



PRIMARY PROGRESSIVE MS: THE BENEFITS OF “NEGATIVE” TRIALS

Of the various forms of multiple sclerosis (MS), the primary progressive subtype (PPMS) offers particular challenges for clinicians. The absence of discrete, recognizable attacks or relapses can make diagnosis difficult, particularly in the early stages of the disease. Pharmacologic management remains a challenge as well, as the few trials that have been conducted in patients with PPMS have not supported the use of any agent.

Nonetheless, these “unsuccessful” studies have provided a wealth of interesting findings that not only shed light on the course of PPMS but may also prove valuable in guiding the design of future trials. At a symposium during the recent 19th Annual Meeting of the Consortium of Multiple Sclerosis Centers in Orlando, researchers

discussed the challenge of diagnosing and treating PPMS and shared information gathered from recent trials.

DIAGNOSTIC DIFFICULTIES

Part of the problem clinicians encounter when making a diagnosis is that the definition of PPMS has been “a moving target” during the past decade, noted Emmanuelle Waubant, MD, PhD, an Assistant Professor of Neurology at the University of California in San Francisco. The various subtypes of MS were redefined in 1996¹; subsequently, two separate sets of diagnostic criteria for PPMS were proposed, each broadly similar but differing in important details. (The most recent of these criteria, formulated by McDonald et al in 2001², are presented in the Table.)

Jerry S. Wolinsky, MD, Professor of Neurology at the University of

Texas Health Science Center at Houston, provided an advance glimpse of the new, simplified, but not yet finalized, diagnostic guidelines that were devised earlier this year at a meeting in Amsterdam. The criteria are notable in that positive cerebrospinal fluid (CSF) findings are no longer required for diagnosis; instead, patients must have disease progression for at least one year plus two of the following three findings: positive brain MRI, positive spinal cord MRI, or positive CSF (Table).

Even with the revised criteria, diagnosis can be tricky. Because age at diagnosis is greater for PPMS than for relapsing-remitting disease—by as much as 10 years, according to some reports—clinicians must consider a wider range of alternate diagnoses. Diagnosis in older patients may be even more

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challenging, he noted, as they may present with concomitant disease unrelated to MS and incidental brain pathology on MRI. Also, older patients may have forgotten long-ago events that, if revealed to their clinician, might have provided keys to a diagnosis, Dr. Wolinsky said. “I’ve followed patients for two or three years who I believed had PPMS. Finally they would reveal something telling, such as the time in high school when they’d have to stop playing basketball because they had double vision and nobody could figure out the cause.”

CONVERSION AND PROGRESSION

Among patients in whom PPMS has already been diagnosed, two clinical issues of particular concern are the rate of disease progression and the possibility that the patient will convert to progressive relapsing MS and begin experiencing attacks. To examine these issues, Drs. Wolinsky and Waubant reviewed data from three phase II and phase III trials that have focused on PPMS patients.

By far the largest of these trials has been the PROMiSe trial, which was launched in 1999.³ Inclusion criteria included progressive neurologic symptoms (including a myelopathic component) for at least six months, no history of prior neurologic attacks, objective pyramidal damage, a score between 3.0 and 6.5 on the Expanded Disability Status Scale (EDSS), and recent CSF testing. All patients also underwent MRI. At least 64% of these patients would have been classified as having “definite PPMS” according to the McDonald criteria.

Subjects were randomized to treatment with glatiramer acetate (20 mg/day) or placebo during a 16-month enrollment period. The study was terminated earlier than scheduled in 2002 after an interim analysis revealed that it was highly improbable that the study would reach statistical significance.

At the time the study was concluded, there had been 41 relapses involving 37 patients, which translates to a rate of about 2% per year. Participants who had gadolinium-enhanced lesions (about 14% of subjects) had a twofold increased risk of relapses.

Because age at diagnosis is greater for PPMS than for relapsing-remitting disease—by as much as 10 years, according to some reports—clinicians must consider a wider range of alternate diagnoses.

Significantly more surprising than the low relapse rate was the low rate of progression seen in the study. The investigators had predicted an annual progression

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Table

DIAGNOSING PPMS

Current Criteria

- Positive CSF
- MRI dissemination in space:
 - evidence of 9 or more T2 brain lesions; or
 - 2 or more cord lesions; or
 - 4-8 brain lesions and 1 cord lesion; or
 - positive VEP with 4-8 MRI lesions; or
 - positive VEP with less than 4 brain lesions plus 1 spinal cord lesion
- MRI dissemination in time or continued progression for 1 year

Tentative Revision

- Disease progression for 1 year (historical or observed)
- 2 of the following 3:
 - positive MRI (9 T2 brain or spinal cord lesions or 4 or more lesions plus positive VEP)
 - positive spinal cord MRI (2 focal T2 lesions)
 - positive CSF (oligoclonal bands on isoelectric focusing, or elevated IgG index)

CSF, cerebrospinal fluid; IgG, immunoglobulin G; MRI, magnetic resonance imaging; PPMS, primary progressive multiple sclerosis; VEP, visual evoked potential.

Source: Wolinsky JS. Primary progressive MS: diagnosis and prognosis. Lecture presented at: CMSC 19th Annual Conference; June 1-5, 2005; Orlando.

THE FUTURE OF THERAPY

Although none of the drugs tested in these studies were more effective than placebo for PPMS, Dr. Waubant advised against jumping to the conclusion that immunosuppressive or immunomodulatory therapies are ineffective in PPMS. She noted that because it may take a year or more for disease-modifying treatments to begin to reverse ongoing disease process, longer clinical trials—of at least three years' duration—would probably be necessary to show clinical benefits. Given the current uncertainty over the optimal design of a PPMS study, Dr. Waubant suggested that conducting phase II trials of new or existing agents may actually be detrimental, because negative results from an inadequately designed trial may lead researchers to discount a medication that may actually be helpful to patients.

Nonetheless, an important new phase II/III clinical trial in PPMS was recently launched. The study is focusing on rituximab, a synthetic antibody that binds to and induces lysis of B

rate of about 50% among the least affected patients (those with an EDSS score between 3.0 and 5.0). After one year, however, the progression rate was only 16% in these individuals; after two years, just 28% had progressed. The rate was slightly higher (34%) among more severely affected patients, though whether this suggests anything about the trajectory of true biological change during the course of the disease or is simply a result of the outcome scales used is absolutely unclear, Dr. Wolinsky said.

The fact that PPMS progressed more slowly than expected reduced the trial's statistical power to detect modest therapeutic benefits from the use of glatiramer acetate. However, it was encouraging news for patients worried about their accumulating disability.

Unexpectedly slow progression was also observed in the two phase II trials that have been conducted, Dr. Waubant noted. (Mitoxantrone and interferon beta-1a were studied.) Findings from the PROMiSE study point to the presence of gadolinium-enhanced lesions, positive CSF findings, and a high T2 burden of disease as predictors of faster progression, according to Dr. Wolinsky.

cells. Although most immunologic research for MS has focused on T cells, increasing evidence suggests that B cells not only play a role in the pathogenesis of PPMS but possibly also in determining the severity of the disease, noted Kathleen Hawker, MD, Assistant Professor of Neurology at the University of Texas Southwestern Medical Center in Dallas.

The trial, which is being conducted at 61 centers in the United States and Canada, is scheduled to enroll 435 patients, who will receive either rituximab or placebo for 30 months. In addition to monitoring clinical outcomes, the investigators will also collect data on immunologic and radiologic measures. "Even if it's a negative trial, we'll learn a tremendous amount about the immunology of this disease," Dr. Hawker concluded.

MSX

–Peter Doskoch

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SLEEP DISORDERS IN MULTIPLE SCLEROSIS



Sleep problems in multiple sclerosis (MS) are common. Identifying them properly and treating them appropriately, however, can be difficult for two key reasons: fatigue is a common MS symptom that can be hard to distinguish from the sleepiness that may characterize a true sleep disorder; and many patients with MS take multiple medications, some of which can interfere with sleep. In a recent presentation at the 19th Annual Conference of the Consortium of Multiple Sclerosis Centers in Orlando, two neurologists with expertise in sleep-related issues provided an overview of the most common sleep disorders and offered MS-tailored strategies for addressing them.

An important first step in identifying treatment for sleep disorders—conducting a thorough sleep-oriented history—is one that’s often overlooked, said David W. Brandes, MS, MD, FAAN, who directs both the Northridge MS Center in Southern California and Northridge Hospital’s Sleep Disorders Center. “Many clinicians have heard their MS patients say, ‘I’m tired all the time.’ However, we need to discover how they are defining ‘tired,’” he said. “Also, are they experiencing any mood disorders, such as depression, or any cogni-

It’s often best to consider devoting an entire patient visit to sleep issues, so that clinicians can explore the issue independently of other MS-related symptoms, the presenters recommended.

tive dysfunction?” Even though some patients with MS may experience both fatigue and sleepiness, asking specific questions, such as whether patients routinely fall asleep while reading, riding in a car, or watching television, can help with the diagnosis and, eventually, with treatment.

It’s often best to consider devoting an entire patient visit to sleep issues, so that clinicians can explore the issue independently of other MS-related symptoms, Dr. Brandes and co-presenter Rock Heyman, MD,

Director of the MS Center of the University of Pittsburgh Medical Center, recommended.

One challenge for health care professionals who treat patients with MS is that few physicians or nurses have received much training in the mechanics of sleep and/or sleep disorders. In addition, the formal study of sleep is a relatively recent development: it wasn’t until the 1970s that sleep disorders were classified and the first associated treatment center was created, Dr. Brandes explained.

TYPES AND CAUSES OF SLEEP DISORDERS IN MS

Of the three major types of sleep disorders, hypersomnia and insomnia are those most likely to occur in individuals with MS. The third type of sleep disorder, parasomnia, is characterized by undesirable physical phenomena that occur primarily during sleep, such as night terrors or sleepwalking. However, parasomnia is uncommon in the general population and tends not to be an issue in MS, Dr. Brandes added.

Both insomnia and hypersomnia could be caused by certain MS medications, noted Dr. Brandes. Antispasticity drugs such as baclofen and tizanidine, or antiseizure medications such as gabapentin or topiramate, may cause daytime sleepiness, as might some antidepressants and antihypertensives. Stimulants such as modafinil, if given too late in the day, or beta interferons, which can produce flu-like symptoms that may be more pronounced if the drug is taken at bedtime, may interfere with the quality of sleep.

Poor sleep hygiene, as well as a variety of medical or metabolic conditions, might also play a role, Dr. Brandes continued. For example, hypersomnia might be caused by sleep-arousal

issues such as obstructive sleep apnea (OSA) or gastroesophageal reflux disease. Central sleep apnea, the loss of the muscular effort required to breathe during sleep, has been reported in neuromuscular disorders, including MS, but it is extremely rare, Dr. Brandes added. Periodic limb movements of sleep occur in up to 65% of patients with MS and are a major issue in disease-related sleep disturbances.

Other factors specific to MS, such as nighttime spasms, neuropathic pain, or nocturia, may result in



Multiple Sclerosis Nursing in 2005: A Global Perspective

CMSC Meeting Highlights

With nearly 1,000 MS health care professionals in attendance, the 19th Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC), held June 1 to June 5 in Orlando, was the largest in history. CMSC Executive Director June Halper, MSCN, ANP, FAAN, noted that this year's meeting also featured more symposia, scientific papers, and posters than had any previous year.

The theme of the 2005 conference was "Navigating the World of Multiple Sclerosis" and featured state-of-the-art information on the latest treatments, research, models of care, and advocacy groups. As in past years, the conference represented a collaborative effort by the CMSC, the International Organization of MS Nurses (IOMSN), and the Latin American Committee for Treatment and Research in MS (LACTRIMS). Highlights included the Presidential Lecture titled "The Potential for Remyelination in MS," given by CMSC Lifetime Achievement Award winner Cedric S. Raine, PhD, DSc. Symposia topics reflected the broad scope of MS care today, and included rehabilitation, pregnancy issues, ethnocultural concerns, alternative medicine, and neuroprotection/neuroregeneration, among many others.

Remembering Dr. Paty

This year's meeting was dedicated to the memory of Dr. Donald W. Paty, who was one of the original founders of the CMSC in 1986 as well as Medical Director of the MS Center at the University of British Columbia in Vancouver. A firm believer in the value of comprehensive, coordinated, and continuous MS care, Dr. Paty was a pioneer in the application of MRI in the study of MS. Due in large part to his efforts, the use of MRI has become standard in clinical trials all over the world.

"Dr. Paty was extremely proud of the CMSC," noted Ms. Halper. "Our impact has been felt throughout the world and we have collaborated with numerous individuals and organizations to meet our mission."

Conference Awards

At the IOMSN dinner, held Wednesday, June 1, at the Walt Disney World Swan and Dolphin Hotel, several awards were presented to commend individuals on their achievements in various areas of MS care and research.

The June Halper Award for Excellence in MS Nursing was presented to two recipients: Josée Poirier, RN, BSc, MSCN of the MS Clinic at Hospital Notre Dame in Montreal; and Marie Namey, RN, MSN, MSCN, of the Mellen Center for MS Treatment and Research at the Cleveland Clinic Foundation in Ohio. The award is

presented to those who exemplify leadership and creativity in caring for people with MS and their families/caregivers. It also recognizes the recipients' "energy of purpose to provide or promote the most up-to-date, comprehensive MS care possible," according to the CMSC.

The Thumbs-Up Award is presented to a person who or organization that has been instrumental in advocating and promoting MS nursing. This year, the award was presented to the MS Trust, an independent United Kingdom-based charity that provides services for those with MS, their caregivers, and their health care professionals.

The IOMSN Hope Award was presented to Christine Martin, PhD, of the Veterans Health Administration MS Center of Excellence-East in Baltimore for her poster, "Empowering Caregivers for Individuals With Multiple Sclerosis." The Hope Award is presented to the author(s) of a poster that best depicts a spirit of optimism in the area of education, clinical practice, or research. (See page 10 for more detailed information on Dr. Martin's poster.)

Selected presentations from the conference, as well as posters and abstracts, are available on the CMSC Web site (www.ms-care.org). Preparations are under way for next year's conference, to be held May 31 through June 4 in Phoenix. **MSX**

Legal Issues in MS Nursing

Although it is not often in the forefront of their mind, clinicians are responsible for the legal implications of day-to-day practice. If a malpractice complaint is filed against a health care professional, it may stir up doubts and fears, and raise questions about his or her own competence and professional integrity.

“The first thing a clinician named in a lawsuit should do is relax, as he or she hasn’t necessarily done anything wrong,” advised Rebecca Berg Solano, Esq, in her presentation titled, “Legal Issues Related to Advanced Practice Nursing,” at the 19th Annual CMSC Meeting in Orlando.

A clinician can be named in a malpractice suit for any number of reasons, explained Ms. Berg, who is a Senior Associate at Wilson, Elser, Moskowitz, Edelman & Dicker LLP in New York City. For example, she noted, the plaintiff’s attorney may know little about the health care system and may have simply named any medical staff member remotely connected to the case.

“Of course, there is always the possibility that the plaintiff’s attorney simply made a mistake and named the wrong person in a lawsuit,” she added.

Settle or Go to Trial?

Ms. Berg pointed out that there are many factors for a clinician to consider in deciding whether to settle a case or go to trial. During this process of deliberation, it’s important to have a competent and trustworthy legal team. The first consideration is whether the clinician feels a malpractice suit is justified and, if so, why.

Other considerations include questions such as: Does the defense attorney think the case can be won? Does the attorney consider the courts where the trial would take place to be “pro-plaintiff” or “pro-defense”? Does the clinician feel emotionally prepared to go through a trial that may continue for weeks or months, and can he or she take the necessary time off from work?

“Sometimes, you won’t have a choice as to whether or not you settle,” noted Ms. Berg. She explained that some malpractice insurance carriers can and will settle a case without the defendant’s consent.

If a malpractice case does go to trial, the plaintiff’s attorney may present evidence from many sources, including the clinician’s own sworn testimony, which is obtained during pretrial discovery. The plaintiff’s attorney may also attempt to garner potentially damaging testimony

from expert witnesses, the clinician’s coworkers, and even the plaintiff’s family.

“The medical records will certainly be brought in,” Ms. Berg cautioned. “The clinician should never alter them, even to change something he or she had been meaning to change or to complete a missing note, as the plaintiff’s attorney might have obtained a copy of the original records.

“While knowing what to expect from a malpractice suit can be helpful, not having the suit brought at all is obviously preferable,” Ms. Berg added (see sidebar).

Real-Life Legal Lessons From MS Nurses

Marie A. Namey, RN, MSN, MSCN, a Clinical Nurse Specialist at the Cleveland Clinic Foundation in Ohio and a founding member of the IOMSN, learned through experience about the need to document patient encounters. She discussed a lawsuit involving a patient who fell out of her wheelchair in Ms. Namey’s office.

“I certainly didn’t think she was harmed,” said Ms. Namey, who therefore didn’t make a written record of the fall. Months later, the patient had filed suit against the hospital. The case was resolved out of court but not before Ms. Namey went through a long deposition—which was much more arduous than necessary due to her failure to document her involvement in the case—and many meetings with lawyers.

Can Lawsuits Be Avoided?

Although there is no way for clinicians to completely eliminate the possibility of legal action, there are ways to minimize the risk, Ms. Berg explained.

Be clear about roles and responsibilities from the start. To a patient, a nonphysician may be indistinguishable from a physician. Therefore, clinicians must make sure their full title and role in the treatment plan is known to the patient.

Documentation is critical. Briefly but accurately record every interaction with a patient, whether it occurs in person or over the phone. “If you don’t, it will be your word against the plaintiff’s,” Ms. Berg warned.

Keep legible notes. “I’ve actually seen depositions and trials in which clinicians couldn’t read their own writing,” related Ms. Berg, noting that a record is worthless if it cannot be deciphered in court.

Be cautious when using e-mail. E-mail is discoverable—that is, it can be used as evidence in a malpractice suit. “It’s potentially a very dangerous form of communication,” Ms. Berg cautioned, “because people often say more in an e-mail than they might in a formal letter or chart.”

Linda Morgante, RN, MSN, CRRN, MSCN, had a distinctly different experience as a defense witness in the case of a patient suing a physician for a misdiagnosis of MS. “I found it very difficult to testify against the patient, with whom I had had a very long-term, close relationship,” acknowledged Ms. Morgante, an Advanced Practice Nurse at Mount Sinai MS Care Center in New York City. “It was important to me, however, to make sure that the truth was known. That was what I’d hoped to accomplish in this case.”

In the end, the jury found in favor of the physician. Ms. Morgante stressed the lesson learned from this situation: “What you write down in a patient’s chart can be just as damaging as what you don’t write down. Be honest but concise.”

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—*Timothy Begany*

Speech, Swallowing, and Cognition Issues in MS

MS can cause a wide variety of disabilities that negatively impact many areas of a patient’s life, including employment and personal relationships. However, the experience of MS—and its symptoms—varies from one patient to the next. That’s why one key to managing disorders of speech, swallowing, and cognition is individualizing treatment for each patient, said Bonnie Schaudé, MA, CCC/SLP during her talk at the CMSC’s recent conference in Orlando.

“It is vital for us, as clinicians, to be aware of how these disorders often seriously impact the quality of life of people with MS,” she pointed out. “However, educating and instructing patients on modifications and compensatory strategies can provide them with tools to adjust to any losses and to maintain performance levels,” she stressed.

Dealing With Speech Difficulties

Forty percent of MS patients report changes in speech, a figure that rises with disease progression, according to Ms. Schaudé. Some common speech disturbances include impaired volume control, harsh vocal quality, and trouble with articulation. The type and severity of these symptoms are related in part to the stage of the disease process and the neural systems involved, Ms. Schaudé noted.

Clinical examination should assess each of these symptoms and therapy should be tailored to the specific impairments and their impact on function, said Ms. Schaudé.

When deciding on treatment options, however, the clinician should consider that the patient might have concomitant cognitive problems that can affect the ability to learn and use new skills, she explained.

Speech interventions may range from teaching energy conservation techniques (for mild speech disturbances) to teaching more appropriate respiratory patterns (for moderate disturbances). In severe cases, devices such as an alphabet board may be needed to assist or replace verbal communication. However, research suggests that early intervention can facilitate later adaptation. “Compensatory techniques that are learned early can be implemented throughout the course of the disease,” said Ms. Schaudé. “That can be very empowering for patients.”

Swallowing Issues

An estimated 19% to 30% of MS patients have chewing and/or swallowing problems in early stages of the disease; this figure may rise to 50% in advanced stages, said Ms. Schaudé. Common symptoms reported include choking on and/or difficulty in swallowing food, liquids, and even saliva, drooling, and feeling as though food is “stuck” in the throat.

“Clinical findings may indicate that the swallow mechanism appears to be within functional limits, even though patients are complaining of difficulties,” said Ms. Schaudé. Therefore, the patient’s perceptions of swallowing problems are critical. “Speech therapists should consider supplementing clinical and radiographic assessment tools with quality-of-life measures to determine the total impact that the swallowing disorder has on the patient and his or her family,” she advised.

Removing distractions may help in reducing symptoms of a swallowing disorder. Changes in posture, modifying food textures to those which are easier to swallow (such as purees), and replacing three large meals with smaller, more frequent meals may also have a significant impact for some individuals, Ms. Schaudé noted.

For cases of more severe swallowing disturbances, additional treatment may involve implementing specific exercises to improve strength and coordination of the swallow mechanism. Behavioral strategies, such as cutting food into smaller pieces and eating more slowly, may also be helpful, said Ms. Schaudé. In advanced stages of MS, alternatives to oral feeding may be necessary if a patient’s health and safety are at risk.

Cognitive Changes

Though they may be so subtle that they fail to show up on less sensitive assessment measures, cognitive changes can profoundly impact a person's quality of life and may affect up to 50% of MS patients. Cognitive impairment may cause problems with memory, attention/concentration, information-processing speed, executive functions, visuospatial skills, and language. "The variability of symptoms may be due in part to the number, location, and activity of MS lesions," explained Ms. Schaude.

Cognitive assessment involves a combination of standardized clinical testing, patient/family interviews, and a home evaluation. Another important aspect of the assessment is a functional cognitive communication evaluation, which involves examining the impact of cognitive changes on the patient's activities of daily living, said Ms. Schaude.

Treatment of cognitive impairment may include cognitive rehabilitation, psychological counseling, and education/family training. Ms. Schaude treated one patient who felt cognitive changes had started to affect his work performance. Neuropsychological testing showed a very slight decline. However, during an interview he revealed that he was depressed over his condition, he was sleeping poorly, his diet was unbalanced, and he no longer exercised. A combination of counseling, medication, and organizational time management strategies helped him deal with these problems; as a result, his work capacity increased.

Ms. Schaude reminded the audience that their goal should be to help MS patients maintain a maximal level of independence and a healthy, productive quality of life. "As one MS patient put it, 'MS doesn't really affect what I do, but rather how I do it,'" she concluded. **MSX**

—David Holzman

MULTIPLE SCLEROSIS CERTIFIED SPECIALISTS

On February 12 through February 26, 2005, candidates took part in the second sitting of the examination for Multiple Sclerosis Specialists developed by the Clinical Care Committee and the Professional Testing Corporation. The successful candidates are now eligible to

use the registered designation of Multiple Sclerosis Certified Specialist (MSCS). Those interested in obtaining information about future sittings of the exam may contact the Professional Testing Corporation at www.ptcny.com.

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sleep deprivation or in nonrestorative sleep. Insomnia—whether sleep-onset or sleep-maintenance in nature—might be caused by MS-related pain, anxiety, or depression, by circadian disturbances, or by substance abuse involving prescription or nonprescription medications.

Because of the many issues that might be involved in sleep problems in MS, clinicians must expand their focus beyond the disease when trying to make diagnoses, both presenters urged. “We have to consider other possible causes of sleep disorders, because people with MS might have coexisting illnesses and use medications for other conditions that are causing or contributing to problems with sleep,” Dr. Brandes advised.

EVALUATION OF SLEEP DISORDERS

When a sleep disorder is suspected, evaluation necessarily becomes a protracted, multistep process, according to Dr. Heyman. The history taking should begin with use of a sleep rating scale, such as the Stanford Sleepiness Scale or the Epworth Sleepiness Scale, and should address familial factors and substance use. Screening for mood disorders, such as depression, might also be warranted. Physical examination of the airway, jaw, tongue, and palate might be helpful in identifying anatomic deviations that may contribute to breathing difficulties during sleep.

Finally, a patient’s use of a sleep diary may help identify a possible disorder or a sleep-hygiene problem, and can offer a starting point for behavioral or pharmacologic treatment, Dr. Heyman said. He cited the example of a patient with MS who, after taking care of her children and spouse during the day, admitted that she often does housework until the early hours of the morning. “She doesn’t want to give up all the things she thinks she has to do—but she’s not placing enough importance on getting a proper amount of sleep,” Dr. Heyman said. When incorporated with the perspective of a patient’s bed-partner, the diary can be particularly useful.

For patients who report that they have slept “enough hours” and yet remain chronically sleepy, and for those whose disorder cannot be readily identified, targeted testing by experienced sleep specialists may be in order. A polysomnograph, or multichannel sleep recording, can identify several issues that may be contributing to a sleep disorder. Dr. Heyman noted that many MS treatment centers offer polysomnograph services without specialist consultations or sleep-specialist referrals, but said that such consulta-

tions may be more effective in ensuring differential diagnosis and fine-tuning treatment.

A multidisciplinary approach—involving a psychiatrist or psychologist, along with a neurologist and MS nurse—may be warranted to obtain a “big-picture” solution to the sleep problem, Dr. Heyman said.

PURSUING TREATMENT STRATEGIES

Treating sleep disorders can be almost as complex as identifying them, especially for patients who take MS medications, both presenters acknowledged. Narcolepsy can be effectively treated with stimulants. Behavioral management, such as biofeedback or progressive relaxation techniques, or the performance of appropriately timed (morning or early evening) exercise, is helpful in alleviating insomnia but can take several months to become effective. Sleep disorders such as OSA can often be successfully treated with simple, noninvasive therapies such as continuous positive airway pressure, which uses a mask-like device during sleep. Patients who pursue this therapy “might need encouragement from their clinicians,” Dr. Heyman noted, as patients may need some time to become accustomed to using the machine.

If it is determined that sleep disturbances are caused by a patient’s medication regimen, Dr. Brandes explained, decreasing doses or changing medication schedules may help. He also stressed the importance of encouraging patients to discuss with their clinicians side effects that might be interfering with sleep, to ensure that an accurate diagnosis is made.

In the treatment of insomnia, clinicians generally are beginning to move away from long-acting (and potentially addictive) benzodiazepines such as diazepam (Valium®) and alprazolam (Xanax®), in favor of newer, nonbenzodiazepine hypnotics such as zolpidem (Ambien®), eszopiclone (Lunesta®), and zaleplon (Sonata®). These drugs also have shorter half-lives than do traditional hypnotics, alleviating the residual sleepiness some patients may experience the next morning.

“Several studies have examined MS lesions and their possible relationship to sleep disorders, with various findings,” Dr. Brandes said. “In some of the studies, patients with brain lesions experienced improvement of sleep problems with the use of steroids.” However, he pointed out, these studies involved small numbers of patients; further studies in this area are needed before any significant conclusions can be made.

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—Bonnie Darves

LITERATURE MONITOR/ NEWS ROUNDUP



EMPOWERING FAMILY CAREGIVERS

A poster based on the National Family Caregiver's Association (NFCA) Family Caregiver Self-Advocacy Training Project won the IOMSN Hope Award at this year's CMSC Annual Conference. This project emphasizes family caregiver self-empowerment through use of a diverse network of professionals and family caregivers who convey the program's philosophy and needed skills. It focuses specifically on improving participants' grasp of medical terminology and their ability to communicate effectively with professionals involved in the patient's care.

"One of the foremost responsibilities of MS caregivers is the necessity of becoming the conduit between patient and provider," noted lead author Christine Martin, PhD. She pointed out that many MS caregivers experience negative feelings, such as helplessness and intimidation, when they interact with clinicians. With that in mind, Dr. Martin and her colleagues Kathleen Costello, RN, MS, CRNP and Mary Ehrmantraut, RN, MS, CRNP adapted the NFCA project for the MS Center of Excellence-East in Baltimore.

The researchers introduced vocabulary and common scenarios regarding MS symptoms and treatments to caregivers. The team also developed a questionnaire—designed to determine the efficacy of the training with regard to self-efficacy, comfort/confidence levels, and knowledge/skill improvement—that was administered to participants before and after the workshop.

Of notable interest were caregivers' improvements in managing power ($P < 0.000$) and confidence in using key principles of effective communication ($P < 0.000$). Participants also experienced improvements in empowerment and communication skills ($P < 0.000$), self-efficacy beliefs regarding the ability to communicate well with health care professionals ($P = 0.021$), and organizational skills needed to provide information and records regarding care recipients ($P = 0.012$).

Martin C, Costello K, Ehrmantraut M. Empowering caregivers for individuals with multiple sclerosis. Poster presented at: 19th Annual Meeting of the Consortium of Multiple Sclerosis Centers; June 1-5, 2005; Orlando.

THE CAREGIVER EXPERIENCE: THE MS PATIENT'S PERSPECTIVE

While past research has shed light on the challenges faced by caregivers of those with debilitating illnesses, few stud-

ies have examined the caregiving experience from the perspective of the patient. A poster presented at the recent CMSC meeting in Orlando brought attention to the issues encountered by those with MS who rely on others for care.

Utilizing a grant from the National Institute on Disability and Rehabilitation Research, Estelle Klasner, PhD, and her colleagues from the University of Washington in Seattle conducted semi-structured interviews with one man and five women with moderate to severe MS who received care from a spouse, friend, or family member. Participants were asked to describe the experience of asking for help from their caregivers. The researchers conducted a phenomenological analysis and discovered three major themes among the participants: the wish to preserve existing family roles, the desire to not be considered a burden by caregivers, and the perceived need of the patient to change personal expectations.

According to the researchers, participants felt that family members viewed them differently than they had before caregiving was required. They also felt that their role in the family had become compromised. "In an effort to avoid becoming a burden on caregivers," Dr. Klasner reported, "the patients reported monitoring the amount of help they asked for and always being aware of not asking for too much." Since patients required assistance from others as part of their adjustment to MS, they realized that they needed to change their personal expectations. As a result, however, the participants felt they had lost their sense of control.

"While the course of MS is variable, many individuals will require care and assistance with a variety of activities," Dr. Klasner noted. "Awareness and understanding of the perspectives of both the caregiver and the person with MS can help to establish and maintain a partnership between both parties."

Klasner E, Dudgeon B, Yorkston K. Asking for help: the experience of individuals with MS. Poster presented at: 19th Annual Meeting of the Consortium of Multiple Sclerosis Centers; June 1-5, 2005; Orlando.

PLEASE SHARE YOUR COMMENTS

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A REVIEW OF CANNABIS-BASED DRUGS IN MULTIPLE SCLEROSIS

There has long been anecdotal evidence of the benefits of cannabis-based drugs in treating some of the symptoms of MS. Current literature suggests that using such drugs for the disease may even promote remyelination. However, a recent review published in *Expert Opinion on Investigational Drugs*¹ shows conflicting results regarding the efficacy of cannabinoids in treating MS.

According to the authors, MS patients have long reported that use of marijuana seemed to relieve their symptoms. In a 1997 survey, MS patients reported improvement in spasticity, pain, tremor, and many other common symptoms of the disease as a result of marijuana use. Experimental studies of the animal form of MS have supported these findings; one report showed an improvement in spasticity and tremor in chronic, relapsing experimental allergic encephalomyelitis.²

In addition, there is some evidence that cannabinoids have a neuroprotective effect in MS. In vitro and animal studies suggest that these substances may reduce oligodendrocyte and neuronal cell death, influence inflammation and microglial migration, and enhance remyelination.

According to the researchers, however, the clinical trials examined in the paper demonstrated inconclusive evidence that cannabinoids improve symptoms, prevent relapses, or offer any neuroprotective benefits to those with MS. The authors cited flaws in some of the study designs, such as a lack of appropriate outcome measures. In addition, difficult pharmacokinetics and dose tolerability impede the ability to draw accurate conclusions. The authors also noted that “any improvement in subjective measures may simply reflect an overall euphoria masking all potential symptoms.”

According to the researchers, the success of future studies of cannabinoids in MS are dependent on improvements in four main areas: a better basic understanding of cell death and survival, as cannabinoids appear to affect both; an improved methodology for measurement of symptom improvement and neuroprotection in clinical trials; increased availability of cannabinoid agonists; and development of clinically useful agents that target the endocannabinoid system and modify cannabinoid receptors by indirect means. According

to the authors, “although this group of compounds has been in medical use for centuries, we are only at the beginning of understanding their potential.”

1. Teare L, Zajicek J. The use of cannabinoids in multiple sclerosis. *Expert Opin Investig Drugs*. 2005;14:859-869.

2. Baker D, Pryce G, Croxford JL, et al. Cannabinoids control spasticity and tremor in a multiple sclerosis model. *Nature*. 2000;404:84-87.

CANNABIS-DERIVED, PRESCRIPTION MS PAIN MEDICATION NOW AVAILABLE IN CANADA

Sativex[®], a spray medication for pain derived from the marijuana plant, can now be obtained by prescription in Canada, according to a June 20 press release from the drug’s manufacturer, Bayer HealthCare. In April 2005, Canada became the first country to approve the new drug.

Studies show that up to 80% of people with MS experience some degree of neuropathic pain, which is often undertreated and undercontrolled, according to William J. McIlroy, MD, National Medical Advisor of the Multiple Sclerosis Society of Canada. Approximately 50% of these patients describe their pain as chronic, and many experience minimal pain relief from current treatment options.

Sativex was developed by GW Pharmaceuticals in the United Kingdom. The approval of the drug was based on the results of a placebo-controlled, parallel group study of 66 patients with MS with neuropathic pain, which showed Sativex provided significantly greater pain relief than did placebo. The drug also reduced pain-related sleep disturbances. The most common side effects were nausea, fatigue, dizziness, and application-site reactions.

Sativex is administered in preselected dosages through a spray pump used under the tongue or inside of the patient’s cheek. This formulation enables the patient to have greater dosage control than would be obtained from an oral tablet.

Canadian patients taking Sativex should be aware that they are not permitted to take the drug out of the country, as current regulations deem it a controlled substance.

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Sativex-Novel cannabis derived treatment for MS pain now available in Canada by prescription [press release]. Bayer HealthCare; June 20, 2005.

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CONTINUING EDUCATION CONFERENCE CALENDAR

September 17–20, 2005

9th Congress of the European Federation of Neurological Societies. Location: Athens, Greece. Contact: EFNS Head Office, Breite Gasse 4-8, 1070 Vienna, Austria; +43 1 889 05 03; fax: +43 1 88905 03 13; e-mail: headoffice@efns.org; Web site: www.efns.org.

September 25–28, 2005

130th Annual Meeting of the American Neurological Association. Location: San Diego. Contact: American Neurological Society, 5841 Cedar Lake Road, Suite 204, Minneapolis, MN 55416; (952) 545-6284; fax: (952) 545-6073; e-mail: ana@llmsi.com; Web site: www.aneuroa.org.

September 28–October 1, 2005

Joint Annual Meeting of ECTRIMS and ACTRIMS. Location: Thessaloniki, Greece. Contact: AKM Congress Service, Clarastrasse 57, PO Box CH-4005, Basel, Switzerland; +41 61 686 7711; fax: +41 61 686 77 88; e-mail: info@akm.ch; Web site: www.akm.ch/ectrims2005MD.

November 12–16, 2005

35th Annual Meeting of the Society for Neuroscience. Location: Washington, DC. Contact: Society for Neuroscience, 11 Dupont Circle, NW, Suite 500, Washington, DC 20036; (202) 462-6688; fax: (202) 462-9740; e-mail: info@sfn.org; Web site: www.sfn.org/am2005.

November 13–15, 2005

MS Trust 9th Annual Conference. Location: Blackpool, UK. Contact: MS Trust, Spirella Building, Bridge Road, Letchworth Garden City, Hertfordshire SG6 4ET, UK; +01462 476700; fax: +01462 476710, e-mail: info@mstrust.org.uk; Web site: www.mstrust.org.uk.

May 31–June 4, 2006

20th Annual Meeting of the CMSC. Location: Phoenix. Contact: Tina Trott, Consortium of MS Centers, Gimbel MS Center, 718 Teaneck Rd, Teaneck, NJ 07666; (201) 837-0727 ext 120; fax: (201) 837-9414; e-mail: tina.trott@mscare.org.



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