

Multiple Sclerosis: Best Practices in Nursing Care

Disease Management,
Pharmacologic Treatment,
Nursing Research

4TH EDITION

Colleen J. Harris, MN, NP, MSCN
Nurse Coordinator/Nurse Practitioner
University of Calgary MS Clinic
Calgary, Alberta
Canada

June Halper, MSN, APN-C, FAAN, MSCN
Executive Director
CMSC/IOMSN
Hackensack, New Jersey
USA



Supported by an educational grant from Teva Neuroscience.

The opinions expressed in these materials are those of the authors and are not attributable to the publisher or the educational grant provider. This publication may include discussion of investigational uses of medications that have not been recognized as safe and efficacious by the Food and Drug Administration and investigational uses of drugs that have been approved for other uses. In weighing the benefits of treatment against the risks, physicians and nurses should be guided by clinical judgment. Dosages, indications, and methods for use of drugs and procedures referred to may reflect the clinical experience of the authors or may be derived from the professional literature or other clinical sources. Consult complete prescribing information before administering any of the drugs discussed.

Ms. Harris has the following relationships to disclose: She has been or is a consultant to Bayer Healthcare Pharmaceuticals, Biogen Idec, EMD Serono, Questcor Pharmaceuticals, Genzyme, and Teva Neuroscience.

Ms. Halper has the following relationships to disclose: She has been or is a consultant to Teva Neuroscience, Questcor Pharmaceuticals, Genzyme, and Novartis and has participated on speakers bureaus for Acorda Therapeutics.

Some of the research cited in this publication may have been funded by Teva Neuroscience, the original funder of the publication.

© International Organization of Multiple Sclerosis Nurses

Reprinted with permission by IOMSN. None of the contents of this publication may be reproduced in any form without the prior written consent of the publisher.

Multiple Sclerosis: Best Practices in Nursing Care

Disease Management,
Pharmacologic Treatment,
Nursing Research

4TH EDITION

Table of Contents

| | |
|--|----|
| Foreword | 2 |
| Introduction | 3 |
| Overview of Multiple Sclerosis | 4 |
| <i>Symptoms and Diagnosis</i> | 4 |
| <i>Disease Classification</i> | 5 |
| Evolution of Multiple Sclerosis Treatment and Nursing Practice | 7 |
| Developing a Model of Multiple Sclerosis Nursing Practice | 8 |
| <i>Definition of a Multiple Sclerosis Nurse</i> | 8 |
| <i>Philosophy of Multiple Sclerosis Nursing Practice</i> | 8 |
| <i>Practice Areas</i> | 8 |
| <i>Practice Areas Across the Disease Trajectory</i> | 9 |
| Domains and Competencies of Multiple Sclerosis Nursing | 11 |
| <i>Multiple Sclerosis Nursing Domains</i> | 11 |
| <i>Knowledge-Based Competencies</i> | 11 |
| <i>Skill-Based Competencies</i> | 11 |
| <i>Specialized Competencies</i> | 12 |
| <i>Matching Nursing Competencies to Nursing Domains</i> | 12 |
| Role of the Nurse in Pharmacologic Therapy of Multiple Sclerosis | 14 |
| <i>Episodic Treatments</i> | 14 |
| <i>Symptomatic Treatments</i> | 15 |
| <i>Medications Used for Disease Modification</i> | 19 |
| <i>Other Disease-Modifying Therapies</i> | 25 |
| Supporting Multiple Sclerosis Nursing Practice Through Research | 26 |
| <i>Limitations of Multiple Sclerosis Nursing Research</i> | 28 |
| <i>Strategies to Facilitate Nursing Research: Buying Time</i> | 29 |
| <i>Recommendations for Multiple Sclerosis Nursing Research</i> | 30 |
| <i>Research Priorities</i> | 30 |
| <i>Enhancing the Professional Practice</i> | 31 |
| Conclusion | 31 |
| References | 32 |
| Original Members of the MS Nurse Specialists Consensus Committee | 37 |

Foreword

Multiple sclerosis (MS) has a major impact on the lives of patients and their families. Its unpredictable course leaves those affected with an uncertain future. Recent advances in understanding about the disease and its treatment have changed the way that healthcare professionals can help patients and their families. Healthcare professionals, in addition to determining an MS diagnosis and providing supportive care, can now direct treatment toward changing the disease course. As a result, MS nurses worldwide are faced with many challenges as they meet the needs of patients in the rapidly changing field of MS. The MS Nurse Specialists Consensus Committee has drawn on research, educational, and practical experiences to develop a new and cohesive model of nursing care in MS—one that will sustain and educate nurses in their clinical practice, promote nursing research, and inspire a new generation of MS nurses as they enter the field. This model is the leitmotif of the International Organization of Multiple Sclerosis Nurses (IOMSN).

A new definition of MS nursing is as follows: The MS nurse is a competent expert who collaborates with those affected by MS and shares knowledge, strength, and hope. As the role of nurses continues to evolve, there is a need to establish a cohesive model of MS nursing practice along with specific standards for best practice in MS nursing care. Nursing practice aims to manage and influence the patient's illness by supporting the use of disease-modifying treatments; facilitating symptom management; promoting safe, maximal function; and supporting a wellness-oriented quality of life. Activities that are essential to patient care can be grouped into 3 categories: establishing care, continuing care, and sustaining care.

Together, these interwoven areas provide a framework for a comprehensive, cohesive model for MS nursing practice that can be applied to care of all MS patients, regardless of disease classification or level of disability.

This monograph, now in its 4th edition, was created by the MS Nurse Specialists Consensus Committee, made up of nurses who specialized in MS care (see page 37 for a complete listing of the committee's original members), and includes valuable new information. Like the previous editions, this monograph is designed to enhance MS nursing care, particularly with regard to disease management, pharmacologic treatment, and nursing research. The information herein was drawn from MS and nursing literature, research in MS and other chronic illnesses, and the years of experience of the distinguished participants in this project. This monograph will assist nurses in fulfilling their universal purpose of providing high-quality, compassionate care of patients and families affected by MS. Specifically, this publication is designed to help nurses:

1. Describe the epidemiology and disease pathology of MS
2. Explain how MS nursing is concomitant to the evolution of new diagnostic technology and treatment approaches
3. Identify domains in MS nursing
4. Identify key competencies within each domain
5. Identify their various roles in caring for patients and families affected by MS
6. Describe the role of MS nursing practice in optimizing MS treatments
7. Describe medications used to treat relapses, to treat MS symptoms, and to modify the disease course
8. Define evidence-based practice in MS nursing
9. Describe limitations and gaps in MS research and proposed work to fill those gaps
10. Identify potential sources of financial support for MS nursing research

We hope the information provides a framework to support the sustained value of the work of nurses who are dedicating their professional careers to the field of MS.



Colleen J. Harris, MN, NP, MSCN
Nurse Coordinator/Nurse Practitioner
University of Calgary MS Clinic
Calgary, Alberta
Canada



June Halper, MSN, APN-C, FAAN, MSCN
Executive Director
CMSC/IOMSN
Hackensack, New Jersey
USA



Introduction

MS is a chronic, frequently debilitating neurological disease that most often affects young adults in the prime of their lives. While nurses contribute significantly to the care of these patients, basic and advanced nursing education has not typically stressed care of patients with chronic and disabling disease. Thus, nurses in MS clinical settings may not always feel prepared to handle the diverse and variable needs of these patients. In addition, rapid advances in technology and medications used for MS, escalating healthcare costs, shorter hospital stays, and an increased emphasis on home care and patient self-care challenge nurses to face increasingly diverse responsibilities in caring for patients with MS. Nurses not only must help meet the healthcare requirements of these patients but often must also serve as the hub of communication, education, advocacy, and counseling for patients, their families or care partners, and other healthcare professionals.

The growing number of MS nurses worldwide requires networking and involvement with one another. The IOMSN was founded for this purpose and now has numerous international affiliates. It is incumbent on MS nurses to share knowledge and experience with one another.

This monograph is intended to be a tool for MS nurses who are seeking clarification of their roles and responsibilities as well as for nurses 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 symptoms, and explores the potential for MS nursing research to improve patient care.

Overview of Multiple Sclerosis

MS is a chronic, inflammatory, neurodegenerative disorder that affects the central nervous system (CNS). The disease is characterized by patchy loss of the myelin sheath that surrounds nerve fibers, visualized on imaging scans as plaques or lesions in the brain and spinal cord. Demyelination disrupts electrical conduction of the nerves in the CNS, producing variable changes in sensory, motor, and cognitive function. In addition, there may be permanent and irreversible axonal loss, accounting for ongoing disability in the spectrum of manifestations of the disease.

The cause of MS is not known. Research suggests that MS is a consequence of an abnormal autoimmune response to myelin, one that develops after exposure to some environmental agent—possibly a virus—in genetically predisposed individuals. When the immune response is triggered, activated lymphocytes migrate across the blood–brain barrier (BBB) into the CNS. Once inside, these cells interact with macrophages and other cells, stimulating production of inflammatory cytokines that break down the BBB. The combined effects of this autoimmune response cause the demyelination, axonal damage, and scarring seen on cranial and spinal magnetic resonance images (MRIs) in patients with MS.¹ Axonal degeneration and axonal

transection may lead to permanent neurological dysfunction and may begin early in the disease course.¹ In addition, brain atrophy may occur early and is thought to reflect irreversible tissue damage.²

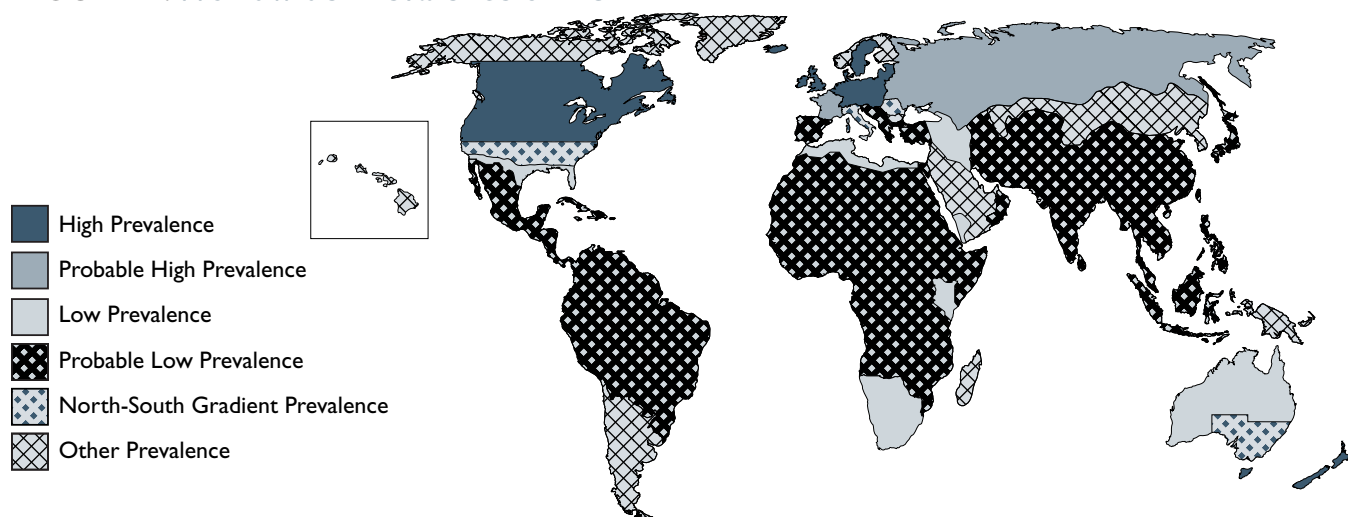
MS prevalence worldwide varies and is highest in northern Europe, southern Australia, the northern United States, and Canada (Figure 1). An estimated 400,000 people in the United States³ and 75,000 people in Canada⁴ have MS. People diagnosed with the disease are typically young, and onset typically begins in early adulthood.⁵ Women are more than 3 times as likely as men to be diagnosed with MS.^{6,7}

MS is unpredictable in its overall course, in the type and severity of symptoms experienced by each patient, and in its long-term outcome. Although the disease is seldom fatal, it can be severely disabling, with approximately one third of patients requiring ambulatory assistance within 10 years of their diagnosis.⁸ Despite these uncertainties, recent advances in disease modification have brought hope to those affected by MS.

SYMPTOMS AND DIAGNOSIS

The symptoms of MS are unpredictable and may be mild, moderate, or severe. Symptoms may appear as an acute attack, also known as an exacerbation or a relapse, or they may become chronic, with clinical and functional deterioration defining disease progression. Each patient differs in the types and intensity of symptoms, depending on the areas of the CNS that are affected.

FIGURE 1. Worldwide Prevalence of MS



Patients with MS may experience fatigue, visual disturbances, weakness, elimination (bowel and bladder) problems, pain and other abnormal sensations, and sexual dysfunction.⁹ Other symptoms include vertigo, tremor, speech difficulties, depression, cognitive changes, and Lhermitte's sign (a sudden transient sensation of electric shock that occurs with forward flexion of the neck).

Because neurological impairments are often transient and symptoms manifest themselves in different ways, MS can be challenging to diagnose. Diagnosis is made by a neurologist after a patient has experienced 2 or more attacks with neurological symptoms referable to 2 or more lesions in the CNS.¹⁰

According to current diagnostic criteria, diagnosis is based upon attacks separated by at least 1 month, lasting 24 hours or more, and occurring independently of any other disease or condition.¹⁰ Fewer than 2 attacks and/or clinical evidence of only 1 lesion requires dissemination of time or space as shown by MRI, positive cerebrospinal fluid (CSF) findings, and/or abnormal evoked potential testing.¹⁰ Insidious neurological progression suggestive of MS requires evidence (retrospective or prospective) of disease progression lasting for at least 1 year as well as 2 out of 3 additional findings (ie, positive brain MRI, positive spinal MRI, positive CSF).¹⁰ Since MS remains primarily a clinical diagnosis, the patient's history, including gender, birthplace, family history, and age when symptoms first began, is critical in the decision-making process. MRI of the brain and spinal cord has become essential to diagnosis, detecting lesions, or plaques, as discrete areas of brightness or high intensity, usually in the white matter of the brain and spinal cord.¹¹ On MRI, MS lesions appear ovoid, and their size may range from a few millimeters to more than a centimeter in diameter. The shape, size, intensity, and location of brain lesions—characteristically, in the periventricular white matter—can also support a diagnosis of MS.¹²

Additional diagnostic procedures may include evoked potential testing (ie, visual evoked potentials [VEPs], brainstem auditory-evoked potentials [BAEPs], or somatosensory-evoked potentials [SSEPs]), which may show slowed nerve conduction even when positive

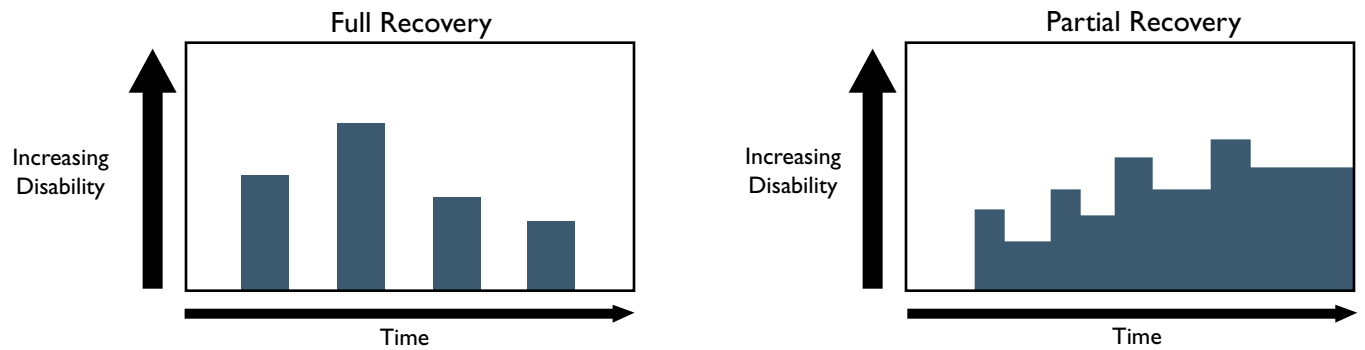
neurological findings are not elicited on examination. Blood tests can help rule out the presence of other chronic or infectious illnesses as potential causes of MS-like symptoms, and analysis of CSF may reveal an unusually high number of cells (mostly monocytes), along with qualitative changes in immunoglobulin detected as oligoclonal bands.¹³

DISEASE CLASSIFICATION

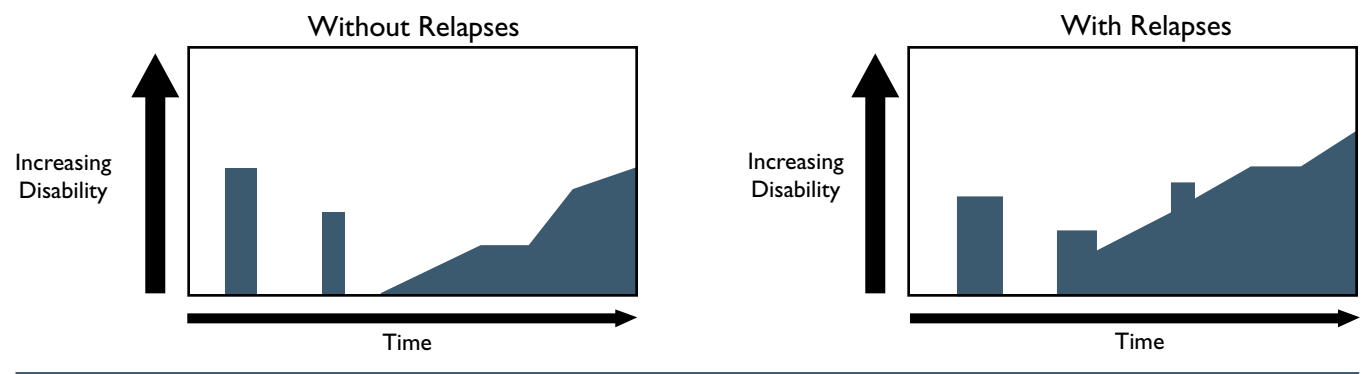
According to internationally accepted terminology, the clinical courses of MS are categorized as relapsing-remitting, secondary-progressive, primary-progressive, and progressive-relapsing.¹⁴ Note that 3 of these classifications consist of relapsing forms of MS, as illustrated in Figure 2. In about 85% of all MS patients, MS follows a relapsing-remitting pattern at onset, with relapses occurring randomly over many years and with minimal accumulation of disability or change in disease progression. In 50% to 70% of patients diagnosed with relapsing-remitting MS, the disease course becomes steadily more progressive over time. This pattern, called secondary-progressive MS, may or may not involve occasional relapses, plateaus, and remissions. Approximately 10% of patients have primary-progressive MS, characterized by a disease course that worsens continuously from onset, with occasional plateaus or temporary improvements. Progressive-relapsing MS is the least common form of MS—affecting only about 5% of patients—and involves continuous disease progression with superimposed relapses.^{14,15}

FIGURE 2. Types and Courses of Multiple Sclerosis

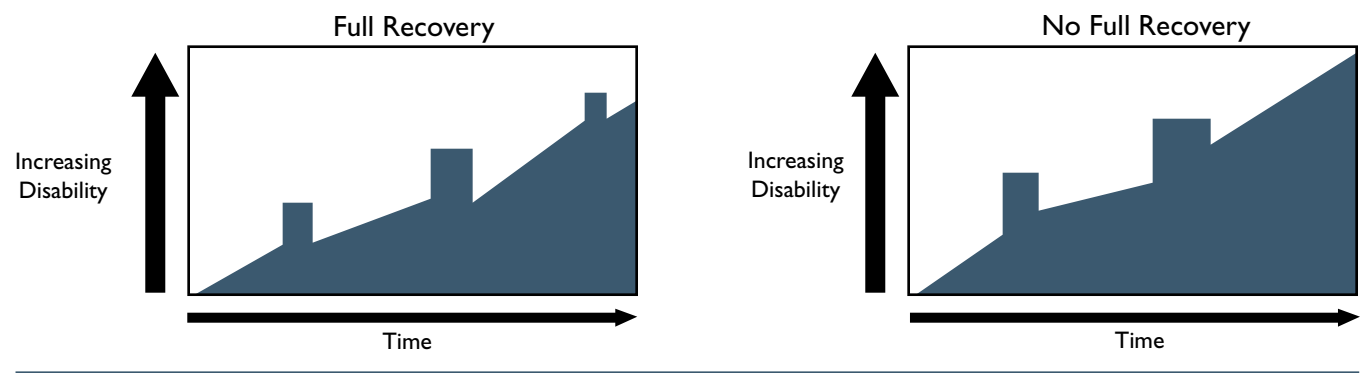
A. Relapsing-remitting



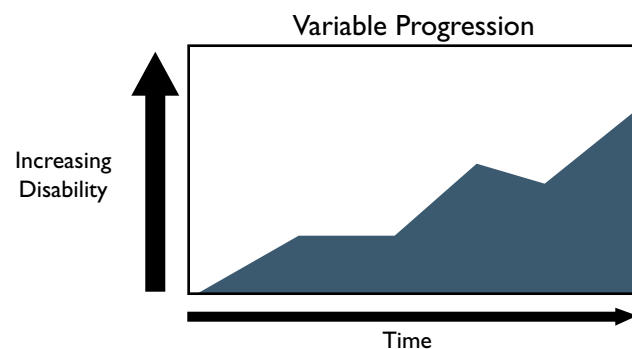
B. Secondary-progressive



C. Progressive-relapsing



D. Primary-progressive



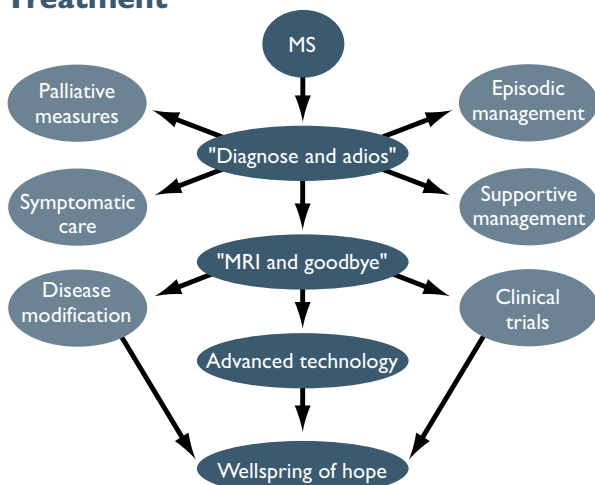
Adapted with permission from Lublin FD, Reingold SC. *Neurology*. 1996;46:907-911.¹² (<http://lww.com>).

Evolution of Multiple Sclerosis Treatment and Nursing Practice

Since the second half of the 20th century, the understanding of MS and its diagnosis and treatment evolved from a hopeless prognosis, characterized in 1948 by the National Multiple Sclerosis Society (NMSS) as the “crippler of young adults,” to a manageable and treatable condition, a new vision of MS. This evolution drew a wide range of healthcare professionals to the field of MS, including specialist nurses, rehabilitation professionals, and counselors.

During the 1970s, 1980s, and early 1990s, MS patient care could be described as a “diagnose and adios” approach, because interventions available at the time could provide temporary relief but had no lasting impact on the disease course (Figure 3). Treatment was mostly palliative and focused on alleviating symptoms and reducing inflammation. Few clinics were devoted specifically to MS, and few nurses were involved in patient care. Even with the advent of MRI technology in the latter part of the 20th century, MS care did not change substantially beyond what Dr. Labe C. Scheinberg described as “MRI and goodbye.”^{15,16}

FIGURE 3. Evolution of Multiple Sclerosis Treatment



Adapted with kind permission from June Halper. The phrases “diagnose and adios” and “MRI and goodbye” were coined by Labe C. Scheinberg, MD.

During the 1990s, MS care improved substantially with the introduction of the immunomodulatory agents interferon β -1a (IFN β -1a; Avonex[®], Rebif[®] 2002), interferon β -1b (IFN β -1b; Betaseron[®]), and glatiramer acetate (Copaxone[®]). The availability and efficacy of immunomodulatory agents and advances in diagnostic and monitoring techniques have brought new hope to patients with MS and their families. These changes, along with cost-containment pressures within the healthcare system and expanding prescriptive authority for advanced practice nurses, brought about a dramatic and ongoing expansion in the roles of nurses who treat patients with MS. Treatment has shifted from a focus on crisis intervention and maintenance to a focus on prevention, symptom management, wellness, and empowerment. The nurse has emerged as a pivotal member of a multidisciplinary team who provides education, skills development, and healthcare delivery for patients with MS and their families.^{16,17}

MS nurses now treat patients in primary, acute, specialized, and rehabilitative settings. MS nurses are educators and advocates. Some have prescriptive privileges, and most work closely with the patient in monitoring and assessing treatment outcomes. MS nurses often initiate, coordinate, or contribute to clinical research. Many are active participants in national and international organizations, such as the IOMSN, that have evolved to support professional education, networking, advocacy, and research on behalf of patients with this perplexing and challenging disorder.

As the role of MS nurses continues to evolve, the need has arisen to establish a cohesive model of MS nursing practice along with specific standards for best practice in MS nursing care. This monograph provides a framework for this model and proposes a philosophy of care that seeks to empower nurses worldwide. The monograph describes many of the responsibilities of MS nursing, encapsulates best practices in patient assessment and treatment, and explores current and potential areas of nursing research in MS—all with the goals of enriching nurses and other professionals and thereby improving the health and quality of life of all those affected by MS.

Developing a Model of Multiple Sclerosis Nursing Practice

DEFINITION OF A MULTIPLE SCLEROSIS NURSE

The MS nurse is a competent expert who collaborates with those affected by MS and shares knowledge, strength, and hope. MS nurses can enhance adaptive and coping skills, facilitate empowerment and a sense of control, and thereby engender hope and positive attitudes among patients with MS and their family members or care partners.¹⁸

PHILOSOPHY OF MULTIPLE SCLEROSIS NURSING PRACTICE

Chronic illness has been described as having a course that can change over time but can be shaped and managed, even if the eventual outcome cannot be modified.¹⁹ As applied to MS, nursing practice aims to both manage and influence the patient's illness by:

- Shaping the disease course by facilitating treatment that interrupts acute episodes and delays the progression of pathology
- Facilitating the management of symptoms and problems that occur in relation to MS
- Enhancing and promoting safe, maximal function
- Supporting wellness-focused quality of life

Because MS is unpredictable in its course and outcome, the philosophy of MS nursing must be flexible, fluid, dynamic, and responsive to changes in the patient's physical and emotional status. In addition, MS nursing care must recognize, react to, and respect demographic, socioeconomic, and cultural boundaries with care that is comprehensive, empathic, and ultimately holistic.²⁰

In this section, to assist in understanding nursing practice issues, MS is viewed across a trajectory from prediagnosis or early diagnosis to advanced-stage disease. Practice issues are discussed for patients grouped as follows:

- Those who have just been diagnosed or have a

probable diagnosis of MS, regardless of how their disease will be eventually classified

- Those with relapsing-remitting MS
- Those with progressive MS, including those with primary-progressive, secondary-progressive, or progressive-relapsing disease
- Those with advanced MS, including patients who have become severely disabled within a brief or substantial length of time

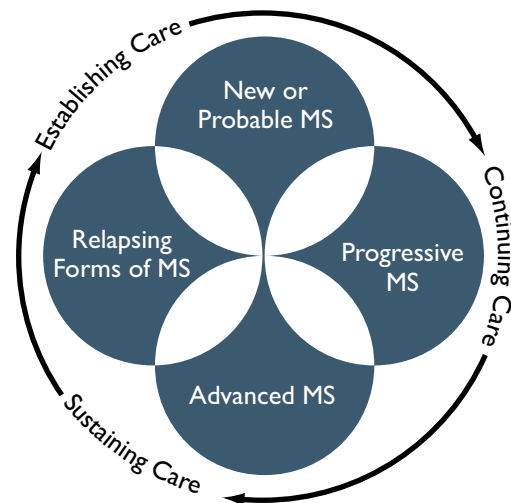
PRACTICE AREAS

Activities that are essential to the care of patients with MS can be grouped into 3 main areas:

1. Establishing care
2. Continuing care
3. Sustaining care

Together, these 3 interwoven areas provide a framework for a comprehensive, cohesive model for MS nursing practice that can be applied to care of all MS patients, regardless of disease classification or level of disability (Figure 4). Although specific activities within each area may be the same for each patient, the emphasis may shift according to the stage of disease.

FIGURE 4. Cohesive Model of Nursing Care in Multiple Sclerosis



Adapted with kind permission from Marie Namey.

Establishing care is the first step toward building relationships and encouraging open communication with patients and their families or care partners. Components of establishing care include building trust,

establishing partnerships, determining information needs, sharing information, and assessing each patient's support network. These activities provide a foundation that promotes empowerment, encourages positive attitudes, and fosters hope, ultimately contributing to the establishment of a strong therapeutic alliance between nurses and those receiving care.

Continuing care focuses on cultivating patient health. As part of continuing care, nurses serve as educators, counselors, and advocates. Nurses teach patients practical approaches for managing disease symptoms and medication side effects, stressing the importance of adherence to treatment. Nurses also help patients implement self-care strategies, such as self-injection; symptom management; and wellness strategies focused on diet, exercise, and coping with stress. Self-care strategies can enhance patients' health and give them a sense of control over their illness. As part of continuing care, nurses may also assist patients with family and vocational issues and guide patients through the many life- and health-related uncertainties associated with MS.

Sustaining care focuses on maintaining patient well-being. In sustaining care, MS nurses coordinate referrals, identify community and information resources, and serve as consultants as patients' and families' needs change. Sustaining care also calls for the establishment of collaborative liaisons between MS nurses and other healthcare professionals—for example, neurologists, primary care physicians, speech and language pathologists, rehabilitation specialists, psychologists, and social workers—as dictated by the patient's physical and emotional needs. In addition, MS nurses may establish liaisons outside the healthcare team, to include government services, religious establishments, and other organizations that can provide assistance and support for patients with MS.

PRACTICE AREAS ACROSS THE DISEASE TRAJECTORY

Patients With New or Probable Diagnoses

For patients with a new diagnosis of MS or symptoms that strongly suggest MS, the nurse's priority is to establish care. Nurses should be aware that patients differ in their reactions to diagnosis.^{20,21} Some patients

experience grief and shock; some, denial; others may feel relieved to find an explanation for their symptoms. Initially, some patients may be unable to absorb much specific information about the disease and treatment options; others may want as much information as possible. Special attention may be needed for patients who are awaiting confirmation of a probable diagnosis, a process that may be prolonged and frustrating.²¹ As part of building trust and open communication, nurses need to carefully assess patients' reactions, coping mechanisms, and information needs.

Patients With Relapsing-Remitting Multiple Sclerosis

For patients with relapsing-remitting MS, the main focus is on continuing care. Sometimes, however, activities for establishing care apply—for example, when a patient has been symptom free for months or years. Research suggests that a relapse represents an “interruption” that precipitates a need for new information to help the patient cope.²² MS nurses will likely find themselves counseling patients to help them contend with the disappointment and discouragement associated with a relapse. Nurses can reestablish communication and reassess information needs to ensure that the continuing care needs of these patients are met.

As part of continuing care for patients with relapsing-remitting MS, nurses need to emphasize the importance of early and sustained treatment with the disease-modifying agents. They can help patients establish realistic expectations and explore treatment options. Nurses can also help patients make informed decisions about the use of complementary or alternative therapies.

Nurses also serve as advocates to ensure that patients have timely and adequate access—through insurance or other healthcare programs or through industry-supported programs—to medications, adaptive equipment, and supplies. Nurses will need to help patients and families cope with the major responsibilities of managing symptoms and complications of MS while maintaining “normal” lives and dealing with the ordinary events and experiences of living.¹⁹ Encouraging patients to develop support networks (eg, through participation in an MS support group) can help.

In sustaining care of patients with relapsing-remitting MS, nurses must recognize the tremendous burden and responsibility that the disease represents to patients and their families.^{19,20} Nurses have to advocate for adequate insurance entitlements and appropriate access to care. They may need to defend patient autonomy with regard to treatment decisions and self-care activities. Sustaining care for patients with relapsing-remitting MS requires continuous evaluation of patients' physical, cognitive, and emotional status. Specific changes, for example, in mobility or cognition, should be assessed and treated when they become evident and when they interfere with activities of daily living. In addition, treatment outcomes and the patient's self-care abilities should be monitored. If patients are doing well on treatment, positive reinforcement can help continue that pattern; if patients are not adhering to treatment, nurses should determine the impediments to adherence and initiate strategies to reverse this trend.

Patients With Progressive Multiple Sclerosis

The nursing care needs of patients with progressive MS are often complex. Sustaining patient trust and maintaining open communication are crucial to effective practice. If the disease worsens, the patient's physical, cognitive, and emotional needs should be continually reevaluated. Safety issues are the key concern. A caregiver or family member may need to be enlisted to assume responsibilities for activities of daily living and other interventions previously managed by the patient. The nurse can assist with training the caregiver and counseling the patient through this change in status. If disability increases, continued counseling and healthcare interventions can help the patient adapt and adjust. Rehabilitation efforts may be employed to reduce the severity of certain symptoms and improve patient independence.^{23,24}

Patients With Advanced Multiple Sclerosis

For patients whose disease has become more advanced, nurses must redefine therapeutic partnerships with patients and with family members or care partners who

ensure that the patient's daily needs are met. If the patient's condition warrants home healthcare or admission to a nursing home, the nurses who provide this care will need to establish new therapeutic relationships. For patients with advanced disease, it is especially important for care to be planned and implemented with attention to individual patient preferences, cultural mores, and previous lifestyle. In addition, because case management issues associated with advanced MS are often complex, nurses need to serve as advocates for quality care.

Continuing care needs of patients with MS shift to providing comfort, ensuring safety, and preventing complications. For example, patients with impaired mobility need interventions that prevent pressure sores. For patients who have difficulty speaking, alternate communication methods need to be devised. For patients who have lost the ability to swallow, alternative feeding methods will be necessary. Although these patients may not be able to care for themselves, they require recreation, stimulation, and support of their daily living activities. These requirements are universal for all people and are especially important for those facing daily losses in function, financial and emotional security, and self-esteem.

As part of sustaining care for patients with more advanced disease, these patients and their families require information and counseling on various issues, including the acceptance of progression of their disease and the need for life planning and advance directives, nursing home placement, and hospice care. Patients may need an opportunity to talk openly and honestly about their feelings. Nurses must be alert to signs of despair, helplessness, and hopelessness in their patients and must make appropriate referrals. Depression and suicide are real phenomena in MS. Patients with advanced disease and their families are often dealing with end-of-life issues, and nurses will want to consider palliative care options used by other patient populations.

Domains and Competencies of Multiple Sclerosis Nursing

The purpose of this section is to continue defining a model for MS nursing by identifying domains and competencies that describe the unique specialty of MS nursing. This model also helps to define best practices.

The domains of MS nursing are the particular areas of knowledge, expertise, and influence provided by nurses who care for patients with MS. Competencies are defined as the specific types of knowledge and skills that fit within and support the nursing domains. The domains and competencies described here have been selected to encompass care of patients over the full life-span trajectory of people with MS—that is, across the continuum from the newly diagnosed patient to advanced-stage disease.

Together, these domains and competencies define the standards and scope of MS nursing practice. They can serve as a guide for nurses who currently specialize in MS care or who plan to pursue this specialty.

MULTIPLE SCLEROSIS NURSING DOMAINS

- *Establish therapeutic partnerships* with MS patients, their families, and other health professionals on the patient's professional healthcare team.
- *Perform comprehensive assessments* to gauge each patient's level of functioning, identify the patient's needs and preferences, understand the patient's learning style, appreciate the patient's lifestyle, and get to know the patient's family.
- *Formulate a collaborative treatment plan*, taking into account the patient's symptoms, level of disability, need for disease-modifying agents, and need for sustained or prolonged care.
- *Initiate and facilitate a treatment regimen* by educating the patient about disease-modifying medications; teaching self-injection; serving as a patient advocate; helping the patient to overcome physical, cognitive, or other obstacles to treatment; and administering treatment when necessary.
- *Monitor the patient's treatment outcomes*, including

adherence; self-care, self-efficacy, and responsibility; side effects and adverse effects of medications; lifestyle changes; and quality of life.

- *Sustain therapeutic alliances* with the patient, family members or care partners, and other health professionals on the patient's healthcare team.
- *Maintain and broaden nursing competencies*, eg, develop new skills; enhance MS knowledge; and initiate, coordinate, or participate in MS research.

KNOWLEDGE-BASED COMPETENCIES

To carry out activities in these various domains, MS nurses should have solid, comprehensive, and current knowledge in the following areas:

1. The diagnostic process, course and pathology of MS, including the trajectory of MS across the life span
2. Pharmacology of therapeutic agents used for acute, symptomatic, and disease-modifying treatments
3. Use of complementary and alternative therapies in MS
4. Use of evaluation tools for monitoring outcomes
5. Basics of rehabilitation practice
6. Community resources—information and resources for patients and families
7. Educational principles, including age-specific learning techniques
8. Psychosocial issues, such as cultural and ethnic considerations, coping, and gender and sexuality issues
9. Reimbursement processes (insurance and managed care plans, Medicaid, Medicare, pharmaceutical industry programs)
10. Healthcare and education strategies that encourage wellness and health promotion
11. Professional expertise, for example, knowledge of nursing theory and models, assessment tools, current technologies, technical nursing skills, and professional organizations

SKILL-BASED COMPETENCIES

Skills necessary to professional nursing care of patients with MS include the following:

1. Communication
 - a. Listen to patient, family, other members of the healthcare team
 - b. Collaborate with other healthcare providers
 - c. Network
 - d. Negotiate

- e. Delegate
- f. Document
- 2. Assessment
 - a. Recognize physical care requirements
 - b. Perform neurological assessment
 - c. Perform functional assessment
 - d. Perform psychological, sociological, and cognitive assessments
 - e. Recognize culture-specific needs
 - f. Detect acute and chronic changes in health
- 3. Counseling
 - a. Provide anticipatory guidance (foresee and forestall problems)
 - b. Define patient's, family's, and nurse's limits and responsibilities
 - c. Listen, motivate, inspire hope, and put MS "in its place"
 - d. Solve problems
- 4. Education and teaching
 - a. Serve as a role model for patients, family members, other nurses, and other members of the professional healthcare team
 - b. Serve as a mentor and preceptor
 - c. Increase awareness about MS in the community
- 5. Advocacy
 - a. Negotiate within the healthcare system
 - b. Promote self-care
- 6. Participate in research
 - a. Establish benchmarks of nursing care
 - b. Examine outcomes of nursing practice

SPECIALIZED COMPETENCIES

The following is a list of skills that may require a unique approach in the care of patients with MS.

- 1. Management of elimination dysfunction
- 2. Assessment and control of pain
- 3. Assessment and reduction of spasticity
- 4. Skin care and management of injection-site reactions
- 5. Infusion skills for intravenous therapies
- 6. Knowledge of advanced technologies (eg, MRI, optical coherence tomography [OCT], rehabilitation innovations)

MATCHING NURSING COMPETENCIES TO NURSING DOMAINS

Table 1 shows how specific skill-based competencies can be matched to MS nursing domains, providing a comprehensive and practical illustration of the scope

of MS nursing practice. For example, as part of *establishing therapeutic partnerships*, nurses listen to and communicate with patients and other health professionals. Nurses assess the patient's psychological, social, and cognitive abilities and maintain sensitivity to cultural, ethnic, and gender issues. Nurses provide anticipatory guidance; establish limits and responsibilities of care for patients, family members, and healthcare professionals; and listen, motivate, and inspire hope in initiating treatment. Education about the disease and about effective treatment and management of symptoms is an essential component of developing nurse–patient partnerships. Furthermore, as part of *establishing therapeutic partnerships*, nurses may need to serve as advocates by negotiating within the healthcare system—ensuring that patients get the medications, equipment, and resources they need—and by promoting patient self-care.

As part of *monitoring outcomes*, MS nurses listen and communicate and must continuously assess and document the patient's functional, psychological, sociological, and cognitive status over time (Table 1). In addition to monitoring the patient's general health status, nurses must be acutely aware of the appearance of, or any changes in, symptoms. Nurses also provide counseling to motivate patients and encourage hope. They provide education about monitoring treatment, serving as role models for patients and families and as mentors and preceptors for their less experienced peers.

Many of the specific skills identified in Table 1 apply across multiple domains. For example, anticipatory guidance is crucial not only for establishing strong therapeutic relationships but also for formulating, initiating, and facilitating treatment. Similarly, the nurse's capacity to listen, motivate, and inspire hope is essential not only to establishing therapeutic partnerships and formulating treatment plans but also to monitoring treatment outcomes and sustaining therapeutic alliances. Recognizing the patient's physical care needs is obviously important to performing a comprehensive assessment, but it is also part of formulating and implementing treatment and monitoring treatment outcomes. These examples illustrate the continuity that exists both within and across domains and competencies.

TABLE I.
Domains and Competencies of Multiple Sclerosis Nursing

| | | DOMAINS | | | | | | |
|---|------------------------------------|-----------------------------------|--|---|------------------|-------------------------------|---|--|
| COMPETENCIES | Establish Therapeutic Partnerships | Perform Comprehensive Assessments | Formulate Collaborative Treatment Plan | Initiate and Facilitate Treatment Regimen | Monitor Outcomes | Sustain Therapeutic Alliances | Maintain and Broaden Nursing Competencies | |
| 1. Communicate | | | | | | | | |
| a. Listen | X | X | | | | X | | |
| b. Collaborate | X | | X | | | X | X | |
| c. Network | | | | | | X | X | |
| d. Negotiate | | | X | X | | X | X | |
| e. Delegate | | | X | | | X | X | |
| f. Document | | X | X | | | X | X | |
| 2. Assess patient care needs | | | | | | | | |
| 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 | | |
| 3. Counsel patients and families | | | | | | | | |
| a. Provide anticipatory guidance | X | | 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 | | |
| d. Solve problems | | | X | X | | X | | |
| 4. Educate | | | | | | | | |
| a. Serve as role model | X | | | X | | X | X | |
| b. Serve as a mentor and preceptor | | | | | | X | X | |
| c. Increase awareness of MS in the community | | | | | | X | X | |
| 5. Advocate | | | | | | | | |
| a. Negotiate within the healthcare system | X | | X | X | | X | X | |
| b. Promote self-care | X | | X | X | | X | X | |
| 6. Participate in research | | | | | | | | |
| a. Establish benchmarks of care | | | | | | | X | |
| b. Examine outcomes of nursing practice | | | | | | | X | |

Role of the Nurse in Pharmacologic Therapy of Multiple Sclerosis

As a primary source of information for patients and families affected by MS, nurses are in an optimal position to provide education about medications. Nurses can provide practical information about indications, effectiveness, and side effects, thereby facilitating patients' treatment decisions, clarifying any misconceptions, and ensuring proper use of medications.

MS nurses also play a substantial role in monitoring adherence. Once a particular medication or medication regimen is started, nurses must know how to assess treatment responsiveness and what side effects to be mindful of. Nurses also serve as advocates, working with insurance companies, managed care organizations, Medicaid and Medicare, and pharmaceutical support programs to make sure that patients can obtain and receive reimbursement for the treatments prescribed. Medications for MS include:

- Episodic treatments—those used to shorten relapses
- Symptomatic treatments—those used to minimize or control specific symptoms, such as spasticity, bowel and bladder problems, and fatigue
- Disease-modifying treatments—immunomodulatory drugs and other agents developed to reduce the frequency and severity of relapses and slow disease progression

This section lists and discusses many of the medications used for the management of MS, along with specific nursing considerations for each medication.

EPISODIC TREATMENTS

In patients with MS, a relapse—also known as an acute attack or an exacerbation—is defined as an episode of new or worsening MS symptoms that lasts more than 24 hours and is not related to metabolic changes (eg, due to fever or intercurrent illness) or steroid withdrawal. Typically, an acute relapse tends to progress over a few days, reaches its peak within a week, then slowly

resolves.²⁵ Relapses often lead to a change in the patient's functional status,²⁶ and resolution may require as long as 6 months.

There is no established standard for management of relapses. Treatment decisions are determined by the healthcare provider on an individual basis. Depending on specific symptoms, no treatment may be suggested—for example, for patients with mild sensory attacks and no functional decline. Most patients who are experiencing acute relapses are given high-dose corticosteroids, usually intravenously but sometimes orally. Treatment is based on the practice patterns of the physician caring for the patient. Unfortunately, there is a paucity of literature documenting the superiority of one route of administration over the other.

Corticosteroids reduce the inflammation in the central nervous system and may help reestablish the integrity of the blood–brain barrier, thereby hastening improvement of symptoms.²⁷

Intravenous methylprednisolone (IVMP) is consistently the treatment of choice. Initially, this anti-inflammatory corticosteroid is given at high, intermittent doses over 3 to 5 days.^{28,29} IVMP can be given in the hospital or at home and may or may not be followed by a gradually tapering dose of an oral corticosteroid.^{28,29} The Canadian model leans toward high dose oral steroids in place of IV administration. ACTH, previously used for relapses during the mid 20th century, is now available but there is no accepted protocol for relapse management.³⁰

During steroid treatment, patients and families need to know what to expect. Nurses can provide education about realistic outcomes and side effects that demand medical intervention. Typical side effects include increased appetite, gastrointestinal upset, nervousness or anxiety, and insomnia. Facial flushing, urinary frequency, and taste disturbance may also accompany corticosteroid treatment. Patients should be encouraged to call their healthcare provider if they experience anxiety or insomnia. Other side effects that may warrant monitoring and medical treatment include glycosuria and severe mood changes or mood swings. Patients should be advised to limit salt and sugar intake while on

corticosteroid treatment, and patients taking immunomodulatory agents (the interferons or glatiramer acetate) should be told not to stop these medications while receiving IVMP or any other treatment for a relapse. During the time of a relapse, it is important to assess whether patients would benefit from other interventions, such as adaptive equipment. For example, for patients who have difficulty walking during an attack, a cane or walker can provide a safe, energy-conserving mobility device. Nurses may also want to discuss temporary modifications to patients' work and physical activities.

SYMPTOMATIC TREATMENTS

Managing the ongoing symptoms of MS is challenging, but effective management can dramatically improve the patient's quality of life. Fatigue, elimination problems, and other common symptoms can be controlled or reduced through education, counseling, and rehabilitation measures. When these strategies are not sufficient, pharmacotherapy may be considered.

Table 2 lists medications used for symptom management in MS. It gives generic drug names, along with specific nursing implications associated with their use, for treatment of various symptoms. The table is not intended to be exhaustive; the most common or problematic symptoms are discussed here, but others that may be alleviated by nursing intervention include tremor, weakness, vertigo, and sexual dysfunction. Excellent reviews of the strategies and medications used to manage these symptoms are available for guidance.²⁸

The first step in symptom management is to determine the factors that are causing or contributing to symptoms. Concomitant medications, concurrent illnesses or other medical conditions may produce new symptoms or alter the severity of the symptoms. If pharmacologic treatment is needed to alleviate symptoms, some general "rules of thumb" apply. First, it is essential to determine whether any contraindications, such as other medical conditions or concomitant medications (including over-the-counter medications and alternative treatments), preclude treatment with a particular agent. Second, nurses need to convey what outcomes patients should anticipate and what side

effects may occur—this can help reinforce positive therapeutic relationships and can help optimize symptom management. Third, patients need to be encouraged to follow up, so that nurses can confirm that medications are working properly and intervene if unexpected outcomes or intolerable side effects occur. Nursing strategies such as dose escalation and dose titration can help patients avoid side effects and increase tolerance of treatment.

Fatigue

Fatigue is the most common—and often the most disabling—symptom associated with MS. Fatigue in patients with MS may occur in several different forms—as activity-related fatigue; as fatigue associated with deconditioning, depression, or neuromuscular exhaustion; or as a lassitude known as "MS fatigue." Treatment of fatigue requires effective energy management, medications, or both. Nurses can suggest behavioral changes such as conditioning programs, exercise, and improved nutrition.³¹ Patients can be referred to an occupational therapist, who can teach them about and help them implement energy-conservation techniques.

Drugs that can provide relief include CNS stimulants such as methylphenidate (Ritalin[®]) and modafinil (Provigil[®]).^{32,33} Patients should be advised that these medications may cause nervousness, restlessness, and insomnia. Antidepressants such as fluoxetine (Prozac[®]) and an antiviral agent, amantadine (Symmetrel[®]), may also be effective for fatigue.^{32,34} Previous literature has also documented the benefit of conditioning programs with graded exercise to reduce fatigue.³¹

Bladder Dysfunction

Bladder dysfunction results from pathology in nerve pathways controlling detrusor function, sphincter function, or both.³⁵ Symptoms of bladder dysfunction—urinary hesitancy, frequency, urgency, and/or incontinence—affect many people with MS. Patients may attribute these problems to the effects of aging or childbirth and simply accept them as such rather than see them as modifiable symptoms of MS, but they should be informed that bladder symptoms can be managed. Dysfunction may manifest as failure to store urine, failure to empty urine,

TABLE 2.
Pharmacologic Management of Selected Symptoms in Multiple Sclerosis

| Symptoms | Treatment | Nursing Considerations | | | | |
|--|---|--|-------------------------|--|--|--|
| Fatigue | <ul style="list-style-type: none"> • CNS stimulants (pemoline, modafinil, armodafinil) • Amantadine • Selective serotonin reuptake inhibitors (SSRIs), eg, fluoxetine | <ul style="list-style-type: none"> • Restlessness or sleep disturbance may occur • Help patients with dosing schedule, titrate doses up | | | | |
| Bladder dysfunction | <ul style="list-style-type: none"> • Anticholinergics (eg, oxybutynin) • Antimuscarinics (eg, tolterodine) • α-Blockers (eg, terazosin) | <ul style="list-style-type: none"> • Determine if urinary tract infection is present • Monitor retention • Monitor fluid balance • Follow overall elimination pattern • Consider contribution of other medications • Provide strategies to avoid side effects, eg, dry mouth | | | | |
| Bowel dysfunction | <table border="0"> <tr> <td><i>Constipation</i></td> <td><i>Urgency/Diarrhea</i></td> </tr> <tr> <td> <ul style="list-style-type: none"> • Stool softeners • Bulk-forming agents • Mini-enemas • Stimulants • Suppositories </td> <td> <ul style="list-style-type: none"> • Bulk-forming agents • Anticholinergics • Antimuscarinics </td> </tr> </table> | <i>Constipation</i> | <i>Urgency/Diarrhea</i> | <ul style="list-style-type: none"> • Stool softeners • Bulk-forming agents • Mini-enemas • Stimulants • Suppositories | <ul style="list-style-type: none"> • Bulk-forming agents • Anticholinergics • Antimuscarinics | <ul style="list-style-type: none"> • Provide bowel training regimens; many of the medications should not be used long-term • Consider contributory effects of other medications, eg, steroids or antibiotics • Consider lifestyle issues • Encourage exercise • Provide diet counseling |
| <i>Constipation</i> | <i>Urgency/Diarrhea</i> | | | | | |
| <ul style="list-style-type: none"> • Stool softeners • Bulk-forming agents • Mini-enemas • Stimulants • Suppositories | <ul style="list-style-type: none"> • Bulk-forming agents • Anticholinergics • Antimuscarinics | | | | | |
| Pain | <ul style="list-style-type: none"> • Anticonvulsants (phenytoin, carbamazepine, gabapentin, pregabalin, lamotrigine) • Tricyclic antidepressants (amitriptyline, nortriptyline) • Duloxetine hydrochloride | <ul style="list-style-type: none"> • Watch for sedation • Start with low doses and titrate up • Monitor outcomes; alter treatment as necessary; supportive measures can help | | | | |
| Spasticity | <ul style="list-style-type: none"> • GABA antagonists (oral or intrathecal baclofen) • α-Agonists (tizanidine) • Anticonvulsants (diazepam, clonazepam, gabapentin) • Botulinum toxin | <ul style="list-style-type: none"> • Time doses to maintain therapeutic blood levels • Titrate doses up (especially with baclofen) • Watch for sedation or cognitive symptoms; may require a change in dosage or medication • Combination treatments may help • Intrathecal baclofen requires surgical insertion of programmable pump | | | | |
| Depression | <ul style="list-style-type: none"> • SSRIs and SNRIs (eg, fluoxetine, sertraline, paroxetine, citalopram, duloxetine hydrochloride) • Tricyclic antidepressants (eg, amitriptyline, nortriptyline) • Atypical antidepressants (eg, venlafaxine, bupropion) | <ul style="list-style-type: none"> • Evaluate type and degree of depression • Consider contribution of medications (eg, with interferons) • Assess family situation/support network • Consider suicide risk • Promote use of psychiatric services • Advise patient that medication effects may take several weeks • Advise patient not to stop medications suddenly • Reassess patient regularly • Paroxetine can be taken in the morning or at night, can help with anxiety • Monitor urinary function with venlafaxine (may cause fluid retention) | | | | |

TABLE 2. (continuation...)
Pharmacologic Management of Selected Symptoms in Multiple Sclerosis

| <i>Symptoms</i> | <i>Treatment</i> | <i>Nursing Considerations</i> |
|---------------------|--|---|
| Walking difficulty | <ul style="list-style-type: none"> • Dalfampridine www.ampyra.com | <ul style="list-style-type: none"> • 10 mg every 12 hours • Do not crush • Consider seizure risk • Monitor for infections • Advise not to increase dosage • Do not take with compounded 4-AP |
| Pseudobulbar Affect | <ul style="list-style-type: none"> • Nuedexta™ (dextromethorphan hydrobromide and quinidine sulfate) www.nuedexta.com | <ul style="list-style-type: none"> • Use for MS or ALS • Maybe used for other types of emotional lability • Not restricted to any types of MS • Dose once daily for 7 days, 1 capsule every 12 hours • Should not be used with quinine, quinidine, mefloquine or MAO inhibitors • Do not use with other drugs that prolong Q-T interval |

or both. Urinary tract infection may be a contributing factor and should be ruled out or treated appropriately before initiating other treatment.

Effective pharmacologic treatments include anticholinergic agents, antimuscarinic agents, and α -blockers.^{32,36} A bladder training program that includes education, elimination of bladder irritants such as caffeine and aspartame, scheduled voidings, and positive reinforcement can also improve bladder functioning and quality of life. Medications include darifenacin (Enablex®), oxybutynin (Ditropan®, Ditropan® XL), a transdermal oxybutynin patch (Oxytrol®), solifenacin succinate (Vesicare®), tolterodine (Detrol®), and trospium chloride (Sanctura™). Patients may also require bladder emptying with either intermittent or permanent placement of a catheter.

Bowel Dysfunction

Patients with MS may have bowel problems that range from constipation to bowel urgency and involuntary bowel movements. Constipation is the most common, and involuntary bowel movements are perhaps the

most distressing. Constipation is best managed with preventive measures, including a high-fiber diet, adequate fluid intake, exercise, and an established bowel program. The nurse can guide and facilitate a bowel program with education and support. If medication is indicated, bulk formers (such as psyllium) or softeners (such as docusate) may be prescribed. If a stimulating laxative is needed, a mild compound such as milk of magnesia may work best. Stronger stimulants and stimulating suppositories or enemas should be regarded as occasional treatments or tools to get a bowel program started—their use on a regular basis should be avoided.

Patients with bowel urgency may benefit from treatment with an anticholinergic agent such as oxybutynin or an antimuscarinic agent such as tolterodine or trospium chloride. These medications have antispasmodic effects that can ease uninhibited bowel spasms that contribute to urgency. Bulk-forming agents, along with a regular bowel routine, can also reduce bowel urgency.

Pain

Pain in MS may be neuropathic or neurological in origin and acute or chronic in duration. Because the pain associated with MS differs from that typically associated with injury, standard pain medications such as aspirin, nonsteroidal anti-inflammatory agents, and narcotic analgesics do not provide relief.

Types of acute pain that occur frequently in patients with MS are *trigeminal neuralgia*, a sharp, stabbing pain in the face, and a burning, aching sensation known as *burning dysesthesia*. Pharmacologic treatments that can provide relief include the anticonvulsants carbamazepine (Tegretol[®], Carbatrol[®]), gabapentin (Neurontin[®]), and lamotrigine (Lamictal[®]).^{32,37} Though often effective for pain, some anticonvulsants may cause sedation; slow titration can minimize this side effect.³⁸ Tricyclic antidepressants such as amitriptyline (Elavil[®]) may relieve pain and can be especially helpful for dysesthesias; they may act by stopping pain conduction through the nerves. A transdermal delivery system, a lidocaine patch (Lidoderm[®]), may provide patients with sustained relief if oral medications are partially effective or are ineffective.

Two other medications that are used to treat acute pain due to MS are pregabalin (Lyrica[®]), an anticonvulsant and analgesic agent also approved to treat neuropathic pain associated with diabetes and fibromyalgia, and duloxetine hydrochloride (Cymbalta[®]), which is also used to treat depression (see below).³⁹ Neither drug has been specifically approved to treat pain associated with MS, but their effectiveness in treating neuropathic pain associated with other diseases make them a suitable option for MS patients.

Chronic pain in patients with MS often manifests as a “pins and needles” sensation or as a burning, aching pain. Chronic pain is often treated with the same medications used for treatment of acute dysesthesias.

Patients with MS also may experience pain as a result of muscle cramping or abnormal musculoskeletal stresses. Musculoskeletal pain can be alleviated by supportive interventions such as an ankle–foot orthosis or by appropriate positioning of seating devices to maintain/sustain appropriate body alignment.

Spasticity

Another common symptom, spasticity, is a major factor in decreased mobility among patients with MS. Spasticity can manifest as stiffness or spasms, may involve pain and discomfort, and may interfere with daily activities. Regular stretching and exercise can reduce stiffness and improve function, but pharmacologic treatment is often necessary.

Effective antispasmodics include baclofen (Lioresal[®]), a γ -aminobutyric acid (GABA) antagonist, and tizanidine (Zanaflex[®]), an α_2 -adrenergic agonist. The anticonvulsant medications diazepam (Valium[®]) and clonazepam (Klonopin[®]) may also be helpful in combination with other medications.²⁸ For many of these medications, it is best to start at low doses, then titrate up, to improve tolerability. Maximizing the dose at bedtime, usually a time of maximal spasticity, is a useful strategy for managing both spasms and the sedative effects of some antispasmodics.

Baclofen is among the most commonly used medications for spasticity, but the drug may cause weakness or sedation.⁴⁰ If weakness limits the use of baclofen, tizanidine is a viable alternative. Baclofen and tizanidine may be used in combination as well. For spasticity that is severely disabling and not responsive to oral drug therapy, intrathecal baclofen, delivered via a programmable pump that is surgically inserted into the abdominal wall, may provide relief.⁴¹ For focal muscle spasticity, which may be resistant to systemic treatment, an injection of botulinum toxin (Botox[®]) can provide temporary relief but may need to be repeated.⁴²

Depression

Both clinical depression and a similar, less severe emotional distress are common in patients with MS. About 50% of patients with MS experience depression at some time during their illness⁹—a rate much higher than that seen in the general population. Rates of suicide among people with MS are also much higher than those seen in the general population.^{9,45} MS nurses must be aware of the symptoms of depression and assess patients with each contact. Appropriate referrals for counseling or psychiatric therapy and recommendations for pharmacologic treatment should be made as needed. If depression is suspected, certain

contributing factors must be considered. Some medications, including baclofen and benzodiazepines, which are used for symptom management, may be associated with depression. Patients should be screened for depression before starting treatment with disease-modifying therapy, and any depressive symptoms should be treated before or during therapy. Note that other medical conditions, such as hypothyroidism, can contribute to a depressed affect and should be ruled out or treated, as appropriate.

An array of medications is available to alleviate depression. Selective serotonin reuptake inhibitors (SSRIs) and selective serotonin and norepinephrine reuptake inhibitors (SNRIs), such as fluoxetine, sertraline (Zoloft[®]), escitalopram oxalate (Lexapro[®]), citalopram HBr (Celexa[®]), paroxetine (Paxil[®] or Paxil CR[®]), and duloxetine, are frequently prescribed. Tricyclic antidepressants, including amitriptyline and nortriptyline, are useful, especially if sleep disturbance accompanies depression. Atypical antidepressants such as venlafaxine (Effexor[®]) and bupropion (Wellbutrin[®]) may also be prescribed.

Walking Problems

Walking and overall mobility can be affected by multiple sclerosis to a greater or lesser extent based on the nature of the disease course, problems with stamina and fatigue, environmental factors such as climate and structural issues (stairs, length of halls, etc.) and demands of activities of daily living. Dalfampridine (Ampyra[®]) has been approved by the FDA to improve walking in multiple sclerosis but it is important that the nurse also ensure that the patient receives appropriate rehabilitative and exercise training to enhance the effect of the medication.⁴³

Emotional Lability (Pseudobulbar Affect - PBA)

Patients with multiple sclerosis can experience a wide range of emotions related to coping with this disorder. One stressful and embarrassing problem is pseudobulbar affect or inappropriate laughing or crying. The associated stress of this problem is obvious and embarrassing. The FDA has approved Nuedexta[™], an oral medication which is a combination of the generic

drug quinidine which prevents cardiac arrhythmia, and the cough suppressant, dextromethorphan. The most common side effects include diarrhea, dizziness, cough, emesis, urinary tract infections, elevated liver enzymes, and flatulence. This medication can interact with other medications (see Table 2).⁴⁴

MEDICATIONS USED FOR DISEASE MODIFICATION

Immunomodulatory Agents

Evidence that MS is more than a demyelinating disease—that axonal transection is the pathology underlying permanent disability, occurs early in the disease course, and causes irreversible damage—has given major impetus to early and aggressive treatment with immunomodulatory agents.¹

IFN β -1a (intravenous [IM] and subcutaneous [SC]), IFN β -1b, glatiramer acetate, and natalizumab (Tysabri[®]) are now fundamental components of treatment for relapsing forms of MS. IFN β -1a and IFN β -1b are recombinant proteins that may exert their effects by inhibiting inflammation and the migration of white blood cells across the blood–brain barrier (BBB).⁴⁶ In contrast, glatiramer acetate, a synthetic polypeptide thought to resemble myelin basic protein, may act by stimulating immune suppressor lymphocytes that then release anti-inflammatory cytokines. Glatiramer acetate may also compete with myelin antigens for binding to antigen-presenting cells, thereby preventing autoimmune reactions that lead to demyelination.⁴⁷ Natalizumab is a monoclonal antibody that may block the migration of activated lymphocytes, which cause damage to the brain and spinal cord, across the BBB.⁴⁸

Natalizumab (Tysabri[®]) is a disease modifying therapy that is administered every four weeks by infusion. There were striking efficacy results on both clinical and MRI endpoints from two clinical trials. Data from AFFIRM revealed a 68% reduction in annual relapse rates compared to placebo and significantly reduced numbers of brain lesions on MRI. Other positive results were reported from SENTINEL such as reduction in annual relapse rate of 54% at years one and two with natalizumab/interferon therapy compared to interferon alone.^{63,64}

TABLE 3. Immunomodulatory Agents for the Treatment of Relapsing-Remitting Multiple Sclerosis^{47-62,68-70,72}

| Generic and brand name | Interferon β -1a | | Interferon β -1b | | Glatiramer acetate | | Natalizumab | | |
|------------------------------|---|---|--|---|--|---|-------------|--|--|
| | Avonex [®] | Rebif [®] | Betaseron [®] | Extavia | Copaxone [®] | Tysabri [®] | | | |
| Manufacturer/distributor | Biogen Idec | EMD Serono | Bayer HealthCare Pharmaceuticals | Novartis Pharmaceuticals | Teva Neuroscience | Biogen Idec and Eian | | | |
| Approval in US | 1996 | 2002 | 1993 | | 1996 | 2005 (reintroduced in 2006) | | | |
| Approval in Canada | 1998 | 1998 | 1995 | | 1997 | 2006 | | | |
| Frequency; route of delivery | Weekly; IM injection | 3 times/week; SC injection | Every other day; SC injection | Every other day; SC injection | Daily; SC injection | Every 4 weeks; IV infusion | | | |
| Administration options | <ul style="list-style-type: none"> • Prefilled syringe • Lyophilized powder • Room temperature–stable formulation | <ul style="list-style-type: none"> • Prefilled syringe • Autoinjector • Room temperature–stable formulation | <ul style="list-style-type: none"> • Prefilled diluent for mixing with lyophilized powder • Autoinjector • Room temperature–stable formulation | <ul style="list-style-type: none"> • Prefilled syringe • Autoinjector • Room temperature–stable formulation | <ul style="list-style-type: none"> • Prefilled syringe • Autoinjector • Room temperature–stable formulation | <ul style="list-style-type: none"> • IV infusion at registered infusion facility | | | |
| Long-term follow-up study | <ul style="list-style-type: none"> • 2 years | <ul style="list-style-type: none"> • 8 years* | <ul style="list-style-type: none"> • 16 years* | <ul style="list-style-type: none"> • 10 years | <ul style="list-style-type: none"> • 10 years | <ul style="list-style-type: none"> • 2 years | | | |
| Key efficacy findings | <p>RRMS</p> <ul style="list-style-type: none"> • 18% reduction in annualized relapse rate • 37% lower risk for progression of disability • 50% fewer lesions at 2 years <p>Monosymptomatic Presentation</p> <ul style="list-style-type: none"> • Significant delay in development of clinically definite MS | <p>RRMS</p> <ul style="list-style-type: none"> • 29%–32% reduction in relapse rate at 2 years, which continued to decrease at year 8 • Significant reduction in disability; time to sustained disability progression significantly prolonged in interferon β-1a SC compared with crossover patients • Significant reduction in active lesions on MRI sustained through 8 years of treatment | <p>RRMS</p> <ul style="list-style-type: none"> • 40% reduction in relapse rate at 16 years • Reduction in rate of severe relapses • Reduction in rate of new lesions detected by MRI <p>Monosymptomatic Presentation</p> <ul style="list-style-type: none"> • Significant delay in development of clinically definite MS | <p>RRMS</p> <ul style="list-style-type: none"> • >80% reduction in relapse rate at 10 years • 62% of patients had stable/improved disability measures; crossover patients who delayed treatment had more frequent relapses and significantly greater risk of disability • Significant reduction in lesions (40% at 9 months, 54% at 18 months); overall 34.2% lower accumulated lesion disease burden for patients always on glatiramer acetate than for crossover patients • Significant reduction in the proportion of lesions that evolve into black holes and hence brain tissue disruption/loss | <p>RRMS</p> <ul style="list-style-type: none"> • 67% reduction in relapses at 2 years • 42% reduction in risk of sustained progression of disability • 92% fewer lesions at 2 years | | | | |
| Common side effects | <ul style="list-style-type: none"> • Headaches • Mild flu-like symptoms • Muscle aches • Anemia • Depression, suicidal ideation, and/or suicide attempts may occur; warranting treatment cessation | <ul style="list-style-type: none"> • Mild flu-like symptoms • Muscle aches • Anemia • Injection-site reactions • Depression, suicidal ideation, and/or suicide attempts may occur; warranting treatment cessation | <ul style="list-style-type: none"> • Flu-like symptoms • Injection-site reactions • Menstrual disorders • Mild neutropenia, anemia, and thrombocytopenia • Abnormal liver function • Depression and/or suicidal ideation may occur; warranting treatment cessation | <ul style="list-style-type: none"> • Injection-site reactions • Postinjection reaction | <ul style="list-style-type: none"> • Headache • Fatigue • Arthralgia • Urinary tract infection • Liver injury • PML (rare) • Malignant melanoma[†] | | | | |
| Patient support programs | <p>Avonex Services</p> <p>US: 800-456-2255</p> <p>www.avonex.com</p> <p>Canada: 1-888-456-2263</p> <p>www.msalliance.ca</p> | <p>MS Lifelines[®]</p> <p>US: 877-447-3243</p> <p>www.ms lifelines.com</p> <p>Multiple Support Program</p> <p>Canada: 888-677-3243</p> <p>www.msprogram.ca</p> | <p>MS PathwaysSM</p> <p>US: 800-788-1467</p> <p>www.ms pathways.com</p> <p>Canada: 800-977-2770</p> <p>www.ms pathways.ca</p> | <p>Shared Solutions[®]</p> <p>US: 800-887-8100</p> <p>www.copaxone.com</p> <p>MSWatch</p> <p>Canada: 800-283-0034</p> <p>www.ms watch.ca</p> | <p>Tysabri Support</p> <p>US: 800-456-2255</p> <p>www.tysabri.com</p> <p>Canadian Tysabri Care Program</p> <p>Canada: 1-888-827-2827</p> | | | | |

* Long-term follow-up studies for both SC IFN β -1a and IFN β -1b may have included patients who stopped therapy, restarted therapy, or used another immunomodulatory therapy at some point before the long-term follow-up visit.
 † As reported in 3 patients with an existing skin lesion/mole. One case occurred during the clinical trial; 2 postmarket cases were reported by Mullen et al. (N Engl J Med. 2008;358:647-648).

Safety concerns due to the occurrence of a condition due to compromise of the immune system, PML (progressive multifocal leukoencephalopathy) resulted in the withdrawal of this therapy in 2004. When it was approved to re-enter the treatment paradigm by the FDA, the TOUCH program was mandated to monitor for potential indications of symptoms indicating this condition. A study is currently underway to determine the validity of an antibody test that may predict the risk of PML in patients treated with natalizumab.

Fingolimod (Gilenya®) is the first oral medication approved by the FDA to modify the disease course in multiple sclerosis. It is indicated to reduce the frequency of exacerbations and delay the accumulation of disability in relapsing forms of MS. Studies are underway to determine potential benefit for persons with progressive MS. Two pivotal trials were the basis of FDA approval. The FREEDOMS I trial and the TRANSFORMS trial resulted in the approval in 2010. As the first oral therapy with potential side-effects, this medication has added to the nurse's role in patient and family education as well as long-term monitoring for potential risks.⁶⁵⁻⁶⁷

The FDA has recommended baseline observations during the first dose of fingolimod along with baseline blood work and evaluation of immunization status, cardiac status, and ophthalmologic examination. It is also recommended that patients be re-evaluated ophthalmologically after three to four months of treatment and in the event that new visual symptoms occur. Patients who develop symptoms of pulmonary or hepatic disease should be tested promptly.⁶⁷

Table 3 summarizes key information for each immunomodulatory agent, including injection routes, findings from recent clinical trials, and resources for further information. As shown in clinical trials, these immunomodulatory agents can modify disease progression, reduce future disability, and improve quality of life for patients with relapsing-remitting MS.^{47-62,68-70,72} The clear benefit of these agents prompted the NMSS to release a consensus statement recommending *early intervention* and *continued treatment* for all patients with MS (Table 4).⁷¹ Thus, for most patients with a confirmed

**TABLE 3. (continuation...)
Immunomodulatory Agents for the
Treatment of Relapsing-Remitting
Multiple Sclerosis**

| Generic and brand name | Fingolimod |
|-------------------------------------|---|
| | Gilenya |
| Manufacturer / distributor | Novartis Pharmaceuticals |
| Approval in US | 2010 |
| Approval in Canada | 2011 |
| Frequency; route of delivery | 0.5 mg orally; daily |
| Administration options | <ul style="list-style-type: none"> • Prescreening recommended • 6 hour observation at first dose |
| Long-term follow-up study | |
| Key efficacy findings | <p>FREEDOMS I</p> <ul style="list-style-type: none"> • Relative risk reduction in relapses – 54 % • Sustained EDSS progression – 30 % relative risk reduction <p>TRANSFORMS</p> <ul style="list-style-type: none"> • Fingolimod and interferon beta-1a SQ – 52 % relative risk reduction in 0.5 mg dose • MRI benefits noted • No differential effect on progression |
| Common side effects | <ul style="list-style-type: none"> • Risk of infection • Macular edema • Changes in pulmonary function • Elevation in liver enzymes • Alterations in blood pressure |
| Patient support programs | Novartis Patient Services: 1-877-408-4974 www.gilenya.com |

TABLE 4.
Recommendations of the Medical Advisory Board of the National Multiple Sclerosis Society on the Use of the Immunomodulators⁷¹

- Initiation of therapy with an immunomodulator is advised as soon as possible following a definite diagnosis of MS with a relapsing course and may be considered for selected patients with a first attack who are at high risk for MS.
- Patients' access to medication should not be limited by frequency of relapses, age, or level of disability.
- Treatment is not to be stopped while insurers evaluate the case for continuing coverage of treatment.
- Therapy is to be continued indefinitely, except in the following circumstances: there is a clear lack of benefit; there are intolerable side effects; new data reveal other reasons for cessation; better therapy becomes available.
- All of the FDA-approved immunomodulatory agents should be included in formularies and covered by third-party payers so that physicians and patients can determine the most appropriate agent on an individual basis. Failure to do so is unethical and discriminatory against a very small percentage of patients.
- Movement from one immunomodulatory drug to another for medically approved reasons should be permitted.
- Immunosuppressive therapy with mitoxantrone may be considered for selected relapsing patients with worsening disease.
- Most concurrent medical conditions do not contraindicate use of the immunomodulatory drugs.
- None of the DMTs have been approved for use by women who are trying to become pregnant, are pregnant, or are nursing mothers.

Adapted from *Expert Opinion Paper: Disease Management Consensus Statement*. © 2007 The National Multiple Sclerosis Society. The full text of the document is available at: <http://www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinion-papers/index.aspx>. Accessed April 6, 2008.

diagnosis of MS (that is, patients who have experienced 2 or more attacks separated by time and space, have clinical evidence of 2 or more lesions in the CNS, or fulfill McDonald MRI criteria described earlier¹⁰), the question is not *whether* to treat with an immunomodulatory agent but rather *which* agent to use.

Currently, patients with clinically isolated syndrome (CIS)—those who have experienced only 1 neurological episode suggestive of MS along with MRI data indicative of MS—are considered to be at high risk for a diagnosis of MS, and immunomodulatory therapy is strongly suggested for them.⁷¹ Data from several trials exploring the potential value of initiating treatment at the first sign of clinical demyelination demonstrated that glatiramer acetate and the β -IFNs can significantly delay the development of clinically definite MS in patients who have had only 1 clinical episode, sometimes referred to as “monosymptomatic” presentation.^{50,73-75} Indications for IM IFN β -1a, IFN β -1b and glatiramer acetate have been expanded to include their use in patients experiencing a first clinical episode who have MRI findings that are consistent with MS.^{68,69} These findings provide further evidence and impetus for early initiation of immunomodulatory therapy and suggest that for some patients, treatment may need to be considered before a second relapse has occurred.

While these studies show that early treatment can delay disease progression in CIS patients, data from long-term follow-up (LTFU) studies involving the randomized populations in the pivotal trials of glatiramer acetate, IFN β -1b, and SC IFN β -1a reveal that these therapies benefit MS patients in the long term.^{52,59,72} Glatiramer acetate has the longest record of patients randomized in the original trial who have been on continuous and consistent therapy.⁷⁶ In an ongoing extension trial examining the efficacy of glatiramer acetate over time, the annual relapse rate declined by 80% over 10 years of treatment, from an average of about 1.18 per year to an average of 1 every 5 years.⁵⁹ Furthermore, 62% of patients continuing glatiramer acetate treatment at 10 years experienced no further change in disability or improved at least 1 step on the Expanded Disability Status Scale (EDSS).⁵⁹ Importantly, a separate analysis

TABLE 5. **Checklist of Patient Questions**

Patients need to consider many factors when making a decision about disease-modifying treatment. This list of questions may be a useful tool for patients.

- What can I expect in terms of disease activity while taking the medication? How will the treatment affect relapses and disease progression?
- How will I feel when taking the medication?
- What are the effects of treatment over a long period of time?
- How many studies have been done to show efficacy? Do studies of the different medications have similar results?
- What if I got pregnant while on the medication? Would my baby be safe?
- Can I breast-feed my baby while on the medication?
- What are the side effects of the medication? Are they manageable? Will they affect my lifestyle?
- If I don't experience side effects, does that mean my therapy is not working?
- Will I have a skin reaction after injection?
- Are there specific reasons why I should not take the medication (for example, spasticity, depression, other medical conditions)?
- Does the severity of the side effects influence the way the medication works?
- Will the treatment affect my menstrual cycle? How?
- Does the treatment require periodic blood tests or any other follow-up?
- Aside from the injection frequency, what are the major differences between the therapies?

comparing outcomes in patients who received glatiramer acetate throughout the trial with those in patients who received placebo for about 30 months demonstrated that delaying treatment was detrimental, in terms of both the frequency of relapses (significant difference between the groups during years 1 and 2) and the risk of disability as measured by a decline of 1 or more EDSS steps (which was significantly greater in patients in whom therapy was delayed).⁷⁶

Unlike in the LTFU study of glatiramer acetate, the patient populations of the LTFU studies of IFN β -1b and SC IFN β -1a included patients who may not have been on the same therapy continuously for the entire follow-up period. Patients examined 16 years after starting IFN β -1b therapy continued to experience up to a 40% reduction in annualized relapse rates.⁷² Furthermore, disability progression as measured by EDSS was slower in patients taking IFN β -1b for longer periods of time; patients reached an EDSS score of 6.0 within a median of 13 years of taking therapy.⁷²

Data from an 8-year LTFU study of SC IFN β -1a in patients randomized in the pivotal trial also reveal a continued benefit in patients.⁵² The annualized relapse rates for the original cohort of patients was 0.67 relapses per patient/year. At follow-up, the annualized relapse rate was slightly lower, at 0.61 relapses per patient/year. Patients available for LTFU had a mean increase of 1.1 on the EDSS scale (mean EDSS score was 3.5)⁵² Those patients randomized to receive high-dose SC IFN β -1a (44 μ g) had better outcomes on relapse rate, disease progression, and T2 burden of disease at LTFU than patients originally randomized to receive placebo.⁵²

All of the available immunomodulatory agents have side effects (Table 3). For example, some cause injection-site reactions, which usually are mild and self-limiting. Some side effects, such as the flu-like symptoms seen with the interferons, may persist for several months.^{68,69} Glatiramer acetate appears to have the mildest side effect profile; rarely, it may cause a transient, benign

postinjection reaction characterized by chest tightness and shortness of breath.⁴⁷

Currently five of the available immunomodulatory agents must be injected. Because many patients find injections painful, difficult, and inconvenient, adherence may suffer. Mild, transient injection-site reactions, such as skin redness, reportedly occur commonly in patients receiving therapy via subcutaneous injection.⁵⁴ More serious reactions, such as skin necrosis and lipoatrophy, are considerably less common. Skin necrosis has been reported in a small percentage of patients treated with IFN β -1b and IFN β -1a administered subcutaneously.⁵⁴ Reports in the literature also indicate that glatiramer acetate has been associated with some instances of lipoatrophy at injection sites.⁷⁷⁻⁸⁰ Many of these injection-site reactions may be lessened or avoided with proper injection techniques and injection-site rotation. Patients receiving therapy via intramuscular injection (IFN β -1a) may also experience reactions at the injection site, including pain and bleeding following injection. Occasionally, patients receiving therapy via intramuscular injection have reported abscesses, which may necessitate surgical intervention and draining.⁵⁴ Fortunately, there are now different delivery systems for disease-modifying therapies that require self-injection. For example, autoinjection systems provide alternatives for patients who are needle-phobic and may also help to minimize injection-site reactions. All of the self-administered immunomodulatory agents are also available in prefilled syringes, which are especially convenient for patients with manual dexterity problems.⁵⁴ Prefilled syringes of glatiramer acetate, SC IFN β -1a, IFN β -1b, and the lyophilized powder form of IM IFN β -1a can be stored at room temperature for up to 30 days (up to 7 days for prefilled syringes of IM IFN β -1a), which may provide convenience for patients who travel frequently. Finally, researchers also are exploring the utility of sustained-release injectable formulations and alternative routes for administering immunomodulatory agents.

Although most of the side effects associated with the immunomodulatory agents diminish as treatment continues, they can undermine treatment adherence. A survey of participants in the CMSC/NARCOMS

Registry—the registry of the Consortium of Multiple Sclerosis Centers/North American Research Consortium on Multiple Sclerosis—demonstrated discontinuation rates ranging from 22% for patients treated with glatiramer acetate to 41% and 70% for patients treated with IFN β -1a administered via intramuscular injection and those treated with IFN β -1b, respectively.⁸¹ Key factors leading to the discontinuation of immunomodulatory therapies included increases in MS symptoms and flu-like symptoms associated with treatment. Fewer than 10% of registrants reported depression and skin reactions as reasons for discontinuing treatment. Interestingly, factors that were not considered adequate reasons for discontinuation included injection-site pain and self-injection or needing assistance with injection.⁸¹

Now that disease modification in MS has expanded to regular infusions and oral therapies, new research on adherence will reveal different issues and concerns as new data emerge.

With regard to nursing roles in immunomodulatory treatment of MS, probably the most important nursing interventions are education and skill development. Patients and their families or care partners need to have a thorough understanding of the treatment options available to them, along with clear and realistic expectations of what the immunomodulatory agents can and cannot be expected to do. They also need to understand what side effects are associated with treatment and how these side effects can be managed. Nurses may want to use a checklist of questions for patients to consider when selecting an immunomodulatory treatment (Table 5).

Once a specific immunomodulatory agent has been chosen, patients need to know how to carry out the self-care aspects of their MS management plan. They will need training in reconstituting and injecting the medication. They may need help with overcoming a fear of needles and self-injecting. Patients with memory deficits may need instruction in the use of specific memory cues to help them remember to take their medication on schedule.

Nurses play a key role in enhancing treatment adherence through patient education and by developing supportive relationships with patients, as mentioned earlier. A great benefit of these drugs has been the hope they have brought to patients with MS—hope that can help to motivate self-care and adherence to treatment.

Nurses must also monitor the patient's response to immunomodulatory therapy, both initially and over time. If patients are having trouble adhering to treatment, the nurse should determine the source of the problem. If adherence problems are related to side effects, nurses can make practical suggestions for managing these effects. If side effects are intolerable, the patient may need to try a different immunomodulatory agent.

In addition, MS nurses often serve as advocates for patients who need immunomodulatory treatment. Nurses may interact with managed care organizations, insurance companies, and other health-benefit programs to help patients obtain treatment. As part of this advocacy effort, nurses may need to write letters describing the medical necessity of the immunomodulatory agents and may need to assist with appeals against denial of benefits.

OTHER DISEASE-MODIFYING THERAPIES

A number of agents and strategies are being used or investigated for treatment of MS. Some can be given orally, such as azathioprine (Imuran[®]); others, including mitoxantrone (Novantrone[®]) and cyclophosphamide (Cytoxan[®]), are given intravenously.

Azathioprine, an immunosuppressive agent often used in transplant patients but also useful for the treatment of rheumatoid arthritis, lupus nephritis, and psoriatic arthritis, appears to reduce relapse frequency and decrease brain inflammation and lesion accumulation in patients with MS.⁸² However, some clinical trials have shown mixed results, along with severe side effects such as anemia and liver damage.⁸³

Mitoxantrone, an antineoplastic agent, has shown promise in treatment of MS. In phase III clinical trials, mitoxantrone given as an IV treatment every 3 months appeared to reduce relapse rates and the progression of disability in patients with advanced forms of relapsing-remitting and

secondary-progressive MS.^{28,84,85} When used in combination with methylprednisolone in patients with signs of residual neurological deficits between relapses, primary and secondary end points such as the percentage of patients without new gadolinium-enhancing lesions, increases in EDSS scores, and annualized relapse rates improved significantly.⁸⁵ However, with long-term use, mitoxantrone has dose-dependent cardiotoxic effects, and its dosage in MS patients is limited to a lifetime cumulative dose of 140 mg/m².⁸⁵

Cyclophosphamide, a potent immunosuppressive drug, has been used to treat MS for many years. Although cyclophosphamide sometimes improves the condition of patients with primary-progressive MS, recent studies have shown that any benefit is modest.⁸⁶ In addition, cyclophosphamide can affect blood clotting and increase susceptibility to infection. One clinical trial has shown that cyclophosphamide may benefit patients with MS who are deteriorating rapidly and have failed therapy with the interferons or glatiramer acetate.⁸⁷

Cladribine (Leustatin[®]) is an agent used to treat leukemia that may work by destroying activated lymphocytes. This agent, which is given intravenously, has shown some benefit in MS but has been associated with lymphopenia and herpes zoster infection.^{28,88,89}

Cladribine was approved in Russia and Australia but subsequently withdrawn from all use by EMD Serono when the European Union and the US FDA did not approve its use in relapsing MS.

Other agents are under investigation as oral therapies for MS. Laquinimod and fingolimod (FTY720) are 2 novel agents that have been shown to be effective in reducing the number of active lesions on MRI^{90,91} and are currently being examined in phase III clinical investigations. BG00012 is under investigation in several studies both alone and in combination with other therapies. Teriflunomide is also being studied in relapsing MS.⁹⁸ Alemtuzumab is delivered by infusion and although has had a higher risk profile than injectable DMTs had had an impressive outcome.⁹³

Intravenous immunoglobulin (IVIg), a treatment that has

been used as a “rescue therapy” for acute relapses, is being studied for its potential to reduce relapse rates and disability in MS. An earlier study demonstrated that in patients with relapsing-remitting MS, IVIg produced reductions in both the relapse rate and the progress of disability and had virtually no side effects. However, IVIg is extremely expensive and therefore may be impractical for long-term treatment until evidence on its efficacy is stronger.^{28,94}

Although cytoxan, azathioprine, and IVIG are used much less frequently than the interferons, glatiramer acetate, natalizumab and Gilenya, nurses need to inform patients about their potential risks, benefits, and side effects. These novel and innovative strategies may offer hope to patients who have not responded to conventional treatments.

While adding new therapies to the MS treatment arsenal is a large part of ongoing MS research, other studies directly comparing the effects of the interferons and of glatiramer acetate have revealed that these therapies are equally effective in reducing disease activity as measured by MRI and annualized relapse rates.⁹⁵⁻⁹⁷ These results add further to the evidence for the efficacy of existing therapies available for patients with relapsing-remitting MS.

Supporting Multiple Sclerosis Nursing Practice Through Research

With the challenges presented by recent advances in technology and new therapeutic agents for MS, along with the continuous changes in the roles and responsibilities of MS nurses, nursing research is essential to documenting the effectiveness of nursing practice outcomes for patients with MS.⁹⁸

Nursing research, performed as a systematic investigation or inquiry to generate new knowledge or validate existing knowledge, can contribute to the understanding of MS and its effects, guide nursing practice, and identify

outcomes of effective nursing interventions. Nursing research may be quantitative or qualitative. It does not focus on an illness or condition purely as a health problem; rather, it examines the physical, emotional, and psychosocial responses of patients and their families to that illness or condition. Nursing research in MS may investigate patient and family responses anywhere along the illness trajectory and seeks to contribute in positive ways to shaping and managing the course of MS.

Nursing research has provided valuable information about caring for patients with MS. For example, recent studies have shown how patients experience and manage fatigue,^{99,100} the impact of illness uncertainty associated with MS on family life,¹⁰¹ and interventions that can help care partners manage stress.^{101,102} MS nurses can use this information in practical ways to gain perspective on their patients' physical and emotional status and to encourage wellness, health-seeking strategies, and empowerment.¹⁰³

Several studies have examined factors that contribute to quality of life among people with MS. One investigation found that marriage, work, health status, and involvement in recreation or social activities are major contributors to a positive outlook.¹⁰³ Several investigations by Fraser and colleagues have found that self-efficacy is a positive force in sustained adherence to complex therapies, and have noted that a belief that one can make a difference can sustain continued care.^{104,105} Another found that factors significantly related to perceived quality of life among patients with MS included involvement in health-promoting behaviors, including exercise, nutrition, and stress management, and taking responsibility for health.¹⁰⁶

Two qualitative studies have examined patient experiences surrounding the diagnosis of MS and living with relapsing MS.¹⁰⁷ Both studies employed phenomenological research methods—approaches used to understand people and their everyday lives under certain circumstances without including preconceived ideas.²¹ In the first study, researchers explored what 5 people experienced before, at the time of, and after diagnosis of MS.²¹ Before diagnosis, these people recalled searching for the reasons for their symptoms and creating possible explanations as a coping mechanism to

TABLE 6.
Funding Sources for Nursing Research

| Organization | Contact Information |
|---|--|
| Agency for Healthcare Research and Quality | Agency for Healthcare Research and Quality 540 Gaither Road, Suite 2000, Rockville, MD 20850 Phone: (301) 427-1364; Web site: www.ahrq.gov |
| American Academy of Nurse Practitioners | AANP Foundation, Inc. P.O. Box 12924, Austin, TX 78711 Phone: (512) 276-5905; Fax: (512) 442-6469; E-mail: foundation@aanp.org Web site: www.aanp.org/default.asp |
| American Association of Colleges of Nursing | American Association of Colleges of Nursing One Dupont Circle, NW, Suite 530, Washington, DC 20036 Phone: (202) 463-6930; Fax: (202) 785-8320; Web site: www.aacn.nche.edu |
| American Nurses Association | American Nurses Association 8515 Georgia Ave., Suite 400, Silver Spring, MD 20910 Phone: (301) 628-5000; Fax: (301) 628-5001; Web site: www.nursingworld.org |
| American Nurses Foundation | American Nurses Foundation 8515 Georgia Ave., Suite 400, Silver Spring, MD 20910 Phone: (301) 628-5227; Fax: (301) 628-5354; E-mail: anf@ana.org Web site: www.anfonline.org |
| International Organization of Multiple Sclerosis Nurses | International Organization of Multiple Sclerosis Nurses 359 Main St./Suite A, Hackensack, NJ 07601 Phone: (201) 487-1050; Fax: (201) 678-2291; Email: info@iomsn.org Web site: www.iomsn.org |
| Midwest Nursing Research Society | Midwest Nursing Research Society 10200 W. 44th Avenue, #304, Wheat Ridge, CO 80033 Phone: (720) 898-4831; Toll Free: 1-866-908-8716; Fax: (303) 422-8894; E-mail: info@mnrns.org Web site: www.mnrns.org |
| National Institute of Nursing Research | National Institute of Nursing Research 31 Center Drive, Room 5B10, Bethesda, MD 20892-2178 Phone: (301) 496-0207; Fax: (301) 480-8845; E-mail: info@nir.nih.gov Web site: http://nir.nih.gov |
| National Institutes of Health | National Institutes of Health (NIH) 9000 Rockville Pike, Bethesda, MD 20892 Phone: (301) 435-0714; Email: grantsinfo@od.nih.gov ; Web site: http://grants.nih.gov |
| National League for Nursing | National League for Nursing 61 Broadway, 33rd floor, New York, NY 10006 Phone: (800) 669-1656 or (212) 363-5555; Fax: 212-812-0393 Email: research@nln.org ; Web site: www.nln.org/aboutnln/grants.htm |
| National Multiple Sclerosis Society | Research Programs Department National Multiple Sclerosis Society 733 Third Avenue, New York, NY 10017 Phone: (212) 986-3240; Fax: (212) 986-7981; Email: info@nmss.org Web site: www.nationalmssociety.org |
| Neuroscience Nursing Foundation | Neuroscience Nursing Foundation 3007 Marx Road, Rice, WA 99167 Phone: (509) 738-2542; Fax: (509) 738-2580 Email: nnf@nnfoundation.net ; Website: www.nnfoundation.net |
| Sigma Theta Tau International | Sigma Theta Tau International 550 West North Street, Indianapolis, IN 46202 Phone: (888) 634-7575 (US/Canada) or (317) 634-8171 (International) Fax: (317) 634-8188; E-mail: research@stti.iupui.edu Web site: www.nursingsociety.org/Research/SmallGrants/Pages/grants_small.aspx |
| Canadian Health Services Research Foundation | Canadian Health Services Research Foundation 1565 Carling Avenue, Suite 700, Ottawa, Ontario K1Z 8R1, Canada Phone: (613) 728-2238, Fax: (613) 728-3527 Email: info@chrsf.ca ; Web site: www.chrsf.ca/AboutUs/funding_granting.aspx |
| Canadian Nurses Foundation | Canadian Nurses Foundation 50 Driveway St., Ottawa, Ontario K2P 1E2, Canada Phone: (613) 237-2133 ext. 242; Toll Free: 1-800-361-8404; Fax: (613) 237-3520 E-mail: info@cnf-fiic.ca ; Web site: www.cnf-fiic.ca |

protect themselves and others from undue anxiety. As symptoms recurred or worsened, patients experienced increasing concern about what might be wrong and entered a phase of worrying, wondering, and waiting for outcomes of consultations and testing. Once an MS diagnosis was confirmed, patients described feelings of shock and numbness that lasted only a few moments for some but days to weeks for others. Afterward, there was the process of informing family members and others of the diagnosis, an experience that was not always positive. Finally, patients described “claiming” the diagnosis as part of adjusting and refocusing on plans and hopes for the future.

The second study examined the experiences of 7 women and 3 men diagnosed with relapsing MS.¹⁰⁷ With analysis of interview data, several themes emerged to describe patient experiences:

- Reliance on social networks
- Adjustment to MS
- Coping with symptoms and inconveniences
- Feelings of hope and hopelessness
- Need for control and independence
- Conflict with physicians, insurance companies, employers, family members
- Relief associated with confirmed diagnosis
- Uncertainty related to the unpredictability of MS
- Loss of independence, employment, relationships, function
- Fear of loss of health, life, support system
- Becoming informed about MS
- Struggle over revealing or concealing MS

Phenomenological studies such as these provide practical, “real-life” information that promotes empathy and understanding among healthcare professionals, thereby facilitating appropriate patient support.

Two exploratory nursing studies have examined the use of alternative therapies—including nutritional therapy, massage therapy, acupuncture, chiropractic treatment, and homeopathy—in small groups of patients who were not taking disease-modifying agents. The first study identified reasons why patients accessed alternative therapies, finding that most patients turned to these treatments because traditional medicine

offered no cure.^{108,109} The second study examined relationships between the use of alternative therapies and differences in symptom severity and functional status. All patients reported reduction in MS symptom severity and improvement in functional status with the use of alternative therapies; however, the greater the number of therapies used, the lower the patients’ functional status scores.¹⁰⁹ MS patients are often interested in alternative therapies, and findings from studies such as these can help nurses in their roles as counselors who help patients make appropriate treatment decisions.

A qualitative study investigation identified the information needs of patients experiencing relapses. The study found that these patients had significant gaps in their understanding of the physical symptoms they were experiencing and the drugs used to treat an acute relapse. Barriers to information access included both external barriers, such as limited computer or Internet access or difficulties accessing libraries, and internal barriers, such as denial, uncertainty, and fear. Results from this study suggest that patients with MS need relevant, specific, and current information to help them remain independent and to empower them to make informed decisions regarding relapse treatment.²²

Nursing research has identified specific physiological and psychological needs of care partners of patients with MS.¹¹⁰ Among the strongest needs identified by caregivers (who were usually spouses) was the need for regular, brief breaks from caregiving to allow rest and relaxation. In addition, all caregivers in the study reported that they received no help from community organizations. The same study asked caregivers how nurses can provide support.¹¹⁰ Caregivers stated that they needed more education about the disease process and the technical aspects of care and more current information on new developments in MS. Caregivers also wanted nurses to listen to and understand them.

LIMITATIONS OF MULTIPLE SCLEROSIS NURSING RESEARCH

To date, nursing research provides better

understanding for MS nursing practice. However, nursing research is hampered by a variety of limitations. For example, there are no standardized definitions for terms such as *caregiver* or *quality of life*, and there are few tools with established validity or reliability for measuring outcomes of nursing interventions. Nursing research is also beset by minimal use of conceptual frameworks, small sample sizes, and sample heterogeneity. Many studies have been performed only once; confirmatory studies are needed. These issues mean that even for the research that has been done, interpretation across studies is difficult.

STRATEGIES TO FACILITATE NURSING RESEARCH: BUYING TIME

Many nurses are overburdened with day-to-day responsibilities and are not expected or encouraged to take the time and effort that careful research would require. However, those nurses who wish to investigate a research question should and can begin to seek funding and support by:

- Identifying funding sources
- Developing grant-writing skills
- Identifying and developing collaborative relationships with other practitioners

Research funds are available from a variety of public and private sources, including those listed in Table 6. Additional information about funding for nursing research can be obtained through the Binghamton University Libraries Web site (<http://library.lib.binghamton.edu/subjects/nursing/nursresearch.html>). The Foundation Center also provides grant information through its Web site (<http://foundationcenter.org>).

Applying for grants is a necessary aspect of obtaining funds for research. Writing a grant application can be an intimidating prospect, but a variety of instructional programs and materials—including courses at colleges and universities, books, and Web sites—are helpful. The National Institutes of Health provide guidance on grant application procedures through its Web site (<http://www.grants.nih.gov>). Many of the organizations that offer funds also provide specific instructions about how to prepare a grant proposal.

TABLE 7. Recently Published Articles of Interest To MS Nurses

Corry M, McKenna M, Duggan M. The role of the clinical nurse specialist in MS: a literature review. *Br J Nurs*. 2011 Jan 27-Feb 9;20(2):86-93. Review.

Espejo C, Montalban X. Dalfampridine in multiple sclerosis: From symptomatic treatment to immunomodulation. *Clin Immunol*. 2011 Jun 25. [Epub ahead of print]

Finlayson M, Van Denend T, Hudson E. Aging with multiple sclerosis. *J Neurosci Nurs*. 2004 Oct;36(5):245-51, 259.

Goektas O, Schmidt F, Bohner G, Erb K, Ludemann L, Dahlslett B, Harms L, Fleiner F. Olfactory bulb volume and olfactory function in patients with multiple sclerosis. *Rhinology*. 2011 Jun;49(2):221-6.

Halbert LA. Breastfeeding in the woman with a compromised nervous system. *J Hum Lact*. 1998 Dec;14(4):327-31. Review.

Kostianovsky A, Maskin P, Noriega MM, Soler C, Bonelli I, Riley CS, O'Connor KC, Saubidet CN, Alvarez PA. Acute demyelinating disease after oral therapy with herbal extracts. *Case Rep Neurol*. 2011 May;3(2):141-6. Epub 2011 Jun 25.

McKeown LP, Porter-Armstrong AP, Baxter GD. The needs and experiences of caregivers of individuals with multiple sclerosis: a systematic review. *Clin Rehabil*. 2003 May;17(3):234-48. Review.

Netherlin JS, Fox S. End-of-Life care concepts in *Journal of Neuroscience Nursing*. *J Neurosci Nurs*. 2006 Oct;38(5):342-8, 353.

Rutschmann OT, McCrory DC, Matchar DB; Immunization Panel of the Multiple Sclerosis Council for Clinical Practice Guidelines. Immunization and MS: a summary of published evidence and recommendations. *Neurology*. 2002 Dec 24;59(12):1837-43.

Shakespeare DT, Boggild M, Young C. Anti-spasticity agents for multiple sclerosis. *Cochrane Database Syst Rev*. 2003;(4):CD001332. Review.

Shakespeare DT, Boggild M, Young C. Anti-spasticity agents for multiple sclerosis. *Cochrane Database Syst Rev*. 2001;(4):CD001332. Review. Update in: *Cochrane Database Syst Rev*. 2003;(4):CD001332.

Shakespeare DT, Young CA, Boggild M. Anti-spasticity agents for multiple sclerosis. *Cochrane Database Syst Rev*. 2000;(4):CD001332. Review. Update in: *Cochrane Database Syst Rev*. 2001;(4):CD001332.

Sorensen PS, Lycke J, Erälälinna JP, Edland A, Wu X, Frederiksen JL, Oturai A, Malmeström C, Stenager E, Sellebjerg F, Sondergaard HB; for the SIMCOMBIN study investigators. Simvastatin as add-on therapy to interferon beta-1a for relapsing-remitting multiple sclerosis (SIMCOMBIN study): a placebo-controlled randomised phase 4 trial. *Lancet Neurol*. 2011 Aug;10(8):691-701.

Zamvil SS, Steinman L. Combining statins with interferon beta in multiple sclerosis: think twice, it might not be all right. *Lancet Neurol*. 2011 Aug;10(8):672-3. No abstract available.

Another challenge in nursing research is patient recruitment. There are various approaches to patient recruitment, one of which is the CMSC/NARCOMS database. More information about access to this database can be obtained through the Consortium of Multiple Sclerosis Centers Web site (<http://www.ms-care.org>).

An important benefit of nursing research is the professional recognition that comes with publication, whether in nursing journals or in other health-related journals. Publication not only serves to release information valuable to the care of patients with MS but can enhance researchers' chances of obtaining additional funding.

Often, collaborative relationships are necessary to performing research. Nurses may need to form liaisons with other nurse researchers and with other professionals within or outside their practice or department to increase sample size, facilitate study design, acquire funding, and perform statistical analyses. In addition, collaborative efforts can facilitate clearance of research proposals through institutional review boards or research committees at hospitals or universities—often a necessary step in initiating research in many academic and medical school settings.

RECOMMENDATIONS FOR MULTIPLE SCLEROSIS NURSING RESEARCH

In conducting research, nurses should be aware of certain practical issues. For example, they will need to identify appropriate statistical tests to validate and enhance data. Consultation with a statistician and the use of computer programs for statistical analysis will be beneficial. To ensure scientific rigor, investigators should use standardized assessment tools and outcomes measures that are objective and specific to nursing practice. Patients selected for a study should form balanced, homogeneous sample populations that are large enough to allow reasonable conclusions to be drawn. When appropriate, theoretical frameworks should guide study design. Replication studies can be important for confirming findings that have been published only once. Nurses also should follow ethical

standards with regard to patient consent and confidentiality, conflict of interest issues, patent and copyright laws, and responsibilities of authorship when the time comes to prepare a manuscript.

RESEARCH PRIORITIES

Published MS nursing research is sparse. There are many gaps and, clearly, no shortage of studies to pursue.

Suggested areas for further study include the following:

- Impact of injection training on injection practices and injection-site reactions or infections
- Impact of autoinjection systems on patient adherence and injection-site reactions or infections
- Identification of the most effective educational approach to injection training
- Barriers to use of early therapy
- Responses to illness and treatment
- Factors that influence patients' view of treatment
- Factors that influence adherence to treatment
- Women's health issues, eg, MS-related issues in pregnancy, breast-feeding, osteoporosis, and hormone replacement therapy with menopause
- Men's health issues, eg, relationships between MS or MS treatments and prostate cancer; reproductive concerns
- Impact of MS on parenting and professional roles
- Studies of symptom management using specific measurable outcomes to determine the most effective interventions
- Identification of the needs of patients newly diagnosed with MS (and their families)
- Identification of the needs of patients with advanced MS (and their families)
- Cultural influences on and cultural responses to diagnosis, treatment, stresses, and coping
- Effect of MS on personal and family relationships (eg, children, couples) regarding issues such as disclosure of diagnosis
- Safety issues in MS, eg, in relation to assistive technology, the home and work environment, and the ability to drive

Findings from nursing studies can help broaden nurses' knowledge and improve professional practice. A wealth of information is available within the environment of MS nursing practice, and research

has the potential to provide valuable, practical information that can enhance the lives of patients affected by MS. Development of research skills could help improve nurses' opportunities to obtain funding, design studies carefully, and conduct systematic qualitative and quantitative investigations.

ENHANCING THE PROFESSIONAL PRACTICE

While participating in MS research, especially research of interest to the nursing practice, is important, many nurses are unable to do so. Funding sources are limited, and the resources and facilities needed to conduct research may not be readily available in a nurse's area of practice. When circumstances hinder the ability to participate in research, it is critical for MS nurses to enhance their professional practice by becoming well versed in the latest research being conducted in the field.

Every month, literature on MS pathogenesis, treatments, and patient care is published. To keep abreast of the latest publications, nurses should make use of searchable databases such as PubMed (www.pubmed.com), a medical literature database maintained by the US National Library of Medicine and the National Institutes of Health, and CINAHL (www.cinahl.com), a database that houses publications geared toward nurses and allied healthcare professionals. Conducting regular searches in these databases to find MS literature and reading articles of interest and importance build upon knowledge and skills that can be translated into changes in practice that may improve patient care. MS patients are becoming increasingly knowledgeable about therapies under investigation and new techniques, and they often look to their nursing team to provide more information. In order to supply their patients with accurate information, it is imperative for nurses to continue to educate themselves by keeping up with research that has been published in peer-reviewed journals.

Table 7 provides a sample list of recently published articles on MS that are of interest to professionals in the field. These articles, as well as those cited throughout this monograph, will help build a solid foundation of continued MS education. Summaries and,

in some cases, the free full text of these articles can be found by searching PubMed. University or hospital libraries may also provide access to the complete articles. Almost all of the relevant journals are available by individual or institutional subscriptions; purchasing a subscription to those journals that publish articles of interest on a regular basis may be worth considering.

Conclusion

Rapid advances in technology and an ever-increasing range of effective medications, along with escalating healthcare costs, shorter hospital stays, and an increased emphasis on home care and patient self-care, have altered the practice environment significantly. With these changes has come a considerable increase in responsibility for nurses who care for patients with MS.

Clearly, nurses have an essential role to play in MS care, one that will continue to evolve. As the mechanisms underlying the development and progression of this disease are further understood, there will be more novel treatment strategies to optimize patient outcomes. Therefore, it is vital for nurses to constantly update their knowledge of MS care, research, and best practices in patient assessment and interventions. Collaboration, expertise, and optimal access to care on the part of nurses will support the MS team's effort to fight the effects of this challenging and complex disease.

References

1. Trapp BD, Peterson J, Ransohoff RM, Rudick R, Mork S, Bo L. Axonal transection in the lesions of multiple sclerosis. *N Engl J Med*. 1998;338:278-285.
2. Simon JH, Jacobs LD, Campion MK, Rudick RA. A longitudinal study of brain atrophy in relapsing MS. *Neurology*. 1999;53:139-148.
3. National Multiple Sclerosis Society. FAQs about MS. Available at: <http://www.nationalmssociety.org/about-multiple-sclerosis/FAQs-about-MS/index.aspx>. Accessed April 1, 2008.
4. MS Society of Canada. Frequently Asked Questions. Available at: <http://www.mssociety.ca/en/information/faq.htm>. Accessed April 1, 2008.
5. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. *N Engl J Med*. 2000;343:938-952.
6. Cutter G, Yadavalli R, Marrie RA, et al. Changes in the sex ratio over time in multiple sclerosis. *Neurology*. 2007;68(suppl 1):A162.
7. Orton SM, Herrera BM, Yee IM, et al. Sex ratio of multiple sclerosis in Canada: a longitudinal study. *Lancet Neurol*. 2006;5:932-936.
8. Weinshenker BG, Bass B, Rice GP, et al. The natural history of multiple sclerosis: a geographically based study, I: clinical course and disability. *Brain*. 1989;112:133-146.
9. Multiple Sclerosis Society of Canada, Quebec Division. Knowledge update on the symptomatic treatment of multiple sclerosis: guide for general practitioners. Available at: <http://www.mssociety.ca/qc/professionals-santeEn.html>. Accessed May 8, 2008.
10. Polman CH, Reingold SC, Edan G, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". *Ann Neurol*. 2005;58:840-846.
11. Fazekas F, Barkhof F, Filippi M, et al. The contribution of magnetic resonance imaging to the diagnosis of multiple sclerosis. *Neurology*. 1999;53:448-456.
12. Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. *Neurology*. 1996;46:907-911.
13. Sibley WA. Diagnosis and course of multiple sclerosis. In: Rao SM, ed. *Neurobehavioral Aspects of Multiple Sclerosis*. New York, NY: Oxford University Press; 1990.
14. van den Noort S, Holland NJ. *Multiple Sclerosis in Clinical Practice*. New York, NY: Demos Medical Publishing; 1999.
15. Halper J, Holland N. An overview of multiple sclerosis: implications for nursing practice. In: Halper J, Holland N, eds. *Comprehensive Nursing Care in Multiple Sclerosis*. 2nd ed. New York, NY: Demos Medical Publishing; 2002:1-14.
16. Halper J. The evolution of nursing care in multiple sclerosis. *Int J MS Care*. 2000;3:13-20.
17. Lesaux J, Jadback G, Harragby CE. Improving the convenience of home-based interferon beta-1a therapy for multiple sclerosis. *J Neurosci Nurs*. 1999;31:174-179.
18. Morgante LA. Integrating the concept of hope into clinical practice. In: Halper J, Holland NJ, eds. *Comprehensive Nursing Care in Multiple Sclerosis*. 2nd ed. New York, NY: Demos Medical Publishing; 2002:213-222.
19. Smeltzer SC. Use of the trajectory model of nursing in multiple sclerosis. *Sch Inq Nurs Pract*. 1991;5:219-234.
20. Fraley AM. *Nursing and the Disabled Across the Lifespan*. Boston, Mass: Jones and Bartlett; 1992.
21. Koopman W, Schweitzer A. The journey to multiple sclerosis: a qualitative study. *J Neurosci Nurs*. 1999;31:17-26.
22. Baker LM. Sense making in multiple sclerosis: the information needs of people during an acute exacerbation. *Qual Health Res*. 1998;8:106-120.
23. Di Fabio RP, Soderberg J, Choi T, Hansen CR, Schapiro RT. Extended outpatient rehabilitation: its influence on symptom frequency, fatigue, and functional status for persons with progressive multiple sclerosis. *Arch Phys Med Rehabil*. 1998;79:141-146.
24. Nolan M, Nolan J. Rehabilitation in multiple sclerosis: the potential nursing contribution. *Br J Nurs*. 1997;6:1292-1295, 1309-1310.
25. Paty GC, Edwards GC, eds. *Multiple Sclerosis*. Philadelphia, Pa: FA Davis; 1998.
26. Lublin FD, Baier M, Cutter G. Effect of relapses on development of residual deficit in multiple sclerosis. *Neurology*. 2003;61:1528-1532.

27. Sears ES, Tindall RS, Zarnow H. Active multiple sclerosis: enhanced computerized tomographic imaging of lesions and the effect of corticosteroids. *Arch Neurol*. 1978;35: 426-434.
28. van Oosten BW, Truyen L, Barkhof F, Polman CH. Choosing drug therapy for multiple sclerosis: an update. *Drugs*. 1998;56: 555-569.
29. Schapiro RT, Schneider DM. Symptom management in multiple sclerosis. In: Halper J, Holland NJ, eds. *Comprehensive Nursing Care in Multiple Sclerosis*. 2nd ed. New York, NY: Demos Medical Publishing; 2002:31-52.
30. Thompson AJ, Kennard C, Swash M et al. 1989 Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. *Neurology* 39:969-971.
31. Krupp LB. *Fatigue in Multiple Sclerosis: A Guide to Diagnosis and Management*. New York, NY: Demos Medical Publishing; 2004.
32. Schapiro RT. Medications used in the treatment of multiple sclerosis. *Phys Med Rehabil Clin N Am*. 1999;10: 437-446, ix.
33. Rammohan K, Rosenberg JH, Pollak CP, Lynn J, Blumenfeld A, Nagaraja HN. Modafinil—efficacy and safety for the treatment of fatigue in patients with multiple sclerosis. *Neurology*. 2000;54:A24.
34. Murray TJ. Amantadine therapy for fatigue in multiple sclerosis. *Can J Neurol Sci*. 1985;12:251-254.
35. Namey MA. Management of elimination dysfunction. In: Halper J, Holland NJ, eds. *Comprehensive Nursing Care in Multiple Sclerosis*. 2nd ed. New York, NY: Demos Medical Publishing; 2002:53-76.
36. Ruscin JM, Morgenstern NE. Tolterodine use for symptoms of overactive bladder. *Ann Pharmacother*. 1999;33:1073-1082.
37. Lunardi G, Leandri M, Albano C, et al. Clinical effectiveness of lamotrigine and plasma levels in essential and symptomatic trigeminal neuralgia. *Neurology*. 1997;48:1714-1717.
38. Hansen HC. Treatment of chronic pain with antiepileptic drugs: a new era. *South Med J*. 1999;92:642-649.
39. Attal N, Cruccu G, Haanpaa M, et al. EFNS guidelines on pharmacological treatment of neuropathic pain. *Eur J Neurol*. 2006;13:1153-1169.
40. Young RR, Delwaide PJ. Drug therapy: spasticity (second of two parts). *N Engl J Med*. 1981;304:96-99.
41. Middel B, Kuipers-Upmeijer H, Bourna J, et al. Effect of intrathecal baclofen delivered by an implanted programmable pump on health related quality of life in patients with severe spasticity. *J Neurol Neurosurg Psychiatry*. 1993;97:204-209.
42. Borg-Stein J, Pine ZM, Miller JR, Brin MF. Botulinum toxin for the treatment of spasticity in multiple sclerosis. New observations. *Am J Phys Med Rehabil*. 1993;72:364-368.
43. Belavic JM. Dalfampridine (Ampyra) for multiple sclerosis. *Nurse Practitioner* 2010 Nov;35(11):7-9.
44. Pioro EP, Brooks BR, Cummings J, et al. Dextromethorphan plus ultra low-dose quinidine reduces pseudobulbar affect. *Ann Neurology* 2010;68(5):693-702.
45. LaRocca NG, Kalb RC. Psychosocial issues in multiple sclerosis. In: Halper J, Holland NJ, eds. *Comprehensive Nursing Care in Multiple Sclerosis*. 2nd ed. New York, NY: Demos Medical Publishing; 2002:93-122.
46. Stone LA, Frank JA, Albert PS, et al. The effect of interferon-beta on blood-brain barrier disruptions demonstrated by contrast-enhanced magnetic resonance imaging in relapsing-remitting multiple sclerosis. *Ann Neurol*. 1995;37:611-619.
47. Copaxone® (glatiramer acetate) [package insert]. Kansas City, Mo: Teva Neuroscience, Inc; 2007.
48. Tysabri® (natalizumab) [package insert]. Cambridge, Mass: Biogen Idec, Inc; 2008.
49. Jacobs LD, Cookfair DL, Rudick RA, et al. Intramuscular interferon beta-1a for disease progression in relapsing multiple sclerosis. The Multiple Sclerosis Collaborative Research Group (MSCRG), [published correction appears in *Ann Neurol*. 1996;40:480]. *Ann Neurol*. 1996; 39:285-294.
50. Jacobs LD, Beck RW, Simon JH, et al. Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis. CHAMPS Study Group. *N Engl J Med*. 2000; 343:898-904.
51. PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) Study Group. Randomized double-blind placebo-controlled study of interferon beta-1a in relapsing/remitting multiple sclerosis [published correction appears in *Lancet*. 1999;353:678]. *Lancet*. 1998;352:1498-1504.

52. Kappos L, Traboulsee A, Constantinescu C, et al. Long-term subcutaneous interferon beta-1a therapy in patients with relapsing-remitting MS. *Neurology*. 2006;67:944-953.
53. Li D, Abdalla JA. Long-term observational follow up of the PRISMS cohort: analyses of MRI BOD shows benefit of high dose, high-frequency IFN beta-1a (Rebif®). *Neurology*. 2004; 62(suppl 5):A153-A154.
54. Frohman EM, Brannon K, Alexander S, et al. Disease modifying agent related skin reactions in multiple sclerosis: prevention, assessment, and management. *Mult Scler*. 2004; 10:302-307.
55. The IFNB Multiple Sclerosis Study Group. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis, I: clinical results of a multicenter, randomized, double-blind, placebo-controlled trial. *Neurology*. 1993;43:655-661.
56. Paty DW, Li DK. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis, II: MRI analysis results of a multicenter, randomized, double-blind, placebo-controlled trial. UBC MS/MRI Study Group and the IFNB Multiple Sclerosis Study Group. *Neurology*. 1993;43:662-667.
57. The IFNB Multiple Sclerosis Study Group and the University of British Columbia MS/MRI Analysis Group. Interferon beta-1b in the treatment of multiple sclerosis: final outcome of the randomized controlled trial. *Neurology*. 1995;45:1277-1285.
58. Stone LA, Frank JA, Albert PS, et al. Characterization of MRI response to treatment with interferon beta-1b: contrast-enhancing MRI lesion frequency as a primary outcome measure. *Neurology*. 1997;49:862-869.
59. Ford CC, Johnson KP, Lisak RP, Panitch HS, Shifronis G, Wolinsky JS; Copaxone Study Group. A prospective open-label study of glatiramer acetate: over a decade of continuous use in multiple sclerosis patients. *Mult Scler*. 2006;12:309-320.
60. Comi G, Filippi M, Wolinsky JS, et al. European/Canadian multicenter, double-blind, randomized, placebo-controlled study of the effects of glatiramer acetate on magnetic resonance imaging-measured disease activity and burden in patients with relapsing multiple sclerosis. *Ann Neurol*. 2001;49:290-297.
61. Wolinsky JS, Comi G, Filippi M, et al. Copaxone's effect on MRI-monitored disease in relapsing MS is reproducible and sustainable. *Neurology*. 2002;59:1284-1286.
62. Filippi M, Rovaris M, Rocca MA, et al. Glatiramer acetate reduces the proportion of new MS lesions evolving into "black holes." *Neurology*. 2001;57:731-733.
63. Rudick RA, Stuart WH, Calabresi PA, et al. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. *NEJM*. 2006; 354:911-923.
64. Major EO. Reemergence of PML in natalizumab-treated patients - new cases, same concerns. *NEJM*. 2009; 361:1041-1043.
65. Kappos L, et al. <http://www.nejm.org/doi/full/10.1056/NEJMoa0909494>.
66. Cohen, J., et al. <http://www.ncbi.nlm.nih.gov/pubmed/20089954>.
67. Gilenya (fingolimod) www.pharma.us.novartis.com/product/pi/pdf/gilenya.pdf.
68. Avonex® (interferon beta-1a). Cambridge, Mass: Biogen Idec, Inc; 2006.
69. Betaseron® (interferon beta-1b). Montville, NJ: Bayer HealthCare Pharmaceuticals; 2007.
70. Rebif® (interferon beta-1a). Rockland, Mass: EMD Serono, Inc; 2008.
71. National Multiple Sclerosis Society. *Expert Opinion Paper: Disease Management Consensus Statement*. Available at: <http://www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinion-papers/index.aspx>. Accessed April 6, 2008.
72. Ebers G, Rice G, Konieczny A, et al. The interferon beta-1b 16-year long-term follow-up study: the final results. *Neurology*. 2006;66 (suppl 2):A32.
73. Filippi M, Rovaris M, Inglese M, et al. Interferon beta-1a for brain tissue loss in patients at presentation with syndromes suggestive of multiple sclerosis: a randomised, double-blind, placebo-controlled trial. *Lancet*. 2004;364: 1489-1496.
74. Kappos L, Polman CH, Freedman MS, et al. Treatment with interferon beta-1b delays conversion to clinically definite and McDonald MS in patients with clinically isolated syndromes. *Neurology*. 2006;67:1242-1249.

75. Comi G. Treatment with glatiramer acetate delays conversion to clinically definite multiple sclerosis (CDMS) in patients with clinically isolated syndromes. Presented at: 60th Annual Meeting of the American Academy of Neurology; April 12-19, 2008; Chicago, IL.
76. Johnson KP, Brooks BR, Ford CC, et al. Glatiramer acetate (Copaxone): comparison of continuous versus delayed therapy in a six-year organized multiple sclerosis trial. *Mult Scler*. 2003;9: 585-591.
77. Drago F, Brusati C, Mancardi G, Murialdo A, Rebori A. Localized lipoatrophy after glatiramer acetate injection in patients with relapsing-remitting multiple sclerosis. *Arch Dermatol*. 1999;135:1277-1278.
78. Mancardi GL, Murialdo A, Drago F, et al. Localized lipoatrophy after prolonged treatment with copolymer 1. *J Neurol*. 2000;247:220-221.
79. Hwang L, Orengo I. Lipoatrophy associated with glatiramer acetate injections for the treatment of multiple sclerosis. *Cutis*. 2001;68:287-288.
80. Edgar CM, Brunet DG, Fenton P, McBride EV, Green P. Lipoatrophy in patients with multiple sclerosis on glatiramer acetate. *Can J Neurol Sci*. 2004;31:58-63.
81. Namey M. Optimizing adherence in multiple sclerosis. *Collective Clin. Forum*. 2007:24-27.
82. Massacesi L, PA, Baraliro A, Pelicano G, et al. MRI evaluation of azathioprine activity on encephalic lesions in relapsing-remitting multiple sclerosis. *Neurology*. 2000; 54:A16.
83. Yudkin PL, Ellison GW, Ghezzi A, et al. Overview of azathioprine treatment in multiple sclerosis. *Lancet*. 1991;338:1051-1055.
84. Millefiorini E, Gasperini C, Pozzilli C, et al. Randomized placebo-controlled trial of mitoxantrone in relapsing-remitting multiple sclerosis: 24-month clinical and MRI outcome. *J Neurol*. 1997;244:153-159.
85. Novantrone® (mitoxantrone) [package insert]. Rockland, Mass: EMD Serono Pharmaceuticals; Melville NY: OSI Pharmaceuticals, Inc; 2007.
86. The Canadian Cooperative Multiple Sclerosis Study Group. The Canadian cooperative trial of cyclophosphamide and plasma exchange in progressive multiple sclerosis. *Lancet*. 1991;337:441-446.
87. Khan O, Zvartau-Hind M, Kamholz J, et al. Efficacy and tolerability of intravenous (IV) cyclophosphamide (CTX) in rapidly deteriorating MS patients resistant to conventional treatment. *Neurology*. 2000;54:A337.
88. Romine JS, Sipe JC, Koziol JA, Zyffoff J, Beutler E. A double-blind, placebo-controlled, randomized trial of cladribine in relapsing-remitting multiple sclerosis. *Proc Assoc Am Physicians*. 1999;111:35-44.
89. Giovannoni G, et al. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. *NEJM*. 2010; 362: 5: 416-416.
90. Polman C, Barkhof F, Sandberg-Wollheim M, Linde A, Nordle O, Nederman T; Laquinimod in Relapsing MS Study Group. Treatment with laquinimod reduces development of active MRI lesions in relapsing MS. *Neurology*. 2005;64:987-991.
91. Comi G, Abramsky O, Arbizu T, et al. The effect of two doses of laquinimod on MRI-monitored disease activity in patients with relapsing-remitting multiple sclerosis: a multicenter, randomized, double-blind, placebo-controlled study. *Neurology*. 2007;68 (suppl 1):A84.
92. Oral Teriflunomide Reduces Relapses in Multiple Sclerosis. <http://www.medscape.com/viewarticle/730605>
93. The CAMMS223 Trial Investigators. Alemtuzumab vs. Interferon Beta-1a in Early Multiple Sclerosis. *N Engl J Med* 2008; 359:1786-1801.
94. Sorensen PS. Intravenous immunoglobulin G therapy: effects of acute and chronic treatment in multiple sclerosis. *Mult Scler*. 1996;1:349-352.
95. Wolansky L, Cook S, Skurnick J, et al. Betaseron vs. Copaxone in MS with triple-dose gadolinium and 3-T MRI Endpoints (BECOME): announcement of final primary study outcome. Presented at: 23rd Congress of the European Committee for Treatment and Research in Multiple Sclerosis; October 11-14, 2007; Prague, Czech Republic.
96. Cadavid D, Wolansky L, Cook S, et al. Betaseron versus copaxone in multiple sclerosis with triple-dose gadolinium and 3 Tesla MRI Endpoints (BECOME): announcement of secondary clinical outcomes. Presented at: 23rd Congress of the European Committee for Treatment and Research in Multiple Sclerosis; October 11-14, 2007; Prague, Czech Republic.

97. Mikol DD, Barkhof F, Chang P, et al. The REGARD trial: a randomized assessor-blinded trial comparing interferon beta-1a and glatiramer acetate in relapsing-remitting multiple sclerosis. Presented at: 23rd Congress of the European Committee for Treatment and Research in Multiple Sclerosis; October 11-14, 2007; Prague, Czech Republic.
98. Gulick EE. Research priorities for nurses caring for persons with multiple sclerosis. *J Neurosci Nurs.* 1996; 28:314-321.
99. Stuijbergen AK, Rogers S. The experience of fatigue and strategies of self-care among persons with multiple sclerosis. *Appl Nurs Res.* 1997;10:2-10.
100. Stuijbergen AK, Rogers S. Health promotion: an essential component of rehabilitation for persons with chronic disabling conditions. *ANS Adv Nurs Sci.* 1997;19:1-20.
101. Wineman NM, O'Brien RA, Nealon NR, Kaskel B. Congruence in uncertainty between individuals with multiple sclerosis and their spouses. *J Neurosci Nurs.* 1993;25:356-361.
102. O'Brien MT. Multiple sclerosis: stressors and coping strategies in spousal caregivers. *J Community Health Nurs.* 1993;10:123-135.
103. Gulick EE. Correlates of quality of life among persons with multiple sclerosis. *Nurs Res.* 1997;46:305-311.
104. Fraser C, Hadjimichael O, Vollmer T. Predictors of adherence to Copaxone therapy in individuals with relapsing-remitting multiple sclerosis. *J Neurosci Nurs.* 2001;3:231-239.
105. Fraser C, Morgante L, Hadjimichael O, Vollmer T. A prospective study of adherence to glatiramer acetate in individuals with multiple sclerosis. *J Neurosci Nurs.* 2004;36:120-129.
106. Stuijbergen AK. Health-promoting behaviors and quality of life among individuals with multiple sclerosis. *Sch Inq Nurs Pract.* 1995;9:31-50; discussion 51-55.
107. Miller CM. The lived experience of relapsing multiple sclerosis: a phenomenological study. *J Neurosci Nurs.* 1997;29:294-304.
108. Fawcett J, Sidney JS, Hanson MJ, Riley-Lawless K. Use of alternative health therapies by people with multiple sclerosis: an exploratory study. *Holist Nurs Pract.* 1994; 8:36-42.
109. Fawcett J, Sidney JS, Riley-Lawless K, Hanson MJ. An exploratory study of the relationship between alternative therapies, functional status, and symptom severity among people with multiple sclerosis. *J Holist Nurs.* 1996;14:115-129.
110. Sato A, Ricks K, Watkins S. Needs of caregivers of clients with multiple sclerosis. *J Community Health Nurs.* 1996;13:31-42.

Original Members of the Multiple Sclerosis Nurse Specialists Consensus Committee

- Wini Breitbach, RN, MSCN, Houston, Texas, retired
- Emily Cerreta, MSN, RN, CNS, NP, *private practice*
- Ismari M. Clesson, RN, MSCN, CCRP, Multiple Sclerosis Center at Shepherd, Atlanta, Georgia
- Kathleen Costello, MS, ANP-BC, MSCN, Johns Hopkins MS Center, Baltimore, Maryland (Group Leader)
- Andrea Censky Dietrich, MSN, BSN, *retired*
- Cira Fraser, APRN, BC, MSCN, PhD, Monmouth University/Maimonides MS Care Center, West Long Branch, NJ (Group Leader)
- Elida Greinel, APN-BC, University of New Mexico, Health Sciences Center, Albuquerque, New Mexico
- June Halper, MSN, APN-C, FAAN, MSCN, Consortium of Multiple Sclerosis Centers, Hackensack, New Jersey (Chairperson)
- Colleen J. Harris, MN, NP, MSCN, University of Calgary MS Clinic, Calgary, Alberta, Canada (Group Leader)
- Nancy J. Holland, RN, EdD, MSCN, Hastings-on-Hudson, New York, retired
- C. Leith Kelley, RN, PhD, *retired*
- Patricia Kennedy, RN, CNP, MSCN, Can Do Multiple Sclerosis, Gainesville, VA
- Deena Lisak, RN, BS, MA, MSCN, Wayne State University, Detroit, Michigan
- Diane Lowden, MSc[A], MSCN, McGill University Health Center, Montreal Neurological Hospital, Montreal, Quebec, Canada
- Heidi Wynn Maloni, PhD, RN, Veterans Affairs Medical Center, MS Center of Excellence East, Washington, DC
- Lynn McEwan, BSN, MScN, CNNC, MSCN, London Health Science Center, Multiple Sclerosis Clinic, London, Ontario, Canada
- Linda Morgante, RN, MSN, CRRN, MSCN, *deceased*
- Marie Namey, RN, MSN, MSCN, Mellen Center for Multiple Sclerosis Treatment & Research, Cleveland Clinic Foundation, Cleveland, Ohio (Group Leader)
- Amy Perrin-Ross, APRN, MSN, CNRN, MSCN, Loyola University Medical Center, Maywood, Illinois
- Dorothea "Dottie" Pfohl, RN, BS, MSCN, University of Pennsylvania Health Systems—Comprehensive Multiple Sclerosis Center, Philadelphia, Pennsylvania
- Julie Saunders, RN, MSN, ANP, *retired* (Group Leader)
- Pauline Weldon, RN, BN, CNN[C], MSCN, Canada, retired
- Phyllis Wiesel-Levison, RN, BSN, *deceased*
- Zo Woods, Teva Neuroscience, Kansas City, Missouri
[Editor's Note: This monograph is supported by an educational grant from Teva Neuroscience.]

*Multiple Sclerosis:
Best Practices in Nursing Care*

Notes

Lined area for notes, featuring horizontal lines and a faint, light blue watermark illustration of a hand holding a flower.

*Multiple Sclerosis:
Best Practices in Nursing Care*

Notes

Lined area for notes, featuring horizontal ruling lines and a faint background illustration of a hand holding a flower.

*Multiple Sclerosis:
Best Practices in Nursing Care*

Notes

Lined area for notes, featuring horizontal ruling lines and a faint background illustration of a hand holding a flower.

