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Feelings of hopelessness are common in patients with multiple sclerosis (MS), which poses a significant threat to an individual's independence and feelings of competence. Because hope has been shown to play an important role in health and coping during chronic illness, it is critical for the MS provider to understand the elements of hope and recognize when the person with MS is struggling with feelings of hopelessness. The MS nurse is the pivotal player in ensuring that the individual with MS maintains a sense of hope throughout the illness. In addition to providing education, counseling and referrals, the nurse can help the MS patient focus on feelings and ideas, recognize personal reasons for living, and establish both short-term and long-term goals.

Use of MRI Technology in Determining Prognosis and Tracking Therapeutic Benefit in Multiple Sclerosis

Timothy Vollmer, MD

Over the past decade, magnetic resonance imaging (MRI) has been increasingly used as a tool to facilitate the diagnosis of multiple sclerosis (MS). Because of the relative insensitivity of commonly used clinical assessment measures, however, clinicians are exploring ways in which MRI can be used to determine a patient's prognosis and track progression of the disease. This article discusses the MRI findings that may be useful in evaluating disease progression in MS; results of recent clinical trials of MS treatment agents that have employed MRI; and potential applications for MRI in clinical practice.

Osteoporosis in Multiple Sclerosis: A Frequent, Serious, and Under-Recognized Problem

Robert M. Herndon, MD; Nirupa Mohandas, MD

Osteoporosis is extremely common in the multiple sclerosis (MS) population, especially in those women with MS who are postmenopausal and not on hormone replacement therapy. It results in part due to causes present in the general population, but is more common in those with MS due to a variety of factors including limited weight-bearing and the use of steroids to treat the disease. This article discusses impact of osteoporosis on the MS patient, the criteria for diagnosing osteopenia and osteoporosis, and treatment options to increase bone mass.

Abstracts from the Annual Meeting of the Consortium of Multiple Sclerosis Centers

June 22-25, 2000

Halifax, Nova Scotia, Canada

The annual meeting of the CMSC offers dozens of platform and poster presentations on every aspect of MS care around the globe, including diagnosis and treatment, epidemiology, physical, occupational, and speech therapy, and emotional and psychosocial report. Read the abstracts from the physicians, nurses, rehabilitation specialists, and other MS care providers who are presenting their innovative research at this year's meeting.

Book Review: Wheelchair Selection and Configuration

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Letter from the Editor



Robert M. Herndon, MD
Editor-in-Chief

Welcome to the New *International Journal of MS Care!*

Dear Colleagues:

As I'm sure you see, the look of the *International Journal of MS Care* has changed. The new look reflects the involvement of a new publisher, Partners in Medical Communications, which has assumed responsibility for the day-to-day operations of the *IJM* and its Website. The fresh new look is also a preview of exciting times ahead for the *IJM* and the CMSC and RIMS. Starting in September, Partners in Medical Communications will begin publishing a printed version of *IJM*, which is available to all members of the CMSC as yet another membership benefit. The printed journal will provide a wonderful opportunity to offer the highest quality educational programs to the international MS community.

What has *not* changed is the *IJM*'s commitment to international, interdisciplinary education of MS providers. As you search through the articles in the June 2000 issue, you will see a wealth of information in the form of original review articles, written by the most respected names in their respective disciplines. As a special department, you will also find the abstracts from this year's CMSC meeting in Halifax—a handy reference tool to use both before and after the conference.

As you know, the *IJM* is the official journal of the CMSC and RIMS. In addition, we have begun discussion with LACTRIMS regarding their use of the *IJM* as their official journal. We hope to bring LACTRIMS into our international community in the near future, and we will keep informed of this development.

Finally, as a result of the international character of the *IJM*, we will be looking for MS experts around the globe (Europe, Latin America, and Australia) to join our Editorial Board. Our goal is to make *IJM* a truly international educational journal, to share the latest scientific findings in MS from around the world and deliver the most up-to-date clinical care information. We welcome your feedback, and invite you to submit articles for publication (please see the section on article submission on this Website). Thank you for your support, and we continue to look forward to bringing you the best in MS.

Robert M. Herndon, MD

Editor-in-Chief

A Fundamentally New View of Multiple Sclerosis

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Abstract

The last decade has been an era of unprecedented progress in our understanding of multiple sclerosis (MS). MS is now considered a destructive process of the central nervous system, initiated by inflammatory demyelination but including prominent axonal pathology. This new knowledge has been acquired from new imaging techniques and traditional histopathologic study. New mechanisms of myelin destruction have been uncovered, and hypothetical new therapies for MS include neuroprotectants. Serial gadolinium-enhanced magnetic resonance imaging (MRI) scans reveal MS as a continuously active process. Brain and spinal cord atrophy, defined by MRI, correlate closely with clinical state. MR imaging techniques therefore are considered the standard tools for monitoring disease activity and severity. These efforts have produced improved therapy for patients with MS. Two classes of agents, interferon beta and glatiramer acetate, have been approved by the US Food and Drug Administration for use. A major challenge for clinicians is to provide early diagnosis and determine appropriate treatment. New neuroprotective and anti-inflammatory drugs are on the horizon.

In the last 10 years, a fundamental paradigm shift has taken place in the way we view multiple sclerosis (MS). MS is now viewed as a continuous process. Although conceptually, MS remains a condition of inflammatory myelin destruction, the role of axonal transection is now recognized. This new knowledge has been acquired primarily through the direct study of MS patients and tissues, through the application of contemporary immunohistochemistry and microscopy and the use of magnetic resonance imaging (MRI), now the standard for monitoring disease activity, severity, and response to therapy. In this review, I will discuss new findings in pathogenesis, monitoring, and treatment of MS.

Pathogenesis

We now recognize MS as continuously active from the onset in most patients. Serial gadolinium-enhanced MRI has shown that many new lesions may occur in some patients every month, even without disease activity. It has been known for more than 100 years that autopsied MS brains show many more demyelinating lesions than can be accounted for by clinical attacks in life. (see Sidebar, "Multiple Sclerosis: A Brief History.") From MRI studies, we now recognize that these lesions accumulate continuously, from early in the disease process.

Mechanisms of myelin injury—the hallmark of MS—have been studied for many years. More recently, the important role of axonal pathology in the development of disability in patients with MS has been revealed. Genetic susceptibility to MS is also considerably clearer.

In the 90s—the Decade of the Brain—epidemiologic descriptions of genetic susceptibility were available. With the Genome Project providing tools, the genetic susceptibility to MS has come into focus. And the likelihood that there is a single gene of major effect—MS as a disease of direct Mendelian inheritance—has been largely excluded. Genomic screening techniques with advanced statistical approaches have led to the identification of genetic loci associated with increased susceptibility to MS. Based on results of this work, MS depends either on independent or interactive epistatic influences of several genes, each with a small individual effect.

The human lymphocyte antigen (HLA) association, which is the most robust and reproducible association, accounts for a significant proportion of genetic susceptibility. Importantly, concordant results have emerged from analysis of sporadic MS and from studies of MS in multiply affected families (favored as a study population because of increased statistical power). Candidate loci and candidate genes are being further investigated. The important work of defining genetic contributors to disease type and severity has begun. Thus, our understanding of genetic susceptibility is being continuously refined.

T-cell autoimmunity to myelin, which had been hypothetical throughout the history of MS research, has now been demonstrated in MS patients. It is also clear that macrophages within the target tissue are major effectors of myelin destruction. It now seems likely that myelin protein-specific antibodies in some cases help to target macrophages to myelin (*Nature Med.* 1999;5:170). In some lesions and some individuals, myelin is destroyed because of primary oligodendrocyte pathology, essentially in the absence of significant inflammation (*Semin Neurol.* 1998;18:337). In these cases, zones of oligodendrocyte death in lesions are confined to periplaque white matter, indicating that myelin is absent from these lesions because the oligodendrocytes have died. Thus, there is distinct heterogeneity in the pathogenesis of MS.

Axonal Pathology

Axonal pathology plays an important role in the development of irreversible and progressive disability in MS patients. This axonal pathology is closely related to inflammation. Immunocytochemical experiments on MS lesions of varying ages by Ferguson *et al.* showed the expression of amyloid precursor protein in damaged axons within the acute MS lesions and in the active borders of less acute lesions (*Brain.* 1997;120:393). Trapp and colleagues (*N Engl J Med.* 1998;338:278) showed, using dual immunofluorescence confocal microscopy, that the axons became physiologically impaired even as myelin was being "peeled away." Spectroscopic studies have identified highly dynamic changes in axonal *N*-acetylaspartate (NAA; a marker of axonal and neuronal integrity) within and near acute MS lesions. Abnormal levels of NAA have also been seen in normal-appearing white matter around MS lesions and within the corpus callosum.

Thus, loss of myelin and oligodendrocytes, along with axonal injury, provide a pathologic substrate for irreversible disability in patients with MS. This new knowledge has been revealed by techniques including immunohistochemistry, advanced microscopic techniques, and MRI.

In summary, axonal pathology is common in patients with early mild disease and occurs in most lesions. Pathologic studies have shown identical axonal damage in lesions that were of extremely recent origin—as little as weeks—and in cases of secondary progressive MS of as long as 30 years' duration. This supports the hypothesis that MS, in addition to being continuously active in most patients most of the time, is a destructive process in most patients most of the time. It indicates a likely pathologic substrate for irreversibility and highlights the

potential need for early and continuous neuroprotective treatment in most patients. It implies that formal neuroprotective strategies should be considered in MS.

Although we still do not know why axonal transection occurs, it is considered likely to result from loss of protection or trophic support of myelin, or both. This hypothesis leads to the corollary concept that remyelination is a major neuroprotective event in itself, as chronically demyelinated axons may not be viable. Studies of ways to protect axons in the context of inflammatory demyelination must now be conducted.

Monitoring

MRI has set a standard for determining how well treatment is working, as well as determining disease activity, disease burden, and disease type. It is a radical change in our thinking that MRI can be used in this way. Thompson and colleagues (*BMJ*. 1990;300:631) reported that MRI had revealed much about the disease process and was valuable in diagnosis, but that it was not helpful in predicting disability in an individual patient. By 1998, brain MRI was being used to predict long-term disability in MS and to determine the type and extent of disability. What changed was a series of extremely dedicated and persistent clinical-radiographic correlative efforts on the part of several groups. The most evident outcome of this work was the demonstration that individuals presenting with clinically isolated syndromes could be stratified accurately with regard to prognosis (see, for example, *Brain*. 1998;121:495). Thus, our view of what MR can do has changed radically.

Disease burden—the cumulative impact of disease—has been difficult to quantify. MRI analysis of the brain shows many abnormalities in patients with MS. It has not been clear which measurement most accurately reflects the total burden of disease: T2-weighted bright spots, T1-weighted "black holes," or magnetization transfer ratio (MTR) all have advocates. It has now become clear that no single MR parameter will provide all the answers.

Rudick, Fisher, and colleagues recently reported a method of quantitating brain atrophy in MS by simple postprocessing of conventional FLAIR images, potentially providing a convenient way to summarize the destructive process in MS (*Neurology*. 1999;53:1698). As MS damages and destroys myelin, axons, oligodendrocytes, and neurons, one outcome of the disease process is brain atrophy. The new measure of brain atrophy relies on calculation from segmented images of a brain parenchymal fraction (BPF), defined as the ratio of brain parenchymal volume to the total volume within the brain surface contour. Rudick, Fisher, and colleagues showed that in the normal population, BPF is a very narrowly distributed function—approximately 87.5% of the head is occupied by brain, regardless of age or gender. In a well-characterized cohort of patients with early relapsing remitting MS (70 placebo cases in a clinical trial; mean age = 36 years; mean duration of disease = five years; mean Expanded Disability Status Scale score = 2.5), the BPF was 83%, and this fraction was also narrowly distributed. Thus, patients with early, mild MS already had significant atrophy ($P < .001$ compared with healthy age-matched controls). Further, during two years of follow-up during the clinical trial, these patients lost a mean of 0.5% of BPF/year, much more than is observed in serial studies of healthy individuals.

Disease Type

MS is an heterogeneous disease. Demyelination can occur independent of perivenous inflammatory changes, supporting the presence of more than one pathophysiologic process leading to demyelination in MS. Narayana and colleagues (*Ann Neurol*. 1998;43:56) performed serial MR spectroscopic imaging for up to two years in patients with early mild MS and correlated their findings with quantitative lesion volumes. In these longitudinal studies, metabolic changes were observed on MR spectroscopic imaging in some subjects before the appearance of lesions on MRI scanning. Regional changes in metabolite levels were dynamic

and reversible in some patients. Transient changes in *N*-acetylaspartate (NAA) levels were sometimes found in acute plaques and indicated that a reduced NAA level does not necessarily imply axon loss, but may signal the reversible altered physiology of demyelinated axons. They observed an inverse correlation between the average NAA within the spectroscopic volume and the total lesion volume. Strong lipid peaks in the absence of gadolinium enhancement and MRI defined lesions were seen in four of the 25 patients, implying demyelination without attendant inflammation. This provocative study therefore reinforced the concept of heterogeneity of pathologic alterations in the brains of MS patients.

MS is a Treatable Disease

It has been demonstrated that treatment modifies the natural history of MS in the short term. However, the biggest task that lies ahead is to extend short-term benefits to a long-term reduction in disability. McFarland and coworkers (*Ann Neurol.* 1995;37:611; *Neurology.* 1997;48:1446) showed that initiation of interferon beta therapy results in abolition of enhancing activity almost immediately, and in a robust and lasting way. Preliminary studies with glatiramer acetate, originally known as copolymer-1, show that it may also show comparable benefit in MRI indices of disease activity in relapsing-remitting MS. The impact of these short-term benefits on long-term disability remains the '\$64,000 question.'

The availability of new treatments imposes challenges upon clinicians: We must diagnose MS early and with stringent accuracy, to take full advantage of MS-specific drugs. As a group of 'treating physicians' we are also faced with the challenge of determining when therapy should be started. If, as posited earlier, MS is, from the day of onset, a destructive process that continues even during asymptomatic periods, clinical progression should ultimately be determined by the magnitude of tissue injury. According to this concept, MS at the tissue level is monophasic and continuous, and patients enter the phase of secondary progressive MS when a threshold of tissue destruction has been exceeded. Closely monitoring patients' rate, extent (by BPF, for example), and location of central nervous system atrophy could help to address the accuracy of this hypothesis and validate brain atrophy as a relevant measure of cumulative disease impact. In patients who have obvious, fulminant MS, disability occurs very quickly and BPF declines rapidly. However, for the great majority of patients, secondary progressive disease begins 10 to 20 years after the onset of MS. This phase of disease poses our greatest challenge and remains highly resistant to treatment.

That's the bad news; the good news is that BPF decline appears to respond moderately to contemporary treatment. Rudick and coworkers (*Neurology.* 1999;53:1698) recently analyzed data from a trial of interferon-beta treatment for relapsing-remitting MS. They detected no differences between placebo and interferon-beta-treated patients during the first year, in regard to BPF decline. However, there was a 55% reduction in progression of atrophy (as measured by changes in the BPF) during the second year of active treatment compared with placebo. Such results are encouraging and suggest that early treatment may modify the risk of subsequent disability.

Other treatments in development include small-molecule antagonists of leukocyte trafficking, blockers of T lymphocyte co-stimulatory signaling, and innovative approaches such as T-cell and DNA vaccines. Given the pace of improved knowledge, innovative uses of sophisticated imaging techniques, and new therapies in the 10 years that comprised the Decade of the Brain, one may be encouraged that the next 10 years may be similarly productive.

Conclusions

The 90s—the Decade of the Brain—has been a period of paradigm shift in our understanding of MS. In addition to the steady progress of understanding myelin breakdown, the role of axonal

pathology has been elucidated. The disease is now viewed as a continuous process from the onset. Monitoring tools—specifically, the use of MRI techniques—have shown tissue changes and have illuminated pathologic events. The systematic study of large numbers of active cases has been, and will continue to be, instrumental in improving our understanding of the immunologic and pathophysiologic mechanisms in MS. We have entered a challenging and exciting era in which MS, for the first time, is a treatable disease. The task that remains before us is to determine the optimal way to use these treatments and develop the next generation of therapies.

Multiple Sclerosis: A Brief History

Identification Of The Disease

- Early 1800s** Tarnswell is the first to observe and describe the onset of MS symptoms.
- 1844** Cruveilhier describe the anatomic lesions responsible for MS.
- 1868** MS is diagnosed for the first time and the clinicopathologic definition first stated by Jean-Martin Charcot still holds today.
- 1878** Discovery of myelin by Louis Ranvier. Other researchers later identify a specific category of myelin-producing cells (oligodendrocytes) and determine the importance of myelin in the conduction of nerve impulses.

Understanding The Disease Process

- 1916** James Dawson identifies initial lesions indicating lymphocyte, macrophage, and plasma cell infiltration into the brain, leading to early demyelination.
- 1922** First discovery of anomalies in the cerebrospinal fluid of MS sufferers. First observations that MS does not occur in a uniform pattern worldwide and the incidence is higher in the Northern hemisphere.
- 1935** Thomas Rivers describes an animal model of a disease resembling MS and suggests an autoimmune basis for the disease, with myelin in the central nervous system being the target of the immune response. An animal model is also developed by Pasteur.
- 1942** Elvin Kabat underlines the significance of these cerebrospinal fluid anomalies within the immune system.
- 1955** The first comprehensive neuropsychological study of a small number of MS patients is carried out. The researchers Ross and Reitan find that patients have severe difficulties performing tasks that involve motor speed, strength and coordination, exhibit intermediate difficulties in abstracting and concept formation, but have preserved verbal ability.
- 1955** John Kurtze develops the first widely used scale enabling categorization of the different stages of MS; a later version of the scale, the Expanded Disability Status Scale (EDSS), is still used

today.

The first controlled trial of MS is published in *Neurology* in 1969 by Tourtellote.

Trying To Find The Cause

- 1970s** Recognition of the characteristics of latent slow virus infection in animals and humans prompts researchers to consider anew the possibility of an infectious origin for the disease.
- 1980s** Many studies examining different aspects of immunologic responses of MS patients are initiated. Some link the condition to HLA associations, some suggest that astrocytes might have a role in the pathogenesis and symptomatology of MS.
- 1981** The first pictures of the brain of an MS patient are obtained by magnetic resonance imaging (MRI), providing the opportunity to visualize MS lesions within the central nervous system. MRI will revolutionize the diagnosis, management, and monitoring of MS.

Further Knowledge And New Therapies For MS

- 1980s** Trials with linoleic acid, linolenic acid and methylprednisolone are attempted. The first studies using interferon alpha and beta to treat MS are conducted.
- 1990s** Axonal pathology, known to be present in MS lesions since the 1880s, is quantitated and shown to be irreversible. MRS studies demonstrate the pervasive nature of axonal and neuronal disruption in MS brains. The relationship between axonal pathology and progression of disability is proposed and intensive studies begin.

Interferon-beta-1b (1993) and –beta-1a (1996) are approved in the United States, and then in the European Community for use in relapsing-remitting MS.

Glatiramer acetate, a synthetic copolymer of four amino acids, is approved in the United States for use in relapsing remitting MS.

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Hope In Multiple Sclerosis A Nursing Perspective

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Abstract

Feelings of hopelessness are common in patients with multiple sclerosis (MS), which poses a significant threat to an individual's independence and feelings of competence. Because hope has been shown to play an important role in health and coping during chronic illness, it is critical for the MS provider to understand the elements of hope and recognize when the person with MS is struggling with feelings of hopelessness. The MS nurse is the pivotal player in ensuring that the individual with MS maintains a sense of hope throughout the illness. In addition to providing education, counseling and referrals, the nurse can help the MS patient focus on feelings and ideas, recognize personal reasons for living, and establish both short-term and long-term goals.

Hope is an essential element of life—it embodies our vision of the future, our opinion of ourselves and others, and our sense of control over the events and direction of our lives. The presence of hope for someone experiencing an illness can provide the energy necessary to promote health and enhance well-being.

Multiple sclerosis (MS) is commonly diagnosed during the most productive years of a person's life, between the ages of 20 and 40. It threatens independence and the ability to make meaningful contributions to the family and to society. This in turn can lead to a loss of feeling competent and self-assured. The disease often arrives in the midst of what are expected to be healthy years, disrupting an individual's confidence in his or her body and health. Because of the unpredictable nature of the disease, some patients with MS may feel that they are unable to plan for the future. Although this is an optimistic time in MS management, with new drug therapies available that can alter the course of the disease in a positive way, MS remains incurable.¹ It comes as no surprise, therefore, that depression, helplessness, and hopelessness are common in patients with MS.^{2,3}

Hope has been shown to play an important role in health, and is indispensable to healthy coping.⁴⁻⁸ Breast cancer patients with highly optimistic attitudes have been found to cope better with their illness, whereas persistent hopelessness may increase the risk of a relapse or death from the disease.⁹ Hope may help a patient with MS to continue functioning more successfully and to remain independent for a longer period of time. Hope may not only bolster a patient's self-esteem and sense of well-being, but also may have a synergistic effect on more conventional medical therapies. Inspiring hope, therefore, should be an integral part of a multidisciplinary approach to the treatment of MS.

Nurses perform an important function in engendering hope.¹⁰⁻¹³ Nurses who care for persons with MS and their families can provide the resources to promote hope and prevent

hopelessness. By virtue of their nurturing care, empathy, and unconditional support of patients with MS, nurses are a healing presence.¹

Elements Of Hope

Hope is often defined as futuristic, an expectation that can be achieved if one is motivated; a realistic goal. In 1965, Lynch¹⁴ defined hope as a sense of the possible, “the best resource of man, always there in the inside making everything possible when he is in action, or waiting to be illuminated when he is ill. It is [our] most inward possession and is rightly thought of according to the Pandora story, as still there when everything else has gone.”

Much of the early work written about the concept of hope centered around these characteristics, and hope began to be explored as a mechanism for coping with illness. Psychologists in particular studied prisoners of war and found that the idea of release helped to sustain them.¹⁵ In addition, Kubler-Ross¹⁶ worked with individuals with terminal illnesses to develop her well-known stages of death and dying. She found that hope for a cure or remission of illness supported people and helped them to cope during difficult times; when individuals stopped expressing hopeful thoughts, death was imminent.

Variables That Support Hope

A variety of underlying characteristics contribute to a patient’s hopefulness or lack thereof. Self-esteem is an essential component of the overall ability of the patient to be hopeful and cope with chronic illness. Significant associations have been found between self-esteem and depression, with only 4% of those with high self-esteem rated as depressed by their nurses, compared with 80% of those with low self-esteem.⁴ Feelings of competence and control of one’s life are related to hope,^{11,17} and an underpinning of faith, whether expressed as conventional religious faith or simply as a feeling of connectedness with a higher being, has also been found to have a positive impact on a patient’s hopefulness.¹⁷

Hopelessness And Despair

Hopelessness and despair also have a number of components. Lynch¹⁴ defined hopelessness as not having the energy for either imagining or wishing. It is a deeply passive state. A person who is hopeless sees no future, makes no plans, and anticipates nothing. There is often a sense of sadness, a loss of interest in life’s pleasures, and a negative attitude that is easily recognized by the nurse.

The Nurse’s Role

In order to intervene in the hoping process, the nurse must recognize the degree of hope that a patient has.¹⁰ In a qualitative study of the lived experience of relapsing-remitting MS, Miller¹⁸ found that hope, in fact, does exist in those with MS. As a frequent caregiver, the nurse is able to observe the patient and assess the patient’s spiritual and emotional health. The nurse can evaluate behaviors that reflect hope, and identify variables that make an impact on the process of hoping.

Hope manifests itself in verbal and nonverbal expressions that mirror a spirit of optimism. “Hope can be a song, a poem, a painting, a flower arrangement, a smile, or a joke.”¹ Table 1 lists some of the behaviors that reflect hope.¹

Table 1. Behaviors That Reflect Hope

Source: Morgante L.¹ Reprinted with permission.

- Verbalizes future goals
- Shows motivation to reach goals
- Expects to accomplish goals
- Imagines a brighter tomorrow
- Reminisces about past successes
- Sees options for self
- Maintains a sense of control
- Anticipates positive outcomes
- Relates to family, friends, or caregivers in supportive and reciprocal ways
- Feels connected to a higher being
- Displays humor
- Relaxes with imagery and visualization

In contrast, signs of hopelessness may also be physical, such as avoiding eye contact, shrugging in response to questions, passivity, motionlessness, or a sad expression. Altered appetite and weight, increased sleep, decreased motivation, and social withdrawal also reflect a hopeless state. Verbal cues include frequent sighing or responses with hopeless content.¹⁰ The inaction and apathy that arise out of despair may result in greater dependence on others to satisfy basic needs, which in turn lowers self-esteem.¹⁰ Lower self-esteem is itself a contributor to hopelessness, and this may lead to what could be called a cycle of despair.

Neither hope nor despair is a static state. They are instead part of an ever-changing process that can fluctuate from moment to moment. Nurses who recognize this can help inspire hope even during the darkest times. All patients have within them the resources to hope. Learning about a person's past coping abilities provides clues to hope. Helping a person to reminisce about previous experiences can aid the caregiver to formulate a plan to hope¹ (see Figure).



Figure. The Dynamic Process of Hope and Despair.

The Tools To Inspire And Sustain Hope

Education, counseling, advocacy, and referrals are tools the nurse uses to enhance hope in persons with MS and their families.¹ Empathy, unconditional positive regard, respect, warmth, commitment, and caring are the underpinnings of a strong therapeutic relationship.¹⁹ Nurses can help the patient focus on feelings and ideas, recognize personal reasons for living, and

establish both short-term and long-term goals.¹⁰ Attainable goals kindle hope, feelings of competence, and higher self-esteem in patients.

Nurses can ensure that resources are available to support hope. In the MS patient this may include ensuring that the patient has access to the workplace. A study by Foote et al⁴ in 1990 showed that employment correlated positively with higher levels of self-esteem and hope. Minor modifications such as grab bars and a chair in the shower can make bathing easier and safer for the patient, and increase a sense of independence.¹ Loss of control over the self and the environment can increase a sense of helplessness, while restoring independence can ignite hope.

Strategies to reinforce hope include discovering and utilizing the patient's support network and resources, building on past hoping mechanisms, and projecting realistic hopes for the future. This may include aiding the patient to formulate and plan for an attainable hope. Creating hope that extends forward into time gives most patients a sense of a future, which severely depressed patients may lack.¹⁰ However, hoping in the moment or "taking it one day at a time" may be appropriate for patients with MS whose fears and anxieties are focused on the future uncertainties surrounding the illness. Fraser⁸ found that hope shifts as individuals move through an experience for long periods of time. Hopes and dreams of recovering at some point in the future undergo a transition to focusing on one day at a time. The experience is reframed to a comfortable place in the present, which promotes a sense of control and renews hope.

Many persons with MS express fear of becoming burdens to their family and friends, and desire to continue making valuable contributions. The nurse may help the patient explore these feelings and pinpoint key relationships, which are vital to hope. Maintaining and strengthening these relationships are crucial to a patient's emotional well-being. The nurse also may serve an important role here, facilitating communication with the patient's friends and family.^{1,10} However, the energy in these relationships must flow both ways. Hopeful people feel needed and valuable to their friends and family.¹⁹

Social isolation resulting from bladder and bowel problems can occur during the course of MS. The nurse can provide practical solutions for disturbing problems that may interfere with a patient enjoying social activities. For example, self-catheterization techniques can be taught and anticholinergic drugs prescribed to assist with urinary urgency and incontinence, and bowel habits can be regularized with a high-fiber diet and high-fiber supplements, giving the patient greater comfort and self-confidence in social situations. This in turn creates a sense of well-being.¹

Finally, the nurse may assist the patient to achieve goals in a very concrete manner. This may be as simple as helping the patient to plan a trip, or as complicated as mustering the resources necessary to aid the patient to enhance intimacy.

Hope vs False Hope

Nurses "weave a tapestry of hope while untangling a web of false hope."¹ Persons with MS can develop unrealistic hopes. An example of this is commonly seen when a person begins treatment with an immunomodulating drug. The patient and family expect to see improvement in MS symptoms after therapy is initiated. Yet they often feel no change, and sometimes feel even worse if side effects occur. Nursing education and counseling regarding realistic expectations are required at the beginning of treatment, and should be reinforced at each follow-up visit. The nurse-patient relationship, built on a foundation of trust and mutual respect, helps persons with MS master the experience within a realistic and hopeful framework.

When MS Becomes Progressive

Although the variable course of MS can cause a patient stress, uncertainty can be a form of hope in itself, as a variety of hopes may be accommodated by an uncertain future.¹⁰ When relapsing-remitting disease becomes progressive, the transition is very difficult for the patient, as certain hopes are destroyed. Treatment options are limited for this course of disease, and the patient's vulnerability and despair often increase.¹ The nurse's goal now becomes supporting the patient in maintaining normalcy and maximizing abilities.

It is important, however, to understand that the patient may need to pass through a period of grieving. Denial is the first step in the process, and is a mechanism that may protect hope for the patient by allowing the individual time to assimilate the new information and adjust.¹ Denial results in a reduction in anxiety, by diminishing the perception of threat to the individual; it is one of the most primitive of defense mechanisms.¹²

Grieving is a natural process that allows us to confront losses. In MS, the losses accumulate over the years, and when the disease changes course and becomes progressive, these losses may seem an unbearable burden. The nurse can assess the patient and watch for signs of distress and unrelenting despair, and provide referrals for counseling if necessary.

Dealing With Young Adults

Although MS typically strikes those in their 20s or older, occasionally adolescents or even children are stricken with the disease. Their coping mechanisms differ from those of more mature adults. Adolescents, in particular, turn to themselves or peers for reassurance and to provide a frame of reference for their problems. In a study of adolescents coping with cancer, Hinds and Martin found that these patients would often attempt to banish despair by telling themselves they could be worse off. However, if parents or health care professionals used this strategy on the patient it would lose its effectiveness.¹¹

Adolescents also practice distraction-based thinking to maintain internal equilibrium, deliberately replacing negative, despairing thoughts with cognitive clutter—thoughts of homework or sports—or by engaging in physical activity and socializing to keep themselves busy and provide mental relief.¹¹ Their coping tends to be more emotionally focused; that is, they attempt to control their response to the disease rather than attempting to manage the disease itself. Emotional-focused coping occurs when individuals feel nothing can be done to modify the threatening condition they face.¹¹

The nurse should keep these differences in mind when endeavoring to foster hope in an adolescent. Although adolescents frequently discount the advice and encouragement adults give them, Hinds and Martin also found that adolescents were influenced by others around them, including clinicians. The attitudes and behaviors of others could provide a positive support network against which hope could grow.¹¹

Maintaining Hope Within Yourself

To inspire hope in others, nurses must feel hopeful themselves.¹ Miller¹⁸ found that persons with relapsing-remitting MS rely on the hopeful attitudes projected by health care professionals. Patients and their families borrow from the nurse's wellspring of hope, and it is vital to renew and replenish that well of hope.

It is difficult sometimes to feel hopeful when caring for those who are seriously and chronically ill; nurses grieve when a patient's condition deteriorates. It is important to recognize personal

sadness and loss, and use the support of other members of the health care team. It is also crucial to implement strategies for self-care, as “Nurturing oneself is a requisite for nurturing others in a more authentic way” (see Table 2).^{1,20} Self-care strategies include regular exercise to promote fitness and health, proper nutrition to keep the body fueled, and relaxation techniques including deep breathing, meditation, and yoga to quiet the mind and re-energize the body. Setting limits, learning to say “no,” and asking for guidance when in doubt are helpful stress reducers. Nurturing one’s own relationships in a supportive manner helps sustain hope, and talking to a confidante helps to relieve anxiety. Networking with peers and professional development help keep the day-to-day work more interesting, and foster self-esteem. Humor and laughter help to lighten the spirit, and even smiling makes one feel better. Making sure that there is something to look forward to each day helps remind one that hope exists for all of us, and is available to those who dare to dream.

Table 2. *Strategies for Self-Care*

Source: Morgante L.¹ Reprinted with permission.

- Savor each moment
- Exercise regularly
- Eat nutritiously
- Network with peers
- Rely on others for guidance when in doubt
- Use your confidante
- Nurture supportive and reciprocal relationships
- Know your limitations
- Expand your knowledge base
- Be inventive
- Share your expertise
- Pamper yourself-massages, facials, manicures, pedicures, etc
- Try deep breathing, relaxation, yoga, and meditation
- Give yourself something to look forward to each day
- Take vacations

Conclusions

Hope is a resource within each of us that can be illuminated to promote healing. Given the importance of the relationship between emotional response and clinical outcomes, more work needs to be done on the concept of hope in patients with MS. Nurses have an excellent opportunity to make a profound difference by exploring variables that support hope in individuals who live with the day-to-day uncertainty of a chronic illness like MS.

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Use of MRI Technology in Determining Prognosis and Tracking Therapeutic Benefit in Multiple Sclerosis

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Abstract

Over the past decade, magnetic resonance imaging (MRI) has been increasingly used as a tool to facilitate the diagnosis of multiple sclerosis (MS). Because of the relative insensitivity of commonly used clinical assessment measures, however, clinicians are exploring ways in which MRI can be used to determine a patient's prognosis and track progression of the disease. This article discusses the MRI findings that may be useful in evaluating disease progression in MS; results of recent clinical trials of MS treatment agents that have employed MRI; and potential applications for MRI in clinical practice.

Although magnetic resonance imaging (MRI) has been generally accepted for the diagnosis of multiple sclerosis (MS), its use in clinical practice for prognostication and tracking of therapeutic effect is not widely practiced. The need for objective surrogate markers in this disease is clear, however. Clinical assessments, such as the Expanded Disability Status Scale (EDSS), are relatively insensitive to change and limited in their ability to evaluate the benefits of therapeutic agents in individual patients in the clinical setting. Furthermore, such measures reveal little about disease pathophysiology and have a poor predictive value with regard to progression of the disease itself.¹

First introduced in 1984, MRI technology offers a method of tracking disease progression and an objective measure of the efficacy of drugs used in the treatment of MS.² To date, this technology has been used mainly in phase III clinical trials as a measure of therapeutic effect. But of equal value is the insight it may provide into the pathophysiology of this disease. Currently, direct correlation between some MRI findings and clinical signs and symptoms is weak: New lesions occur five to 10 times as often as clinical relapses.³⁻⁵ Evidence indicates, however, that axonal loss may accumulate in relatively asymptomatic patients until it reaches a threshold beyond which compensatory mechanisms fail.⁶ It is at this point that symptoms begin to manifest. Furthermore, there are compelling data from atrophy measures that MRI provides evidence that precedes and predicts disability, which has important implications for both prognostication and treatment.

Since its introduction, MRI equipment has evolved considerably. The development of equipment that generates higher magnetic fields has resulted in better image resolution. Fields of 1.5 Tesla (T) are now common, and equipment that generates fields of 3 T will soon be announced for neurologic applications. These new MRIs will be faster and have improved contrast and resolution, which will translate into more accurate diagnosis. Sequencing techniques are always being optimized, and the development of new contrast agents is under investigation. Software innovations have also facilitated new applications, such as three-dimensional volumetric analysis. While refinements of some measures need to be made, and reproducibility issues still

exist, the technology allows a glimpse into the course of a disease that until now has remained a mystery.

MRI Measures

A number of measures are used to evaluate disease progression in MS. Two of the more common are T1- and T2-weighted lesion measures.

T2 Lesions

The most common MRI measure done in patients with MS is the total brain lesion volume (TLV), a measure of unenhanced T2-weighted scans (see Figure 1). Because T2 scans reveal considerable activity, yet do not distinguish between edema, gliosis, demyelination, and axonal loss, their correlation with clinical impairment is weak.^{7, 8} Moreover, the TLV fails to take the location of lesions into account, although the clinical relapse rate is to a great extent dependent upon the location of active lesions.⁹ Despite these limitations, the T2 lesion measure remains a valuable gauge of overall disease activity, often indicating subclinical activity.

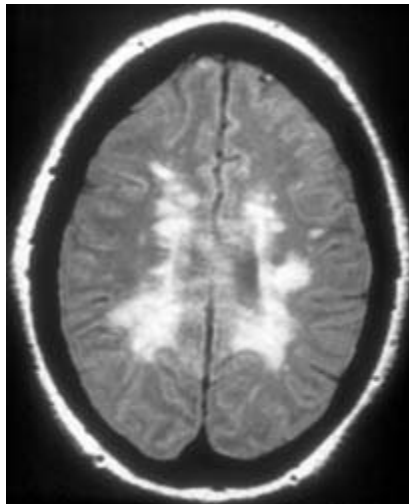


Figure 1. Unenhanced MRI scan showing the presence of MS plaques. Image courtesy of Gordon Sze, MD.

NOTE: You can click on this image to see a larger version in a new browser window.

T1 Lesions

The “black holes,” or areas of hypointensity, seen in unenhanced T1 lesions may correlate more highly than TLV with disability (see Figure 2). These areas, which are seen much less frequently than the high-signal areas seen on T2, are thought to be more pathologically specific. In postmortem studies, the degree of hypointensity has correlated well with the degree of axonal loss and has also shown an association with magnetization transfer ratios (MTRs), implying the presence of demyelination.¹⁰ Most studies indicate a higher correlation between T1 results and EDSS scores than with T2 results.

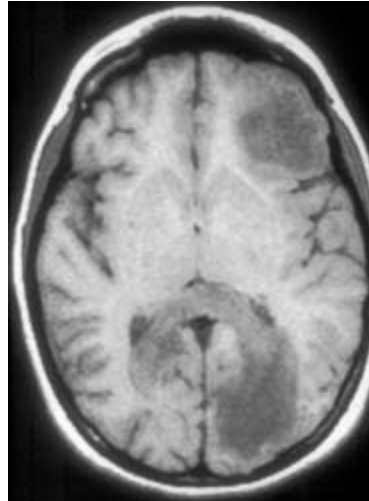


Figure 2. Nicknamed “black holes,” the areas of hypointensity seen on T1-weighted images are believed to indicate that MS is a disease not only of demyelination but also of axonal destruction. Image courtesy of Gordon Sze, MD.

NOTE: You can click on this image to see a larger version in a new browser window.

Both T1 and T2 scans are time consuming and require proper repositioning of the patient, to ensure the accuracy of the imaging. T1 scans, however, are subject to greater inter-rater variability due to a degree of subjectivity in determining which lesions qualify as black holes. Results from ongoing phase III clinical trials may substantiate the value of T1 lesions as surrogate markers in MS.

Gadolinium Enhancement

Gadolinium enhancement allows further differentiation of lesions. Lesions that brighten after enhancement indicate an area of blood-brain barrier (BBB) breakdown (see Figure 3). Although enhancing lesions do not always result in the same degree of tissue destruction,¹¹ the number and volume of these types of lesions are known to correlate with the inflammatory stage of the disease.⁸ The value of gadolinium-enhanced imaging is given additional weight in a recent study by Waubant et al.¹² That study explored the relationship between serum levels of metalloproteinase-9 (MMP-9) and tissue inhibitor of MMP-type 1 (TIMP-1) and MRI activity in patients with relapsing-remitting MS (RRMS). MMP-9 is known to be expressed by activated T lymphocytes crossing the BBB in experimental autoimmune encephalomyelitis (EAE).¹³ Their findings indicate that changes in the levels of these enzymes occur up to two months before the appearance of gadolinium-enhanced lesions, and represent a possible initial stage of the disease.

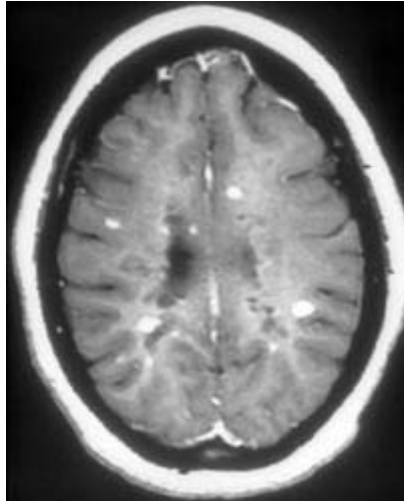


Figure 3. This MRI scan with gadolinium enhancement shows active plaques (bright areas). Image courtesy of Gordon Sze, MD.

NOTE: You can click on this image to see a larger version in a new browser window.

Spinal Cord and Cerebral Atrophy

Spinal cord and cerebral atrophy are significant consequences of MS. Severe tissue destruction may cause shrinkage and reorganization within the structure of the central nervous system.¹¹ This progressive loss of brain and spinal cord tissue may begin at the onset of the disease. Although much of the disability in MS has been thought to be the result of spinal cord disease,⁷ this places undue emphasis on locomotion while ignoring the visual and cognitive elements of the disease, as well as the symptom of fatigue, all of which, at least partially, are cerebral in origin, and are arguably of greater significance to the patient.

Spinal cord atrophy does, however, demonstrate a strong positive correlation with EDSS scores. Patients with MS who had atrophy at one or more of four spinal levels (C5, T2, T7, and T11) scored significantly higher on EDSS than those without evidence of atrophy.¹⁴ Shrinkage of the spinal cord circumference may reflect the pathologic process responsible for this disease; that is, the axonal loss and demyelination in lesions and normal-appearing white matter (NAWM).¹⁰

A study by Filippi et al¹⁵ of spinal cord atrophy at the C5 level revealed a difference in the degree of atrophy in patients with benign MS versus those with secondary progressive disease (SPMS). Both this study and the study by Kidd et al¹⁴ used a manual outlining technique, which has poor scan-rescan reproducibility.⁷

A 1996 study by Losseff et al also found an extremely strong correlation ($P < .001$) between spinal cord area and both EDSS scores and disease duration as measured at the C2 level using a semiautomated technique to delineate cord boundaries.⁷ Accurate MRI readings at the C2 level are easier to obtain, as the cord can lie in the middle of the cerebral spinal fluid (CSF), with the result that cord/CSF contrast is maximized. Measurements can be obtained quickly, and both inter-rater and intrarater variability is reduced over other imaging techniques. Additionally, repositioning errors have a minimal effect on scan-rescan. Conversely, C5 level measurements lack sufficient cord/CSF contrast for automated contouring to work, and thus require manual outlining technique, which further reduces reproducibility.⁷

Also of interest, a recent serial study by Stevenson et al of cord atrophy in patients with MS revealed that those patients with primary progressive disease (PPMS) showed the greatest degree of spinal cord change.¹⁶ These patients are well known to have low brain T2 lesion

loads.¹⁰ The Stevenson study also demonstrated that ongoing atrophy of the spinal cord was measurable over a period of one year. This finding was not reflected in EDSS scores, however, possibly as a consequence of a lack of responsiveness in this measure. There is also little correlation between EDSS scores and the number or volume of spinal cord lesions as seen by T2 imaging.¹⁰

While spinal cord atrophy measurement shows promise as a tool to gauge clinical disease and pathologic change, a measure of brain atrophy may prove even more useful as a method of assessing ongoing disease. A number of techniques have been developed to accomplish this, and recent developments in registration methods have improved the accuracy of serial three-dimensional MR brain images.¹⁷ However, quantifying brain atrophy remains more complex than measuring spinal cord atrophy.

Some methods require the extraction of the brain from the skull via imagery. Technologic advances have allowed serial volume acquisitions to be registered and subtraction images to be produced, yielding an automated measure of change in cerebral volume.¹⁰ This technique was used by Losseff et al in an 18-month study in 1996. The authors found that while baseline T2 lesion load, T2 lesion load changes, and gadolinium volumes did not correlate with progressive atrophy, there were trends suggesting a positive association.¹¹ Results of the study also implied a correlation between atrophy and worsening disability, and noted a slower rate of atrophy in patients who did not have increasing disability.¹¹

Brain ventricle and sulcal enlargement and decreasing corpus callosum were used to gauge brain atrophy and as markers of disease progression in a recent study by Simon et al. This two-year study evaluated brain atrophy in patients with RRMS and mild to moderate disability based on annual MRI measurements.⁸ Atrophy measures included third and lateral ventricle width, brain width, and corpus callosum area.⁸ The authors found that the magnitude of changes based on these measures was on the order of 5% per year. These atrophy measures correlated with MR measure of cumulative past insult, T2 lesion volume at study entry, and disease duration at entry. The particular significance of this study is its use of measures that do not require specialized software.

The brain parenchymal fraction (BPF) was used to measure whole brain atrophy in RRMS by Rudick et al in a 1999 post-hoc study of the treatment effect of interferon beta-1a (IFN β -1a) in patients with RRMS. The BPF was defined as a ratio of the brain parenchymal volume to the total volume within the brain surface contour. This method demonstrated reduced variability caused by variation in brain size and a high retest reproducibility. Even in patients with mild clinical disability, the investigators found a mean BPF that was 5 SD below the mean of healthy age- and gender-matched controls, reflecting the view that this disease is active during periods of clinical remission.¹

Of importance in this investigation was the finding that IFN β -1a had no effect on brain atrophy during the first year of the study, but was associated with a reduction in atrophy in the second year.¹ The authors suggested that treatment effects of this agent were ongoing in the first year, but only evident in the second year of the study. This suggests that there are secondary effects resulting from the initial inflammatory phase that are active in a longer time frame. These secondary effects may include axonopathy with Wallerian degeneration resulting in secondary neuronal death, which may follow the initial inflammatory event by weeks to months. Consequently, cerebral atrophy may represent the sum total of demyelination, axonal transection, subsequent neuronal death, and secondary changes in the neuronal-associated astrocyte populations.

Magnetization Transfer Ratios

The MTR is an indirect measure of tissue integrity. In areas of demyelination, there is an

indirect reduction in tissue signal intensity (see Figure 4). Reduced MTR values, indicating demyelination, have been seen in both lesions and NAWM in patients with MS. These values have shown moderate correlation with EDSS scores.¹⁰

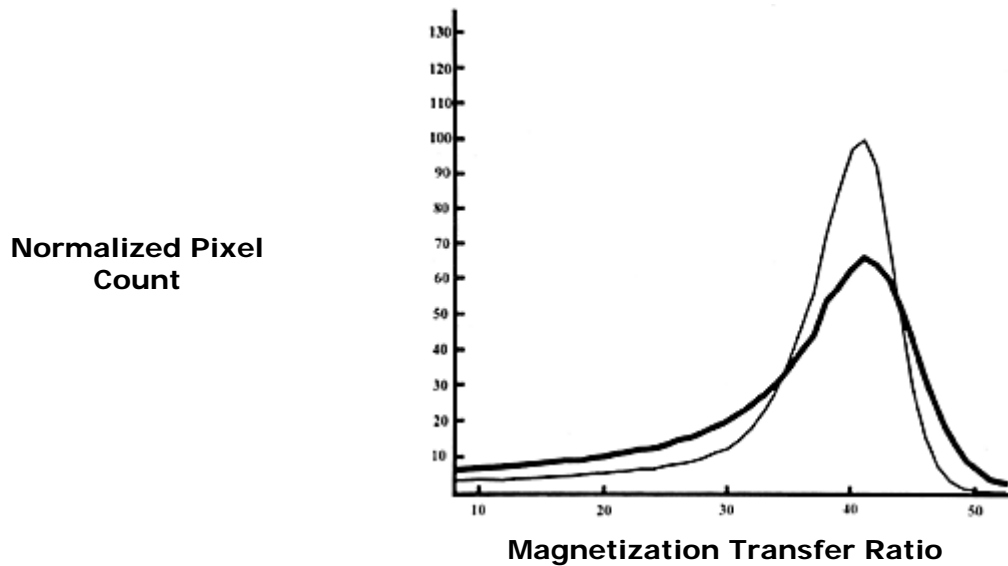


Figure 4. The magnetization transfer ratio, an indirect measure of tissue integrity in MS, shows reduced values in areas of demyelination. Image courtesy of Gordon Sze, MD.

More recently, histograms constructed from calculated MTR values have combined data from both lesions and NAWM. Histogram analysis by Tortorella et al has shown lower MTR and peak values in patients with RRMS and PPMS than in normal subjects, and still lower values in patients with SPMS than in those with RRMS. They also found that average histogram MTR ($P < .0001$) and T2 lesion load ($P = .001$) correlated highly with brain volume. The authors concluded that microscopic changes account for an important fraction of the MS lesion load and may contribute to brain atrophy, and that these changes tend to be more evident in patients with SPMS.¹⁸

Magnetic Resonance Spectroscopy

Magnetic resonance spectroscopy (MRS) complements conventional MRI by quantifying the chemical pathology within both lesions and NAWM. The reduction of *N*-acetylaspartate (NAA) implies the loss or dysfunction of axons, as this chemical is assumed to be present only in neuronal cell bodies and axons (see Figure 5). These reductions are seen in the NAWM of MS patients, and even in those patients with PPMS, who are known to have small TLVs. The changes in the lipid portion of the spectra evident in acute or enhancing lesions with this technique most likely indicate inflammation or demyelination.¹⁰

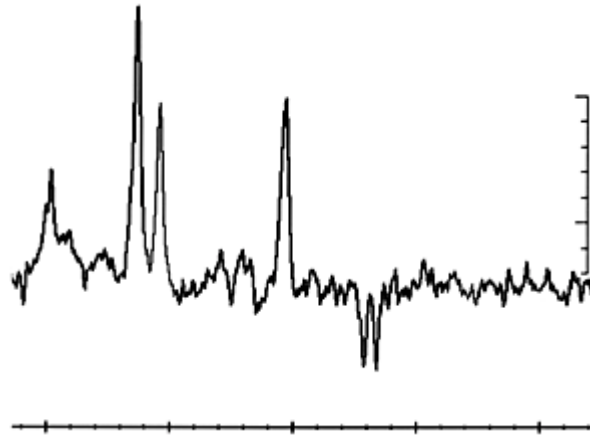


Figure 5. Magnetic resonance spectroscopy findings in MS are characterized by decreased N-acetylaspartate, suggesting axonal destruction. Image courtesy of Gordon Sze, MD.

In an attempt to establish a new measure of disease load in MS, Gonen et al recently used the whole brain's NAA concentration to quantify the extent of neuronal loss in MS. Total brain NAA was determined by proton MRS. Findings indicated that whole brain NAA was lower in patients with RRMS than in matched controls, with the difference being greater in older subjects than in younger, suggesting that a progressive neuronal cell loss is a significant feature of the disease. Moreover, the authors proposed that whole brain NAA provides a quick, highly reproducible measure of disease progression and possibly of treatment efficacy in MS.¹⁹

MRI Results Of Recent Clinical Trials In Multiple Sclerosis Therapy

Glatiramer Acetate

Previous studies of glatiramer acetate treatment in patients with RRMS using serial MRI have demonstrated a significant effect of treatment on the number of gadolinium-enhancing lesions, volume of gadolinium-enhancing disease, number of new and expanding T2 lesions, and volume of T2 disease.^{20,21} Of interest, the magnitude of the MRI effect of treatment with glatiramer acetate on disease activity as measured by gadolinium approximates the treatment effect on relapse rate (approximately a 30% decrease). This has been interpreted as being consistent with the proposed mechanism of action of glatiramer acetate, which suggests that glatiramer acetate works through a bystander suppression mechanism. This mechanism of action implies a need for an anti-glatiramer immune response to gradually develop as a consequence of repeated injections of this drug.

More recently, glatiramer acetate was evaluated in the treatment of RRMS in a placebo-controlled trial by Ge et al. Results were measured with both T2- and T1-weighted images, before and after gadolinium enhancement. The study confirmed the previously documented effect of glatiramer treatment on new lesion formation as measured by gadolinium enhancement and new and enlarging T2 lesions. The study did not show a significant effect on T2 volume of disease (possibly related to the small size of the study). Of interest, the BPF was calculated as well. Patients in the glatiramer acetate-treated group showed significantly less brain atrophy than placebo controls. The authors found that even in this small study the data provided evidence of a slowing in progressive brain atrophy with glatiramer acetate treatment for RRMS, and reinforced the value of brain atrophy as a measure of clinical efficacy.²²

Interferon β -1b

Previous studies have shown a significant treatment effect of IFN β -1b on new and enlarging T2

lesions and gadolinium-enhancing disease activity. The magnitude of these effects ranges between a 70% and 90% decrease in disease activity. Treatment effect was also seen by TLV and persisted through at least five years.^{4,23} More recently a placebo-controlled trial of IFN β -1b in patients with SPMS evaluated treatment efficacy using proton density (PD)/T2 brain scans to measure TLV. A subgroup of patients also underwent monthly gadolinium-enhanced and PD/T2-weighted brain MRI. Results indicated that IFN β -1b had a substantial effect on disease progression in patients with SPMS, reducing the accumulation of new inflammatory disease. The treated group had a significant reduction in TLV at the first follow-up, indicating a significant effect of treatment on inhibiting new lesion development in SPMS similar to that seen in RRMS.²⁴

Interferon β -1a

Several trials have also demonstrated the efficacy of IFN β -1a in the treatment of MS as measured by MRI. The PRISMS trial (Prevention of Relapses and Disability by Interferon β -1a Subcutaneously in Multiple Sclerosis) evaluated the effect of IFN β -1a on RRMS using PD/T2 and gadolinium-enhanced T1 scans in a placebo-controlled study. As with the IFN β -1b study, a subgroup underwent monthly scans, while all patients had biannual MRIs. Actively treated patients had significantly reduced T2 activity compared with placebo, and in the subgroup undergoing monthly scans, reduction in activity became statistically significant after only two months of treatment.²⁵ Some of the patients received higher doses of IFN β -1a, and the authors found that PD/T2 scans were better able to detect a dose-effect response than gadolinium-enhanced T1 scans, with higher doses of the agent evidencing greater efficacy.²⁵

A reanalysis of the MRI data from an earlier study of IFN β -1a (Avonex) in RRMS has shown a significant effect of treatment on reducing progression of cerebral atrophy as measured by the BPF.¹ The BPF is calculated using semiautomated software and has been found to be reproducible and reliable. Of interest, the study suggests that atrophy as measured by the BPF is detectable in RRMS patients with the shortest disease duration, suggesting this is an early phenomenon in the progression of MS. Also, unlike the effect of IFN β -1a on measures of inflammation and myelin damage, the treatment effect on cerebral atrophy was not detectable in the first year of treatment, but appeared in the second year. The explanation for this observation is not yet clear.

Mitoxantrone

A placebo-controlled study of mitoxantrone in patients with RRMS evaluated the efficacy of the drug using T2-weighted scans. While clinical findings showed some reduction in the number of patients with confirmed progression of the disease as measured by EDSS, MRI data revealed only a trend towards a reduction in new T2 lesions. The investigators felt that the failure to measure TLV and the use of different brands of MRI machines might have caused this discrepancy.²⁶

Practical Applications Of MRI Technology To Clinical Care

There is a developing consensus that MRI has substantial value as a surrogate marker in evaluating treatment of MS, not only in clinical trials but also in the individual patient. Some have gone so far as to suggest that MRI is not a surrogate marker, but that it directly visualizes the evolving pathology in the brain.²⁷ Yet few neurologists use this measure to monitor a patient's progress or to evaluate current therapy. This is despite the fact that a number of trials have shown a correlation between a variety of MRI measures and long-term prognosis, as well as clear indications of therapeutic effect in a number of agents used in the treatment of MS. In addition, MRI measurements have revealed differences between the types of MS, with PPMS, for example, demonstrating the greatest spinal cord atrophy and the lowest TLV, and SPMS having the lowest MRS values. Findings such as these might have valuable applications to clinical practice not only in diagnosis, but also in assessing prognosis, identifying initial

treatment effect, and in monitoring persistence and/or magnitude of treatment in patients on disease course-altering therapies.

Cost issues have been a deterrent to MRI in the past. But the true cost of an MRI in many areas of the US is between \$350 and \$500, as reflected by the National Institutes of Health fee rate for MRI as well as the reimbursement rate for cranial MRI by managed health care plans. This is certainly competitive with many of the specialized blood tests that are ordered for patients, such as the IFN β neutralizing antibody test. Moreover, when the cost of treatment is taken into account—often \$12,000 to \$15,000 per year—the cost of an MRI either annually or biannually, to monitor the effectiveness of an agent, may be reasonable. This is particularly true in that current estimates of the incidence of neutralizing antibodies to IFN β in treated RRMS patients range from 5% to 35%. There are approximately 100,000 RRMS patients being treated with IFN β in the US. Since the cost of treatment exceeds \$10,000 per year, even if only 5% of patients on interferon therapy develop neutralizing antibodies, the cost of treatments that may have no opportunity of benefit would be \$50 million per year in the US alone. Of even greater importance however, is the cost to the patient in terms of ongoing demyelination, axonal loss, and accumulating disability that may be preventable by switching to an alternative therapy.

Detecting new lesions by gadolinium enhancement or T2 MRI may be the most sensitive way to detect onset of treatment effect with interferon and, possibly, immunosuppressive therapies. Detecting the onset of treatment effect by glatiramer acetate in individual patients by MRI remains challenging. At this point, brain atrophy appears to be the best indicator of disease progression and may prove the most useful for clinical application.²⁸ MRS NAA measures and MTR histograms hold promise for more sensitive indicators in the future, and may help distinguish pathologically between the various types of MS. As resolution improves and techniques become more automated and reproducible, it may become possible to pinpoint with greater accuracy the ongoing neuronal damage that is the hallmark of this disease and to document its initial stages. With normative data, these techniques may allow us to prognosticate more accurately, which will assist us in selecting patients for treatment and identifying an adequate treatment response in the individual patient.

Clearly, neurologists and radiologists can use the MRI experience in clinical trials to design more sensitive and effective imaging protocols for facilitating prognosis, monitoring disease course, and assessing treatment effect in MS patients in the clinical setting. Also, further improvements in the clinical imaging of MS will occur as specialized image analysis software becomes generally available. Since the effectiveness of current therapies is variable between patients, the development of tools to monitor disease activity and treatment effect in a given individual are key to the rational management of MS. Currently, the judicious use of MRI offers the most promise in terms of assisting neurologists in optimizing the application of currently available therapies to the needs of our patients.

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Osteoporosis in Multiple Sclerosis: a Frequent, Serious, and Under-Recognized Problem

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Abstract

Osteoporosis and fractures are extremely common in the multiple sclerosis (MS) population, especially in those women with MS who are postmenopausal and not on hormone replacement therapy (HRT). There is evidence of significantly increased fracture risk in MS patients who have been on steroids, although this appears to be due to increased falls in addition to osteoporosis. Additionally, evidence has indicated that high-dose pulse methylprednisolone has little effect on osteoporosis, but decreased mobility is a very significant factor in decreased bone density. Osteoporosis in MS results in part from causes present in the general population, but is significantly aggravated by immobility and probably by other drugs used to treat MS and its complications, including drugs known to increase bone loss (eg, diphenylhydantoin). Fractures in MS are a particularly serious problem in that the resulting immobility causes deconditioning. A fracture—any fracture—is a much more serious problem in those with MS than in the general population. For example, use of narcotics for pain control in the MS patient with a fracture can convert constipation to obstipation or even bowel obstruction. Deconditioning resulting from injury-related immobility recovers much more slowly than in healthy individuals, and may never return to the preinjury level. Often a fracture converts an individual from being ambulatory to permanent wheelchair status. With preventive measures and moderately effective therapy available, it is important to identify those at risk and initiate appropriate treatment.

Osteoporosis is a common and frequently serious problem in the general population, causing an estimated 1.3 million fractures per year in the United States alone.¹ While there are few studies on the subject, osteoporosis appears to be even more common and more serious in those with multiple sclerosis (MS),² but is seriously under-recognized. It causes considerable morbidity and occasional mortality in those affected.

Both osteoporosis and falls contribute to fractures in the MS population.² Low bone mass in these patient predicts fracture risk.³⁻⁶ In the MS population, falls are common and are a significant factor contributing to fractures.² In the authors' experience, a painful fracture, often a hip or vertebral fracture, converts an individual who is ambulatory with walking aids to a wheelchair-dependent state. Since the lack of coordination and weakness experienced by many of those with MS leads to falls, the risk of fractures in this population is quite high. Despite this, a Medline search for articles in the past decade with the key words *multiple sclerosis* and *fracture* yielded only two articles.^{2,7}

The severity of this problem is emphasized by an examination of results from the first eleven patients in whom we obtained vertebral bone density measurements after we became aware of the problem (see Table 1). Seven of our eleven patients meet criteria for osteoporosis, and the remaining four have osteopenia. All but three are men (owing to population bias of the

Veterans Administration medical center); however, this emphasizes the importance of this problem in men as well as women.

Table 1. Results of Bone Density Assessments in a Sample of MS Patients.

Age	Gender	T-score	EDSS*	Fracture?	Other factors
65	M	-5.9	8.5	no	
55	M	-5.1	8.5	no	seizures, low testosterone
69	M	-4.6	7	patella	
64	M	-4.6	7	no	
60	M	-4.4	7	no	
60	M	-3.1	7	tibia	
56	F	-2.7	7	ankle	postmenopausal, on HRT
56	F	-2.5	2.5	no	postmenopausal, on HRT
40	F	-2.2	9	no	premenopausal, African-American
53	M	-1.6	5	no	on Dilantin (phenytoin)
59	M	-1.2	7	no	

*Kurtzke Extended Disability Status Scale rating (0 = normal; 7 = wheelchair self-transfer; 10 = dead from MS).

It has long been possible to carry out some measures, such as calcium and vitamin D supplementation and hormone replacement therapy (HRT), to reduce the risk of osteoporosis; but until quite recently, there was no effective treatment that would significantly reduce fracture risk in those with established osteoporosis. With the development of bisphosphonate drugs (eg, alendronate [Fosamax[®]] and etidronate [Didronel[®]]) and the advent of the selective estrogen receptor modifiers (SERMs), there are now therapies that have been shown not only to increase bone density but to significantly reduce the risk of fractures.⁸⁻¹¹ Alendronate can be used at a low dosage to prevent bone loss and at a higher dosage to increase bone density.

Most of those who deal with neurologic disease consider management of osteoporosis outside their area of expertise and interest. Nevertheless, it is essential that we, as health professionals, become aware of the effects of the medications we use to treat neurologic diseases (eg, steroids, immunosuppressive agents, and antiepileptic drugs) on bone mass. We need to see that osteoporosis is identified when present and, once identified, is properly treated. Additionally, we need to identify those at risk and take steps to prevent or minimize bone loss.

Causes of Osteoporosis

Some of the most common causes of osteoporosis are listed in Table 2.^{12,13} The rate in postmenopausal white women who are not on hormone replacement is extremely high, and that risk is significantly increased by the presence of decreased mobility. Causes that are particularly likely to contribute to osteoporosis in the MS population are listed in Table 3. In addition to those with known risk factors for osteoporosis, one should check for osteoporosis in any individual with fractures that are inexplicable or are the result of seemingly trivial trauma.

There are several methods of determining bone density. The two most common are dual-energy x-ray absorptiometry (DEXA) and quantitative computerized tomography (QCT). The

former is less expensive, more accurate, takes only 10 minutes, and exposes the individual to minimal radiation.^{14,15} Both provide a value in terms of standard deviations (SD) or T-score relative to age matched controls. A T-score of -1 equals -1 SD; -2 equals -2 SD, and so on. A bone density T-score of -1 to -2.5 is defined by the World Health Organization (WHO) as osteopenia, and a T-score less than -2.5 is defined as osteoporosis.¹⁴ Severe osteoporosis is defined as a value -2.5 SD or lower, with concomitant fragility fractures. We have seen values as low as -5.9 in a male wheelchair patient with MS.

The relative risk of fracture is 2.0 for each SD below normal; that is, the risk of fracture doubles for each SD below normal.^{6,8} Anyone who is at risk should be evaluated and considered for preventive therapy, even if not yet osteoporotic. Those with osteoporosis require treatment to reduce fracture risk. While the risk of osteoporosis is significantly less in patients of races other than Caucasian, it should not be ignored.

Table 2. General Risk Factors for Osteoporosis

Common risk factors

- Hypogonadism (particularly in postmenopausal women not receiving hormone replacement)
- Chronic or recurrent use of corticosteroids
- Small bone structure
- Body weight under ideal
- Family history of osteoporosis
- Caucasian race
- Low dietary calcium intake
- Immobility
- Sedentary lifestyle
- Cigarette smoking
- Alcohol abuse (> 5 oz/day)
- Aging

Metabolic Causes

- Vitamin D deficiency
- Malabsorption syndromes
- Hyperthyroidism
- Hyperparathyroidism
- Lactose deficiency
- Uremia
- Hypogonadism
- Cushing's syndrome
- Multiple myeloma
- Paget's disease of bone
- Malignancies causing weight loss

Medications and Drugs

- Long-term anticonvulsant drugs (especially diphenylhydantoin)
- Long-term heparin
- Caffeine
- Synthroid

Table 3. Common Causes of Osteoporosis in MS

Immobility, especially decreased weight-bearing activity
Underweight
Hypogonadism
Postmenopausal women not receiving hormone replacement
Testosterone deficiency in males with MS
Repeated corticosteroid use

Evaluation of Individuals With Osteoporosis

Although osteoporosis is common in the elderly (particularly those who are disabled), once a diagnosis is made, some basic evaluation is indicated to discover or rule out possible causes other than, or in addition to, the obvious ones. A general history and physical examination will usually be adequate to detect evidence of malignancy, hyperthyroidism, or Cushing's syndrome, although evidence for the latter is often ignored in individuals who have been on steroids in the recent past. Serum calcium and phosphorus should be checked at least twice, and a 24-hour urine calcium analysis should be done to rule out hyperparathyroidism. If there is a possibility of hyperparathyroidism, levels of parathyroid hormone should be measured using parathyroid hormone by radio immunoassay (iPTH) evaluation. A panel of hepatic function tests should be completed to rule out liver disease, and serum creatinine and blood urea nitrogen (BUN) levels should be measured to rule out renal disease. A check of 25-hydroxy vitamin D level will rule out vitamin D malabsorption or deficiency. Additionally, serum protein and urine protein electrophoresis should be considered to rule out multiple myeloma. If any of these tests are positive, appropriate further investigation and evaluation and treatment by an internist is warranted. In men with MS, a measurement of testosterone level is indicated, since they have an increased risk of hypogonadism.

Management of Osteoporosis

Disease management in individuals with both MS and osteoporosis has two major aspects. The first is prevention of falls and resultant fractures, and the second is prevention of and/or treatment for the osteoporosis itself; both are important. Fractures cause major disease management problems in persons with MS, making fracture prevention as important an aspect as treatment, which takes a considerable time to have an effect.

Complications of Fracture

Fractures have serious consequences in MS. Patients need to be educated about the risks for fracture as well as about measures to prevent falls. The restricted activity incident to a fracture regularly leads to deconditioning to a point where ambulation is no longer possible. If ambulation is possible, it may take weeks or months of therapy to regain lost physical capabilities. Expected mortality rate is 6.3% in the total population; after a hip fracture the expected mortality rate is 36.7%.¹⁵ While mortality may not actually reach the expected rate of 36.7% in the MS population, it is certainly going to be significant.

Ileus (obstruction of the intestines) is one complication of fracture. Due to narcotic use to control pain, the bowels—normally sluggish in MS—become essentially paralyzed. Most physicians are unaware of the seriousness of this problem and the need for preventive

measures. Another complication resulting from decreased mobility is thrombophlebitis, with the associated risk of pulmonary embolism. This is particularly significant following fracture of one of the lower extremities. Additionally, individuals with a Kurtzke EDSS rating of 6 or higher almost always have some respiratory compromise and may have some dysphagia when stressed. Those whose rating is EDSS 7 or higher almost always have a markedly decreased respiratory capacity¹⁷—often as little as 1 L—accompanied by a weak ineffective cough. Following a painful fracture, these individuals are at risk for aspiration pneumonia, which can be life threatening.

Prevention of falls

Many of those with MS have a tendency to fall, but do not worry much about the risk falls represent. Often, denial is a big part of this problem. Individuals with MS and their families need to be educated and made aware of these risks. They need to know if their bones are weak and to realize that a fracture is a much more serious problem in MS than in those who are healthy. Individual assessment of the situations in which falls occur and development of strategies for fall prevention are part of this education.

Physiatrists, physical therapists, and MS nurses can play an important role in the education process. Nurses are more likely to be aware of falls, because they spend a great deal of time with patients and assume the most responsibility for patient education and situational risk assessment. Physical therapists and physiatrists are in the best position to assess physical capacity, to recommend or prescribe appropriate balance-aid equipment, and to help with the educational process.

A host of devices are available to reduce the risk of falls; these include canes and crutches, walkers, grab bars, bath and shower seats, and bedside commodes and urinals. Evaluation of where and when falls occur, education in preventive measures, and provision of appropriate aids are important in avoiding fracture.

Prevention and Treatment of Osteoporosis

The relative efficacy and associated risks/adverse events for agents used to treat osteoporosis are listed in Table 4. Alendronate is the only drug proven to decrease the risk of extremity fractures, whereas both alendronate and raloxifene (Evista[®]) decrease the risk of vertebral fractures.^{9-11,18} In addition, nasal salmon calcitonin has been shown to reduce the risk of fracture at the spine by approximately one third (Novartis Corp., data on file). HRT has long been known to reduce osteoporosis and fracture risk, but good data on this are hard to find.

Raloxifene is in the SERM category of drugs, and its only listed indication for use is the prevention of osteoporosis in postmenopausal women. It appears not to have been tested in premenopausal women, and there are little data on its use in men. Its mode of action is similar to HRT, and the two should not be used concurrently. Alendronate, on the other hand, can be used in addition to HRT and can also be used in premenopausal women. We prefer to use alendronate for its proven effect on both extremity and vertebral fractures and greater effect on bone density. Alendronate can be irritating to the esophagus, is poorly absorbed in the presence of food, and requires special precautions. It should be taken first thing in the morning with a full glass (8 oz) of water. Nothing else—neither food nor medicine—should be taken for 1 hour afterward. It is important for patients to remain upright during this period to minimize the risk of esophageal irritation, which is the most common complication. Patients should not lie down until they have eaten.

Measures to reduce or prevent osteoporosis in those with MS include education regarding adequate calcium and vitamin D intake, avoidance of smoking and excessive alcohol intake, and regular exercise, particularly weight-bearing exercise. Smoking cessation is particularly important. In menopausal and postmenopausal women, HRT is indicated. The concern that

estrogen might make MS worse has been expressed, but there is no good evidence that estrogen adversely affects the disease process. Patients who are on chronic steroid therapy, regardless of the reason, should be on a preventive regimen for osteoporosis.

Assuming that we have eliminated or have treated causes of osteoporosis other than steroid effects and immobility, treatment is based on calcium and vitamin D supplementation and use of one of the available therapeutic agents. We recommend a regimen of calcium carbonate (or another calcium compound) 500 mg to 650 mg bid, vitamin D 400 IU qid, and alendronate 5 mg to 10 mg a day. In postmenopausal women, HRT is also indicated. Raloxifene might be used in place of HRT in this circumstance, but there is no data available on combined usage of alendronate and raloxifene.

Studies have shown that treatment with alendronate can reduce the risk of vertebral compression fracture, hip fracture, and wrist fracture by about 50% in the first 2 years of treatment as compared to raloxifene, which reduces vertebral compression fractures but has no demonstrated effect on extremity fractures. Given the significance of fractures in the MS population, it behooves us to identify those with osteoporosis and initiate therapy.

Table 4.⁹⁻¹³ *Fracture Risk Reduction With Agents Used for Osteoporosis Prevention and Treatment.*

Treatment	Relative Fracture Risk With Use		Risks and Side Effects
	Spine	Hip	
Hormone replacement	0.4-0.6	~0.6	Increased risk of thrombophlebitis, uterine bleeding, breast enlargement; slightly increased risk of uterine cancer
Raloxifene (Evista [®])	0.5	NS	3.1-fold risk of thrombophlebitis
Calcitonin (Miacalcin [®] , Calcimar [®])	~.65	NS	Nausea; allergic hypersensitivity reactions
Alendronate (Fosamax [®])	0.47	0.49	Esophageal irritation; [†] ulcers; flatulence
Etidronate (Didronel [®])	NS	NS	Must be given in 14-day cycle repeated every 3 months; not approved for treatment of osteoporosis in US; does increase bone density

NS = no statistically significant effect demonstrated.

[†]Must be administered on an empty stomach with a full glass of water, with no food or medicine for 1 hour post-dose. The patient must remain upright during this time.

Summary

Osteoporosis is a common, serious, and treatable condition in persons with MS—particularly those with reduced mobility—and results in fractures in a significant proportion of this population. Since effective treatment is available, it is incumbent upon us as MS professionals

to identify those at risk for osteoporosis and those who already have this condition. Once identified, appropriate intervention to reduce the risk of fracture is imperative.

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Abstracts from the Annual Meeting of the Consortium of Multiple Sclerosis Centers

June 22-25, 2000
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The annual meeting of the CMSC offers dozens of platform and poster presentations on every aspect of MS care around the globe, including diagnosis and treatment, epidemiology, physical, occupational, and speech therapy, and emotional and psychosocial report. Read the abstracts from the physicians, nurses, rehabilitation specialists, and other MS care providers who are presenting their innovative research at this year's meeting.

Platform Presentations

1. The Effects of Cognitive-Behavioral Therapy in Patients with MS-Associated Personality Disorder

Ralph Benedict, PhD

2. A Web Site Focusing on Complementary and Alternative Medicine for Multiple Sclerosis

Allen Bowling, MD, PhD

3. Submaximal Fitness Testing and Client-Monitored Interval Training Have a Positive Effect on Deconditioning

Sandra Brunham, BSR(PT), MSc

4. Multiple Sclerosis in Latin America: Changing Concepts, Current Status

Jose A. Cabrera-Gomez, MD

5. A Comparison of Rehabilitation Against Standard Therapy in Multiple Sclerosis (MS) Patients Receiving IV Steroid Treatment

Jenny Craig

6. Comparison of Exacerbations among Breast- vs. Formula-Feeding Mothers with MS

Elsie Gulick, PhD, FAAN, RN

7. Changes in Health-Related Quality of Life in Persons with Multiple Sclerosis

Wilma Hopman, MA (Psych)

8. Effect of Variable Dosing Regimens of Intravenous Methylprednisolone (IVMP) on Recovery During an Acute Exacerbation in Multiple Sclerosis Patients Admitted to Hospital

Deena Lisak, BS, MA

9. Efficacy and Safety of Provigil® (Modafinil) for the Treatment of Fatigue in Patients with Multiple Sclerosis (MS)

Joanne Lynn, MD

10. Effectiveness of an Energy Conservation Course for Individuals With Multiple Sclerosis

Virgil Mathiowetz, PhD, OTR

11. The Consequences of MS: Disability Increases the Odds of Being Separated or Divorced

Metz LM, Rose SM, Patten SB, Murray TH, Lagendyk LE, McGuinness SD, Fisk JD, Reimer M, Brown M, and Jacobs P

12. The Effect of a Supervised Aquatics Program on the Health-Related Quality of Life for Persons with Progressive Multiple Sclerosis

Tammy Roehrs, MA, PT

13. Determinants of Health-Related Quality of Life in Multiple Sclerosis: The Role of Illness Intrusiveness

Marla Shawaryn, PhD

14. Bone Density in Women with MS

Suzanne Smeltzer, RN, MS, EdD, FAAN

15. Caregiver Burden: Meeting the Needs of People who Support the Person with Multiple Sclerosis

Judy Wollin, RN, PhD

16. MS Treatment Patterns at the End of the 20th Century

Timothy Vollmer, MD

17. Interferon Beta Therapy Combined with Steroids and Azathioprine in Relapsing-Remitting MS: Toleration and Effect

Veronita Ticha, MD

18. Rehabilitation Helps In Coping With Fatigue

Soile Niemi

The Effects of Cognitive-Behavioral Therapy in Patients With MS-Associated Personality Disorder

Ralph Benedict, PhD; A Shapiro; C Miller; and L Jacobs

Disorders of personality in MS have been reported for at least a century. Recent work shows a significant correlation between abnormal imaging and acquired traits such as euphoria, social disinhibition, and egocentric speech. We tested the effectiveness of a cognitive-behavioral intervention called Neuropsychological Compensatory Training (NCT), designed to mitigate the influence of MS-associated personality disorder (MAPD). Fifteen patients were randomly assigned to one of two treatments: active (NCT) and placebo (nonspecific supportive counseling). All patients exhibited signs of MAPD. Most were euphoric, and all had difficulty with egocentric speech. Fifteen normal volunteers, matched to the patient group on age and education, were also studied at baseline. NCT included 12 weekly one-hour sessions, involving both the patient and a designated caregiver. There were three objectives: 1) teach patient and caregiver to understand the neurologic basis of abnormal behavior, 2) improve capacity to appreciate the perspective of others, and 3) diminish the frequency of socially aggressive behavior. Patients assigned to the placebo condition received standard supportive

psychotherapy from a Master's-level counselor naive to the active condition objectives and techniques. The counselor was well trained in general psychotherapy but not knowledgeable in the neuropsychological foundations of MS. Treatment effects were examined with a Social Aggression Scale adapted for MS (MSSAS). MSSAS scores exceeded 4 in all MS patients, and were lower than 4 among all controls. Pre/post treatment change scores were greater for the actively treated group ($t = 3.2, P < .01$). A reliable difference was also found on the Excessive Speech subscale ($t = 2.4, P < .05$). We conclude that the NCT intervention developed here had a significant positive impact on cognitively and socially impaired MS patients. This is the first behavioral intervention reported for patients that would have been labeled euphoric in previous descriptive studies.

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A Web Site Focusing on Complementary and Alternative Medicine for Multiple Sclerosis

Allen Bowling, MD, PhD; Thomas Stewart, JD, PA-C

Introduction: Many people with multiple sclerosis (MS) use complementary and alternative medicine (CAM). Health care professionals, including those who specialize in MS, generally have little or no knowledge, training, or experience with CAM and may face liability if they include CAM in their practices. Lay books on CAM do not have detailed, objective MS-relevant CAM information. This lack of readily accessible CAM information creates an unsafe and unhelpful environment for people with MS who are interested in CAM.

Method: To provide objective and useful information about CAM to people with MS, we have developed a Web site (www.ms-cam.org) that covers more than 50 different types of CAM. Potential risks and benefits for MS and its associated symptoms are identified, as are potential drug interactions. The evidence-based information was obtained from the scientific and clinical literature and is presented in a format that is easily accessible to most people with MS. The Web site also serves as a data collection tool: In anonymity, visitors are asked demographic information and are encouraged to disclose their own experiences with CAM, through threaded conversations and surveys. The Web site is operated by the Rocky Mountain MS Center, a nonprofit organization.

Data: Data will be presented about the demographics of Web site users, the most frequently visited topics, and the content of the threaded discussions.

Conclusion: The Web site is a novel source of MS-specific CAM information for people with MS. The Web site may also be a valuable tool for obtaining data about patterns of CAM use and the self-perceived benefits and harms of different CAM therapies.

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Submaximal Fitness Testing and Client-Monitored Interval Training Have a Positive Effect on Deconditioning

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Objective: Deconditioning or lack of fitness, is a predictable sequel of chronic progressive disabling conditions such as MS. Physiotherapy often neglects the areas of fitness testing and aerobic exercise in adults with neurologic conditions. Adults with MS find exercising for health and fitness increasingly difficult and fatiguing as their condition progresses. Guidelines for fitness testing and aerobic exercise at submaximal, self-paced rates have been developed by the American College of Sports Medicine and are appropriate for adults with MS. This presentation describes a program that was effective in changing fitness levels in adults with neurologic conditions.

Subjects: Thirty-four adults with various neurologic conditions, including MS, who were not receiving any other forms of rehabilitation or exercise, attended an outpatient fitness program.

Methods: Interval training—standard exercise equipment, customized for the individual, with on/off ratios of one to five minutes on, 30 to 60 seconds off, were used. Clients were taught to monitor their submaximal efforts using the Borg Scale of Perceived Exertion. Heart rate, blood pressure, and oxygen saturation levels were monitored throughout the eight-week program. Clients exercised once a week at the program and twice a week at home. Pre- and post-program assessments were determined by distance covered during self-paced six-minute walk, wheel, or arm pedal tests.

Results: Significant gains in endurance ($P > .0001$) were achieved by the group.

Conclusion: Fitness can be safely and effectively addressed in adults with neurologic conditions.

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Multiple Sclerosis in Latin America: Changing Concepts, Current Status

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Interest in multiple sclerosis (MS) has steadily increased in Latin America. Despite considerable regional differences, recent observations in several countries point to an apparently increasing incidence and a prevalence higher than traditionally believed. There are also unique characteristics among the MS Latin-American populations such as a highest prevalence among Mestizos but affecting as well Caucasians and across the continent, consistent reports of MS not affecting nonmixed Indoamerican groups with strong Mongoloid genetics. Brazil, Cuba, and Martinique report a prevalence in Afro-Americans and mulattos higher than similar groups elsewhere. Cubans and Cuban-Americans residing in Florida, USA show a greater percentage of primary/progressive forms (40 per 100,000), while Cubans living on the island show an identical tendency, both areas being located practically within the same latitude. MS in Cuba demonstrates great variation in zonal prevalence (4.3 to 106 per 100,000) apparently related to a characteristically variable racial distribution in the island. Puerto Rico claims a high concentration. Mexico has experienced a 29-fold increase since the original reports from the 1970s—producing a change from a prevalence of 1.6 to 12 per 100,000, as current studies indicate. Argentina and Uruguay have the strongest Caucasian genetic influence in Latin America, and both have consistent national prevalence figures: 15.6 to 17.50 per 100,000 in Argentina, 17.6 per 100,000 in Uruguay. This review also discusses the limitations encountered in Latin America to study MS and the factors that have contributed to the apparent prevalence increase.

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A Comparison of Rehabilitation Against Standard Therapy in Multiple Sclerosis (MS) Patients Receiving IV Steroid Treatment

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Background: There is evidence to support the use of intravenous methylprednisolone (IVMP) in the treatment of MS relapse but very little research to support physiotherapy as being of benefit. Previous research studies have focused on rehabilitation or drug management alone. It is felt among therapists that steroids, given in conjunction with appropriate therapy, will lead to a better functional outcome.

Aim: To evaluate the benefits of IVMP and therapy compared to IVMP alone, in relation to disability and quality of life.

Study design: This will be a randomized controlled study of patients who are admitted to the Neurology wards at WCNN and who are confirmed by a consultant neurologist to have had a definite relapse of MS in the previous eight weeks that is severe enough to warrant IVMP (1g IV daily for 3 days).

Baseline assessments will be administered to both groups before IVMP commences. The control group will be managed by standard routine. The treatment group will be given multidisciplinary team assessment and treatment and appropriate follow-up. Measures will be repeated at one

and three months. The Outcome Measures are Guy's Neurological Disability Scale, Motor Club Assessment, Barthel Index, and SF-36 & Kurtzke Expanded Disability Status Scale.

Initial results: The sensitivity to change of the outcome measures in a cohort of 25 consecutive patients will be analyzed and routine British practice described, allowing normative data and power calculations to be established.

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Comparison of Exacerbations among Breast- Versus Formula-Feeding Mothers with MS

Elsie Gulick, PhD, FAAN, RN, June Halper, MSN, RN, CS, FAAN

Purpose: Exacerbation rates in mothers with MS increase significantly during the first three to six months postpartum compared to the pregnancy period. Increased levels of cortisol and either low or high levels of prolactin have immunosuppressant effects. Immune suppression is a deterrent to MS exacerbations. Increased levels of cortisol and prolactin accompany breast-feeding. The purpose of this study was to compare the prevalence of MS exacerbations during the first six postpartum months between breast-feeding (BF) and non-breast-feeding (NBF) mothers with MS.

Sample: The sample of 62 BF and 16 NBF mothers completed ADL level of functioning, MS symptom and postpartum support scales with established reliability and validity at 1, 3, and 6 months after birth, and weekly diaries to report percent of infant feedings by breast or formula and mother and infant health status. Mothers averaged 33.0 years (standard deviation [sd], 4.4) in age, 5.4 years (sd, 4.1) since MS diagnosis, and 15.2 years (sd, 1.9) of education, with no significant differences between groups and no differences for ADL functioning; level of postpartum support; or motor, elimination, and sensory symptoms at one, three, and six months. The NBF group reported more brainstem symptoms at one month and more emotional distress symptoms at three and six months than the BF group (all $P < .05$).

Study findings: Findings indicated 18 (29%) BF and seven (43%) NBF mothers had neurologist-confirmed MS exacerbations. Average number of months to first exacerbation was 2.7 with a range of 0.4 to 5 for BF, and 2.1 with a range of .8 to 6 for NBF mothers. Of the BF mothers, three (4.9%) had a second and one (1.9%) had a third exacerbation, compared to four (25%) who had a second and two (13%) who had a third exacerbation for NBF mothers. More symptoms were reported by mothers with MS exacerbations than those not reporting exacerbations for motor, brainstem, sensory, and elimination at one, three, and six months (all $P < .05$).

Further study: Results of this study will be helpful in counseling women with MS who are contemplating pregnancy or breast-feeding. Further study is warranted to determine if serum levels of prolactin and cortisol affect the immune regulatory system (ie, CD4+, CD8+ T cells and NK cells) in breast-feeding compared with formula-feeding mothers.

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Changes in Health-Related Quality of Life in Persons with Multiple Sclerosis

Wilma Hopman, MA (Psych)

Background: Over the past 20 years, it has become increasingly apparent that the patient's point of view is an important component in the assessment of health care outcomes, particularly for chronic disease, where quality rather than length of life may be more relevant. Accordingly, measurement of health-related quality of life (HRQL) is being used to supplement clinical measures in the assessment of health. In a previous study, we did a cross-sectional analysis of HRQL in persons with multiple sclerosis. The present study was undertaken to measure changes in HRQL over a four-year period in the same group.

Methods: Individuals who participated in the previous study were contacted to see if they would be willing to take part in a follow-up assessment of HRQL. Forty-five patients agreed to complete the SF-36 and a questionnaire to collect demographic and other information. Clinical data were abstracted from patient charts. Changes in each of the eight domains of the SF-36 were calculated by subtracting follow-up scores from baseline scores. Linear regression models were developed to determine which factors were associated with changes in HRQL.

Results: A significant deterioration in health status was observed in the physical functioning, role physical, general health, and social functioning domains. In contrast, slightly over 50% of those surveyed showed an improvement in the mental health domain. Sex, family history of MS, and use of interferon beta were some factors that were significantly associated with changes in HRQL.

Conclusions: Assessment of HRQL over time reveals a number of significant changes, which may be related to demographic and clinical characteristics. A better understanding of how these factors affect HRQL may contribute to improved patient care and decision making.

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Effect of Variable Dosing Regimens of Intravenous Methylprednisolone on Recovery During an Acute Exacerbation in Multiple Sclerosis Patients Admitted to Hospital

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Objective: To investigate the beneficial effects of variable dosing regimens of intravenous methylprednisolone (IVMP) in MS patients admitted to a hospital for the treatment of an acute exacerbation. To study the relationship between demographic variables and response to treatment with IVMP.

Background: Acute exacerbations of MS are routinely treated with IVMP. While the beneficial effects of IVMP in the treatment of an acute exacerbation are well known, there is no consensus regarding the optimal dose of IVMP during an acute exacerbation. Most physicians treat an acute exacerbation of MS with 1 to 7 g of IVMP administered over three to seven days with or without prednisone taper. Furthermore, definitions of high- and low-dose IVMP are arbitrary.

Design/methods: We performed a retrospective chart analysis of 200 consecutive admissions with an admitting diagnosis of "acute exacerbations of MS" to a teaching hospital affiliated with Wayne State University. All 200 patients received IVMP. Definition of high- and low-dose IVMP was based on variable dosing regimens of IVMP administered. Low-dose IVMP was defined as a total dose of < 3 g given over three to five days. High-dose IVMP was defined as ≥ 3 g (up to a maximum of 10 g) given over three to five days. The primary outcome was the difference between Kurtzke's Disability Scale EDSS on admission and after the last dose of IVMP.

Results: At the time of submission of this abstract, 95 admissions had been reviewed. Using the definitions proposed by Lublin et al, 49 patients had relapsing-remitting (RR) and 46 patients had secondary progressive (SP) MS with superimposed exacerbations. Mean length of hospital stay ($n = 95$) was 5.1 days. Overall ($n = 95$), mean EDSS scores on admission and upon completion of treatment with IVMP were 5 and 5.1, respectively (reduction in mean EDSS -0.77 , $P < .00001$), indicative of a treatment effect. However, there was no significant difference in mean EDSS reduction between the high- and low-dose IVMP groups (-0.78 and -0.73 , respectively, $P > .05$). Treatment with IVMP (high- and low-dose) showed a significant reduction in mean EDSS in patients with RRMS compared to SPMS (-1.1 and -0.42 , respectively, $P = .0002$). RRMS treated with high-dose IVMP showed significant reduction in mean EDSS compared to high-dose-treated SPMS patients (-1.08 and -0.44 , respectively, $P = .0003$). Similarly, RRMS treated with low-dose IVMP also showed a significant reduction in mean EDSS compared to low-dose-treated SPMS patients (-1.25 and -0.29 , respectively, $P = .009$). Within the RRMS group ($n = 49$), treatment with low-dose IVMP led to a greater reduction in mean EDSS (-1.25) than did high-dose IVMP (-1.08); but this difference did not reach statistical significance ($P > .05$). Conversely, within the SPMS group ($n = 46$), treatment with high-dose IVMP showed a greater reduction in mean EDSS (-0.45) compared with low-dose IVMP (-0.29); but this difference was not significant ($P > .05$).

Conclusions: Our preliminary analysis indicates that MS patients treated with IVMP during an acute exacerbation show a significant improvement in clinical outcome. However, we were unable to demonstrate a significant therapeutic difference between high and low doses of IVMP for the entire group ($n = 95$) analyzed so far. RRMS treated with high- or low-dose IVMP appear to demonstrate significant improvement compared to SPMS. We also observed that RRMS and SPMS patients appeared to improve more with low- and high-dose IVMP, respectively. We are continuing to analyze and complete 200 consecutive admissions. Details of the analysis will be presented, including relationship between gender, admission EDSS, disease duration, type of neurologic deficits on admission, and response to treatment as well as time to subsequent exacerbation.

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Efficacy and Safety of Provigil® (Modafinil) for the Treatment of Fatigue in Patients With Multiple Sclerosis (MS)

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Introduction: Fatigue is a frequent symptom and primary cause of disability in patients with MS. Modafinil, a novel wakefulness-promoting agent, is effective and well tolerated for the treatment of excessive daytime sleepiness in patients with narcolepsy. This study evaluated the efficacy and safety of modafinil for the treatment of fatigue in patients with MS.

Methods: Patients age 18 to 65 years with a diagnosis of MS, a stable disability level of ≤ 6 on the Kurtzke EDSS, and a mean score of at least 4 on the Fatigue Severity Scale (FSS) were enrolled in a nine-week, forced-titration, placebo-controlled study. Exclusion criteria included a diagnosis of narcolepsy, sleep apnea, clinically significant major disease, and recent use of medications affecting fatigue. Patients received placebo during weeks one and two (baseline), 200 mg/d modafinil during weeks three and four, 400 mg/d modafinil during weeks five and six, and placebo during weeks seven through nine. Efficacy was evaluated using the 9-item FSS, a visual analogue scale for fatigue (VAS-F), the 21-itemed Modified Fatigue Impact Scale (MFIS), and the 8-item Epworth Sleepiness Scale (ESS). All efficacy measures were assessed by patients, who were blinded to treatment. Adverse events (AEs) were recorded throughout the study.

Results: Seventy-two patients (mean age, 44 years; MS type: 74% relapsing/remitting, 7% primary progressive, 19% secondary progressive) were enrolled and received treatment. Modafinil 200 mg/d significantly improved fatigue compared with placebo on all three fatigue scales. Mean scores were: FSS, 5.5 versus 4.6 for placebo ($P < .0001$), VAS-F, 5.4 versus 4.5 ($P = .0031$), and MFIS, 37.7 versus 44.7 ($P = .0002$). Mean fatigue scores for modafinil 400 mg/d were not significantly different from placebo. Mean ESS scores were significantly improved ($P < .0001$) with both doses of modafinil when compared with the mean score at screening. The most frequent AEs were headache (placebo, 15%; 200 mg, 17%; 400 mg, 11%), asthenia (placebo, 8%; 200 mg, 3%; 400 mg, 15%), and nausea (placebo, 6%; 200 mg, 11%; 400 mg, 6%). No serious AEs were reported. Sixty-four patients (89%) completed the study.

Conclusion: Modafinil 200 mg/d significantly improves fatigue and is well tolerated in patients with MS.

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Effectiveness of an Energy Conservation Course for Individuals with Multiple Sclerosis

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Fatigue is a common MS symptom that can impact most aspects of daily activities and quality of life. Education on energy conservation principles is a common occupational therapy (OT) intervention for dealing with fatigue, but research regarding its efficacy is limited. This study examined the outcomes of an energy conservation (EC) education program for 54 individuals who have MS. Three research questions were addressed: 1) Does the EC course increase EC behaviors in participants with MS? 2) Does the integration of EC principles into daily activity result in reduced impact of fatigue on participant's lives? 3) Does the integration of EC principles improve the perceived quality of life and self-efficacy of persons with MS?

Participants volunteered for the study by responding to an advertisement placed by the MS Society. To be included, participants needed to be literate adults with MS living independently in the community, be able to attend at least five out of each six sessions, and experience fatigue severe enough to interfere with daily activities. Participants' data were eliminated if they experienced an exacerbation during the study, had fatigue medication changes, or had cognitive problems that interfered with new learning. A repeated measure design was used: a six-week control group (support group), followed by the six-week no-intervention period. The three dependent variables (fatigue, self-efficacy, and quality of life) were measured using the Fatigue Impact Scale (FIS), the Self-Efficacy Gauge, and SF-36 health survey, respectively. Results indicate that fatigue, self-efficacy, and some aspects of quality of life improved significantly following the EC course and were maintained six weeks later. These improvements were not seen after the support group only. These results support using EC education as an effective intervention for managing fatigue for individuals with MS.

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The Consequences of MS: Disability Increases the Odds of Being Separated or Divorced

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Objective: While many suspect that marital breakdown is often disease-related, evidence for this association is lacking. This study evaluates the relationship between marital status and MS while controlling for age and gender.

Methods: A population-based sample of 219 patients from two Canadian MS clinics (in Calgary and Halifax) was recruited and was stratified by EDSS severity group (0.0 to 2.5, 3.0 to 5.5, 6.0 to 8.0, 8.5 to 9.5). Patients were interviewed and examined for relationships between variables. Multivariate analysis, restricted to patients over age 29, used EDSS, age, gender, site, duration since symptom onset, duration since diagnosis, age at onset, number of relapse days in past two years, and whether disease was currently stable.

Results: The probability of being divorced or separated was statistically related to age and EDSS group, but not to gender. The probability of divorce/separation for patients with EDSS between 8.5 and 9.5 was nearly double that expected in the general populations (SMR = 1.88, $P = 0.056$). Odds ratios for divorce/separation increased as disability severity increased when compared to the least disabled group (EDSS < 3.0). The odds ratio for EDSS group 3.0 to 5.5 was 2.0 (95% CI 0.7 to 5.9); for EDSS group 6.0 to 8.0 it was 2.7 (95% confidence interval [CI], 1.0 to 7.6); and for EDSS group 8.5-9.5 it was 5.7 (95% CI, 1.7 to 19.5). Controlling for EDSS group, the probability of divorce/separation decreased with age (odds ratio, 0.96 for a one-year increase in age; 95% CI, 0.93 to 1.0).

Conclusions: Greater disability increases the odds of being separated or divorced for those with MS. This association is better appreciated when the divorce/separation rates of more disabled groups are compared with the least disabled group. The lower rate in the least disabled group probably reflects differences between the demographic profiles of the MS population and the general population.

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The Effect of a Supervised Aquatics Program on the Health Related Quality of Life for Persons With Progressive Multiple Sclerosis

Tammy Roehrs, MA, PT, Marjorie Padula, MD, PhD, Rifaat Bashir, MD

Purpose: The purpose of this pilot study was to evaluate the effects of a regular aquatic exercise intervention on the quality of life of persons with either primary or secondary chronic progressive multiple sclerosis (MS).

Methods: Thirty-one subjects categorized with progressive MS consented to participate. In a crossover design, each subject was scheduled for 12 weeks of aquatic exercise intervention and 12 weeks of no intervention. The Multiple Sclerosis Quality of Life Inventory (MSQLI), the Medical Outcomes Study Short Form (SF-36; a component of the MSQLI), the Beck Depression Inventory II (BDI), and the State Trait Anxiety Inventory (STAI) were administered before and after each 12-week session. Two-way RM ANOVA was used to determine the effect of exercise and session order on these scores.

Results: Twelve subjects withdrew from the study, owing to exacerbations, excessive fatigue, systemic infections, lack of caregiver support, or dissatisfaction with the class. Of the remaining 19 subjects, 14 attended at least 50% and eight subjects attended at least 75% of the exercise sessions. Barriers to compliance included transportation issues, inclement weather, isolated neurologic symptoms, illness, and social activities. Data from the group that attended 75% of the exercise classes were evaluated. Significant improvements with exercise were found in the following subscales of the SF-36: bodily pain, social functioning, and general health. Session order had a significant effect on the general health subscale of the SF-36.

Conclusions: The data suggest that exercise may have a positive effect on persons with MS. For future studies, we suggest evaluating the relationships of level of disability to: 1) improvement in quality of life, and 2) compliance and attrition.

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Determinants of Health-Related Quality of Life in Multiple Sclerosis: The Role of Illness Intrusiveness

Marla Shawaryn, PhD, Kathleen Schiaffino, PhD, Nicholas LaRocca, PhD

Multiple sclerosis (MS) is a common demyelinating chronic illness that primarily affects young adults. It is characterized by its progressive and unpredictable nature and poses many physiological and psychological challenges to both the individual and the family. Recent research has examined the impact of MS on health-related quality of life (HRQL). HRQL facilitates study of disease impact not only from a medical or physiological perspective, but also from social, psychological, and economic vantage points. This study was focused on clarifying the relationship between MS and HRQL by investigating how illness intrusiveness may play an intermediary role between the impact of MS and HRQL.

Participants consisted of 90 individuals with MS who were recruited from the Medical Rehabilitation Research and Training Center for Multiple Sclerosis at Saint Agnes Hospital in White Plains, New York. They completed brief neuropsychological measures and self-report questionnaires measuring HRQL, psychological adjustment, and illness intrusiveness.

Results indicated that physical aspects of HRQL, both generic and MS-specific, were significantly predicted by disease severity, whereas mental and emotional aspects of HRQL were predicted by information processing speed. Disease severity and information processing speed predicted depression and well-being. The extent to which individuals viewed the MS as intrusive mediated the manner in which disease severity predicted each of the following: physical HRQL, fatigue, and depression.

Implications of the current research underscore the need for broader scopes of assessing MS and its impact on the individual. The data also serve in supporting the use of HRQL as it is broadly defined in assessing outcome in chronic illness. While in most cases physical indices of disease predict physical quality of life, and cognitive assessment predict mental and emotional quality of life, the individual's perception of MS is a major determinant of adjustment. This points to the need for psychological intervention in helping individuals adapt to MS.

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Bone Density in Women with MS

Suzanne Smeltzer, RN, MS, EdD, FAAN, Vanessa Zimmerman, Lilia Fernandes

Many women with MS are at risk for osteoporosis because of their inability to engage in weight-bearing exercise, use of steroids to treat exacerbations, and a low calcium intake that is common in many women. Their risks increase with the decreased estrogen production that characterizes menopause. Despite these risks, few women with MS report participating in bone density testing. This study examined the risks for osteoporosis and the results of bone mineral density (BMD) screening in 89 women with MS. Subjects, who participated in one of two MS workshops underwent peripheral BMD screening at the calcaneus. BMD results were categorized as normal, osteopenia, or osteoporosis by WHO standards for fracture risk. Subjects also completed a short questionnaire about risks for osteoporosis (eg, Caucasian, menopausal, thin frame, history of broken bone, family history of osteoporosis, low calcium intake, lack of regular exercise). Subjects were also asked if they ever had BMD testing before, and if testing had ever been recommended to them.

The mean age of the sample was 49.1 (SD \pm 10.1), with a range of 29 to 74. The number of risk factors of osteoporosis ranged from 1 to 8 with a mean of 4.6. BMD test results revealed that 49.4% of women had normal bone density, 32.6% had osteopenia, and 18% had osteoporosis. Despite risks for decreased bone density in this group of women, only 28.7% of them reported taking calcium supplements, 17.2% reported use of hormone replacement therapy, and 9.2% reported use of other medications to prevent or reduce risk of osteoporosis. Only 17.4% reported previous BMD testing and 32.1% reported ever receiving a recommendation for testing. These findings suggest the need for greater attention to detection, prevention, and treatment of osteoporosis in this high-risk group.

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Caregiver Burden: Meeting the Needs of People who Support the Person with Multiple Sclerosis

Judy Wollin, RN, PhD

Reliance on informal arrangements to support the person with MS is an increasingly common phenomenon. The impact of the caregiver role, the identification of stresses likely to prevent a continuation of the role, and the resources needed by caregivers to continue in the role formed the focus of this Australian-based research.

The views of 34 people who care for a person with MS were collected using mail-out surveys, in order to identify their views on the impact of the role. The results indicated that caregivers

provide between two and 10 hours of physical, emotional, financial, or informational support to the person with MS every day. People who support the person with MS are usually married to them, provide care out of love, and are overtaxed with day-to-day tasks—and thus have reduced physical, emotional, and financial resources to draw on.

Caregivers felt their efforts were appreciated in 82% of cases. But where caregivers did not feel appreciated correlated with request for assistance in their supporting role with request for overnight assistance ($r = .391, P < .01$). Needing care overnight correlated with "supporting has reduced my health" ($r = .501, P < .01$). The level of support needed overnight correlated to several variables, needing help ($r = .398, P < .01$), home respite care ($r = .500, P = .01$), and calls for help to meet expectations ($r = .448, P < .01$). Those caregivers who had neither help with housework from other household members or family members not living at home identified the need for help in their supporting role ($r = .509, P < .01$). In addition, being responsible for dependent household members correlated with reduced health ($r = -.418, P < .01$). The analysis indicates that if the caregiver feel unappreciated then they are likely to need additional resources to continue in the supporting role. This has important implications for support agencies.

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MS Treatment Patterns at the End of the 20th Century

Timothy Vollmer, MD, Weija Ni, PhD, Olympia Hadjimichael, MPH

We investigated the treatment patterns among 6,902 MS patients, using data gathered in the NARCOMS Registry from January 1998 to December 1999. The sample approximates the characteristics of the MS population in the US, with 74% female, 91% Caucasian, and a mean age of 47.

The majority of the patients (89%) have visited neurologists either for treatment or for consultation. Symptomatic therapies are used by 78% of the patients, and the use rate is highly correlated ($P < .001$) with degree of disability, as measured by functional performance in each of the eight domains—mobility, hand, vision, fatigue, cognition, bladder/bowel, sensory and spasticity. Various kinds of alternative drugs are used by 40% of the patients.

The immunologic therapies made available in the past decade, in particular the ABC drugs (Avonex[®], Betaseron[®], and Copaxone[®]), have had considerable impact on the treatment of MS, with 62% of all relapsing-remitting patients in the registry sample reporting usage. Single-drug users were 20% for Avonex, 17% for Betaseron, and 6% for Copaxone. The rest (19%) used more than one drug. On average, 39% of all ABC users discontinued treatment after 12 months, either entirely or by switching to another drug. There is a statistically significant correlation between use of ABC drugs and, respectively, higher income, more education, and shorter years of disease. There is also some indication that younger patients and those who have insurance coverage other than, or in addition to, Medicare and Medicaid are more likely to

use these drugs. Neurologists (97%) mostly prescribe ABC drugs. Most users (65%) rate their on-drug experience as either good or very good.

We will present additional data from the rapidly expanding database and discuss how MS can be better managed in the new millennium with improvements in therapy, as well as long-term outcomes of these treatments.

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Interferon Beta Therapy Combined with Steroids and Azathioprine in Relapsing-Remitting MS, Tolerant and Effect

Veronita Ticha, MD, Eva Haurdova, MD, Iveta Novakova, MD

Introduction: Interferon beta was introduced for RR MS therapy in the Czech Republic in autumn 1996, after the inclusion criteria and rules for reimbursement were set down. At present, 606 patients are being treated with interferon beta in the Czech Republic—67.6% with interferon beta1b and 32.4% with interferon beta1a. Patients are followed regularly in seven MS Centers by the departments of neurology in university hospitals.

Patients and methods: 112 patients (from 226 treated with interferon in our MS Center), 69 female and 43 male, EDSS 2.8 ± 0.75 , duration of MS 6.5 ± 2 years, median age 31, completed two or more years of interferon therapy. Relapse rate decreased from 1.7 ± 0.6 to 0.5 ± 0.5 (reduction by 68%), while the reduction of the relapse rate in the studies with interferon beta in RR MS was about 30%. We analyzed this group of 112 patients retrospectively to clarify the unexpected effect of the therapy.

Results: More than 80% of patients were treated with low-dose oral steroids when starting the interferon therapy and 40% of patients used combined immunosuppressive therapy with steroids and azathioprine or methotrexate. Progression in EDSS, relapse rate, and adverse effects were followed and compared in a group of patients with interferon monotherapy, a group that received combined interferon and steroid therapy, and a group treated with interferon and combined immunosuppressive therapy with steroids and azathioprine or methotrexate. No serious adverse effects requiring the therapy to stop occurred. Mild hepatotoxicity and leukopenia were observed in all groups of patients, more frequently in patients with interferon and combined immunosuppressive therapy; but lowering the dose of azathioprine often led to normalization of laboratory parameters.

Conclusions: Combined interferon and immunosuppressive therapy with steroids and azathioprine or methotrexate is well tolerated, and the suspected synergic effect of different immunomodulators may be important in looking for the optimal individual therapy in MS patients.

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REHABILITATION HELPS IN COPING WITH FATIGUE

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Fatigue is one of the most disabling symptoms in Multiple Sclerosis (MS). However, methods to control MS-fatigue are few in numbers. For the purpose to develop rehabilitative methods, we organized a two weeks rehabilitation course for MS patients with fatigue.

The participants of the course were 10 MS patients with definitive MS diagnoses and fatigue as one of the three most disabling symptoms. The rehabilitation intervention consisted of individual examination performed by the neurologist and physiotherapist, group physiotherapy, occupational and neuropsychological evaluations and group meetings as well as individual therapy when needed. Dimensions of fatigue were evaluated with questionnaires, interviews and different kinds of measurements. By the means of this course, we wanted to find out whether multidisciplinary approach could improve the patients` ability to cope with fatigue.

The results showed that multiprofessional evaluations and training could help the patients analyse their fatigue more profoundly and after that cope with this harmful symptom better.

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Poster Presentations

1. Diversity, Diagnosis, and Disability: A Three-dimensional Look at Multicultural/Multifaith Communities in Multiple Sclerosis

Marvin Anderson, BA, MA, PhD

2. Assessing Lower Extremity Function in Multiple Sclerosis by Reaction Time

RR Apache, ABD

3. Multiple Sclerosis in Children

Brenda Banwell, MD, FAAP, FRCP(C)

4. Autonomic Dysreflexia in Multiple Sclerosis: Case Study

Anne Bateman., RN, MS, CNP

5. Measuring Change in Outcomes for Multiple Sclerosis Patients

Heather Becker, PhD

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Gillian Murphy, BSc

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Rebecca Polss, LSW

29. The Art and Skill of Caring for a Loved One with MS: An Interdisciplinary Caregiver Training Model

Lee Shaugnessy, BA

30. Determinants of Health-Related Quality of Life in Multiple Sclerosis: The Role of Illness Intrusiveness

Marla Shawaryn, PhD

31. Caregiver Burden Assessment Instrument: Helping Health Professionals Identify Caregiver Needs—An Australian Trial

Nancy Spencer, PhD

32. Collaborations in Care-Building Bridges for People with MS and their Families across Communities: The NMSS and MS Clinical Facilities

Wendy Sullivan CSW

33. A Program for New Therapies in MS: The Nova Scotia Experience

Pauline Weldon, RN, BN

34. Nursing Time Index for New Therapies in Multiple Sclerosis

Pauline Weldon, RN, BN

35. A Description of Multiple Sclerosis (MS) Patients in Long-term Care Centers Using the Continuing Care Needs Determination Instrument (CCNDI)

Sharon Williams, PhD

36. The Informational Needs of the Newly Diagnosed Person with MS and their Family

Judy Wollin, RN, PhD

37. Urinary Incontinence, a Precursor to Increased Social Handicap: A Critical Variable in Assessing Handicap in People With MS

Judy Wollin, RN, PhD

38. MS Treatment Patterns at the End of the 20th Century

Timothy Vollmer, MD

39. Effect of Race in the Treatment of MS

Timothy Vollmer, MD

40. Development and Uses of the NARCOMS Registry

Timothy Vollmer, MD

Diversity, Diagnosis, and Disability: A Three-dimensional Look at Multicultural/Multifaith Communities in Multiple Sclerosis

Marvin Anderson, BA, MA, PhD, Debra Orton, BA

Introduction: Given the increasing ethnic, cultural, and religious diversity of the greater Toronto area as well as other urban communities throughout Ontario, the regional manager determined that some volunteers and staff did not have the resources or knowledge required to serve the culture-specific needs of those individuals with MS and their family members from multicultural, multifaith communities.

Purpose: The purpose of this educational program was to provide both MS volunteers and staff with the kinds of skill and knowledge needed for greater sensitivity to the cultural/religious mores and etiquette unique to multifaith communities—from the initial stage of diagnosis of MS to the ongoing support offered to the client and his/her family.

Method: An informal survey was completed with the chapters in Central Ontario East. It was discovered that the chapters within the greater Toronto area had clients with multicultural/multifaith backgrounds. At the time of this survey, four out of thirteen chapters were presently experiencing frustration in providing the best possible service to clients and their families with a multicultural/multifaith background. The staff and volunteers identified that

it was difficult to provide quality services or to know the needs of the clients when it was hard to communicate effectively with clients who have a background different from those of the staff.

Results: In order to improve service outcomes, it was necessary to identify and prioritize the methods in which services were being provided to persons with MS who have a diverse background. This workshop was designed to introduce caseworkers to cultural and religious differences, methods for servicing MS clients with diverse backgrounds, and how to work within the family structure of multicultural/multifaith communities.

Presentation: This presentation will detail the following program components; an overview of program development, key factors related to working in multicultural/multifaith communities, and survey results outlining the validity of this training program for case workers.

Assessing Lower Extremity Function in Multiple Sclerosis by Reaction Time

RR Apache, ABD, DH Mattson, MD, PhD, DG Jackson, RN, BSN

Reaction time (RT) and movement time (MT) were measured in 178 ambulatory multiple sclerosis patients during a regularly scheduled clinic visit. The purpose of this study was to examine the criterion validity of a RT/MT test measure. Criterion validity of the test measure was assessed by evaluating RT and MT against the derived Expanded Disability Status Scale (EDSS), the pyramidal Functional System Score, and a timed 25-foot walk. Results indicate that RT and MT has a moderate-to-good relationship with EDSS ($r = .86$). The criterion validity of RT and MT for the MS patients was comparable to that of the timed 25-foot walk ($r = .78$). In conclusion, lower extremity RT and MT of ambulant multiple sclerosis patients are reliable, valid, and sensitive to various degrees of disability severity.

Multiple Sclerosis in Children

Brenda Banwell, MD, FAAP, FRCP(C)

Approximately 2% of MS cases are diagnosed before the patient's 18th birthday. As many as 20% of adult MS patients recall transient symptoms during childhood or adolescence that may well have represented the first episodes of demyelination. Given recent studies suggesting that early treatment with immunomodulatory agents may reduce the neurologic sequelae of MS, prompt identification and appropriate treatment of pediatric patients is imperative.

Most children with MS are managed by pediatric neurologists with limited experience in MS, or by adult neurologists with expertise in MS but a lack of experience in issues of pediatric health, psychosocial, or psychoeducational needs. The impact of MS on long-term educational and vocational planning, on a child's self-esteem, and on family and peer relationships is probably profound, but few reports have studied these issues. In order to address the needs of pediatric MS patients and their families, a multidisciplinary pediatric multiple sclerosis clinic has now been established at the Hospital for Sick Children. This clinic is designed to offer comprehensive medical, nursing, and allied health professional assessments. Patient and parent support is provided by a social worker, and by a member of the Multiple Sclerosis Society staff.

We report the clinical features and current management of five children (four male, one female; age nine to 15 years) with clinically definite MS. Presenting features, with onset at a mean age of 8.7 years, were hemiplegia (two children), brainstem and cerebellar dysfunction (two

children), and hemisensory loss (one child). Currently, two children are treated with Betaseron,© one child with Avonex©, and one child with Copaxone©.

The clinical course and management of these children and a review of the pediatric MS literature will be presented.

Autonomic Dysreflexia in Multiple Sclerosis: Case Study

Anne Bateman, RN, MS, CNP, Gary Goldish, MD

Autonomic Dysreflexia (AD) is a recognized hypertensive crisis in a person with a T7 or higher spinal cord injury. AD is the result of an uninhibited sympathetic reflex response to noxious stimuli below the level of the spinal cord injury. A MEDLINE search failed to identify cases of AD as a complication of multiple sclerosis (MS), although it seems to be a recognized theoretical possibility, especially with dense lesions at or above T7. We present what may be the first documented case of AD in MS. A 54-year old man with a 19-year history of MS was transferred from his nursing home to our Veterans Administration Medical Center with a several day history of blood pressure instability. He was admitted to the transitional unit and was noted to have severe fluctuations of blood pressure, from 76/42 to 180/18 mm Hg. When the Spinal Cord Injury Disorder Team saw the patient in consultation, he was complaining of a severe headache. He had flushing above T7 and a blood pressure of 190/100 mm Hg. The patient's bladder was catheterized, and he had immediate relief of headache and normalization of blood pressure. Details of this case will be presented along with survey results from the Consortium of MS Centers on the awareness of AD as a complication of MS. We feel that awareness of this condition by MS care providers will decrease potentially life-threatening delays in treatment.

Measuring Change in Outcomes for Multiple Sclerosis Patients

Heather Becker, PhD, Alexa Stuijbergen, PhD, RN EAAN, Gayle Timmerman, PhD, RN

In intervention studies, our ability to detect change is often hampered by lack of measures that are sensitive to meaningful change in targeted outcomes. We used Goal Attainment Scaling (GAS), a measure of individualized treatment-induced change, to assess outcomes in a randomized clinical trial of a health promotion intervention among women with multiple sclerosis. GAS enables comparisons among individuals in their relative success in achieving predetermined goals. We considered GAS appropriate for this study because the intervention was designed to be individualized to each woman's specific situation, and goal setting was already an integral part of the intervention. Fifty-eight women (average age, 43 years), whose MS had been diagnosed an average of nine years previously, were randomly assigned to the intervention condition. They participated in eight sessions designed to provide them with the knowledge, skills, and support necessary to improve their overall health behaviors. At the conclusion of these sessions, the group facilitator helped them identify goals they felt would be achievable within the following three months in five areas: lifestyle adjustment, nutrition, physical activity, stress management, and health care responsibility. These goals became the zero points on each individual's scales. Better- and worse-than-expected outcomes were then identified and scaled from -2 to +2. Women indicated their status on each scale before the intervention status on each goal during six weeks, three months, and six months follow-up telephone calls. The percentage of women who achieved or exceeded their goals increased across time. Between 40% and 65% of the women had reached their goals immediately after the educational program, and 59% to 84% reported having achieved them six months later. Gains were greatest in the nutrition area; after six weeks, 79% reported meeting or exceeding their goal.

"We're Listening": Attending to the Psychological Need of Individuals Living with MS and Their Significant Others

Cathy Benbow, MSW, Ontario College of Certified Social Workers, Wilma Koopman, MScN

Individuals with MS in Canada are served through regional clinics. The London Health Sciences Center MS Clinic in London, Ontario, developed a formal MS needs assessment with the goal of determining the needs of the individuals living with MS using the MS clinic as well as the needs perceived by their significant others. The prominent results of the psychological needs assessment will be highlighted and the implications for clinical practice will be discussed.

The Value of Systematically Examining Eye Movements in Patients with Multiple Sclerosis

Roongroj Bhidayasiri, MD, Deborah Downey, John Stahl, Robert Ruff, John Leigh

Introduction: Standard clinical methods for evaluating patients with multiple sclerosis (MS) do not allow systematic coding of visual and oculomotor defects, even though abnormalities in these systems are common.

Methods: We examined the vision (acuity, fields, color, and ophthalmoscopy) and horizontal and vertical eye movements of 33 MS patients (six female) seen consecutively in our outpatient clinic; the examination typically took 10 minutes to perform. Strabismus, nystagmus, saccadic dysmetria, internuclear ophthalmoplegia, and impairment of smooth pursuit, the vestibulo-ocular reflex (VOR) and vergence were assigned a value of one for present/abnormal or zero for absent/normal. Patients were assigned to the normal or abnormal group according to oculomotor (OM) score (scores greater than 2 were considered abnormal). Statistical comparisons were made using the Mann-Whitney rank sum test.

Results: Ten patients (all male) had abnormal OM scores (median, 4.75); their ages and duration of illness were similar to those of the 23 patients with normal OM scores. All 33 patients showed some evidence of involvement of the visual system, but visual acuity was significantly lower ($P = .015$) in the abnormal OM group. The abnormal OM group had significantly greater Kurtzke EDSS scores ($P = .009$) than the normal OM group. The abnormal OM group had greater Kurtzke FSS scores and greater pyramidal, and cerebellar functions, but these differences were not significant ($P > .25$). Sensory, bowel/bladder, and mental functions showed no differences in the two groups.

Conclusion: In our study, patients with abnormal eye movements were the most disabled. In evaluating and following patients with MS, it seems worthwhile to perform a systematic examination of eye movements. The brainstem and cerebellar pathways involved in the control of eye movements are well established and may provide a sensitive way of monitoring any individual plans.

Disability Years Avoided and Cost-Effectiveness Are a Function of Time from MS Onset to Treatment and of Treatment Duration

Murray Brown, PhD, Skedgel C, Murray TJ, Fisk J, Sketris I

Objective: To demonstrate how expected disability years avoided (DYA), costs (C), and C/DYA for treatments that slow MS disability progression vary with treatment start date relative to MS onset (TS) and treatment duration (TD).

Methods: Expected health outcomes and net treatment costs were simulated, using the Multiple Sclerosis PhamacoEconomic Evaluation Tool (MS PEET), over the natural history of MS for female and male onset cohorts with an initial relapsing remitting (RR) diagnosis. Data elements included EDSS progression in RR MS onset cohorts over 25 years, RCT results of delayed EDSS progression, direct drug treatment costs, and direct public sector health costs avoided. Other MS PEET variables included eligibility for funded treatment, compliance, antibody buildup, 'mild,' 'moderate,' and 'severe' EDSS weights and discount rates. Sensitivity analyses compared DYA, C, and C/DYA results across scenarios that vary TS and/or TD.

Results: 1) Treatment start effect: With TD held constant, expected DYA/person (intention to treat basis (ITT) increased, but less than proportionately, as TS increased (over range one to 20 years since onset). 2) Treatment duration effect: With TS held constant (TS range one to 15 years since MS onset), expected DYA/person (ITT) increased more than proportionately as TD increased (eg, from 10 to 20 years). 3) On an intention-to-treat basis, C/DYA/person declined (less than proportionately) with increases in TS and/or TD.

Discussion: Higher expected DYA/person treated (and lower C/DYA, as TS increases) reflects increased relative risk of EDSS progression to higher disability levels. Higher expected DYA/person treated (and lower C/DYA, as TD increases) illustrates the importance of long-term compliance for medications that alter the course of disease progression. Simulation models such as MS PEET facilitate analysis of the determinants of long-term treatment and cost consequences for chronic disease.

Sub-Maximal Fitness Testing and Client-Monitored Interval Training Have a Positive Effect on Deconditioning

Sandra Brunham, BSR(PT), MSc(Rehab)

Objective: Deconditioning, or lack of fitness, is a predictable sequel of chronic progressive disabling conditions such as MS. Physiotherapy often neglects the areas of fitness testing and aerobic exercise in adults with neurologic conditions. Adults with MS find exercising for health and fitness increasingly difficult and fatiguing as their condition progresses. Guidelines for fitness testing and aerobic exercise at submaximal, self-paced rates have been developed by the American College of Sports Medicine and are appropriate for adults with MS. This presentation describes a program that was effective in changing fitness levels in adults with neurologic conditions.

Subjects: Thirty-four adults with various neurologic conditions (including MS) who were not receiving any other forms of rehabilitation or exercise attended an outpatient fitness program.

Methods: Interval training on standard exercise equipment, customized for the individual, with on:off ratios of one to five minutes on, 30 to 60 seconds off, was used. Clients were taught to monitor their submaximal efforts using the Borg Scale of Perceived Exertion. Heart rate, blood pressure, and oxygen saturation levels were monitored throughout the eight week program. Clients exercised once a week at the program and twice a week at home. Pre- and post-program assessments were determined by distance covered during self-paced 6-minute walk, wheel, or arm-pedal tests.

Results: Significant gains in endurance ($P < .0001$) were achieved by the group.

Conclusion: Fitness can be safely and effectively addressed in adults with neurologic conditions.

Analyses of Nursing Home Residents with MS

Robert J. Buchanan, PhD, David Graber, PhD, Suojin Wang, MD

Nursing homes are a principal provider of health services for people with advanced MS. This study profiles nursing home residents with MS in the United States, describing the services and care they receive. The resident profiles also include a comprehensive description of demographic characteristics of nursing home residents with MS. In addition, the study analyzes variations in these resident profiles by payment source, gender, and race. These analyses provide a better understanding of which nursing home residents have MS and identifies their other medical conditions and the care they receive. The results of the study have significant public policy implications, documenting any differences in resident profiles and the care or services provided to residents with MS who are insured by Medicare, Medicaid, private health insurance or self-pay residents.

This study presents the results of a unique set of analyses of nursing home residents with MS, made possible recently with the availability of the "Minimum Data Set (MDS) for Nursing Home Resident Assessment and Care Screening" from the US Health Care Financing Administration. Between June 22, 1998 and January 25, 1999, there were 13,331 nursing home residents with MS in the MDS data set. This research was funded by a Pilot Research Project Grant from the National Multiple Sclerosis Society.

A Review of Mobility Measures and Their Applicability and Utilization by Comprehensive Multiple Sclerosis Centers

Angela Chan, MHSc, BPT

All individuals with multiple sclerosis (MS) who score 5 or higher on Kurtzke's Expanded Disability Status Scale experience mobility difficulties, which intensify as their MS progresses. According to the International Classification of Impairment, Disability, and Handicap, although a mobility problem is not an impairment, it has an impact on almost all of an individual's activities, including their ability to participate in the community and society.

Methods: This paper will review mobility measures reported in the literature ($n = 15$) and identify utilization of measures in clinical settings to determine where gaps exist between the literature and clinical practice. Mobility outcome measures were reviewed under the following domains: transfers, ambulation distance, timed ambulation, dependence of ambulation, community ambulation, type of measurement scale, test environment, mode of collection (ie, self-report or direct observation), and whether it was developed and/or validated in the MS population. Clinical practice information on use of mobility measures was collected through a survey of MS Consortium Centers members.

Results: The results showed great variability amongst the measures in several domains. Also, there was minimal utilization of these mobility measures in clinical practice. Although centers consistently reported recording a descriptive analysis of gait, there was variability between the centers in the walking distance selected for timed walk. Disability measures were rarely used in clinical practice.

Conclusion: Results from the current study confirm that a gap exists between the mobility measures reported in the literature and clinical practice. This gap provides an opportunity for Consortium members to collaborate on selecting one or more impairment and disability measures, which could be utilized across all practice settings. This standardization of practice across centers will facilitate multicenter research activities and single-center longitudinal studies, support evidence-based practice, and provide an objective way to measure treatment effectiveness.

The Needs of Caregivers

Noreen Comeau, RN, Tamika Wallen, RN

Caregivers are an at-risk population. Their needs could have many implications for healthcare providers, depending on the age-group being examined and their health, status, social capital, and human capital. The added stress of caring for loved ones who are no longer able, or at least limited in their ability, to care for themselves, often leads to or increases the possibility that the caregiver will become ill or will him/herself be in need of care. "The devaluation of caring, coupled with its invisibility, can place those who are cared for, whether by family members of human service organizations, in a position of extreme dependency on others" (Hooyman & Gonyea, 1995, p 152). In the literature review, most of the information available on caregivers and caregiver issues is written for women and about women, and most surveys show that the majority of caregivers are women (Sherman & Sherman, 1999, p 1). "The designation of caregiving as a 'woman's role' has resulted in the fact that respondents to research surveys and interviews have been overwhelmingly women" (Hooyman & Gonyea, 1995, p 137). "In our culture, men are portrayed as uncaring takers ... In fact, caring is seen almost solely as a feminine trait" (Dominguez, 1995, p 16). Since multiple sclerosis affects young people between the ages 20 and 40 years, and women twice as often as men, the caregiver population for persons with MS is young and predominantly male. The purpose of this paper is to assess the needs of the caregivers of the persons with multiple sclerosis (MS) who attend a self-group in Lewiston-Auburn, Maine. The results of the needs assessment will be utilized in future planning of programs for caregivers in Maine.

Multiple Sclerosis Care Within the Veterans Health Administration

Deborah Downey, RN, MN, CRRN

The Austin Data Center of the Department of Veterans Affairs Health Administration (VHA) tracks patients by a number of methods, including ICD-9 codes. Coding information on patients, followed by specialties, has not always been accurate for a variety of reasons. The Veterans Affairs Special Interest Group (VA-SIG) is a special interest group within the Consortium of Multiple Sclerosis Centers, which is committed to guiding and improving multiple sclerosis care within the VHA. As part of the VA-SIG, the Clinical Care Committee is currently undertaking a survey to determine patient demographics, availability of specialty care, dedicated multiple sclerosis clinics, availability of emerging multiple sclerosis therapies, and utilization of Spinal Cord clinics, services, and providers. Data collection is currently ongoing, with completion anticipated to occur on June 1, 2000. It is expected that data through that date will be presented and serve as the basis for the Clinical Care Committee to set direction and goals for the subsequent year's activities.

Predictors of Adherence to Copaxone® Therapy in Individuals with Relapsing-Remitting Multiple Sclerosis

Cira Fraser, RN, CS, PhD, Olympia Hadjimichael, MPH, Timothy Vollmer, MD

Purpose and Research Question: The purpose of this study was to evaluate psychological, biophysical, and sociodemographic variables as predictors of adherence to Copaxone® therapy in individuals with Relapsing-Remitting Multiple Sclerosis (MS). The research question: Are characteristics such as self-efficacy, self-esteem, hopefulness, level of disability and sociodemographic factors significant predictors of adherence to Copaxone® among those with Relapsing-Remitting MS?

Background: Since Copaxone® is a daily subcutaneous injection, individuals with MS are challenged by the daily routine of preparation and administration of this medication. Despite the challenges, some individuals with MS adhere to treatment with injectable medications with little or no difficulty while others struggle to adhere and soon abandon the daily task. It is crucial to identify predictors of adherence to Copaxone® therapy. Those at risk need to be identified early and provided with individualized support at the onset of therapy to promote adherence.

Methods: Potential participants were identified from the NARCOMS Patient Registry database (n=600) and Shared Solutions™ patient database (n=600). **Inclusion Criteria:** Relapsing-Remitting MS. **Exclusion Criteria:** Taking multiple immunomodulating drugs; Booklets completed by other than person with MS.

Booklets containing four instruments (MS Self-Efficacy Scale, Herth Hope Index, Rosenberg Self-Esteem Scale, and Performance Scales) and sociodemographic data sheets were mailed to 1200 individuals. Total number responding n = 594. Total meeting criteria n = 341. The adherent group included 225 individuals. The nonadherent group included 116 individuals.

Findings: Logistic Regression revealed four significant predictors of adherence: The MS Self-Efficacy (Control Subscale) ($p = .0007$), Herth Hope Index ($p = .0310$), doctor perceived as most supportive of Copaxone therapy ($p = .0211$), and previous use of Avonex and/or Betaseron ($p = .0330$). The higher the score on the MS Self-Efficacy Scale (Control Subscale), the more likely the individual will adhere to Copaxone®. The individual with a score of 900 is 3.67 times more likely to adhere to Copaxone® than an individual with a score of 400. The lower the score on the Herth Hope Index, the more likely the individual will stop Copaxone®. The individual with a score of 28 is 2.76 times more likely to stop Copaxone® than an individual with a score of 48. Those who perceive the doctor as most supportive of Copaxone® therapy are more likely to be adherent. Those who have previously taken Avonex and/or Betaseron are more likely to be nonadherent.

Implications: The Multiple Sclerosis Self-Efficacy (Control Subscale) and the Herth Hope Index show promise of being useful to predict adherence. Further testing is recommended. Physician support should be conveyed to all individuals starting and maintaining on Copaxone® therapy for MS. Greater support needs to be provided to those who have previously taken immunomodulating drugs.

Current Issues and New Directions in MS Vocational Rehabilitation

RT Fraser, PhD, CRC, D Clemmons, PhD, CRC, E Johnson, MS, K Johnson, PhD

This paper reviews information relevant to the first 90 vocational rehabilitation referrals to a demonstration project at the University of Washington MS Rehabilitation Research and Training Center. Key points include:

1. An occupational profile of the first 50 individuals engaging in vocational rehabilitation services through our project, with implications for the primary vocational rehabilitation needs of the population.
2. A description of the first 40 individuals dropping out of the project with review of causes of drop-out.
3. Presentation/discussion of the neuropsychological screening battery developed specifically for this project, and its utility for vocational planning.
4. Identification of key barriers for project enrollees to successfully engage in both the project and the state vocational rehabilitation system. Implications for effective service delivery within the US national/state vocational rehabilitation system will be discussed.
5. A review of our efforts and success in developing a home-based vocational option for persons with MS, and the range of placement approaches our project offers.
6. A review of placement outcomes over the first 18 months of the project, with the most successful placement approach and the most frequent accommodations highlighted.
7. Effective merging of Social Security subsidy and paid work alternatives as a placement option.
8. Identification of the best predictor variables of placement and successful job retention.

Neuropsychological Rehabilitation for MS Patients: Effects on Metacognition and Daily Functioning

Hamalainen P, Seinela A, and Ruutianinen J, Masku Neurological Rehabilitation Centre, Masku Finland

Cognitive deficits are one of the most harmful symptoms in multiple sclerosis (MS). Neuropsychological assessment methods have been extensively developed, but rehabilitation of cognition is still at its early steps in MS.

In Masku Neurological Rehabilitation Centre, we have developed three models of neuropsychological treatment in MS. 1) Information / family weekends for MS patients who are concerned about cognitive deficits; 2) inpatient rehabilitation courses of six days for cognitively affected MS patients and their spouses; 3) inpatient cognitive rehabilitation courses over three weeks for MS patients. The rehabilitation intervention has consisted of information at general as well as at individual levels, neuropsychological assessment and feedback, individual counseling, and group meetings. We have evaluated the effectiveness of rehabilitation intervention by questionnaires assessing the change in patients' metacognitive skills and daily coping abilities.

We found that after the rehabilitation intervention, the metacognitive skills of patients improved and everyday coping was easier. For the spouses, the most important gain was the increment of understanding towards their husband/wife's cognitive problems. The patients and spouses seemed to benefit from the course up to one year after the course.

The results suggest that rehabilitation courses are not only an effective way of treating patients with cognitive deficits, but also a great help to their family members.

The Prevalence, Etiology, and Impact of Pain in Multiple Sclerosis

Amanda Howarth, B Med Sci, MSc

A quantitative study was designed to explore the experience of pain in multiple sclerosis (MS). The study involved an anonymous questionnaire randomly sent to 913 people with MS. The purpose of the questionnaire was to identify the prevalence of the problem of pain in multiple sclerosis and also to start and explore how the problem has been clinically dealt with and the impact it is having on individual's lives. The questionnaire also asked what treatments had been tried and whether they had been found to be effective.

Analysis of the 436 questionnaires returned revealed that 316 (72.5%) of the patients experience pain, with the prevalence of pain increasing with time since onset of disease.

It is apparent from literature reviewed and the exploratory study undertaken that acknowledgement of, and proposals for the treatment/management of this difficult problem are sparse. It is necessary for the issue of pain in MS patients to be addressed with appropriate research and education pertinent to MS. This may facilitate the implementation of management and treatment strategies necessary to allow MS patients to achieve an acceptable quality of life. Recommendation for this will be proposed.

Comparison of Quantitative Sensory Testing to the Standard Clinical Examination and Self-Assessment

Michael Kaufman, MD

Sensory testing was performed for 32 patients with MS who had mild or no sensory complaints and for 30 age-matched controls. Quantitative testing for the detection of a cold stimulus and for the extinction of a moderate vibratory stimulus was done in the hands and feet. There was overlap for the thresholds for these sensations between MS patients and controls. In order to detect a significant number of abnormalities involving patients with sensory complaints, values for quantitative testing were chosen that identified four of 30 controls as abnormal. Standard clinic assessment of sensation was done for pin, vibration, and joint position sense in the hands and feet. The self-reported sensory inventory asked about temperature sensitivity and position sense for the feet. In these patients, quantitative sensory testing was slightly more sensitive than standard clinical assessment in detecting abnormalities, but identified as abnormal some MS patients and controls without sensory complaints. There was little congruence for the abnormalities identified by the three methods; consequently, the test frequently identified different sensory modalities as normal or as abnormal in the examined limb. More patients reported sensory abnormalities than could be detected by either quantitative testing or by the clinical examination. The Spearman correlation coefficients between quantitatively measured threshold for cold and the severity of the self-reported sensory inventories for temperature were greater than -0.5 . This argues that quantitative sensory thresholds for cold accurately reflected sensory changes, even if the absolute cold threshold was within the normal range. Quantitative sensory testing has the advantage of providing a continuous outcome measure that can be followed over time. This advantage may be especially useful in following patients in clinical trials.

Physical Therapy Intervention Following Treatment with IV Steroids for an Acute Exacerbation of MS

Daniel Kelly, PT, François Bethoux, MD, RP Kinkel, MD, Deborah Miller, PhD

The Mellen Center conducted a recent pilot study on the outcome of 48 patients treated with intravenous methylprednisolone (IVMP) for an acute relapse of MS. Prerelapse EDSS was between 1.0 and 7.5. The subjects were followed for four months. Most of the decrease in disability occurred within four weeks, and disability scores started to increase after four weeks in 40% of the subjects. Indicators of subjective health status showed minimal changes throughout the period of observation. These results suggested that residual symptoms, such as fatigue, continue to affect the patient's daily functioning and quality of life despite the initial beneficial effect of IV steroids. These patients usually do not receive any additional therapy and are left to cope with their difficulties by themselves.

To determine if these patients with minimal to moderate disability can benefit from a short course of comprehensive outpatient rehabilitation (consisting of occupational and physical therapy) after IV steroid treatment for an MS relapse, a single-blind controlled study was designed and is currently being conducted at the Mellen Center. The physical therapy treatment includes aerobic exercise, strengthening, flexibility, and functional mobility training. It is anticipated that patients in the treatment group will be able to improve their general condition and to better manage specific symptoms and will consequently utilize less in terms of health care resources.

This presentation will describe the study design, the rationale for the physical therapy elements included in the rehabilitation program, and preliminary observations on the feasibility and short-term results of the PT intervention.

A Rapid Screening of the Presence of Dysphagia in MS Patients

Isabella Koch, Ornella Zamparini, M. Rosaria Stabile, Francesca Meneghello, Francesco Piccone, Paolo Tonin; Hospital S. Camillo, Dept. Of Neurorehabilitation, Venice, Italy

Introduction: Dysphagia may cause severe consequences but is still underestimated in MS patients. If dysphagia is detected early, the associated morbidity can be substantially reduced. However, complete clinical evaluation is time-consuming and could be useless for many patients. Unfortunately, the existing questionnaires for dysphagia screening are unsuitable for MS patients. For that reason, we elaborated a new rapid screening questionnaire specifically designed to select MS patients for clinical and instrumental evaluation.

Methods: Fifty MS patients without a previous diagnosis of dysphagia (EDSS score between 4.0 and 7.5; 48 female and 32 male; age ranging from 18 and 64 years; 1 to 34 years from onset) who were admitted to our hospital for a period of rehabilitative treatment, have been screened. The environmental aspects of nutrition were similar for all subjects. The questionnaire consisted of 23 items regarding three different aspects: the alimentary habits, the dysphagic symptoms, and the social implications. All patients who reported signs of dysphagia on the questionnaire underwent a complete functional evaluation of the deglutition. Each questionnaire administration required 10 minutes.

Results: Twenty-five percent of the patients reported signs of dysphagia, of various degrees of severity. In all of these patients, the functional evaluation confirmed the presence of dysphagia.

Conclusions: Our data confirm that dysphagia is an underestimated symptom in MS patients. This questionnaire seems to be a rapid, reliable, and easy instrument to detect early dysphagia, as well as a useful tool for monitoring the outcome of this symptom.

Combined Treatment of Relapsing Multiple Sclerosis (MS) with Interferon beta-1a and Prednisone

Oldrich Kolar, MD, PhD; Han W, Huler KKH, Mercer JE, Muckway MA

Background: Multiple sclerosis (MS) is essentially a continuous pathologic process involving the central nervous system (CNS). Optimal treatment of MS should prevent relapses or progressive neuropsychiatric symptoms of the disease.

Materials and methods: From the total of 214 MS patients with relapsing MS on Avonex® in 168 individuals (137 women, median age 44, range 23 to 66 years; 30 men, median age 42.5, range 25 to 59 years) who experienced a relapse of neurologic symptoms or in whom, at the beginning of treatment with Avonex, exhibited persistent abnormal neurological findings following preceding attacks that were established, continuous treatment with interferon beta-1a (30 µg intramuscularly once a week) and prednisone (7.5 to 15 mg/kg/d) was initiated. The median duration of the treatment was 23 months (range, 1 to 41 months). To prevent osteoporosis, the patients were treated with calcium, vitamin D, testosterone, and (when indicated by bone density studies) alendronate with or without raloxifene.

Results: The relapse rate in the MS patients treated with Avonex and prednisone was 32%. In 12 instances, relapse of neurologic symptoms was associated with clinically established infections. During the treatment, four patients experienced traumatic fractures (2.3%) and two individuals (1.2%) were found to have stress fractures. No side effects requiring permanent discontinuation of the combined continuous therapy were encountered.

Conclusion: In our open-label study of 168 MS patients treated with combined continuous therapy with interferon beta-1a and low-dose of prednisone, the relapse rate was lower as compared with previously published data on MS patients undergoing monotherapy.

Continuous, Simultaneous Treatment with Interferon –beta-1a, Prednisone and Azathioprine in Multiple Sclerosis (MS)

Oldrich Kolar, MD, PhD; Han W, Huler KKH, Muckway MA, Wire MR

Background: Multiple sclerosis (MS) is essentially a continuous inflammatory and metabolic central nervous system (CNS) disorder with a highly individual rate of advancement. In MS patients, optimal immunomodulatory-immunosuppressive (IMIS) therapy should prevent relapses and/or progressive neuropsychiatric symptomatology.

Materials and methods: In 28 MS patients with EDSS 3.5 to 7.5 (16 women, median age 43, range 21 to 57 years; 12 men, median age 44, range 18 to 44) who experienced relapse and progressive neurologic symptomatology on continuous treatment with interferon-beta-1a (Avonex 30 U intramuscularly weekly and prednisone 7.5 to 15 mg/d) treatment was 18 months (range, 1 to 36 months).

Results: In nine patients in this series (33%), no stabilization of neurologic symptomatology was observed. In seven patients (25%), persistent improvement exceeding one point in the EDSS rating was noticed. The remaining 12 MS patients (40%) in this series show currently stable symptomatology. No laboratory or clinical findings requiring discontinuation of the combined continuous IMIS therapy in our MS patients were established.

Conclusions: In some MS patients, combined IMIS therapy including interferon beta-1a, prednisone, and azathioprine is superior to combined therapy with interferon beta-1a and

prednisone. In our series of 28 MS patients with progressive neurologic symptomatology on continuous combined therapy with interferon beta-1a and prednisone, stabilization and improvement in clinical findings were established in 67% of the individuals studied. Persistent, subclinical activity of the MS process in our patients cannot be excluded.

Independent Living Empowerment and Advocacy Program (ILEAP)—A Disease Management Interdisciplinary Model for Maintaining Independence in MS

Lavonne Kraft, MA

The desire to remain at home for as long as possible prevails in the minds of most people with MS. That need is heightened in young people with families, especially when children reside in the home. The long-term care benefit option for those with progressive illness often reveals gaps in the full continuum of care needed to maintain optimal independence. In May 1999, the Colorado Chapter of the National MS Society initiated a pilot project, ILEAP, to begin addressing risk factors identified through service delivery within this population. Risks include: accelerated loss of function, family breakdown, abuse, depression, suicidality, premature institutionalization, social isolation, poor disease management, underutilization of available benefits and resources, and a decline in self-esteem and self-advocacy skills. The overall goal for ILEAP participants is a measurably improved overall quality of life. The primary objectives were identified as: 1) living independently in the safest, least restrictive environment possible, 2) empowerment of the individual through advocacy, 3) improved emotional and physical health of the person with MS, and 4) improved emotional and physical well-being of family members. These objectives are met through a well-coordinated array of services, including case management, home health care through approved agencies, volunteer home helpers, Seniors' Companions, financial assistance for independent living aids, training and counseling for caregivers, and support services. Outcome measurements are being implemented for key objectives. For example, the BHS (Beck Hopelessness Scale) is being implemented on a pre- and posttest basis from the onset of the program. Preliminary outcomes will be available in May 2000. Additional outcomes will be measured for each program objective. To date, 30 families are receiving services (91% female patients, with an average age of 41 years).

Oral Rather than IV Steroid Therapy for MS Patients Results in Savings to the Health Care System

Metz LM, Harris CJ, Moore A, Peters S, Patry D, Bell RB, Yeung M, Power C, and Murphy WF

Objectives: While high-dose pulse oral steroids can be safely and effectively administered to people with MS (Metz et al, *Neurology* 1999), intravenous (IV) therapy remains the standard in many centers. The purpose of this study was to determine the proportions of patients who choose oral versus IV therapy and the savings to the health care system over a one-year period (1999) in a Canadian MS clinic (Calgary).

Methods: All MS patients who received a course of steroids through the clinic were offered a choice of oral prednisone (1250 mg every other day for five doses) or IV methylprednisolone (1 g every other day for five doses). IV steroids were administered in an outpatient unit or in the patient's home. The cost of IV treatment was derived from analysis of treatment costs in another Canadian MS clinic (Robson et al, *CJNS* 1998). The reported cost of \$714.64 (Canadian) for four outpatient doses (including the cost of the drug) was multiplied by 1.25 to arrive at a five-dose cost of \$893.30 per patient. There was no cost to the health care system for oral therapy because patients covered this cost themselves (cost, \$35.00).

Results: During 1999, 116 MS patients were prescribed pulse steroids through the clinic. Ninety-three percent (108 out of 116) chose oral therapy. All IV treatments were given on an outpatient basis. The total cost to the health care system to treat 116 patients was \$7,146.40. The cost would have been \$103,622.80 if all 116 had been treated intravenously as outpatients; more, had they been treated at home. The one-year saving was therefore at least \$96,476.40.

Conclusion: This study provides evidence that MS patients, when given a choice, usually choose oral therapy and that oral therapy greatly reduces costs to the health care system. Oral steroids should be considered a first-line option when pulse steroid treatment is indicated.

The Consequences of MS: Disability Increases the Odds of Being Separated or Divorced

Metz LM, Rose SM, Patten SB, Murray TH, Lagendyk LE, McGuinness SD, Fisk JD, Reimer M, Brown M, and Jacobs P

Objective: While many suspect marital breakdown is often disease-related, evidence for this association is lacking. This study evaluates the relationship between marital status and MS while controlling for age and gender.

Methods: A population-based sample of 219 patients from two Canadian MS clinics (Calgary/Halifax) was recruited and stratified by EDSS severity group (0.0 to 2.5; 3.0 to 5.5; 6.0 to 8.0; 8.5 to 9.5). Patients were interviewed and examined for relationships between variables. Multivariate analysis, restricted to patients over age 29, used EDSS, age, gender, site, duration since symptom onset, duration since diagnosis, age at onset, number of relapse days in past two years, and whether disease was currently stable.

Results: The probability of being divorced or separated was statistically related to age and EDSS group, but not to gender. The probability of divorce/separation for patients with EDSS between 8.5 and 9.5 was nearly double that expected in the general population (SMR = 1.88, P = .056). Odds ratios (in comparison with the least disabled group [EDSS < 3.0]) for divorce/separation increased as disability severity increased. The odds ratio for EDSS group 3.0 to 5.5 was 2.0 (95% CI 0.7 to 5.9); for EDSS group 6.0 to 8.0, it was 2.7 (95% CI, 1.0 to 7.6); and for EDSS group 8.5 to 9.5, it was 5.7 (95% CI, 1.7 to 19.5). Controlling for EDSS group, the probability of divorce/separation decreased with age (odds ratio = 0.96 for a one year increase in age, 95% CI 0.93 to 1.0).

Conclusions: Greater disability increases the odds of being separated or divorced for those with MS. This association is better appreciated when the divorce/separation rates of more disabled groups are compared with the least disabled group. The lower rate in the least disabled group probably reflects differences between the demographic profile of the MS population and the general population.

Effect of Betaseron® Dose Titration on Side-Effect Profile in Multiple Sclerosis

Melanie Morash, BScN

Betaseron has been approved for use in secondary progressive multiple sclerosis patients since 1999.

Like all medications, Betaseron® has side effects. Betaseron's adverse effects tend to be more severe in the secondary progressive patient population than in the relapsing-remitting population.

Empirical evidence suggests that slow titration with small doses of Betaseron reduces the severity of these adverse effects. Currently, no titration protocol exists to guide the administration of Betaseron.

This paper will review a small pilot study done to determine what titration protocol is most effective in reducing the severity of Betaseron's adverse effects.

The results of this study will form the basis for further research with a greater number of participants.

Presentation will be in poster format.

An Audit of Swallowing Problems in a Disabled Population of Multiple Sclerosis Patients in Northern Ireland

Gillian Murphy, BSc (Hons) Speech & Lang., Stanley Hawkins, MD, FRCP

The British Artificial Nutrition Survey 1999 reports 12,000 cases of patients receiving home enteral tube feeding, 76.6% because of dysphagia alone. Among the patients who were between the age of 30 and 40 years, multiple sclerosis was the most common diagnosis. Speech and Language Therapy Clinical Guidelines (May 1998) report an approximately threefold increase in referrals for assessment of dysphagia in patients with a progressive neurologic disorder. A high percentage of this group has a diagnosis of multiple sclerosis. The Multiple Sclerosis Society of Great Britain and Northern Ireland (1998) highlights the current evidence regarding the importance of dietary factors in multiple sclerosis, and the risk factors associated with inappropriate/inadequate feeding management are outlined in the Speech and Language Therapy Guidelines.

Multiple sclerosis is a disease that fluctuates; consequently, the nature of a patient's swallowing disorder will fluctuate also. To date, criteria for use of percutaneous endoscopic gastrostomy (PEG) tube feeding in multiple sclerosis patients have been "random," the tubes often being used almost as an emergency procedure when, owing to dysphagia, a patient's nutritional status has become much less than adequate. Within the Northern Ireland Neurology Service, 50 MS patients have been assessed in detail in the past two years.

We will present an audit of swallowing management in multiple sclerosis and the importance of adequate nutrition and access for medication. The lack of standard criteria used when considering PEG tube insertion in patients with multiple sclerosis will be discussed, and a potential need for more standardized assessment criteria highlighted.

Information and Referral: A Most Important Mission

Rebecca Polss, LSW

Life crisis: For many people, being diagnosed with a chronic illness such as multiple sclerosis (MS) is the first "life crisis" they have ever faced. Questions about what the diagnosis means and how it will affect one's life—career, roles, and health—can cause tremendous emotional

turmoil. Exact answers to these questions do not exist. Yet, the need to know more, to gather information, or to simply talk about this life-crisis persists. When MS is newly diagnosed, most information comes from health care providers. Otherwise, many people with MS isolate themselves because they feel that no one understands their issues and concerns. With organizations like the National Multiple Sclerosis Society (NMSS) in place, there is no reason for people with MS to experience isolation.

Knowledge is power: In this era of technology, information—accurate and inaccurate—abounds. The NMSS is a nationally recognized resource for accurate and up-to-date information about MS. This includes MS facts, symptom management, emotional coping, and lifestyle adjustment issues.

Getting this information out to the MS community, professionals, and clients is the challenge. The Greater Delaware Valley Chapter has met this challenge through the creation of its Resource Room, and particularly its Resource Connection—a state-of-the-art information and referral service now serving as a model for the development of the national information and referral protocol.

The Resource Room: The Greater Delaware Valley Chapter's Resource Room consists of two components—a lending library and a computerized information and referral service. The poster will illustrate the following:

- 1) Information and referral as the cornerstone of the NMSS Programs Department.
- 2) Major elements needed to create an information and referral system.
- 3) Benefits of an effective information and referral system.
- 4) Daily operation of the Resource Room.

The Art and Skill of Caring for a Loved One with MS: An Interdisciplinary Caregiver Training Model

Lee Shaugnessy, BA, Kathy Jensen, LCSW, Connie Holmes, LCSW, Judy Gentner, OTR, Sandy Williamson, MS, CANP, CRRN, Jan Jerome, LCSW, Stacey Sweet, and Linda Purdum

Although the current network of health care depends heavily upon the use of family caregivers to provide essential services to our patients with MS, often those caregivers have little or no hands-on training in the tasks that are required of them. In a pre-program questionnaire, family caregivers indicated a lack of confidence in their mastery of skills such as transferring, bowel and bladder management, medication monitoring, and ADL assistance. They also expressed doubts about their emotional preparedness for the task of caregiving. Professionals in Denver, Colorado resolved to ameliorate these gaps and to provide a "tool kit" to some of our family caregivers. In October 1999, the Rocky Mountain MS Center, the National MS Society — Colorado Chapter, and the Denver VA MS Clinic presented a two-weekend workshop entitled "The Art and Skill of Caring for a Loved One with MS." This cooperative effort was attended by 30 participants (55%) who said that they had never attended any kind of caregiver support or training program. This was an interdisciplinary program, incorporating presentations by social workers and social work students, an occupational therapist, a nurse practitioner, a family caregiver, an education coordinator, and medical equipment suppliers. Goals of the program were to provide hands-on skills training to family caregivers, increase the health and safety of both the caregivers and care recipients, enhance awareness of resources available to

caregivers, provide guidelines to begin long-term planning, and provide emotional support and interaction with other caregivers. A report on the program will be provided, as well as data from two follow-up phone interviews to measure change in the participants' knowledge base and use of resources.

Determinants of Health-Related Quality of Life in Multiple Sclerosis: The Role of Illness Intrusiveness

Marla Shawaryn, PhD, Kathleen Schiaffino, PhD, Nicholas LaRocca, PhD

Multiple sclerosis (MS) is a common demyelinating chronic illness that primarily affects young adults. Its progressive and unpredictable nature poses many physiological and psychological challenges to both the individual and the family. Recent research has examined the impact of MS on health-related quality of life (HRQL). HRQL facilitates study of disease impact not only from a medical or physiological perspective, but also from social, psychological, and economic vantage points. This study was focused on clarifying the relationship between MS and HRQL by investigating how illness intrusiveness may play an intermediary role between the impact of MS and HRQL.

Participants were 90 individuals with MS recruited from the Medical Rehabilitation Research and Training Center for Multiple Sclerosis at Saint Agnes Hospital in White Plains, New York. They completed brief neuropsychological measures and self-report questionnaires measuring HRQL, psychological adjustment, and illness intrusiveness.

Results indicated that physical aspects of HRQL, both generic and MS-specific, were significantly predicted by disease severity, whereas mental and emotional aspects of HRQL were predicted by information processing speed. Disease severity and information processing speed predicted depression and well-being. The extent to which individuals viewed the MS as intrusive mediated the manner in which disease severity predicted each of the following: physical HRQL, fatigue, and depression.

Implications of the current research underscore the need for broader scopes of assessing MS and its impact on the individual. The data also serve in supporting the use of HRQL as it is broadly defined in assessing outcome in chronic illness. While in most cases, physical indices of disease predict physical quality of life and cognitive assessment predicts mental and emotional quality of life, the individual's perception of MS is a major determinant of adjustment. This points to the need for psychological intervention in helping individuals adapt to MS.

Caregiver Burden Assessment Instrument: Helping Health Professionals Identify Caregiver Needs; an Australian Trial

Nancy Spencer, PhD

The caregiver is an important resource in the support of the people with MS living in the community. Hence the assessment of the caregiver's sense of burden is important for community organizations wishing to improve the care of the person with MS.

Supporting a person with MS is a long-term caring role most often assumed by spousal partners. In previous research, it was noted that caregivers provide care out of love and are usually overtaxed with day-to-day tasks with reduced physical, emotional, and financial

resources to draw on. It is practical interventions aimed at supporting the family as well as the person with MS that are likely to be successful (Buchanan, 1997).

This research, with a sample of 14 caregivers, trailed an instrument to be used by health professionals when assessing the burden perceived by caregivers. The instrument developed for an Australian setting was based on previous research into caregiver burden (Wollin et al, 1999).

The instrument trailed is a variant of one used in previous research into the needs of caregivers (Braithwaite, 1997; Guest & Novak, 1987). The questionnaire contained 17 items addressing the practicalities of looking after a chronically ill person: the physical well-being of the person with MS, the home, meal preparation, and the caregiver's own health and well-being.

Caregivers have indicated that help around the home—including cooking, cleaning, and mowing the lawns—is often needed. The pressures associated with the day-to-day demands of life, in addition to supporting the person with MS, often lead caregivers to feel that they are not meeting their own expectations, need a break, and need to feel appreciated. The new instrument will assist health professionals to direct caregivers to the three important support services—community nursing, counseling, and home help.

Collaborations in Care—Building Bridges for People with MS and their Families Across Communities: The NMSS and MS Clinical Facilities

Wendy Sullivan, CSW, Deborah Hertz, MPH

The National Multiple Sclerosis Society (NMSS) and the 106 affiliated MS specialty clinical facilities across the US have developed collaborative models for partnerships in care. The collaborative efforts of the NMSS and MS clinical facilities bridge the gap in services so people with MS and their families can function as independently as possible within the limits of their disease. Through these collaborations, individuals with MS, their families, friends, and the community are provided with the tools (ie, health care, education, information, community referrals, advocacy, social support, rehabilitation, vocational services, and counseling) to help them manage the unpredictable and emotional effects of MS. Individuals with MS and their families acquire the necessary skills, supports, and health care to foster independent community living at the appropriate level of their capacity.

This presentation will highlight how the collaborative relationships developed in affiliation models strengthen the quality, access, and use of health care by people with MS. It will demonstrate the role of the NMSS as the advocating, connecting link that relates and interacts with health, human service, and community agencies. This enables people with MS and their families to develop strategies and strengthen resource utilization to improve the quality of their lives with MS.

This poster will present: 1) an overview of affiliation models; and 2) two models of affiliations used in Rochester, NY and Pittsburgh, PA.

A Program for New Therapies in MS: The Nova Scotia Experience

Pauline Weldon, RN, BN, Jock Murray, MD, FRCPC, Nancy Shaver-LeForte, RN

The program for New MS Therapies supported by the Department of Health of Nova Scotia is organized and coordinated through the Dalhousie MS Research Unit (DMSRU). This program is a

structured program that coordinates the education, assessment, prescription, training, and follow-up of patients on the new immunomodulatory drugs for MS. Although access to the programs is only through the DMSRU, a patient who fulfills the criteria for therapy and attends a required education session will have full coverage for the therapy.

Patients may be referred by their family physicians or neurologist or may come from the clinic population. All prospective candidates for therapy are required to attend an education session delivered by the nurse coordinator to provide an understanding of the benefits, limitations, side effects, and responsibilities with these therapies. Eligibility is determined by one of the clinic neurologists according to set criteria, including 1) clinically definite relapsing-remitting or secondary progressive MS; 2) EDSS 6.5 or less; and 3) no contraindications. Exceptions are possible for patients with a usually malignant course or very abnormal MRI who do not completely fulfill the criteria. In the first 18 months, 1,194 patients were assessed, 355 attended the education session, and 276 patients were funded for therapy. Seventy-nine candidates attended the education program but elected not to accept therapy, even though it would be completely funded.

Although rigidly controlled, the program has been very well accepted by government, patients, and physicians and has an unusually high compliance rate (100% at six months and 94% in the first year of the program). A further report on the first two years of the program will be presented.

Nursing Time Index for New Therapies in Multiple Sclerosis

Pauline Weldon, RN, BN, CNN(C)

Nurses who work with MS patients have seen a role change in the decade since the availability of the new therapies. The hours of involvement are not always predicted accurately. Patients' reactions to beginning therapy differs.

This presentation will present findings of a pilot study to determine the possibility of developing a work load index to pre-determine nursing hours needed on an individual-case basis.

All patients received the same preinitiation education. The study coordinator performed an interview, and the patients were asked to fill out a Depression Inventory and MS Quality of Life questionnaire. Past history was also reviewed from patient's records.

Upon initiation of therapy, patients recorded in their diaries any interaction they had with a health care professional. The study coordinator also kept a record of interactions recording content and length of conversation. Patients were followed for three months following initiation of therapy.

Patients were matched for four variables across all four therapies. Interactions were plotted on grids and analyzed at completion of the study by a descriptive analysis.

A Description of Multiple Sclerosis (MS) Patients in Long-term Care Centers Using the Continuing Care Needs Determination Instrument

Sharon Williams, PhD, Warren S, Beaulne P, Hollander M, Lyle M, Schalm C, Wanke M

Published estimates suggest that up to 10% of Canadian MS patients reside in long-term care centers, but their characteristics have rarely been described. Some long-term care centers have begun to collect standardized client assessments, which will provide this information.

Recently, Alberta Health and Wellness developed an assessment tool, the CCNDI, which includes measures of activities of daily living (ADL), cognition, depression, behavior problems, social involvement, and informal support. Items for this tool relevant to facility-based care were derived from the Minimum Data Set: Version 2 and the Alberta Assessment and Placement Instrument (AAPI), which have been tested for reliability and validity. The sample consisted of 1,845 long-term care residents (15% of the total) from centers province-wide.

Of the residents sampled, 5% were diagnosed with MS. They represented 49% of the chronically disabled service clients between ages 18 and 55 and 25% of these clients across all ages. Sixty-nine percent of MS patients were female. Their average age was 53 at admission and 58 at assessment. Thirty-eight percent were married, and 58% had graduated from high school or college/university. Seventy-two percent scored severely impaired on physical ADL, but only 34% showed any instrumental ADL impairment. Fifty-four percent gave no indication of need for cognitive care. Forty-eight percent gave no indications of depression, and 38% gave no indications of behavior problems. As for social involvement in community life, 35% accepted invitations to most group activities. Overall, only 19% of MS patients showed no sense of social involvement. On average, MS patients received 47 hours of informal support per week from family or friends and required 196 minutes per day of formal care, according to a staff time-use analysis.

Such information provided by databases using tools like the CCNDI would be helpful in planning special program needs for long-term care center clients with MS.

The Informational Needs of the Newly Diagnosed Person with MS and their Families

Judy Wollin, RN, PhD

The aim of the study was to identify from people with MS (and their families) what information (as well as in what format and at what point in the course of the disease) they felt would assist them and their family. Without this necessary information, people—particularly those with a chronic disease—are handicapped when making decisions relating to their health and lifestyle.

A Queensland-wide cross-sectional self-report study design was used. The research participants felt that people with MS should be provided with information about how MS would affect them (73%), how to manage their MS (57%) and how to treat MS (50%). Doctors, usually the neurologist, were the recommended source of information about MS. Nurses were recommended by 21% of participants. The preferred format for information included one-on-one sessions (68%), group sessions (62%), pamphlets (56%), and books (53%).

The people with MS and their family and friends who participated in this research wish to be provided with a range of information. They recommended that the newly diagnosed and their families be provided with information that reflects their personal needs; is provided in person in both group and individual sessions; and that includes research aimed at cures, therapies, counseling, and support services early in the course of the disease. Currently doctors are the preferred source of information. Nurses have an increasing presence in supporting people with MS and—as the value of a team approach to supporting the person with MS and his or her family becomes the norm—the opportunity to play an increasingly significant role.

Urinary Incontinence, a Precursor to Increased Social Handicap: A Critical Variable in Assessing Handicap in People with MS

Judy Wollin, RN, PhD

Handicap is the disadvantage—judged from the perspective of the society they live in—experienced by a person with an impairment or disability experience. Handicap is the loss of social status and cues rather than functional ability (Badley, 1995; WHO, 1992). The use of a single variable—"pad use to manage urinary difficulties such as leaking"—is offered as an indicator of impending handicap in MS. A positive response to the question "Do you use pads to manage urinary difficulties such as leaking?" is a precursor to unemployment. Since unemployment is strongly linked to social disadvantage—clinicians may find being alerted to impending social disadvantage by using this single prompt allows a window of opportunity for a more detailed assessment and appropriate interventions.

Fatigue and mobility difficulties have been cited as factors contributing to unemployment (Edgley et al, 1991; LaRocco et al, 1985). In contrast, in this research the use of pads to manage urinary incontinence was found to be a better indicator of impending unemployment. The logistic regressions indicated that fatigue and mobility difficulties are not as significant as "pad use" in explaining employment status.

By seeking information about a person's continence status with the question "Do you use pads to manage urinary difficulties such as leaking?" clinicians give permission for this taboo to be addressed, validate concerns about incontinence, and provide much-needed accurate information about incontinence and its management (Norton et al, 1998). Early intervention with advice on MS and the range of strategies that can be used to manage urinary incontinence (eg, intermittent self-catheterization) may delay unemployment, poverty, and associated social handicaps.

MS Treatment Patterns at the End of the 20th Century

Timothy Vollmer, MD, Weijia Ni, PhD, Olympia Hadjimichael, MPH

We investigated treatment patterns among 6,902 MS patients, using data gathered in the NARCOMS Registry from January 1998 to December 1999. The sample approximates the characteristics of the MS population in the US, with 74% female, 91% Caucasian, and a mean age of 47.

The majority of the patients (89%) have visited neurologists either for treatment or for consultation. Symptomatic therapies are used by 78% of the patients; the use rate is highly correlated ($P < .001$) with degree of disability, as measured by functional performance in each of the eight domains: mobility, hand, vision, fatigue, cognition, bladder/bowel, sensory, and spasticity. Various kinds of alternative drugs are used by 40% of the patients.

The immunologic therapies made available in the past decade, in particular the ABC drugs (Avonex[®], Betaseron[®], and Copaxone[®]), have had considerable impact on the treatment of MS, with 62% of all relapsing-remitting patients in the registry sample reporting usage. Single-drug users were 20% for Avonex, 17% for Betaseron, and 6% for Copaxone. The rest (19%) used more than one drug. On average, 39% of all ABC users discontinued treatment after 12 months, either stopping entirely or switching to another drug. There is a statistically significant correlation between use of ABC drugs and, respectively, higher income, more education, and

shorter years of disease. There is also some indication that younger patients and those who have insurance coverage other than, or in addition to, Medicare and Medicaid are more likely to use these drugs. Neurologists (97%) mostly prescribe ABC drugs. Most users (65%) rate their drug experience as either good or very good.

We will present additional data from the rapidly expanding database and discuss how MS can be better managed in the new millennium with improvements in therapy, as well as long-term outcomes of these treatments.

Effect of Race in the Treatment of MS

Timothy Vollmer, MD, Olympia Hadjimichael, MPH, Weijia Ni, PhD

We investigated the effect of race in the treatment of MS in the United States, using data from the NARCOMS Patient Registry. Among all MS patients who registered in the database during 1998-1999, 91% were Caucasian; 4.5% were African-American; 1.8% were Hispanic-Latino; 1.1% were Native American; and the rest included Asian or Pacific Islander, Asian Indian, Semitic/Arab, and others.

The two largest groups, Caucasians and African-Americans, are compared in the analysis. The two groups do not differ in age distribution, gender, relapse rate, or average disease length. However, compared to Caucasians, African-Americans have fewer years of education, lower income, and less insurance coverage (all comparisons reached statistical significance: $P < .05$). A significantly higher proportion of African-American patients report that their employment has been adversely affected as a result of MS-related disability.

Regarding MS-related treatments, Caucasians report higher use of symptomatic therapies (77% vs 67%; $P < .005$) and alternative drugs (38% vs 23%; $P < .005$). Although the two groups do not differ significantly in functional performance measured in eight domains (mobility, hand, vision, fatigue, cognition, bladder/bowel, sensory, and spasticity), as well as the Patient-Determined Disease Steps (PDDS), a surrogate measure of EDSS. The use-rate of ABC drugs (Avonex[®], Betaseron[®], and Copaxone[®]) and other immunologic therapies does not differentiate the two race groups. Neither is there a difference between the two groups in the proportion of patients who discontinued these therapies.

Our data show a clear group difference in the use of symptomatic (thought not immunologic) therapies, which may be related to socioeconomic differences between Caucasians and African Americans. The pattern may also reflect an overall discrepancy in health care delivery between the two race groups.

Development and Uses of the NARCOMS Registry

Timothy Vollmer, MD, Olympia Hadjimichael, MPH, Weijia Ni, PhD

We present the historical development of the NARCOMS Registry since 1993, when it was established as a project of the Consortium of MS Centers. Patient recruitment started slowly in 1996 and reached 3,000 in early 1998. Subsequent collaborative efforts with the VA and NMSS rapidly enriched enrollment, which has currently surpassed 15,000 MS patient participants.

The NARCOMS Registry is patient-driven; potential participants are contacted through various means and provide an adequate representation of the MS population. Collected data include

demographic information, MS-related medical history, immunologic and symptomatic therapies, utilization of health care services, and a series of patient-assessed performance scales that reflect disability in mobility, hand, vision, sensory and bladder function, fatigue, cognition, and spasticity.

The first milestone in utilizing the registry's data was in 1998, with a survey of registrants on determinants of adherence to injection therapy in MS. Two additional surveys have been conducted since then.

The second milestone in 1999 was in facilitating recruitment for two multicenter clinical trials. Individual centers have also used the registry to enhance clinical trial recruitment.

Other developments: The first update of the registrants' data was mailed to them in January of 2000. Updates are scheduled for every six months.

Online enrollment and updates will be available to patients through the Internet in the spring of 2000.

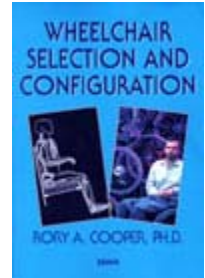
An international collaboration is underway to coordinate registries from various countries in order to maximize research opportunities.

A direct benefit to registrants since the fall of 1999 was the distribution of MSQR (a quarterly joint publication with EPVA), which provides research news.

Future work will include continued expansion of the registry database, increased access and use of the registry to consortium members, increased membership involvement in organizational and research teams, and development of the Cooperative Studies section of NARCOMS. Data will be presented on the current development and use of the NARCOMS Patient Registry and Cooperative Studies research news.

Book Review

The Editors of the *International Journal of MS Care* are constantly evaluating reference books that can be of assistance to MS care providers around the world. If you have questions on any of the books reviewed here, or have any suggestions on additional books to be reviewed, please contact us at IJMSC@partmedcomm.com.



Wheelchair Selection and Configuration

by Rory A Cooper, PhD

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410 pages

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Wheelchair Selection and Configuration is a reference book and textbook. It is laid out well, with goals for the reader appearing at the beginning of each chapter. In Chapter 1, the author gives the reader a history lesson on the development of the chair as a mobility device, and introduces us to the psychological factors involved in wheelchair usage. In Chapter 2, we get an introduction to principals of measurement and its overall importance in wheelchair usage. This is continued with a very in-depth lesson in physics in Chapter 3.

Chapters 4 and 5 are somewhat overdone, in this reviewers opinion. However, they are academic in nature. Chapter 6 addresses wheelchair standards in depth; this is valuable information for those involved with wheelchair purchasing. In Chapters 7 through 12, the author details types of wheelchairs and specialized usage, as well as selection of specialized seating designs and cushions. Assessment for the proper wheelchair is very important, and these considerations are covered in Chapter 13.

This book is not light reading, but for the person with a keen interest in wheelchair technology it is worthwhile reading and a good text for rehabilitation specialists.

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