The current wisdom is that multiple sclerosis (MS) is an autoimmune disease. However, the evidence for this is circumstantial, according to Subramaniam Sriram, MD, PhD, whose talk at the 2003 National Multiple Sclerosis Society’s Research Symposium in New York focused on infection as a possible trigger of MS.

**THINKING BEYOND AUTOIMMUNITY**

“We need to think outside the autoimmune concept,” said Dr. Sriram, who is the William Weaver Professor of Experimental Neurology and Professor of Microbiology and Immunology at the Vanderbilt University Medical Center in Nashville, Tennessee. He noted that identifying the specific autoantigen (or autoantigens) responsible for MS has continued to elude researchers. In addition, autoimmunity cannot provide a wholly satisfactory disease model because immunosuppressive treatment of MS has been only partially effective. Therapies such as anti-CD4 antibodies, anti-tumor necrosis factor antibodies, and altered peptide ligands—which are successfully employed to cure experimental allergic encephalitis (an autoimmune disease in animals that mimics MS), as well as human autoimmune diseases such as lupus erythematosus and thyroiditis—have not been fully successful in the treatment of MS. “Calling MS an autoimmune disease is an unsatisfactory answer to me,” he said.

Rather than regarding MS as a single autoimmune disease entity, Dr. Sriram suggested regarding it as a syndrome, a heterogeneous disease caused by “autoimmunity that is an interplay between host immunity and environmental pathogens.” Focusing exclusively on autoimmunity ignores the role of infectious organisms in the disease process and leads to “incomplete cure of the disease,” Dr. Sriram cautioned.

**HOST GENETICS AND ENVIRONMENTAL PATHOGENS**

MS is “the ultimate expression of an interaction between the host and the pathogen,” Dr. Sriram said. “We live in a sea of pathogens. Some bacteria cause diseases in some people, but not in all people.” Rather, the genetic predisposition of the host creates vulnerability to a disease process triggered by the pathogen.

Genetic and infectious diseases are closely linked—not two separate disease entities—according to Dr. Sriram. Regarding them as utterly different is based on two misconceptions. The first is that genetic tendencies do not play a role in determining who will contract a disease after exposure to a pathogen, and who will not. The second is that diseases with higher incidences in siblings and twins are due exclusively to genetic factors and do not have an environmental component. “However, the reality is that all infections have a genetic component.
and a pathogen does not affect everyone equally,” Dr. Sriram stated.

He pointed to leprosy as an example of a “classic infectious disease,” which has a 52% concordance rate in monozygotic twins, versus a 22% rate in dizygotic twins. This implies that some common genetic tendency predisposes some, but not all, exposed individuals to contract the disease. The concordance rate of disease expression in MS in monozygotic versus dizygotic twins is 25% to 30% and 2% to 5%, respectively—a pattern closely resembling that seen in infectious diseases, he said. MS, which is generally regarded as unrelated to the environment, may well be caused by an infectious organism invading a person with genetic vulnerability. Understanding MS in that light requires deeper comprehension of the nature of both genetic and infectious diseases.

**GENETIC DISEASES: EITHER PURPOSEFUL OR SELF-LIMITING**

Genetic diseases remain active in a population over several generations only if they serve a useful purpose, such as protection against infection. Dr. Sriram explained. One example of this process is sickle cell disease, which has been prevalent in Africa for thousands of years and confers some protection against malaria in affected individuals. If the African population were placed in an environment without risk of malaria, the incidence of sickle cell disease would decrease over time. This has indeed taken place in the African-American population in the United States, where sickle cell disease is gradually declining.

“A genetic disease that provides no benefit to the population will die out over a period of 100 or 200 years,” Dr. Sriram said. MS has been present in the human population for much longer than this. “On the other hand, highly damaging infectious disease will persist indefinitely in human populations. So, when you have a disease such as MS that is present for a number of generations, has a negative impact on fitness, and is fairly prevalent, we have to think of it as triggered by an environmental factor and therefore an infection.”

**EXPANDING THE CONCEPT OF INFECTION**

Our understanding of MS does not fit the classic profile of an infectious disease because of the narrowness of the term, which has persisted since nineteenth-century German microbiologist Robert Koch established criteria to define “infectious diseases.” These criteria state that the infectious agent cannot be present in normal, healthy people, that it must be possible to isolate and identify the pathogen, and that the disease must be communicable to animals.

“The problem is that a number of known infectious diseases do not fulfill the criteria proposed by Koch. These include syphilis, leprosy, and many viral infections that cannot be induced in animals,” commented Dr. Sriram. In addition, an infection or infectious pathogen may be widespread but will only cause disease in a few individuals, or the same organism can be responsible for different pathological diseases. “We need to get outside the constraining effects of Koch’s postulates,” he said.

Dr. Sriram pointed to peptic ulcer disease, Whipple’s disease, and reactive arthritis as examples of diseases once attributed to other causes such as stress or autoimmunity and now understood to be caused by infectious agents. He predicts that MS will soon move into the infectious phase as well.
The epidemiology of MS supports the view that it is an infectious disease, said Dr. Subramaniam Sriram. There are a few case reports of clusters of MS outbreaks, such as observed in Key West, Florida several years ago. In addition, the well-known study by John F. Kurtzke, MD on the epidemiology of MS in the Faroe Islands—an isolated group of islands in the North Atlantic Ocean between Iceland and Norway—clearly suggests an environmental factor in the development of MS. Dr. Kurtzke believed the British troops’ five-year occupation of the island during World War II introduced MS to the Faroese population. Studies of this population show that an MS epidemic breaks out approximately every 13 years. An illness associated with periodic outbreaks is more likely to be infectious than autoimmune in nature, according to Dr. Sriram.

While a single infectious agent has not been identified, several have been associated with MS (Table). Dr. Sriram focused on two organisms: human herpesvirus 6 (HHV-6) and Chlamydia pneumoniae.

**HHV-6 and MS**

HHV-6 is the causative agent in roseola and has been linked to several diseases, including AIDS-associated encephalomyelitis. The organism infects the lymphocytes but can also infect other host cell types. “An active HHV-6 infection can cause inflammation, setting the stage for a chronic, virologically mediated process in the central nervous system,” said Dr. Sriram. “This could lead to infection of the oligodendrocytes (myelin-producing cells) in the brain, leading to myelin loss.”

HHV-6 has been found in the brains of people with MS and in some healthy controls as well. This suggests that the presence of HHV-6 is not specific to MS. However, HHV-6 may still be implicated in the MS disease process. Dr. Sriram compared HHV-6 to the *Helicobacter pylori* bacteria, which is present in a large number of people but causes peptic ulcer disease only in a small subset of individuals. Interestingly, one study found that increased HHV-6 antibodies were significantly correlated with clinical exacerbations in MS. “There is clearly some evidence that we should be looking into this further,” he said.

**Chlamydia pneumoniae and MS**

Dr. Sriram reported on research conducted in his laboratory on *C pneumoniae*. This organism infects the macrophages, which are the cells thought to be involved in immunity against infectious agents. *C pneumoniae* lies dormant within the macrophages for a number of years before being dispersed to several regions of the body, including the central nervous system. It then reactivates periodically. “We can think of this organism as causing a relapsing, remitting disease,” remarked Dr. Sriram.

What is the evidence that *C pneumoniae* is involved in MS? Research in animal models suggests the development of autoimmunity to myelin antigens following infection with *C pneumoniae*. In addition, some research has suggested that the DNA of the organism can be found in the cerebrospinal fluid of MS patients, but not in controls. However, this finding is controversial and has not yet been validated.

Several recent studies more strongly support the link between *C pneumoniae* and MS. A seroepidemiologic study conducted at Harvard Medical School followed more than 60,000 female nurses for a number of years. Researchers reported that high *C pneumoniae* antibody titers were moderately associated with the risk of relapsing-remitting MS (RRMS) and strongly associated with the risk of progressive MS. Mean antibody titers were similar in women with RRMS and controls but were elevated in women with RRMS and controls but were elevated in women with progressive forms of the disease.

A study conducted by researchers in the Netherlands also suggested an association between MS and *C pneumoniae*. Hintzen and colleagues followed 73 patients with relapsing-remitting disease for a mean of 1.7 years. During this time, they monitored MS disease activity and evaluated patients for the presence of antibodies to several organisms, including *C pneumoniae*. The researchers reported an increased risk of MS relapse in those who developed upper respiratory infection with *C pneumoniae*.

“I believe that the role of infectious agents in MS is inescapable,” concluded Dr. Sriram. “I think we need to change old views to accommodate novel pathogens.”

—Rosalee L. Blumer

### REFERENCES

OVERCOMING BARRIERS TO PATIENT ADHERENCE

Disease modifying agents such as glatiramer acetate (Copaxone®) and the interferons (Avonex®, Betaseron®, and Rebif®) are currently the best available treatments for multiple sclerosis (MS), yet only half of the MS patients in the United States are being treated with one of these therapies.1 2

“Getting MS patients on a treatment regimen and keeping them on one can be challenging.” said Howard Zwibel, MD, during his presentation at the 2003 CMSC Annual Conference in San Diego. There are no definitive data on the long-term side effects of glatiramer acetate and the interferons, he noted. However, he believes the disease-modifying therapies are overall both safe and effective, despite some of their short-term side effects. “In order to increase adherence,” he emphasized, “we have to better inform patients about MS treatments and make them more aware of the potential risks.”

PATIENT CHOICE IN DRUG SELECTION

Long-term adherence to disease-modifying treatment for MS has been disappointing low, remarked Dr. Zwibel, who is Director of the Multiple Sclerosis Center at Doctors’ HealthSouth in Coral Gables, Florida. Perceived lack of improvement and continued disease progression are the main reasons patients cite for discontinuing MS therapy. In addition, MS patients may resist treatment because they have difficulty accepting that they have MS, or they hope the course of their disease will prove benign. Uncertainty about the long-term benefits of therapy, fear of injections or side effects, concern about not being able to follow a complex medication regimen, and having limited or no medical insurance are also significant barriers to adherence.1

Knowing what patients want from MS therapy may help in addressing these issues. “Patient preferences and perceptions about MS therapy have an important impact on both choice of treatment and compliance,” said Dr. Zwibel. In marketing surveys, the major concerns of people with MS were minimizing disability and maintaining a high quality of life. Notably, they viewed glatiramer acetate and the interferons as being equally effective in slowing the progression of disability and reducing relapse.3

Although patients expressed a desire to have all of their treatment options explained to them in detail, only 57% reported that they received such information from their health care providers. About 30% had several, though not all, of the disease-modifying therapies explained to them, while 14% received detailed information about only one MS drug.3 “Clearly, we are not getting our patients all of the information that is out there,” remarked Dr. Zwibel.

Only about 30% of MS patients made their decisions based on information provided to them by their physician. In most cases, individuals ended up researching the available MS treatments themselves. In addition, the patient and clinician collaborated on a decision only 56% of the time (see Table, page 9).3 “This finding concerns me,” Dr. Zwibel said, “because a joint decision is the best route to patient adherence.”

SIDE EFFECTS AND SAFETY ISSUES

Clinicians should never assume that patients have read about potential adverse effects on medication labels and package inserts. “If we do not tell patients about all of the potential problems or if we pass them off lightly, we have not fully done our jobs and we will contribute to noncompliance,” Dr. Zwibel asserted.

While the long-term side effects of disease-modifying agents for MS remain unknown, adverse event reporting to the FDA has not associated the use of these drugs with the development of cancer, serious infections, or other major illnesses, he said. Short-term, relatively mild effects currently appear to be the major concern, he added.

Injection-site erythema is the most common early side effect of glatiramer acetate, affecting approximately 60% of those taking the drug. However, a much less common
MS Nursing Research: Focus on Outcomes

The use of outcome measures has helped nurses articulate their special value to the well-being of patients. However, many measures currently used to evaluate outcomes do not identify or acknowledge the unique contribution of nurses, especially when it comes to treating a chronic, progressive disease such as MS, according to Diane Lowden, MSc(A), MSCN during her presentation at the last CMSC conference in San Diego.

Why Study Outcomes?
Ms. Lowden, a Clinical Nurse Specialist in the Multiple Sclerosis Program at the Montreal Neurological Hospital of the McGill University Health Centre, provided three important reasons why MS nurses should focus on nursing outcomes research.

First, one of the unique qualifications of MS specialist nurses is their accountability for the care provided, which includes quality of care, patient satisfaction, efficient use of resources, and clinical behavior. Nursing-specific outcomes should be measured to ensure that MS nurses are setting and reaching the highest possible standards of accountability.

Secondly, MS nurses must demonstrate their value in the health care system because their worth may be largely overlooked by traditional outcome methods. “There remains a gap in outcomes studies in nursing because the focus is typically on costs and lengths of stay and not on equally important measures such as symptom resolution and reduction, adherence, well-being, and patient and family knowledge and satisfaction with care,” she pointed out.

Finally, “there is a need for ‘hard’ evidence that we make a difference,” said Ms. Lowden. According to a 1998 article in Advanced Practice Nursing Quarterly, there has been a scarcity of published evidence that nursing research has been used to influence public health policy. The study’s author, Ann B. Hamric, remarked that research is a powerful tool that nurses can and should use to make a difference in regulatory legislation. Although this is slowly changing, nursing outcomes research could have significant implications for policies relating to MS patient care, added Ms. Lowden.

MS-Specific Outcomes
Ms. Lowden discussed some of the ideas presented by the Working Group on Outcomes during the 2002 Advanced Practice Nurse Advisory Meeting in Niagara-on-the-Lake, Canada. The group developed a comprehensive model that identified eight outcomes and described each outcome’s specific relation to MS:

- **Adherence**—includes treatment, rehabilitation, and follow-up;
- **Cost**—takes into account direct and indirect costs such as length of office or hospital visit, equipment, medications, lost work days, etc;
- **Symptom resolution and reduction**—specifically includes spasticity, fatigue, bladder symptoms, and pain, as well as mood and mobility issues;
- **Complication prevention**—the primary focus is on prevention of urinary tract infections, pressure ulcers, and pneumonia;
- **Well-being**—involves patient’s mood and ability to cope, sense of hope, and stress reduction;
- **Satisfaction with care by patient and family**—includes patient satisfaction with access to care; availability, comprehensiveness, and delivery of care; and the perception of being well cared for;
- **Continuity of care and care management**—factors include reduced number of emergency room, office, or clinic visits and fewer long-term care admissions;
- **Patient and family knowledge**—signifies that patients and family have an idea of what to expect in terms of treatment, symptoms, and disease course, as well as knowledge about medications, resources, care plan, etc.
The working group on outcomes also provided suggestions for interventions and ways of measuring each outcome (see sidebar).

Alligators, Swamps, and MS
The many difficulties involved in treating MS can present significant roadblocks to nursing research, said Ms. Lowden. She paraphrased an old adage to illustrate her point: “When you are up to your neck in alligators, it is difficult to think about draining the swamp.” She likened the alligators to the day-to-day workload, unpredictable crises, patients’ unrelenting symptoms, and innumerable phone calls dealt with routinely by MS nurses. “The swamp is the big picture of MS—the emotional, physical, and social consequences of the disease and the patient and family issues that arise during the coping process,” she said.

This hectic, emotionally trying environment leaves the MS nurse with “no time to think,” said Ms. Lowden. In addition, there is no reimbursement for outcomes research, limited access to libraries and computers for most nurses, and a lack of necessary databases to capture care. The support of colleagues and a supportive management environment are the exceptions rather than the rule, she added.

Finding the Bridge Over the Alligators
One important way MS nurses can overcome these obstacles is by actively disseminating information, suggested Ms. Lowden. This can be done by publishing articles in medical journals, presenting at conferences, educating oneself and others, becoming politically involved, and promoting advocacy. She also advised collaborating with other MS colleagues, offering nursing student research grants, and seeking out mentors as ways of obtaining research assistance. In addition, finding members of hospital staff or university faculty to help with research questions, design, and statistical analysis may prove beneficial, as can the assistance of academic nurses who have research training as well as access to resources. Ms. Lowden concluded her talk by encouraging MS nurses to take advantage of funding sources such as the International Organization of Multiple Sclerosis Nurses. MSX

—Rosalee L. Blumer

REFERENCES
CMSC Rehab Therapists Group Forms

As recently as 20 years ago, people with MS were advised to avoid physical activity because it was thought that exercise could increase symptoms or might enhance disease activity. Over the past several years, however, research has begun to dispel these myths by showing that exercise and rehabilitation can improve function and quality of life for MS patients. These relatively new findings, together with an increasingly interdisciplinary approach to MS treatment, have set the stage for the emerging role of the rehabilitation therapist in MS patient care.

“There are unique challenges for rehabilitation therapists treating people with MS,” says Brian Hutchinson, PT, President of the Heuga Center in Edwards, Colorado, which provides innovative medical and wellness programs for families affected by chronic diseases such as MS. Mr. Hutchinson is also one of the founders of the new International Organization of Multiple Sclerosis Rehabilitation Therapists (IOMSRT), which became a special interest group of the CMSC in 2002.

“We officially formed a year ago, but the organization has been about three years in the making,” says Mr. Hutchinson. “The idea came about as a result of the rehabilitation roundtable discussion at a CMSC conference a few years ago. We saw the success of the IOMSN and felt that it was important for rehabilitation therapists to try to become more cohesive and to share ideas with one another.”

With 50 members currently, most from the United States and Canada, the IOMSRT is still in its infancy. Mr. Hutchinson says the organization is trying to increase its membership and international scope through meetings at the annual CMSC conferences as well as other MS-related events. “We’re using a grapevine method of getting word out,” he explains, “because we don’t have a lot of funding for mass mailings and other promotional activities.”

Primary membership in the IOMSRT is geared toward physical and occupational therapists and speech-language pathologists with an interest in MS, but associate (nonvoting) memberships are available for interested parties from other occupational fields. For further information, e-mail Mr. Hutchinson at bhutchinson@heuga.org.

Coordinating MS Research in the US

The MS care community in the United States lacks a coordinated means of developing clinical trials, recruiting patients, and maintaining a persistent, qualified network of investigators. These deficiencies have slowed progress in the discovery of new MS treatment and care strategies.

To address these needs, MS health care professionals formed the Multiple Sclerosis Cooperative Studies Group (MSCSG). Operating under the direction of the CMSC, the group’s mission is “to identify and conduct high-quality research that will further the understanding of MS disease and its effects, reduce disease activity, and advance MS therapeutics—all to improve the quality of life of MS patients.” The MSCSG’s broad objectives include developing a cooperative infrastructure for MS research, increasing MS patients accessibility to clinical trials, and facilitating the transfer of research findings to MS providers in order to have an impact on clinical practice.

To view the 2003 MSCSG prospectus or to download a registration form, go to www.mscare.org.
Botulinum Toxin Injections for Neurogenic Bladder Dysfunction

There seems to be no end to the medical uses of botulinum toxin (Botox®), and one application that is gaining interest in the field of MS care is for treatment of bladder dysfunction caused by detrusor-sphincter dyssynergia (DSD).

At the CMSC conference earlier this year, researchers from the Mellen Center for MS Treatment and Research at the Cleveland Clinic reported the results of their trial, which used botulinum toxin injections to treat documented DSD in 12 MS patients.1

The patients (10 female; mean age 51.2) had three sessions of 100-IU botulinum toxin injections into the external sphincter, spaced four-weeks apart. Improvement over baseline was determined on the basis of post-voiding residual volume (PVR); patients’ voiding diaries recording frequency, urgency, leakage, and retention; patients’ perception of the severity of urinary symptoms; and quality of life measures based on two standard urological questionnaires.

After the treatment period, there was significant improvement in PVR, patient-reported urinary frequency, and perception of urinary symptoms, but quality of life scores and the other parameters did not change significantly. The authors, led by Francois A. Bethoux, MD, concluded that botulinum toxin injections appear to relieve some of the symptoms of DSD, but that further study of this treatment modality is needed.1

Positive results in MS patients also have been reported at other centers. Nine MS patients with DSD received external sphincter injections of botulinum toxin (100 IU) in a study performed at the University of Pittsburgh.2 At baseline, all had urinary retention, hesitancy, urgency, and infection history, and four required intermittent catheterization. After the injections, all were able to void spontaneously. The authors reported that patients experienced no acute complications, such as general paralysis or respiratory depression, and that no patients developed stress incontinence during the follow-up period.

A larger study from Taiwan published recently by Kuo3 enrolled 103 patients with urinary dysfunction from a variety of causes, including 29 with DSD. Botulinum toxin doses ranged from 50 to 100 IU. This author reported a success rate of 84.5%; 39% of patients reported excellent results and 46% had significant improvement. Among patients for whom treatment was successful, mean maximum voiding pressure, maximal urethral closing pressure, and post-void residual pressure had improved significantly at evaluations two to four weeks after treatment. Interestingly, 39 out of 45 patients were able to have their indwelling catheters removed or intermittent catheterization discontinued.

Botulinum toxin was first applied to the treatment of bladder conditions in 1998. Published literature reviews on this modality note that the best indication seems to be DSD caused by either MS or incomplete spinal cord injury.4 The effects of the injections last between two and nine months, depending upon the dose and the number of injections given.3,4

An obvious downside is the high cost of the botulinum toxin (about $400 for 100 units) if the patient’s insurance does not cover the procedure.

**REFERENCES**


INTERESTED IN SHARING YOUR KNOWLEDGE WITH THE WORLD? JOIN THE IOMSN!

The IOMSN is the only organization dedicated to the education of MS nurses around the world. If you wish to join the IOMSN, you can access it on the World Wide Web at www.iomsn.org, or contact the organization at:

**IOMSN**

c/o Bernard W. Gimbel MS Comprehensive Care Center

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Teaneck, NJ 07666

(201) 837-0727
post-injection systemic reaction, which affects about 10% of glatiramer acetate users, includes chest pain, flushing, palpitations, anxiety, dyspnea, and urticaria. These symptoms are usually transient, not cardiac in origin, and require no treatment.4 “Patients should be told about this possible reaction beforehand to reduce anxiety and avoid unnecessary trips to the emergency department,” advised Dr. Zwibel.

With the interferons, there are high rates of injection site reactions, headache, and flu-like symptoms (Figure).5 These agents are also associated with liver function abnormalities and may lead to liver damage. “It is best that patients be aware of the potential for such events so they can make informed decisions and monitor their response to the drug,” he remarked. In addition, regular patient monitoring may allow for early detection and avert long-term liver damage, noted Dr. Zwibel.

Data from the IFNB Multiple Sclerosis Study Group showed that flu-like symptoms from interferon beta-1b diminished over time, declining to around 8% within one year of starting treatment and typically dropping to around that level after only two months.6 Interferon treatment has been associated with skin necrosis but this does not usually occur with glatiramer acetate. Patients receiving interferon therapy should also be monitored for lipoatrophy (subcutaneous tissue loss) because, although rare, this side effect is irreversible.

Fatigue is a possible side effect of glatiramer acetate but significantly more so with the interferons. Few patients receiving glatiramer acetate develop flu-like symptoms. Clinicians should check the package insert of each MS medication for specifics about risks to pregnant women, the possibility of medication-related depression and seizures, and the need for thyroid and hematological monitoring during treatment.

**ADHERENCE**

Several factors affect patient adherence to treatment regimens. These include the number of drugs the person is taking, the frequency of dosing, and the ease of administration, said Dr. Zwibel. The number and severity of side effects, adverse drug reactions, comorbid conditions, and duration of the illness are equally significant. Data presented at the 1999 American Academy of Neurology meeting in Toronto suggested that adherence to therapy was greatest with glatiramer acetate (78.4%), followed by interferon beta-1a (58.6%), and interferon beta-1b (30.6%).7 Patients cited disease progression (25.4%), lack of improvement (22.1%), and side effects such as fever, flu-like symptoms, or joint pain (11.7%) as reasons for discontinuing therapy.8

Close follow-up is necessary for improving adherence

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**PATIENT INVOLVEMENT IN SELECTION OF MS THERAPIES**

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<thead>
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<th>Patient assessment of information given by clinician:</th>
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<tr>
<td>• All treatment options given in detail</td>
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**How did doctor handle treatment decisions?**

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<tr>
<td>• Let patient decide independently</td>
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<td>• Recommended one or two treatments</td>
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**Research by patient into treatment options**

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<tr>
<td>• Did further research</td>
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<td>• Based decisions on information received from clinician</td>
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**Who made the final decision about medication?**

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<td>• Patient and clinician together</td>
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Source: Howard Zwibel, MD.

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*Figure. Meta-analysis of adverse events with interferon agents versus placebo.*

to MS treatment. Follow-up should include pre-assessment calls, injection training, regular compliance calls, and even checking up on those who were only seeking a second opinion. “Patients should be seen every three to six months,” Dr. Zwibel recommended.

A team approach is vital as well. He stressed that “the patient, family, and health care providers need to be part of a team that promotes long-term adherence to treatment.”

REFERENCES

3. Teva Neuroscience; Serono Inc/Pfizer, and Berlex Laboratories marketing surveys.

LITERATURE MONITOR/NEWS ROUNDUP

NO SAFETY DATA FOR USE OF NASAL SPRAY INFLUENZA VACCINE IN MS PATIENTS

Because the new nasal spray for influenza immunizations is a live, attenuated vaccine, it should not be used in people with MS who are receiving immunosuppressive medications such as chronic steroids, mitoxantrone, cyclophosphamide, azathioprine, or methotrexate, warns Dennis Bourdette, MD, Chair of the Multiple Sclerosis Council’s Immunizations Guidelines Development Panel. In addition, the effects of interferon beta in response to live vaccines is unknown, he says.

“There are no safety data on this nasal spray,” says Dr. Bourdette. He recommends traditional inactivated influenza vaccine over the nasal spray form because “there are good safety data in MS” and because “inactivated vaccine may be less likely to provoke systemic response” than would live vaccine. However, he adds, receiving the nasal form of the vaccine “is preferable to not being vaccinated at all.”

REHAB PLUS STEROIDS BENEFITS MS PATIENTS AFTER RELAPSE

Combining intravenous steroids with rehabilitation is superior to steroid therapy alone for treating relapse in MS patients, according to researchers at the Centre for Neurology and Neurosurgery in Liverpool, United Kingdom.

The trial included 40 patients (27 female) with confirmed MS relapses severe enough to warrant intravenous methylprednisolone (IVMP) at a dose of one gram daily for three days. The subjects were randomized into two groups, both of which received IVMP treatment. However, one group received multidisciplinary team (MDT) care as an adjunct to steroid therapy.

The primary outcome measures were Guy’s Neurological Disability Scale (GNDS; a questionnaire in which the subject replies yes or no to a series of symptom-related questions), and the Amended Motor Club Assessment (AMCA), which measures motor impairment. Secondary measures included self-report questionnaires regarding independence of personal care, functional performance of activities of daily living, and other issues related to disability and quality of life. Assessments were performed during the first and third months of the study.

After three months, MS patients who underwent rehabilitation combined with steroid therapy experienced a statistically significant improvement in measures of GNDS and AMCA, as well as most secondary measures, compared with the steroid-only group. The authors concluded that “a problem-focused, team-integrated approach to the steroid management of MS relapse in the acute setting, including access to appropriate levels of therapy, is of benefit to patients in terms of motor function, disability, and aspects of health-related quality of life.”

STRESS MAY TRIGGER MS EXACERBATIONS

Stressful events are associated with increased exacerbations in relapsing-remitting multiple sclerosis (RRMS), according to a recent study. “In patients with MS the experience of at least one stressful event during a period of four weeks was associated with double the risk of an exacerbation within the next week,” reported researchers from Erasmus Medical Center in Rotterdam, the Netherlands.

The trial involved 73 RRMS patients ages 18 to 55. All subjects could walk with a cane or better (score of 0 to 0.6 on the Expanded Disability Status Scale) and had experienced at least two exacerbations in the previous 24 months. Patients with other serious conditions were excluded. Data were collected during regular office visits once every eight weeks, and additional visits were arranged within three days after patients reported symptoms of either infection or exacerbation. Once a week, patients recorded in diaries any stressful events from the following week. The diaries were independently evaluated by two neurologists in order to exclude stress directly connected to existing signs or symptoms of MS. The average follow-up time was 1.4 years.

Seventy of the 73 participants reported at least one stressful event, such as job-related stress, financial difficulties, or an illness or death in the family. A total of 457 stressful life events not related to MS were reported. During the study, 134 exacerbations occurred in 56 patients and 136 infections occurred in 57 patients. Statistical analysis showed that stress was associated with a doubling of the exacerbation rate during the subsequent four weeks.

Infections were associated with a threefold increase in the risk of exacerbation but this effect was found to be independent of stress. “Certain types of psychological stress can suppress immune reactions, and this could lead to increased susceptibility to infections,” the researchers noted. However, they found no evidence for increased infections associated with stressful life events.

“It will not be easy to tackle these factors in a given patient,” they added, “because both infections and stressful events cannot simply be eradicated from patients’ lives.” However, the authors suggested that MS patients and their caregivers can gain insight from the knowledge that stressful events not related to MS were reported. During the next week, reported researchers from Erasmus Medical Center in Rotterdam, the Netherlands.

STRESS MAY TRIGGER MS EXACERBATIONS

Stressful events are associated with increased exacerbations in relapsing-remitting multiple sclerosis (RRMS), according to a recent study. “In patients with MS the experience of at least one stressful event during a period of four weeks was associated with double the risk of an exacerbation within the next week,” reported researchers from Erasmus Medical Center in Rotterdam, the Netherlands.

The trial involved 73 RRMS patients ages 18 to 55. All subjects could walk with a cane or better (score of 0 to 0.6 on the Expanded Disability Status Scale) and had experienced at least two exacerbations in the previous 24 months. Patients with other serious conditions were excluded. Data were collected during regular office visits once every eight weeks, and additional visits were arranged within three days after patients reported symptoms of either infection or exacerbation. Once a week, patients recorded in diaries any stressful events from the following week. The diaries were independently evaluated by two neurologists in order to exclude stress directly connected to existing signs or symptoms of MS. The average follow-up time was 1.4 years.

Seventy of the 73 participants reported at least one stressful event, such as job-related stress, financial difficulties, or an illness or death in the family. A total of 457 stressful life events not related to MS were reported. During the study, 134 exacerbations occurred in 56 patients and 136 infections occurred in 57 patients. Statistical analysis showed that stress was associated with a doubling of the exacerbation rate during the subsequent four weeks.

Infections were associated with a threefold increase in the risk of exacerbation but this effect was found to be independent of stress. “Certain types of psychological stress can suppress immune reactions, and this could lead to increased susceptibility to infections,” the researchers noted. However, they found no evidence for increased infections associated with stressful life events.

“It will not be easy to tackle these factors in a given patient,” they added, “because both infections and stressful events cannot simply be eradicated from patients’ lives.” However, the authors suggested that MS patients and their caregivers can gain insight from the knowledge that stressful events may be linked to increased disease activity.


FATIGUE IN MS RELATED TO IMPAIRED NERVOUS SYSTEM

Fatigue in MS patients may be associated with sympathetic vasomotor dysfunction—an impairment of the part of nervous system concerned with preparing the body to react to stressful situations or emergencies—according to findings from a study conducted in Germany and Switzerland.

Sixty patients with clinically definite MS and 36 healthy controls were included in the trial. The researchers performed various measures of autonomic function to determine its relationship to fatigue. The assessments included electrocardiogram (ECG), heart rate, deep breathing, blood pressure responses to postural changes, and sustained handgrip. Fatigue was measured by self-administered questionnaires, including the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS).

The results showed that MS patients had a significantly lower median heart rate when standing compared with healthy participants. MS patients also had a significantly lower sustained handgrip than did healthy subjects. An analysis conducted within the MS patient group indicated that autonomic dysfunction was more pronounced among patients with MS-related fatigue. Those without fatigue did not differ from healthy subjects in any of the autonomic test parameters.

According to the researchers, these findings suggest that fatigue in MS patients “may be related to hypoadrenergic orthostatic response due to a sympathetic vasomotor lesion.”

Orthostatic hypotension is involved in other conditions, such as pure autonomic failure and multiple system atrophy, they noted, and its association with weakness, lethargy, and fatigue, resembles its association with MS-related fatigue in this trial.

Although the correlation between autonomic data and fatigue scores was “weak to moderate” in this study, the authors added that “a sympathetic vasomotor lesion similar to that seen in orthostatic intolerance may be one but not the only factor contributing to fatigue.” They speculated that treatments to alleviate orthostatic hypotension, such as increased fluid intake or sympathomimetics, may help to ameliorate MS-related fatigue.


CONTINUING EDUCATION CONFERENCE CALENDAR

February 9–13, 2004
Multiple Sclerosis Nurse Update Meeting. Location: Altamonte Springs, Fla. Contact: Carole Mulken, Serono Symposia International, One Technology Place, Rockland, MA 02370; (781) 681-2352; fax: 781-681-2915; e-mail: carole.mulken@serono.com; Web site: www.seronosymposia.org.

April 17–20, 2004
American Association of Neuroscience Nurses 36th Annual Meeting. Location: San Antonio, Tex. Contact: AANN, 4700 W Lake Ave, Glenview, IL 60025; (847) 375-4733; fax: (847) 375-6333; e-mail: info@aann.org; Web site: www.aann.org.

April 24–May 1, 2004
American Academy of Neurology 56th Annual Meeting. Location: San Francisco. Contact: AAN, 1080 Montreal Ave, Saint Paul, MN 55116; (800) 879-1960 or (651) 695-2717; fax: (651) 695-2791; e-mail: lstrachota@aan.com; Web site: http://am.aan.com.

September 4–7, 2004
8th Congress of the European Federation of Neurological Societies. Location: Paris. Contact: EFNS Head Office, University Campus, Courtyard 1, Alser Strasse 4, A-1090 Vienna, Austria; +43 1 889 05 03; fax: +43 1 889 05 03/13; e-mail: headoffice@efns.org; Web site: www.kenes.com/efns2004.

October 3–6, 2004
129th Annual Meeting of the American Neurological Association. Location: Toronto. Contact: ANA, 5841 Cedar Lake Rd, Suite #204, Minneapolis, MN 55416; (952) 545-6284; fax: (952) 545-6073; e-mail: lorijanderson@msn.com; Web site: www.an euroa.org.

October 6–9, 2004
Joint Annual Meeting of ECTRIMS and RIMS. Location: Vienna. Contact: ECTRIMS 2004 c/o Congress Service, PO Box Clarastrasse 57, CH-4005 Basel, Switzerland; +41 61 686 77 11; fax: +41 61 686 77 88; e-mail: info@ akm.ch; Web site: www.akm.ch/ectrims2004.

CMSC 2004 ANNUAL MEETING
The 2004 Annual Meeting of the Consortium of Multiple Sclerosis Centers will be held on June 2–6, 2004 in Toronto. The theme is “The Art and Science of Multiple Sclerosis Care.” Presentations that address timely issues involving MS patient care and basic and clinical research, as well as those that reflect collaboration between specialties, are encouraged. Go to www.mscare.org for abstract submission forms and registration information. Contact: Tina Trott, Executive Assistant, Consortium of Multiple Sclerosis Centers, c/o 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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