Nursing Management of the Patient with Multiple Sclerosis

AANN and ARN Clinical Practice Guideline Series

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Preface

In 1997, the American Association of Neuroscience Nurses (AANN) created a series of patient care guidelines, the AANN Reference Series for Clinical Practice, to meet its members' needs for educational tools. To better reflect the nature of the guidelines and the organization's commitment to developing each guideline based on current literature and evidence-based practice, the name of the series was changed in 2007 to the AANN Clinical Practice Guideline Series. This guideline represents a milestone in the series because AANN has now partnered with the Association of Rehabilitation Nurses (ARN) and the International Organization of Multiple Sclerosis Nurses (IOMSN) in the development of this guideline. This is the second guideline to be developed collaboratively between AANN and ARN and promotes evidence-based practice for the adult patient with multiple sclerosis (MS) across the continuum of care.

Nursing care of patients with MS and their families or care partners has evolved from a focus on interventions during periods of crisis to a focus on symptom management, wellness, prevention of disease worsening, and empowerment. The goal of this guideline is to offer evidence-based recommendations on nursing activities that have the potential to maximize outcomes for adults with MS. Not all recommendations concern activities independently performed by registered nurses (RNs), but nurses are responsible for implementing and monitoring the outcomes of these activities. The evidence presented here may help nurses make appropriate choices when caring for patients with MS. Dependent on scope of practice regulations, advanced practice nurses may have independent or collaborative responsibilities for activity performance; thus, this guideline may assist them in the management of patients with MS.

Resources and recommendations must describe the best practices that can enable RNs to provide optimal care for persons with MS. Accordingly, adherence to these guidelines is voluntary, and the ultimate determination regarding their application must be made by practitioners in light of each patient's individual circumstances. This reference is an essential resource for nurses providing care to the adult patient with MS. It is not intended to replace formal learning but rather to augment clinicians' knowledge base and provide a readily accessible reference tool. The nursing profession, AANN, ARN, and IOMSN are indebted to the volunteers who have devoted their time and expertise to this valuable resource, which was created for those who are committed to excellence in the care of patients with MS.

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I. Search Strategy and Levels of Evidence

A. Search strategy

A computerized search of MEDLINE, Cochrane, and the Cumulative Index to Nursing and Allied Health Literature was performed by using *multiple sclerosis*, *symptom*, *disease management*, *nursing*, and *education* as keywords. The search was restricted to works in English and adults. The reference lists of identified articles were also searched for additional, relevant references including books, guidelines, and articles. A panel of nursing experts determined the level of evidence for each study included in the guideline, summarizing the level of evidence for each recommendation.

B. Levels of evidence supporting the recommendations

- Class I: Randomized controlled trial without significant limitations or meta-analysis
- Class II: Randomized controlled trial with important limitations (e.g., methodological flaws or inconsistent results), observational studies (e.g., cohort or case-control)
- Class III: Qualitative studies, case study, or series
- Class IV: Evidence from reports of expert committees and/or expert opinion of the guideline panel, standards of care, and clinical protocols.

The Clinical Practice Guidelines recommendations for practice are established on the basis of the evaluation of the available evidence (AANN, 2005; adapted from Guyatt & Rennie, 2002; Melnyk, 2004):

- Level 1 recommendations are supported by Class I evidence.
- Level 2 recommendations are supported by Class II evidence.
- Level 3 recommendations are supported by Class III and IV evidence.

II. Scope of the Problem: Definition, Natural History, and Epidemiology of Multiple Sclerosis (MS)

A. Definition

1. MS is a progressive, inflammatory, neurodegenerative demyelinating disease of the central nervous system (CNS) predominantly affecting white matter (Miller et al., 2008). It is the most common nontraumatic cause of neurologic disability in young adults (Fleming & Carrithers, 2010). The cause of MS is unknown; however, research suggests that an abnormal autoimmune response to myelin develops in genetically susceptible individuals after exposure to one or more environmental agents.
2. The autoimmune cascade results in an inflammatory response against self-antigens in the CNS, causing demyelination and axonal damage. Scarring visible at magnetic resonance imaging (MRI) represents these pathological changes. Demyelination in the CNS disrupts conduction in nerves, causing the hallmark sensory, motor, and cognitive signs and symptoms of MS (De Jager et al., 2009; Harris & Halper, 2004; Thrower, 2009; Trapp et al., 1998).
3. MS may present as a case of monosymptomatic or polysymptomatic neurologic abnormality. Most early cases are characterized by periods of disease freedom with superimposed relapses characterized by signs and symptoms of CNS dysfunction (Confavreux, Vukusic, Moreau, & Adeleine, 2000).

B. Epidemiology

1. MS affects approximately 400,000 people in the United States alone, and more than 50,000 Canadians (Costello & Halper, 2010a**;** Miller et al., 2008). The projected prevalence rate of MS for the white population in the year 2000 was 191/100,000, and the incidence rate was 7.3/100,000 person years at risk (Kantarci & Weinshenker, 2005; Kantarci & Wingerchuk, 2006). There are 12,000 new cases of MS diagnosed per year in the United States (Alonso & Hernán, 2008).
2. Review of incidence data suggests the lifetime risk of MS is 2.5% for women and 1.4% for men (Alonso & Hernán, 2008). MS is generally at least twice as common in women as it is in men, with some data suggesting the male-to-female ratio is as high as 1:4 (Beck et al., 2003; Kantarci & Wingerchuk, 2006; Vukusic & Confavreux, 2007).
3. The age of onset peaks between 25 and 35 years of age. Men may have a later onset of disease and a worse prognosis (Kantarci & Wingerchuk, 2006; Vukusic & Confavreux, 2007). Despite the young age of disease onset and the potential for neurologic disability, the life expectancy of people with MS is only slightly reduced (Compston et al., 2006). Fifty percent of MS patients will die from causes other than MS (Sadovnick, Eisen, Ebers, & Paty, 1991).

C. Types of MS

1. There are four defined clinical types of MS: relapsing-remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), and progressive-relapsing MS

(PRMS). These types are described by relapses, remission, and chronic progression (increasing disability as time passes). Relapse can be followed by full or partial recovery. Disease severity varies considerably among people with MS, no matter the type ascribed to them (Compston et al., 2006).

2. Initially, 85% of cases are RRMS, and 15% are PPMS. When a person with RRMS begins to acquire disability, SPMS is said to occur. This phase of the disease evolves owing to progressive axonal injury. The median time to conversion from RRMS to SPMS is 19 years, and 75% will reach this phase by 25 years. Approximately 40% of progressive cases (SPMS and PPMS) still experience relapses (Compston et al., 2006; Frohman et al., 2005; Kantarci, 2008; Runmarker & Andersen, 1993). Nonetheless, in progressive patients, the course of disability progression is not affected by relapses (Confavreux, Vukusic, & Adeleine, 2003).
3. There is a theory that the clinical subtypes of MS may be separate phenotypes of one disease process. The differing types of MS may represent various points along the spectrum of MS. However, distinct pathophysiological processes have not yet been identified (Confavreux & Vukusic, 2006; Lublin, 2010).

D. Natural history of the disease
   1. Despite the unpredictable nature of MS, results of cohort studies provide general prognostic factors.
   2. Better disease prognosis is associated with younger age at onset, female sex, monosymptomatic presentation (particularly optic neuritis or sensory symptom), complete recovery from relapse, a long interval between presentation and second event, relapsing course, and a low number of relapses (Lisak, 2001; Miller et al., 2008).
   3. Poor long-term prognosis has been associated with male sex; older age at disease onset (> 40 years); motor, cerebellar, or sphincter symptoms at initial presentation; polysymptomatic presentation; frequent attacks in the first 5 years; short interval between first two attacks; short time to reach an Expanded Disability Status Scale (EDSS) score of 4; and a progressive course (Bergamaschi, Berzuini, Romani, & Cosi, 2001; Compston & Coles, 2002; Confavreux, Vukusic, Moreau, & Adeleine, 2000; Riise et al., 1992; Trojano et al., 1995; Vukusic & Confavreux, 2007). *Note: A standard measure of disability in MS is the EDSS score. Higher EDSS scores indicate higher levels of disability (Kurtzke, 1983).*

E. Genetics
   1. Family history is the strongest known risk factor for MS. In fact, MS is 20–40 times more common among first-degree relatives, with a rapid decrease in risk with degree of relatedness (Ascherio & Munger, 2008; Kantarci, 2008; Kantarci & Wingerchuk, 2006; Vukusic & Confavreux, 2007; Weinshenker, 1996).
   2. There have been at least 13 genetic susceptibility loci identified by scientists (Australia and New Zealand Multiple Sclerosis Genetics Consortium [ANZgene], 2009; International Multiple Sclerosis Genetics Consortium, 2007; De Jager et al., 2009), and it has been suggested that 10–50 genes are related to genetic susceptibility to MS (Baranzini, 2010).

F. Environmental risk factors
   1. The estimated genetic risk of MS is 25%–35% based on monozygotic twin studies (Kantarci, 2008). Incomplete penetrance of heritability provides evidence that there are environmental factors at play in MS susceptibility. MS is more common in Europe, the United States, Canada, New Zealand, and Southern Australia than in Asia, the tropics, and the subtropics. The incidence and prevalence increases with latitude relative to the equator. Review of the MS literature suggests there may be attenuation in the latitude gradient, or *MS belt*, reinforcing the role that environmental factors play in MS etiology (Ascherio & Munger, 2008; Bakshi, Hutton, Miller, & Radue, 2004; Franciotta, Salvetti, Lolli, Serafini, & Aloisi, 2008).
   2. Additionally, migrant studies suggest one assumes the risk of one's final place of residence, rather than of one's birthplace, if migration occurs in childhood (Zivadinov et al., 2009).
      a. The strongest support for environmental risk factors is based on geographic distribution and studies of migration to Israel, from the United Kingdom to South Africa, from the United Kingdom to Australia, and from the United Kingdom to the United States (Alter, Kahana, & Loewenson, 1978; Alter, Leibowitz, & Speer, 1966; Dean & Kurtzke, 1971; Hammond, English, & McLeod, 2000; Kurtzke, Beebe, & Norman, 1985).
      b. Studies show that the risk of MS is low in migration from the Far East to the United Kingdom and North America as compared with that of migration from India, when

the risk of MS increases in the second generation. Typically, migration studies are not able to establish timing of environmental exposures (Ebers, 2008; Elian, Nightingale, & Dean, 1990).

3. Other strong environmental factors associated with MS include lack of vitamin D exposure, smoking, and the Epstein-Barr virus (EBV).
   a. Past sun exposure and vitamin D supplementation have been associated with decreased risk of MS (Coo & Aronson, 2004; Marrie, 2004; Munger, Levin, Hollis, Howard, & Ascherio, 2006; Munger, et al., 2004; Soilu-Hänninen et al., 2005).
   b. Heavy smoking (defined as more than 25 pack-years) increases MS risk by approximately 70%, and the increase in risk is dose responsive (Ascherio & Munger, 2007; Hedström, Bäärnhielm, Olsson, & Alfredsson, 2009; Hernán et al., 2005; Hernán, Olek, & Ascherio, 2001). Among MS patients, smoking is associated with higher levels of disability, greater number of enhancing T2 and T1 lesions, greater lesion volume, and more brain atrophy (Zivadinov et al., 2009).
   c. Data from several Class II studies support the association of EBV with MS. There is evidence that the presence of EBV in plasma is associated with increased risk of MS (Wagner, Munger, & Ascherio, 2004). MS risk increases sharply after EBV infection (Levin, Munger, O'Reilly, Falk, & Ascherio, 2010).

G. MS symptoms
   1. MS is associated with numerous symptoms, and MS symptoms vary widely from individual to individual. Symptoms of MS are unpredictable and often interfere with activities of daily living (ADLs).
   2. Primary symptoms of MS are caused by the dysfunction of nerve conduction because of demyelination, inflammation, and axonal loss in the CNS (Lisak, 2001).
   3. MS symptoms include spasticity, fatigue, pain, disturbance of elimination (bladder or bowel), unilateral vision loss, vertigo, Lhermitte's sign, sexual dysfunction, cognitive dysfunction, ataxia, tremor, depression, oculomotor dysfunction, dysarthria or dysphonia, dysphagia, and seizure (Compston et al., 2006; Lisak, 2001; Harris & Halper, 2004; Stuke et al., 2009).
   4. A relapse (also known as an *attack* or *exacerbation*) is defined as a new neurologic symptom, or worsening of previous symptom(s), lasting more than 24 hours that does not have an alternative explanation. Pseudorelapses are related to infection or heat exposure and do not represent new disease activity.

H. Effect of the diagnosis
   1. An MS diagnosis is a life-altering event. MS is a chronic, often disabling disease that may affect the physical, economic, psychological, and social aspects of a patient's life. The unpredictable nature and varied symptoms of the disease mean that patients face a future of uncertainty.
   2. Managing MS consists of primarily managing the symptoms that are associated with the disease. For example, time management and conservation of energy have been the recommended forms of managing fatigue. If tremors and gait imbalance are the major presenting symptoms, medications and/or physical therapy have been shown to be helpful.
   3. The financial effect of MS should be considered, because treatment can be costly. There are a number of disease-modifying therapies (DMTs), including interferon-beta-1a (IFN β-1a), IFN β-1b, glatiramer acetate, and natalizumab. Other DMTs being used or investigated include mitoxantrone and cyclophosphamide. Both direct and indirect costs may or may not be reimbursed by insurance plans, which vary individually. Costs and quality of life (QOL) are significantly correlated with functional capacity (Kobelt, Berg, Atherly, & Hadjimichael, 2006).
   4. Debilitating diseases with no cure can be a burden financially for patients and families. Patients with MS may face loss of employment. In addition, the financial effect of the disease may be related to the cost of needed services, other care providers, and possibly the need to modify the patient's home environment to accommodate changing abilities.
   5. RRMS affects a majority of the MS population. Although there are several DMTs for RRMS, not all are available for the same cost. Goldberg and colleagues (2009) evaluated the 2-year effectiveness of four DMTs used for RRMS—glatiramer acetate, IFN β-1an intramuscular (IM) injection, IFN β-1a subcutaneous (SC) injection, and IFN β-1b SC injection. These four DMTs are the most cost-effective treatments for RRMS (Goldberg et al.).
   6. QOL may be affected by the financial costs related to MS (De Judicibus & McCabe, 2007). Life-altering decisions can create an enormous amount of uncertainty, followed by

making adjustments to accommodate the change. Financial stress can be caused by loss of income and the strain that patients and their families undergo as they adjust to loss and the possible increased need to cover the cost of required medical and related services (De Judicibus & McCabe).

7. The disease affects the caregivers as well. In a small qualitative study in the United Kingdom, interviews were conducted of 8 partners who lived and cared for a person with MS (Mutch, 2010). The study showed that disability due to MS significantly affected their lifestyles after 20 years of marriage; partners felt obligated to continue caring for the affected spouse and consequently lost their identity as husband or wife. Partners also yearned for independence and were not satisfied with their own QOL because MS care was a daily occurrence (Mutch, 2010). Caregivers also go through life-altering decisions and changes secondary to their partner's health, and as a result they have their own needs (Corry & While, 2008). As the disease progresses, caregivers may be increasingly required to care for the patient because of the debilitating nature of the disease (Buhse, 2008). As a result, caregiver burden becomes a cluster of physical, social, economic, and psychological responses—caregivers who are highly burdened were shown to have lower QOL and higher risk for depression (Buhse). Further study of the caregiver population is needed.

Recommendations: The model of nursing care in MS includes establishing, continuing, and sustaining care along the MS spectrum of new or probable MS, relapsing forms of MS, progressive MS, and advanced MS (Level 3). Nurses should facilitate treatment and symptom management, promote and enhance function, and support a QOL of adults with MS and their family-care partners that is wellness focused (Level 3). Nurses use evidence-based knowledge to determine an effective course of action for MS patients with specific needs (Level 2). Nurses act as advocates to ensure that patients and their family-care partners have access to needed care and assistance in using resources crucial to managing MS (Level 2). Nurses should help patients locate and develop appropriate resources and initiate contacts as needed (Level 2).

III. Classification of MS

A. Introduction

1. MS is an immune-mediated disease of the CNS with inflammatory and degenerative characteristics (Siva, 2006). The clinical course may be variable. In 1996 a formal classification of MS clinical subgroups was proposed from an international survey of MS clinicians, and standardized definitions for the most common clinical courses of MS were defined.
   a. The clinical course was defined by the following descriptions: RRMS, PPMS, SPMS, PRMS, benign MS, malignant MS (Lublin & Reingold, 1996).
   b. The terms *benign* and *malignant* MS are used to describe relatively mild and very progressive courses of MS, respectively. Both are relatively rare.
2. When patients receive a disease diagnosis under one of the above classifications, both the patients and families may need further explanation to understand the disease's clinical course; the importance of disease-modifying therapy and symptom management, if appropriate; and the need for regular follow-up with the neurologist and other care providers.

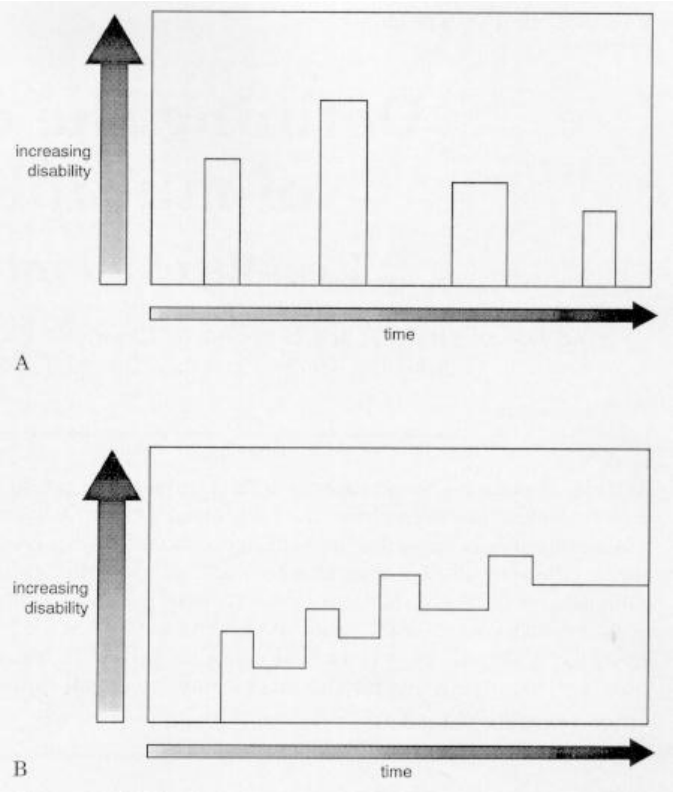
B. RRMS

1. RRMS is marked by periods of acute decline or exacerbations in neurologic function followed by a variable degree of recovery with stable periods between attacks (Lublin & Reingold, 1996). Patients may experience total or partial remission of symptoms (**Figure 1**).
2. *Relapse* (exacerbation) is the appearance of a new symptom or reappearance of a prior symptom lasting more than 24 hours (Lublin & Reingold, 1996). *Pseudoexacerbation* refers to changes in neurologic function triggered by infection, fever, heat, and fatigue. These relapses occur from decompensation of existing CNS scars and are not indicative of new inflammatory CNS lesions (Birnbaum, 2009).
3. Onset of neurologic changes may occur over several hours or appear over days to weeks. Symptoms may be focal and can spread over other body regions. A relapse may last from a few days to several weeks or more. Full or partial recovery may occur with the disease remaining stable between relapses. This relapsing-remitting course is seen in approximately 80%–85% of patients (Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000). Treatment with immune-modulating therapies and corticosteroids is indicated.

C. PPMS

1. PPMS presents with a gradual onset of symptoms that worsen over time with minor fluctuations that progress and do not reverse (**Figure 2**).

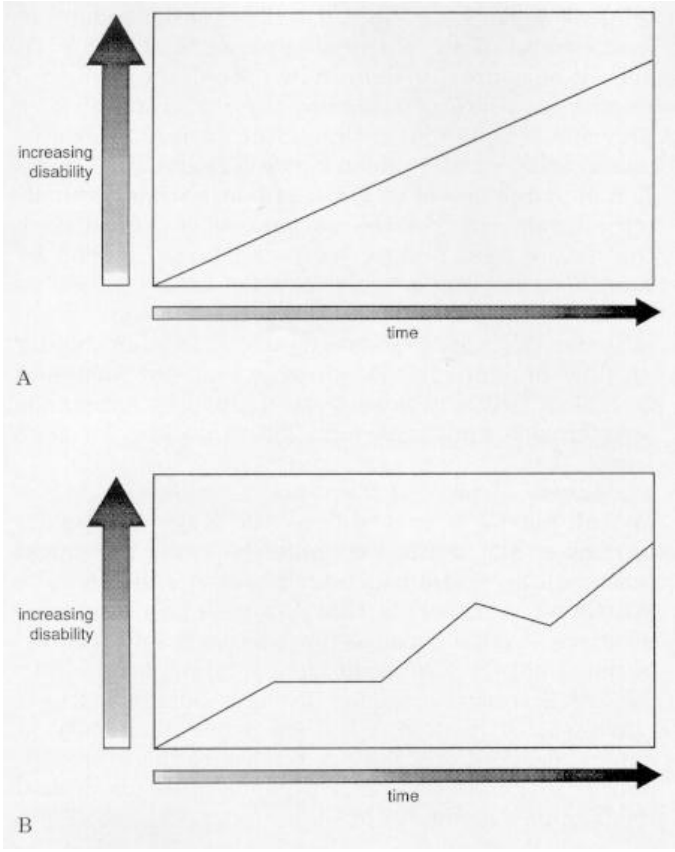
Figure 1. Characterization of the natural history of relapsing-remitting multiple sclerosis



Relapsing-remitting (RR) MS is characterized by clearly defined acute attacks with (A) full recovery or (B) sequelae and residual deficit upon recovery. Periods between disease relapses are characterized by lack of disease progression. From Lublin, F. D., & Reingold, S. C. Defining the clinical course of multiple sclerosis: Results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis Neurology, 46*(4):907–911. Reproduced with permission from Wolters Kluwer Health.*

2. PPMS occurs in 10%–15% of patients, and age of onset is approximately 10 years older than that seen in RRMS (mean of 40 years versus 30 years).
3. Most common presenting symptoms include progressive spastic paraparesis, usually in the lower extremities, as well as impaired mobility with weakness, stiffness, and dragging of the legs. Exercise-related fatigable weakness, urinary urgency, urge incontinence, and erectile dysfunction are also common (Miller & Leary, 2007).
4. PPMS may vary significantly from patient to patient. Some may experience profound disability within 1–2 years, whereas in others, progression may occur over decades. The pathophysiology of PPMS is thought to be different from that of RRMS, and, therefore, long-term immune-modulating therapies are not indicated for treatment (Birnbaum, 2009).

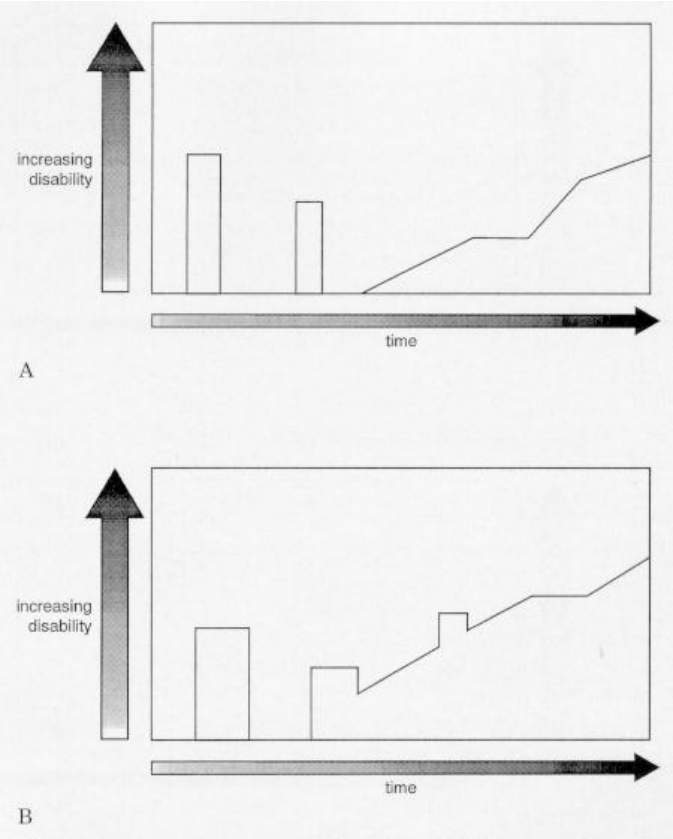
Figure 2. Characterization of the natural history of primary progressive multiple sclerosis



Primary progressive (PP) MS is characterized by disease showing progression of disability from onset (A) without plateaus or remissions or (B) with occasional plateaus or temporary minor improvements. From Lublin, F. D., & Reingold, S. C. Defining the clinical course of multiple sclerosis: Results of an international survey. National Multiple Sclerosis Society (US) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis Neurology, 46*(4):907–911. Reproduced with permission from Wolters Kluwer Health.*

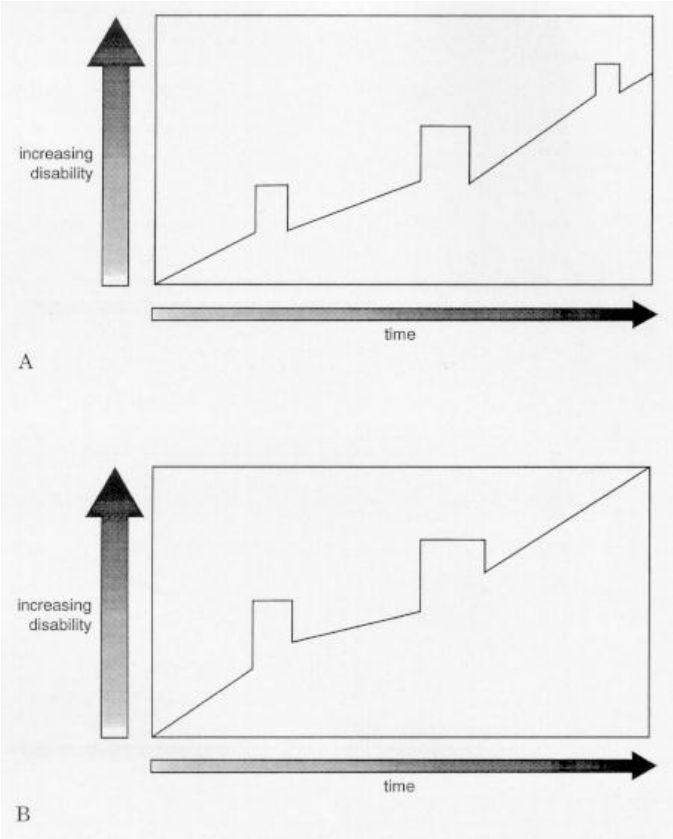
D. SPMS
   1. SPMS is seen as the long-term outcome of RRMS, which occurs once the baseline between relapses becomes progressively worse. Patients experience a gradual worsening of the disease that is independent of continued exacerbations (**Figure 3**; Lublin & Reingold, 1996).
   2. Approximately 50% of patients with RRMS will develop SPMS with time. The frequency of relapses decreases, and patients experience an increase in disability. The transition from RRMS to SPMS may be rapid or gradual. SPMS patients also present with fewer acute inflammatory changes at brain and spine magnetic resonance imaging (MRI); therefore, long-term immune-modulating therapies are not indicated for treatment (Birnbaum, 2009).

Figure 3. Characterization of the natural history of secondary progressive multiple sclerosis



Secondary progressive (SP) MS begins with an initial RR course, followed by (A) progression of variable rate that may also include (B) occasional relapses and minor remissions. From Lublin, F. D., & Reingold, S. C. Defining the clinical course of multiple sclerosis: Results of an international survey. National Multiple Sclerosis Society (US) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis Neurology, 46*(4):907–911. Reproduced with permission from Wolters Kluwer Health.*

Figure 4. Characterization of the natural history of progressive-relapsing multiple sclerosis



Progressive-relapsing (PR) MS shows proession from onset but with clear acute relapses (A) with or (B) without full recovery. From Lublin, F. D., & Reingold, S. C. Defining the clinical course of multiple sclerosis: Results of an international survey. National Multiple Sclerosis Society (US) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis Neurology, 46*(4):907–911. Reproduced with permission from Wolters Kluwer Health.*

E. PRMS
   1. PRMS appears to progress clinically as seen in PPMS with acute relapses, and full recovery may or may not occur. There is continued progression between relapses (**Figure 4**; Lublin & Reingold, 1996).
   2. PRMS has a progressive onset with acute inflammatory activity in the CNS with relapses. These relapses can respond to short-term antiinflammatory therapies. The benefit of long-term immune-modulating therapies is uncertain at this time (Birnbaum, 2009).

F. Benign MS
   1. All neurologic systems of patients with benign MS appear to be fully functional 15 years after the onset of disease (Lublin & Reingold, 1996).
   2. This form of the disease is characterized by a full recovery and normal functioning after a symptomatic period. It is thought to occur in about 5%–10% of cases of MS (Sayao, Devonshire, & Tremlett, 2007).

G. Malignant MS
   A brief time after disease onset, the disease progresses rapidly and may lead to significant disability or death within 5 years of diagnosis; it is thought to be extremely rare (Lublin & Reingold, 1996).

H. Other types
   The MS spectrum includes idiopathic inflammatory demyelinating diseases including the following:
   1. Subclinical multiple sclerosis (SCMS), which presents with incidental lesions at MRI without clinical signs and symptoms.
   2. Clinically isolated syndrome (CIS), which is a onetime neurologic episode consistent with demyelination or CNS inflammation (Siva, 2006). CIS may include optic neuritis, transverse myelitis, or isolated brain stem or cerebellar syndromes. Patients with CIS are at high risk of developing MS (Halper, Costello, & Harris, 2006).

3. Other demyelinating diseases that may present as MS are acute disseminated encephalomyelitis and neuromyelitis optica (or Devic's disease) (Wingerchuk, Lennon, Lucchinetti, Pittock, & Weinshenker, 2007).

I. Implications for patients
   1. Some patients may have some familiarity with MS; however, they may have an incorrect understanding of MS. Patients and families may imagine the worst case scenario and anticipate a rapid decrease in function and the need for assistive devices, including a wheelchair.
   2. Patients and their families need a realistic view of MS along with an understanding about the disease-modifying agents and symptom-management strategies.

   Recommendations: Nurses caring for patients with MS need an understanding of the various types of MS and should be familiar with the typical clinical course of each type in order to
   - provide explanations and initiate patient education and counseling for patients and their families
   - provide information and counseling to help patients and care partners develop a realistic picture of the disease, the benefits of treatment, and expectations related to its management
   - help patients and their families cope with a new diagnosis of MS, adopt a healthy lifestyle, and maintain a positive and hopeful perspective
   - emphasize health-promotion strategies and preventive health care and screening, including the importance of regular follow-up with their neurologist and other healthcare providers (Level 3).

IV. Immunogenetics and Pathogenesis

A. General background
   1. Up to 20% of MS patients have a family member affected by the disease (Compston & Coles, 2002).
   2. The risk of developing MS is 20–30 times higher for siblings of affected individuals than for the general population (3:1) (Compston & Coles, 2002).
   3. An important role for the genetic factors in determining MS susceptibility is suggested by familial aggregation of the disease as well as high incidence in some ethnic populations (e.g., Northern European ancestry).
   4. Genes that code for major histocompatibility complex (MHC) are part of the human leukocyte antigen (HLA) system cluster on chromosome 6 (Ben-Zacharia & Morgante, 2005; de Jong et al., 2002; Olerup et al., 1987).
   5. HLA genes help T cells distinguish self from nonself (Ben-Zacharia & Morgante, 2005; de Jong et al., 2002; Olerup et al., 1987).
   6. Variations in several HLA genes are seen in autoimmune disease, when the body mounts an immune response (Ben-Zacharia & Morgante, 2005; de Jong et al., 2002; Olerup et al., 1987.).

B. Pathophysiology of MS (Halper, Costello, & Harris, 2006)
   1. The etiology of MS is not known.
   2. It is hypothesized that MS is a virus-induced immune-mediated disease.
   3. Lesions include acute plaques with active inflammatory infiltrates and macrophages, and chronic, inactive demyelinated scars.
   4. Irreversible axonal damage and loss are caused by inflammation, demyelination, and scarring.
   5. Brain atrophy may be useful in measuring disease progression and effects of long-term therapy.

C. Blood-brain barrier (BBB) in MS
   1. BBB is formed primarily by tight junctions between endothelial cells that are disrupted in MS and result in lesion formation in the brain and CNS (Riskind, 2007).
   2. Proinflammatory cytokines such as interleukin (IL)-1β that is expressed in MS lesions may contribute to BBB permeability (Argaw et al., 2006).
   3. With BBB disruption, immune cells and other molecules that assist in the migration of these immune cells called *adhesion molecules*, which are the target of MS therapies (natalizumab), and chemokines that may attract and stimulate the migration of leukocytes could also play a role in MS pathology. Chemokines could also play a role in the recruitment of oligodendrocytes and could be involved in remyelination (Riskind, 2007).

D. T cell and B cell pathogenesis of MS
   1. Cellular and humoral immunity (Halper, Costello, & Harris, 2006).
      a. Cellular immunity consists of cytotoxic T cells (cluster of differentiation [CD] 8) and T-helper (TH) cells (CD 4).
      b. Humoral immunity includes B lymphocytes and antibodies.
      c. B cells recognize antigens outside of cells; T cells recognize antigens from inside host cells and those on the cell surface.

d. Humoral immunity involves B cells producing antibodies that work by mechanisms including neutralization, opsonization, and complement activation.
e. Cellular immunity involves T cells with receptors on the cell surface.
f. T cells are activated by antigen presentation.

2. The general consensus is that MS is a disease related to an imbalance of antiinflammatory versus proinflammatory cytokines.
3. Proinflammatory TH-1 (CD 4+) and antiinflammatory TH-2 (CD 4+)
   a. Proinflammatory cytokines (TH-1): IL-2, IL-10, IFNγ, TNFα
   b. Antiinflammatory cytokines (TH-2): IL-4, IL-10, IL-13, transforming growth factor (TGF) β (Akira, Takeda, & Kaisho, 2001)
4. T cells in the periphery are activated by antigen present cells (APC).
   a. Activated TH-1 cells migrate across the BBB.
   b. In the CNS, the T cells are reactivated by an APC and secrete proinflammatory cytokines including CNS inflammation via activation macrophages and other T cells and B cells (Neuhaus, Archelos, & Hartung, 2003).
5. Recently discovered additional CD4+ subset TH-17
   a. TH-17 cytokines IL-17, IL- 6, TNFα, and IL-17 are expressed in MS lesions (Akira, Takeda, & Kaisho, 2001).
6. B cell pathogenesis
   a. B cells have the capacity to stimulate T cells (Bar-Or, 2010).
   b. B cells produce antibodies to components of the CNS, including myelin. This may help determine the extent of tissue injury in MS.
   c. Antibodies bind with complement to attack and destroy the myelin sheath (complement fixation).
   d. Complement fixation is especially effective with oligodendrocytes, resulting in an influx of calcium. This promotes phagocytosis of oligodendrocytes.
   e. B cells may secrete more IgM, IgG, and IgA and bring about an antigen-dependent T cell response (Bar-Or, 2010).

E. Neurodegeneration in MS (Trapp & Nave, 2008)
1. Trapp and colleagues (1998) performed autopsies and biopsies on patients with MS, and they demonstrated greater axonal damage than had been previously appreciated.
2. Axonal loss can be seen at MRI and magnetic resonance (MR) spectroscopy (Filippi et al., 2003).
3. Neurodegeneration is a major contributor to CNS atrophy.
4. Neurodegeneration occurs with inflammation.
5. Controversy remains regarding the relationship between inflammation and neurodegeneration.
6. Causes of neurodegenerative processes:
   a. Failure of sodium channel homeostasis.
   b. Excess glutamate, nitrous oxide, proteases, cytokines, CD8 cells, oxidative products, and free radicals generated by activated immune and glial cells.

F. Remyelination (Chari, 2007; Franklin & Kotter, 2008)
1. Remyelination appears to be considerable in the majority of the MS population; however, CNS remyelination does not occur as well as peripheral nervous system (PNS) remyelination.
2. Remyelination is a natural reparative process in MS during which new myelin sheaths are formed over demyelinated axons.
3. Remyelination varies from individual to individual.
4. It is observed in individuals both early and late in the course of disease.
5. It is present in all types of MS.
6. Favorable factors for remyelination are as follows:
   a. Presence of oligodendrocyte precursors near the active edges of inflammatory lesions.
   b. Migration and development into mature oligodendrocytes.
   c. Inflammation appears to be necessary.
   d. Clearance of myelin debris generated during demyelination.

Recommendation: Well-designed multidisciplinary research is needed for a more complete understanding of the pathophysiology of MS (Level 3).

V. Assessment and Diagnostic Process

A. Introduction
1. A clinical diagnosis of MS is based on neurologic examination. Laboratory testing and MRI provide supporting evidence of a diagnosis.
2. Diagnostic criteria have evolved over several decades and include the use of clinical (e.g., history and physical) and paraclinical

data (e.g., MRI, serum and cerebrospinal fluid [CSF] sampling, visual evoked potentials, and somatosensory and brain stem evoked potentials). Other potential causes of CNS demyelination must be excluded before MS is diagnosed (Costello & Halper, 2010b; Harris & Halper, 2004, 2008; Miller et al., 2008; Poser et al., 1983).

B. Diagnostic criteria for MS
   1. The McDonald criteria were created to present a better and more reliable diagnostic scheme to diagnose MS (Polman et al., 2005; Polman et al., 2011). The McDonald criteria use history of clinical attack(s) along with MRI lesion distribution (e.g., dissemination in space) and lesion occurrence over time (e.g., dissemination in time and space via MRI, CSF, evoked potentials) to aid in the diagnosis of MS (Polman et al., 2011). Diagnosis is often made by a neurologist on the basis of the McDonald criteria (Harris & Halper, 2004, 2008; Polman et al, 2005).
   2. These criteria may allow a more reliable diagnosis to be made sooner than otherwise possible (Bakshi et al., 2008). The criteria were most recently revised in 2010.
   3. The 2010 revisions to the McDonald criteria for diagnosis of MS (Polman et al., 2011) are as follows:
      a. When the clinical presentation includes two or more attacks and objective clinical evidence indicating two or more lesions in different locations, no further confirmation is needed.
      b. If two or more attacks occur and clinical evidence indicates only one lesion, dissemination in space must be provided by means of MRI, or a diagnosis of MS can be made by using the appearance of two or more lesions at MRI plus a positive CSF.
      c. In cases in which an individual has experienced one attack but objective clinical evidence indicates two separate lesions, MRI is not required to prove dissemination in space. However, MRI can prove dissemination in time, as can the occurrence of a second attack. Dissemination in time can be established in one of two ways: (1) detection of Gadolinium (Gd) enhancement at least 3 months after the initial event or (2) detection of a new T2 lesion at any time compared with reference imaging performed at least 30 days after the initial clinical event.
      d. In clinically isolated syndromes in which an individual has experienced only one attack and clinical evidence indicates one lesion, an abnormality at MRI as defined in the criteria or two lesions at MRI plus a positive CSF would satisfy the definition of dissemination in space. Dissemination in time could be confirmed at MRI by the occurrence of a second attack.
   4. The most common presentations of MS include the following:
      a. Sensory disturbances such as numbness, paresthesias, pain, or Lhermitte's sign.
      b. Motor abnormalities including corticospinal, abnormal deep tendon reflexes (DTRs), positive Babinski response, or spastic limb weakness.
      c. Visual problems including brain stem and eye movement abnormalities, and optic neuritis.
      d. Cerebellar gait ataxia, limb ataxia, and tremor.
      e. Fatigue.

C. Assessment tools
   1. Assessing a patient with MS begins with the initial observation of the patient in any setting and includes observing his or her ability to move (walking, assistive devices), affect, balance and coordination, hygiene, speech.
   2. Although a clinical neurologic examination provides baseline information about how the nervous system is functioning, there are findings specific to MS. This information will help identify the areas of the CNS that may be affected by demyelinating lesions (Rudick, 2004; van den Noort & Holland, 1999).
      a. Brain stem: internuclear ophthalmoplegia (INO), and nystagmus
      b. Cerebellar: scanning speech, intention tremor, truncal ataxia, gait ataxia, and dysarthria
      c. Motor symptoms: pyramidal tracts—weakness typical of upper motor neuron lesions, spasticity, hyperreflexia, dysarthria, clonus, and extensor plantar responses
      d. Motor symptoms: corticobulbar tracts—emotional lability
      e. Sensory symptoms
         - Not always visible but can be elicited with testing.
         - Sensory loss may affect gait and other motor function leading to clumsiness of fine movements and loss of dexterity.

f. Higher cortical function
   - Short-term memory dysfunction
   - Managing complex tasks
   - Speed of information processing
   - Visual-spatial dysfunction
   - Verbal fluency

3. Patient interviews provide the greatest information to guide caring for the patient with MS and improving his or her QOL. Through this process, nurses can discern if symptoms are constant or intermittent and how they affect the lives of patients at home, at work, and in the community. Skilled interviewing will involve asking for information not necessarily offered by the patient.
4. Examples of topics to address include the following:
   a. ADLs: dressing, bathing, eating, and grooming
   b. Bowels: constipation, incontinence, and diarrhea
   c. Bladder: frequency, urgency, incontinence, and infections
   d. Sexual function: loss of libido, erectile dysfunction, loss of sensation, and relationship issues
   e. Vision: decreased acuity and constant or intermittent inability to distinguish colors, especially red
   f. Cognition: word-finding problems, memory issues, poor concentration, and inability to understand what is being said
   g. Mood: depression, anxiety, depletion, irritability, sadness, anger, and mood fluctuations
   h. Diet and fluids: decreased fluids to manage bladder, and inability to get food, prepare food, or feed self
5. EDSS is a standard measure of disability in MS (Kurtzke, 1983).
   a. EDSS is a widely used MS outcome measure administered by a professional trained in its use (Coulthard-Morris, 2000).
   b. The EDSS is based on an evaluation of a patient's functional systems scores as determined by means of a standardized neurologic examination and an assessment of the patient's walking ability. The EDSS is a 20-point scale from 0 to 10 in half-point increments (**Table 1**; Kurtzke, 1983).
      i. 1–3 indicates minimal disability and the patient is ambulatory.
      ii. 4–7 indicates moderate disability and the patient is ambulatory with assistive device.
      iii. 8–10 indicates severe disability and the patient is confined to a wheelchair (Coulthard-Morris, 2000).
   c. Functional systems (FS) scores are used in the evaluation of a patient's EDSS. FS scores measured during a neurologic examination include visual, brain stem, pyramidal, cerebellar, sensory, bowel and bladder, and cerebral and mental function. FS scores are rated on a scale from 0 (normal function) to 6 (unable to perform the function; Kurtzke, 1983).
   d. On the basis of results from cohort studies, once an EDSS score of 4 is reached, there is a progression of disability regardless of initial good prognosticators. An EDSS score of 4, therefore, heralds the onset of SPMS (Hutchinson, 2009). Longer intervals to progression to subsequent EDSS levels are present in those with initial RRMS (versus those with PPMS), those with complete recovery from first relapse, and those with longer time from MS onset to second episode (Confavreux, Vukusic, & Adeleine, 2003; Confavreux, Vukusic, Moreau, & Adeleine, 2000).
   e. The risk of reaching an EDSS score of 6 is only 20% at 10 years for the person with one or fewer relapses in the first 2 years of the disease. Approximately 50% of people with MS need to use a walking aid after 15 years (Weinshenker et al., 1989a, 1989b). Freedom from major disability after 25 years occurs in approximately 10% of people with MS (Kantarci et al., 1998). If an EDSS score stays at or below 2 for more than 10 years, there is a 90% chance of disease stability (Kantarci et al., 1998; Pittock et al., 2004). In contrast, most people experiencing 5 or more relapses within the first 2 years of disease onset require use of a cane at 10 years (Weinshenker, 1994).
6. The Multiple Sclerosis Functional Composite (MSFC; Kurtzke, 1983; Fischer, Jak, Kniker, Rudick, & Cutter, 2001) includes three outcome measures:
   a. Nine-hole peg test—arm assessment measurement
   b. Timed 25-foot walk test—leg assessment measurement.

Table 1. Expanded Disability Status Scale (EDSS)

EDSS Score	Clinical Finding
0.0	Normal neurologic examination
1.0–1.5	No disability
2.0–2.5	Minimal disability
3.0–3.5	Moderate disability
4.0–4.5	Fully ambulatory and self-sufficient despite severe disability
5.0–5.5	Walking restricted to 100–200 meters
6.0–6.5	Needs unilateral or bilateral constant assistance
7.0–7.5	Restricted to wheelchair; can wheel self and transfer alone
8.0–8.5	Restricted to bed or chair; retains some self-care functions
9.0–9.5	Helpless bed patient
10.0	Death due to MS

Note. From Kurtzke, J. F. (1983). Rating neurologic impairment in multiple sclerosis: An expanded disability status scale. *Neurology, 33*(11), 1444–1452.

c. Paced auditory serial addition test (PASAT)—cognitive assessment measurement.

7. The Multiple Sclerosis Symptom Checklist (MSSC) is a 26-item self-report measure designed to assess for the presence of 26 disease symptoms common in MS patients (Gulick, 1989). The tool consists of five subscales assessing motor function, sensory disturbance, mental and emotional concerns, bowel and bladder elimination, and brain stem symptoms. Homogeneity reliability has been determined through the use of the Cronbach alpha with subscale scores ranging from .78 to .87 (Gulick, 1989). Total scale Cronbach alpha has been shown to be .89. Scores are determined through the use of a six-point scale with responses ranging from *never* to *always*. Higher scores indicate an increase of symptoms (Gulick, 1998).

Recommendations: A comprehensive assessment should be completed, including the following areas: physical, cognitive, sensory, and bowel and bladder function. The baseline functional assessment can be used to compare with future neurologic examinations (Level 2). For assessment of function, frequency of evaluation has not been extensively studied. Nurses should complete an initial assessment of function and monitor on an ongoing basis for any changes in condition (Level 3).

D. Assessment charts
   1. Cranial nerve assessment (**Table 2**)
   2. Assessment of motor symptoms; range of motion and muscle strength (**Table 3**)

E. Assessment of reflexes (**Table 4**)

F. Diagnostic testing

The diagnosis of MS is essentially a clinical diagnosis. The McDonald criteria are used along with other diagnostic tools, because a neurologic examination alone may not provide enough evidence. These tests are used not only for early detection of the disease but also for evaluating the efficacy of current and new treatments (Laron et al., 2009).

1. Evoked potentials: An evoked potential test measures the time it takes for nerves to respond to stimulation. The size of the response is also measured. An advantage and reason for using evoked potential in diagnosis is the ability to detect abnormal signs and lesions in patients who have isolated symptoms. Nerves from different areas of the body may be tested.
   a. Visual evoked potential (VEP) is the most commonly used evoked potential test in the diagnosis of MS. VEP tests help identify optic neuritis (ON) or other demyelinating conditions along the optic nerve and optic pathways (Laron et al., 2009; Turker et al., 2008).

      The McDonald criteria have incorporated VEPs into the diagnosis of MS. VEPs are recommended in patients with MRI showing 4 or more, but fewer than 9, T2 lesions consistent with MS (Evans & Boggs, 2010; Laron et al., 2009).
   b. Brainstem auditory evoked response (BAER)
      i. BAER measures the function of the auditory nerve and auditory pathways in the brain stem. It provides information about changes in the neurophysiologic status of the peripheral nervous system and CNS (Evans & Boggs, 2010; Laron et al., 2009).
      ii. BAERs are considered if clinical symptoms indicate the possibility of a lesion outside the brain. An abnormal BAER would support the diagnosis of MS (Laron et al., 2009).
   c. Somatosensory evoked potential (SSEP)
      i. Sensory disturbances are common findings in patients with MS. SSEPs detect clinical abnormalities but mainly explore the lemniscal pathway, which is responsible for transmitting touch, vibration, and conscious proprioception. In the spinal cord, the dorsal columns are responsible for conduction of the activity that is demonstrated by the SSEP, and it involves the lemniscal,

Table 2. Cranial Nerve Assessment

Cranial Nerve	Function	Assessment	Expected Findings
I: Olfactory	Sense of smell	Tools: two different scents such as clove, vanilla, or coffee. Have patient close eyes and close one nostril, then identify scent.	
II: Optic	Central and peripheral vision	Tools: Snellen chart or available print version and two index cards. Have patient identify writing or symbols. Assess peripheral vision by facing patient nose to nose 12 inches away. Have patient cover one eye with index card and you cover mirror image of eye (patient right eye, your left eye). Extend arm and have patient note when he or she sees fingers moving. Assess upper, middle, and lower range of inner and outer aspect of eye. You should see finger movement at about the same time as the patient. If you (the examiner) have poor peripheral vision, you will not be able to do this examination.	Comfortably and accurately reads or identifies small figures. Peripheral vision intact.
III: Oculomotor	Pupillary constriction	Tool: penlight. Hold penlight 12 inches from patient eyes. Next, have patient look at distant object then bring object close to patient eyes. Assess 6 cardinal positions of gaze.	Pupils constrict equally in response to light. Eyes are accommodating with convergence and constriction of pupils. Equal extraocular movement.
IV: Trochlear	Movement of eyes toward nose	Assess 6 cardinal positions of gaze.	Eye movement is smooth toward nose.
V: Trigeminal	Sensation and motor function of face	Tools: cotton ball and dull end of an object such as a pen, reflex hammer, or tongue depressor. Test sensation on face. Have patient close eyes and identify when he or she feels touch. Wisp cotton ball against cornea. Have patient open jaw against resistance.	Corneal reflex intact. Sensation intact on forehead, jaw, and cheek. Adequate jaw strength.
VI: Abducens	Lateral movement of eyes away from the nose	Assess 6 cardinal positions of gaze.	Eye movement is smooth away from nose.
VII: Facial	Facial expression	Ask patient to smile, frown, or puff out cheeks.	Equal facial expression.
VIII: Acoustic	Hearing	Whisper next to patient ear but not in patient view to prevent lip reading.	Able to understand whisper.
IX: Glossopharyngeal X: Vagus (assess IX and X together)	Tongue and throat movement	Tools: tongue depressor, penlight Have patient say "ahh." Test gag reflex.	Uvula retracts evenly. Soft palate rises. Gag reflex intact.
XI: Spinal Accessory	Shoulder shrug	Shrug shoulders against resistance.	Raises shoulders with equal force.
XII: Hypoglossal	Tongue movement	Ask patient to stick out his or her tongue.	Tongue sticks out midline.

Table 3. Assessment of Motor Symptoms: Muscle Strength

Assess joint movement of head and neck and major joints of upper and lower extremities. Grade muscle strength by using muscle strength scale.

Grading Muscle Strength	Finding
0	No visible muscle contraction
1	Visible muscle contraction with no or trace movement
2	Limb movement when gravity is eliminated
3	Movement against gravity but not resistance
4	Movement against resistance supplied by examiner
5	Full strength

Table 4. Assessment of Reflexes

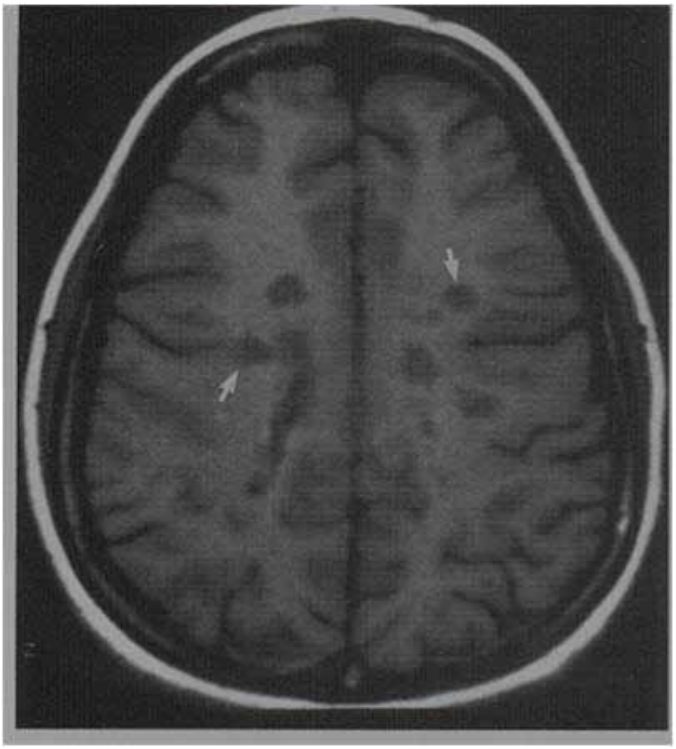
Assess Reflexes	
Reflex	Nerve Innervation
Biceps	C5, C6
Triceps	C7, C8
Brachioradialus	C5, C6
Patellar	L3, L4
Achilles	SI, S2
Plantar Reflex (Babinski)	L5,SI
Reflex Grading Scale Finding	
0	Absent reflex
1+	1+ Diminished
2+	2+ Present, normal finding
3+	3+ Increased
4+	4+ Increased with clonus
5+	5+ Increased with sustained clonus

thalamocortical, and extralemniscal pathways (Evans & Boggs, 2010).

ii. SSEPs are useful in diagnosing clinically silent MS lesions. One third of abnormal SSEPs occur unilaterally. Studies that compared SSEPs with VEPs found equal sensitivity in revealing lesions in patients with MS (Evans & Boggs, 2010; Gronseth & Ashman, 2000).

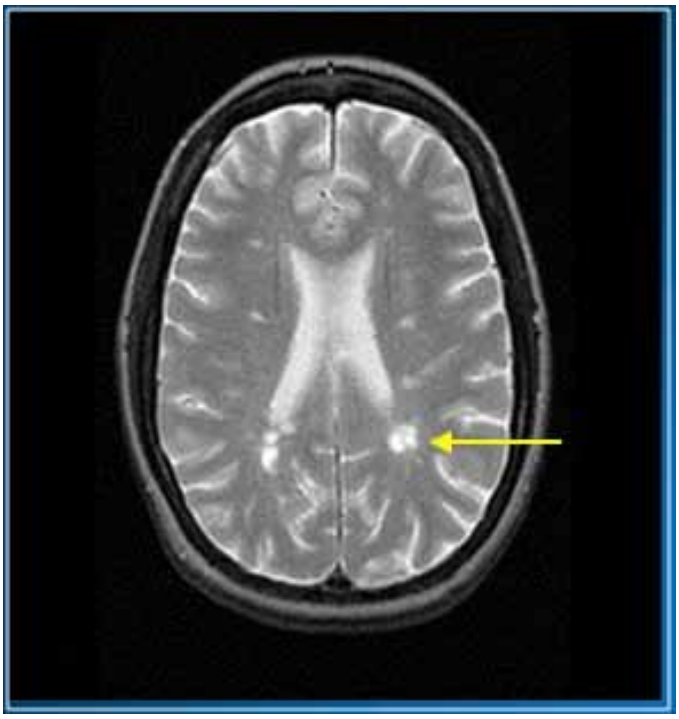
2. Optical coherence tomography (OCT)
   a. OCT is a new optical imaging technique that measures a cross-section of the retinal nerve fiber layer (RNFL) thickness with high resolution and good reproducibility. The RNFL consists of the unmyelinated axons of retinal ganglions that become myelinated past the lamina cribrosa and the optic nerve. If the RNFL is affected as seen in patients with MS, it will show a retrograde degeneration that follows the damage of the optic nerve or optic tract.
   b. Benefits found with OCTs are that they are easy to perform, time efficient, and less costly than MRI. MRI is considered the standard evaluative technique for diagnosis of MS. OCT has been used as a potential substitute to measure of axonal loss and neuroprotection in MS (Laron et al., 2009).
3. MRI
   a. MRI is one of the most important diagnostic tests used in diagnosing MS. In MS, clinical features seen at MRI include multiple plaques or lesions throughout the CNS, which is composed of the brain, optic nerves, and spinal cord (Traboulsee & Li, 2006).
   b. MRI will show abnormalities in approximately 95% of patients with clinically definitive MS (Nielsen, Korteweg, & Polman, 2007).
   c. Two types of images are used during brain MRI: T2-weighted and T1-weighted images (Traboulsee & Li, 2006).
      i. T1-weighted images appear dark (**Figure 5**), and T2-weighted images appear bright (**Figure 6**).
      ii. Fluid-attenuated inversion-recovery (FLAIR) MRI is also useful for lesion detection (**Figure 7**).
      iii. When brain MRI results are normal or equivocal, spinal cord MRI is useful (**Figure 8**).
      iv. Spinal cord lesions are found in approximately 50%–90% of patients with clinically definitive MS (Traboulsee & Li, 2006).
      v. The characteristic MS lesion appears bright at T2-weighted MRI (secondary to inflammation, edema, demyelination, axonal loss, and/or Wallerian degeneration) and is found in the periventricular, juxtacortical, or infratentorial white matter (Bakshi, Hutton, Miller, & Radue, 2004).
   d. Lesions can occur in any CNS tissue where there is myelin (e.g., the brain, spinal cord, or optic nerves; Traboulsee & Li, 2006).
   e. In the brain, the periventricular (surrounding the ventricles) region is the typical location where white matter lesions are located (**Figure 9**).
   f. Juxtacortical lesions are located in the temporal lobes at the grey-white matter junction (Figure 9; Traboulsee & Li, 2006).
   g. Dawson's fingers are lesions that are perpendicular to the ventricles. These lesions are a unique feature of MS (**Figure 10**; Traboulsee & Li, 2006).

Figure 5. T1-weighted axial image



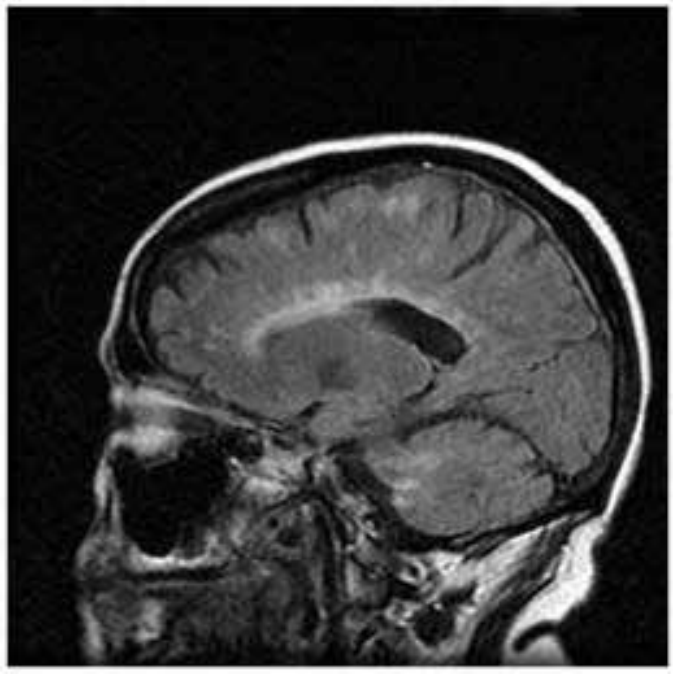
T1 images emphasize the differences between tissues and show good anatomic detail, but do not demonstrate pathology best. Abnormalities show up dark on T1 images. Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN).

Figure 6. T2-weighted axial image



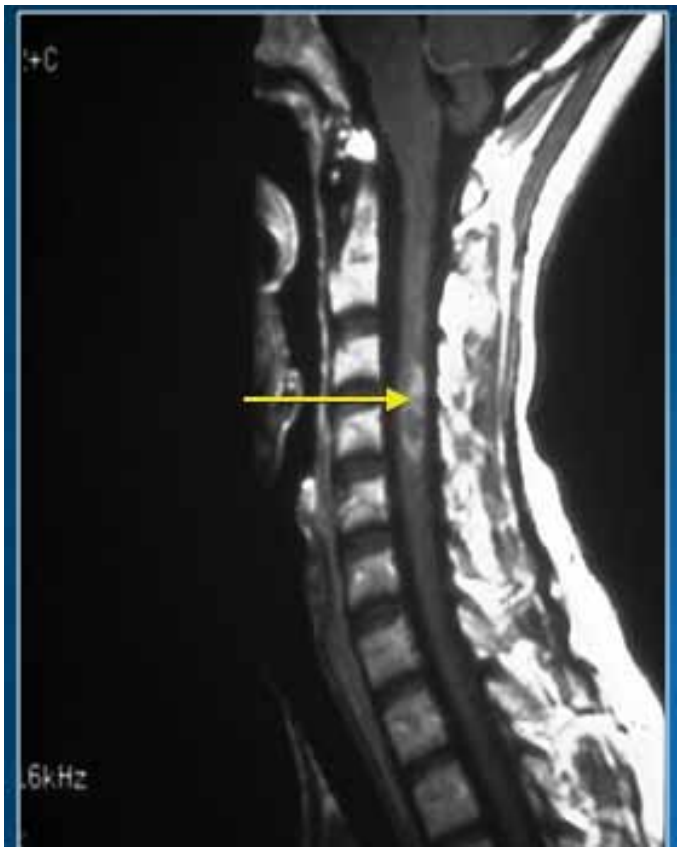
T2 images are sensitive to increased water content and may be superior at demonstrating pathological changes. Gray matter appears lighter than white matter. MS lesions appear hyperintense or bright. Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN).

Figure 7. Sagittal FLAIR image



A FLAIR image is a type of T2 image with superior capability for demonstrating demyelinating lesions and shows both new and old lesions clearly. Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN). Original MRI image provided to IOMSN by William Stuart, MD.

Figure 8. Spinal cord MRI showing cord lesion



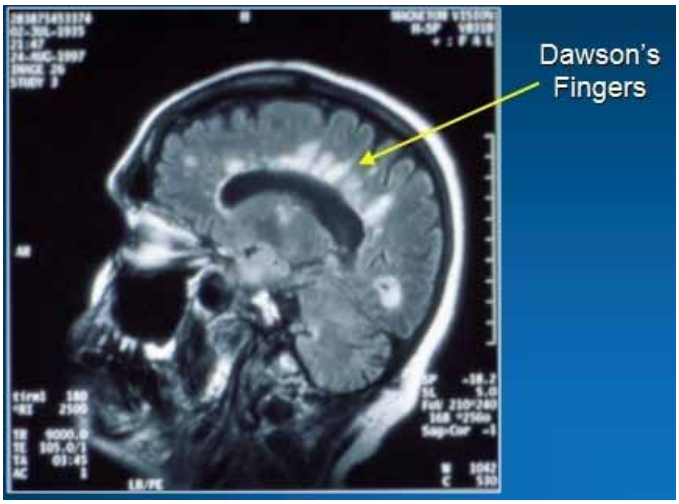
Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN).

Figure 9. Axial FLAIR imaging showing periventricular and juxtacortical lesions

Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN). Original MRI image provided to IOMSN by William Stuart, MD.

h. Areas of hypointensity are called *black holes*. Chronic black holes are lesions that are nonenhancing and typically persist for a minimum of 6 months after they first appear (Traboulsee & Li, 2006). If these hypointense areas persist, they represent axonal loss. Permanent disability may be related to axonal loss (**Figure 11**; Bakshi, Hutton, Miller, & Radue, 2004).

Figure 10. MRI demonstrating Dawson's fingers



Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN).

i. There is some consensus that patients with PPMS have fewer lesions in the cerebrum and possibly less enhancement in the CNS (Bakshi et al., 2008).

j. Gadolinium is used to detect new disease activity (inflammation). Gadolinium does not typically cross the BBB. New MS lesions coincide with disruption of the BBB and appear on T1-weighted images as gadolinium-enhanced lesions (Traboulsee & Li, 2006). The lesions appear bright and often have a ringlike pattern around them (**Figure 12**). On average, enhancement lasts approximately 4 weeks, with a gradual decrease during the next 2–4 weeks (Traboulsee & Li, 2006).

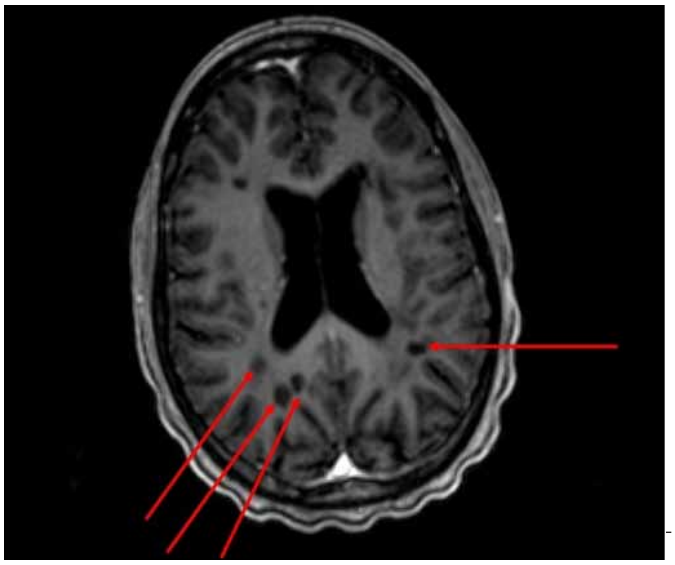
k. The Consortium of MS Centers has published an MRI protocol for the diagnosis and follow-up of patients with MS. These guidelines provide details of the clinical use of MRI for patients with MS.

4. Brain parenchymal fraction (BPF) is another method of using MRI techniques to evaluate the clinical course of MS through measurement of cerebral atrophy. In comparison with controls, patients with MS display an increased loss of brain volume, and a means of measuring this is through calculation of BPF (Rudick et al., 1999), which is considered a sensitive indicator of disease severity (Dörr et al., 2011).

G. Laboratory testing

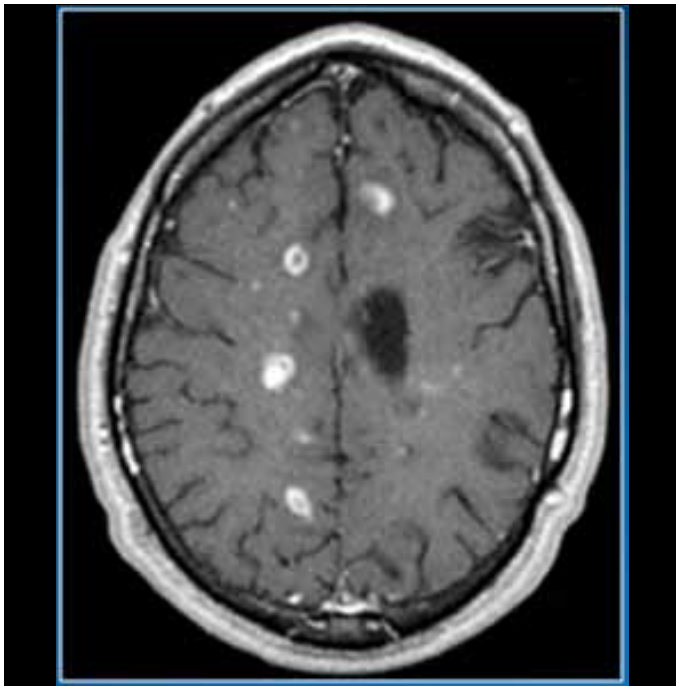
The MS diagnosis is generally based on clinical signs and symptoms and MRI, VEP, and laboratory analyses (specifically CSF) See previous discussion of McDonald criteria (Polman et al., 2011).

Figure 11. MRI demonstrating "black holes"



Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN). Original MRI image provided to IOMSN by William Stuart, MD.

Figure 12. MS lesions on enhanced T1 weighted MRI



T1-weighted gadolinium-enhanced MRI showing new and active lesions that appear bright, reflecting areas of blood-brain disruption. Courtesy of the International Organization of Multiple Sclerosis Nurses (IOMSN).

1. CSF tests: Examining CSF may identify abnormal cells or antibodies that suggest the presence of MS. It has been the focus of testing and research for many years (Rammohan, 2009).

a. CSF is examined by means of a lumbar puncture (spinal tap). CSF is clear and colorless in all MS patients (Rammohan, 2009).

2. Tests performed on CSF include oligoclonal bands (OCBs), IgG Index, Myelin Basic Protein (MBP), Kappa Light Chains, glucose, albumin index, protein level, and white blood cell level.
   a. Oligoclonal bands: OCBs are immunoglobulins (IgG, IgM, or IgA) or proteins of the immune system that are generated by plasmablasts and plasma cells in the CSF or CNS compartment (Awad et al., 2010). In addition to MRI, the presence of OCBs in the CSF is the most consistent laboratory abnormality found in patients with MS. If OCBs are present, less stringent criteria are needed to satisfy the dissemination in space criterion (Polman et al., 2011).
      i. A positive test for OCBs is the presence of two or more IgG bands in the CSF that are not present in a blood serum sample obtained at the same time (Awad et al., 2010; Freedman et al., 2005; Link & Huang, 2006; Rammohan, 2009).
      ii. According to Rammohan (2009), identification of OCBs is invaluable for diagnosis of MS. Villar and colleagues (2009) stated that the presence of OCBs is characteristic of MS, and Fromont and colleagues (2005) stated that the detection of OCBs in a patient's CSF is the gold standard laboratory test for MS.
      iii. Tintoré and colleagues (2008) examined whether OCBs added to MRI findings as a predictor of a second attack and the development of clinically definite MS and disability in patients with clinically isolated syndrome (CIS). The authors found that the presence of OCBs doubles the risk for having a second attack, independent of MRI findings, but does not seem to influence the development of disability.
   b. IgG Index: An increase in the level of IgG in the CSF can be due to the increased production of IgG in the CNS. This increase in production can be seen with MS as with other diseases. The increase in IgG can be due to leakage of plasma proteins into the CSF as might be seen with inflammation or trauma.
      i. The IgG Index is calculated from IgG and albumin measurements in the CSF and blood serum. The calculation is

$$\text{IgG Index} = \frac{\text{IgG (CSF)/IgG (serum)}}{\text{Albumin (CSF)/Albumin (serum)}}$$

      (Hische, van der Helm, & van Walbeek, 1982; Link & Huang, 2006).
      ii. An elevated IgG Index indicates an increase in the production of IgG within the CNS. It is elevated in about 70% of cases of MS. Because of the low sensitivity of the IgG Index, it cannot be recommended as the primary laboratory test or replace the CSF OCB in the diagnosis of MS. However, when elevated, it can be used as an additional tool in the diagnosis of MS and help to rule out other diseases that mimic MS (Link & Huang, 2006).
   c. Myelin Basic Protein (MBP): MBP is the major component of myelin, and increased concentrations of myelin in CSF indicate that demyelization is occurring. Increased levels of MBP have been found during active demyelination. Levels may be elevated in the CSF of patients with MS; however, it is thought not to be specific for MS, because other inflammatory diseases of the CNS can increase the level of MBP in the CSF. It may be used to help rule out other diseases that mimic MS (Rammohan, 2009).
   d. Other CSF studies performed not specific for MS
      i. Color and clarity: All aspects of CSF analysis help to distinguish between other causes of systemic inflammation and diseases that could possibly mimic MS. CSF in patients with MS is generally clear and colorless.
      ii. Glucose: Usually normal in MS.
      iii. Albumin index: Used to rule out the leakage of protein into the CSF from blood caused by either a damaged BBB or a traumatic spinal tap.
      iv. Protein level: Normal or slightly elevated; most patients with MS have normal total protein counts even during an acute exacerbation (Rammohan, 2009).
   e. White blood cell (WBC) level: Higher than normal CSF WBCs (predominantly mononuclear cells) are found in MS, whereas

very high CSF WBC counts (>50 x 10 L) are unusual for MS.

3. Peripheral Blood Tests: May be helpful to rule out other disease processes that mimic MS (Calabresi, 2004).
   a. Advancements in paraclinical investigations, especially MRI, CSF, and visual evoked potential testing, together with the need for a definitive diagnosis at the earliest time possible, are imperative for the physician to begin treatment in a timely manner. In making the diagnosis, a precondition should include the exclusion of diseases that mimic MS (Courtney, Treadaway, Remington, & Frohman, 2009). Multiple tests are needed to rule out other conditions or diseases that have similar signs and symptoms that affect the CNS and that can be confused with MS (Calabresi, 2004).
   b. **Table 5** lists some of the diseases that mimic MS. This table is not all-inclusive but lists many of the diseases most frequently mentioned in the literature. (See also Courtney, Treadaway, Remington, and Frohman, [2009] and Rolak and Fleming, [2007], who provide a more extensive list of diseases that mimic MS).
   c. Continued refinement of techniques will generate additional information, better methods of storage, and data analysis that use bioinformatics. The resulting increased availability of information from research studies on CSF will help clinicians diagnose and treat MS as well as conduct further research. Advances from these studies will help to change the course of MS and empower the patient and physician to treat MS more effectively in the future (Rammohan, 2009).

H. Diagnostic research studies: Biomarkers
   1. Introduction: A number of different biomarkers have been used to diagnose and differentiate the different types of MS and treat MS.
      a. *Biomarkers*, or biological markers, are naturally occurring substances that can be used as indicators of biological processes and pathogenic processes including disease states such as MS. Some biomarkers are useful in assessing responses to therapeutic interventions.
      b. Discovery of new biomarkers for MS relies on advances in proteomics research along with microarray gene expression analyses together with the analysis of antigens. It is hoped that this will establish specific biomarkers for MS (Harris & Sadiq, 2009).
   2. Disease Activation Panel of Biomarkers
      a. Biomarkers being researched include a panel of biomarkers that measure MS disease activation: interleukin-6, nitric oxide, osteopontin, and fetuin-A (Harris & Sadiq, 2009).
      b. Interleukin-6: Interleukins (ILs), also called *lymphokines*, are a subgroup of the cytokines and carry messages between cells. They are communicating proteins that initiate or suppress inflammation. There are more than 30 known ILs at this time.
      c. Nitric oxide (NO) and NO synthesis: NO is a free radical signaling molecule that has a complex biochemistry. Evidence points to the role that NO plays in the pathogenesis of MS and its role in various aspects of MS such as inflammation, oligodendrocyte injury, synaptic transmission changes, axonal degeneration, and neuronal death (Encinas, Manganas, & Enikolopov, 2005). Its action may have both positive and negative effects in MS.
      d. Osteopontin: Osteopontin has been found in the plasma levels of patients with MS during relapses. In a study of MS patients and healthy subjects, plasma osteopontin levels were significantly increased in patients with RRMS and also correlated with the IgG Index. This finding suggested that bone-related molecules such as osteopontin and vitamin D have immunomodulary functions and are correlated with the IgG Index in patients with RRMS (Vogt, ten Kate, Drent, Polman, & Hupperts, 2010). Osteopontin is significant in MS as it works with integrin a4b1 to block lymphocyte entry to the brain and to reduce relapses (Steinman, 2009).
      e. Fetuin-A: Fetuin-A is a protein found in blood serum; 95% of it is derived from the liver. It is implicated in the CNS as responsible for increasing the permeability of the BBB by activating matrix metalloproteinase. In patients with active MS, a significantly higher level of CSF fetuin-A is noted than in patients with inactive disease (Yan, Rammal, Dinzey, Donelan, & Sadiq, 2007). Fetuin-A protein can be used to predict the level of disease activity and to promote

Table 5. Differential Diagnosis of Diseases that Mimic MS

Name and Description of Disease	How It Mimics MS	Diagnostic Studies to Differentiate
Acute Disseminated Encephalomyelitis (ADEM) Monophasic demyelinization occurring with or just after infection, vaccination, or other immune-altering event (Courtney, Treadaway, Remington, & Frohman, 2009; Rolak & Fleming, 2007).	Frequently it is preceded by a viral infection (Gasperini, 2001). Symptoms can be identical to MS, including involvement of optic nerve, brain, and spinal cord. Fifteen percent of patients may have lesions on the brain.	MRI lesion may be hemorrhagic and involve the gray matter (Rolak & Fleming, 2007). CSF—mild to moderate pleocytosis (elevated WBCs in the CSF) and mild to moderate elevated protein MBP. CSF beta-1 globulin in MS (Chopra, Abraham, & Abraham, 2002). Gasperini (2001) states that using unenhanced serial MRI may be helpful, because with ADEM many lesions resolve and new ones do not develop, but with MS, some lesions resolve but new lesions develop.
Neuromyelitis Optica or Devic Syndrome Monophasic	Abrupt onset of optic neuritis, transverse myelitis, brain stem tegmentum syndrome (vomiting, oculomotor, and vestibular problems); 10% to 50% have brain lesions (Courtney, Treadaway, Remington, & Frohman, 2009). Frequently, it is preceded by a viral infection (Gasperini, 2001).	CSF—marked pleocytosis (neutrophil component) and protein and albumin levels. Absent OCBs and normal IgG Index. At MRI, lesions noted affecting the optic nerve and spinal cord but with myelitis extending over 3 or more continuous segments of the spinal cord (Rolak & Fleming, 2007).
HIV-Associated Infections	Occurs in high-risk patients that may have a decreased CD4 cell count and positive serology. May cause optic neuritis, myelopathies, changes in mental status, and focal deficits (Rolak & Fleming, 2007).	Increased total protein and cell count in CSF; 0 OCBs; multiple cerebral white matter lesions at MRI indistinguishable from those of MS (Gasperini, 2001). Positive HIV serology.
Lyme Disease Tick exposure infected by tick-borne spirochete, *Borrelia burgdorferi*. (Courtney, Treadaway, Remington, & Frohman, 2009).	Can cause consistent focal neurological findings	Western blot. Diagnosis made based on symptoms and evidence of tick bite. Enzyme-linked immunosorbent assay (ELISA); indirect fluorescent antibody (IFA); positive polymerase chain reaction test (PCR) may be used to detect a current (active) infection by detecting the genetic material (DNA) of the Lyme disease bacteria (Rolak & Fleming, 2007; Courtney, Treadaway, Remington, & Frohman, 2009). Intrathecal synthesis of IgG and OCBs have been reported (Gasperini, 2001).
Myasthenia Gravis Disease in which weakness occurs because the nerve impulses responsible for initiating movement are not able to reach muscle cells.	In myasthenia gravis, the symptoms tend to fluctuate throughout the day, and they often worsen at night. Droopy eyelids; facial weakness; impaired eye coordination; and weakness of the limbs, neck, shoulders, hips, and trunk are typical. Patients usually do not experience loss of sensation, and fatigue is localized (Rolak & Fleming, 2007).	MRI, CSF, and visual evoked response (VER) are normal. Eighty percent of patients have an elevated serum acetylcholine receptor antibody test result (Rolak & Fleming, 2007).
Pernicious Anemia Vitamin B12 deficiency	May cause central nervous system (CNS) deficits, especially progressive myelopathy. Rare MRI abnormalities (Rolak & Fleming, 2007).	Serum B12 low; complete blood count may be abnormal; methylmalonic acid and homocysteine are often abnormal (Rolak & Fleming, 2007).
Progressive Multifocal Leukoencephalopathy (PML) CNS infection by John Cunningham (JC) virus in immunosuppressed patient.	Can have multifocal CNS deficits. It occurs in immunocompromised patients. The deficits are usually progressive rather than relapsing. Death may occur within weeks to months if untreated (Rolak & Fleming, 2007; Courtney, Treadaway, Remington, & Frohman, 2009).	The MRI is abnormal, usually shows lesions in white matter that are larger and more confluent than those seen with MS. CSF polymerase chain reaction (PCR) may be positive for JC virus, but brain biopsy may need to be performed for definite diagnosis (PCR is a laboratory test to detect the genetic material of an infectious disease) (Rolak & Fleming, 2007).
Systemic Lupus Erythematosus (SLE)	Systemic involvement includes hematologic, skin, and kidney changes. Common in young women and may affect the nervous system, especially the optic nerve and spinal cord. MRI changes of white matter are common. Up to 60% of patients have OCB and IgG abnormalities in CSF (Rolak & Fleming, 2007).	Antinuclear antibody (ANA) titers levels are in increased SLE; positive serology: double-stranded DNA autoantibodies and ANA (Rolak & Fleming, 2007).
Syphilis CNS infection by spirochete *Treponema pallidum* (Courtney, Treadaway, Remington, & Frohman, 2009; Rolak & Fleming, 2007)	Can cause optic neuritis, myelopathies, and other focal neurological changes (Rolak & Fleming, 2007).	Tests for syphilis include serum VDRL, rapid plasma regain (RPR) test, fluorescent treponemal antibody absorption (FTA-ABS). CSF-protein (90%), WBC (90%), CSF VDRL (positive 80%). MRI usually normal. Infection considered rare except in HIV-positive or immunocompromised patients (Rolak & Fleming, 2007).

Continued

Table 5. Differential Diagnosis of Diseases that Mimic MS *Continued*		
Sarcoidosis Granulomatous multisystem angiotensin disease of unknown cause (Rolak & Fleming, 2007)	Often systemic symptoms, especially in the lungs. May involve optic nerve or spinal cord (Rolak & Fleming, 2007). Involvement of the optic nerve with pain in one or both eyes and blurred vision are of importance. Facial nerve relapsing-remitting palsies may occur (Gasperini, 2001).	CSF-protein, mononuclear pleocytosis, angiotensin-converting enzyme level. Chest X ray is a very helpful tool. Serum and CSF ACE levels may be increased. Rare patients have OCB in CSF. MRI may show white matter lesions and meningeal enhancement. Positive biopsy of skin lesions, lymph nodes, or lung is definitive diagnosis (Rolak & Fleming, 2007).
Sjögren Syndrome Chronic inflammatory and autoimmune disease	Systemic symptoms with dry eyes, dry mouth, and also arthritis and vasculitis (Courtney, Treadaway, Remington, & Frohman, 2009; Rolak & Fleming, 2007).	Positive serology for SS-A (Ro) and SS-B (La) autoantibodies (Courtney, Treadaway, Remington, & Frohman, 2009; Rolak & Fleming, 2007). MRI may show white matter lesions, and CSF may show OCBs with increased IgG. Biopsy of the salivary gland can be definitive (Rolak & Fleming, 2007).

faster and better therapeutic decisions by healthcare providers.

3. Neurodegeneration proteins indicative of disease progression. Disease activity in MS is mainly due to inflammation; however, disease progression is most likely due to neurodegeneration (Harris & Sadiq, 2009).
   a. CSF biomarkers (proteins) that reflect the pathological process of MS are indicative of demyelination as well as neuronal, axonal, and glial loss and regeneration (Tumani et al., 2009).
      i. Neurofilaments
         a) Studies have shown that an increase in these antibodies may serve as a marker of axonal damage in MS (Giovannoni, 2010; Salzer, Svenningsson, & Sundström, 2010; Teunissen, Dijkstra, & Polman, 2005).
         b) Antibodies to neurofilaments have been identified in the serum and CSF of patients with MS. They have been detected in relapsing as well as progressive disease and are thought to be a marker of progressive axonal injury (Rammohan, 2009).
      ii. Total tau protein levels in CSF
         a) Tau protein is a protein localized in neuronal axons, and because axonal damage has been proposed as the major cause of permanent clinical disability in patients with MS, it is thought that it can serve as a biochemical marker to evaluate axonal damage (Brettschneider et al., 2005).
         b) Studies have been both positive and negative for use of tau protein as a clinical marker of axonal injury (Brettschneider et al., 2005; Guimarães, Cardoso, & Sá, 2006; Jiménez-Jiménez et al., 2002; Terzi, Birinci, Cetinkaya, & Onar, 2007; Valis, Talab, Stourac, Andrys, & Masopust, 2008).
      iii. N-acetylaspartic acid—may be an important neuron specific marker of disease severity and possible progression (Jasperse et al., 2007; Teunissen et al., 2009).
      iv. B cell chemokine CXCL13 (also known *as B lymphocyte chemoattractant* [BLC]). Chemokines are a group of molecules that attract leukocytes (WBCs) from blood to the brain when there is infection and/or an immune response. B cells are a type of WBC that develops in the bone marrow and works as part of the immune system of the body. They have many receptors that recognize invading organisms and as a result release antibodies to fight the invaders. B cells play a role in the pathogenesis of MS. CSF and CNS tissues of patients with MS contain B cells along with plasma cells, antibodies, and immunoglobulins, which suggests the need for more research toward B cell–targeted therapies (Racke, 2008).
      v. Nogo-A
         a) Nogo-A is a protein that is a strong neurite inhibitor (Oertle et al., 2003). It plays a role in restructuring axonal regeneration (or regrowth) after injury and in structural plasticity (i.e., ability of the neural pathways to reorganize as a result of new input) in the CNS. Proteins that affect remyelination and regeneration are proteins that are thought to provide

important information about MS related to predicting disease subtypes and progression (Lehmensiek et al., 2007).

b) Results from several studies on Nogo-A suggest that it has multiple functions at the cell surface and intercellular level (Harris & Sadiq, 2009; Oertle et al., 2003). Nogo-A plays an important role for oliodendrocyte differentiation, which is important in myelin repair in autoimmune diseases such as MS (Pernet, Joly, Christ, Dimou, & Schwab, 2008), thus Nogo-A may have a beneficial effect during the inflammatory process of MS but could be negative for the process of myelin repair at a later date.

vi. Apolipoprotein (ApoE)

a) ApoE is a transport protein that has been associated with clinical features of MS. Liu and colleagues (2009) reported that ApoE was decreased in patients with MS. It has also been identified in CIS as one of the proteins that may have a relevant effect on early identification of disease. However, further validation is needed (Lehmensiek et al., 2007).

b) ApoE is considered to be a neurotropic factor. Therefore, any decrease in intrathecal ApoE synthesis could possibly contribute to the progression of multiple sclerosis.

vii. BDNF protein

a) Expression of BDNF has been associated with neural regeneration; it is usually found wherever innervations are present.

b) An increased number of BDNF positive cells have been found in the inflammatory lesions of those with MS (Stadelmann et al., 2002), and agents used to treat MS have been found to activate cells capable of producing BDNF (Yoshimura et al., 2010; Ziemssen, Kümpfel, Klinkert, Neuhaus, & Hohlfeld, 2002), with higher levels of BDNF apparently playing a role in the disease process.

Recommendation: Nurses should familiarize themselves with published and ongoing research efforts in the area of biomarkers for MS disease diagnosis and progression to provide patient education regarding laboratory testing and respond to questions from patients (Level 3).

VI. Disease Management

A. Management of MS

1. The management of MS is directed toward disease modification, relapse management, and symptom management. Treatment aims include decreasing the frequency and number of relapses, limiting disability, and relieving symptoms (Compston & Coles, 2002; Goodin et al., 2007).
2. There are presently six disease-modifying treatments (DMTs) approved for use in the United States and Canada to treat relapsing forms of MS: glatiramer acetate (Copaxone®); natalizumab (Tysabri®); and the interferons (IFNs), intramuscular IFN β-1a (Avonex®), subcutaneous IFN β-1a (Rebif®), subcutaneous IFN β-1b (Betaseron®, Extavia®), and fingolimod (Gilenya™). Randomized clinical trials support the favorable effects of DMTs on MS-related disease activity as monitored by means of MRI, relapse rate, and sustained disability (Comi, Filippi, & Wolinsky, 2001; INFB Multiple Sclerosis Study Group & the University of British Columbia MS/MRI Analysis Group, 1995; Jacobs et al., 1996; Johnson et al., 2003; O'Connor, 2005; Rudick, 2005; Prevention of Relapses and Disability by Interferon β-1a Subcutaneously in Multiple Sclerosis [PRISMS] Study Group, 1998). Mitoxantrone (Novantrone®) is an immunosuppressant approved to treat secondary progressive, progressive-relapsing, and worsening RRMS not responding to other DMTs (Edan et al., 1997; Hartung et al., 2002). The key features of DMTs for MS are summarized in **Table 6**.
3. Tolerance of and willingness to adhere to treatment regimen and the risk/benefit ratio drive treatment decisions of the person with MS and the prescriber (Freedman et al., 2008; Goodin, 2004; Goodin et al., 2007; Ross, 2008).
4. Nurses are responsible for monitoring the response to DMT, including skin site reactions (**Figures 13–15**). Strategies to manage tolerability issues associated with MS therapies are presented in **Table 7**.
5. Intravenous methylprednisolone or oral steroids are most commonly used to treat relapses (Thrower, 2009).

Recommendations: Nurses need to be aware of the mechanism of action of MS medications to educate and counsel patients about expected benefits and adverse effects of medication therapy (Level 3). Nurses need to be aware of the role of personal patient preference and drug regimen complexity related to tolerance of and willingness to adhere to treatment protocols (Level 2).

B. Economic considerations
   1. Financially, these treatments can be costly and a significant burden to patients and families. Both direct and indirect costs may or may not be reimbursed by insurance plans, which vary individually. Kobelt and colleagues (2006) studied the estimated current costs and QOL of patients taking disease-modifying medications, the total average annual cost in 2004 was $47,215 (U.S. dollars) per patient. Of the total average cost, it was determined that 53% was for direct medical and nonmedical costs, while 37% was related to losses in productivity, including short-term absence, reduced working time, and early retirement. Approximately 10% of the yearly costs were attributed to informal care. Costs were significantly correlated with functional capacity (Kobelt, et al.).
   2. Affordability of disease-modifying agents: Studies have shown that some medications may be more affordable than others. Newer medications would likely be more expensive than existing ones that have been used for a longer time. Natalizumab (Tysabri®) has been shown to reduce relapses and slow disease progression, but the assessment of lifetime cost-effectiveness of natalizumab versus other disease-modifying drugs is inadequate (Earnshaw, Graham, Oleen-Burkey, Castelli-Haley, & Johnson, 2009). Earnshaw and colleagues (2009) show that direct costs (remaining lifetime) for patients receiving glatiramer acetate or natalizumab compared to costs associated with symptom management were only $408,000; $422,208; and $341,436, respectively. Glatiramer acetate was more cost-effective than natalizumab. Long-term evidence showed that glatiramer acetate has similar, if not improved, clinical benefits, despite 1- and 2-year relapse rates being better for natalizumab (Earnshaw, Graham, Oleen-Burkey, Castelli-Haley, & Johnson, 2009).
   3. RRMS affects the majority of the MS population. Although there are several DMTs for RRMS, not all are available for the same cost. Goldberg and colleagues (2009) analyzed the 2-year effectiveness of four DMTs used for RRMS—glatiramer acetate, interferon (IFN) β-1a IM injection, IFN β-1a SC injection, and IFN β-1b SC injection. Variables included relapses, disability progression, and direct medical costs. Medical savings were considered in an event of an avoided relapse and disability progression prevention. It was found that without DMT, patients had more relapses and pronounced disability progression. The four DMTs previously mentioned are the most cost-effective treatments for RRMS (Goldberg et al.).

   Recommendation: Nurses can serve as advocates for MS patients related to ensuring connection with medication support services (Level 2).

C. Immunotherapies reveal aspects of MS
   Disease-modifying medications' mechanisms of action provide evidence for understanding of pathways in MS (Compston & Coles, 2002; Franklin & Kotter, 2008; Olek, 2005; Chari, 2007; Yong, 2002; Neuhaus, Archelos, & Hartung, 2003).
   1. Glatiramer acetate
      a. Blockade of antigen presentation
      b. Bystander suppression
      c. Regulation of the T cells by CD 8 suppressor cells
      d. Enhanced neuroprotection and remyelination
   2. Interferon β
      a. Stimulation of antiinflammatory cytokine production
      b. Inhibition of VLA-4 interaction with vascular cell adhesion molecules (VCAMs) by reducing increasing soluble VCAM-1
      c. Inhibition of synthesis and transport of matrix metalloproteinases
   3. Fingolimod
      a. Targets sphingosine-1-phosphate-1 receptor on lymphocytes entrapping in lymphoid tissue
   4. Monoclonal antibodies—reduce occurrence of contrast-enhancing lesions suggesting:
      a. Circulating immune cells expressing α-4 integrins are responsible for much of the CNS cellular infiltration in MS.
      b. Augmentation of low levels of natural killer cells and their function may correct defects in or provide a better level of T cell regulation.
      c. Circulating B cells are important pathogenic components of immune responses in MS.
      d. Circulating lymphocytes and monocytes are important in demonstrating contrast-enhancing MS lesions.

Table 6. Key Features of the Disease-Modifying Agents

Agent (Brand Name)	Interferon ß-1b (Betaseron®, Extavia®)	Interferon ß-1a (Avonex®)	Interferon ß-1a (Rebif®)	Glatiramer acetate (Copaxone®)	Natalizumab (Tysabri®)	Mitoxantrone (Novantrone®)	Fingolimod (Gilenya™)
Description	• Recombinant agent, produced in E. coli • Unglycosylated • Amino acid sequence differs from naturally occurring interferon with a serine substituted for the cysteine residue at position 17	• Recombinant agent produced from Chinese hamster ovary cells • Glycosylated • Identical in amino acid content and sequence to human β-interferon	• Recombinant agent produced from Chinese hamster ovary cells • Glycosylated • Identical in amino acid sequence to human ß-interferon	• Synthetic polypeptide • Approximates the antigenic structure of myelin basic protein	• Recombinant humanized monoclonal antibody produced in murine myeloma cells	• Synthetic antineoplastic anthracendione	Binds to the sphingosine-1-phosphate receptor, or S1P receptor on immune cells, including T cells and B cells. Induces immune cells to remain in lymph nodes, inhibiting them from migrating into the brain and spinal cord.
Indication (United States)	Relapsing forms of MS to reduce frequency of relapses, CIS	Relapsing forms of MS to slow accumulation of physical disability and decrease frequency of relapses, CIS	Relapsing forms of MS, to delay accumulation of physical disability and decrease frequency of relapses	RRMS to reduce frequency of relapses, CIS	Relapsing forms of MS to delay accumulation of physical disability and reduce frequency of relapses	SPMS, PRMS, or abnormally worsening RRMS, for reducing neurological disability and frequency of relapses	Reducing the frequency of clinical relapses and delaying the accumulation of physical disability in relapsing forms of MS.
Dosage/ Route/ Administration	0.25 mg/l subcutaneous injection every other day	30 µg/l intramuscular injection weekly	22 µg or 44 µg/l subcutaneous injection 3 times weekly, preferably on same 3 days and at the same time (e.g., late afternoon or evening)	20 mg/l subcutaneous injection daily	300 mg/IV infusion over 1 hour every 4 weeks	12 mg/m^2 (cumulative lifetime dose not to exceed 140 mg/m^2)/ IV infusion administered for 5 to 15 minutes every 3 months	0.5 mg orally daily
Nursing Considerations	• Injection-site rotation and skin management • Laboratory monitoring* • Neutralizing antibodies • Hematological/ hepatological abnormalities • Flu-like symptoms, depression, other side effects	• Injection-site rotation and skin management • Laboratory monitoring • Neutralizing antibodies • Hematological/ hepatological abnormalities • Flu-like symptoms, depression, other side effects	• Injection-site rotation and skin management • Laboratory monitoring • Neutralizing antibodies • Hematological/ hepatological abnormalities • Flu-like symptoms, depression, other side effects	• Injection-site rotation and skin management • Immediate post-injection reaction, lipoatrophy, other side effects	• Only available under TOUCH® Prescribing Program • PML, hypersensitivity reactions, signs of liver injury, other side effects	• Cardiotoxicity (increases with cumulative dose): • Patients should be monitored for evidence of cardiotoxicity prior to each dose, and total cumulative lifetime dose is not to exceed 140 mg/m^2 • AML • Other side effects	Requires 6 hours first dose monitoring. Caution should be used in patients who may be at risk of developing bradycardia or heart blocks, macular edema, active infections, hypertension, hepatic dysfunction, and respiratory disorders.

AML, acute myelogenous leukemia; CIS, clinically isolated syndrome; IV, intravenous; PML, progressive multifocal leukoencephalopathy; PRMS, progressive-relaping MS; RRMS, relapsing-remitting MS; SPMS, secondary-progressive MS.

**Laboratory monitoring for hematological/hepatological changes is done usually at month 3, 6, 9, 12, 18, 24 and annually after that. Neutralizing antibodies can be detected at 12–24 months.*

Adapted with permission from Costello, K., & Halper, J. (Eds.). (2010). Multiple Sclerosis: Key issues in nursing management—adherence, cognitive function, quality of life. *(3rd edition.). Washington, D.C.: Expert Medical Education.*

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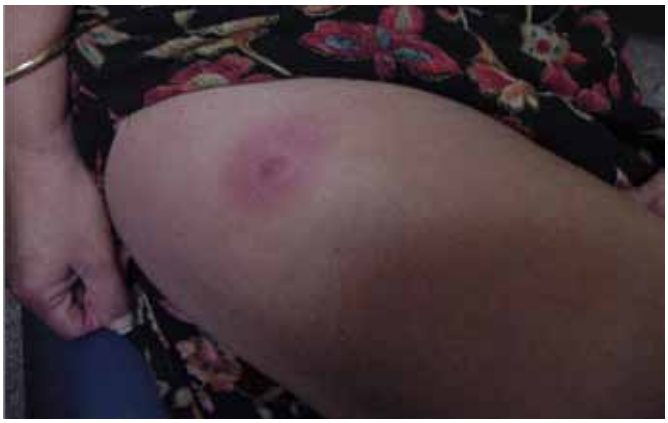
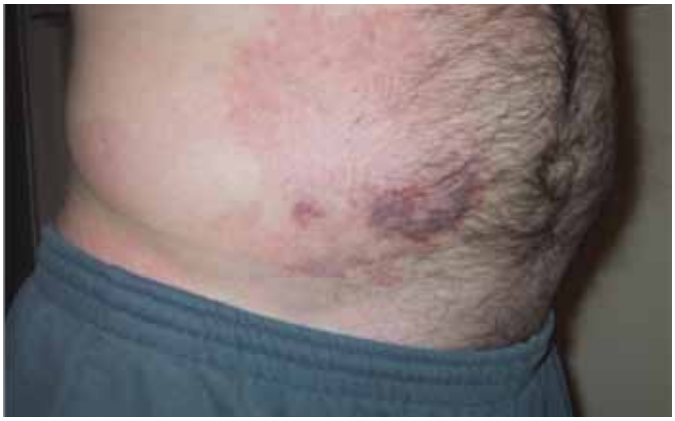
Figure 13. Erythema, Interferon β-1a SC



Courtesy of Colleen Harris, MN MSCN

Figure 14. Erythema, bruising, glatiramer acetate



Courtesy of Kathleen Costello, MS ANP-BC MSCN

Figure 15. Lipoatrophy

Courtesy of Colleen Harris, MN MSCN

i. Natalizumab—directed against α-4 integrins
ii. Daclizumab—directed against CD25, the α chain of IL-2 receptor
iii. Rituximab—directed against CD20 on B cells
iv. Alemtuzumab—directed against CD52 on T and B cells and monocytes

5. Estriol
   a. Increases IL-10 and IL-5 and decreases interferon γ and TNF-α
   b. Provides further support of shift toward antiinflammatory responses and is typically favorable in relapsing MS
6. Studies of agents that have been shown to worsen MS also provide evidence for understanding of pathways in MS (Panitch, Hirsch, Schindler, & Johnson, 1987).
   a. Interferon γ—augments helper T cell-1 response
   b. Granulocyte colony-stimulating factor—stimulates autoreactive lymphocytes
   c. Antitumor necrosis factor α agents—blocks beneficial effects of tumor necrosis factor α, suggesting it may have immunomodulatory neuroprotective properties

Recommendations: Nurses must be aware of patient responsiveness to therapy and serve as advocates for follow-up with appropriate interdisciplinary team providers (Level 3). Nurses should monitor MS patients for medication-related side effects and use appropriate strategies to manage their manifestations (Level 2).

VII. Clinical Features and Symptom Management

A. Clinical features overview
   1. MS is first and foremost a clinical diagnosis.
   2. Clinical manifestations in MS depend on which portion of the CNS is affected. The demyelination or destruction of the myelin sheath of axons in the CNS most frequently affects the optic and oculomotor cranial nerves and the cerebellar, corticospinal, and posterior column systems. Clinical manifestations include abnormalities of vision and eye movement, motor skills, coordination, and gait, as well as spasticity and sensory disturbances, such as pain and paresthesia (Hoeman, 2008). The interruption of neural conduction in the demyelinated nerves is manifested by a variety of symptoms, depending on the location and extent of the lesion (Hoeman, 2008; Porth & Matfin, 2008; Swann, 2006).
   3. People with MS may experience a wide range of symptoms. These may vary from person to person, and symptoms may vary within one individual patient (Halper, Costello, & Harris, 2006). The varied range of symptoms includes fatigue, mobility, spasticity, numbness and tingling in the extremities, general weakness, visual impairments, bowel and bladder dysfunction, sexual dysfunction, cognitive

disabilities, depression, anxiety, and diminished self-efficacy (Rumrill, 2009). Common symptoms of MS are shown in **Table 8** (Halper, Costello, & Harris, 2006).

a. MS symptoms may be managed in a variety of ways including education, counseling, physical and occupational therapy, rehabilitation, and medication. **Table 8** provides a summary of the various pharmacologic measures for selected MS symptoms.

B. Sensory symptoms

1. Paresthesias: Paresthesia can be present at any state of the disease (Peterson, Kornbluth, Marcus, Saulino, & Hung, 2004).
   a. Paresthesia is evidenced as numbness, tingling, a burning sensation, or pressure and can range from annoying to severe in MS patients (Porth & Matfin, 2008).
   b. Symmetric paresthesis (tingling and numbness) may occur in an unpredictable pattern in dorsal column symptoms in patients with spinal cord involvement. In patients with cerebellar involvement, paroxysmal attacks include sensory (and motor) symptoms, such as paresthesias, dysarthria (and ataxia and tonic head turning) (McCance, Huether, Brashers, & Rote, 2010). Loss of neuroprotective sensation may place patient at increased risk of pressure ulcer development.
   c. A common paroxysmal symptom, Lhermitte sign, is a shocklike or tingling sensation, shooting down the trunk or limbs during active or passive flexion of the neck. Sensory stimulation, voluntary movement, hyperventilation, and emotional stress may be inciting events (McCance, Huether, Brashers, & Rote, 2010; Porth & Matfin, 2008).
2. Pain: Pain is a complex symptom of MS and usually involves the sensory system (Halper, Costello, & Harris, 2006). Acute and chronic pain may occur in MS.
   a. It is subjective and is identified by the individual with MS.
   b. It is difficult for an observer to measure pain.
   c. Acute pain and paroxysmal disorders
      i. Trigeminal neuralgia may be associated with transmission of nerve impulses in severe regions of demyelination.
      ii. Tonic spasms, at times, may be related to spasticity. Simple flexor spasms may be related to movement or noxious stimuli.
      iii. Lightning-like extremity pain.
      iv. Painful Lhermitte's sign.
      v. Optic neuritis results in inflammation around the pain-sensitive meninges near the optic nerve and retrobulbar pain.
   d. Chronic pain with insidious onset
      i. Dysesthetic extremity pain
      ii. Bandlike pain in torso or extremities
      iii. Back pain with radiculopathy
      iv. Headache related to demyelinating lesions
3. Management strategies (Halper, 2007b; Maloni, 2007)
   a. Nonpharmacologic
      i. Rehabilitation evaluation for physical therapy, occupational therapy
      ii. Gait training
      iii. Seating
      iv. Assistive devices
      v. Energy conservation
      vi. Avoidance of tight clothing or noxious stimuli
      vii. Moist heat
   b. Pharmacologic
      i. If symptoms appear to be related to relapse, short course of corticosteroids
      ii. Nonsteroidal antiinflammatory drugs (NSAIDs)
      iii. Antispasticity agents
         a) baclofen (Liorseal®)
         b) tizandine (Zanaflex®)
      iv. Antiseizure medications
         a) phenytoin (Dilantin®)
         b) gabapentin (Neurontin®, Gabarone®)
         c) pregabalin (Lyrica®)
         d) carbamazepine (Tegretol®)
      v. Antidepressant medications
         a) Trazadone (Desyrel®)
         b) Amitryptilline (Elavil®) switched sequence
   c. Complementary and alternative medicine (CAM)
      i. Massage
      ii. Guided imagery
      iii. Yoga
      iv. Tai chi
      v. Relaxation techniques
   d. Surgical intervention for severe and intractable pain

Table 7. Symptoms of Multiple Sclerosis

Common	Less Common	Rare
Fatigue	Dysarthria, scanning speech, dysphagia	Decreased hearing
Depression	Lhermitte's sign	Convulsions
Focal muscle weakness	Ataxia	Tinnitus
Visual changes	Vertigo	Mental disturbance
Bowel, bladder, sexual dysfunction	Tremor, incoordination	Paralysis
Gait problems, spasticity		
Paresthesias		
Neuropathic pain		
Cognitive dysfunction		

Table 8. Pharmacologic Management of Selected Symptoms in Multiple Sclerosis

Symptom	Treatment	Nursing Considerations
Fatigue	CNS stimulants (pemoline, modafinil) Amantadine Selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine)	Restlessness or sleep disturbance may occur Help patients with dosing schedule, titrate doses up
Bladder dysfunction	Anticholinergics (e.g., oxybutynin) Antimuscarinics (e.g., tolterodine) α-blockers (e.g., terazosin)	Determine if urinary tract infection is present Monitor retention Monitor fluid balance Follow overall elimination pattern Consider contribution of other medications Provide strategies to avoid side effects (e.g., dry mouth)
Bowel dysfunction	Constipation Stool softeners Bulk-forming agents Mini-enemas Stimulants Suppositories Urgency or diarrhea Anticholinergics Antimuscarinics	Provide bowel training regimens; many of the medications should not be used long term Consider contributory effects of other medications (e.g., steroids or antibiotics) Consider lifestyle issues Encourage exercise Provide diet counseling
Pain	Anticonvulsants (phenytoin, carbamazepine, abapentin, amotrigine) Tricyclic antidepressants (amitriptyline, nortriptyline) Duloxetine hydrochloride	Watch for sedation Start with low doses and titrate up Monitor outcomes; alter treatment as necessary; supportive measures can help
Spasticity	GABA antagonists (oral or intrathecal baclofen) α-Agonists (tizanidine) Anticonvulsants (diazepam, clonazepam, gabapentin) Botulinum toxin	Time doses to maintain therapeutic blood levels Titrate doses up (especially with baclofen) Watch for sedation or cognitive symptoms; may require a change in dosage or medication Combination treatments may help Intrathecal baclofen requires surgical insertion of a programmable pump
Depression	SSRIs and serotonin-norepinephrine reuptake inhibitors (e.g., fluoxetine, sertraline, paroxetine, citalopram, duloxetine hydrochloride) Tricyclic antidepressants (amitriptyline, nortriptyline) Atypical antidepressants (e.g., venlafaxine, bupropion)	Evaluate type and degree of depression Consider contribution of medications (e.g., with interferons) Assess family situation and support network Consider suicide risk Promote use of psychiatric services Advise patient that medication effects may take several weeks Advise patient not to stop medications suddenly Reassess patient regularly Paroxetine can be taken in the morning or at night and can help with anxiety Monitor urinary function with venlafaxine (may cause fluid retention)

From Singer, B., Lucas, S., Kresa-Reahl, K., Perrin Ross, A., & Blake, P. (2008). Optimizing adherence to multiple sclerosis therapies: Managing tolerability and monitoring safety. *International Journal of MS Care, 10*(4), 113–126. *Reproduced with permission.*

Recommendations: The nurse should conduct intermittent assessment for pain, dysthesia, and spasticity (Level 2). Evaluate for the loss of neuroprotective sensation and the potential for pressure ulcer development (i.e., ensure full body assessment; Level 2). Evaluate the patient for triggering and alleviating factors (Level 2). Evaluate the effectiveness of pharmacologic therapies and advocate for evaluation by the interdisciplinary team (Level 1). Provide patient with emotional support and evaluate for anxiety (Level 2). Provide patient and family education related to availability of adjuvant treatment and possible surgical interventions; assess patient's willingness and readiness to incorporate alternative therapies into treatment regimen (Level 3).

C. Visual and hearing impairment
   1. Visual Iimpairment
      a. The demyelination or destruction of the myelin sheath most frequently affects the optic and oculomotor cranial nerves and the cerebellar, corticospinal, and posterior column systems. Vision problems are often the first sign of MS (National MS Society, 2009).
      b. Twenty-five to forty-eight percent of persons initially experience optic neuritis (Peterson, Kornbluth, Marcus, Saulino, & Hung, 2004; Plant, 2008). This manifestation of optic nerve axonal loss is highly suggestive of MS. Diplopia and eyeball pain are common subjective findings (McCance, Huether, Brashers, & Rote, 2010). High-dose glucocorticoids have been used traditionally to accelerate recovery, and NSAIDs may be useful for pain management (Halper, Costello, & Harris, 2006).
      c. Subjective visual symptoms that may present unilaterally or bilaterally include impaired central vision (blurring, fogginess, haziness) and impaired color perception. Signs include decreased central visual acuity; central or paracentral scotoma (area of diminished vision); acquired color vision deficit, especially to red and green; defective papillary reaction to light; and a variety of field defects (McCance, Huether, Brashers, & Rote, 2010).
      d. Internuclear ophthalmoplegia, nystagmus, and dysarthria are the most common brain stem symptoms. May have significant effect on ADLs because of diplopia or inability to focus. These brain stem lesions involving cranial nerves III through XII may be followed by deafness, vertigo and vomiting, tinnitus, facial weakness, and facial sensory deficit. Bilateral internuclear ophthalmoplegia (lateral gaze paralysis) is considered diagnostic of MS. If it is acute, treatment may include high-dose glucocorticoids to accelerate recovery (Halper, Costello, & Harris, 2006); otherwise, treatment is for symptoms. There is currently no approved U.S. Food and Drug Administration (FDA) treatment. Prism lenses may be helpful in some individuals with diplopia.
      e. Nystagmus may be present in patients who have cerebellar involvement with MS and reflects cerebellar and corticospinal involvement (McCance, et al.). Nystagmus is also included in the description of the Charcot triad, described by a combination of nystagmus, dysarthria, and intention tremor (McCance, Huether, Brashers, & Rote, 2010). For nystagmus, some benefit has been found with the following pharmacologic agents (Halper, Costello, & Harris, 2006):
         i. Gabapentin (Neurontin®, Gabarone®)
         ii. Memantine (Namenda®)
         iii. 4-aminopyridine
         iv. Levetiracetam (Keppra®)
   2. Hearing impairment
      a. The MS patient's ability to understand speech is markedly worse with sensorineural hearing loss (Suckfüll, 2009).
      b. Young persons with hearing loss should have MS considered as a possible diagnosis. Bilateral sequential hearing loss may be considered an MS manifestation (Oh, Oh, Jeong, Koo, & Kim, 2008).

   Recommendations: Encourage regular eye examinations (Level 3). Be aware of the potential for hearing changes and assess as needed (Level 3). Provide education regarding the patient's particular visual and hearing symptom experience (Level 3). Support the patient as visual and hearing impairment may reduce overall function (Level 2). Promote safety through education and counseling related to effective lighting, scanning, and environmental modifications (Level 2).

D. Fatigue
   1. Fatigue is an individual's subjective lack of physical and/or mental energy that is perceived as impeding his or her typical or desired activities of life (Johansson, Ytterberg, Gottberg, Widén Holmqvist, & von Koch, 2009).
   2. Fatigue is considered the most common and disabling symptom of MS; it affects between

75% and 95% of all persons with the disease (Egner, Phillips, Vora, & Wiggers, 2003).

3. Higher levels of general fatigue are observed in RRMS compared with the other three subtypes, and with increasing disease severity. DMT generally has no effect on fatigue levels (Hadjimichael, Volmer, & Oleen-Burkey, 2008).
4. Fatigue is categorized into primary and secondary forms, which are often difficult to differentiate.
    a. Primary fatigue can directly result from MS neuropathology.
    b. Secondary fatigue follows from a number of common MS comorbidities, including depression, medication side effects, pain, psychosocial characteristics, thyroid dysfunction, vitamin B12 deficiency, anemia, and sleep disorders (Johnson, 2008). Most research to date has found fatigue to be of the secondary rather than the primary form.
5. Trojan and colleagues (2007) differentiated fatigue into three categories: (1) general or overall, (2) physical, and (3) mental. They found that sleep quality, pain, and self-efficacy were the strongest predictors of general fatigue; self-efficacy and physical activity level were most predictive of physical fatigue; stress level and self-efficacy were the strongest predictors of mental fatigue.
6. Relationships between physical fatigue and increased MS disease severity have been observed (Debouverie, Pittion-Vouyovitch, Brissart, & Guillemin, 2008).
7. Depression has not been found to be a strong predictor of physical fatigue in MS (Debouverie, Pittion-Vouyovitch, Brissart, & Guillemin, 2008; Trojan et al., 2007), although it has shown relationships with mental fatigue (Schreurs, de Ridder, & Bensing, 2002).
8. Along with depression, fatigue is a predictor for decreased cognitive functioning in MS (Diamond, Johnson, Kaufman, & Graves, 2008).
9. Assessment of fatigue
    a. Involves informal questioning of patients and their care partners
    b. Formal assessment by means of instruments/tools: the Modified Fatigue Impact Scale (MFIS), the Fatigue Severity Scale (FSS), or the Neurological Fatigue Index-MS (NFI-MS)
10. Management of fatigue (Bergamaschi, Romani, Versino, Poli, & Cosi, 1997; Costello, Halper, & Harris, 2003; Kos, Kerckhofs, Nagels, D'Hooghe, & Ilsbroukx, 2008; Krupp, 2004; Markowitz, 2010; Mills, Young, Pallant, & Tennant, 2010; Penner & Calabrese, 2010)
    a. Nonpharmacological strategies
        i. Gradual exercising
        ii. Maintain realistic expectations
        iii. Energy conservation techniques (Fragoso, Santana, & Pinto, 2008)
            a) Pace activities
            b) Space activities
            c) Divide activities
            d) Do strenuous activities early in the morning
            e) Minimize effort
            f) Prioritize tasks
            g) Schedule and plan activities
            h) Schedule rest periods
        iv. Keep cool during exercises
            a) Exercise in air-conditioned environment
            b) Drink ice water
    b. Complementary and alternative methods
        i. Vitamins
        ii. Nutrition
        iii. Caffeine
        iv. Carnitine
    c. Pharmacological interventions
        i. Fatigue responds to some pharmacotherapy regimens, including amantadine (Symadine®, Symmetrel®), modafinil (Provigil®) and armodafinil, selective seratonin reuptake inhibitors (SSRIs).
        ii. Less commonly used are amphetamines such as methylphenidate or amphetamine and dextroamphetamine composite (Adderall®).
        iii. Aminopyridine is a possible modulator of increased conduction and increasing fatigue.
        iv. A key point for all medications for MS patients is to initiate at a low dose and increase based on effectiveness and tolerance.

Recommendations: Nurses should be aware of and assess for secondary causes of fatigue to include depression, medication side effects, pain, and sleep disorders (Level 2). Nurses should educate and counsel patients regarding energy conservation strategies, including the role of body temperature control (Level 2). The nurse should be aware of the optimal timing of medication administration to enhance energy level and to avoid interrupting sleep (Level 3).

E. Impaired mobility
   1. Physical activity is markedly decreased in MS populations compared with that in healthy controls, and this appears to be related to disease severity (Motl, 2008). However, it is not clear if disease severity itself is the culprit. Because fatigue and motor dysfunction frequently present in MS, persons affected by the disease often avoid physical exercise, believing it may worsen fatigue or have no beneficial effect.
   2. Hand dysfunction has been found to be more common at testing in patients with MS when compared with that in other patients (Krishnan & Jaric, 2008). This dysfunction may include loss of strength and/or coordination.
   3. Disabling tremor or ataxia is a common feature of MS and occurs in almost 80% of patients at some point during their disease. Research on strategies to treat disabling tremor or ataxia with pharmacotherapy, neurosurgery, or rehabilitation has not demonstrated effective treatment (Mills, Yap, & Young, 2007).
   4. A symptom cluster of pain, depression, and fatigue has recently been observed to be a strong barrier to exercise, and functional impairment is a predictor of the presence of the symptom cluster (Motl & McAuley, 2009).
   5. Assessment (Halper & Ross, 2010; Schapiro, 2007)
      a. Subjective history
      b. Objective assessment of motor strength, muscle tone, balance, and sensory function. Specific tests include: the timed 25-foot walk, timed up and go test, expanded disability status scale (EDSS), and driving evaluation.
   6. Management of mobility disturbance
      a. Exercise therapy: identified as an effective treatment for MS. Results of trials show strong evidence that exercise therapy compared to no exercise therapy had positive effects on muscle power function, exercise tolerance functions, and mobility-related activities (Rietberg, Brooks, Uitdehaag, & Kwakkel, 2005). Exercise improves self-efficacy, which in turn reduces fatigue, pain, and depression in patients with MS (McAuley, White, Rogers, Motl, & Courneya, 2010). Meta-analyses have shown that exercise training is associated with a small improvement in walking mobility (Snook & Motl, 2009) and quality of life (Motl & Gosney, 2008) among patients with MS.
         i. Exercise therapy was not found to be effective in reducing fatigue or in reducing the perception of disability compared to no exercise therapy. No evidence was found to suggest that exercise therapy was harmful, and it is reasonable to promote exercise in patients with MS who are not experiencing an exacerbation (Rietberg, Brooks, Uitdehaag, & Kwakkel, 2005).
         ii. Resistance exercise has been found to have a positive effect on function in patients with MS. A randomized clinical trial of exercise versus control group demonstrated that supervised and intense resistance training of the lower extremities improves muscle strength and functional capacity in patients with RRMS and moderate impairment. Importantly, in patients, these improvements persisted after 12 weeks of self-guided physical activity (Dalgas et al., 2009). Resistance training of moderate intensity seems to be well tolerated and to have beneficial effects for patients with MS.
         iii. Elevated core body temperature can sometimes present a barrier to exercise (generating Uhthoff's phenomenon), but this can be addressed by the use of affordable cooling equipment (Schwid et al., 2003).
      b. Use of adaptive equipment: bracing, cane, walker, scooter, wheelchair. Ensure training on safe use and proper maintenance. The patient is referred for evaluation for use of automobile hand controls; OT/PT consultation is obtained as appropriate (Halper & Ross, 2010; Schapiro, 2007).
      c. Electrical stimulation devices: WalkAide®, Bioness® (Halper & Ross, 2010; Schapiro, 2007)
      d. Pharmacologic therapy: dalfampridine, fampridine-SR (Ampyra)

Recommendations: Identify functional effect of impaired mobility and collaborate with interdisciplinary team members to promote optimal mobility within the patient's limitations (Level 3). Evidence-based treatment interventions for mobility optimization include exercise promotion

(Level I). Educate patient and care partners regarding treatment, therapy recommendations, medications, and support adherence (Level 3). The nurse should encourage safety by reinforcing appropriate and safe use of adaptive equipment and aides (Level 2). Assess for the psychological effect of reduced mobility and/or increased disability (Level 2).

F. Bladder and bowel symptoms
   1. In MS with spinal cord involvement, bowel and bladder symptoms occur. Some MS patients lose voluntary control over bladder and bowel function (Pellat, 2008).
   2. Bladder symptoms
      a. There are three types of bladder dysfunction: storage dysfunction, emptying dysfunction, and combined dysfunction. In MS, bladder dysfunction affects QOL (Rantell, 2009).
      b. Incontinence is preceded by urgency and hesitancy. Flaccid bladder may occur with retention problems, although bladder dysfunction most often involves a spastic bladder.
      c. Some patients with spinal cord disease may have combined incomplete emptying and bladder overactivity (Pellat & Geddis, 2008).
   3. Bowel dysfunction
      a. Neurogenic bowel dysfunction may occur in MS. This may include fecal incontinence or constipation, and at times may involve both (Wollin, Bennie, Leech, Windsor, & Spencer, 2005), and is often an underreported symptom of MS (Bywater & While, 2006). In severe cases of MS, constipation is common (McCance, Huether, Brashers, & Rote, 2010).
      b. Bowel dysfunction has a significant effect on the QOL of patients with MS, but research in this area is limited (Coggrave, 2008; Coggrave, Wiesel, & Norton, 2006).
   4. Evaluation of urinary elimination in MS patients can be multidimensional (Betts, D'Mellow, & Fowler, 1993; DasGupta & Fowler, 2003; O'Leary & Dierich, 2010)
      a. Laboratory assessment
         i. Urinalysis; urine culture and sensitivity (UTIs, diabetes, hematuria)
         ii. Cytology (bladder cancer)
         iii. Blood urea nitrogen (BUN), creatinine levels (renal dysfunction)
      b. Urodynamics—group of tests which together measure bladder function and pressure
      c. Uroflowmetry (volume of urine voided over time), postvoid residual (PVR; urine volume after void)
      d. Radiologic tests
         i. Abdominal computed tomography (CT) scan
         ii. Renal ultrasound (renal and upper urinary tract status)
         iii. Cystoscopy (study of bladder lining and urethra)
      e. Bladder diary—voiding patterns typical over 24–72 hours
      f. Diary of food and fluid intake
   5. Urinary management strategies (Betts, D'Mellow, & Fowler, 1993; DasGupta & Fowler, 2003; O'Leary & Dierich, 2010)
      a. Nonpharmacologic
         i. Behavior management—establishing voiding schedule, diet instruction to limit irritants and to increase fluid intake, measures to limit fluid retention, environmental assessment of toilet locations, proper use of absorbent products, biofeedback, and infection prevention strategies
         ii. Intermittent self-catheterization (ISC)—used for chronic retention to improve continence and to preserve renal function. Frequency depends on voids per day and resulting retention.
         iii. Long-term indwelling catheters—suprapubic catheter recommended for individuals who cannot toilet themselves, cannot perform intermittent catheterization, or have medical issues from incontinence. Urethral catheters should be used short term only (i.e., several weeks, not months) because of the damage that can occur in the urethra and other complications.
      b. Pharmacologic
         i. Anticholinergics—side effects of oral forms include dry mouth, blurred vision, flushing, palpitations, nausea, constipation, drowsiness, confusion, and urinary retention.
         ii. Alpha-adrenergic blocker—side effects include site reactions, sleepiness, or blurred vision.
         iii. Botulinum toxin (off-label use) injection into bladder. Side effects: pain, urinary retention, hematuria, and infection.

Recommendations: Nurses should work with the patient, care partner, and other members of the interdisciplinary team to develop an appropriate bladder management program (Level 3). Assess all patients for urinary dysfunction and assess effectiveness of treatments or behavioral strategies over time (Level 3). Encourage discussion of symptoms and effect on QOL and role function and assist with coping strategies (Level 3). Assess for infection and assist in management strategies to reduce risk of infection, stone formation, or worsening of neurologic condition (Level 3).

6. Evaluation of Bowel Function (DasGupta & Fowler, 2003; Walker, 2009)
   a. Assessment of frequency and type of movement, time of day, use of any medication, laxatives and enemas, absorbent products, comorbid conditions, and assistance needed with toileting
   b. Further testing as warranted
      i. Laboratory—complete blood cell count, complete metabolic profile (CMP), pancreatic enzymes, stool culture, and hemoccult testing
      ii. Imaging—abdominal flat plate, barium enema, defecography, colonic transit studies, upper GI, and CT scan of abdomen
      iii. Other tests—manometry and electromyography
7. Bowel management strategies
   a. Nonpharmacologic
      i. Behavior management—establishing consistent schedule, diet instruction to limit irritants and to increase fluid intake, addition of dietary fiber in foods the patient can tolerate, environmental assessment of toilet locations, proper use of absorbent products, and biofeedback
      ii. Use of reflexes. Stimulation of gastrocolic and duodenocolic reflex. The best time is 30–45 minutes after a meal or hot beverage or after digital stimulation or enema.
   b. Pharmacologic
      i. Suppositories, bulk-forming agents, stool softeners, laxatives (osmotic and stimulant), and rectal stimulants. (Caution: large-volume enemas can overdistend the bowel.)

Recommendations: Nurses should work with the patient, care partner, and other members of the interdisciplinary team to develop an appropriate bowel management program (Level 3). Assess all patients for disorders of bowel function and assess effectiveness of treatments or behavioral strategies over time (Level 3). Encourage discussion of symptoms and effect on QOL and role function and assist with coping strategies (Level 3). Assess for effectiveness of management strategies and effectiveness of medications, understanding that bowel interventions may take a long time to become effective and that worsening of symptoms without any relief from strategies may indicate disease progression (Level 3).

G. Sexual dysfunction and reproductive issues
   1. Sexual dysfunction is common in MS because of its direct neurophysiologic effects, consequences of secondary conditions of MS (e.g., fatigue, altered sensation, muscle spasms, bowel and bladder problems, vaginal dryness), and the psychological and cognitive changes that occur in MS (McCabe, 2002; Smeltzer, 2002).
   2. Neurogenic impotence may accompany sphincter symptoms.
   3. Despite the incidence of sexual dysfunction, many patients with MS remain interested in intimacy, sexual relationships, childbearing, and parenting (McCabe, 2002; Smeltzer, 2002).

Recommendations: Nurses must consider MS patients' interest in sexuality and intimacy rather than assume that they are asexual or uninterested (Level 2). Nurses should provide information, education, counseling, and resources about issues related to sexuality, reproductive function, pregnancy, and parenting (Level 3).

H. Dysphagia
   1. Permanent and transitory swallowing disorders (dysphagia) occur with high frequency in patients with MS (Calcagno, Ruoppolo, Grass, De Vincentiis, & Paolucci, 2002; Prosiegel, Schelling, & Wagner-Sonntag, 2004), occurring in 34.4% of patients with primary and secondary progressive MS (Calcagno, Ruoppolo, Grass, De Vincentiis, & Paolucci). Swallowing disorders may be present long before the person with MS experiences any other related symptoms. Patients with a mild form of MS may experience problems swallowing fluids, and patients with more advanced MS may develop difficulties swallowing solid foods (Bogaardt et al., 2009).

2. A close relationship between dysphagia and both brain stem impairment and severity of illness has been noted. The potential risk of aspiration and malnutrition, and the high efficacy of swallowing rehabilitation suggest that all MS patients should have a careful evaluation of deglutition functionality, especially those with brain stem impairment and a high grade of disability level (Calcagno, Ruoppolo, Grass, De Vincentiis, & Paolucci, 2002).
3. The most common MS-related swallowing disorders in the oral and pharyngeal areas are delays in triggering the pharyngeal swallow. This can cause particular difficulties with liquid swallowing, including aspiration (Logemann, 2000). Reduction in tongue base activity reduces the pressure generated during the swallow, allowing residual food to remain in the pharynx and be aspirated when the patient resumes breathing. These disorders can be mild, without causing any significant difficulties such as aspiration or inefficient swallow, or they can be more severe and require therapeutic (behavioral) management (Logemann, 2000).
4. Dysphagia evaluation
    a. Assessment: problem onset, duration and severity; symptom characteristics; observation of choking, delayed swallowing, chewing difficulties; nutritional status, food and liquid intake, weight; cough or increasing hypophonia may indicate new or pending problems.
    b. Referral should be made to a speech/language pathologist (SLP) for evaluation and treatment.
    c. Additional assessment as needed may include video-fluoroscopic study (modified barium swallow; Frenette, Harris, Klassen, & McEwan, 2001).
5. Dysphagia management
    a. Ensure alert and minimize distractions at mealtimes; provide supervision as indicated.
    b. Monitor patient for signs and symptoms of swallowing difficulty, aspiration pneumonia (Frenette, Harris, Klassen, & McEwan, 2001).
    c. Safe swallowing practices
        i. Proper positioning
        ii. Double swallow
        iii. Chin tuck
        iv. Other techniques as prescribed
    d. Collaborate with dietician and SLP for dietary modifications; ensure consistency and ordered texture of liquids and solids.
    e. Suctioning if indicated
    f. Monitor weight on ongoing basis.
    g. Education of patient and family regarding safety measures to include use of suction apparatus and Heimlich maneuver
    h. Advanced or worsening swallowing may result in the need for tube feedings via nasogastric (NG) tube temporarily or via percutaneous endoscopic gastrostomy (PEG) on a permanent basis. Educate and counsel patients and care partners about feeding options as disease progresses.
    i. Other treatment options may include neuromuscular electrostimulation because it was successful in reducing pooling saliva and in reducing aspiration in patients with MS (Bogaardt et al., 2009).

Recommendations: Assess the patient regularly for swallowing difficulties (Level 2). Nurses should work with the patient, care partner, and other members of the interdisciplinary team to develop an appropriate dysphagia management program (Level 3). Monitor weight at each visit (Level 3). Educate and counsel the patient and care partner to reinforce safe swallowing practices (Level 3).

I. Cognitive dysfunction
    1. Recent studies suggest a high prevalence rate for cognitive impairment, ranging between 40% and 70%, depending on the population and setting studied (Chwastiak & Ehde, 2007; Siepman et al., 2008). The most common cognitive impairments found in MS include memory, sustained attention, and slowed information processing speed (Amato, Zipoli, & Portaccio, 2006; Nocentini et al., 2006).
    2. The relationship between MS disease subtype and magnitude of cognitive impairment remains unclear (Kalmar, Gaudino, Moore, Halper, & DeLuca, 2008). Huijbregts and colleagues (2004) demonstrated that cognitive profiles in RRMS versus progressive MS differ in severity and character, with patients with RRMS showing isolated deficits in working memory and those with progressive MS showing more global deficits.
    3. Cognitive impairment has been related to the presence of other symptoms including fatigue, spasticity, bowel or bladder dysfunction, and fine motor functioning (Kalmar, Gaudino, Moore, Halper, & DeLuca, 2008). Information

processing speed has demonstrated relationships with depression and fatigue (Diamond, Johnson, Kaufman, & Graves, 2008).

4. Relationships have been found between MRI measures and cognitive dysfunction in MS (Archibald et al., 2004; Calabrese et al., 2010). Some studies suggest a link between cognitive impairment and progression in the EDSS (Lynch, Parmenter, & Denney, 2005), whereas others do not (Kalmar, Gaudino, Moore, Halper, & DeLuca, 2008).
5. Cognitive impairment has also been linked to employment status; however, education level, fatigue, and workplace characteristics were equally important contributors (Pompeii, Moon, & McCrory, 2005).
6. Evaluation of cognitive impairment
   a. Brief batteries and clinical assessments are under investigation for reliability and validity.
   b. Informal evaluation of cognitive strengths and deficits by nursing professionals
   c. Refer for formal neuropsychological evaluation by neuropsychologist, SLP, occupational therapist or other trained provider
7. Management of cognitive impairment
   a. Cognitive rehabilitation (Mattioli, Stampatori, Zanotti, Parrinello, & Capra, 2010).
      i. Direct retraining of impaired functions
      ii. Memory exercises
      iii. Attention training
      iv. Compensatory strategies
      v. Notebooks, lists, organizers
      vi. Substitution strategies
      vii. Time and energy management
   b. Pharmacologic management
      i. Disease-modifying therapy (Freedman et al., 2008)
      ii. Anticholinesterase inhibitor treatment with donepezil (Krupp et al., 2004)
      iii. Antifatigue agents, stimulants
      iv. SSRIs

Recommendations: Nurses should work with the patient, care partner, and other members of the interdisciplinary team to develop an appropriate cognitive management program and reevaluate on an ongoing basis (Level 3). The nurse should screen for factors that could increase cognitive problems such as medications, sleep disturbance, inadequately treated pain, and other untreated symptoms (Level 2). Nurses need to recognize and acknowledge the distressing nature of cognitive deficits (Level 3). Patients should be provided with verbal and written instructions regarding the need to reduce distractions and implement safety measures (Level 3).

J. Mood dysregulation
   1. Anxiety: Lifetime prevalence of any anxiety disorder in MS is 36%, compared with 25% in the general population (Korostil & Feinstein, 2007). Generalized anxiety disorder lifetime prevalence in MS is substantially higher at 18.6% than in the general population, where it is only 3% (Korostil & Feinstein). Lower EDSS scores, fatigue, pain, and younger age at disease onset have been associated with symptoms of anxiety (Beiske et al., 2008).
   2. Sleep disorders are also common in MS, with a cumulative prevalence of all forms of sleep dysfunction reaching 47.5% (Merlino et al., 2009).
   3. Depression
      a. Prevalence studies demonstrate that depressive symptoms occur in MS with a range from 31.4% (Beiske et al., 2008) to 41.8% (Chwastiak & Ehde, 2007). Studies of lifetime prevalence of major depressive disorder in MS find rates ranging from 22.8% to more than 50%, which is significantly higher than that of the general population (Patten, Beck, Williams, Barbui, & Metz, 2003).
      b. Depression has been linked to neurobiological changes in brain structure and function in persons with MS (Passamonti et al., 2009). Beta interferon, a commonly used disease modifying therapy, has also garnered interest as a potential cause of the increased depression prevalence rate (Pandya & Patten, 2002), but this association has not held up in more rigorous studies (Patten & Metz, 2002).
      c. A direct relationship between depression and disease severity has not been found. Studies have found no relationship between depression and increased EDSS scores (Brajković et al., 2009; Dahl, Stordal, Lydersen, & Midgard, 2009). Comorbid fatigue and younger age of MS onset have been associated with depressive symptoms (Beiske et al., 2008).
      d. Depression has been shown to have direct effects on multiple aspects of functional impairment, including disease severity, adherence to disease-modifying treatments, and multiple QOL domains (Chwastiak & Ehde, 2007; Paparrigopoulos, Ferentinos,

Kouzoupis, Koutsis, & Papadimitriou, 2010).

e. Effective treatment of depression, including telehealth modalities (Egner et al.), has shown significant improvements in quality of life (Hart, Vella, & Mohr, 2008).
f. Studies have found the suicide rate in persons with MS to be twice that of a non-MS sample (Caine & Schwid, 2002). Suicidal ideation is common in MS and appears to be associated with depression, alcohol abuse, and social isolation. Further, the severity of depression and not the presence of major depression alone is a strong predictor of suicide intent (Feinstein, 2002).
g. Despite the availability of effective treatment and the high prevalence of depression and suicide in MS, less than 30% of MS patients with depressive symptoms actively seek care (Sollom & Kneebone, 2007).
h. Assessment of depressive symptoms and suicidality
    i. Ongoing assessment and monitoring for depressive symptoms with standardized instruments (e.g., PSQ-9, Beck Depression Inventory II, Center for Epidemiologic Studies Depression Scale [CES-D])
    ii. Positive endorsement of items should prompt screening for suicidality.
    iii. Evaluate medication profile for drugs that may influence mood.
    iv. Consult and refer with the multidisciplinary team as indicated by assessment.
i. Management of depressive symptoms
    i. Acknowledge existence of complex and diverse changes caused by MS and their effect on patients and care partners.
    ii. Activity and exercise (Reitberg, Brooks, Uitdehaag, & Kwakkel, 2005; Springer, Clark, Price, & Weldon, 2001)
    iii. Counseling/cognitive behavioral therapy (Thomas, Hillier, Galvin, & Baker, 2006)
    iv. Pharmacologic management (Table 8)

Recommendations: Nurses should work with the patient, care partner, and other members of the interdisciplinary team to manage depression appropriately (Level 2). Other roles are to assist patients and care partners to adjust to changes involved in living with MS (Level 2); identify the physical, emotional, spiritual, and educational needs of the patient and family (Level 2); reinforce the importance of medication regimen and be aware of medication side effects (Level 2); be alert to cues related to mood changes and treatment outcomes (Level 2); and encourage participation in a regular pattern of exercise to improve mood (Level 1).

VIII. Patient and Care Partner Education

A. General concepts for patient and care partner education
    1. Successful combination requires prepared educator and motivated, ready learner
    2. More effective when every member of multidisciplinary team works toward agreed-on patient and family outcomes
    3. Adult learning theory (Knowles, Holton, & Swanson, 2005)
        a. Because most people with MS are adults, andragogy rather than pedagogy (focus is on children) usually applies. Adult learning theory is based on principles that adults assume responsibility for learning and that learning improves when the topic directly relates to their lives.
        b. Assumptions of learning
            i. Adults with MS seek information with a desire to improve their ability to cope with the issues that MS presents in their lives.
            ii. Learning is enhanced if patients perceive education as increasing control over their lives.
    4. Domains of learning: Teaching patients with MS and their care partners typically addresses the domains of knowledge (cognitive), attitudes (affective), and behaviors (psychomotor).

B. Goals (Holland, 2002; London, 2009; Syx, 2008)
    1. Patient and family education provides MS patients and their families with information needed to promote active participation in care, and enables patients and families to make informed choices about health behaviors and engage in self-care with confidence and competence.
    2. Additional objectives include promoting maximum health potential toward wellness, coping and adaptation of the patient and family, and empowerment toward improved quality of life and hope.
    3. Specific goals of patient and family education in MS include (Halper, 2007a)

a. Understanding the diagnosis and successfully coping with the potential effects on one's life
b. Planning in critical areas such as relationships, parenting, employment, and lifestyle
c. Preventing potentially disabling outcomes, with specific goals related to new symptoms

C. Role of the nurse (Halper, 2007a; Craven & Hirnle, 2008)
1. Assist individuals with activities that contribute to health or recovery that patients perform unaided when possible (patient must have strength, will, and knowledge)
2. Help individuals carry out prescribed therapy
3. Contribute to behavior change, resulting in the knowledge and skills necessary to maintain and improve health
4. Assess and reassess patient understanding and behavioral change
5. Promote and encourage adherence to treatment

D. Concepts of learning
1. Experience is the richest source of adult learning. Although many patients and family members have not had previous experience with MS, most individuals have experienced health-related issues that require coping skills.
2. Readiness to learn is important. Adults typically need and want to be self-directing, which encourages independence.
3. Problem-solving approach to learning is preferred. Adults typically learn best when information is presented in real-life context.

E. Learning needs in MS

The complexity of MS and its management result in a variety of learning needs for patients and their families. The scope and depth of information listed below depend on the patient's and family's preferences (Fraser, Hadjimichael, & Vollmer, 2003; Halper, Costello, & Harris, 2006; Heesen, Köpke, Richter, & Kasper, 2007; Köpke, Kasper, Mühlhauser, Nübling, & Heesen, 2009; Kennedy, 2005; Pfohl, Costello, & Kennedy, 2005).

1. MS
a. Definition
b. Epidemiology
c. Pathophysiology
d. The disease course; classifications of MS; long-term needs
e. Diagnosis: McDonald criteria
f. Diagnostics: laboratory and diagnostic tests

2. Treatment of the disease
a. Provide information about all treatment options so patient can make an informed commitment to therapy. Adherence is greater when information includes realistic expectations.
b. Include information on basic clinical trial outcomes, mechanism of action, treatments (administration, adverse effects and management, resources for information and financial assistance)
c. Disease-modifying therapies
d. Adherence (discuss benefits and identify barriers to adherence)

3. MS-related symptoms
a. Common symptoms
b. Uncommon symptoms
c. Management of symptoms

4. Plan of care
a. Developed by the patient and the healthcare team to include goals and interventions that will delay progression of disability
b. Discuss when patient should call healthcare provider, and review process specific to your office routine

5. Role of team members (Craven & Hirnle, 2008)
a. Physicians
i. Primary care physician: Emphasizes the importance of regular and ongoing follow-up of all primary healthcare needs, including preventive care and appropriate screening. Often, patients with MS ignore general health screening and checkups with primary care physicians.
ii. Neurologist: Provides ongoing follow-up and management of MS and MS-related symptoms

b. MS nurses/advanced practice nurse (APN) or physician's assistant (PA)
i. Provides ongoing follow-up and management of MS and MS-related symptoms
ii. Healthcare promotion
a) Assesses patient and family for health risks
b) Facilitates learner involvement in setting healthy goals
c) Guides and supports problem solving and decision making
d) Promotes self-care strategies to enhance wellness
e) Reinforces health-promoting behaviors
f) Models healthy behaviors
g) Encourages primary health care and preventive health screenings

c. Other health care professionals
i. Rehabilitation specialists: physiatrist, physical therapist, occupational therapist, SLP
ii. Specialists: urologist, orthopedist, gynecologist, psychiatrist
iii. Counselor/Psychologist/Licensed-certified Social Worker (LCSW)
iv. Case Manager

6. Relapse management options
a. Support network
i. Benefits of staying socially connected
ii. Family and friends
iii. MS support groups
iv. MS organizations
v. Religious organizations
vi. Volunteer support
b. Resources
i. Healthcare providers
ii. MS organizations
iii. Literature
iv. Websites

F. Factors that affect learning (Chiovetti, 2006; Donaldson, Rutledge, & Pravikoff, 1999; Giger & Davidhizar, 2004; Glick, 2005; London, 2008)
1. Patient's understanding of the health problem
2. Health beliefs and practices
3. Cultural competence
a. Defined as working relationship within a system of language and culture that is dependent on history and heritage
b. Cultural health benefits
i. Affect how individuals think and feel about health and health problems
ii. Affect when and from whom they seek health care
iii. Affect how they respond to healthcare recommendations
iv. Provide a context through which meaning is gained
v. Cultural values guide actions and decision making that facilitates self-worth and self-esteem
c. Influence of culture on the individual: each patient is culturally unique
i. Identify patients at risk and adapt teaching method
ii. Promote cultural literacy
4. Health literacy (will affect how nurse teaches patients and their families; Cutilli, 2005)
a. Defining attributes
i. Reading and numeracy skills
ii. Comprehension
iii. Capacity to obtain, understand, and use information in healthcare decision making
b. Health literacy empowers individuals to
i. navigate healthcare system
ii. act appropriately in new health-related circumstances.
c. Consequences of health literacy
i. Increased healthcare knowledge
ii. Improved health status
iii. Adherence to healthcare recommendations
iv. Appropriate use of healthcare services
5. Support system and role of the family
a. Recognize the power and importance of family
b. Assess the extent to which others (family, significant other, friends, support groups) may enhance learning and offer support and encouragement
6. Cognitive dysfunction
a. Approximately 50% of individuals with MS will experience cognitive dysfunction, which may affect their ability to concentrate, learn, and recall new information and make it difficult for them to follow the plan of care.
b. Providing information verbally as well as in writing enables patients, families, and care partners to review information later.
7. Learning style
a. Individualize learning for patient's preferred learning style.
b. Select tools to meet the patient and family's needs.
c. Use a variety of teaching methods.
8. Economic factors
a. Financial concerns regarding healthcare costs may affect the patient's ability to adhere to treatment recommendations.
b. Financial concerns may increase anxiety, which in turn may affect learning.
9. Emotional state
a. Patients with MS may experience mood disorders such as depression, which can significantly affect readiness to learn.
b. Be alert to symptoms, discuss with patient and family, and refer the patient for intervention as needed.
10. Acute illness, such as relapse or an illness unrelated to MS, can affect patient's readiness and ability to learn.

11. Psychomotor ability
    a. Physical disability may lead to difficulty in performing demonstrations requiring coordination and strength.
    b. Modify teaching strategy and include family and/or care partner for support.

G. Plan: Teaching strategies
   1. Lectures and groups
      a. Involve learners and individualize the teaching session by using interactive exercises.
      b. Connect content to real-life experiences.
      c. Ask open-ended questions that require thought.
   2. One-to-one discussions with patient and family
      a. Give the patient and family time to take notes. At end of the session, ask patient and family to discuss their notes to ensure accuracy of information.
      b. The act of writing may help patients understand and remember the information.
   3. Demonstrations, such as injection technique
      a. Choose appropriate hands-on tools.
      b. Demonstrate procedure several times, then ask the patient and family to return demonstration.
      c. Acknowledge and reinforce success.
   4. Pamphlets, books, pictures
      a. Discuss written information. Allow time for questions and answers.
   5. Audiovisuals
      a. Choose videos and DVDs that are 20 minutes or less in length; use clear, direct, and accurate language; and are culturally appropriate
   6. Internet programs
      a. Use recognized authorities and provide patients with a list of recommended websites. Ensure the information is evidence based and current (i.e., are certified by the Health On the Net Foundation [HON]).

H. Models of learning for wellness and healthcare promotion (Anspaugh, Hamrick, & Rosato, 1991; Stuifbergen, Becker, Rogers, Timmerman, & Kullberg, 1999; Stuifbergen, Seraphine, & Roberts, 2000)
   1. Wellness: an expanded idea of health, meaning more than "absence of disease." The presence of well-being and dignity in the lives of individuals, communities, and cultures. It is the holistic integration of six interactive dimensions that continually influence each other.
      a. Environmental: healthy setting and self protection
      b. Physical: nutrition, fitness, and lifestyle changes
      c. Social: respect, relationships, intimacy, and and tolerance
      d. Spiritual: life meaning, purpose, and values
      e. Intellectual: learning, growth, and new challenges
      f. Emotional: stress management, acceptance, and expression of feelings
   2. Clark (1986) describes wellness as striving in a positive way, unique to an individual. People can have MS and strive to be well and enjoy life with meaning and purpose.
   3. Processes to promote wellness
      a. Provision of accurate information
      b. Individual goal setting
      c. Enhancement of self-efficacy
      d. Patient recognizes the need for learning and acceptance of new information.
      e. Patient believes in his or her own ability to make and implement appropriate behaviors.
      f. Patient and family assume responsibility for health care and self-monitoring.

Recommendations: Nurses should use an evidence-based and wellness-focused approach to education and counseling to assist patients with MS and their families to adhere to the treatment regimen, manage their symptoms, and cope with their chronic disease (Level 3). The nurse should screen for factors that could influence the ability to learn, such as cognitive difficulties and health literacy issues, and adapt teaching as appropriate (Level 2).

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