



## THE EMERGENCE OF BIOMARKERS IN MS

Most evidence suggests that multiple sclerosis (MS) is an autoimmune disorder in which the body's defense mechanisms misidentify myelin as a foreign object, triggering its destruction. Some researchers have begun to focus on finding molecules that react to the normal components of myelin, especially antibodies that help to identify immune system targets. Such molecules are referred to as biologic markers, or biomarkers.

A biomarker can be defined as a "characteristic that is objectively measured and evaluated as an indicator of normal biologic processes or pharmacologic responses to a therapeutic intervention."<sup>1</sup> Biomarkers for the damage and repair mechanisms of MS are often sought in the body fluids (cerebrospinal fluid, blood, and urine) of MS patients.

A symposium at the recent Consortium of Multiple Sclerosis (CMSC) meeting in Scottsdale, Arizona focused on the emergence of antibodies as biomarkers in MS. According to Thomas Berger, MD, MSc, Head of the Neuroimmunological and Multiple Sclerosis & Research Unit in the Clinical Department of Neurology at Innsbruck Med-

ical University in Austria, the ability to identify such markers is vital for the "further understanding of the pathogenesis of MS, as well as for the diagnosis and classification of disease activity, rational design of treatment regimens, monitoring of treatment, prediction of disease progression, and effects of disease-modifying therapy." He added that "biologic markers for the different pathophysiologic processes will individualize MS diagnostics, staging, prognosis, and treatment monitoring in the future." (Examples of antibody biomarkers in MS are listed in the Table.)

### WHAT CAN BIOMARKERS TELL US ABOUT MS?

Claude Genain, MD, Associate Professor of Neurology at the University of California, San Francisco and a Scientist at the California Pacific Research Institute, chaired the CMSC symposium and posed some important questions about MS biomarkers:

- Could MS onset be predicted with a biomarker?
- Could stage of disease progression be determined for individual patients?

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- Could the type of MS or course of the disease be predicted?
- Could the risk for a child or a young adult developing MS be detected?

Finding answers to the above questions could help determine when to start treatment, which is currently a controversial topic, noted Dr. Genain. Two articles in a recent issue of *Archives of Neurology*<sup>2,3</sup> debated the costs and benefits of early treatment versus a “wait-and-see” approach to MS. In the future, biomarkers that predict disease severity and/or disease course may provide much needed answers.

However, in order for biomarkers to be truly useful, certain conditions must be met. Dr. Genain explained that biomarkers should be a “robust measurement” with the ability to be consistently performed and repeated at most scientific laboratories. In addition, he pointed out, “biomarkers should be easy for doctors—as well as patients—to understand.”

## ANTIBODIES AS DIAGNOSTIC MARKERS

Biomarkers already play a role in the diagnosis of MS—but not a definitive

one. For instance, the detection of oligoclonal immunoglobins (Ig) is an important diagnostic marker in MS. However, the antigen specificities of oligoclonal Ig bands have yet to be defined. In addition, several studies have searched for autoantibodies directed against myelin and nonmyelin target antigens in the serum and cerebrospinal fluid of people with MS. However, most antibodies found thus far in MS patients also have been found in people with other neurologic conditions and even in some healthy controls.<sup>4</sup>

“None of these studies convincingly demonstrated an MS-specific antibody response to a certain central nervous system (CNS) target antigen,” said Dr. Berger.

The antibody to a component of myelin called myelin oligodendrocyte glycoprotein (MOG) has been found to play a role in destroying myelin in experimental allergic encephalomyelitis (EAE), but it is still unclear what role anti-MOG plays in humans.

Dr. Genain and colleagues have been trying to develop more accurate tests to determine the significance of antibodies that target myelin in MS.

In one study<sup>5</sup>, they found that about a third of normal control subjects and patients with relapsing-remitting disease had signs of antibodies against MOG in their system. In contrast, almost all patients with progressive MS tested positive for anti-MOG. However, several other antibody suspects that have been found to react to myelin components were not more prevalent in those with progressive disease than in those with relapsing-remitting disease or in healthy individuals. “

According to Dr. Genain, the anti-MOG antibodies appear to be clearly different from other antibodies in this disease. This means that either the antibodies are causing the disease process, or they are a strong marker of tissue destruction by some other process. “In either event,” said Dr. Genain, “conducting surveys of anti-MOG antibodies in MS will be useful for diagnosing more severe forms of MS and for giving a prognosis and an index of tissue damage.

“This study appeared to be the first simple, reliable, and inexpensive blood test to correlate so strongly with clinical parameters in MS. Its use in combination with other disease

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## Table

### ANTIBODY BIOMARKERS AND PATHOPHYSIOLOGIC PROCESSES IN MS

Pathophysiologic processes	Examples of potential use as a biomarker
Inflammation	Neuromyelitis optica (NMO)-IgG Anti-myelin antibody
Demyelination	NMO-IgG Anti-myelin antibody
Remyelination and repair	Anti-Nogo-A antibody

Adapted from Berger et al. *Future Neurol.* 2006.<sup>4</sup>

markers such as MRI would greatly enhance our understanding of what causes the different types of MS and how each should be treated. We can also envision that therapies against antibodies or B cells will be useful to treat this disease,” added Dr. Genain.

Galactocerebroside, the major glycolipid of CNS myelin, is a known target for pathogenic demyelinating antibody responses in EAE. Dr. Genain co-authored a study that was led by Menge et al, in which anti-galactocerebroside (alpha-GalC) IgGs were quantified from sera of MS patients and in marmoset EAE.<sup>6</sup> The researchers found that alpha-GalC antibodies appear MS-specific and are not found in healthy subjects, unlike the antibodies against myelin proteins. In addition, when present, alpha-GalC antibodies identify mostly relapsing-remitting MS and may be an indicator of ongoing disease activity.

#### ANTIBODIES FOR REGENERATION AND REPAIR

“We are not only fortunate to establish patients’ risk for disease progression, or immunopathogenic stage of their disease, but also the capacity for regeneration and repair,” stated Dr. Berger.

In fact, a protein called Nogo-A

has been shown to aid in the promotion of axonal regrowth. This molecule suppresses regeneration and axonal sprouting, explained Dr. Berger. One study in an animal model showed that immunization against Nogo-A, which is expressed exclusively in the CNS, prevents demyelination in EAE. Dr. Berger and colleagues found that patients with a relapsing-remitting disease course had most of the anti-Nogo-A antibody.<sup>4</sup> “Thus, anti-Nogo-A antibodies might be used in the future to determine the endogenous potential of axonal regrowth and therefore repair in MS patients,” he stated. Patients with secondary progressive disease course who had higher anti-Nogo-A antibody still had relapses. “These are patients who harbor the capacity of repair—especially, of course, in the relapsing-remitting population.”

Another important molecule involved in this active process of regeneration is called p75(NTR), according to Dr. Berger. “Antibodies against p75(NTR) are correlated with relapsing-remitting disease course and lower Expanded Disability Status Scale scores, indicative for a greater repair potential in this group of patients.” It has been shown that p75(NTR) antibodies bind to oligodendrocytes of remyelinated areas.<sup>7</sup>

“Nogo-A antibodies are already starting to be tested in Phase I trials for stroke and spinal trauma,” he added.

#### FUTURE DIRECTIONS

“MS is a very heterogeneous disease indicative of different pathologic situations,” related Dr. Berger. “Our major goal is to individualize management and treatment of patients. Simple biomarkers would help to differentiate pathologic subtypes of MS. Then we could target patients individually, average their risk and prognosis, and adjust the therapeutic algorithm. I am convinced we will find appropriate use of biomarkers in the near future.”

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—Linda Ruiz

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## WHAT'S NEW IN PEDIATRIC MS?

“The field of pediatric MS is expanding with respect to both clinical investigation and basic research,” said Brenda Banwell, MD, of the Hospital for Sick Children in Toronto, at the 20th Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) in Scottsdale, Arizona. “Children, by virtue of their young age, are uniquely close to the biologic onset of the MS disease process. Thus, the potential environmental triggers and earliest aspects of abnormal immune cell behavior can be best studied in pediatric MS patients.”

The incidence of childhood MS is not known, but conservatively, about 5% of all MS patients have disease onset prior to age 18.<sup>1</sup> Dr. Banwell stressed that the relative rarity of childhood-onset MS requires a team effort. In terms of clinical care, health care providers worldwide are sharing their experience and treatment protocols and are carefully documenting key features of the disease in children—especially very young children, who may have somewhat different features of the disease. Additionally, a number of genetic and immunologic studies are exploring factors that influence patient age at disease onset and whether childhood onset is related to a heightened predisposition.

### IMPACT OF MS ON CHILDREN

“Until recently, we did not know much about the cognitive impact of MS in kids. However, what we did know is that the disease process affects myelin development at a critical time,” explained William MacAllister, PhD, a Neuropsychologist at the National Pediatric MS Cen-

ter at Stony Brook University Hospital in New York, who was also a presenter at the CMSC symposium. Dr. MacAllister added that more recent data have demonstrated that cognitive dysfunction present early in the course of the disease is likely to progress in many children, making cognition an important disease parameter to monitor over time.

In one study currently in press, Dr. MacAllister and colleagues looked at MS-related cognitive impairment in 37 children with the disease; average patient age was 14.8 years, and average age at disease onset was 13 years. The investigators found that half of the children reported significant fatigue; approximately 37% showed symptoms of cognitive dysfunction (eg, attention,

memory, and language impairment). The single greatest predictor of cognitive dysfunction was patient level of neurologic dysfunction as measured by the Expanded Disability Status Scale score. Other predictors included number of relapses and disease duration. Of note, MRI findings did not seem to have a strong clinical relation to cognitive performance.

Furthermore, Dr. MacAllister pointed out that children are also likely to show a greater degree of cognitive deficit than are adults with comparable disease severity. “In adults, the cognitive functions have already developed, so MS will lead to impairment. In kids, the cognitive functions are just starting to develop. As a result of this, the MS disease

process may actually inhibit future cognitive development. This is why longitudinal studies are so important,” he stressed.

In addition to cognitive defects, children and teenagers with MS face unique psychosocial challenges, added Jennifer Boyd, RN, MHSc, MSCN, a Clinical Nurse Specialist at The Hospital for Sick Children in Toronto. At the CMSC conference, Ms. Boyd reported findings from a qualitative study on children with MS that was performed at her clinic.

Study participants—12 children who had relapsing-remitting MS and were between the ages of 8 and 18—acknowledged the presence of stressors, including intermittent and ongoing symptoms, unpredictability of relapses, uncertain future, lifestyle re-

“In kids, the cognitive functions are just starting to develop. As a result, the MS disease process may actually inhibit future cognitive development,” said Dr. MacAllister.

strictions, treatment regimens, and school absenteeism. In turn, the children reported using a variety of coping strategies (eg, maintaining a positive outlook, incorporating distraction techniques, and accepting the need for treatment) to manage stress.<sup>1</sup>

Ms. Boyd noted that most children experienced both positive and negative changes in relationships with family and friends after diagnosis—and disliked being treated “differently” because of the disease.

“The participants also reported MS-related challenges in school, such as difficulty in learning, memory, and concentration problems, and the need to work harder to obtain the same grades,” Ms. Boyd added.

*continued on page 9*



## Multiple Sclerosis Nursing in 2006: A Global Perspective

### CMSC Meeting Highlights

With over 1,200 MS health care professionals in attendance, the 20th Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC), which took place May 31 to June 3 at the Westin Kierland Resort and Spa in Scottsdale, Arizona, was the largest in history.

The theme of this year's conference was "Celebrating 20 Years of Excellence in MS Care and Research." Visitors attended lectures and workshops on MS pathology, basic fundamentals of MS care, advanced concepts in research and clinical practice, discussion of technological advances in disease diagnosis and treatment, and new avenues in providing symptomatic and rehabilitative care.

### A Rich History

The conference provided an opportunity for CMSC members to look back at past accomplishments. From the first official meeting in Minneapolis in 1987, the CMSC has grown by leaps and bounds. Organizational milestones include the founding of the CMSC North American Research Committee on Multiple Sclerosis (CMSC-NARCOMS), which maintains a patient registry, Web site, expert forum and research registry to

promote MS research (1993), the first issues of the *International Journal of MS Care* (2000) and *MS Exchange* (1997), the first seating of the Multiple Sclerosis Certified Specialist (MSCS) Exam (2004), and the founding of the MS Coalition (2005).

### Conference Awards

On Saturday, June 3, several awards were presented to clinicians involved in MS care for their achievements in patient care and/or research.

The CMSC Lifetime Achievement Award was presented to Robert Herndon, MD, for his decades-long commitment to neuroscience research, MS patient care, and education of MS specialists. In addition, Dr. Herndon has served as past-president of the CMSC and is the founding and current editor of the *International Journal of MS Care*.

The June Halper Award for Excellence in Nursing was given to Barbara Johnson, BSN, CRRN, MSCN, recently retired from the Bernard W. Gimbel Multiple Sclerosis Comprehensive Care Center at Holy Name Hospital in Teaneck, NJ. This award commends recipients on leadership and creativity in the care of MS patients and their families.

The IOMSN Hope Award was received by Maria Milazzo, RN, MS, William MacAllister, PhD, Pamela Block, PhD, Nino Slota, MS, Anita Belman, MD, and Lauren Krupp, MD, for

their poster, "A Weekend Retreat for Teens With Multiple Sclerosis." (A full article on the camp appeared in the May issue of *MS Exchange*.) The Hope Award is presented annually in recognition of the poster that best represents a spirit of optimism and possibility related to MS clinical care or education.

The Labe C. Scheinberg Award, given in memory of Dr. Scheinberg and in recognition of outstanding work in MS neurorehabilitation, was presented to Meesha Schartzter, SPT, Amanda Brandt, SPT, Kortney Bomia, SPT, Heather Scott, SPT, Donna Przybylski, PT, and Donna Fry, PT, PhD. Their winning poster was entitled, "Body Weight Support Treadmill Training in Patients With Multiple Sclerosis."

The IOMSN Thumbs-Up Award celebrates those who advocate and promote MS nursing. This year's recipient was Heidi Maloni, DNScc, RN, CNRN, ANP, MSCN, of The Catholic University of America in Chevy Chase, Maryland.

Selected presentations from the conference, as well as posters and abstracts, are available on the CMSC Web site ([www.ms-care.org](http://www.ms-care.org)). Preparations are currently under way for next year's CMSC conference, to be held May 30 to June 3 in Washington, DC.

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—Krista Binetti

## Pulmonary Complications in the MS Patient

Pneumonia and upper respiratory conditions are common causes of morbidity and mortality in patients with multiple sclerosis (MS), said Jodie K. Haselkorn, MD, MPH, who chaired the Pulmonary Rehabilitation program at the recent Consortium of Multiple Sclerosis Centers (CMSC) meeting. However, the medical literature provides the MS specialist little guidance in appropriate monitoring of deficits or treatment strategies. Dr. Haselkorn is an Associate Professor of Rehabilitation Medicine at the University of Washington and Director of the Multiple Sclerosis Center of Excellence at the West VA Puget Sound Health Care System.

“Pulmonary muscle strength and endurance is reduced in a large portion of our patients with MS, including those who are less disabled,” agreed Donna Fry, PT, PhD, Associate Professor and Interim Director of Physical Therapy at the University of Michigan-Flint. “Yet, pulmonary muscle weakness often isn’t considered in the MS population, and is not even listed as a symptom on the National Multiple Sclerosis Society Web site<sup>1</sup>,” she added.

### Causes of Pulmonary Impairment in MS

Richard B. Goodman, MD, Associate Professor of Pulmonary and Critical Care Medicine at the University of Washington in Seattle, also presented at the symposium and has been collaborating with Dr. Haselkorn’s MS Center of Excellence to screen patients with clinical respiratory symptoms by measuring their pulmonary function. According to Dr. Goodman, “it is clear that many MS patients have measurable pulmonary impairment.”

Dr. Goodman reported on the work of Joshua Benditt, MD, Professor of Medicine at the University of Washington, who has been studying respiratory function in general muscular diseases.<sup>2</sup> “Dr Benditt has broken respiratory complications into three mechanistic categories: 1) bulbar weakness (glottic and pharyngeal muscles), which manifests as aspiration complications and impaired cough coordination; 2) inspiratory muscle weakness (diaphragm muscle), which presents with dyspnea and ventilatory insufficiency symptoms; and 3) expiratory muscle weakness (abdominal muscles), with resultant cough force im-

pairment,” reported Dr. Goodman. He added that, in MS, “impairments in any of these categories can result from plaques in the brain stem or spinal cord, from disease impairment, or from complications related to the treatment of MS-related spasticity.”

### Appropriate Screening Tools

Dr. Goodman uses spirometry to screen symptomatic patients who present to the pulmonary function laboratory. He evaluates forced vital capacity (FVC), forced expiratory volume in one second, maximal inspiratory pressure, and maximal expiratory pressure. He also monitors serum bicarbonate levels, because they serve “as a marker of ventilatory insufficiency in patients with measurable impairment of FVC, particularly in patients with diaphragm dysfunction.”

Spirometers are portable and simple to operate, added co-presenter Toni Chiara, PhD, PT, a researcher at the Malcolm Randall VA Medical Center in Gainesville, Florida and adjunct faculty member at the University of Florida. Their use is not limited to the respiratory therapist, she stressed.

Another useful tool for pulmonary assessment is the manometer, which Dr. Chiara said is helpful for getting “serial measurements of your patients in the clinic.” The Index of Pulmonary Dysfunction (IPD) is an MS-specific tool for pulmonary function assessment, Dr. Chiara explained. The higher the patient’s score (which ranges from 4–11), the greater the level of pulmonary impairment. The IPD consists of four questions: 1) Does the patient report a history of choking when he or she swallows?; 2) Does the patient report his or her cough is normal or weak?; 3) Does the evaluator perceive the cough as normal, weak, or absent?; and 4) On a maximal inhalation, how long can the patient count on one breath? The impulse oscillometry system, previously a research tool now available for clinical use, measures airway resistance.

### Improving Pulmonary Function

A number of trainers on the market boost inspiratory or expiratory muscle strength, or both. Dr. Chiara cited several studies that examined expiratory muscle strength training in MS patients. Some used trainers, but one study<sup>3</sup> performed by nurses, used music therapy. All studies reported that training helped MS patients to some degree.

## The Role of the MS Specialist

Dr. Haselkorn stressed that MS specialists should effectively monitor their patients for decreases in respiratory function. In addition, MS clinicians should have knowledge of the role of exercise in strengthening inspiratory and expiratory muscles and prevention strategies for upper respiratory infections and pneumonia, such as the influenza vaccination, which has been proven not to exacerbate MS.

The goals in managing pulmonary complications in MS patients, added Dr. Goodman, are to “improve and stabilize gas exchange, ameliorate symptoms, improve sleep quality, extend survival, and improve quality of life.”

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—Barbara Merchant

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## Managing Injection-Site Reactions in MS Patients

Although not a cure, disease-modifying drugs (DMDs) are effective in reducing the frequency and severity of relapses and slowing disease progression in MS. However, one major issue with injectable therapies for MS is the inevitable skin reactions that patients experience due to frequent injection of drugs with immunogenic properties.

Drug side effects may impact adherence and, therefore, limit the efficacy of prescribed therapies. Both patients and clinicians tend to put greater focus on adverse events that affect quality of life, such as flulike symptoms and fatigue. However, it is essential that the less intrusive, but more visible, problem of skin reactions not be neglected.

### Common Skin Reactions

As the injectable agents used to treat MS have immunogenic properties, it is not surprising that all patients will ex-

perience some degree of skin reaction. This may manifest as transient pain upon injection, a mild burning sensation, or full-blown abscess, infection, or loss of vital tissue.

Subcutaneous (SC) therapy occasionally results in mild reactions such as erythema and swelling. Granulomas, ulcers and, in some cases, skin necrosis and abscesses, have been reported with SC interferon (IFN) therapy.

Glatiramer acetate for injection can result in localized redness and hardening of the skin around the injection site. Additionally, a small number of patients receiving this agent have experienced lipoatrophy, characterized by irregular areas of skin depression, similar in appearance to cellulite. It is believed to be caused by damage to fat cells from frequent injections and lack of proper rotation of injection sites. Lipoatrophy is thought to be permanent, and may have a significant psychological impact. Therefore, clinicians need to educate patients on the possibility of lipoatrophy so that patients will be able to identify it, and discontinue injecting in areas where it is found. Clinicians should also instruct patients to rotate injection sites, as this may help to prevent the occurrence of lipoatrophy.

Some patients receiving IFN therapy via intramuscular (IM) injection experience pain and transient bleeding following injections. Rarely, abscesses characterized by swelling and site discomfort have been reported, as has skin necrosis.

### Factors That Influence the Occurrence of Skin Reactions

Factors that influence the occurrence of skin reactions among patients administered DMDs may be patient-related (eg, overweight patients may have difficulty reaching the muscle when administering a drug via intramuscular injection) or drug-related.

DMDs can occasionally exacerbate existing dermatologic conditions such as eczema and psoriasis. In general, patients who have fair skin and coloring (those who burn easily in the sun) are more likely to develop skin reactions.

Injecting in the same place without site rotation can lead to problems. Some patients routinely inject in an area that is frequently or permanently numb because this reduces the pain of injection. However, this can lead to overuse of particular sites and chronic skin damage.

## Managing Skin Reactions

There are a number of measures that patients and clinicians can take to minimize skin reactions. Perhaps the most crucial is ongoing reinforcement of proper injection technique. It is not enough to educate patients when they initially begin therapy. Repeated reiteration of the importance of site rotation and awareness of possible reactions can go a long way toward ensuring that patients adhere to therapy and maximize its efficacy.

Needle selection is critical when administering DMDs. Longer needles are appropriate for IM injection, while shorter needles are usually better for SC injection. However, in those with less muscle mass, a shorter needle may be suitable for IM injection. Conversely, patients with excess subcutaneous fat may do better with a longer needle for SC injection.

Injection of DMDs frequently results in pain and burning. Ensuring that the drug is at room temperature before injection is helpful, as is application of ice. However, applying ice for longer than 30 seconds may constrict blood vessels and increase the risk that the medication will not reach the circulation. Applying a topical anesthetic for approximately 30 minutes prior to injection can reduce pain and burning. It is essential that the cream be washed off before injecting to avoid introducing the cream into the injection site. Alcohol wipes and perfumed moisturizers should be avoided. Mild soap and water is adequate to clean the injection site; the area must be thoroughly dry before injecting. Tissues are recommended to dry the skin because they are essentially sterile.

Frequently, patients are taught to expel air bubbles from the syringe prior to injection. This should be avoided, as this involves pushing some of the fluid out of the tip of the needle, and the solution can irritate the skin.

MS patients should avoid excessive sunlight because this can cause the skin to harden and dry out, making injection more difficult. Injection sites can become inflamed again after exposure to sunlight; peeling of a site can potentially lead to infection and further com-

plications. In addition, it has been postulated that smoking should be avoided, as chronic nicotine use results in vasoconstriction.

Repeated injection in the same site can cause long-term problems, such as skin necrosis and/or abscesses. In rare cases, these may require surgical debridement and skin grafting. With the more frequent injection regimens, patients should try to avoid using the same site within the same two-week period.

## The Clinician's Role

Clinicians should inspect patients' skin at each visit and review injection techniques. If a skin reaction is suspected during a telephone interaction, the patient should be seen as soon as possible. Patients should routinely be asked to demonstrate their injection technique to the clinician.

As with all aspects of MS, clinicians need to keep the lines of communication open. Some patients are reluctant to acknowledge that they are experiencing skin problems because they are concerned that their clinician will be disappointed in them. Others may view skin reactions as an unavoidable result of injectable therapy. MS clinicians must play an active role in educating patients about appropriate injection techniques, not only upon initiation of therapy but throughout the disease course.

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## PREDICTORS OF MS IN CHILDREN

“Being able to predict the course and timing of disease progression in children with MS would be useful for therapeutic decision making and family planning. Yet, such predictions remain difficult, especially in children younger than 10,” said Marc Tardieu, MD, PhD, Professor of Pediatrics (Neurology) at the Université Paris, who also presented at the CMSC conference. “To that end, our research has focused on identifying prognostic factors predictive of relapse and disability after a first episode of acute central nervous system (CNS) inflammatory demyelination in pediatric MS.”

In one study currently in press, Dr. Tardieu and colleagues followed 197 children (mean age at disease onset, 11.3 years) for 5.5 years; only 9% were lost to follow-up. Notably, 14% of the children were younger than 6.

The investigators defined MS as two clinical attacks separated by more than 30 days. Seventy-three percent of the children reached the study outcome of a second attack; the mean interval between the first and second attack was 15.5 months. Analysis showed that the rate of second attack was greater in female

“The most important next steps in the care of children with MS will require expansion of collaborative networks of clinicians and scientists dedicated to the study of childhood-onset MS,” said Dr. Banwell.

patients and/or those who experienced a second attack in less than one year, had no mental change at disease onset, and/or met childhood MS MRI criteria (ie, corpus callosum long axis perpendicular lesions on initial MRI and/or sole presence of well-defined lesions).

Dr. Banwell also discussed the impact of MS on executive functions—higher order cognitive functions such as reasoning, inhibition, emotional control, and shifting attention between tasks—as well as ways to manage and treat cognitive impairment. He explained that executive functions in children are an

## NETWORK SPONSORS PROGRAM FOR CHILDREN WITH MS AND THEIR FAMILIES

The MS Society of Canada and the National MS Society (USA) recently launched Young Persons With MS: A Network for Families With a Child or Teen With MS. The initiative is a collaborative program to provide critical support to young people with MS and their families, announced Jon Temme, National Vice President of Client Services of the MS Society of Canada, at the recent CMSC conference.

Educational resources provided by the network will help youngsters and parents learn about the disease, manage symptoms, and adapt to changes brought about by MS. *Kids Get MS Too*, a handbook for parents written by specialists in childhood MS, provides a wide range of information on pediatric MS. An activity book called *Mighty Special Kids* includes educational games, activities, and age-appropriate articles for children with MS (ages 5 to 12).

Other features of the program include teleconferences to introduce parents to pediatric MS specialists, and telephone and e-mail support groups. For more information, call (toll-free): (866) KIDS-W-MS (866-543-7967) or send an e-mail query to [childhoodms@nmss.org](mailto:childhoodms@nmss.org). United States residents can also contact their local Society chapter at (800) FIGHT-MS (800-344-4867).

“In this study, we have defined prognostic factors in childhood-onset MS,” related Dr. Tardieu. “In addition, we have developed a possible scoring method to predict the evolution of the disease in children. This could be very beneficial to clinicians in making treatment decisions for these patients.”

### NEXT STEPS

Dr. MacAllister anticipates that future studies will focus on the im-

area of increasing interest because the process of myelination shows a general posterior to anterior progression, with the frontal lobes—which play an important role in higher order cognitive functions—not reaching functional maturity until late adolescence. In the majority of children with MS, the disease strikes at a time when these areas are still developing. As a result, the myelination and the disease are “fighting it out,” Dr. MacAllister explained.

All presenters agreed that a teamwork approach is vital in the study and treatment of pediatric MS. “The most important next steps in the care of children with this disease will require expansion of collaborative networks of clinicians and scientists dedicated to the study of childhood-onset MS,” concluded Dr. Banwell.

MSX  
—Kathleen Wildasin

### REFERENCE

1. Boyd JR, MacMillan LJ. Experiences of children and adolescents living with multiple sclerosis. *J Neurosci Nurs*. 2005;37:334-342.



## LITERATURE MONITOR/ NEWS ROUNDUP

### SEXUAL FUNCTION IN WOMEN WITH MULTIPLE SCLEROSIS

A poster entitled, “Factors Associated With Sexual Function in Women With Multiple Sclerosis<sup>1</sup>” won the Research Award for Best Poster at the 20th Annual Conference of the Consortium of Multiple Sclerosis Centers (CMSC) in June. The researchers, from the University of Pittsburgh and Duquesne University, aimed to identify demographic, urinary symptom distress, and disability level factors associated with sexual dysfunction in female MS patients. They found that sexual dysfunction was most consistently predicted by visual dysfunction, pain disability, and gait disability.

Sixty-eight women with relapsing MS (mean age:  $48.5 \pm 10$  years) were recruited into the study and completed the Patient-Determined Disease Steps (PDDS) and Performance Scale Questionnaires, Urge-Urinary Distress Inventory (U-UDI), the Female Sexual Function Index (FSFI)<sup>2</sup>, and the Health Related Quality of Life Short-Form 36. The majority were Caucasian, with an  $11 \pm 8.3$  year history of MS. Median PDDS score was 3.0 (indicating gait disability). Performance Scale ratings showed minimal depression, vision disability, and cognitive disability. Participants had mild pain and mild gait, bladder, sensory, and spasticity disability; fatigue disability was moderate.

Sexual dysfunction was most consistently predicted by visual dysfunction, in terms of arousal, orgasm, lubrication, and overall sexual satisfaction. Other sexual response predictors were pain disability (strong predictor of decreased sexual arousal and satisfaction) and gait disability (strong predictor of difficulty in achieving orgasm).

1. Borello-France D, DiBlassio J, Marx S, et al. Factors associated with sexual function in women with multiple sclerosis. Poster presented at: 20th Annual Conference of the Consortium of Multiple Sclerosis Centers; May 31-June 3; Scottsdale, Arizona.

2. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther.* 2000;26:191-208.

### RETREAT FOR TEENS WITH MS IMPROVES QUALITY OF LIFE, TREATMENT COMPLIANCE

A recreational retreat for teens with MS, designed to improve participants' quality of life (QOL), was reported on in a poster that won the Hope Award at the 20th Annual CMSC Conference. The authors, from the National Pediatric MS Center in Stony Brook, NY, reported that the twenty-eight teens who attended the program showed significant improvement in QOL and in medication compliance at program's end.

Participants from the United States and Canada attended the four-day camp during the summers of 2004 and 2005. During the retreat, attendees participated in activities such as kayaking, sailing, swimming, a ropes' course, and a drumming cycle. Additionally, they took part in team-building activities and a drama workshop.

All attendees participated in a structured interview and completed self-report questionnaires. “Enhancement of well-being, a feeling of cohesion, and a sense of ‘not being defined by MS’ were described by participants,” according to the au-

thors. Importantly, medication compliance increased among participants at the end of the retreat. “One attendee who had discontinued her therapy returned home and restarted her treatment,” the authors related.

The authors stressed that the estimated 150,000 MS patients under age 18 usually face limited resources, with little opportunity to contact other MS patients of the same age. It was reported that recreational retreats may be one way “to bring . . . teens together and improve quality of life.”

Milazzo M, MacAllister W, Block P, et al. A weekend retreat for teens with multiple sclerosis. Poster presented at: 20th Annual Conference of the Consortium of Multiple Sclerosis Centers; May 31-June 3; Scottsdale, Arizona.

### TREADMILL TRAINING IMPROVES GAIT VELOCITY IN MS PATIENTS

Body weight support treadmill training (BWSTT) improves gait velocity, and possibly dynamic balance, in patients with MS, according to the poster that won the Labe C. Scheinberg Award at the recent CMSC conference.

The researchers conducted a single-subject, A1B1A2B2 time-series study; each phase lasted four weeks. The two study participants both had relapsing-remitting MS and an Expanded Disability Status Scale (EDSS) score of 4. Subject 1 was 62 years old; subject 2 was 59. At intake, both patients completed the Modified Fatigue Impact Scale, the Health-Related Quality of Life Short-Form 36, and an activities-specific Balance Confidence Scale. The six-minute walk test and a sit-to-stand test were performed once during each phase to measure endurance and functional lower extremity strength, respectively. During each session, gait velocity and dynamic balance were also mea-

sured. Subjects self-reported their level of perceived exertion during each session.

“Gait velocity improved significantly in both subjects during both intervention phases,” reported the authors, from the University of Michigan-Flint and McLaren Regional Medical Center. However, while subject 1 showed significant improvement in dynamic balance during the first intervention phase, subject 2 did not approach statistically significant improvement in this outcome measure. The authors related that the Timed Pick-up Test used in this study may not be sensitive enough to detect significant improvement in dynamic balance.

Schutzer M, Brandt A, Bomia K, et al. Body weight support treadmill training in patients with multiple sclerosis. Poster presented at: 20th Annual Conference of the Consortium of Multiple Sclerosis Centers; May 31-June 3; Scottsdale, Arizona.

## IDENTIFYING NEEDS OF MS PATIENTS, CAREGIVERS

Receipt of pertinent medical information, rehabilitative and therapeutic services, and life skills assistance is currently an unmet need for many MS patients, stated the authors of a poster presented at the recent CMSC conference. Their data uncovered a need for further research to determine which programs and services would most benefit these patients.

Seven hundred and sixty-two MS patients completed a survey designed to elicit informational, education, programmatic, and service needs. More than half of respondents reported being at least moderately affected in 13 of 16 possible symptom categories.

Eighty-four percent of respondents stated that an important need is information on new medications, treatment, and research. Other needs rated as high priorities were exercise information (77%), fatigue management (74%), problem-solving and coping mechanisms (74%), and complementary/alternative therapy (72%).

When asked to rate 13 program areas currently provided by the Multiple Sclerosis Association of America in order of importance, respondents rated publications and brochures as most vital. Educational awareness events and therapeutic programs with social aspects (eg, water exercise and Tai Chi classes) were rated second and third, respectively. Compared with five other potential program offerings, respondents rated rehabilitation services as being most important. Such programs, along with those that provided life-management skills, were deemed even more necessary to patients than were those that offered financial assistance.

Montague A, Rapp R, Burks J, Cutter G. A needs assessment survey of MS patients and care partners. Poster presented at: 20th Annual Meeting of the Consortium of Multiple Sclerosis Centers; May 31-June 3; Scottsdale, Arizona.

## PHYSICAL ACTIVITY AMONG PERSONS WITH MS

Physical activity that is obtained through everyday activities can help MS patients to adhere to the Centers for Disease Control and Prevention (CDC) guidelines for physical activity, according to researchers from Rutgers University and Mount Sinai School of Medicine. According to

their poster presented at the recent CMSC conference, housework, yard work, caretaking, walking, and recreation may provide benefits similar to those of more structured physical activity programs.

The authors analyzed self-reported data from 123 MS patients who completed the Yale Physical Activity Survey. Physical activity information was viewed in relation to disability status, as determined by the Patient-Determined Disease Steps.

The majority of respondents reported participating in three or more hours of total physical activity per week, regardless of disability level. Such activities “contribute significantly to [the] CDC’s recommendation for a minimum of 30 minutes of physical activity on most, if not all, days of the week,” the authors concluded.

Gulick EE, Goodman S. Physical activity among persons with multiple sclerosis. Poster presented at: 20th Annual Conference of the Consortium of Multiple Sclerosis Centers; May 31-June 3; Scottsdale, Arizona.

### PLEASE SHARE YOUR COMMENTS

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# CONTINUING EDUCATION CONFERENCE CALENDAR

## **September 2-5, 2006**

10th Congress of the European Federation of Neurological Societies. Location: Glasgow, UK. Contact: EFNS Head Office, Breite Gasse 4-8, A-1070 Vienna, Austria; +43 1 889 05 03; fax: +43 1 889 05 03 13; e-mail: headoffice@efns.org; Web site: [www.kenes.com/efns2006](http://www.kenes.com/efns2006).

## **September 27-30, 2006**

22nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis. Location: Madrid. Contact: AKM AG, Clarastrasse 57, PO Box CH-4005, Basel, Switzerland; +41 61 686 77 77; fax: +41 61 686 77 88; e-mail: [info@akm.ch](mailto:info@akm.ch); Web site: [www.akm.ch/ectrims2006](http://www.akm.ch/ectrims2006).

## **October 8-11, 2006**

131st Annual Meeting of the American Neurological Association.

Location: Chicago. Contact: ANA, 5841 Cedar Lake Road, Suite 204, Minneapolis, MN 55416; (952) 545-6284; fax: (952) 545-6073; e-mail: [julieratzloff@llmsi.com](mailto:julieratzloff@llmsi.com); Web site: [www.aneuroa.org](http://www.aneuroa.org).

## **October 14-18, 2006**

36th Annual Meeting of the Society for Neuroscience. Location: Atlanta. Contact: Society for Neuroscience, 1121 14th Street, NW, Suite 1010, Washington, DC 20005; (202) 962-4000; fax: (202) 962-4941; e-mail: [info@sfn.org](mailto:info@sfn.org); Web site: [www.sfn.org](http://www.sfn.org).

## **November 2-4, 2006**

MS Trust 10th Annual Conference. Location: Bournemouth, UK. Contact: MS Trust, Spirella Building, Bridge Road, Letchworth Garden City, Hertfordshire SG6 4ET; +44 14 6247 6700; e-mail: [info@mstrust.org.uk](mailto:info@mstrust.org.uk); Web site: [www.mstrust.org.uk](http://www.mstrust.org.uk).



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