers and the axons themselves. When the myelin sheath is destroyed and the nerves are damaged, then the ability to conduct signals between the CNS and other parts of the body is disrupted.

The exact cause of MS is unknown, although it is thought to be primarily an autoimmune response to antigens. It can occur anytime between the ages of 10 and 80 years; however, the first attack usually occurs in young adults between 20 and 40 years of age. Females are two times more susceptible to MS than males. There is also a strong genetic link, especially in those people of northern European ancestry.

There is no set pattern to MS as far as which nerve cells are attacked and thus virtually any neurologic symptom can appear with MS depending on where the MS lesion occurs. The disease is insidious and unpredictable with four primary subgroups:

Relapsing MS (new symptoms appear in discrete episodic attacks [called relapses, flare-ups, or exacerbations] of worsening function followed by partial recovery periods)

Primary progressive MS (characterized by gradually worsening neurologic function without remission)

Secondary progressive MS (relapsing MS in the beginning may progress to progressive MS without relapses)

Progressive relapsing MS (progressive MS from the beginning but with episodes of increased worsening of neurologic function)

The disease follows no set pattern and it is often difficult to determine which type of MS a person has. Relapsing forms of MS appear to have active and quiet periods; however, evidence indicates that inflammatory lesions are continually developing until a neurologic threshold is reached and triggers an exacerbation (relapse). Typically relapses occur every 1–2 years, but occurrence is unpredictable and symptoms may differ from one relapse to another. Progressive MS also differs considerably in the rate of progression and degree of disability may vary over time (Fox, 2010).

The prognosis and life expectancy for individuals with MS are highly variable and depend on the subtype

Beatrice Turkoski, PhD, RN, Graduate Faculty—Advanced Practice Nursing, Kent State University College of Nursing, Kent, OH.

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Table 1. Sources of Information about Multiple Sclerosis

National Multiple Sclerosis Society - http://www.nationalmssociety.org

- Disease Management Consensus Statement about use of current disease-modifying agents (.pdf)
- Recommendations Regarding the Use of Cannabis in Multiple Sclerosis (.pdf)
- Assessment and Management of Cognitive Impairment in Multiple Sclerosis (.pdf)
- Changing Therapy in Relapsing Multiple Sclerosis: Considerations and Recommendations (.pdf)
- Rehabilitation: Recommendations for Persons with Multiple Sclerosis (.pdf)
- Management of MS-Related Fatigue (.pdf)
- Recommendations Regarding Corticosteroids in the Management of Multiple Sclerosis (.pdf)
- Nurse's Quick Reference (A guide to nursing management in MS) (.pdf)
- Multiple Sclerosis: The Nursing Perspective (.pdf)
- Multiple Sclerosis: The Nurse Practitioner's Handbook (.pdf)

Multiple Sclerosis Foundation - http://www.msfocus.org

of the disease and the degree of disability the individual experiences across time. Many individuals with MS are only mildly or moderately affected. In other cases, over time the damage may become cumulative and widespread with permanent gradually progressive neurologic deterioration (Compston & Coles, 2008; Fox, 2010).

Signs and Symptoms—The Effects of MS on the Body

A major challenge in diagnosing MS is that there is no one set pattern of symptoms that all individuals with MS experience. Symptoms are not the same for everyone, anyone with MS can experience any of a wide range of neurologic symptoms, and any of these symptoms may be mild, moderate, or very severe. Early signs and symptoms of MS can be gradual and relatively benign at first or the first attack can be devastating and extremely debilitating. In addition, the severity of neurologic effects may fluctuate over time and differ greatly between one relapse and another.

Vision problems (double vision, red-green distortion, blurry vision) are often one of the first symptoms some people have of MS. Fatigue is also a very common early indication of MS and may often occur when there are no other signs or early indications of disabilities. Multiple sclerosis fatigue is different and is generally more severe than normal fatigue: it can occur in the morning after a good night's rest, tends to worsen throughout the day, may be aggravated by heat and humidity, and may come on very suddenly. Fatigue is also one of the primary reasons that people with MS leave the workforce.

Most individuals with MS experience also some degree of mobility impairment due to either unilateral or bilateral muscle weakness or spasticity in their extremities. Multiple sclerosis can also cause dyscoordination, impaired balance, and numbness or loss of sensation that may affect mobility and physical activity. Bowel and bladder problems, speech and swallowing problems, and cognition problems are also common effects of disrupted axonal transmission.

The type of symptoms that occur is determined by the location of the nerve damage. Lesions in the cerebrum and cerebellum can cause balance, speech coordination problems, and tremors. Lesions in the motor nerve tracts are responsible for muscle weakness, spasticity, paralysis, vision problems, and bowel or bladder problems. Lesions in sensory nerve tracts may cause loss of sensation (numbness) or sensations of prickling or burning.

Diagnosing Multiple Sclerosis

Currently, there are no specific set of symptoms or physical findings and no one laboratory test that can, alone, confirm a diagnosis of MS. However, many times a careful medical history and a neurologic examination can be enough for a presumptive diagnosis. A neurologic examination must confirm that (1) there is neurologic evidence of damage in at least two separate areas of the CNS (including the brain, spinal cord, and optic nerves); (2) evidence that the damage occurred at least 1 month apart; and (3) a fair certainty the damage has no other reasonable explanation (e.g., exposure to certain toxins can also cause demyelination).

Then, even when there is a family history and clear neurologic evidence, magnetic resonance imaging (MRI) may be used to detect specific areas of demyelination and confirm the diagnoses. An MRI can also differentiate old lesions from those that are new or active and they are often used to monitor the disease progression. Evoked potential tests, where electrodes are placed on various parts of the head and body, may be used to help identify the area where the disruption in nerve transmission is occurring. A spinal Tap may also be used as a part of diagnosis.

Treating MS

Treatments for MS are aimed at (1) addressing the symptoms, (2) treating exacerbations, and (3) modifying the disease progression.

Strategies to Address MS Effects on the Body

Managing the symptoms of MS is a challenge because symptoms vary from individual to individual and may vary from episode to episode in the same person. Some people may experience mild symptoms for the course of the lifetime, whereas others may be more seriously affected right from the beginning and may experience progressively worsening symptoms. Most symptoms, however, can be managed with lifestyle modifications, assistive devices, physical therapy that focuses on maintaining function, and/or medications that target a specific symptom.

A major lifestyle modification for most people with MS involves adjusting their daily activities to address fatigue (Ayag, 2012). Fatigue affects more than 80% of people with MS and may often occur when there are no

other signs or early indications of disabilities. Multiple sclerosis fatigue is different and is generally more severe than normal fatigue. It can occur in the morning after a good night's rest, tends to worsen throughout the day, may be aggravated by heat and humidity, and may come on very suddenly. Thus, most individuals with MS will need to rearrange their entire daily schedule in order to pace all activity and ensure adequate rest periods.

Gait problems are very common among people with MS. These may be due to muscle weakness or spasticity, balance problems, or severe loss of sensation. Muscle weakness or spasticity may respond to specific targeted exercises or antispasticity medications. However, depending on the degree of disability, gait problems may require the use of mobility aids such as a cane, a walker, or, in extreme cases, a wheelchair.

When nerves that control bowel or bladder functions are affected, dietary changes and appropriate fluid intake may be all that is needed. In some situations, appropriate medications may be used to promote evacuation or facilitate bladder emptying. Swallowing difficulties may be addressed also with a change in diet and eating patterns or consult with a speech therapist.

Most medications used to address the symptoms of MS are not specific for use with MS. However, there is one medication approved specifically to address symptoms of MS. Dalfampridine (Ampyra) is used to improve walking speed for individuals with MS who have gait problems. It has been shown to help even those who use assistive devices such as a cane or walker. Dalfampridine is a potassium channel blocker that acts to prevent the leakage of potassium from demyelinated axons so there is less interruption of neuronal signals. It is contraindicated for individuals with a history of seizures or mild to moderate renal impairment and patients taking dalfampridine should be monitored for adverse effects such as urinary tract infection, dizziness or balance disorder, or rarely, MS relapse (Turkoski, Lance, & Tomsik, 2011).

Addressing the effects of MS on the body can differ greatly from person to person. Individuals (and their care providers) will need to address the changes that occur in their body. But, for most people with MS, any spontaneity in life is often no longer possible; constant caution, awareness, and preplanning are necessary to manage the effects of MS.

Treating Exacerbations

Exacerbations of MS are triggered by an inflammation in the central nervous system that damages the myelin sheath that protects the nerves. Exacerbations may last from a few days to several weeks or even months and can be mild or severe. Often they are self-limiting and require only symptom management. However, severe exacerbations are treated with high-dose corticosteroids (prednisone or methylprednisolone) to reduce the inflammation and lessen the extent of the axonal damage.

Disease-Modifying Agents

Before there were any disease-modifying agents available, there was little that could be done to slow the progression of MS. Up until now there were only eight disease-modifying agents to treat relapsing forms of MS and only one of these was oral. However, with the recent Food and Drug Administration approval of teriflunomide (Aubagio) there are now nine, two of which are oral. The Medical Advisory Board of the National Multiple Sclerosis Society has recommended that treatment with a disease-modifying agent should start immediately following the diagnosis of a relapsing form of MS. The Board further recommends that treatment should continue indefinitely unless there is clear evidence of no benefit or side effects are intolerable.

The currently available disease-modifying drugs are not designed to make anyone with MS "feel better," and they will not cure the disease. Rather, they primarily focus on the immune dysfunction and may lessen the frequency of exacerbations, slow the progression of relapsing forms of MS, and reduce the risk of significant disability. Currently, there is no agent approved for treating primary progressive disease.

The following is a brief overview of the nine disease-modifying agents currently approved for use with MS. Major cautions, limitations, and side effects are identified (Sandofi, 2012; Turkoski et al., 2011).

Beta interferons (first-line therapies)**:** Avonex (interferon beta-1a), Betaseron (interferon beta-1b), Extavia (interferon beta-1b), and Rebif (interferon beta-1a).

- *Action*. All of the beta interferon agents act to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations for patients who have experienced a first clinical episode and have MRI results consistent with MS. The exact mechanism of how they work to reduce frequency of relapses is unknown.
- *Pregnancy Risk Factor*. C.
- *Administration*. Avonex: Intramuscular weekly; Betaseron and Extavia: subcutaneous every other day:
- Rebif. subcutaneous three times a week.
- *Cautions*. Interferons have been associated with severe psychiatric events (mania, depression, psychosis, and suicidal ideation). They should be avoided in presence of severe psychiatric disorders. Extreme caution and close monitoring are required for persons exhibiting symptoms of depression or seizure disorder. Caution should be used with preexisting cardiovascular, pulmonary, or hepatic impairment. No known interactions with other medication other than a possible increase in levels of theophylline derivatives or Zidovudine when used concurrently with beta interferons.
- *Monitoring*. Liver function tests, thyroid function, hematology, and complete blood cell (CBC) count with differential should be done before administering an interferon and repeated periodically throughout treatment.
- *Reactions*. Rare anaphylactic reactions have occurred; the patient should be educated about signs and symptoms. Flu-like reactions (sometimes severe) are associated with interferon: the use of analgesics and antipyretics is recommended; these reactions may lessen over time.
- *Patient education*. Not a cure for MS. Appropriate injection procedure if self-administered. Contact the prescriber if any severe or prolonged reactions.

Glatiramer Acetate (Copaxone).

- *Action*. Induces and activates the T-lymphocyte suppressor cells that are specific against the myelin antigens, for example, blocks the autoimmune attach on myelin.
- *Pregnancy Risk Factor*. B.
- *Administration*. subcutaneous daily
- *Cautions*. Avoid use concurrently with BCG, live vaccines, natalizumab (Tysabri), roflumilast, and topical tacrolimus.
- *Adverse effects*. Immediate postinjection reaction (flushing, chest tightness, dyspnea, palpitations) self-resolving and occurs less often with subsequent injections. Nausea, rash, infection, and flu-like symptoms.
- *Patient education*. Not a cure for MS. May reduce severity and incidence of exacerbations. Rotate and monitor injection sites daily. Appropriate injection procedure for self-administration is important to prevent severe skin and tissue damage. May experience postinjection reaction with first infection and occasionally with subsequent injections. Contact the prescriber for unusual or prolonged reactions.

Fingolimod (Gilenya).

- *Action*. Causes inflammatory cells (lymphocytes) to get trapped in lymph nodes so there are fewer lymphocytes available in the CNS, which reduces central inflammation and neuron damage.
- *Pregnancy Risk Factor*. C.
- *Administration*. Oral daily.
- *Cautions*. Do not use in presence of acute or chronic infections (may increase risk of infection due to reduction of lymphocytes). Use caution with concurrent immunosuppressant, immune modulation, or antineoplastic medications. Use caution with severe hepatic impairment, history of diabetes, or uvelitis. Avoid concurrent use with BCG, live vaccines, natalizumab, roflumilast, and topical tacrolimus.
- *Monitoring*. Ophthalmic examination should be done prior to therapy and 3–4 months after treatment starts (macular swelling). Electrocardigram, CBC, liver enzymes, and bilirubin prior to treatment. CBC periodically during treatment. Evaluate need for varicella vaccine before starting therapy. Blood pressure throughout therapy. Observe for 6 hours following first dose—severe bradycardia may develop.
- *Adverse effects*. Immediate postinjection reaction (bradycardia may occur within 1 hour of therapy with maximal decrease occurring 6 hours after the dose). Flu-like symptoms, diarrhea, cough, opportunistic infection, and vision changes.
- *Patient education*. Not a cure for MS. May reduce severity and incidence of exacerbations. Need to have heart rate monitored for 6 hours following first dose.
- Explain possible reactions and instruct client to contact the prescriber if signs of opportunistic infection or if side effects are severe or unusual.

Natalizumab.

- *Action*. Monoclonal antibody—interferes with the movement of potentially damaging immune cells from bloodstream to brain and spinal cord.
- *Limitations*. Reserved for cases where there has been inadequate response or inability to tolerate any other agent. Patients must be enrolled in Tysarbi Care Program.
- *Pregnancy Risk Factor*. C.
- *Administration*. Intravenous (over 1 hour) every 4 weeks.
- *Caution*. Not to be used with any other disease-modifying agent. Increases risk for progressive multifocal lukoencephalopathy (PML), which causes death or severe disability as a result of JC virus. Prior use of immune suppressing drugs increases the risk of developing PML. Discussion with patients should review the benefits and risks of PML.
- *Monitoring*. Liver enzymes, CSF analysis, MRI scan. Test for antibodies to JC virus prior to therapy. Monitor response every 6 months (Tysarbi Care Program). Observe closely during and for 1 hour following infusion for hypersensitivity reaction: patients who demonstrate an infusion hypersensitivity reaction should discontinue immediately and not be re-treated.
- *Adverse effects*. Infusion reaction. Hepatotoxicity, increased fatigue, visual field defects, anxiety, cognitive changes, aphasia, ataxia, opportunistic infection.
- *Patient education*. Not a cure for MS. May experience infusion reaction (you will be monitored during and after infusion). Identify possible adverse effects and instruct the client to contact the prescriber if adverse effects are severe or prolonged.

Mitoxantrone (Novantrone).

- *Action*. A type II topoisomerase inhibitor that disrupts DNA synthesis in cells (antineoplastic chemotherapy drug).
- *Limitations*. Approved for both secondary progressive and relapsing-remitting MS who have not responded to first-line agents.
- Cytotoxic. Total cumulative lifetime dose is limited according to body mass to limit cardiac problems.
- *Pregnancy Risk Factor*. D (pregnancy should be ruled out before beginning therapy.)
- *Administration*. Intravenous every 3 months over 2–3 years (until maximum lifetime cumulative dose is reached).
- *Cautions*. Myelosuppression (not recommended in presence of preexisting myelosuppression), myocardial toxicity—(risk increases with cumulative dosing), increases risk of acute myelogenous leukemia, should not be used in presence of hepatic impairment. Desiccant—avoid extravasation (can cause severe tissues damage).
- Risks of cardiotoxicity should be discussed with the patient.
- *Monitoring*. Pregnancy status (before and during treatment); cardiac status (electrocardigram with

left ventricular ejection fraction) prior to each dose and at appearance of any cardiac symptoms (individuals with MS should have cardiac monitoring annually following discontinuation of therapy due to delayed cardiotoxicity); CBC count and liver function tests prior to infusions.
- *Adverse effects*. Cardiotoxicity, acute myelogenous leukemia, hypersensitivity reactions, myelosuppression, gastrointestinal upset, hyperglycemia, opportunistic infections, gastrointestinal upset (diarrhea, constipation, nausea, and vomiting), hair lose, mouth sores, and edema.
- *Patient education*. Not a cure for MS. Urine, saliva, tears, sweat, and white of eyes may turn blue-green for 24 hours postinfusion. Identify possible adverse effects and instruct the patient to notify the prescriber if any effects are severe or prolonged.

Teriflunomide (Approved September 13, 2012).

- *Action*. Teriflunomide is a pyrimidine synthesis inhibitor that acts to reduce the number of activated lymphocytes in the central nervous system.
- *Limitations*. Approved for relapsing forms of MS.
- *Pregnancy Risk Factor*. Pregnancy contraindicated (pregnancy registry available).
- *Administration*. Oral daily–-with or without food.
- *Cautions*. Avoid use in presence of hepatic impairment, pregnancy, or serious infection. If necessary, to discontinue may require accelerated elimination procedure (effects may continue for up to 2 years). Avoid concurrent use with leflunomide, hormonal contraceptives.
- *Monitoring*. Pregnancy (before, during, and for 2 years following discontinuation), signs and symptoms of infection (immunosuppression effect), blood pressure, CBC count (prior to therapy), and liver function tests (6 months prior to therapy and at least monthly for 6 months). Monitor INR in concurrent use of warfarin. Monitor response with the concurrent use of drugs metabolized by CYP2C8 or CYP1A2.
- *Adverse effects*. Hepatotoxicity, immunosuppression, alopecia, diarrhea, nausea, paresthesia (peripheral neuropathy that is not related to the MS), hypertension, renal failure, severe skin reaction, hypertension.
- *Patient education*. Not a cure for MS. May reduce severity and incidence of exacerbations. Will need to have laboratory testing on regular basis. Must avoid pregnancy for up to 2 years following discontinuation (can cause severe harm to fetus) malformation. Explain possible reactions and instruct client to contact the prescriber with signs of hepatic changes, skin reaction, opportunistic infection, numbness in extremities that is different from symptoms of MS, or if side effects are severe or unusual.

The choice of whether or not to use a disease-modifying medication and the decision about which one to use must be a matter for the individual and their professional care provider to make. None of these agents are curative and none will repair neurologic damage that has been done. Early use of disease-modifying agents, however, may reduce the number of relapses and slow the progress of inflammatory destruction and may provide individuals with MS considerable more time without serious disability.

Conclusion

The diagnosis of MS is challenging, the efficacy of any current treatment is variable, a cure is nonexistent, and the symptoms make daily life difficult for the majority of those who have to live with MS. While some people experience a mild and fairly benign form of MS, others have a more severe form that causes muscle weakness or spasticity, balance incoordination, or sensory deficit and fatigue. Any of these effects of MS can increase the risk for an injury that would place them in an orthopaedic care setting.

Nurses with knowledge of MS can optimize the quality of care for patients who have MS by developing care protocols that address the challenges of MS and the effects of MS on the body (Ayag, 2012). One major consideration in care planning is recognizing that, for the individual with MS, a specific daily routine for activity, rest, diet, and elimination is not just a whim or a quirk. For patients with MS, intolerance for flexibility or resistance to change in routine is not just stubbornness, but rather it may be the only way these individuals maintain some control over their symptoms. A nurse can play a pivotal role in educating multidisciplinary team members about MS to and advocating to schedule all activities around the goal of preserving patient strength and reducing undue fatigue.

Medication education for both peers and patients is another nursing responsibility. Many professionals are not well informed about the MS-disease modifying drugs and the rationale behind their use. And, individuals with MS who are using one of these medications may benefit from additional teaching and reinforcement for self-administered injection procedures.

Whether a patient enters the orthopaedic care area as a result of MS damage or because of something unrelated to the MS, the nurses who understand MS will be invaluable. Having MS is, for most people, a constant challenge and having caregivers who are understanding and knowledgeable about MS will not only optimize care but will also lessen the patient's anxiety and fear.

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