

# MOVING FORWARD:

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*Adherence to Therapy and  
the Role of Nursing in  
Multiple Sclerosis*



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# *Continuing Education Information*

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## **TARGET AUDIENCE**

This educational activity is designed to meet the needs of nurses who treat or who have an interest in patients with multiple sclerosis (MS).

## **NEEDS ASSESSMENT**

MS nurses are increasingly challenged in their practice with complex issues related to MS: disease modification, symptomatic management, psychosocial issues, and sustaining adherence to complex protocols such as disease-modifying therapy. As the profession advances in scope of practice and stature within the MS community, nursing clinicians are challenged by the complexity of multiple sclerosis: how to explain the central nervous system to patients; why adherence to disease-modifying therapies is so important when there are no visible benefits; how to manage and reduce side effects of powerful medications. This monograph will address knowledge needs and practice gaps in these important areas of MS nursing.

## **LEARNING OBJECTIVES**

- Examine emerging information about the immunology of MS and its pathologic implications for patient care.
- Identify the clinical courses of multiple sclerosis and the rationale for early intervention.
- Cite effective and comprehensive strategies in the management of multiple sclerosis symptoms and incorporate this information into best practices.
- Integrate strategies to sustain adherence to complex protocols into all nursing activities.

## **CONTINUING EDUCATION CREDIT**

This continuing nursing education activity is co-provided by Nurse Practitioner Alternatives (NPA) and the International Organization of Multiple Sclerosis Nurses (IOMSN).

NPA is a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Laurie Scudder, DNP, NP, served as nurse planner and reviewer for this activity.

This activity has been awarded 2.0 contact hours (1.0 contact hours are in the area of pharmacology). Code: IOMSN M050113.

In order to earn credit, please read the entire activity, complete the online posttest and earn a minimum score of 70%, and complete the online evaluation tool. The posttest and evaluation tool will be available beginning July 1, 2013 at [www.iomsn.org](http://www.iomsn.org). Approximate time to complete this activity is 120 minutes.

This program expires July 1, 2014.

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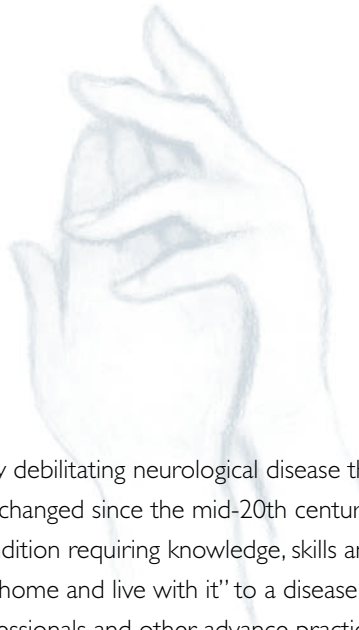
# Moving Forward:

Adherence to Therapy and the  
Role of Nursing in Multiple Sclerosis

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# Foreword



Multiple sclerosis (MS) is a chronic, frequently debilitating neurological disease that most often affects young adults in the prime of their lives. The spectrum of MS has changed since the mid-20th century from an incurably, hopeless and debilitating disorder to a complex and challengeable condition requiring knowledge, skills and a nimble cadre of health care professionals. It also has evolved from a picture of "just go home and live with it" to a disease requiring proactive and, at times, aggressive approaches to its management. Nursing professionals and other advance practice clinicians have become and will continue to be essential professional figures in the successful management of multiple sclerosis.

The goals of the MS health care professional are to provide education about the multifaceted aspects of multiple sclerosis and to assist people with MS adhere to treatments, manage their symptoms and cope with a long-term chronic illness. It has become increasingly obvious that what is needed are methods that can be adapted for each situation and each environment, along with evidence-based approaches to caring for all those affected by multiple sclerosis.

This monograph is intended to be a tool for nursing and advance practice clinicians who seek clarification of their roles and responsibilities as well as for those interested in pursuing MS care as a specialty. It provides an overview of the MS disease process, proposes a definition and model for MS nursing, identifies medications used to manage MS and control its symptoms, and explores many strategies that have proven effective in sustaining adherence in a dynamic disease.

A stylized, handwritten signature in blue ink that reads "June Halper".

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Funding for this educational activity was provided by an educational grant from EMD Serono, Inc. We appreciate the expertise and support of Lori Saslow, a medical writing consultant on behalf of the IOMSN, for her assistance in manuscript development, preparation and editing.

# Overview of Multiple Sclerosis

## INTRODUCTION

Multiple sclerosis (MS) is a progressive, inflammatory disease of the central nervous system (CNS) that causes demyelination and axonal damage.<sup>1</sup> This chronic disease is a leading cause of neurologic disability in young adults,<sup>2</sup> affecting 2.1 million people worldwide, approximately 400,000 people in the US, and at least 50,000 people in Canada.<sup>1,3,4</sup> MS is more common among women, with studies suggesting that the ratio of women to men is 3:1.<sup>5,6,7,8</sup> Men may experience onset of disease at an older age and may have a poor prognosis as compared to women.<sup>7,8</sup>

Although the onset of MS typically occurs in young adults between the ages of 25 and 35, it may be diagnosed in children under age 16 and may also appear in adults over age 50. Data indicate that approximately 3 to 5% of MS patients experience symptoms prior to age 18.<sup>9,10</sup> Children may experience symptoms similar to adults; however, symptoms such as seizures and lethargy, which may occur in children, are not common among adult patients with MS.<sup>10</sup> Evidence shows that disease-modifying therapies are safe and well tolerated in children, although the effectiveness of DMTs requires further study. The National Multiple Sclerosis Society (NMSS) reports that people diagnosed over age 50 are more likely to have a progressive course that often is expressed in the ability to walk.

It is important for nurses to provide education to patients and their families about the typical clinical course of MS and the patient's personal profile of the disease, risks and benefits of treatment, expectations related to the disease, and the importance of monitoring and follow-up with the health care team.

## CLINICAL COURSE AND NATURAL HISTORY

Four clinical courses of multiple sclerosis have been identified,<sup>11</sup> although it is anticipated that these may be redefined during 2013 based on recent evidence utilizing radiologic information. These include the

relapsing-remitting form (RRMS) of the disease, which is identified by exacerbations or relapses followed by total or partial remission of symptoms. RRMS is seen in 80 to 85% of patients with MS.<sup>12</sup> Over time approximately 50 to 70% of patients initially diagnosed with RRMS will develop a steady progression with or without relapses. This type of MS is secondary progressive MS (SPMS). Primary progressive MS (PPMS) occurs without the typical pattern of relapses and remission; PPMS, where progression is steady and leads to increasing disability, occurs in approximately 10% of patients. The least common clinical course is progressive-relapsing MS (PRMS), in which a patient follows an initial course of PPMS and then may experience exacerbations, remission and continual progression between relapses. This occurs in only 5% of patients.<sup>11,13,14</sup> Other descriptions of MS include benign MS, malignant MS and other types included in the MS spectrum (Table 1).

The overall course of MS is unpredictable, and the symptoms patients may experience are wide-ranging in type and severity. Good disease prognosis is associated with younger age of onset, complete recovery from a relapse, a lengthy interval between the initial and second event, and fewer relapses.<sup>1,15</sup> Poor prognosis is associated with the male sex; older age (over 40 years at disease onset); initial presentation involving motor; cerebellar or sphincter symptoms; multiple symptoms at first presentation; frequent attacks within the first five years of diagnosis; the first two attacks occurring within a short time frame; short interval to reaching an Expanded Disability Status Scale (EDSS) score of 4.0; and a diagnosis of progressive course of MS.<sup>8, 16-20</sup>

MS may lead to severe disability and can shorten a person's life span.<sup>21</sup> Data indicate that there is a 46% decrease in all causes of mortality for patients who start treatment early in the course of the disease.<sup>22</sup> These studies indicate that patients should begin treatment with a disease-modifying therapy soon after an MS diagnosis. Early treatment has been shown to slow the progression of the disease, delay disability, and lessen the impact upon length and quality of life. When early treatment is coupled with adherence to therapies, the benefits to patients are seen in decreased risk of clinical and radiographic relapses and reduced disability.<sup>23</sup>

Offering information to patients about life expectancy and long term prognosis is common in managing patients with other chronic illnesses such as heart disease, diabetes and cancers.<sup>24,25,26,27,28,29</sup> At times, treatment decisions may be based on survival data.<sup>30,31</sup> Survival outcome in MS has become increasingly important as a factor in the decision-making process in the treatment of MS.<sup>32</sup> If treatment can slow the progression of disease and improve the prognosis, it will become increasingly vital to share this information with patients. The goal is to reduce the risk of premature mortality and sustain adherence.

**TABLE I.**  
**Types and Courses of Multiple Sclerosis**

<i>Types of MS</i>	<i>Percentage of patients with clinical course; comment on types</i>	<i>Additional comments</i>
Relapsing-remitting multiple sclerosis (RRMS)	80 to 85% of patients <sup>12</sup>	RRMS marked by relapses and exacerbations followed by recovery and stability between attacks <sup>11</sup>
Secondary progressive multiple sclerosis (SPMS)	50% of patients with RRMS will develop SPMS over time <sup>33</sup>	SPMS patients experience gradual worsening of disease
Primary progressive multiple sclerosis (PPMS)	10 to 15% of patients	Gradual onset of symptoms that worsen over time; <sup>11</sup> progression is variable among patients <sup>33</sup>
Progressive-relapsing multiple sclerosis (PRMS)	5% of patients	Progression continues between relapses <sup>11</sup>
<u>Other Descriptions:</u> Benign MS	May occur in 5 to 10% of cases of MS <sup>34</sup>	Full recovery occurs after patient experiences neurologic symptoms <sup>34</sup>
Malignant MS	Rare	May lead to significant disability or death within five years <sup>11</sup>
Radiologically isolated syndrome (RIS)		Lesions appear on MRI but no clinical signs or symptoms
Clinically isolated syndrome (CIS)	An initial MS-like neurologic episode, such as optic neuritis	Patients with CIS are at high risk of developing MS <sup>35</sup>
Other demyelinating diseases	Acute disseminated encephalomyelitis (ADEM) and neuromyelitis optica (NMO) may present as MS <sup>36</sup>	A number of diseases mimic MS, including HIV-associated infections, Lyme disease, myasthenia gravis, pernicious anemia, progressive multifocal leukoencephalopathy (PML), systemic lupus erythematosus and syphilis.



## IMMUNOLOGY AND PATHOGENESIS OF MS

MS is an autoimmune/neurodegenerative disease of the central nervous system (CNS). Although the etiology of MS is unknown, genetics, environmental effects and possible infectious agents are various factors that may contribute to MS-related immune dysfunction. MS involves breakdown of the blood-brain barrier (BBB), acute and chronic inflammation, demyelinated scarring, and irreversible axonal damage. Destruction of the CNS myelin and oligodendrocyte loss is the primary pathology of MS. The major cause of neurologic disability is axonal loss. Brain atrophy may be helpful in determining disease progression and the effects of long-term therapy.<sup>35,37,38</sup>

There are two distinct components of immune system activity: innate immunity and adaptive immunity. Innate immunity causes the body to react to foreign substances and is a trait of all healthy individuals. In adaptive immunity, exposure to a pathogen is required to stimulate an immune response. When the innate immune system is not adequate to fight pathogens, the adaptive immune system is activated. Adaptive immunity is slower to respond and involves different subsets of T-cells, B-cells, and antibodies produced specific to antigens and complement. Within the CNS, the immune system in one area of the body can react one way, and may react another way in a different area of the body; it is important to recognize that all cells within the CNS do not behave in the same manner.<sup>35,39</sup>

When T-cells are activated by the presentation of antigen, these T-cells may be differentiated into lineages of concern in MS, including Th-1, Th-2 and Th-17 cells. Th-1 cells are considered more pro-inflammatory because of the cytokines and macrophages they produce. In models of MS, Th-2 is not considered a primary inflammatory cell and is considered to have anti-inflammatory properties. Th-17 is also an inflammatory cell.<sup>35,39</sup>

B-cell activation is part of adaptive immunity and is involved in the pathology of MS. B-cells can create and react to the environment, and involve a complex interaction of costimulatory molecules for activation. T-cells also help to activate B-cells to become an effector B-cell or plasma cell.<sup>39</sup> B-cells produce antibodies to components of the CNS, including myelin. This may help determine the extent of tissue injury in MS.

Monocytes, macrophages, microglia and dendritic cells are involved in the pathology of MS based on the amount of destruction they cause to the myelin and to axons directly. These substances can lead to axonal death. All of these cells interact with the others by production, not just of the antigens that present on the surface of cells but also of chemicals that transmit a signal from one cell to another, thereby leading to an environment where cells can be activated.<sup>40</sup>

In MS, Th-1 cells are stimulated in the periphery by an antigen, such as a virus particle. Once activated, these cells produce chemokines and matrix metalloproteinases that break down the BBB and help to recruit various immune cells into the CNS. With these substances in the CNS, these cells become reactivated and release damaging cytokines, interferon gamma, TNF-alpha, TNF-beta and IL-2.<sup>35,38</sup>

Treatment with disease-modifying therapies (DMTs) include immunomodulating and immunosuppressive agents that have a positive effect on immune response. Interferon beta inhibits T-cell proliferation and synthesis of inflammatory cytokines such as IFN-gamma and TNF-alpha. Glatiramer acetate induces suppressor T-cells. Mitoxantrone provides a broad spectrum of immunosuppression and also some B-cell suppression.<sup>35</sup> Natalizumab is a monoclonal antibody that binds to VLA-4 expressed on lymphocytes and monocytes, which reduces recruitment of immune cells to sites of inflammation.<sup>41</sup> Dimethyl fumarate has been shown to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) transcriptional antioxidant pathway that protects cells. Fingolimod appears to prevent some potentially damaging T-cells from leaving the lymph nodes. Teriflunomide reduces lymphocyte activation by inhibition of a mitochondrial enzyme which may lead to immunosuppression and reduced inflammation.<sup>42</sup>

## CLINICAL FEATURES AND DIAGNOSIS

A clinical diagnosis of MS is based on patient history and neurologic findings. Laboratory testing and magnetic resonance imaging (MRI) provide supporting documentation of a diagnosis. Diagnostic workup may include other paraclinical evidence such as MRI, cerebrospinal fluid (CSF), visual evoked potentials, optical coherence tomography (OCT), and somatosensory and



brain stem evoked potential. Other possible conditions and potential causes of CNS demyelination must be excluded before making a diagnosis of MS.<sup>1,43,44,45</sup>

The McDonald criteria, updated in 2010, provides a reliable method for diagnosing MS.<sup>46,47</sup> The McDonald criteria use the patient's history of clinical attacks combined with lesion distribution shown on MRI (dissemination in space) or the occurrence of lesions over time (as shown by CSF, evoked potentials, or dissemination in time and space via MRI).<sup>47</sup> The updated criteria allows for dissemination in time and dissemination in space to be shown on a single scan, which allows for a more rapid diagnosis of MS. The McDonald criteria should be applied for patients who present with CIS or with symptoms of a CNS demyelinating disease.<sup>48</sup>

The 2010 revisions to the McDonald criteria for the diagnosis of MS includes the following:<sup>47</sup>

- Clinical presentation of two or more attacks and objective clinical evidence of two or more lesions in different locations, no additional information is needed for diagnosis of MS.
- Clinical presentation of two or more attacks and clinical evidence of only one lesion, then dissemination in space must be shown by MRI or appearance of two or more lesions on MRI and a positive CSF is diagnostic of MS.
- When there is one attack and clinical evidence of two or more lesions, dissemination in time must be demonstrated.
- In cases where an individual has one attack and clinical evidence of one lesion as seen in CIS, demonstration of dissemination in space and in time is required. For dissemination in space, an abnormality on MRI of two lesions plus a positive CSF is acceptable. Dissemination in time may be shown on MRI or by occurrence of a second attack.

The most common clinical presentations of MS<sup>49</sup> include:

- Sensory disturbances: numbness, parathesias, neuritic pain, Lhermitte's sign, diminished vibratory sense, impaired position sense
- Motor abnormalities: corticospinal, abnormal deep tendon reflexes, positive Babinski response, spastic limb weakness
- Visual pathway problems: brain stem and eye movement abnormalities, optic neuritis including dimming or visual loss, loss of color vision, visual field defect
- Cerebellar: gait ataxia, limb ataxia, tremor

Symptoms experienced by people with MS can vary based on the location of lesions in the brain or spinal cord and result from myelin and axonal damage in specific areas of the CNS.<sup>50,51</sup> MS can be a frustrating disease because of the unpredictable nature of symptoms and the unpredictability of how patients will feel and function on a day-to-day basis. Common symptoms of MS are shown in Table 2.

**TABLE 2.**  
**Symptoms of Multiple Sclerosis<sup>49</sup>**

### **Common symptoms of MS**

- Fatigue
- Depression
- Focal muscle weakness
- Visual changes
- Bowel, bladder and sexual dysfunction
- Gait problems, spasticity
- Paresthesias
- Neuropathic pain

### **Less-common symptoms of MS**

- Dysarthria, scanning speech and dysphagia
- Lhermitte's sign
- Ataxia
- Vertigo
- Cognitive dysfunction
- Tremor, incoordination

**TABLE 2. (CONT.)**  
**Symptoms of Multiple Sclerosis<sup>49</sup>**

**Rare symptoms of MS**

- Decreased hearing
- Seizures
- Tinnitus
- Mental disturbance
- Paralysis

MRI has become a vital diagnostic tool, particularly when the individual does not experience two clinical attacks, as required by the McDonald Criteria. This is the preferred method of brain imaging, and it is able to detect subclinical lesions. Active inflammation may be identified using gadolinium (Gd) contrast enhancement.<sup>48,52</sup> Current guidelines recommend that baseline brain MRIs with gadolinium be conducted in all patients with suspected MS. Brain lesions detected by MRI may provide evidence of dissemination in time and dissemination in space. If the brain MRI is not diagnostic or if the presenting symptoms indicate spinal cord involvement, a spinal cord MRI with gadolinium is recommended in addition to the brain MRI.<sup>53</sup>

There are a few well-defined methods for measuring progression of disease in MS. There are two disability rating scales: the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC). Changes in MRI is another method of evaluating progression of disease. MRI changes can be measured using T1-weighted gadolinium-enhanced lesions, measurement of brain atrophy and new or expanding T2-weighted lesions.

The EDSS, a widely used outcome measure in clinical trials, is a method of quantifying disability in MS. It is based on an evaluation of a patient's functional system scores (Table 3). The 10-point scale is measured in half-point increments. 1-3 indicates that the patient is ambulatory and has minimal disability. 4-5.5 indicates moderate disability, and 6-7 that the patient requires

an assistive device for ambulation. 8-9 denotes severe disability and the patient is confined to a wheelchair or is bedridden; 10 indicates death.<sup>54</sup>

**TABLE 3.**  
**Expanded Disability Status Scale (EDSS)<sup>54</sup>**

- 0:** Normal neurological exam
- 1.0-1.5:** No disability
- 2.0-2.5:** Disability is minimal
- 3.0-3.5:** Disability is mild to moderate
- 4.0-4.5:** Disability is moderate
- 5.0-5.5:** Increasing limitation in ability to walk
- 6.0-6.5:** Walking assistance (cane, crutch or brace) is required
- 7.0-7.5:** Restricted to wheelchair
- 8.0-8.5:** Confined to bed, chair or wheelchair; patient continues some self-care functions
- 9.0-9.5:** Completely dependent
- 10.0:** Death due to MS

Other useful clinical study measures include the Multiple Sclerosis Functional Composite (MSFC), the MS Quality of Life-54 (MSQOL-54), the MS Quality of Life Inventory (MSQLI), the Minimal Assessment of Cognitive Function in MS (MACFIMS), and the Symbol Digit Modalities Test (SDMT) (Table 4).

**TABLE 4.**  
**Clinical Study Measures of Multiple Sclerosis**

<i>Measure</i>	<i>Description</i>
Multiple Sclerosis Functional Composite (MSFC) <sup>55,56,57</sup>	Consists of three quantitative tests of neurologic function, including the Paced Auditory Serial Addition Test (PASAT) to assess cognition, the 9-hole peg test to measure right- and left-arm scores, and the 25-foot timed walk, useful for leg assessment. It provides a precise measure of impairment in MS and has excellent predictive validity. It measures upper-extremity function and cognitive function as well as mobility and leg function. Generally, it is not useful beyond EDSS 6.5.
MS Quality of Life-54 (MSQOL-54) <sup>55</sup>	Based on the Health Status Questionnaire Short Form-36 (SF-36), this 54-item scale measures overall quality of life, health distress, sexual function, cognitive function and energy.
MS Quality of Life Inventory (MSQLI) <sup>55</sup>	Covers most areas of concern for MS patients that relate to quality of life and includes more detail than the MSQOL-54. It includes the following 10 subscales: <sup>55</sup> <ul style="list-style-type: none"> <li>• Health Status Questionnaire (SF-36)</li> <li>• Modified Fatigue Impact Scale (MFIS)</li> <li>• MOS Pain Effects Scale (PES)</li> <li>• Sexual Satisfaction Scale (SSS)</li> <li>• Bladder Control Scale (BLCS)</li> <li>• Bowel Control Scale (BWCS)</li> <li>• Impact of Visual Impairment Scale (IVIS)</li> <li>• Perceived Deficits Questionnaire (PDQ)</li> <li>• Mental Health Inventory (MHI)</li> <li>• MOS Modified Social Support Survey (MSSS)</li> </ul>
Minimal Assessment of Cognitive Function in MS (MACFIMS) <sup>58</sup>	Evaluates major cognitive domains, including processing speed, working memory, verbal learning and memory, visual learning and memory, verbal fluency, executive function and visual-spatial ability.
Symbol Digit Modalities Test (SDMT) <sup>59,60</sup>	Measures visual processing speed and working memory. It is a reliable and sensitive test used for screening of cognitive impairment in MS.

## MANAGEMENT OF MULTIPLE SCLEROSIS

Great advances have been made in the treatment of multiple sclerosis, a chronic and disabling disease. The management of MS is focused on modifying disease, treating relapses and managing symptoms. Recent data on survival in MS presents a strong case for starting early and continuous treatment with approved disease-modifying therapies.<sup>22,32</sup> Patients need information about the various options available in the treatment of the disease. Managing MS should include decreasing the relapses patients experience, slowing the onset of disability and alleviating symptoms.<sup>17,61</sup>

It is important for patients to understand that while these medications are not curative and relapses may still occur, early treatment with disease-modifying therapies is effective. In addition to several effective injectable and infusible DMTs, there are three new oral agents that are also effective in limiting disability and slowing progression of the disease. Patients may indicate certain personal preferences about the type of therapy and the complexity of the regimen, and health care providers should keep in mind how these factors may relate to a patient's tolerance of and motivation to adhere to treatment.

When making treatment decisions, there are a number of issues to consider and many benefits and risks to weigh. Various treatment decisions may be based on safety, tolerability, convenience, required monitoring and pregnancy concerns. Since 70% of patients are female, pregnancy considerations often come into play. Other issues to consider when making treatment decisions include cost, patient preferences, physician experience and the patient response to therapy. Evidence-based studies and the mechanism of action of the various agents may also play a role in the shared decisions made by health care providers in collaboration with patients.

### Injectable Disease-Modifying Therapies

Currently, there are five disease-modifying treatments administered by injection that are approved for use in the United States and Canada to treat relapsing forms of MS. These injectable therapies include glatiramer acetate (Copaxone®), interferon beta-1a (Avonex®), interferon beta-1a (Rebif®) and interferon beta-1b

(Betaseron®, Extavia®). Glatiramer acetate is believed to reduce inflammation in the CNS and may possibly restore normal immune regulation. The interferon beta agents are thought to interfere with MS by suppressing the immune response and limiting activated cells from crossing the blood-brain barrier. These therapies are each administered either subcutaneously or intramuscularly, and have differing schedules, ranging from injection once a day to once a week. For the most up-to-date information about these agents, please refer to the insert (Appendix I) included inside the back cover of this monograph.

The injectable disease-modifying therapies have comparable efficacy and are generally well tolerated. These therapies have been in use since the 1990s, and no new adverse effects have occurred with any of these agents in over 15 years.<sup>62</sup> Side effects of injectable therapies (Appendix I) often occur within the first several months of therapy and then subside gradually. These side effects can be managed, and most patients do not require discontinuation of therapy.

At times, adherence to an injectable therapy regimen may be an issue. Some patients find injections painful, difficult to perform and inconvenient to their lifestyle. In addition, patients may become discouraged because improvement in their symptoms may not be evident. MS nurses can help by working with patients to set realistic expectations and goals. Adherence may also be improved by including family and caregivers in the management plan and offering information about support and networking opportunities for the patient. If cost is an issue, information about pharmaceutical company support programs can be provided to patients and their families. Please refer to Appendices 3 and 4 in the back pocket of this monograph for informative websites about MS and for information about pharmaceutical company contacts. Additional strategies to improve adherence are presented in the following sections.

### Infusible Disease-Modifying Therapies

Two medications, Natalizumab (Tysabri®) and Mitoxantrone (Novantrone®), are both administered by intravenous infusion. Both agents are FDA-approved

for the treatment of MS. When infusible therapies are selected for treatment, appropriate evaluations and ongoing monitoring of patients before and after therapy is required. Additional concerns involving infusible therapies include managing side effects patients may experience, working with patients on a manageable schedule of therapy and providing office logistics needed to support MS infusion therapy.

Natalizumab is administered every four weeks as a two hour infusion (one hour treatment; one hour observation - in the United States). It is a monoclonal antibody and works by inhibiting the migration of T-cells and B-cells into the CNS. The key features associated with natalizumab are shown in Appendix I. Although it is a highly effective therapy,<sup>63</sup> natalizumab treatment increases the risk of progressive multifocal leukoencephalopathy (PML) in patients, and this risk increases with the duration of therapy. Natalizumab is considered a first-line therapy for the treatment of MS, yet it is often recommended as a second-line treatment for patients who have not had an adequate response to therapy or are unable to tolerate an alternate DMT.

In 2005, natalizumab was voluntarily withdrawn from the market due to the PML risk, and was rereleased in 2006 with safety requirements incorporated into the TOUCH<sup>®</sup> program. Restrictions of the program are that patients and prescribers must be enrolled in the program to prescribe and receive natalizumab. Only registered pharmacies and infusion locations authorized by the TOUCH program can administer the agent. In addition, patients must be closely monitored for possible adverse effects every four weeks, and again evaluated at three and six months after infusion and every six months thereafter.<sup>64</sup>

Studies have shown that therapy with natalizumab may lead to reactivation of the JC virus in patients with MS who were previously infected, and may also be associated with a transient reduction in JC virus-specific cellular immune response.<sup>65</sup> It is unclear whether the risk of PML is increased in patients treated with natalizumab in combination with interferon beta as compared to natalizumab alone. Currently, the risk of PML in people receiving more than 24 infusions is estimated at one in

1,000 cases.<sup>66</sup> However, for those who are JCV positive and have had prior immunosuppressant therapy, the risk would be greater at 11/1000 cases.<sup>67</sup>

Mitoxantrone is a chemotherapeutic agent that is administered intravenously every three months. It is approved to treat secondary progressive MS, progressive-relapsing MS, and worsening RRMS that is not responsive to other DMTs.<sup>68,69,70</sup> In treating MS, it suppresses the amount and activity of white blood cells that activate the MS attack in the CNS. Because mitoxantrone suppresses the immune system, those receiving treatment are at higher risk of infection. It is advisable for patients treated with mitoxantrone to avoid contact with others who are sick and to avoid dental treatment for approximately two to three weeks following infusion. The major adverse effect associated with the use of mitoxantrone is cardiomyopathy, which may lead to heart failure and acute myelogenous leukemia.<sup>71</sup> Other effects are noted in Appendix I. Treatment with mitoxantrone is limited to a lifetime use of 140 mg/m<sup>2</sup> due to the cumulative cardiotoxicity of the agent.<sup>68</sup>

## Oral Disease-Modifying Therapies

The most recent additions to the treatment options for MS are the oral disease-modifying therapies. To date, there are three oral therapies available for the treatment of relapsing forms of MS: fingolimod (Gilenya<sup>™</sup>), teriflunomide (Aubagio<sup>®</sup>), and dimethyl fumarate (Tecfidera<sup>™</sup>). Laquinimod is an agent that is being studied for potential benefit as a DMT and may be approved in the future based on research outcomes. Both health care providers and patients have hope that this agent, as well as many under investigation, will add to the armamentarium of treatment options in the future.

Fingolimod was the first oral immunomodulator/ immunosuppressant approved for the treatment of relapsing forms of MS. It is taken once daily and acts by entrapping lymphocytes, mostly T-cells, within the peripheral lymph nodes.<sup>72</sup> The Phase III TRANSFORMS trial demonstrated good outcomes with use of the oral agent, including a lower annualized relapse rate, fewer active lesions and a greater percentage of patients remaining relapse-free.<sup>73</sup> Use of fingolimod requires

careful observation for six hours after the first dose to monitor patients for cardiovascular signs and symptoms. Bradycardia and second-degree atrioventricular block were seen during clinical trials.<sup>73,74</sup> Other side effects are shown in Appendix 2.

Teriflunomide was approved by the FDA more recently for relapsing forms of MS, including RRMS, and is taken orally once a day. This agent acts in MS by decreasing the proliferation of T-cells and B-cells that are thought to be involved in the inflammatory process in MS.<sup>75</sup> Trials of teriflunomide show a reduction in annualized relapse rate, reduced risk of 12-week sustained disability progression, and a reduced number of Gd-enhancing lesions.<sup>76</sup> The major adverse effects of concern are the hepatotoxicity and the risk of teratogenicity that is included as a warning on the labeling of Aubagio®. Appendix 2 lists the other common side effects of the agent.

The most recent entry into the MS therapeutic armamentarium is dimethyl fumarate (Tecfidera™). The agent is administered daily on a BID schedule. Dimethyl fumarate is a derivative of fumaric acid, which is an agent commonly used for the treatment of psoriasis.<sup>77</sup> In MS it acts as an immunomodulator, and it appears to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway, which is a promising protective mechanism in neurodegenerative diseases.<sup>72,78</sup> The effectiveness of dimethyl fumarate was demonstrated in two trials showing an annualized reduction rate at two years, and a reduction in the two-year risk of relapses.<sup>79,80</sup> While the medication is well tolerated, the major side effects include lymphopenia and flushing.<sup>81</sup> Other side effects are listed in Appendix 2.

### Symptom Management

Managing the symptoms of MS is a challenge, but effective management can dramatically improve the patient's quality of life. Symptoms such as fatigue, bowel and bladder dysfunction, pain, and other common symptoms can be controlled or minimized through rehabilitation, education and counseling. When these strategies are not sufficient, pharmacotherapy may be considered.

Table 5 lists the various medications used for symptom management in MS. The table is not intended to be exhaustive; it is an attempt to reflect the most common or problematic symptoms, and the various interventions that may help patients.

Before determining the treatment of symptoms, it is important to exclude any factors that may be causing or contributing to symptoms. Concomitant medications, concurrent illnesses or other medical conditions may produce new symptoms or alter the severity of symptoms. If pharmacologic treatment is needed to alleviate symptoms, it is essential to determine if there are any contraindications. Nurses need to ensure that patients understand what to expect in terms of outcomes and anticipated side effects of the intervention. Finally, patients need to be encouraged to adhere to the suggested medication regimen and follow-up, as needed, so that nurses can confirm that the interventions are effective. If patients experience intolerable side effects as a result of disease-modifying therapies, there are various strategies such as dose escalation and dose titration that can help patients avoid side effects and increase tolerance to treatment.

**TABLE 5.****Pharmacologic Management of Selected Symptoms in Multiple Sclerosis\***

<i>Symptoms</i>	<i>Treatment</i>	<i>Nursing Considerations</i>
Fatigue	<ul style="list-style-type: none"> <li>• CNS stimulants (modafinil, armodafinil)</li> <li>• Amantadine</li> <li>• Selective serotonin reuptake inhibitors (SSRIs), eg, fluoxetine</li> </ul>	<ul style="list-style-type: none"> <li>• Restlessness or sleep disturbance may occur</li> <li>• Help patients with dosing schedule; titrate doses up</li> </ul>
Bladder dysfunction	<ul style="list-style-type: none"> <li>• Anticholinergics (eg, oxybutynin)</li> <li>• Antimuscarinics (eg, tolterodine)</li> <li>• <math>\alpha</math>-Blockers (eg, terazosin)</li> </ul>	<ul style="list-style-type: none"> <li>• Determine if urinary tract infection is present</li> <li>• Monitor retention</li> <li>• Monitor fluid balance</li> <li>• Follow overall elimination pattern</li> <li>• Consider contribution of other medications</li> <li>• Provide strategies to avoid side effects, eg, dry mouth</li> </ul>
Bowel dysfunction	<p><i>Constipation</i></p> <ul style="list-style-type: none"> <li>• Stool softeners</li> <li>• Bulk-forming agents</li> <li>• Mini-enemas</li> <li>• Stimulants</li> <li>• Suppositories</li> </ul> <p><i>Urgency/Diarrhea</i></p> <ul style="list-style-type: none"> <li>• Bulk-forming agents</li> <li>• Anticholinergics</li> <li>• Antimuscarinics</li> </ul>	<ul style="list-style-type: none"> <li>• Provide bowel training regimens; many of the medications should not be used long-term</li> <li>• Consider contributory effects of other medications, eg, steroids or antibiotics</li> <li>• Consider lifestyle issues</li> <li>• Encourage exercise</li> <li>• Provide diet counseling</li> </ul>
Pain	<ul style="list-style-type: none"> <li>• Anticonvulsants (phenytoin, carbamazepine, gabapentin, pregabalin, lamotrigine)</li> <li>• Tricyclic antidepressants (amitriptyline, nortriptyline)</li> <li>• Duloxetine hydrochloride</li> </ul>	<ul style="list-style-type: none"> <li>• Watch for sedation</li> <li>• Start with low doses and titrate up</li> <li>• Monitor outcomes; alter treatment as necessary; supportive measures can help</li> </ul>
Spasticity	<ul style="list-style-type: none"> <li>• GABA antagonists (oral or intrathecal baclofen)</li> <li>• <math>\alpha</math>-agonists (tizanidine)</li> <li>• Anticonvulsants (diazepam, clonazepam, gabapentin)</li> <li>• Botulinum toxin<sup>42</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Time doses to maintain therapeutic blood levels</li> <li>• Titrate doses up (especially with baclofen)</li> <li>• Watch for sedation or cognitive symptoms; may require a change in dosage or medication</li> <li>• Combination treatments may help</li> <li>• Intrathecal baclofen requires surgical insertion of programmable pump</li> </ul>



**TABLE 5. (CONT.)**  
**Pharmacologic Management\***

Depression	<ul style="list-style-type: none"> <li>• SSRIs and SNRIs (eg, fluoxetine, sertraline, paroxetine, citalopram, duloxetine hydrochloride)</li> <li>• Tricyclic antidepressants (eg, amitriptyline, nortriptyline)</li> <li>• Atypical antidepressants (eg, venlafaxine, bupropion)</li> </ul>	<ul style="list-style-type: none"> <li>• Evaluate type and degree of depression</li> <li>• Consider contribution of medications (eg, with interferons)</li> <li>• Assess family situation/support network</li> <li>• Consider suicide risk</li> <li>• Promote use of psychiatric services</li> <li>• Advise patient that medication effects may take several weeks</li> <li>• Advise patient not to stop medications suddenly</li> <li>• Reassess patient regularly</li> <li>• Paroxetine can be taken in the morning or at night; can help with anxiety</li> <li>• Monitor urinary function with venlafaxine (may cause fluid retention)</li> </ul>
Walking difficulty	<ul style="list-style-type: none"> <li>• Dalfampridine<sup>42</sup></li> </ul>	<ul style="list-style-type: none"> <li>• 10 mg every 12 hours</li> <li>• Do not crush</li> <li>• Consider seizure risk</li> <li>• Monitor for infections</li> <li>• Advise not to increase dosage</li> <li>• Do not take with compounded 4-AP</li> </ul>
Pseudobulbar Affect	<ul style="list-style-type: none"> <li>• Nuedexta™ (dextromethorphan hydrobromide and quinidine sulfate)<sup>42</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Use for MS or ALS</li> <li>• Maybe used for other types of emotional lability</li> <li>• Not restricted to any types of MS</li> <li>• Dose once daily for seven days, one capsule every 12 hours</li> <li>• Should not be used with quinine, quinidine, mefloquine or MAO inhibitors</li> <li>• Do not use with other drugs that prolong Q-T interval</li> </ul>

\*Adapted with permission from: Harris C, Halper J, eds. *Multiple Sclerosis: Best Practices in Nursing Care—Disease Management, Pharmacologic Treatment, Nursing Research*. 3rd ed. Hackensack, NJ: International Organization of Multiple Sclerosis Nurses; 2010.

# Roles of The MS Nursing Professional

The role of the MS nurse includes providing education about the multifaceted aspects of multiple sclerosis and assisting people with MS in adhering to treatment, managing symptoms and coping with a long-term chronic illness. Thus the MS nurse must remain alert to factors that affect the ability of people with MS and their families to manage this disease, which may include cognitive difficulties, health literacy issues and cultural differences. Nurses need to employ teaching methods that can be adapted as needed for the situation and environment, along with an evidence-based approach to educating people with MS and their families, with a focus on wellness.<sup>82</sup> Good communication skills with the patient, family members and others on the health care team—including listening, collaborating and negotiating—are paramount. The roles of the MS nurse fall roughly into the following five categories.

## ASSESSMENT, SETTING GOALS AND PROMOTING WELLNESS

Nurses must assess the person with MS and his/her family for health risks, and facilitate the family's involvement in setting healthy goals and in overall problem solving and decision-making. It also falls upon the MS nurse to reinforce self-care strategies that enhance wellness, to model healthy behaviors and to encourage primary health care and preventive health screenings.<sup>82</sup> This means:

- Performing comprehensive assessments to gauge each person's level of functioning and his/her needs and preferences
- Understanding each patient's learning style and lifestyle, and getting to know the families and caregivers for each patient
- Recognizing physical care requirements; performing neurological, functional, psychological, sociological and cognitive assessments; and maintaining sensitivity to cultural, ethnic and gender-based considerations

## EDUCATION

MS is a complex chronic disease with an unpredictable course, and those affected—both the patient and his/her family—face an uncertain future. This unknown prognosis for each individual with the disease underscores the importance of setting appropriate expectations and fostering a realistic perspective. For example, people with MS need to understand that disease-modifying therapies improve prognosis over the long term, but that these treatments may not necessarily help them feel better in the short term. As with any long-term illness, the management of MS requires nurses to remain involved with their patients over many years.

Continuing education in genetics and genomic education is of great interest among the nursing profession.<sup>83</sup> MS nurses should maintain an awareness of the evolving science of genomics and how it may impact ethical, legal and social issues involved in communicating with patients about genomics in health care. This may include issues of confidentiality, decision-making, informed consent and genetic testing. Although MS is not directly inherited, genetic factors may help identify those who are susceptible to environmental triggers such as germs or viruses, which may play a role in causing MS.<sup>84</sup> It is therefore important for nurses to develop competency in genomics so they may guide their patients appropriately.<sup>85</sup>

It is imperative for nurses to keep the lines of communication open between themselves and those with MS, their families and their caregivers about the complexity and progress of the disease and its management. These discussions should cover:

- A definition of MS, as well as the person's diagnosis, symptoms and the course of the disease
- Treatment of the disease, including developing and maintaining a plan of care and managing relapses
- The role of multidisciplinary team members involved in the treatment plan, support networks and available resources. The preferences of the person with MS and his/her family members must be considered in this process.

MS nurses must be able to clearly communicate the process for diagnosing MS, the course and pathology of MS across the life span and educational strategies that encourage wellness and health promotion. If genetics is a concern, health care providers must incorporate translation of these issues into the care and education they provide. Essentially, MS nurses must serve as mentors and role models for patients, family members, other nurses and other members of the professional health care team. Ideally, the role of the MS nurse also should include community outreach to increase public awareness about the disease.

### MANAGING SYMPTOMS, TREATMENT AND FACILITATING BEHAVIOR CHANGE

A primary responsibility of the MS nurse is to assist people with MS in adhering to prescribed therapy and to encourage them to understand and adopt the behaviors needed to maintain and improve their health. This involves continually monitoring each person's overall understanding of the disease and his/her actual behavioral changes, and providing the person with ongoing management of the disease and its related symptoms. The MS nurse helps people with MS to participate in activities that contribute to wellness, health or recovery that the individual can perform independently, if possible, assuming the person has the strength, will and knowledge to do so.<sup>82,86</sup> This means:

- Formulating a collaborative treatment plan, taking into account the person's symptoms, level of disability, need for disease-modifying agents and need for sustained or prolonged care
- Facilitating treatment by teaching the person with MS and family members about disease-modifying medications and helping him/her to overcome physical, cognitive or other obstacles to treatment
- Knowing the pharmacology of therapeutic agents, the use of complementary and alternative therapies in MS and the basics of rehabilitation
- Monitoring treatment outcomes, including the use

of evaluation tools for adherence and self-care; management of pain, side effects and adverse reactions of medications; and noting adaptation to lifestyle changes and quality of life issues

- Detecting acute and chronic changes in health and providing counseling including anticipatory guidance and problem-solving; and defining the limits and responsibilities of the patient, family and nurse
- Listening, motivating, inspiring hope, and putting MS "in its place"

### ECONOMIC AND ADVOCACY ISSUES

MS is becoming an ever more expensive disease to treat, and it often presents a huge economic burden to those who have it, as well as to their families. Those affected with MS face difficulties in terms of employment and employability. There are direct and indirect costs to family members and caregivers, and treatment decisions are affected by the cost of first-line therapies versus other therapy options. Unfortunately, MS nurses often are not trained to handle these financial challenges, nor do they necessarily have the expertise to become a patient advocate and to help guide the person with MS and family members on ways to fund treatment.

Therefore, it is important for MS nurses to have an understanding of reimbursement policies and processes of insurance policies and managed care plans, Medicaid and Medicare funding, and pharmaceutical industry programs. With knowledge of the logistics of the health care system, MS nurses can more effectively advocate for their patients, and may be able to negotiate and operate within that system in the best interests of their patients. With changes in health care on the horizon, it will also be vital for the MS nurse to become familiar with Accountable Care Organizations (ACOs).

## **A MULTIDISCIPLINARY, COLLABORATIVE APPROACH**

It is essential for MS nurses to be aware that they are treating an individual with MS, and that each individual is unique. MS nurses must be mindful of the complete health picture of each individual they treat. In order to facilitate optimum overall health care for people with MS, MS nursing must be a mutual, collaborative effort with other nurse specialists, health professionals, and colleagues from specialties outside of MS and neurology, including primary-care practitioners.

Such a collaborative, multidisciplinary approach is optimal not just for those with MS and their family members but for MS nurses, too, who often work in isolation and who can benefit from outside professional support and networking opportunities. Unfortunately, while the creation of a supportive professional network for MS nurses is important, it does not happen routinely. Professional networking and collaboration is readily available to MS nurses, and organizations that encourage this type of collaboration are listed in Appendix 3. For the benefit of MS nurses and their patients, it is recommended that MS nurses establish and sustain therapeutic partnerships and alliances with MS patients, their families and care partners, and other health professionals on the patient's professional health care

team. Nurses must know how to tap into community resources in order to provide the best information for people with MS and their families. Professional organizations can also be helpful to nurses. Ultimately, to be successful, the MS nurse must be ready and able to educate, and those with MS must be motivated to learn. This happens most effectively when a multidisciplinary team works toward agreed-upon outcomes together with patients, their families and their care partners.

Another benefit of a multidisciplinary, collaborative approach to MS nursing is that it enables nurses to broaden their professional competencies—for example, developing new skills, participating in MS research, establishing benchmarks for nursing care and examining outcomes of nursing practice. A nurse's professional expertise should include current technical nursing skills and knowledge of advanced technologies, e.g., magnetic resonance imaging (MRI) techniques and guidelines and innovations in rehabilitation technology, as well as proficiency with the use of electronic medical records (EMR). MS nursing is broad-based in scope and can include competencies more often associated with social workers, psychologists and rehabilitation specialists. Table 6 provides a comprehensive and practical illustration of the scope of MS nursing practice.

**TABLE 6.****Domains and Competencies of multiple Sclerosis Nursing\*****DOMAINS**

<b>COMPETENCIES</b>	<b>Establish Therapeutic Partnerships</b>	<b>Perform Comprehensive Assessments</b>	<b>Formulate Collaborative Treatment Plan</b>	<b>Initiate and Facilitate Treatment Regimen</b>	<b>Monitor Outcomes</b>	<b>Sustain Therapeutic Alliances</b>	<b>Maintain and Broaden Nursing Competencies</b>
<b>1. Communicate</b>							
a. Listen	X	X			X	X	
b. Collaborate	X		X			X	X
c. Network						X	X
d. Negotiate			X	X		X	X
e. Delegate			X	X		X	X
f. Document		X	X		X		X
<b>2. Assess patient care needs</b>							
a. Recognize physical care requirements		X	X		X		
b. Perform neurological assessment		X			X		X
c. Perform functional assessment		X	X	X	X		X
d. Perform psychological, sociological, and cognitive assessments		X	X	X	X		X
e. Recognize culture-specific needs	X	X	X				X
f. Detect acute and chronic health changes		X			X		
<b>3. Counsel patients and families</b>							
a. Provide anticipatory guidance	X		X	X			
b. Define limits and responsibilities	X		X	X		X	
c. Listen, motivate, inspire hope, put MS “in its place”	X		X	X	X	X	
d. Solve problems			X	X	X	X	
<b>4. Educate</b>							
a. Serve as role model	X			X	X	X	X
b. Serve as a mentor and preceptor					X	X	X
c. Increase awareness of MS in the community						X	X
<b>5. Advocate</b>							
a. Negotiate within the healthcare system	X		X	X		X	X
b. Promote self-care	X		X	X	X	X	X
<b>6. Participate in research</b>							
a. Establish benchmarks of care							X
b. Examine outcomes of nursing practice							X

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# The Concept of Adherence and Nursing Strategies

## IMPORTANCE OF ADHERENCE; STRATEGIES; BARRIERS TO ADHERENCE

Adherence, from a nursing perspective, can be defined as an active, voluntary and collaborative participation of the patient in a mutually agreeable course of behavior or treatment that results in a desired preventive or therapeutic outcome. The key elements of adherence include a partnership, mutually established goals and a therapeutic alliance between the patient and health care provider. Nonadherence, when a person does not take medication, follow a diet and/or execute lifestyle changes as prescribed by a health care provider,<sup>87</sup> may result in negative consequences to the health of the patient. Poor adherence will reduce the overall effectiveness of prescribed therapy. It is important to help the patient feel as though he/she is a valued and respected partner on the health care team who actively collaborates in the treatment plan and participates in shared decision-making.<sup>88</sup>

Lack of adherence to treatment of chronic diseases is a wide-ranging problem throughout the world. In developed countries, adherence to long-term therapies for chronic diseases is approximately 50%. The result of poor adherence is reduced effectiveness of patient outcomes and increased health care costs. In addition to improving therapeutic outcomes, adhering to prescribed medical regimens enhances patient safety.<sup>87</sup>

Adherence is composed of three categories: acceptance, persistence and compliance. Before patients can adhere to a long-term medication regimen, they must first accept the necessity for it. Patients newly diagnosed with MS may not show signs or symptoms of the disease for

months or years, and may not perceive the need for treatment. With education, patients begin to understand the disease process and accept the importance of treatment; once treatment begins, patients need to persist, or continue with regular therapy. Patients are not properly adhering to a medication regimen unless they are also complying with the instructions for taking the medication, which means taking the correct dose of the medication on the right day and at the right time. A patient is not truly adherent unless all three conditions are met.<sup>89</sup>

Nonadherence is a major problem in the treatment of chronic illnesses. According to a report by the National Association of Chain Drug Stores, for every 100 prescriptions written, 50 to 70% are sent to a pharmacy, 48 to 66% leave the pharmacy with the patient, 25 to 30% are taken properly and 15 to 20% are refilled as prescribed.<sup>90</sup>

In MS, adherence to disease-modifying treatments (DMTs) can limit the number of relapses and MS-related hospitalizations. In a large study of 43,054 MS patients in a US managed care database, the risk of MS-related relapse during follow-up was 35% higher for nonadherent patients and 54% higher for patients who discontinued therapy, as compared to the adherent group. In addition, the risk of MS-related hospitalization during follow-up was 54% higher for the nonadherent and 73% higher for the discontinued group versus adherent patients.<sup>91</sup>

The WHO has identified five important dimensions that affect adherence (Table 7). One factor under the health care team and health system is the communication and relationship between the health care provider and the patient.<sup>87</sup> Patients who see themselves as having a high-quality relationship with their health care provider are more inclined to adhere to treatment.<sup>23</sup> In MS, it is often the nurse who partners with the patient from the time of diagnosis throughout the person's journey with this lifelong disease. Adherence to therapy starts with the development of a strong relationship between the health care provider and the patient. Typically, it is the MS nurse who walks the walk with the patient as he/she lives with this long-term disease. The MS nurse is the constant

in the clinic and when patients and their families are coming to grips with the disease. It is the nurse who is there when the patient leaves for college, starts a first job, gets married, has children and advances in a career.

An open and honest relationship between health care providers and patients is another important factor in a patient's ability to adhere to therapy.<sup>89</sup> MS nurses are in a unique position to support the patient throughout the disease. A patient's willingness to adopt behaviors and attitudes that serve to improve health is also key, especially when he/she is faced with obstacles or unpleasant experiences such as preparing and administering a daily injection and managing medication-related side effects.<sup>92</sup>

Other factors which impact adherence are listed in Table 7. Social and economic factors include social support networks, health literacy, cost of medication and transportation, access to facilities, employment, and family function. Medical condition-related factors include whether the patient has any comorbidities that complicate treatment. Therapy-related factors include patients' experience with the side effects of therapy and the complexity of the medical regimen. With MS, one concern may be the patient's ability to master certain techniques, such as self-injection. The last factor identified by the WHO is patient-related concerns. This incorporates the beliefs, perceptions and expectations of the patient. It is important to determine whether a patient's expectations of therapy are realistic. Self-efficacy, or a patient's confidence and ability to manage his/her disease, falls under this category.<sup>87</sup>

A number of predictors indicate whether patients will adhere to therapy (see Table 8). Self-efficacy, how a patient measures his/her ability to complete tasks and reach goals, is an important predictor of adherence. The beliefs that a person holds regarding his/her power to effect a situation influence both the power that person has to face his/her challenges competently and the likelihood that the person will make positive choices. Other important predictors include hope, how a person perceives support from their health care providers and previous use of disease-modifying therapies (DMTs). Differences are apparent between patients who have

just started therapy versus patients who have tried a number of medications over time and have been unhappy with the results. Spousal/family support, how a person perceives the benefits of adherence and the use of injection devices for parenteral medication are also predictors of adherence.<sup>89</sup> Injection devices such as RebiSmart™ have demonstrated a positive benefit on adherence for patients with RRMS.<sup>93</sup> Rebidose® has also been a positive addition to the injection market, and many users find it helpful.<sup>94</sup>

**TABLE 7.**  
**Dimensions of Adherence**

- Health care team and health system-related factors
- Social and economic factors
- Medical condition-related factors
- Therapy-related factors
- Patient-related factors

**TABLE 8.**  
**Predictors of Adherence**

- Self-efficacy
- Hope
- Perceived health care provider support
- No previous use of DMTs
- Spousal/family support
- Perceived benefits of adherence
- Use of an injection device for parenteral medications

There are numerous predictors of nonadherence. Literacy level, depression and cognitive impairment are significant predictors. Some patients have a good understanding of MS, and they believe in the benefits of treatment. Others may believe that medications are harmful. Patients may be tired of injections; injection fatigue is another predictor of nonadherence. Side effects, cost barriers and lack of access to care may be indicators of nonadherence and may lead to patients' missing medication dosing and appointments. Table 9 summarizes factors that commonly affect adherence.



In an online survey, Treadaway, et al evaluated 798 patients at 17 neurology clinics to determine the reasons patients missed a dose of disease-modifying injection therapy for MS. The nonadherent rate across all therapies was about 38%. The most common reason (58%) that the participants listed for missing injections was that they simply forgot to administer a dose. Other factors included injection-site reactions, pain at the injection site, depression, fatigue and being tired of injections. This study underscores the importance of developing strategies to improve adherence rates to optimize effective treatment of MS.<sup>95</sup>

**TABLE 9.**  
**Factors Affecting Adherence**<sup>23,101,102</sup>

- Low literacy
- Depression
- Lower cognitive function or cognitive impairment
- Lack of insight into illness
- Lack of belief in efficacy of treatment
- Belief that medications are not important or are harmful
- Being tired of taking medications
- Side effects or fear of side effects
- Cost of medication, copayment or both
- Barriers to access care or medications
- Homelessness
- Psychiatric disease
- Substance abuse
- Forgetfulness
- Anger; stress, anxiety
- Complexity and/or inconvenience of medication regimen
- Inadequate follow-up or discharge planning
- Missed appointments
- Lack of support system

There are many barriers to patient adherence to DMTs (see Table 10). The most common reasons for nonadherence are injection-related reasons, such as anxiety or pain, and simply forgetting to take medication.

Symptoms of the disease and the cognitive decline that often accompanies MS can impede patients' ability to adhere to the complex therapeutic regimen, and the result may be missed doses and missed appointments. Patients experiencing cognitive impairment, depression and anxiety may have difficulty adhering to the complexities of the dosing regimen, ongoing safety monitoring and office visits. Symptoms of disease such as impaired visual function and spasticity may also affect adherence.<sup>23,89,96</sup>

**TABLE 10.**  
**Barriers to Adherence**<sup>23,89,96</sup>

- Injection-related reasons (anxiety, skin reaction, pain)
- Forgetting to take the medication
- Disease symptoms
  - Impaired visual function
  - Lack of manual dexterity
  - Spasticity
- Cognitive impairment, depression, anxiety
- Perceived lack of efficacy of medication
- Coping with adverse events
- Complacency
- Treatment fatigue

Often patients have unrealistic expectations of the efficacy of a medication, and at the first sign of relapse or progression they discontinue the DMT. MS is different from diseases such as diabetes, in which blood glucose is checked to measure the effectiveness of insulin therapy. In MS, there are no specific markers of efficacy to determine whether a medication regimen is working optimally.<sup>89</sup> It is important for patients to understand that relapses may still occur during treatment and that although we don't have a cure, we can slow the progression of the disease. Patients also need to know that even though they may not be experiencing symptoms, subclinical disease may be ongoing.

Adverse events are also associated with nonadherence. The most common events leading to clinical intervention include flu-like symptoms, depression, injection-site reactions, elevated liver enzymes, fatigue, transient postinjection reactions such as tachycardia, flushing and

dyspnea, and lipoatrophy.<sup>89,97</sup> Other barriers noted were complacency and treatment fatigue due to the chronic nature of the disease.<sup>89</sup> Other side effects reported in the newer oral medications include alopecia, gastrointestinal distress, flushing and diarrhea (see Appendix 2). All patients who start a new medication will need close observation, which may include laboratory surveillance on a regular basis. Patients need to be made aware of the personal responsibility they have to take these medications.

There are several strategies for improving adherence in patients with MS (Table 11). One key concept is that patients may be more willing to adhere to MS treatment if the focus and goal of therapy is health and the maintenance of an independent lifestyle.<sup>88</sup> It is also important for the nurse to stress that treatment can help maintain the function and quality of life, and that relapses may be more severe and occur more frequently when patients are nonadherent.<sup>89</sup>

Strategies to promote adherence to DMT include training and education in proper injection technique. Reeducation on technique may help, particularly for patients who have been on injectable therapy for long periods of time. Management of injection-site reactions may include warming the medication to room temperature, using autoinjectors, rotating injection sites and using a site map. To minimize pain at the injection site, local anesthetics, topical analgesics and briefly applying ice before each injection is recommended.<sup>97</sup>

To combat treatment fatigue, it is important to reinforce the concept that the goal of DMT use is to maintain the person's health and enhance the quality of life. The nurse should address specific symptoms by incorporating pharmacologic or nonpharmacologic intervention. Readjusting the injection schedule may be helpful at times.

Other helpful strategies to improve adherence include the use of reminder systems, enlisting help from the family or caregivers, and contacting various patient assistance programs, if needed (see Appendix 4 for a list of patient assistance programs).

Adverse events such as flu-like symptoms and injection-site reactions are a major barrier to adherence in MS

therapy. Adverse event mitigation techniques such as gradual dose titration and use of analgesics combined with nursing support was shown to improve treatment in patients treated with interferon beta-1b. In the Success of Titration, analgesics, and BETA nurse support on Acceptance Rates in MS Treatment (START) trials, 78% of participants were considered adherent after 12 months. With improved adherence rates, relapse rates can be minimized and nursing support can help patients improve self-management and reduce injection anxiety.<sup>98</sup>

There are three new oral disease-modifying therapies for the treatment of MS. While these therapies may improve tolerability over injectable and infusible therapies, more research and information is needed before definitive statements can be made about the advantages of oral medications. Generally, the benefits of oral medications include the following: increased comfort for the patient; convenience of route and dosing; fewer visible reminders of disease; and that no specific training is required.

The use of oral medications may improve adherence. In a recent study by Agashivala, et al, patients taking fingolimod were less likely to discontinue therapy, and when they did discontinue, they did so later than patients using injectable MS therapies.<sup>99</sup> However, in the case of cancer chemotherapy, the use of oral medications does not necessarily lead to improved adherence. Use and effectiveness of oral medications for cancer therapy has increased in recent years, yet patients continue to face the challenge of adhering to life-saving chemotherapy regimens and are at risk of receiving a suboptimal dose if they do not adhere to therapy. Education about oral medication and the importance of therapy is recommended to improve adherence of oral chemotherapy for patients with cancer.<sup>100</sup>

One of the best tools available to nurses for patient assessment and adherence to medication is asking questions. It is important to uncover any negative attitudes toward taking medication and to ask questions such as: Are you able to take your medication as prescribed? Have you missed any doses in the past week, and, if so, how many? Do you use a pill organizer? Can you show me the site of your last three injections? At follow-up appointments, the nurse should act as the patient's cheerleader. Encourage

maintenance of therapy and monitoring as needed, and discuss side effects, medication effectiveness, missed doses and continued affordability.<sup>88</sup> Asking patients how they pay for therapy and if they need help in reducing medication costs can be helpful.

It is important to consider tolerability and safety issues associated with DMTs when optimizing adherence to therapy. Safety issues are a challenge and may pose a serious health risk to the patient. Appropriate management of adverse effects and ongoing monitoring of patients will help maximize effectiveness of treatment and ensure patient safety. To improve adherence and ensure the safety of patients, routine monitoring is essential for all patients receiving injectable and oral medications.<sup>97</sup>

The role of the nurse as educator is key to improving treatment adherence and managing the care of the patient. When the nurse is imparting knowledge about disease-modifying therapies, it is important to be aware that people have different learning styles; different

teaching methods should be used to adapt to the needs of the patient. Educational tools such as posters, flip charts or models may engage the patient and improve comprehension and retention of information. In addition, brochures, pamphlets, clinical studies, articles and websites enable patients to review information at their own convenience.<sup>88</sup> How-to videos on self-injection, patient testimonies and strategies on how to treat symptoms and slow progression of the disease are effective for patients who are visual learners.

It is an ongoing challenge and an important collaborative team effort for nurses to help patients adhere to therapy. Safety assessments and monitoring adherence should be part of each patient visit. Helping patients to maintain a realistic outlook, using pharmacologic and nonpharmacologic strategies in symptom management, and working on an individualized approach for each patient using the elements of good communication will help improve adherence and optimize therapeutic outcomes.

## TABLE II

### Strategies to Combat Barriers to Adherence<sup>23,89</sup>

#### **Barrier: Unrealistic patient expectations; lack of knowledge about MS; patient complacency**

##### **Suggested Interventions:**

- Provide education about MS, relapses and DMTs: relapses may occur during therapy but may be more frequent and severe without treatment.
- Explain to patients that while their disease appears to be in remission, MS may be active at the subclinical level.
- Inform patients that DMTs are considered preventative therapy to stabilize their disease and to maintain the function and quality of life.

#### **Barrier: Fear of injections**

##### **Suggested interventions:**

- Utilize motivational interviewing techniques
- Educate or reeducate about proper injection preparation and technique
- Dispel fears about injection safety
- Consider cognitive-behavioral therapy or relaxation techniques
- Suggest mindfulness training<sup>103</sup>
- Ask family, caregivers and significant others to support the patient
- Try a thinner-gauge or shorter needle<sup>97</sup>
- Use an injection device

**Barrier: Cognitive impairments and/or forgetfulness**

**Suggested interventions:**

- Evaluate patient's ability to perform injections and to follow through with medical monitoring, if needed
- Assess patient's cognition and memory
- Adjust the frequency and complexity of regimen, if needed
- Arrange for reminders via telephone, text message, alarms or notes
- Enlist a family member, caregiver or pharmacist to help with treatment plan, and, if needed, to prepare and administer injections
- Consider switching to a DMT with less frequent dosing or use premixed therapies in prefilled injectors
- Use dosette pill boxes or packaging
- Refer patient and family to support services for people with cognitive challenges (e.g., Alzheimer's Association or National Family Caregivers Assistance)

**Barrier: Adverse effects such as flu-like symptoms and/or injection-site reactions/pain**

**Suggested interventions for flu-like symptoms:**

- Educate on specific symptoms to expect and that symptoms will likely lessen with time
- Titrate dose gradually to prescribed regimen
- Recommend acetaminophen or nonsteroidal anti-inflammatory agents before and/or after injection, as required
- Readjust injection schedule to days and times when symptoms will be least disruptive
- Offer low-dose oral steroids at start of treatment; consider sleep aids; try reducing dose of DMT<sup>97</sup>

**Suggested interventions for injection-site reactions/pain:**

- Recommend site rotation or site mapping
- Wash hands thoroughly before injection
- If cleaning injection site with alcohol, allow to completely dry
- Switch to cleaning with soap and water instead of alcohol
- Warm medications to room temperature before injection
- Apply a cool or warm compress to injection site for 30 to 60 seconds before injection
- Consider use of autoinjectors, if available<sup>104</sup>
- Use local anesthetics or pretreat with ice to minimize pain
- Consider switching to an oral treatment plan

**Barrier: Fatigue and/or being tired of injections**

**Suggested interventions:**

- Emphasize importance of DMT for maintaining health and quality of life
- Evaluate and readjust injection schedule to accommodate patient's lifestyle
- Consider use of mindfulness training<sup>103</sup>
- Evaluate for depression and initiate treatment, if needed
- Consider change to DMT with less frequent dosing schedule
- Review with the patient the impact of treatment on their disease course

**Barrier: Family support and/or financial concerns**

**Suggested interventions:**

- Work with a social worker for assistance in navigating system/finances and evaluating need for home care, if necessary
- Refer patient to medication assistance programs for DMTs offered by pharmaceutical companies (see resource list in Appendix 4)

## UTILIZATION OF TECHNOLOGY

There are many health technologies that can assist people with MS to better manage their disease. Telemedicine, first used in the 1970s for long-distance provider-to-provider consultations, has expanded to allow patients and care providers to consult remotely online, by phone or by other electronic means. This removes several barriers to care, such as distance, mobility and time.<sup>105</sup> Telehealth goes beyond clinical care to include long-distance remote education, outreach and other consumer health support services.<sup>106</sup>

Information devices, reminders and dispensers are relatively simple and easy to use. Advanced devices may provide audible and verbal reminders in addition to automatically organizing and dispensing medication based on specific criteria. Other advanced tools can detect whether a person has ingested and metabolized the medication, log and report information to the clinician, and alert caregivers of missed doses.<sup>107</sup>

Technology such as autoinjection devices may prove useful for people requiring injections. Studies have reported that autoinjection devices can improve patient satisfaction and their experience with self-injection.<sup>108,109,110</sup> Strategies that incorporate injection devices into a patient management plan could improve treatment outcomes by increasing patient adherence to disease-modifying therapy.<sup>96,104,111</sup> RebiSmart™, approved for use in Canada and throughout Europe, is an example of one such technological advance. It is an adjustable electronic injection device that administers a preset dose of interferon beta-1a and provides information messages, visual and auditory signals, adjustable comfort settings, access to injection history and automatic guidance through the process.<sup>112</sup>

Numerous other reviews and studies have demonstrated positive outcomes from the use of technology, particularly cell phones.<sup>113-115</sup> Mobile health (mHealth) provides consumers with education and dosing reminders, connects them with the pharmacy for refills, and can notify caregivers of missed doses via cell phone apps.<sup>107</sup> However, technology works best when combined with in-person counseling, good communication between care provider and patient, and

an awareness by the caregiver of any underlying issues that may enhance or stifle success—such as health literacy, social support, cultural background and care coordination.

## MOTIVATIONAL INTERVIEWING

Motivational interviewing (MI) is an evidence-based technique that focuses on the importance of promoting behavior change. The underlying goal is to address and understand what a person needs to become more intrinsically motivated. Motivational interviewing embodies a philosophy and communication style that helps people increase motivation by resolving ambivalence. It uses a gentle, patient-centered counseling method to elicit behavior change, and has been found effective in fostering change across a wide range of health behaviors. A meta-analysis spanning 25 years supports the long-lasting positive effects of MI in targeting behavior change.<sup>116-122</sup>

Behavior change is needed to reduce many health risks, including nonadherence to treatment. The challenge for MS nurses is to create the milieu in which patients may embrace change.<sup>117</sup> The trusting relationship between nurses and patients through repeated primary-care encounters provides a strong foundation for MI.<sup>116,123</sup>

Health care professionals often argue for change, yet their patients resist. However, with MI, the focus is on helping patients through their ambivalence toward change and adaptation by encouraging the individual, not the practitioner, to voice arguments for and against change. Thinking aloud about change encourages action. People may resist being told what to do; ironically, acknowledging the freedom not to change is sometimes what makes change possible.<sup>117</sup>

When they act as patient advocates, primary-care providers enhance the likelihood that efforts to promote healthy behaviors will be accepted.<sup>116</sup> Yet education alone is not sufficient to inspire the sustained behavioral changes needed for ongoing self-management of a chronic disease such as MS. By overcoming barriers to self-care, nurses empower patients to take ownership of their treatment and improve outcomes.<sup>117,124</sup>

## Theoretical Basis of MI

The theoretical underpinning of MI includes the transtheoretical model of change.<sup>116,119,120,125</sup> This model describes the process of change as long-term and dynamic, and incorporates individual variables. Patients move through stages of change, though not always in a linear fashion, allowing room for the ups and downs most experience while attempting to incorporate new self-care strategies into their routines.<sup>126</sup> This theory recognizes that change is not the result of a single decision; it unfolds in stages of “motivational readiness,” in which individuals acknowledge the need for change, contemplate and prepare for change, make the change and work to consolidate the behavior. Movement through these stages is flexible and, at times, patients may fall back to a previous stage.<sup>117,127</sup>

With its foundational concept that readiness for change is crucial, the transtheoretical model is useful for reaching MS treatment goals and provides a structure upon which nurses can build a nonjudgmental therapeutic relationship that takes into account individual needs. Using this model, interventions are based on the stage of readiness.<sup>117,127,128</sup>

- Pre-contemplation: Patient shows awareness of the problem, but lacks the intention to change.
- Contemplation: Patient indicates a readiness to change, and is open to information.
- Preparation: Patient exhibits determination to change, and develops a plan.
- Action: Patient makes changes and progresses, with support, toward a goal.
- Maintenance: Patient reaches goals, and behavioral changes are sustained.
- Relapse: Patient returns to previous behaviors.

Adults move toward self-management when they can see that a change will benefit them and when they are confident that they can make the change successfully. To help achieve change, nurses must develop strong supportive interventions that encompass the following:<sup>129</sup>

- teaching individuals to manage their illness to the maximum degree possible
- tailoring programs and offering ongoing support
- following up regularly

It is essential that this self-management support involve a paradigm shift in the patient-caregiver relationship toward a collaborative partnership.<sup>124</sup> Thus embracing the spirit of MI encompasses being collaborative rather than authoritarian, evoking autonomy and motivation, and taking a patient-oriented approach. MI is not a quick fix, nor a way to trick people into change. It is not easy to learn, as it involves a complex set of skills used in a flexible, collaborative manner. MI is useful when working with both genders and with ages ranging from adolescence to older adults, and may be particularly effective with ethnic groups, due to its nonconfrontational approach.<sup>116,118,119,121,123,130,131,132</sup>

## Strategy and Technique

MI uses guided communication based on four principles: (1) expressing empathy, (2) noting discrepancies between desires and actions, (3) rolling with resistance, and (4) supporting self-efficacy.<sup>116,119,120,121,123,130</sup> Often the practitioner has a specific behavior change in mind and gently guides the individual to consider why and how to pursue this goal.<sup>117</sup>

An important step in collaborating with patients includes identifying barriers to self-management. There are five categories of barriers to self-management: (1) physical barriers such as disabilities, (2) psychological barriers such as depression and low self-efficacy, (3) cognitive barriers such as poor health literacy or dementia, (4) economic barriers such as cost of medications and lack of insurance, and (5) social and cultural barriers such as gender and ethnic considerations.<sup>124,133</sup>

MI requires a shift away from feeling responsible for a person's behavior and movement toward helping the individual verbalize reasons and means for change.<sup>117</sup> It comprises two phases: motivation to change and commitment to change.<sup>116,118,130</sup> The core communication skills required for effective motivational interviewing are (1) open-ended questioning to encourage engagement, (2) reflective listening that summarizes a person's



## MOTIVATIONAL INTERVIEWING CASE STUDY

In this case study, various elements of motivational interviewing are demonstrated, as highlighted below.

**Patient Profile:** 19-year-old man with recent diagnosis of clinically definite relapsing-remitting multiple sclerosis. He recently started therapy with interferon beta-1a that he administers by subcutaneous injection. He phones the clinic several times a day with concerns about his MS symptoms and therapy. The MS team is concerned about his mental health, and his neurologist does not think he is taking his medications as prescribed.

He calls his MS nurse in an agitated state, requesting assistance dealing with his MS.

Telephone interaction using concepts of motivational interviewing:

MS Nurse: James, is it okay if we spend some time discussing some of the challenges you have been experiencing with your disease and your therapy? **(Open question inviting conversation)**

James: It would be nice to talk to someone, because it just seems that I was told I have MS and to go home and take shots for the rest of my life. Everybody thinks I should just carry on like nothing is wrong, but in fact I could end up in a wheelchair someday. I am having trouble sleeping and I am so scared.

MS Nurse: It sounds like you are overwhelmed with getting a diagnosis and then having to start an injectable therapy all at the same time. There is a lot to learn about your illness, and lots to learn about your therapy. Are these some of the challenges you are facing? **(Listening by reflection)**

James: Yes—it is just too much. I am only 19 and now I have to change my entire life. My mom told me that I can't drink, smoke or eat junk food anymore. She reminds me about taking my shots all the time. I am reminded about having this stupid disease all the time and I worry about having a relapse.

### Informing strategy—elicit-provide-elicit

MS Nurse: Do you think your mom is worried about your having a relapse as well? **(Elicit)** Often the people who care the most about us are affected by the diagnosis as well. They sometimes do not understand the disease and, often without meaning to, they make you worry more. **(Provide)** Do you think your mom's reaction to your MS is making you anxious? **(Elicit)**

James: Well, maybe, but I am really trying not to worry her. I gave her the books you gave me on MS and I am doing my shots by myself, so I don't see why she is so upset. This is happening to me, not anyone else.

### **(Elicit the focus of informing, provide information, and then determine patient understanding)**

#### Informing strategy—chunk-check-chunk

MS Nurse: I understand how you must feel. Sometimes when we can include our family in the education about the disease and therapy, it helps them to be less worried. If they understand more, then they can be supportive. **(Chunk)** Is this something you would consider? **(Check)**

James: Well, I probably owe that to my mom, because she has been good to me. It is hard for me to talk about it, though.

MS Nurse: Others have reported that is difficult to talk to their families about their illness and medication therapy. This is not unusual. **(Chunk)** Would you like your mom to come to the clinic to learn more about MS and your medication? **(Check)**

### **(Provide chunk of information, check to make sure patient understands, then provide another chunk of information)**

#### Outcome

James: Would you do that? That would be great, but I would like to come with her, to make sure she understands.

MS Nurse: Of course. Perhaps when we meet with your mom we could also go over some of the things that are worrying you. Would that be OK with you?

James: Yes, I really think that this is what I need right now. Can we do it soon?

**The patient has been guided to a solution to the current issue, he feels listened to, and appropriate information has been provided by the nurses at the right time.**



experience and accepts ambivalence, and (3) informing that explores what the patient knows or would like to know, and that avoids giving unwanted information.<sup>117,124</sup> Most importantly, MI instills hope and optimism.<sup>116</sup>

These MI principles can be expressed via the “rule” mnemonic device:<sup>117</sup>

**R**esist the righting reflex  
**U**nderstand motivations  
**L**isten  
**E**mpower

The intent in asking open-ended questions is to better understand an individual's personal situation. Good reflective listening is a complex clinical skill that ensures understanding, communicates caring, and involves attention to detail, providing the patient with the freedom to resolve ambivalence and discuss issues. It also entails recognizing and affirming when a person states that he/she has taken steps toward change. Informing, as a vehicle for educating about a condition and its treatment, is not so much information provision as it is an information exchange in the context of a collaborative relationship. In health care settings, these communication styles might shift several times within a consultation, and this is a marker of good practice.<sup>117</sup>

Done correctly, motivational interviewing helps to facilitate change, with the practitioner doing more listening than talking. Like many skills, proficiency is gained with practice.<sup>116,130</sup> Incorporating this technique into the unique model of MS nursing will help to enhance patient outcomes in the face of the challenges posed by multiple sclerosis.

### **SELF-EFFICACY, SELF-MANAGEMENT AND DECISION-MAKING SKILLS**

From the time of diagnosis and continuing throughout the course of the disease, patients with MS must make multiple decisions regarding medical care, lifestyle and quality of life issues. How people respond to the diagnosis and use their decision-making skills may reflect their previous experience with the health care system. Research has shown that patients with MS want an active role in their health care and that they are likely to attempt to incorporate healthy practices as part of their

lifestyle. Yet many are asymptomatic for long periods and thus may develop a false sense of security. To complicate matters, personal preferences and health care beliefs may change over time, changing a patient's readiness to act as a self-care manager.<sup>134</sup>

Readiness for self-care management is to a degree determined by self-efficacy, which is a patient's own judgment and confidence in his/her ability to organize and implement a new, stressful or unexpected action and to persist despite challenges.<sup>3,23,124,135</sup> How each person perceives this ability is key, as perception strongly influences both the expenditure of energy and its duration, especially when the person is faced with obstacles or unpleasant experiences.<sup>92</sup>

A growing body of evidence suggests that adherence is strongly linked to self-efficacy. Self-efficacy is thus critical, especially because daily MS therapy does not result in an immediate payoff but rather the promise of a future benefit, such as fewer relapses.<sup>92,136,137</sup> In a recent study on adherence to antiretroviral therapy (ART) for treatment of human immunodeficiency virus (HIV), improvements in self-efficacy increased adherence to ART treatment. In this study, the authors recommend that nurses work with patients to improve treatment self-efficacy by using adult learning techniques and strategies to improve health literacy, which will lead to improved adherence to ART, reduced viral load and enhanced immune status of the individual with HIV.<sup>138</sup>

In patients with chronic illness, adherence rates are typically lower over time as compared to those with acute illness. MS patients are more likely to adhere to treatment over the long term if they stay on treatment throughout an initial period of approximately six months. Since patients with MS are at risk of diminished adherence over time, it is important for health care providers to encourage and support self efficacy, starting with the initial contact with the patient and continuing over the long term.<sup>23</sup>

The MS Self-Efficacy scale (MSSE) can be a useful tool for determining a patient's level of self-efficacy. This 18-item scale comprises two subscales: one measures a patient's belief in his/her ability to manage MS, and the other measures a patient's concept of his/her ability

to function with MS. The 18 items are rated from 10 to 100, with 10 equating *very uncertain* and 100 *very certain*, indicating a person's belief in his/her ability to perform specific behaviors.<sup>23,139</sup>

There are four main sources of self-efficacy: mastery of experiences, vicarious experiences (modeling), verbal persuasion from a significant other and physiologic feedback. Successful use of one or more of these sources helps individuals gain a greater sense of control over chronic diseases. A person's perception of self-efficacy evolves with experience and knowledge, which in turn influences the likelihood that a behavior will be adopted. In addition, setting concrete goals and devising an action plan about which a person feels confident increases self-efficacy because the individual becomes an active participant in his/her treatment.<sup>124</sup> However, it is worth noting that self-efficacy among people with MS is subject to variables that may include gender and type of MS.<sup>139</sup>

Bandura has suggested that successful performance of tasks enhances self-efficacy.<sup>140</sup> With regard to MS patients, this includes education about treatment and practicing treatment techniques in the presence of a nurse, as well as the availability of telephone support, role models and support groups, all of which can empower individuals to achieve realistic expectations and adherence.<sup>139</sup> Informed patients are more likely to actively participate in their care, make wiser decisions and adhere to treatment.<sup>134</sup>

An environment of mutual respect between nurse and patient helps in the exploration of each patient's preferences in the decision-making process. Nurses must assess each person's attitudes, along with his/her willingness and ability to participate in making decisions, and then tailor interactions accordingly. Likewise, nurses should ensure that patients have relevant information on options to help guide them through the decision-making process. Yet nurses must be careful not to impose their own value systems. Instead, they should be guided by each patient's beliefs and values, which can be determined by asking simple questions that can provide insight into how patients prefer to make decisions.<sup>134</sup>

Health care providers' working in collaboration with patients to make treatment decisions using a process of

shared decision-making is becoming more commonplace in health care settings. Generally, people want information about their health care choices and to be involved in decisions about their care. Shared decision-making involves health care providers and patients working together to review evidence-based information about tests, therapies and management of disease and deciding on options for care based on medical evidence and the patient's preferences.<sup>141,142</sup> If patients are given information appropriate to their health concerns, have a chance to weigh the information, and understand how it applies to them and their beliefs/culture/lifestyle, they are more likely to feel empowered and supported to make decisions about treatment options (including medication, rehabilitation or lifestyle changes). If patients choose to make "no" their decision, it is important for MS nurses to avoid pushing their own opinions, values and judgments, and to support, educate and assist patients in making informed decisions as they continue to live with MS.

## HEALTH CARE LITERACY AND CULTURAL ISSUES

Nurses play a critical role in educating people with MS and their families about the disease. They should keep a person's level of health literacy in mind when providing instructions, to ensure comprehension<sup>82</sup> and to sustain adherence.

In its landmark report *Health Literacy: A Prescription to End Confusion*, the Institute of Medicine defined health literacy as, "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."<sup>143</sup> Health literacy involves a person's comprehension as well as the ability to use health-related information for their own or their family members' health and well-being.<sup>144</sup> Some 90 million individuals have problems with health literacy, which has been linked to greater risk of poor health status, increased hospitalizations and death.<sup>145</sup> Poor health literacy negatively affects a person's medication adherence, communication with care providers, ability to follow care plans, understanding of hospital discharge instructions, self-management of their condition or disease, and ability to navigate the health system, resulting in poorer overall health and more emergency department visits and hospitalizations.<sup>146</sup>

Health literacy incorporates numerous elements, including educational level, reading proficiency, mathematical skills, comprehension, problem-solving abilities, information processing, task complexity, sensory impairments (e.g., visual or hearing loss), age, culture and ethnicity.<sup>82,144,147</sup> There is increasing evidence of a causal relationship between health literacy and treatment outcomes.<sup>143</sup> In a small study of heart patients, Chen, et. al, found that higher health literacy improved patient self-care. Better patient self-care reduced incidence of emergency department visits, hospital admissions and death, and decreased the cost of care.<sup>148</sup>

There is substantial evidence that adults aged 65 and older are less health literate than the rest of the population, due to variables that include gender, education, race, socioeconomic status and cognitive changes, in addition to advancing age. This lack of health literacy may lead to less preventive care, lack of knowledge about their medications and increased hospitalization.<sup>149</sup>

### **Culture's Role in Health Literacy**

Increasingly, nurses are working with diverse cultural groups. Every person is unique and brings a different perspective on his/her culture and traditions to health care. Culture affects how an individual perceives health and disease and how he/she makes health care decisions.<sup>82</sup> Culture and health literacy are intertwined in a person's attainment, understanding and use of available health information.

Nurses educating individuals about MS must consider their patients' cultural background, belief system and traditions. For example, Singleton and Krause point to family structure and hierarchy, personal understanding of illness, perceived roles of family and self in the health continuum, and modes of communication and learning as important predeterminants in how a person approaches health.<sup>150</sup> Nurses who demonstrate cultural competency, including translation if applicable, can improve communication and education and enhance a person's understanding of disease<sup>151</sup> from the time of the first encounter.

Assessing a person's level of health literacy and cultural perceptions will alert nurses of the potential need to

adapt educational materials and approaches, as well as the degree of adaptation required.<sup>82</sup>

### **Compensating for Low Health Literacy**

Several strategies have proven effective for educating people with low health literacy about chronic disease management and the importance of medication adherence. Motivational interviewing can empower patients to improve their health status through changes in behavior. As mentioned previously, motivational interviewing involves asking open-ended questions, using an approach known as reflective listening and informing the patient by sharing information in a nonjudgmental and nonthreatening manner. This strategy can lead to new insights about the patient regarding what he/she would most like to learn or what he/she already knows about the disease or medication will help to focus the conversation and allow the recipient to set the direction and tone of collaboration.<sup>124</sup>

It is also important for nurses to master good listening skills. Empathetic responses will help the patient feel that the health care professional is truly paying attention. Phrases such as "Let me make sure I understand what you are saying" or "Can you tell me more about ..." will help clinicians assess a patient's perspective.<sup>144</sup>

During the period of adaptation to a chronic illness, the patient's emotions and stress are heightened, which may affect the ability of anyone, even one with good health literacy skills, to absorb, process and remember instructions. Using simple language will facilitate the patient's understanding of written instructions. Employing a "teach back" of instructions will help ensure comprehension. Offering assistance will help people navigate the complexity of the health system—such as discreetly offering to complete insurance paperwork, using simplified forms and helping with referrals or follow-up appointments.<sup>152</sup>

Assessment tools that measure medication use and gauge a patient's understanding may be greatly beneficial to care providers. Cameron, Ross, et al. created and piloted the MUSE—Medication Understanding and Use Self-Efficacy scale—a modified version of existing communication and self-efficacy measures. Among the 267 participants in their study, they found that MUSE

scores accurately predicted patient understanding of medication instructions and the self-confidence to comply as instructed.<sup>153</sup>

Health literacy is a sensitive topic and one that people are reluctant to discuss; however, nurses should make every effort to assess a person's level of comprehension. With this knowledge and understanding, MS nurses can begin to address the needs of those with reduced health literacy by ensuring clarity in dosing instructions, administration of treatment and appointment schedules, which will reduce the likelihood of medication nonadherence.<sup>154</sup>

## OUTCOME MEASURES

Outcome measures are important to help justify health care practices and techniques to improve adherence. Two important outcome measures to measure the effectiveness of therapy and the efficacy of techniques to improve adherence are the Multiple Sclerosis Functional Composite (MSFC) and the Multiple Sclerosis Treatment Adherence Questionnaire (MS-TAQ).

The MSFC (Table 4) is a clinically meaningful measure that has excellent test-retest reliability. It may be more responsive to change as compared to the EDSS, and it has significant correlations with the sickness impact profile and the Short Form-36. In addition, MSFC scores also correlate well with MRI changes. Limitations of the MSFC include practice effects with relation to the PASAT and the 9-hole peg test. Recommendations for future research include adding a test to measure visual function, possibly utilizing an improved method of assessing cognition, and developing improved techniques to understand the clinical relevance of MSFC scores and changes.<sup>155,156</sup>

The MS-TAQ is a self-report questionnaire that helps health care providers quantify adherence and identify barriers to adherence with a focus on MS disease-modifying therapies. This questionnaire can be used to prompt discussion and enhance communication between patients, their families and their health care providers. These questions (Table 12) can help to hone in on the various factors that affect adherence. Potentially, the MS-TAQ can be used online to enable patients to take ownership of their personal adherence to therapy and ultimately improve their own health outcomes by improving adherence.<sup>157</sup>

**TABLE 12.**

### Questions Included in the MS-TAQ<sup>157</sup>

1. Which drug are you currently taking for treatment of MS?
2. During the past four weeks, how many days were you supposed to take this medication?  
(Possible responses: every day; every other day; three times a week; once a week; once a month)
3. During the past four weeks, did you manually inject, use an autoinjector or both?  
(Possible responses: manual injection only; autoinjection only; both manual and auto; neither; medication taken orally)
4. During the past four weeks, how often was your injection done by someone else?  
(Possible responses: never; a few times; about half the time; most of the time; all or nearly all of the time)
5. During the past four weeks, did you miss or forget to take any doses of this medication? (Yes/No)
6. How many doses of medication did you miss or forget?
7. Additional questions may address the following:
  - Factors associated with missing or forgetting a dose
  - Occurrence of adverse effects
  - Interventions used to prevent or treat adverse effects
  - Ease and/or difficulty in adhering to prescribed therapy
  - Patient satisfaction with treatment

It is an ongoing challenge and an important collaborative team effort for nurses helping patients adhere to therapy. Safety assessments and monitoring adherence should be part of each patient visit. Helping patients to maintain a realistic outlook, using pharmacologic and nonpharmacologic strategies in symptom management, and working on an individualized approach for each patient using the elements of good communication will help improve adherence and optimize therapeutic outcomes.

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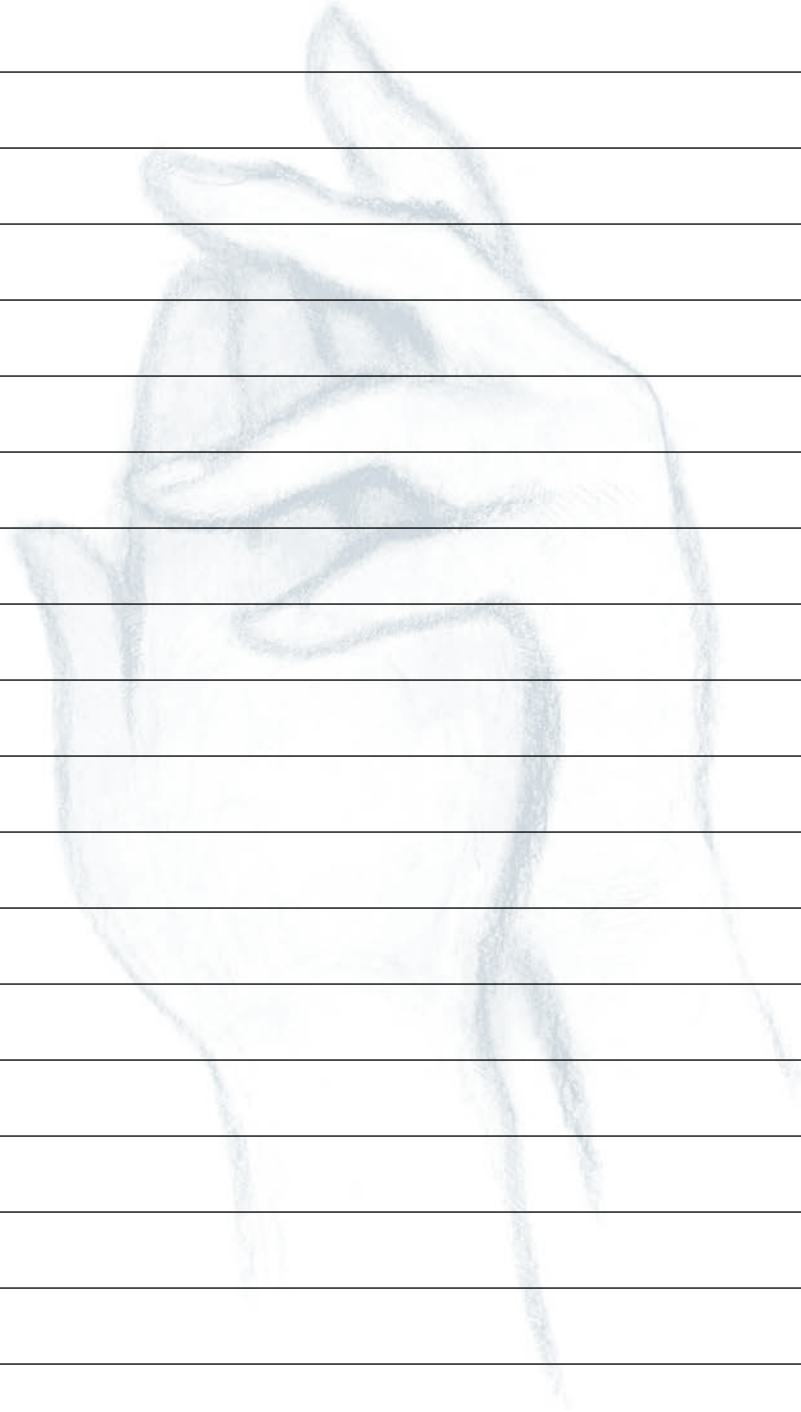
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# *Moving Forward:*

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Adherence to Therapy and the  
Role of Nursing in Multiple Sclerosis

## Notes



# *Moving Forward:*

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Adherence to Therapy and the  
Role of Nursing in Multiple Sclerosis

## Notes



# Moving Forward:

## Adherence to Therapy and the Role of Nursing in Multiple Sclerosis

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### CONTINUING EDUCATION POSTTEST

To receive contact hours, please read the program in its entirety, answer the following posttest questions, and complete the program evaluation. A certificate will be awarded for a score of 70% (8 correct) or better. A certificate will be mailed within 4 to 6 weeks.

Awarded 2.0 of continuing nursing education (1.0 in the area of pharmacology). There is no charge for the CNE credit.

***This program expires on July 1, 2014.***

**By Mail:** IOMSN | 359 Main St. Suite A | Hackensack, NJ | 07601

**By Fax:** 201-678-2291

**Via the Web:** Applicants can access this program at the International Organization of MS Nurses' website, [www.IOMSN.org](http://www.IOMSN.org).

Click on Moving Forward in the Monograph box and follow instructions to complete the online posttest and evaluation forms.

#### PLEASE SELECT THE BEST ANSWER.

1. Roger is a 42-year-old engineer seen by a neurologist with 4 day onset of diplopia, dizziness and nausea. His examination shows visual acuity 20/20 OD 20/30 OS, left optic pallor, right internuclear ophthalmoplegia and impaired tandem gait. Head CT and blood work are normal. He reports an episode of left visual blurring 12 years ago. Based on the 2010 McDonald's Diagnostic Criteria, Roger is diagnosed with:
  - a. Clinically Isolated Syndrome (CIS)
  - b. Relapsing-remitting MS (RRMS)
  - c. Benign MS
  - d. Unable to make a diagnosis at this time
2. Jenny is a 28-year-old hairstylist and a married mother of a three-year-old daughter. She was recently diagnosed with CIS after an episode of right upper limb numbness and weakness. In discussing treatment options with Jenny, what would be the most important consideration in treatment decision making?
  - a. Complexity of treatment regimen
  - b. Side effect profile
  - c. Family planning
  - d. All of the above
3. The type of immunity most commonly affected by MS is:
  - a. Innate immunity
  - b. Adaptive immunity
  - c. Inherited immunity
  - d. Genetic immunity
4. Lucia is a 22-year-old Latina female (her primary language is Spanish, although she speaks limited English) who was recently diagnosed with relapsing-remitting multiple sclerosis. Her MS team consists of a neurologist and a PA, who both agreed that she should begin a disease-modifying therapy. She comes to see the clinical nurse with questions about the value of this type of treatment versus braces for her legs, since she recently watched a telethon for muscular dystrophy, in which rehabilitation was emphasized as vitally important. What is your next step?
  - a. Provide Lucia with literature in Spanish about multiple sclerosis
  - b. Show Lucia a chart with information about how medications work against MS
  - c. Ask for a family meeting to include her circle of support in proposed treatment
  - d. Arrange for a translator who can assist you in explaining MS and the prescribed therapy
5. James has had MS for 14 years and has had a spotty history of adherence to any prescribed treatments, including DMTs. He sees his private neurologist annually, who continues to renew his prescriptions (on James's insistence), even though he is aware that the



- patient skips many doses of his DMTs and his medication for spasticity. The neurologist is concerned about the patient's record of non-adherence, so he contacts the nursing program that supports the patient's current DMT. You are the nurse assigned to visit James. During your visit, you will:
- Do a comprehensive assessment of his environment
  - Review his knowledge about MS and the value of DMT
  - Ask James to share how MS has impacted his personal and professional life
  - Review the importance of adherence
6. **Melanie is 27 years old and was diagnosed with MS three years ago. She started an injectable therapy shortly after her diagnosis. During the first two years, she was quite confident in her treatment and her ability to follow the plan. She was involved in the initial decision to begin the treatment because it seemed to fit her lifestyle best. She has had no exacerbations since starting therapy and her MRI's have shown no new or enlarging lesions. Her provider tells her she is doing well. Her time with the provider decreases at each visit and he asks few questions beyond inquiring about her symptoms. She now has less enthusiasm for her treatment and is skipping more doses each month. She feels that her MS is stable or mild and that her provider is not concerned, so she is not, either. Your next step would be:**
- Stop the therapy, as her MS is not active at this time
  - Ask her if she'd like to try a different therapy
  - Revisit her initial reasons for choosing to take a therapy and the expectations of that therapy
  - Lessen the number of visits with her provider each year
7. **Paul is a 32-year-old financial analyst who works 60+ hours per week. He was diagnosed with MS three years ago and started on a daily injectable disease-modifying therapy. He exercises every day, plays pickup basketball frequently and enjoys going to clubs. His busy lifestyle was becoming a problem for his chosen therapy. Paul has had only one mild exacerbation in three years. He asked to change to an oral medication to "make it easier for him." It is agreed that changing to an oral medication would be appropriate. As the nurse who is working on this with him, you might suggest the following:**
- Utilize his calendar system (smartphone, paper calendar, and/or computer) to remind him to take his medication
  - Carry his medication with him to remind him to take it
  - Double up on medication when he forgets
  - Tell him that missing pills won't make that big a difference
8. **According to a growing body of evidence, adherence to disease-modifying therapies is linked to:**
- Self-awareness
  - Self-efficacy
  - Self-determination
  - Self-motivation
9. **All of the following techniques can be used by an MS nurse to help a patient starting an injectable medication enhance his/her sense of self efficacy, EXCEPT:**
- Arranging for all injections to be given by a nurse in the physician's office
  - Educating the patient about strategies for managing side effects
  - Informing the patient about support groups
  - Encouraging the patient to practice self-injections with a qualified nurse
10. **What is a core communication skill that is required for effective motivational interviewing?**
- Closed-ended questioning
  - Telling the patient what you think they need to know
  - Reflective listening that summarizes and accepts a patients' ambivalence
  - Informing the patient that a behavior change is necessary
11. **The MS -TAQ, used as an outcome measure, focuses on:**
- Adherence
  - Walking
  - Bladder management
  - Spasticity

# Moving Forward:

## Adherence to Therapy and the Role of Nursing in Multiple Sclerosis

### PROGRAM EVALUATION FORM

Please complete the program evaluation and answer the questions with as much detail as possible. We value your comments and refer to them when making decisions on future CE activities. Please fax this form to **(201) 678-2291** or **complete it online** as instructed below.

5 = Strongly Agree

4 = Agree

3 = Neutral

2 = Disagree

1 = Strongly Disagree

**At the end of this program, I was able to:** *(Please circle the appropriate number on the scale.)*

1. Examine emerging information about the immunology of MS and its pathologic implications for patient care.	5	4	3	2	1
2. Identify the clinical courses of multiple sclerosis and the rationale for early intervention.	5	4	3	2	1
3. Cite effective and comprehensive strategies in the management of multiple sclerosis symptoms and incorporate this information into best practices.	5	4	3	2	1
4. Integrate strategies to sustain adherence to complex protocols into all nursing activities.	5	4	3	2	1

**To what extent was the content:**

1. The objectives clearly relate to the purpose / goals of the activity.	5	4	3	2	1
2. The content was evidence based, rigorously scientific and met my expectations.	5	4	3	2	1
3. This program was presented fairly and objectively and will impact my practice.	5	4	3	2	1
4. Overall I would rate this presentation.	5	4	3	2	1
5. This program will affect my practice.	5	4	3	2	1

Please identify how you will change your practice as a result of attending this activity. *(Check all that apply)*

- ☐ This activity validated my current practice; no changes will be made.
- ☐ I will change the management and/or treatment of my patients.  
Please specify: \_\_\_\_\_
- ☐ I will create/revise protocols, policies, and/or procedures.  
Please specify: \_\_\_\_\_
- ☐ Other (Please specify): \_\_\_\_\_

Please indicate any barriers you perceive in implementing these changes. *(Check all that apply)*

- |   |  |
|---|--|
| <input type="checkbox"/> Cost                           | <input type="checkbox"/> Lack of administrative support          |
| <input type="checkbox"/> Lack of experience             | <input type="checkbox"/> Lack of opportunity (patients)          |
| <input type="checkbox"/> Reimbursement/insurance issues | <input type="checkbox"/> Lack of time to assess/counsel patients |
| <input type="checkbox"/> Patient compliance issues      | <input type="checkbox"/> Lack of professional guidelines         |
| <input type="checkbox"/> No Barriers                    | <input type="checkbox"/> Other, please specify: _____            |

Will you attempt to address these barriers in order to implement changes in your knowledge, skills, and/or patients' outcomes?

- ☐ No. Why Not? \_\_\_\_\_
- ☐ N/A
- ☐ Yes. How? \_\_\_\_\_

## Absence of Commercial Bias, Scientific Objectivity, and Fair Balance

IOMSN and NPA strive to ensure that any educational activity offered for credit meets all requirements of the Standards for Commercial Support. Toward that end, please tell us about your experience in this activity. *(Please circle your answer.)*

1. Were you provided with disclosure of relevant financial relationships of all persons affecting the content of this activity ..... Yes No
2. Were product names avoided in this activity, or if used were all products referenced by their trade name? ..... Yes No
3. Was presentation/monograph free of commercial bias? ..... Yes No
- If you answered NO in #3, please identify which presentation was not free of commercial bias.

## Educational Needs

How did you hear about this activity? \_\_\_\_\_

What different topic would you like to see covered in future IOMSN activities? \_\_\_\_\_

Any other comments? \_\_\_\_\_

## There is no fee for this educational activity.

	1	2	3	4	5	6	7	8	9	10	11
Posttest Answer Key											

## Request for Credit *(Please PRINT clearly).*

Name \_\_\_\_\_ Degree (RN, BSN, etc.) \_\_\_\_\_

Employer \_\_\_\_\_

Mailing Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ Zip Code \_\_\_\_\_

Email Address \_\_\_\_\_ Phone \_\_\_\_\_ Fax \_\_\_\_\_

Signature \_\_\_\_\_ Date Submitted \_\_\_\_\_

**By Mail:** IOMSN | 359 Main St. Suite A | Hackensack, NJ | 07601

**By Fax:** 201-678-2291

**Via the Web:** Applicants can access this program at the International Organization of MS Nurses' website, [www.IOMSN.org](http://www.IOMSN.org). Click on Moving Forward in the Monograph box and follow instructions to complete the online posttest and evaluation forms.

## Appendix 1a: Key Features of the Disease-Modifying Agents, Injectable Therapies<sup>1-7</sup>

Agent (Brand Name)	Interferon $\beta$ -1b (Betaseron®, Extavia®)	Interferon $\beta$ -1a (Avonex®)	Interferon $\beta$ -1a (Rebif®)	Glatiramer acetate (Copaxone®, Glatopa™)	Peginterferon $\beta$ -1a (Plegridy™)
<b>Description</b>	<ul style="list-style-type: none"> <li>Recombinant agent, produced in E. coli</li> <li>Unglycosylated</li> <li>Amino acid sequence differs from naturally occurring interferon with a serine substituted for the cysteine residue at position 17</li> </ul>	<ul style="list-style-type: none"> <li>Recombinant agent produced from Chinese hamster ovary cells</li> <li>Glycosylated</li> <li>Identical in amino acid content and sequence to human <math>\beta</math>-interferon</li> </ul>	<ul style="list-style-type: none"> <li>Recombinant agent produced from Chinese hamster ovary cells</li> <li>Glycosylated</li> <li>Identical in amino acid sequence to human <math>\beta</math>-interferon</li> </ul>	<ul style="list-style-type: none"> <li>Synthetic polypeptide</li> <li>Approximates the antigenic structure of myelin basic protein</li> </ul>	<ul style="list-style-type: none"> <li>The “pegylated” form of interferon; polyethylene glycol is attached to molecules of interferon, which lengthens the effect of interferon and allows for less frequent dosing.</li> </ul>
<b>Indication<sup>a</sup> (United States)</b>	Relapsing forms of MS to reduce decrease 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
<b>Dosage/ Route/ Administration</b>	0.25 mg/l subcutaneous injection every other day	30 $\mu$ g/l intramuscular injection weekly	22 $\mu$ g or 44 $\mu$ g/1 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 (Copaxone® and Glatopa™) Or 40 mg/l subcutaneous injection three times weekly (Copaxone® only)	125 mcg every two weeks subcutaneous
<b>Considerations</b>	<ul style="list-style-type: none"> <li>Injection-site rotation and skin management</li> <li>Depression and/or suicidal ideation, warranting treatment cessation</li> <li>Laboratory monitoring<sup>b</sup> <ul style="list-style-type: none"> <li>Neutralizing antibodies</li> <li>Hematologic/ hepatologic abnormalities</li> </ul> </li> <li>Pregnancy Category: C</li> </ul>	<ul style="list-style-type: none"> <li>Injection-site rotation and skin management</li> <li>Depression, suicidal ideation, and/or psychosis may occur, warranting treatment cessation</li> <li>Laboratory monitoring<sup>b</sup> <ul style="list-style-type: none"> <li>Neutralizing antibodies</li> <li>Hematologic/ hepatologic abnormalities</li> </ul> </li> <li>Pregnancy Category: C</li> </ul>	<ul style="list-style-type: none"> <li>Injection-site rotation and skin management</li> <li>Depression, suicidal ideation, and/or suicide attempts may occur, warranting treatment cessation</li> <li>Laboratory monitoring<sup>b</sup> <ul style="list-style-type: none"> <li>Neutralizing antibodies</li> <li>Hematologic/ hepatologic abnormalities</li> </ul> </li> <li>Pregnancy Category: C</li> </ul>	<ul style="list-style-type: none"> <li>Injection-site rotation and skin management</li> <li>Pregnancy Category: B</li> </ul>	<ul style="list-style-type: none"> <li>Injection-site rotation and skin management</li> <li>Depression and/or suicidal ideation, warranting treatment cessation</li> <li>Laboratory monitoring<sup>b</sup> <ul style="list-style-type: none"> <li>Neutralizing antibodies</li> <li>Hematologic/ hepatologic abnormalities</li> </ul> </li> <li>Pregnancy Category: C</li> </ul>
<b>Common Side Effects</b>	<ul style="list-style-type: none"> <li>Flu-like symptoms</li> <li>Injection site reactions</li> <li>Menstrual disorders</li> <li>Mild neutropenia, anemia, and thrombocytopenia</li> <li>Abnormal liver function</li> </ul>	<ul style="list-style-type: none"> <li>Headaches</li> <li>Mild flu-like symptoms</li> <li>Muscle aches</li> <li>Anemia</li> </ul>	<ul style="list-style-type: none"> <li>Mild flu-like symptoms</li> <li>Muscle aches</li> <li>Anemia</li> <li>Injection site reactions</li> </ul>	<ul style="list-style-type: none"> <li>Skin and injection site reactions</li> <li>Postinjection reaction</li> <li>Lipoatrophy</li> </ul>	<ul style="list-style-type: none"> <li>Flu-like symptoms</li> <li>Injection site reactions</li> <li>headache</li> <li>Muscle and joint pain</li> </ul>

Adapted with permission from Costello K, Halper J, eds. Multiple Sclerosis: Key Issues in Nursing Management: Adherence, Cognitive Function, Quality of Life. 3<sup>rd</sup> ed. Washington, DC: Expert Medical Education; 2010.

## NOTES - Appendix 1a

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CIS, clinically isolated syndrome; MS, multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis.

<sup>a</sup> Interferon  $\beta$ -1b, Interferon  $\beta$ -1a, and Glatiramer acetate are approved for use in the US and Canada.

<sup>b</sup> Laboratory monitoring for hematologic/hepatologic changes is done usually at months 3, 6, 9, 12, 18 and 24 and annually thereafter. Neutralizing antibodies can be detected at 12 to 24 months.

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CURRENT AS OF August 15, 2015. This monograph insert will be updated periodically online. Please check the CMSC website at [www.ms-care.org](http://www.ms-care.org) for the most up-to-date information on disease-modifying therapies for multiple sclerosis.

## Appendix 1b: Key Features of the Disease-Modifying Agents, Infusible Therapies<sup>1-3</sup>

Agent (Brand Name)	Alemtuzumab (Lemtrada®)	Mitoxantrone (Novantrone®)	Natalizumab (Tysabri®)
<b>Description</b>	<ul style="list-style-type: none"> <li>Monoclonal antibody that targets CD52, a protein on T and B cells</li> </ul>	<ul style="list-style-type: none"> <li>Synthetic antineoplastic anthracendione</li> </ul>	<ul style="list-style-type: none"> <li>Recombinant humanized monoclonal antibody produced in murine myeloma cells</li> </ul>
<b>Indication<sup>a</sup> (United States)</b>	Relapsing forms of MS	SPMS, PRMS or abnormally worsening RRMS, for reducing neurological disability and/or frequency of relapses	Relapsing forms of MS to delay accumulation of physical disability and reduce frequency of relapses
<b>Dosage/ Route/ Administration</b>	Two annual treatment courses: 12mg/day IV on 5 consecutive days followed by 12 mg/day on 3 consecutive days. 12 months later.	12 mg/m <sup>2</sup> (cumulative lifetime dose not to exceed 140 mg/m <sup>2</sup> ) IV infusion administered for 5 to 15 minutes every 3 months	300 mg IV infusion over 1 hour every 28 days
<b>Considerations</b>	<ul style="list-style-type: none"> <li>Serious side effects include autoimmune thyroid disease, autoimmune cytopenias, infections and pneumonitis</li> <li>Boxed warning indicates risk of serious autoimmune conditions, life-threatening infusion reactions and notes an increased risk of thyroid cancer, melanoma and lymphoproliferative disorders.</li> <li>Only available under the LEMTRADA REMS program<sup>b</sup></li> <li>Pregnancy Category C</li> </ul>	<ul style="list-style-type: none"> <li>Cardiotoxicity increases with cumulative dose</li> <li>Patients should be monitored for evidence of cardiotoxicity prior to each dose, and total cumulative lifetime dose is not to exceed 140 mg/m<sup>2</sup></li> <li>Pregnancy Category: D</li> </ul>	<ul style="list-style-type: none"> <li>Only available under TOUCH<sup>TM</sup> Prescribing Program</li> <li>Patients are monitored for signs and symptoms of PML prior to each infusion and for infusion-related reactions during drug administration; follow-up visits 3 months after first infusion and 6 months thereafter with TOUCH prescriber<sup>c</sup></li> <li>Laboratory monitoring</li> <li>JCV antibody prior to initiating treatment and every 6 months if negative</li> <li>Pregnancy Category: C</li> </ul>
<b>Common Side Effects</b>	<ul style="list-style-type: none"> <li>Rash</li> <li>Headache</li> <li>Pyrexia</li> <li>Nasopharyngitis</li> <li>Nausea</li> <li>Urinary tract infection</li> <li>Fatigue</li> <li>Insomnia</li> <li>Upper respiratory infection</li> <li>Herpes viral infection</li> <li>Urticarial</li> <li>Pruritus</li> <li>Thyroid gland disorders</li> <li>Fungal infection</li> <li>Arthralgia</li> <li>Pain in back or extremity</li> <li>Diarrhea</li> <li>Sinusitis</li> <li>Oropharyngeal pain</li> <li>Paresthesia</li> <li>Dizziness</li> <li>Abdominal pain</li> <li>Flushing</li> <li>Vomiting</li> </ul>	<ul style="list-style-type: none"> <li>Cardiotoxicity</li> <li>AML</li> <li>Alopecia</li> <li>Upper respiratory tract infection</li> <li>Increased fatigue</li> <li>Nausea</li> <li>Menstrual irregularities</li> <li>Urinary tract infection</li> </ul>	<ul style="list-style-type: none"> <li>Hypersensitivity reactions and anaphylaxis; increased lymphocyte, monocyte, and eosinophil counts</li> <li>Urinary tract infection</li> <li>Liver injury</li> <li>PML (rare)</li> </ul>

## NOTES - Appendix 1b

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AML, acute myelogenous leukemia ; IV, intravenous; MS, multiple sclerosis; PML, progressive multifocal leukoencephalopathy; PRMS, progressive-relapsing MS; RRMS, relapsing-remitting MS; SPMS, secondary-progressive MS.

<sup>a</sup> Alemtuzumab and Natalizumab are approved for use in the US and Canada.

<sup>b</sup> Lemtrada REMS (Risk evaluation and mitigation strategy) Program: Initial REMS Approval. Department of Health & Human Services: <http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM425409.pdf>. And Lemtrada REMS program enrollment forms and resources: <http://www.lemtradarems.com/resources>. Accessed: May 18, 2015.

<sup>c</sup> TYSABRI risk minimization action plan: summary of TOUCH. Department of Health & Human Services. [www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM107197.pdf](http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM107197.pdf). Accessed: May 18, 2015.

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CURRENT AS OF August 15, 2015. This monograph insert will be updated periodically online. Please check the CMSC website at [www.msca.org](http://www.msca.org) for the most up-to-date information on disease-modifying therapies for multiple sclerosis.



## Appendix 2: Key Features of the Disease-Modifying Agents, Oral Therapies<sup>1-10</sup>

Agent (Brand Name)	Dimethyl Fumarate (Tecfidera®)	Fingolimod (Gilenya®)	Teriflunomide (Aubagio®)
<b>Description</b>	<ul style="list-style-type: none"> <li>Mechanism of action is unknown. It has been shown to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway. The Nrf2 pathway is involved in the cellular response to oxidative stress.<sup>10</sup></li> </ul>	<ul style="list-style-type: none"> <li>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.</li> </ul>	<ul style="list-style-type: none"> <li>Inhibits proliferation of stimulated T- and B-lymphocytes.</li> <li>Selectively and reversibly inhibits dihydroorotate dehydrogenase (DHODH), which diminishes the number of activated T- and B-cells available to migrate into the CNS.</li> <li>Basic functions of resting lymphocytes preserved.</li> <li>Normal immune surveillance maintained.</li> </ul>
<b>Indication<sup>a</sup> (United States)</b>	Relapsing forms of MS, including RRMS to reduce measures of disease activity including relapses and brain lesions, and to slow disability progression.	To reduce the frequency of clinical relapses and delay the accumulation of physical disability in relapsing forms of MS.	For the treatment of relapsing forms of MS.
<b>Dosage/ Route/ Administration</b>	Starting dose: 120 mg twice a day, orally, for 7 days; after 7 days, 240 mg twice a day, orally	0.5 mg once daily, orally	7 mg or 14 mg once daily, orally
<b>Considerations</b>	<ul style="list-style-type: none"> <li>Obtain CBC within six months of starting therapy; CBC recommended annually.</li> <li>May decrease lymphocyte counts; may cause flushing and diarrhea</li> <li>Pregnancy Category: C</li> </ul>	<ul style="list-style-type: none"> <li>Requires at least six hours of monitoring after the first-dose.</li> <li>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.</li> <li>Pregnancy Category: C</li> </ul>	<ul style="list-style-type: none"> <li>Six months before starting therapy, obtain serum transaminase and bilirubin levels.</li> <li>Recommendations include monitoring ALT levels at least once a month for six months after initiating therapy.</li> <li>Obtain CBC within six months before start of therapy.</li> <li>Before starting therapy, screen patients with tuberculin skin test.</li> <li>Monitor blood pressure before start of therapy and continue monitoring periodically.</li> <li>Boxed warning indicates that severe liver injury may occur and there is a risk of teratogenicity.</li> <li>Pregnancy Category: X</li> </ul>
<b>Common Side Effects</b>	<ul style="list-style-type: none"> <li>Flushing</li> <li>Headaches</li> <li>GI symptoms (abdominal pain, nausea, vomiting, diarrhea)</li> <li>Dose-related elevations in liver enzymes</li> </ul>	<ul style="list-style-type: none"> <li>Risk of infection (herpes virus infections; lower respiratory tract infections)</li> <li>Hypertension</li> <li>Macular edema</li> <li>Changes in pulmonary function</li> <li>Elevation in liver enzymes</li> <li>Alterations in blood pressure</li> <li>Lymphopenia</li> <li>Possible malignancies (e.g. skin cancer)</li> </ul>	<ul style="list-style-type: none"> <li>Diarrhea</li> <li>Nausea</li> <li>Dyspepsia</li> <li>Increased liver enzymes</li> <li>Alopecia</li> <li>Skin rashes</li> <li>Infections</li> <li>Neutropenia</li> <li>Paresthesia</li> <li>Hypertension</li> </ul>

ALT, serum alanine aminotransferase; CBC, Complete blood count; CNS, Central Nervous System.

Notes:

<sup>a</sup> Dimethyl fumarate, fingolimod, and teriflunomide are approved for use in the US and Canada.

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## REFERENCES - Appendix 2

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CURRENT AS OF August 15, 2015. This monograph insert will be updated periodically online. Please check the CMSC website at [www.ms-care.org](http://www.ms-care.org) for the most up-to-date information on disease-modifying therapies for multiple sclerosis.

## Appendix 3: CMSC-Recommended Web Resources

*The following is a list of organizations and websites for health professionals involved in the care of MS patients.*

*The list is adapted courtesy of the CMSC, whose Website Editorial Review Board reviews the sites.*

*For convenient links to these sites, access the list at <http://www.mscares.org/?page=WebResources>.*

### MEDICINE

#### **American Academy of Neurology (AAN)**

Association website for neurologists and neuroscience professionals. It offers clinical practice tools and guidelines, CME and resources.

(<http://www.aan.com>)

#### **MedlinePlus: Health Information from the National Library of Medicine**

(<http://www.nlm.nih.gov/medlineplus/>)

#### **National Center for Complementary and Alternative Medicine**

This NIH organization explores CAM in the context of rigorous science. The website includes fact sheets, consensus statements, databases, a clearinghouse of CAM info and a clinical trial section.

(<http://nccam.nih.gov>)

#### **National Library of Medicine (NLM) Gateway**

Retrieval system allows for simultaneous searching in multiple databases.

([https://wwwcf.nlm.nih.gov/hsr\\_project/home\\_proj.cfm](https://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm))

#### **Neurosciences on the Internet**

Searchable index of Internet neuroscience resources.

(<http://www.neuroguide.com>)

#### **Rocky Mountain MS Center Living Well**

The Rocky Mountain MS Center in Colorado is a patient-centered, nonprofit organization providing information on clinical care, symptoms, wellness strategies and complementary care for MS. There is a one-time \$20 membership fee.

(<http://livingwell.mscenter.org/>)

#### **The Whole Brain Atlas**

A graphic site with good anatomical models to aid in patient and professional education.

(<http://www.med.harvard.edu/AANLIB/home.html>)

### MULTICULTURAL

#### **Agape Clinic and Baylor Community Care**

A resource to help health care professionals understand Hispanic communities. It offers bilingual resources and links to translation sites.

([https://bearspace.baylor.edu/Charles\\_Kemp/www/agape.htm](https://bearspace.baylor.edu/Charles_Kemp/www/agape.htm))

#### **Latin America Committee for Treatment and Research in Multiple Sclerosis (LACTRIMS)**

LACTRIMS represents clinical services in MS throughout Latin America and some portions of the United States.

(<http://www.lactrim.net>)

#### **Multicultural Health Clearinghouse of the University of Illinois**

This site provides health and wellness information and links to other health resources.

(<http://www.mckinley.illinois.edu/multiculturalhealth/index.htm>)

#### **Office of Minority Health**

US government Office of Minority Health site offers conference links, publications, statistics and an extensive listing of government resources.

(<http://www.minorityhealth.hhs.gov>)

#### **Rehabilitation in Multiple Sclerosis (RIMS)**

RIMS is a network of MS centers in Europe involved in clinical care and rehabilitation in MS. Focuses on an interdisciplinary, multidisciplinary team approach to MS care.

(<http://www.eurims.org/>)

### NURSING

#### **American Association of Neuroscience Nurses (AANN)**

Certifying organization for neuroscience nurses. It develops a core curriculum and standards of practice for neuroscience nursing.

(<http://www.aann.org>)

#### **American Nurses Association (ANA)**

An organization representing 2.6 million RNs through its state organizations. This is a full-service site with many offerings, including a listing of useful websites.

(<http://www.nursingworld.org>)

#### **Association of Rehabilitation Nurses (ARN)**

Certifying organization for rehabilitation nurses. The website offers CE articles, conference information, a journal, certification information and practice tests, and opportunities for networking.

(<http://www.rehabnurse.org>)

#### **International Organization of Multiple Sclerosis Nurses (IOMSN)**

The first and only international organization focused solely on the needs and goals of professional nurses, anywhere in the world, who care for people with multiple sclerosis.

(<http://www.iomsn.org>)

### NUTRITION

#### **Academy of Nutrition and Dietetics**

Includes resources for health professionals and consumers: a nutrition tip of the day, nutrition fact sheets, how to find a nutrition professional in your area and a catalog of educational materials for purchase.

(<http://www.eatright.org>)

#### **Food Medication Interactions**

Two comprehensive, well-documented handbooks of interest to health care professionals: the Food Medication Interactions Handbook and the Herb-Drug Interactions Handbook.

(<http://www.foodmedinteractions.com>)

#### **Quackwatch**

Nonprofit organization that focuses on health care-related frauds, hoaxes, myths and fallacies. It critiques alternative medicines, dubious products and questionable advertisements. Its information is well documented.

(<http://www.quackwatch.com>)

#### **United States Department of Agriculture Food and Nutrition Information Center**

This website provides a wealth of information on general nutrition for professionals and consumers.

(<http://fnic.nal.usda.gov/>)

### OCCUPATIONAL THERAPY

#### **AbleData**

A federally funded project, this database contains information on more than 30,000 assistive technology products, from white canes to voice output. Provides information on how to contact manufacturers and distributors of these products.

(<http://www.abledata.com/>)

#### **The American Occupational Therapy Association, Inc. (AOTA)**

(<http://www.aota.org>)

#### **The Association for Driver Rehabilitation Specialists (ADED)**

Supports driver education professionals and equipment modifications for people with disabilities. A membership directory helps in locating local driver rehabilitation specialists.

(<http://www.driver-ed.org>)

#### **Automotive Mobility Solutions: National Mobility Equipment Dealers Association (NMEDA)**

A nonprofit trade association of mobility equipment dealers: vehicle modifications and equipment installation, equipment manufacturers, driver rehabilitation specialists etc.

(<http://www.nmeda.com/>)

#### **Canadian Association of Occupational Therapists (CAOT)**

(<http://www.caot.ca/>)

#### **The Center for Universal Design**

A national research, information, and technical assistance center that evaluates, develops and promotes universal design in housing, public and commercial facilities, and related products.

(<http://www.ncsu.edu/ncsu/design/cud/>)

#### **Closing the Gap, Inc.**

Resources for computer technology in special education and rehabilitation.

(<http://www.closingthegap.com>)

#### **Rehabilitation Engineering and Assistive Technology Society of North America (RESNA)**

A resource for technology-related services, information and referrals. Resources and links to other sites provided.

([www.resna.org](http://www.resna.org))

#### **Trace Research and Development Center**

The Trace Center is currently working on ways to make standard information technologies and telecommunications systems more accessible and usable by people with disabilities.

(<http://trace.wisc.edu>)

### PATIENT INFORMATION

#### **CareGiving**

Provides a support system for caregivers (professionals or family members) through tips, real-life stories and message boards.

(<http://www.caregiving.com>)

### **Computer Literate Advocates for Multiple Sclerosis (CLAMS)**

Advocates computer communications for support, companionship and information for those with MS. Offers resources for finding MS care professionals, recommended by others with MS.

(<http://www.clams.org>)

### **ElderWeb**

Helps older adults cope with the expanding world of technology. Has links to long-term care information, as well as an expanding library of articles and reports.

(<http://www.elderweb.com>)

### **Healthfinder**

Consumer resource from the Department of Health and Human Services. Provides access to the latest government health news and other health topics of interest.

(<http://www.healthfinder.gov>)

### **MSWatch**

Chat site developed by a person with MS; it is a popular way to communicate with others who have MS via the message boards. Sponsored by Teva Canada Innovation, but site is unbiased.

(<http://www.mswatch.ca>)

### **Multiple Sclerosis Association of America**

A national nonprofit organization dedicated to enhancing the quality of life for those affected by MS. MSAA provides ongoing support and direct services to individuals with MS and their families.

(<http://www.mymsaa.org/>)

### **Multiple Sclerosis Foundation**

Great source of basic information about MS. Website has an interactive multimedia MS library and online forum. Users can also subscribe to MSFocus, a quarterly magazine, Support Group News, a bimonthly publication, and MSFYI, an Internet newsletter.

(<http://www.msfocus.org>)

### **Multiple Sclerosis International Federation (MSIF)**

Advocacy group that works in partnership with MS societies and the research community to represent those with MS. Patients can access MS symptoms, definitions and publications.

([www.msif.org](http://www.msif.org))

### **Multiple Sclerosis Society of Canada**

Information about the disease, progress in MS research, available services, fund-raising opportunities and quick access to the MS Society.

(<http://www.mssociety.ca>)

### **Multiple Sclerosis Society UK**

The MS Society is the UK's largest advocacy group for people with MS. The Society is the main source of reliable information about MS and the leading UK funder of MS research.

(<http://www.mssociety.org.uk>)

### **Multiple Sclerosis Trust**

A leading independent UK organization for people with MS, families and UK-based health professionals.

(<http://www.mstrust.org.uk>)

### **National Multiple Sclerosis Society**

Outstanding resource for individuals with MS and their families that provides information pertaining to living with MS, MS treatment, scientific progress, publications, and its organization structure and functions.

(<http://www.nationalmssociety.org>)

### **Nursing Home Patient Rights**

Consumer site explains federal and state law and steps in filing a complaint against a nursing home.

(<http://www.nursinghomepatientrights.com/>)

## **PHARMACY**

### **Centers for Disease Control and Prevention**

Public health guidelines, vaccine and travel information, and CDC publications.

(<http://www.cdc.gov/>)

### **Centers for Disease Control Vaccines & Immunizations**

Current guidelines regarding vaccines.

(<http://www.cdc.gov/vaccines>)

### **Center for Food Safety and Applied Nutrition**

Site providing adverse drug reaction information for herbal products and supplements.

(<http://www.fda.gov/food/default.htm>)

### **CNN Health**

Consumer health information on the news.

(<http://www.cnn.com/health>)

### **DrugDigest from Express Scripts**

Provides drug and disease information for consumers.

(<http://www.drugdigest.org/>)

### **US Department of Health and Human Services**

<http://www.hhs.gov/>

### **Food and Drug Administration**

Drug information, including approvals, shortages, news etc.

(<http://www.fda.gov/drugs/>)

### **Healthfinder**

Government-sponsored consumer resource on prevention and self-care, the latest government health news, Medicare and other health topics of interest across all ages.

(<http://www.healthfinder.gov>)

### **Immunization Action Coalition**

Educational resources for health care professionals and patients.

(<http://www.immunize.org>)

### **Mayo Clinic**

Provides information on more than 8,000 prescription and OTC medications, as well as health information.

(<http://www.mayoclinic.org>)

### **National Council on Patient Information and Education (NCPIE)**

Links to timely guidelines, tips and resources to help patients use their medications safely and appropriately.

(<http://www.talkaboutrx.org>)

### **National Institutes of Health**

Information on disease states, research and federal health programs.

(<http://www.nih.gov/>)

### **National Institutes of Health National Center for Complementary and Alternative Medicine**

(<http://www.nccam.nih.gov>)

### **National Library of Medicine**

A searchable listing of abstracts of medical literature.

([www.nlm.nih.gov](http://www.nlm.nih.gov))

### **SafeMedication**

Provides user-friendly, easy-to-read information on more than 700 drug products.

(<http://www.safemedication.com>)

### **WebMD**

Information on prescription and herbal medications, drug news and product recalls, and links to health information.

(<http://www.webmd.com>)

## **PSYCHOLOGY AND NEUROPSYCHOLOGY**

### **American Psychological Association Division 22: Rehabilitation Psychology**

Division 22: Rehabilitation Psychology

(<http://www.apa.org/about/division/div22.aspx>)

### **American Psychological Association Division 40: Clinical Neuropsychology**

(<http://www.div40.org>)

### **International Neuropsychological Society**

Multidisciplinary nonprofit organization dedicated to promoting research, service and education in neuropsychology, and to enhancing communication among the scientific disciplines.

(<http://www.the-ins.org>)

### **National Academy of Neuropsychology**

The National Academy of Neuropsychology is a professional society that includes clinicians, scientist/practitioners and researchers interested in neuropsychology.

(<http://nanonline.org>)

### **Neuropsychology Central**

General neuropsychological information and neuropsychology search engine.

(<http://www.neuropsychologycentral.com>)

## **SPEECH LANGUAGE PATHOLOGY**

### **American Speech-Language-Hearing Association**

Professional association for speech-language pathologists and audiologists; advocacy organization for people with communications disorders.

(<http://www.asha.org>)

### **Dysphagia Research Society**

Broad-based resources for swallowing and swallowing disorders.

(<http://www.dysphagiaresearch.org/>)

## Appendix 4: Pharmaceutical Company Support Programs

*Companies that distribute the major disease-modifying drugs provide valuable services that are available to people with MS, whether or not they are taking the company's drug. Among the most valuable are the nurse hotlines, which are staffed by nurses specializing in MS. Contact information for these services is listed below. The websites contain a variety of information for MS patients, families and health care professionals.*

### ABOVE MS™

ABOVE MS™ is a free service that provides patients, their care partners and health care professionals with information, assistance and for support with relapsing MS, Avonex® and Plegridy™. Members can create a personal web profile to gain access to several tools. For more information call 800-456-2255, where support services are available Monday through Friday 8:30 am to 8:00 pm EST, or visit <https://www.abovems.com>.

### Ampyra®

Health care professionals, patients and care partners with questions about Ampyra® can call 888-881-1918 or visit [www.ampyra.com](http://www.ampyra.com) for more information and to sign up to receive updates on the therapy.

### Aubagio®

For information about Aubagio® and the MS One to One program, patients can call 855-676-6326 or visit [www.aubagio.com](http://www.aubagio.com).

### BETAPLUS®

BETAPLUS® provides free comprehensive programs and services for patients taking Betaseron® and other people with MS, and their families. Available services include an injection training program, reimbursement services, support groups and nurse support. For more information call 800-788-1467 or visit [www.betaseron.com/betaplus](http://www.betaseron.com/betaplus).

### Extavia® Go Program™

For questions about Extavia® or the Extavia® Go Program™, call 866-398-2842 Monday through Friday 8:00 am to 9:00 pm EST, or visit <http://www.extavia.com/info/PatientSupport/patient-support-program.jsp>.

### Gilenya®

For information about Gilenya's Patient Services Program, call 800-445-3692 or visit [www.gilenya.com](http://www.gilenya.com).

### Lemtrada®

For information about Lemtrada® and the MS One to One program, patients can call 855-676-6326 or visit [www.lemtrada.com](http://www.lemtrada.com).

### MS LifeLines®

MS LifeLines® is an educational tool for people living with MS. People taking Rebif® can also find facts and support for their therapy through this free service, as well as register for events, sign up to receive an information kit, read profiles of other patients and get tips on living with MS. For more information call 877-447-3243 anytime, day or night—a live representative is always available to take your call—or visit [www.mslifelines.com](http://www.mslifelines.com).

### Shared Solutions®

Shared Solutions® is a free patient support program available to anyone with MS and anyone who has been touched by MS, including care partners, friends and family. Patients taking Copaxone® receive additional materials and services related to Copaxone therapy. This program is designed to help patients, their families and caregivers with counseling, reimbursement issues, self-injection training and adherence reminders. For more information call 800-887-8100 to speak with an MS certified nurse, or visit [www.copaxone.com](http://www.copaxone.com).

### Tecfidera®

For information about Tecfidera®, call ABOVE MS™ at 800-456-2255 from Monday through Friday 8:30 am to 8:00 pm EST, or visit [www.tecfidera.com](http://www.tecfidera.com).

### Tysabri®

Patients who are interested in learning more about Tysabri or who are currently taking Tysabri can register to learn more about the drug and the TysabriTOUCH® Prescribing Program. Patient support services, financial assistance programs and a mentor program are also available through the ABOVE MS™ program. For more information call 800-456-2255 Monday through Friday 8:30 am to 8:00 pm, or visit [www.tysabri.com](http://www.tysabri.com).



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