The Transverse Myelitis Association Newsletter

Volume 7 Issue 2 Spring 2007

From the Editor
Sandy Siegel

I have two important issues to address in this column. The first concerns a program focused on quality medical care for people with the neuroimmunologic disorders. The second issue concerns the ways we distribute information to our members. Both issues will need your participation to succeed!

The Transverse Myelitis Association is developing a network of physicians interested in caring for patients who have long-term symptom management issues from TM, NMO, ADEM and ON. I presented my vision for this network of physicians in my column in the TMA Journal Volume I. We are initiating this project by establishing a network of family practice or general practice physicians and pediatricians.

We have formed a team to manage this important project. Dr. Angela Middleton is a family practice physician in Virginia who also has transverse myelitis. Dr. Benjamin Greenberg is the Co-Director of the Johns Hopkins TM Center and serves on the TMA Medical Advisory Board. Dr. Greenberg and the other physicians associated with the Johns Hopkins TM Center have a strong and long-term commitment to providing education to physicians about the acute and long-term treatment of the neuroimmunologic disorders. This education component will be a critical element of the physician network. I will also serve on this team.

Angie, Ben and I recently had a meeting exclusively devoted to our work on this project. We recognize the many challenges involved in accomplishing this task and we have accepted that it will take a long time to develop. We also recognize the critical value of this endeavor and we are committed to doing the work required, however long it takes. The results for all of you will be a network of family practice physicians and pediatricians who have access to information about the neuroimmunologic disorders, information regarding the treatment strategies for the symptoms of these disorders, and experience with caring for people with these disorders. It will often be the general practitioner that has openings available on short notice, when it may take weeks to get in with the specialist. This is by no means an attempt to phase out the specialists, but to give you more guidance as far as the resources that are available for your medical care. Your general practitioner should know you better than any of your physicians, because their training requires them to look at the whole picture.

We need your help! If you are currently seeing a family physician or pediatrician who is providing you with excellent medical care, including the treatment of your or your child's symptoms from TM, NMO, ADEM or ON, we need for you to send us their names and contact information. This information can be submitted on a form that has been set up by Jim on our web site: http://www.myelitis.org/pnr/ or you can send me the information via an email or by letter. Please provide the physician's complete name, mailing address, phone number, and if possible, an email address. Please identify whether the doctor is a family/general practice physician, an internal medicine physician or a pediatrician. We are also asking you to provide us with all of *your* contact information in connection with this reference in case we need additional information from you about the basis of your recommendation. In your referral, please include how long you have been seeing this physician and please confirm with the doctor's office that this physician is accepting new patients. If this project proves successful, we also hope to eventually extend it to include other specialists, such as neurologists, urologists, psychiatrists, etc. As many of you already know, some specialists are more knowledgeable than others when it comes to these rare neuroimmunologic disorders.

The symptoms from TM, NMO, ADEM and ON are complex and difficult to manage. Some people have remarkable recoveries from their immune attacks. Unfortunately, even for those who have good recoveries, there are often symptoms from myelin and neuronal damage in the spinal cord that will go on for the long term. Symptoms such as nerve pain, paresthesias, spasticity, depression, and fatigue typically involve focused attention from a physician. Multiple treatment strategies are frequently required before the most effective therapies or combinations of therapies are found. There are no silver bullets and there is most definitely not a one-size fits all approach for treating these symptoms.

Because the symptoms of these disorders are so difficult, finding effective treatments and going through the process of finding quality medical care, in

general, can become a very frustrating and demoralizing process for many people. I am not overstating the magnitude of the problem. I have very first-hand evidence regarding this issue, because when many of you become significantly frustrated with this process, you often call me or send me an email message seeking help.

Not every medical or health issue you experience will derive from the myelin and neuronal damage that occurred in your spinal cord. It is important to be working with a physician who can determine which of your issues are neurological and which issues could be associated with a different diagnosis, e.g., having bladder dysfunction from TM doesn't make you immune from having your prostate grow to the size of a grapefruit.

The goal of our physician network project is to help people find the highest quality medical care. If you are currently receiving medical care from a physician who you would recommend to others in the TMA community, please take the time to get me this information. We are an international organization and we are very interested in serving our international membership. Please send us the names of your physicians who you would recommend from around the world. If you are a physician and would be interested in serving on the physician network team, we would appreciate your participation.

The TMA considers patient, caregiver and medical professional education among the most important services we provide to our membership. We know that the better informed you are, the more effective you will be in advocating for your medical care. The costs of providing you with this critical service have recently increased in a very substantial way. Postage costs have the single largest impact on our ability to provide you with information. This past May the United States Postal Service very significantly increased their rates. The postal service created a premium rate for all mail that has to be manually sorted; those pieces that are too large or too thick to be sorted through their machines. Unfortunately, almost everything we mail is too large and too thick to be automated mail.

The new postal rates will significantly increase our costs for mailings in the United States. New TMA members receive a packet of information that used to cost us $2.07 in postage. The new postage cost for this packet is $2.47. We are going to experience similar increases in the mailings of the TMA journals and membership directories.

While the mailings in the United States will be more costly, we believe we can absorb these additional costs and not reduce either the frequency or the size of our mailings for our national members. Unfortunately, this is not going to be possible for our mailings to international members. The cost of mailing the new member packets and journal to the majority of our international members was $6 for a single envelope; and this was for a letter post economy rate, the lowest-cost international option. The US postal service has terminated this class of mail with the changes imposed in May. The new rate for the lowest class of international mail is over $10 for a single envelope. It is just not possible for the TMA to manage those increased postage costs.

We are very fortunate and so grateful to a number of our international support groups who have taken on the responsibility for printing the TMA publications and mailing this information to TMA members. Our support group in the UK does all of the printing and mailings for members in the UK and to our membership across Europe. These mailings go to well over 700 members. In addition to taking on the work of printing and mailing these publications, our UK support group also raises their own funds to cover these costs. We owe Geoff Treglown, Lew Gray, Sally Rodohan and the UK support group a tremendous debt of gratitude for their willingness to take on this important work and we urge our members in the UK and Europe to contribute generously to support these efforts.

Errol White and the Australia support group also do the printing and mailings for our members in Australia and New Zealand. Jenny Moss and Mart Uys and our support group from South Africa have recently taken on the responsibility for these mailings to our members in South Africa. By their taking on this critical work, they have made it possible for our members in these countries to receive all of the information mailed by the TMA.

The increase in postage costs is going to significantly change how we distribute information to our international members who do not live in a region of the world covered by the three support groups doing these mailings. The regions that will be impacted by these changes include South and Central America, all of Asia, the Middle East, India, Pakistan and the Pacific.

The TMA will continue to do biennial mailings of the membership directories. For our international members, these will become regional directories which list members only from your region of the world. To honor the privacy of our members, we will not post any of these directories on our web site. Consequently, there is no other way for us to get this critical support information to our members. The new member packets will provide detailed guidance regarding the information that is posted on our web site, and the many ways to learn about the neuroimmunologic disorders and to find support. We will continue to mail the

newsletters to international members twice a year, and we will mail the regional directories biennially. The TMA journals will need to be read from our web site. Thus, it is very important that you check our web site often for new postings and information. The entire archives of our newsletters and journals can be found under the link ***newsletters***.

The TMA has large numbers of members in Canada, Brazil and India. We need people to volunteer to do the printing and mailings to people in your country and region of the world so that all of our international members have the same access to this critical information. The amount of work involved in each mailing is very small. Also, we are not asking you to bear the costs of these mailings; the TMA will pay for the printing and postage costs. If you can help us with this important work, please get in touch with me.

To change our publication and mailing practices was an extremely difficult decision for us. Pauline and I gauge the value of these mailings by thinking about what it would have meant for us to receive this new member packet in the mail when she was first diagnosed. We were totally on our own and we had absolutely no information. The information is critical; so is the envelope showing up in the mailbox, or whatever the receptacle for collecting mail looks like in Bangladesh. When people are given the diagnosis of a disorder that they've never heard anything about and wouldn't have the slightest idea where to find another person who has it, having something tangible representing a network of people who care about what is happening to them, offering information to help them manage their medical care and offering guidance and support through this difficult journey is just an invaluable gift. We know and understand; and that is why we will continue to mail information to everyone; it just can't be the big $10 envelope.

The TMA is an international organization. We are as concerned about our members in Pakistan as we are for our members in Ohio. If you live in a region of the world where we need your help, please consider providing our members in your country with this important service. Get into your membership directory and see if you can't find a group of people who will be willing to take on this effort together. I am not asking you to do something that you are unable to do. If I figured out how to do all of this stuff, so can you.

Please take good care of yourselves and each other.

Douglas A. Kerr, M.D., Ph.D. will be speaking at the first UK TM Conference on Saturday 13th October 2007 in London.

Medical Approach to the Management of Neuropathic Pain

D. Joanne Lynn MD
The Ohio State University MS Center

Adapted from a presentation at the 2006 Rare Neuroimmunologic Disorders Symposium

This article focuses on the medical treatments for neuropathic pain. I am not a pain specialist or an anesthesiologist. I am a neurologist in an MS clinic; my experience derives from treating people with neuropathic pain who come to our clinic. I am going to describe the types of pain and clinical manifestations of neuropathic pain, the various ways that pain neurons respond to injury and how different medications may modulate the pain pathways. Finally, I will describe the first and second line medications that we use for the management of neuropathic pain.

We have more information about neuropathic pain in MS patients than we do from any of the other neuroimmunologic diseases. From various surveys of large MS clinic populations, 45% to 55% of patients report that they have some sort of pain syndrome. In the past, it was believed that pain was not a symptom of MS. This is obviously not the case. A large survey with 1672 respondents was administered to determine the pain syndromes that were found with MS (Archibald, et al. 1994). Trigeminal neuralgia was reported by 2% of the patients. This is one of the most difficult pains; a stabbing, lancinating pain in the face, which may be triggered by speaking or chewing. We sometimes have to admit people to the hospital who have flares of trigeminal neuralgia, because they cannot eat or stay hydrated. Lhermitte's sign was reported by 9% of the MS patients in this survey. This is an electric feeling that spreads down the body when you bend your head forward. Dysesthetic pain was re-

ported by 18.1%. Back pain was identified by 16.4%. Back pain may or may not be directly related to the MS. Painful tonic spasms were reported by 11% of the patients. Sometimes people with spinal cord disorders experience spasms of the hand or leg which occur as constant or intermittent contractions and can be very painful.

Dr. Douglas Kerr has reported from his experience at the Johns Hopkins Transverse Myelitis Center that during the acute phase, 80-94% of patients have numbness, paresthesias or band-like dysesthesias (Krishnan, et al. 2004). Kerr also indicates that pain or dysesthesias are the most debilitating long-term symptom in approximately 40% of TM patients (Kerr 2001, in Griffin and McArthur, Current Therapy in Neurologic Disease).

There are different types of pain. Nocioceptive pain is caused by activation of pain receptors from injuring tissue. The causes can be somatic, such as from a skin burn, muscle tear or pulled ligament or from visceral structures, such as infection of the gall bladder, bowel obstruction and distention. Neuropathic pain is different from nocioceptive pain. Neuropathic pain is from injury or dysfunction in the nervous system and can occur in the peripheral or the central nervous system. Within the nervous system, the injury starts sending off abnormal signals interpreted as "I'm experiencing pain" even though there is no discernable active tissue damage.

There are a number of different neuropathic pain sensations or experiences. Dysesthesias are spontaneous unpleasant sensations which occur without a clear cause. For instance, it might feel as though you are being stabbed by a knife, but you are not. Allodynia refers to pain perception produced by a normally non-noxious stimuli, such as lightly brushing the skin. Hyperpathia or hyperalgesia refers to prolonged or exaggerated pain from a pinprick or other lightly painful stimulus. For instance, when I am doing a neurological exam and touch the skin with a pin that might evoke a sensation that is briefly, transiently uncomfortable, for someone with this type of pain, it might cause a spreading or prolonged painful feeling.

When we are treating someone with pain, it is important for us to try to determine the cause. It is helpful when patients give these issues some thought so that they come to their appointments being able to describe their pain. During our assessment, we want to know the location of pain. We want to identify the character of the pain; is it stabbing, burning, hot, cold, ripping, squeezing? We are seeking some descriptive words for the pain. If a person says that it is "bad" pain or that it is "painful all over;" that information is less helpful for us in determining the cause of the pain. We are interested in the pain's intensity and the temporal pattern; is it acute or chronic. We also want to know if there are exacerbating or ameliorating factors; what kinds of things make it better or worse.

This is a list of common neuropathic pain syndromes or causes:
Painful diabetic neuropathy
Post-herpetic neuralgia
Cancer-associated
Spinal cord injury
Complex regional pain syndrome
Multiple Sclerosis
Trigeminal Neuralgia
Post-stroke pain
HIV-related pain

People with diabetes get peripheral nerve disease. They can experience burning and pain that can be so difficult that they do not even want the sheets to touch their feet. This type of pain is very common, because diabetes is so common. People that have herpes zoster or shingles may also develop the pain syndromes that occur acutely with the shingles outbreak or may follow the recovery. Both diabetic neuropathy and post-herpetic neuralgia are so common and so standard that they are most often used as neuropathic pain syndrome models to study drug treatments. Many of the drugs that I present in this article were studied in the context of these diseases. These drugs are not studied in disorders that are rare, such as in TM or in MS. Pain is common in TM and MS, but it is difficult to study, because people have such a wide variety of characteristics associated with their pain. Spinal cord injury pain could include TM. People with strokes can have pain from injuries to the spinal cord or higher pain pathways or centers.

We often talk about different kinds of neuropathic pain qualities in describing the sensations. The pain can be steady; often described as burning, hot or sometimes cold. It may be paroxysmal shock-like or stabbing. It may be pain to touch (allodynia). It can be deep, aching pain. Often the pain is the most difficult at night.

There are non-pharmacologic treatments of pain. We rely on physical therapists to help with modalities, such as application of heat and cold and gradual, graded therapeutic exercise. We may use acupuncture and transcutaneous nerve stimulation. If pain is difficult to manage, we may need to look into sleep quality and management of depression. Every pain syndrome is made worse by depression. We need to treat the associated depression which is found in high percentages of people with chronic pain. Psychological approaches are important non-pharmacologic treatments of pain. These may include cognitive therapies, such as relaxation and imagery hypnosis, biofeedback, behavioral therapy and music and art therapy.

I am going to provide an overview of the pharmacologic treatments for neu-

ropathic pain. To many patients, the long list of medications is baffling and frustrating. Some people just do not want to try any more drugs. It is important to understand the different types of medications and why we are trying these as treatments for neuropathic pain.

Optimally, management of neuropathic pain would be guided by knowledge of the underlying problem and its resultant mechanisms of pain production. For instance, if you had stabbing pain, it would be great if we knew exactly where in the nervous system the malfunctioning circuit was located, what specific neurotransmitter system was dysfunctional and what drug would fix the problem. That is just not the way it is for almost all of the pain syndromes. The pain results from multiple processes and we have not been able to define them with a sufficient degree of detail or specificity. We have very little information about the specific sites or mechanisms of dysfunction for various pain syndromes.

Wherever nerves are injured or in the normal appreciation of pain, pain receptors trigger electrical impulses of nerve fibers. That information then enters the spinal cord and the neuron releases a chemical neurotransmitter - often glutamate. Glutamate activates second order neurons that carry pain signals to the thalamus and other areas in the brain and brainstem where pain appreciation is modulated and controlled.

What do we know about the mechanisms of neuropathic pain? Nerve fibers bring pain information, for instance, from limbs or from skin and there are several different kinds of sodium channels that are needed for firing of these nerve fibers. One type of Na+ channel is found only on nociceptive (carrying information about pain) sensory neuron fibers. If you have damage to that type of nerve, it can cause an increase in the numbers of sodium channels. That increase in sodium channel density impacts the function of the nerve with resultant hyper-excitability and spontaneous or recurrent nerve discharge or sensitization. The nerve can start to fire on its own, without a stimulus and it can feel like stabbing or a shock. You might also get recurrent nerve discharges. For example, it might be set off once by being bumped and then it keeps going off. The whole system becomes sensitized to the point where it will fire off more easily; there is a lower threshold to fire caused by this kind of injury.

We have some drugs that modulate this sodium channel activity and help neuropathic pain. Some of these are anti-seizure medicines, such as carbamazepine (Tegretol®), oxcarbazepine, and Lidocaine. Some are tricyclic antidepressants, such as phenytoin (Dilantin®), topiramate (Topamax®), and lamotrigine (Lamictal®).

There are two subunits of voltage gated calcium ion (Ca++) channels that are upregulated on the dorsal root ganglion (on the nerve fibers) and spinal cord dorsal horn neurons (spinal cord neurons) after injury. If the function or number of these channels is abnormal, it can be associated with allodynia; a stimulus that would not normally be painful becomes painful. Both gabapentin (Neurontin®) and pregabalin (Lyrica®) bind to these subunits and inhibit the high voltage Ca++ channels. There are other medications that also bind to Ca++ channels.

Nerve damage can produce excitatory neurotransmitters and chemicals (peptides) which may cause central sensitization in the spinal cord and brain pathways for pain. These nerve injuries may also cause damage (toxicity) to descending pain control pathways that inhibit pain (inhibitory neurons that use neurotransmitters, such as norepinephrine - NE, dopamine - DA, serotonin – 5-HT and endogenous opioids). If the systems that control our pain appreciation pathways are damaged, then there will be increased problems with pain. There are medications that can increase the activity of the inhibitory neurotransmitters to help decrease pain perception.

There are three main classes of drugs that we use to treat neuropathic pain: antidepressants, anticonvulsants or anti-seizure drugs, and analgesics, which include opioids. Antidepressants are a well-established older therapy; we have used them for decades. These are the antidepressants that were around before fluoxetine (Prozac®). They were not optimal for the treatment of depression, because of their high side-effect profile. They are good for treating pain, however, because we can use lower doses that are associated with fewer side effects. There are numerous studies which have demonstrated pain relief without an antidepressant effect in many types of neuropathic pain, including diabetic neuropathy, post-herpetic neuropathy, headache, facial pain and low back pain.

The neurotransmitters that are affected by the antidepressants are norepinephrine, dopamine, and serotonin. The tricyclic antidepressants are older medications, such as amitriptyline (Elavil®) and nortriptyline (Pamelor®). These are primarily a combination of serotonin and noradrenaline reuptake blockade. They have some other effects, including peripheral sodium channel blockade and weak NMDA antagonism.

These medications work to inhibit neuropathic pain by blocking the reuptake of one or more of these neurotransmitters. A nerve sends information via a chemical mechanism out to the next

adjacent nerve. The information is a pain signal that is interpreted by the brain as, "You are having pain." The transmission of pain information from one nerve to another can be decreased by slowing reuptake of these neurotransmitters back into the releasing nerve after each nerve firing. This is one mechanism that can inhibit the transmission and perception of pain.

When we treat neuropathic pain with nortriptyline (Pamelor®) and amitriptyline (Elavil®) the guidelines are to start low and increase slowly. There also have to be accommodations for age. If the person is younger than 65, then perhaps start with 25 mg qhs; if older than 65, then start with 10 mg qhs. The dose is also dependent on the person's weight. If we need to increase the dose, we increase gradually; 10 – 25 mg q 1-2 weeks. We also have to look for various side effects, including glaucoma, urinary obstruction, and asthma. The traditional tried and true method was to keep increasing the drug until pain relief was achieved or the person experienced a significant side-effect. We exercise more care today in watching for the side effects of these medications. The side-effects from tricyclic antidepressants include: dry mouth, constipation, weight gain, urinary retention, tachycardia, and drowsiness. Dry mouth can be helped with sugar free lozenges or artificial saliva. We will discontinue these medications, if there is urinary retention or tachycardia. For drowsiness, we will decrease the dose.

Some of the newer antidepressants have been evaluated as treatments for pain. These are the selective serotonin reuptake inhibitor (SSRI) agents (agents that selectively affect neuron systems with serotonin receptors), including fluoxetine (Prozac®), paroxetine (Paxil®) and sertraline (Zoloft®). The results from studies of the SSRIs in the treatment of painful diabetic neuropathy suggest that these agents are less effective than agents that affect both serotonin and norepinephrine. These drugs are great for the treatment of depression, but are not very effective for neuropathic pain.

Another group of newer antidepressants are serotonin-norepinephrine reuptake inhibitors. Venlafaxine (Effexor®) inhibits both norepinephrine and serotonin at 150 mg/d but not 75 mg/d. It has been effective in pain treatment, but it is not being used as a first line medication. Duloxetine (Cymbalta®) is FDA-approved for the treatment of painful diabetic neuropathy. It has relatively few side-effects, and is also used to treat depression, so it has the benefit of being a two-for-one drug.

There is a group of antidepressants that are norepinephrine-dopamine reuptake inhibitors; two neurotransmitter systems. Bupropion (Wellbutrin®) inhibits both norepinephrine and dopamine reuptake. It has been reported to be effective in the treatment of both peripheral and central pain syndrome. There are a number of medications in this group so there are options. There is a low side-effect frequency, but bupropion can cause weight loss, occasional agitation or insomnia. We make decisions about medications on an individual basis and attempt to match medications with a particular set of issues. For instance, a person might have a problem with sleepiness or insomnia, and we would select the appropriate medication accordingly.

For all antidepressants we should consider the FDA black box warnings for increased risk of suicidality in depressed patients treated with antidepressants. Special attention and consideration in this regard needs to be focused on adolescent and pediatric patients. This really means that we should continue to do what we have always done; when using these drugs for pain, we assess for comorbid depression and suicidality.

The next class of medications for neuropathic pain are the antiepileptic drugs. Gabapentin (Neurontin®) is FDA approved for post-herpetic neuralgia or zoster (for patients in the United States) and for neuropathic pain in general in the United Kingdom. It blocks the sodium channels (Ca++) and inhibits excitatory neurotransmitter release. It may decrease the process of central sensitization resulting in lower thresholds for pain. It has a good side effect profile for most people. There is great variation in how much gabapentin a person can handle; some people cannot handle 900 mg/day, while others are able to tolerate above 3600 mg/day.

Pregabalin (Lyrica®) is a newer drug that is a presynaptic calcium (Ca++) channel blocker that reduces excitatory neurotransmitter release. It is FDA approved for painful diabetic neuropathy and post-herpetic neuralgia. It comes in 50 and 75 mg tablets and we can give up to 600 mg/day. It can cause sedation and ataxia as you push up. It will be interesting to see how this medication works for some of the pain syndromes that we see in transverse myelitis.

Carbamazepine (Tegretol®) is an older drug that is FDA approved and has been especially effective for the treatment of trigeminal neuralgia, the facial pain seen in MS, and also shock-like pains. Carbamazepine can cause sedation and balance problems. There are other anti-seizure medicines that are not first line drugs; they may not be as good and they are not as well studied. Oxcarbazepine (Trileptal®) is related to carbamazepine and there has been one positive study in painful diabetic neuropathy. Other antiepileptic drugs include Lamotrigine (Lamictal®), a second line drug that has been shown to be effective against neuropathic pain of several different etiologies, including spinal cord injury. Valproate (Depakote®) is useful for migraine prophylaxis and one study has shown a

benefit for painful diabetic neuropathy. Multiple toxicities and drug-drug interactions make it a second line drug (Kochar, et al. 2004). There have been no randomized controlled trials for the use of the selective GABA reuptake inhibitor Tiagabine (Gabitril®) for the treatment of neuropathic pain conditions.

There are various topical agents that we use for neuropathic pain. There is the lidocaine patch 5% (Lidoderm®) and Capsaicin, a cream made from the chili pepper. Capsaicin affects pain fibers. It burns when it is initially applied. It may then cause some degeneration of neurofibers, and that may create benefit in the long run. There are also some topical NSAIDs and topical antidepressants that are available.

There are also some miscellaneous agents that have been used for neuropathic pain. Baclofen (Lioresal®) is a GABA-A receptor agonist that is mainly used for the treatment of spasticity. It has also been reported to be effective in treating trigeminal neuralgia. Clonidine has been effective in the treatment of cancer-associated neuropathic pain, but requires study in non-cancer neuropathic pain.

Opioids have generally been underutilized for the treatment of neuropathic pain. In addition to working on opioid receptors, opioids also decrease glutamate receptor activity. Physicians who are not anesthesiologists or pain doctors are typically reticent to use opioids and neurologists tend to be conservative. There have been some studies in the past that have reported that opioids are less effective for neuropathic pain compared to tissue injury (somatic) pain. It is certainly appropriate for a patient with moderate to severe pain who has not responded to other types of treatment and who is willing to accept the discipline of a structured opioid prescription program to use these medications.

Opioids may be associated with tolerance; there may be a need to increase the dose over time to maintain effectiveness. It may also be associated with physical dependence and with unpleasant withdrawal symptoms when stopping the drug. Less often, there may be addiction; drug seeking behavior to satisfy drug craving despite harm. For most people with a pain syndrome, they do not develop addiction or drug seeking behavior when using opioids as a legitimate treatment.

Setting up an opioid prescription program helps to reduce the risk of addiction. Having scheduled appointments on a regular basis reduces risk for abuse. There can be an agreement with the patient that they obtain all of the analgesics or opioids through one doctor and one pharmacy. There can be a written contract that sets limits and may agree to urine testing. Some of the opioids are tramadol (Ultram®), morphine or extended release morphine, oxycodone, fentanyl patch and vicodin or percocet for breakthrough pain.

Finally, I want to discuss combination therapy for the treatment of neuropathic pain. Patients consider a 30% improvement in pain to be significant. In many treatment trials only 1 out of 3 to 4 patients treated will experience moderate improvement. It is difficult to identify the underlying pain mechanisms in a patient. Due to these uncertainties, it is sometimes important to try multiple agents. A common approach used in combination therapy is to start with one drug and titrate up until maximum benefit or intolerable side effects result. In one study (Gilron, 2005), a combination of gabapentin and morphine was found to be more effective than each drug used separately.

It is important for patients to remain hopeful and persistent in their efforts to obtain effective treatment for their neuropathic pain. Fortunately, there are a large number of drugs that are effective for treating neuropathic pain. Finding the appropriate treatments is a great challenge and it is important to have a good partnership with your physician in working through the treatments. It is a trial and error process to find the most useful drug or combination of drugs at the right doses with the least side effects to treat neuropathic pain.

Acute transverse myelitis in childhood

Center-based analysis of 47 cases

F.S. Pidcock, MD
C. Krishnan, MHS
T.O. Crawford, MD
C.F. Salorio, PhD
M. Trovato, MD
D.A. Kerr, MD, PhD

CME

Address correspondence and reprint requests to Dr. F.S. Pidcock, Department of Physical Medicine and Rehabilitation, Kennedy Krieger Institute, Johns Hopkins Medical Institutions, 707 North Broadway, Baltimore, MD 21205
pidcock@kennedykrieger.org

ABSTRACT Objective: To relate clinical characteristics associated with acute transverse myelitis (ATM) in children with functional outcomes at follow-up. **Methods:** We identified 47 patients for whom ATM occurred under the age of 18 years. Chart analysis, clinical evaluation, and administration of functional measures were completed. **Results:** The age at onset clustered between ages 0 to 2 and 5 to 17. Febrile illness had occurred in 47% and vaccination in 28%. Major disability at the nadir of the clinical course was noted. Eighty-nine percent were unable to walk, required assisted ventilation, or both. At a median of 3.2 years after acute illness, 43% were unable to walk 30 ft and 21% required a walker or other support, 68% experienced urinary urgency, 50% required bladder catheterization, 54% were troubled by persistent dysesthesias, and 75% had numbness. Factors associated with a better functional outcome included older age at time of diagnosis, shorter time to diagnosis, lower sensory and anatomic levels of spinal injury, absence of T1 hypointensity on spinal MRI obtained during the acute period, lack of white blood cells in the CSF, and fewer affected spinal cord segments. Neither rapid progression to maximum impairment in less than 1 day nor any antecedent illness, immunization, or trauma was associated with a worse outcome. **Conclusion:** Persisting disability was present in many children with acute transverse myelitis. Urinary problems and sensory symptoms were the most common issues. Age at onset below 3 years was associated with worse functional outcomes. **NEUROLOGY 2007;68:1474-1480**

Acute transverse myelitis (ATM) is a rare disorder with about 1,400 new cases diagnosed in the United States per year.[1,2] In approximately 20%, the acute illness occurs at younger than 18 years.[3]

Diagnostic criteria and a classification scheme for ATM were recently established by the Transverse Myelitis Consortium Working Group.[4] The diagnosis requires both the presence of spinal cord inflammation, as defined by CSF pleocytosis, elevated CSF IgG index, or gadolinium enhancement on a spinal MRI, and the absence of an identified CNS infection. The diagnosis also requires exclusion of acute myelopathy secondary to a known underlying disease and from compressive myelopathies. Depending on the series, 6 to 43% of patients with ATM develop signs and symptoms sufficient to make the diagnosis of multiple sclerosis (MS), 8 to 16.5% manifest features of a systemic mixed connective tissue disorder, and up to 5% are found to have localized nonpyogenic infection of the spinal cord[1,2,5] (Johns Hopkins Transverse Myelitis Center [JHTMC] case series). Idiopathic ATM accounts for about 10 to 45% of all cases of ATM.[1,2,6-10]

We evaluated a large cohort of patients under age 18 who developed ATM. This cohort was evaluated and treated at a tertiary referral center. Information is provided on antecedent factors, acute clinical and paraclinical features, and functional and ambulatory outcome measures at the time of onset of ATM and at follow-up and treatment. This study qualified for institutional review board exemption (under 45 CFR 46,101 [b][4] on 20 September 2001 [protocol number 01-09-20-16e]).

See also page 1447

From the Department of Physical Medicine and Rehabilitation (F.S.P., C.F.S., M.T.), Kennedy Krieger Institute, Johns Hopkins Medical Institutions, and Department of Neurology (C.K., T.O.C., D.A.K.), Johns Hopkins University School of Medicine, Baltimore, MD.

Disclosure: The authors report no conflicts of interest.

METHODS Case selection and data collection. All patients evaluated at the JHTMC between January 2000 and February 2004 who met established criteria for acute or remote transverse myelitis under age 18 were included.[4] Patients with disease-associated ATM were included. All information collected was coded to protect confidentiality and entered into SPSS 11.5.0 for analysis.

Retrospective clinical data were collected from chart review and from the history obtained at the time of evaluation at the JHTMC. This included demographic items (age at onset, sex, geography), antecedent factors (immunizations, infectious disease, trauma), description of the acute illness (onset of first neurologic symptom, time to nadir, time to diagnosis, acute symptoms), bladder function, and reported sensory symptoms. Vaccinations within 30 days of onset of ATM were confirmed by review of medical records. Laboratory data collected included the extent and type of spinal cord lesions seen on MRI, CSF white blood cell (WBC) counts, and protein. Treatment variables assessed included use of IV or oral corticosteroids, IV immunoglobulins, acyclovir, and plasmapheresis.

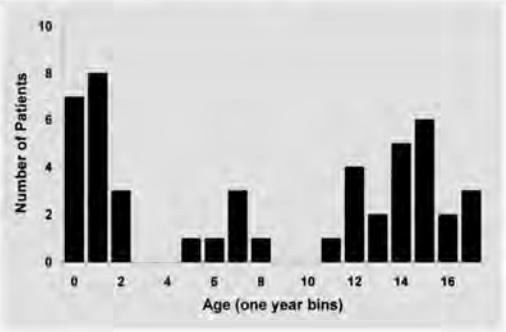
Assessment of function. Ambulatory ability was assessed at the time of presentation to the JHTMC using all retrospective information available from the functional nadir of the acute illness if that had passed. Patients were assigned an ordinal scale score according to an adaptation of the Hughes Functional Disability Scale (HFDS; 0 = normal, 1 = minor symptoms, fully capable of manual work, 2 = able to walk more than 30 ft without assistance, 3 = able to walk more than 30 ft with assistance, 4 = bed bound/wheel chair bound, 5 = requires assisted ventilation, 6 = death).[11] Functional independence following the acute phase of illness was assessed using the WeeFIM for children.[12] For those who were older than age 18 at follow-up, the adult FIM was used to assess functional independence.[13] This follow-up information was collected at an average of 8.0 years (CI: 4.5 to 11.9 years) following the acute onset of disease.

The FIM and the WeeFIM are instruments that measure functional performance of daily skills in 18 separate domains including self-care, toileting, mobility, transfers, communication, cognition, and social interaction. The 18 content items are scored from 1 to 7 based on the individual's level of independence in performing the skill.

Summary data for level of independence at follow-up for each ability area were calculated by grouping patients into three groups, complete dependence, modified dependence, and independence, based on the need for assistance determined by standard rating criteria for the WeeFIM and FIM. WeeFIM and FIM scores at follow-up were then summed into the three domains of activities of daily living (ADL), continence, and mobility. In addition, because younger children are not expected to be completely independent with all activities, all scores were transformed into functional quotients (FQs) based on normative data for each item.

Statistical analysis. The data were analyzed using multiple regression models. Functional outcome was examined using the summed FQ scores for ADL, mobility, and continence. The following predictor variables were examined: age at onset, season of onset, preceding immunization, preceding trauma, the combination of both immunization and trauma, treatment modality, time to nadir, and time to diagnosis. Because of the skewed nature of the distribution of some data, discrete variables were calculated for extent of lesion (zero to three, four to seven, or greater than seven involved segments), CSF pleocytosis (none vs abnormal), rostral border of the sensory level based on exam, and rostral border of the lesion based on MRI (cervical level vs thoracic or lower). In addition, log-transformed values of CSF white blood cells were used for analysis of distribution. Spearman rho correlations were performed between the score on the HFDS at the time of diagnosis and functional outcome scores at the time of follow-up.

Figure 1 Distribution of age at onset of acute transverse myelitis



Factors that predicted functional outcomes were examined for three domains (ADL, continence, mobility) and for the total WeeFIM and FIM scores at follow-up, using multiple regression. All regression models were first run using raw score ratings from the WeeFIM and FIM as the outcome variable and controlling for age in the regression models. The regressions were then rerun using functional quotients as the outcome variable to control for age. As the significance of predictor variables was the same using both methods, only the FQ analyses are reported for simplicity.

RESULTS Patients included. We studied 47 patients with an acute onset of transverse myelitis at younger than 18 years. Eighty-nine percent (42/47) of the patients had monophasic idiopathic transverse myelitis, two patients had recurrent TM, and three patients had TM that was later identified to be associated with another disease, specifically neuromyelitis optica, acute disseminated encephalomyelitis, and systemic lupus erythematosis. In one case MS was diagnosed at a later time. There were two deaths in this cohort during the interval of follow-up, both due to respiratory failure associated with a very high cervical cord lesion. Seven of the subjects were evaluated at the JHTMC as adults at an average of 35 years following their acute illness as children. The data from the acute phase on these seven cases are not complete.

Demographic features and risk factors. The distribution of age at time of onset is bimodal (figure 1). There appears to be at least two peaks of incidence. One is narrow involving toddlers under age 3 and a second is broader ranging between ages 5 and 17 with increasing frequency in older ages. Males and females are equally affected, with a ratio of 1.04.

An infectious disease, defined by two recorded oral temperatures above 101.5 °F, two recorded serum WBC elevations above 11,000 cells/mm^3, or positive PCR or serologic studies preceding the onset of neurologic symptoms, was reported in 47% of cases (22/47). This occurred at an average of 11 ± 10 days (mean ± SD) prior to first neurologic symptom. Twenty-eight percent of cases (13/47) had a confirmed immunization or allergy shot within 30 days (mean 14 ± 7 days, mean ± SD) of the first symptom of ATM. Vaccines given were polio (three cases), measles–mumps–rubella,[3] hepatitis B,[2] diptheria–tetanus–pertussis,[2] influenzae,[2] varicella,[1] small pox,[1] Japanese B encephalitis,[1] *Haemophilus influenzae*,[1] and allergy shots.[1] Two patients received a combination of three vaccinations. In eight cases, both antecedent immunization and illness were reported. Antecedent trauma, usually a twist or fall, was described in 13% of cases (6/47) at an average of 8 days before the onset of acute neurologic symptoms.

Identified treatment modalities included IV steroids in 70% (32/46) cases, IV immunoglobulin in 33% (15/346), oral steroids in 28% (13/46), plasmapheresis in 15% (7/46), and acyclovir in 11% (5/46). Twelve patients reported none of the above treatments. Most of these patients had ATM in the more distant past before high-dose steroid treatment of acute CNS inflammatory disorders became common.

Acute clinical characteristics. The mean time from the onset of acute symptoms to functional nadir was about 2 days in these children; 68.2% of cases were assigned a diagnosis of TM within 7 days of the onset of symptoms. Ninety-one percent of subjects (40/44) described sensory loss or numbness in the initial phase of ATM. Eighty-nine percent (42/47) reported weakness, 85% (40/47) urinary dysfunction, and 75% (30/40) reported pain. Eighty-nine percent (42/47) were bed bound/wheel chair bound or required assisted ventilation during the initial phase of ATM.

The rostral border of clinical sensory loss was cervical in 25% (9/36), thoracic in 53% (19/36), lumbar in 5% (2/36), sacral in 3% (1/36), and unclear in 14% (5/36) of the investigated cohort.

Acute MRI and CSF characteristics. MRI of the spinal cord was obtained in 38 cases. T2 signal abnormalities were identified at cervical levels in 50% of these cases (19/38) and at thoracic levels in 40% (15/38). One patient had multifocal lesions, one had a single sacral level lesion, one had conus level lesion, and one had T2 abnormalities involving the entire spinal cord. Two patients had a normal spine MRI. The findings on T1 signal imaging were reported in 21 cases. A hypointense lesion was identified in 38% (8/21). Gadolinium infusion demonstrated lesion enhancement on T1-weighted images in 74% (26/35) of cases. The rostral–caudal extent of the lesions measured on spine MRI ranged from one vertebral segment to the entire spinal cord in one patient. The average number of segments spanned was six segments.

An elevated CSF WBC was apparent in 50% (17/34) of patients, with a mean WBC count of 136 ± 67 cells (range from 6 to 950 cells). An elevated CSF protein level was found in 48% (14/29) of the patients with a mean value of 173 ± 75 g/dL (range 45 to 1,120 g/dL). CSF WBC count and protein were normal in 31% (9/29) patients. Oligoclonal bands and elevated IgG index were reported in less than 5% of the cohort.

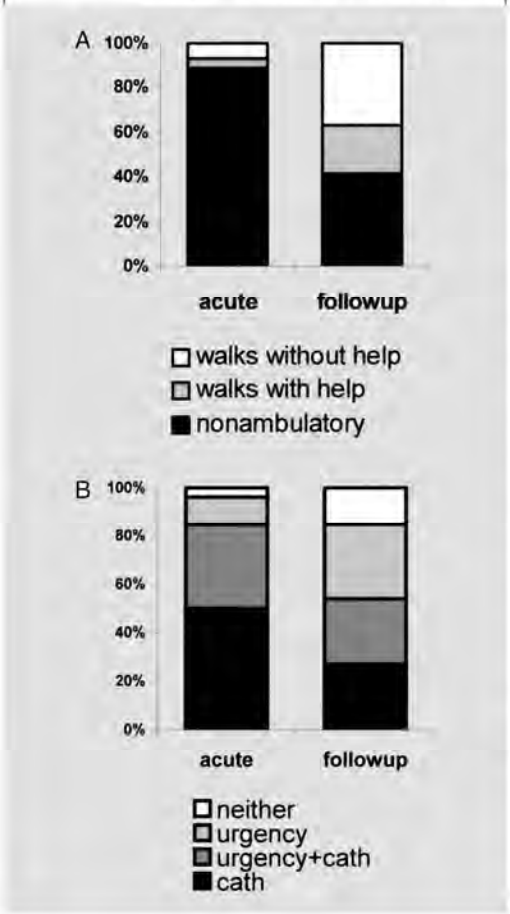
Sensory and motor characteristics. Information about sensory symptoms was collected in 38 patients. During the acute phase of illness, positive sensory complaints (burning, tingling, or electric shock sensations) were present in 23, disquieting numbness was apparent in 27, and a combination of the two was reported in 10. Positive sensory phenomenon resolved at follow-up in 52% (12/23), whereas numbness resolved in only 30% (8/27). At follow-up, new sensory complaints that were not part of the acute illness included positive phenomenon in 12 and numbness in 3. At follow-up, a total of 54% (15/28) of patients still experienced positive sensory dysesthesias, and 75% (21/28) reported numbness.

The need for bladder catheterization during the acute phase of illness was 82% (36/44) compared with 50% (22/44) at follow-up. Urinary urgency was reported in of 46% (13/28) of patients during the acute phase of illness. This resolved in four of these patients. Seven patients acquired urgency as urinary function improved during the interval of follow-up. Overall, 68% (19/28) of patients experienced urinary urgency at follow-up (figure 2).

Of the 42 patients nonambulatory at the nadir of acute illness, 52% (22/42) were able to walk at least 30 ft with or without the help of a walker or some form of support at the time of follow-up. Acute-illness requirement for ventilator assistance was related to later impairment in ambulation. Only 39% (5/13) of these patients were later able to walk, whereas 59% (17/29) of those patients who were confined to bed during the acute period of illness without ventilator assistance were able to walk. A higher level of sensory impairment or MRI-identified lesion was not related to later walking with or without mechanical aids. Ambulation of 30 ft or more was reported in 66% (6/9) of patients with a cervical sensory level and 42% (8/19) with a thoracic sensory level. This level of ambulation was

(A) Ambulation ability (Hughes Functional Disability Scale) acutely and at follow-up. (B) Bladder management acutely and at follow-up

Figure 2 Ambulation ability and bladder management acutely and at follow-up



achieved by 44% (4/9) of patients with a cervical lesion identified on MRI and 58% (7/12) with a lesion on MRI rostrally extending to the thoracic spinal cord. Overall, 36% (17/47) of the patients were able to walk 30 ft independently, and an additional 21% (10/47) required a walker or other form of support to walk more than 30 ft (figure 2).

Functional outcomes. The WeeFIM was used for patients under age 18 and the FIM for those older than 18 at follow-up. The distribution of patients in the categories of independence, modified dependence, and complete dependence according to their performance in the skill areas of self-care, sphincter control, transfer ability, locomotion, communication, and social cognition is reported in table 1.

At follow-up, the majority of patients had independence in all skill areas with the exception of sphincter control. Locomotion, defined as the ability to walk or use a manual wheelchair for at least 150 ft, was eventually achieved by 67% (22/33). Modified dependence was reported in 30% (10/33) for sphincter control and locomotion, 18% (6/33) for transfers, and 12% (4/33) for self-care. Twenty-four percent (8/33) of patients reported that they were completely dependent for sphincter control. This degree of dependence was reported by 18% (6/33) of patients for performing transfers, 15% (5/33) for self-care activities, and 3% (1/33) for locomotion.

There was no significant relationship between season of the year, preceding trauma, preceding immunization, time to nadir, or protein in lumbar puncture to any measure of functional outcome at follow-up.

Normal WBC count in the CSF was associated with a trend for better outcome on the mobility domain in the combined WeeFIM/FIM analysis (mobility FQ 84 vs 64, $p = 0.069$). A greater number of WBC in CSF predicted worse functional mobility outcome ($R^2 = 0.18$, $p < 0.05$).

Age at onset under age 3 was associated with worse outcome at follow-up in the ADL domain (FQ older age = 91, FQ younger age = 74; $p < 0.05$) and the bowel/bladder control domain (FQ older age = 75, FQ younger age = 50; $p < 0.01$) in the WeeFIM/FIM analysis. Across all ages, younger age at onset was associated with worse bowel/bladder control at follow-up ($R^2 = 0.165$, $p < 0.019$).

Diagnosis within 7 days of the onset of symptoms was associated with better functional outcome in ADL ($R^2 = 0.165$, $p < 0.05$) and continence ($R^2 = 0.134$, $p < 0.05$). Those patients diagnosed within 7 days had an average ADL FQ of 95 (i.e., 95% of typical for age) and an average continence FQ of 77, as opposed to children diagnosed more than 7 days after the onset of symptoms, who had an average ADL FQ of 76 and continence FQ of 57. Not surprisingly, a higher rostral border of the sensory level of spinal cord injury at the time of diagnosis was predictive of worse ADL outcome (FQ 93 vs 66; $R^2 = 0.225$, $p < 0.05$).

Table 1 WeeFIM and FIM summary

Skill Area	Independence, % (n)	Modified dependence, % (n)	Complete dependence, % (n)
Self-care	73 (24/33)	12 (4/33)	15 (5/33)
Sphincter control	46 (15/33)	30 (10/33)	24 (8/33)
Mobility (transfer)	64 (21/33)	18 (6/33)	18 (6/33)
Locomotion	67 (22/33)	30 (10/33)	3 (1/33)
Communication	93 (26/28)	7 (2/28)	—
Social cognition	93 (26/28)	7 (2/28)	—

Table 2 Comparison with four other pediatric series

Ref. no.	JHTMC	16	15	14	9
Year of publication	2007	2003	1998	1986	1953
No.	47	24	8	21	25
Collection period, y	2000-2004	1965-1995	1993-1996	1966-1983	1929-1952
Sex, M:F	1.04	0.85	1.66	0.9	0.5
Mean age, y	8.3 (0-17)	7 (0-19)	8.5 (2-15)	10 (0.6-14)	8 (0.5-15)
Age at onset <3 y, %	38	13	12.5	10	8
Acute phase cervical level, %	25	12	0	20	11
Acute phase thoracic level, %	53	85	50	75	60
Acute phase lumbar level, %	5	0	0	5	26
Acute phase sacral level, %	3	0	12.5	0	0
Acute phase level unclear, %	14	0	37.5	0	0
Acute sphincter dysfunction, %	85	95	75	85	95
Chronic bladder dysfunction, %	50	33	*	29	38
Deaths	2	1	0	0	1
Abnormal CSF findings, % (n)	71 (24/34)	62 (15/24)	50 (4/8)	91 (19/21)	60 (12/20)
Abnormal MRI findings, % (n)	94 (34/36)	66 (4/6)	50 (4/8)	ND	ND

*Insufficient or unavailable information.
JHTMC = Johns Hopkins Transverse Myelitis Center; ND = not done.

Similarly, lower level of the rostral border of the lesion on MRI was also associated with better outcome for both ADL and mobility. Children with thoracic or lower level lesions had an average ADL FQ of 89 and an average mobility FQ of 81 compared with children with higher lesions, who had an average ADL FQ of 62 and an average mobility FQ of 51 ($R^2 = 0.25$, $p < 0.05$). The extent of the MRI lesion at diagnosis (number of segments involved) was also predictive of outcome, with fewer involved segments being associated with better outcome for ADL and mobility ($R^2 = 0.17$, $p < 0.05$ and $R^2 = 0.26$, $p < 0.05$,). T1 hypointensity was associated with worse scores on the HFDS at follow-up (Mann–Whitney U $p < 0.05$) and a trend toward worse continence outcome (FQ 83 vs 54, $p = 0.057$).

Patient scores on the HFDS at nadir were correlated with functional outcome at follow-up across all three domains (ADL rho = 0.61, $p < 0.001$; continence rho = 0.57, $p < 0.01$; mobility rho = 0.72, $p < 0.001$).

Although length of time to follow-up was not statistically related to better outcomes, there was a trend for improvement in WeeFIM/FIM scores for mobility ($p = 0.052$) and ADL skills ($p = 0.063$).

Evaluation of treatment modalities did not show an advantage of one treatment method over another. The patients who did not receive treatment tended to have better functional outcomes for ADL (FQ 99 vs 77, $p < 0.05$) and mobility (FQ 88 vs 66, $p < 0.05$). They were the patients who had considerably longer follow-up times (277 vs 41 months, $p < 0.001$). Their average HFDS on presentation was 3.83 compared with 4.17 for the group that reported treatment, suggesting that this group was less severely impaired than the group that did receive therapy; however, this difference was not significant. One specific treatment, oral steroids, was associated with a better functional outcome in the area of mobility (FQ = 95 vs 55, $p < 0.001$).

DISCUSSION This largest reported single case series of patients with ATM concentrates upon individuals with diagnosis by newly established criteria, in a single academic referral center, over an interval of 4 years. Previous case series, including 8 to 25 cases each accrued at single centers over mostly longer intervals of 4 to 25 years (table 2),[9,14-16] were similar to the current series in age at presentation, initial symptoms, and initial course. Other features of these case series are more difficult to compare, owing to the nonspecific and descriptive nature of previously reported outcomes, as, for example, regarding sensory findings, MRI features, continence, or the amount of assistance required for ambulation.[15] This study is the first to use common validated measures of functional outcome.[11-13] Other factors limiting comparison include potential biases in ascertainment related to severity of presentation, length of time in which cases were collected, and the absence of modern diagnostic criteria requiring a surrogate marker of spinal inflammation.

An unexpected feature of this case series is an apparent bimodal age distribution at time of presentation. A substantial peak, comprising 38% of the total, was under age 3, in contrast to a combined 10% of those in all previous studies combined.[9,14-16] Whether this group represents a different form of ATM or a developmentally regulated vulnerability to otherwise typical ATM cannot be discerned from these data. This group of children, however, clearly has greater long-term disability as a consequence of their illness and requires further investigation.

The report of an immunization being given within 30 days of onset of ATM in 28% of our cases was initially viewed as surprising. However, the large fraction of younger children affected, the current recommended vaccination schedule for children, and the lack of any single vaccine association within this group all undermine a potential causal link between vaccination and ATM. In addition, no significant relationship between a preceding illness, immunization, or trauma and worse outcome was noted.

The rapidity of progression of symptoms did not predict a worse outcome. This suggests that deterioration in clinical status during the first 24 hours after presentation should not be used by itself as a negative prognostic factor. This is in contrast to the findings reported by other authors.[14,16]

We observed normal CSF WBC counts in 50% of cases. This is similar to findings reported in other case series of 38 and 52%.[14,16] Normal CSF WBC count in our series was associated with better outcome in mobility. The predictive value of this finding was not reported in other studies.[14,16]

Consistent with previous reports,[14,16,17] impaired bladder control is the most common long-term neurologic deficit following ATM. Recovery of motor function within 20 days of presentation has been associated with a more favorable prognosis for less severe urinary sequelae.[18] In our cohort, we found a strong correlation between Hughes scale at presentation and WeeFIM/FIM bowel and bladder control at follow-up.

The requirement for assistance with transfers (36%) or for self-care activities (27%) at follow-up is not reported in previous studies. Daily living skills remain compromised in many children, and rehabilitation needs are great. Long-term issues that may require attention include skin integrity, hygiene, nutrition, pain, arthritis, constipation, urinary incontinence, and spasticity.[3]

The persistence or occurrence of uncomfortable sensory phenomena suggests that management of ongoing pain is also an important part of the long-term management of children following ATM. Chronic sensory findings have been reported in 46% of children with ATM, but whether these reflect disquieting sensations or numbness is not discussed.[16] Early assessment and intervention of dysesthetic or painful symptoms may be necessary to prevent chronic pain in these children. Referral to a comprehensive pain management program would be appropriate depending on the severity of symptoms and the degree to which the child's life is interrupted.

Previously reported cases series in children have not characterized the MRI findings in pediatric ATM to the extent possible in this series. In another case series, MRI abnormalities in four and normal MRI findings in two of six cases are reported.[16] In that series, one child had multifocal lesions in the cervical region and conus medullaris and three had isolated thoracic level lesions. T1 signal abnormality was identified in two of these cases. Our data suggest that MRI lesions often extend over many segments in children rather than the more typical one to three segments in adults. Current MRI techniques appear to be quite sensitive in diagnosing ATM: Thirty-six of 38 cases meeting diagnostic criteria for ATM had abnormal MRI findings.

Features of the initial diagnostic MRI may be of assistance in predicting outcome in children. Our analysis suggested that the location and extent of T2 lesions on MRI were associated with functional skills at follow-up. Not surprisingly, lower thoracic level of involvement results in better performance on tasks that assess function of the upper extremities. MRI confirmed involvement of fewer segments was associated with better outcome in the areas of ADL and mobility. Why the effect of lesion size was not also apparent in the recovery of continence is unclear.

MRI features of T1 hypointensity at the time of diagnosis independently correlated with worse ambulation outcome. In MS, this finding in the brain is thought to indicate more serious axonal loss.[19] The importance of its presence in the spinal cord has not been defined. Although edema of the spinal cord is a potential alternative cause of T1 hypointensity, the observation that T1 hypointensity correlates with poorer prognosis suggests a more ominous pathology such as severe axonal loss and a poorer prognosis.

The effect of specific treatment modality on functional outcome is not clear. Our finding that treatment with IV steroids did not improve outcome contrasts with that of a previous study that reports an association between high-dose IV methylprednisolone treatment and an increased proportion of patients walking independently or achieving full recovery.[16] We found that treatment with oral steroids

was associated with a better outcome in the area of mobility, which contrasts with another previous study that found no improvement in outcome in their steroid-treated group.[14] Despite these conflicting findings regarding outcomes, steroids given either IV or orally remain the standard first-line intervention for treatment of acute inflammatory conditions including ATM. Better outcomes in the group that received no treatment are likely a reflection of the milder course of disease in these individuals and the decision to forego the use of steroids.

Shorter time to diagnosis was associated with better outcomes. This finding requires cautious interpretation because we do not know the relationship between early treatment and subsequent skills. Additional studies should be undertaken to address this issue.

The finding that longer time to follow-up was associated with better outcome for mobility and ADL skills suggests that some functional recovery occurs. This may be related to primary neurologic recovery or may be the result of rehabilitation. Additional longitudinal studies are needed to determine the trajectory of recovery in these patients and to delineate the factors accounting for the improvements.

This is a large cohort of children with ATM in which associations between preceding factors, diagnostic tests, clinical findings at follow-up, and functional skills at follow-up are reported. Limitations include the referral nature of the sample and the wide range of time to follow-up. These observations should be expanded through collaborative programs that involve multiple clinical centers using the recent strict diagnostic criteria. The effects of initial intervention on outcome and the effects of rehabilitation interventions on outcome are two important issues that require further study.

Received July 26, 2006. Accepted in final form February 1, 2007.

REFERENCES

1. Berman M, Feldman S, Alter M, et al. Acute transverse myelitis: incidence and etiologic considerations. Neurology 1981;31:966–971.
2. Jeffery DR, Mandler RN, Davis LE. Transverse myelitis. Retrospective analysis of 33 cases, with differentiation of cases associated with multiple sclerosis and parainfectious events. Arch Neurol 1993;50:532–535.
3. Kerr DA, Krishnan C, Pidcock F. Acute Transverse Myelitis. In: Singer HS, Kossoff EH, Hartman AL, Crawford TO, eds. Treatment of pediatric neurologic disorders. Boca Raton: Taylor and Francis, 2005:445–451.
4. Transverse Myelitis Consortium Working Group. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology 2002;59:499–505.
5. de Seze J, Stojkovic T, Breteau G, et al. Acute myelopathies: clinical, laboratory and outcome profiles in 79 cases. Brain 2001;124:1509–1521.
6. Altrocchi PH. Acute transverse myelopathy. Arch Neurol 1963;9:21–29.
7. Christensen PB, Wermuth L, Hinge HH, et al. Clinical course and long-term prognosis of acute transverse myelopathy. Acta Neurol Scand 1990;81:431–435.
8. Lipton HL, Teasdall RD. Acute transverse myelopathy in adults. A follow-up study. Arch Neurol 1973;28:252–257.
9. Paine RS, Byers RK. Transverse myelopathy in childhood. Am J Dis Child 1968;85:151–163.
10. Ropper AH, Poskanzer DC. The prognosis of acute and subacute transverse myelopathy based on early signs and symptoms. Ann Neurol 1978;4:51–59.
11. The Guillain–Barré Syndrome Study Group. Plasmapheresis and acute Guillain–Barré syndrome. Neurology 1985;35:1096–1104.
12. Uniform Data System for Medical Rehabilitation. The WeeFIM System clinical guide, version 5.01. Buffalo: UDSMR, 2000.
13. Uniform Data System for Medical Rehabilitation. The FIMware user guide and self-guided training manual, version 5.20. Buffalo: UDSMR, 1999.
14. Dunne K, Hopkins IJ, Shield LK. Acute transverse myelopathy in childhood. Dev Med Child Neurol 1986;28:198–204.
15. Knebusch M, Strassburg HM, Reiners K. Acute transverse myelitis in childhood: nine cases and review of the literature. Dev Med Child Neurol 1998;40:631–639.
16. Defresne P, Hollenberg H, Husson B, et al. Acute transverse myelitis in children: clinical course and prognostic factors. J Child Neurol 2003;18:401–406.
17. Ganesan V, Borzyskowski M. Characteristics and course of urinary tract dysfunction after acute transverse myelitis in. Dev Med Child Neurol 2001;43:473–475.
18. Leroy-Malherbe V, Sebire G, Hollenberg H, et al. Neurogenic bladder in children with acute transverse myelopathy. Arch Pediatric 1998;5:497–502.
19. van Waesberghe JH, Kamphorst W, De Groot CJ, et al. Axonal loss in multiple sclerosis lesions: magnetic resonance imaging insights into substrates of disability. Ann Neurol 1999;46:747–754.

Idiopathic transverse myelitis

Corticosteroids, plasma exchange, or cyclophosphamide

B.M. Greenberg, MD, MHS
K.P. Thomas, MD
C. Krishnan, MHS
A.I. Kaplin, MD, PhD
P.A. Calabresi, MD
D.A. Kerr, MD, PhD

Address correspondence and reprint requests to Dr. B.M. Greenberg, Department of Neurology, Johns Hopkins University School of Medicine 600 N. Wolfe St., Baltimore, MD 21287-5371
bgreenb7@jhmi.edu

ABSTRACT Transverse myelitis is a focal disorder of the spinal cord in which an immune-mediated process results in neural injury. In this large retrospective study, we compare patients who received one of four treatments to identify the most effective therapies. We identified subsets of patients who received clinical benefit from plasma exchange or cyclophosphamide being included in their treatment regimen. **NEUROLOGY 2007;68:1614–1617**

Transverse myelitis (TM) is a monofocal inflammatory disorder of the spinal cord in which an immune-mediated process results in neural injury. Fifty percent of patients experience loss of all movement in their legs, over 80% experience sensory changes, and almost all patients experience autonomic symptoms.[1]

Several small studies support the administration of corticosteroids in patients with TM, but other investigations have suggested they may not be effective.[2,3] The varied results are likely due to the fact that only a subset of patients with TM respond adequately from steroid therapy, whereas other patients require more aggressive therapies.[4] At the Johns Hopkins Transverse Myelitis Center, we routinely offer daily doses of IV methylprednisolone (MP; 1,000 mg) for 3 to 5 days unless there are compelling reasons to avoid this therapy.

Often, patients have TM with coexisting systemic rheumatologic disorders.[5] Although no controlled information currently exists regarding the use of other treatments, some clinicians consider pulse dose IV cyclophosphamide (CP) for these patients. In this article, we review the clinical and paraclinical features and outcome data of patients who met the recently established criteria for idiopathic TM (Transverse Myelitis Consortium Working Group).

From the Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD.
Supported by the Transverse Myelitis Association, Bruce and Deborah Downey, and the Katie Sandler TM Research Fund.
Disclosure: The authors report no conflicts of interest.

Table 1 Cohort characteristics

Characteristics	Treatment groups				Test of significant difference
	IV MP (n = 66)	PLEX (n = 32)	IV CP (n = 13)	PLEX + IV CP (n = 11)	
Mean ± SEM age at onset, y	43.9 ± 2.23	38.6 ± 3.4	41.62 ± 4.5	41 ± 5.5	NSS
Gender, % women	58	56.3	92.3	54.5	NSS
Recurrent TM, %	34.8*†	46.9*§	84.6%*‡	81.8†§	p = 0.001
Mean ± SEM time to nadir at attack, d	9.96 ± 1.44	5.7 ± 1.09	4.9 ± 1.4	9.9 ± 2.6	NSS
Mean ± SEM time to follow-up, mo	20.4 ± 2.23	16.06 ± 2.57	20.92 ± 4.0	10.4 ± 2.8	NSS
% (n) with systemic autoimmune disease	20.0 (13/66)*	12.5 (4/32)†	69.2 (9/13)*‡	0 (0/11)†§	p = 0.00
% (n) with multifocal lesions	9.4 (6/64)*	9.7 (3/31)†	38.5 (5/13)*‡	36.4 (4/11)†§	p = 0.009
% (n) with gadolinium enhancing lesions	85.5 (53/62)	71 (22/31)	76.9 (10/13)	100 (11/11)	NSS
Mean extent of lesion	5.4 ± 0.66	9.7 ± 1.17	8.5 ± 1.75	8.8 ± 1.88	p = 0.006
Level of signal abnormality (rostral border)	53% cervical 42% thoracic	69% cervical 31% thoracic	85% cervical 15% thoracic	64% cervical 36% thoracic	
% (n) patients with CSF pleocytosis	67.2 (41/61)	66.7 (20/30)	84.6 (11/13)	45.5 (5/11)	NSS
% (n) patients with elevated protein	66.7 (40/60)	60.7 (17/28)	100 (9/9)	80 (8/10)	NSS
% ASIA A at nadir	10.6*	34.3*	30.7	36.4	p < 0.02

*†‡§Used to compare treatment groups within a category. Values with matching symbols are the ones that achieve significance. For example, when comparing treatment groups in terms of percent with recurrent TM, there was a greater percentage of patients with recurrent TM in the third and fourth treatment group vs the first (*) and a greater percentage of patients with recurrent TM in the third and fourth group vs the second group (†), but there was no significant difference when comparing Groups 1 and 2.
MP = methylprednisolone; PLEX = plasma exchange; CP = cyclophosphamide; TM = transverse myelitis; ASIA = American Spinal Injury Association.

METHODS We collected information on the acute clinical and paraclinical features of patients who presented with idiopathic TM to the Johns Hopkins Transverse Myelitis Center between 2001 and 2005. Information was collected on demography, antecedent factors, description of the acute illness, serology, and functional status during acute attack. MRI and lumbar puncture results were also collected. All patients were followed for a minimum of 6 months.

We obtained institutional review board approval to examine the clinical records of these patients. Complete data for was available for 122 patients, and they are included in this analysis.

Outcome measures. Outcome was measured on an Expanded Disability Status Scale (EDSS). ΔEDSS scores were calculated as the difference between the acute and follow-up functional status. We also utilized the American Spinal Injury Association (ASIA) classification of myelopathy, which rates patients on an A, B, C, D, or E scale. In this rating scale, a normal patient is rated as ASIA E and a patient with complete loss of motor and sensory functions from a spinal cord injury is rated as ASIA A.

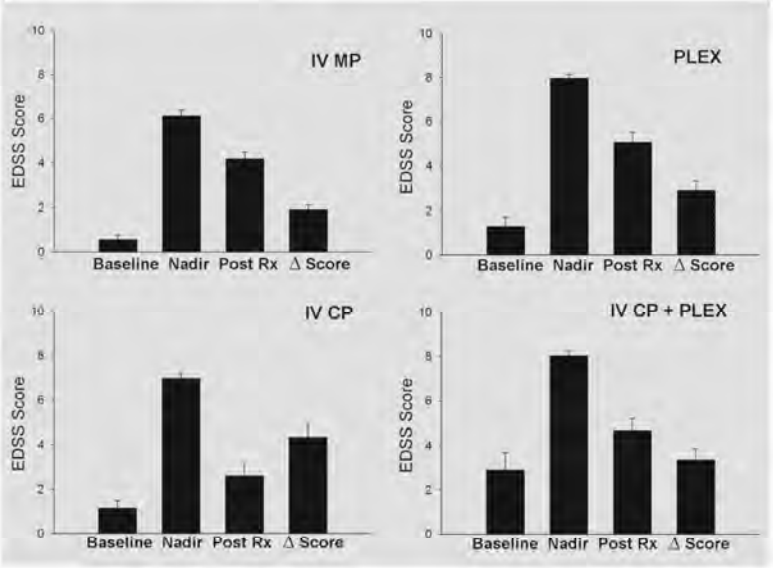
Statistical analysis. SPSS 12.0 was used for the statistical analyses. χ^2 tests were used to analyze the differences between groups for nominal variables. Group differences were analyzed using the Kruskal–Wallis test for continuous variables. Differences between two independent samples were analyzed using the Mann–Whitney *U* test. Significance was assessed at the 0.05 level.

RESULTS All 122 patients met the recently established criteria for the diagnosis of idiopathic TM and received 3 to 5 days of IV MP. Sixty-six patients received no other therapy, 32 patients additionally received five exchanges of 1.1 plasma volumes every other day (PLEX), 13 patients additionally received IV CP (750 to 1,000 mg/m^2), and 11 patients additionally received IV CP and PLEX.

The four treatment groups were similar in terms of various demographic and clinical features (table 1). In the IV CP group, there were more women, more patients with systemic autoimmune disease (systemic lupus erythematosus, Sjogren syndrome, type I diabetes, Hashimoto thyroiditis, Grave disease, mixed connective tissue disorders, etc.), more patients with recurrent TM, and more patients with multifocal lesions. There were no significant differences in average CSF white blood cell count or average protein levels among treatment groups (table 1).

Patients in the IV MP group had a nadir EDSS of

Figure Measure of treatment effects



Disability measured as EDSS at baseline, nadir, post-treatment, and change in EDSS score for patients treated with IV steroids alone, PLEX, IV CP, and PLEX + IV CP. EDSS = Expanded Disability Status Scale; MP = methylprednisolone; PLEX = plasma exchange; CP = cyclophosphamide.

Table 2 Outcomes based on ASIA scores at nadir

	ΔEDSS	
Treatment groups	ASIA A (acute)	Non ASIA A (acute)
IV MP (n = 66)	0.3 ± 0.2	2.1 ± 0.2*
PLEX (n = 32)	0.5 ± 0.2	4.1 ± 0.4*
IV CP (n = 13)	3.0 ± 1.3	4.9 ± 0.5
PLEX + IV CP (n = 11)	4.4 ± 0.7	2.8 ± 0.6

*Achieves significance ($p < 0.001$) when comparing ASIA A and non-ASIA A patients.
ASIA = American Spinal Injury Association; EDSS = Expanded Disability Status Scale; MP = methylprednisolone; PLEX = plasma exchange; CP = cyclophosphamide.

6.1 ± 0.5, and only 10.6% of the patients were classified as ASIA A. At follow-up, the mean EDSS of this group was 4.2 ± 0.3 (ΔEDSS 1.9 ± 2.1). Patients in the PLEX group were more likely to be ASIA A at nadir and had a higher nadir EDSS (7.9 ± 0.3). ΔEDSS was 2.9 ± 0.4 in the PLEX therapy group. Patients in the IV CP group had nadir disability similar to the IV MP patients, but recovered more function as reflected in their lower posttreatment EDSS (2.6 ± 0.61; $p < 0.05$) and higher ΔEDSS (4.4 ± 0.6; $p < 0.05$). Patients in the combination IV MP, PLEX, and IV CP group had the highest baseline EDSS (2.9 ± 1.7), the highest nadir EDSS (8.0 ± 0.5; $p < 0.05$ vs the IV MP group), and the highest percentage of patients who were ASIA A (36.4%; $p < 0.05$ vs the IV MP group). Despite this, these patients recovered to an EDSS of 4.7 ± 0.5, which was virtually identical to the outcome of the less severe IV MP patients (figure).

We found little evidence of recovery in the ASIA A patients treated with either IV MP (ΔEDSS 0.3 ± 0.2) or PLEX (ΔEDSS 0.5 ± 0.2) (table 2). However, there was significant improvement in the ASIA A patients treated with IV CP (ΔEDSS 3.0 ± 1.3) or IV CP/PLEX (ΔEDSS 4.4 ± 0.7). Of the non-ASIA A patients, there was a benefit from PLEX compared to IV MP (ΔEDSS 4.1 ± 0.4 vs 2.1 ± 0.2; $p < 0.001$). In this cohort of non-ASIA A patients, the addition of IV CP to PLEX therapy did not have an additive benefit. The ΔEDSS for the patients receiving IV MP, PLEX, and IV CP was 2.8 ± 0.03 vs 4.1 ± 0.4 in the patients receiving IV MP combined only with PLEX (table 2).

Of the 13 patients who transitioned from IV steroids to IV CP, 70% had evidence of an autoimmune condition. This subset of the IV CP group had a significant response to this regimen with a ΔEDSS of 4.4 ± 0.5.

DISCUSSION Our retrospective review has generated the following conclusions: 1) In our patients with TM who do not have an ASIA A level of disability at nadir or a history of autoimmune disease, PLEX provided benefit beyond steroids, but IV CP did not; 2) in patients who are ASIA A at presentation, PLEX alone is not helpful, whereas a combination of IV CP with PLEX showed benefit.

We recognize, however, that these should be viewed as only provisional conclusions because the data reflect uncontrolled, retrospective analysis. The distinct differences among the treatment groups (percentage with recurrent disease and percentage with autoimmune conditions) highlight the inherent biases that were a part of treatment strategies in this cohort. Nonetheless, this review suggests that ASIA A patients receive significant benefit from medical regimens that include CP. If a patient's disability did not reach a level of ASIA A, the addition of IV CP to their regimen was not of significant benefit, whereas the group of patients receiving combination PLEX and IV MP did better than the group receiving IV MP alone.

Received May 17, 2006. Accepted in final form February 27, 2007.

REFERENCES

1. Transverse Myelitis Consortium Working Group. Proposed diagnostic criteria and nosology of acute transverse myelitis. Neurology 2002;59:499–505.
2. Trevisani V, Castro A, Neves NJ, Atallah A. Cyclophosphamide versus methylprednisolone for treating neuropsychiatric involvement in systemic lupus erythematosus. Cochrane Database Syst Rev 2006;(2):CD002265.

3. Barile-Fabris L, Ariza-Andraca R, Olguin-Ortega L, et al. Controlled clinical trial of IV cyclophosphamide versus IV methylprednisolone in severe neurological manifestations in systemic lupus erythematosus. Ann Rheum Dis 2005;64:620–625.
4. Weinshenker BG, O'Brien PC, Petterson TM, et al. A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease. Ann Neurol 1999;46:878–886.
5. Kovacs B, Lafferty TL, Brent LH, DeHoratius RJ. Transverse myelopathy in systemic lupus erythematosus: an analysis of 14 cases and review of the literature. Ann Rheum Dis 2000;59:120–124.

Myelitis and Rheumatological Syndromes: Diagnostic Challenges and the Need for Research

Julius Birnbaum, MD
Johns Hopkins Clinic for Neurological Rheumatic Disease

I. Introduction

Although myelitis can occur in the context of isolated neurologic syndromes (i.e., multiple sclerosis, Devic's syndrome), it is less appreciated that myelitis can emerge in the context of rheumatologic diseases. Systemic rheumatic syndromes - lupus, Sjogren's syndrome, scleroderma - are diseases characterized by deleterious inflammation directed against **any** organ. Therefore, a crucial diagnostic challenge in the evaluation of myelitis is the elucidation of symptoms suggestive of systemic rheumatic syndromes. When rheumatic disease goes undetected, flares or progression of myelitis can worsen, and ongoing inflammation can damage other organs. A central theme of this article is that myelitis patients who are not adequately and comprehensively screened for rheumatological syndromes are being incompletely evaluated, especially as rheumatic disease is a risk factor for new flares of myelitis.

Unfortunately, neurologists lack the specialized training to detect subtler manifestations of rheumatic disease. In July, 2007, under the aegis of the Johns Hopkins Transverse Myelitis Center, I will be starting a unique Clinic wholly dedicated to evaluating myelitis or other neurological syndromes in the context of rheumatic disease. I have completed full Residency training in Neurology, and am currently completing a Rheumatology Fellowship. Below, I discuss why my dual training in Neurology and Rheumatology has afforded me a unique diagnostic and prognostic perch to optimize care of patients with neurologic rheumatic disease.

For purposes of this article, myelitis refers to an inflammatory syndrome affecting the spinal cord, causing weakness, pain, and/or bowel or bladder difficulties. Within the past years, the term "myelitis" has been further subcategorized by the longitudinal extent of spinal cord inflammation. Specifically, "transverse" myelitis refers to inflammation limited to less than 3 vertebral segments on MRI (the vertebral segments are bones encasing the spinal cord); in contrast, "longitudinal" myelitis (or "longitudinal extensive myelitis") refers to inflammation spanning 3 or more vertebral segments. The term "mylelitis" will be used to encompass both diagnostic entities of "transverse," as well as "longitudinal" myelitis. Both "transverse" and "longitudinal" myelitis can occur in the context of rheumatic disease. An ongoing research interest is whether for patients with rheumatic disease, the pattern of "longitudinal" versus "transverse" myelitis has important mechanistic or prognostic differences. A paradigmatic approach to both types of myelitis occurring in the context of rheumatic disease is discussed below.

II. The diagnosis of rheumatic disease -- the premium of a patient-physician dialogue

As indicated above, most neurologists are familiar with the diagnostic criteria of multiple sclerosis (MS) and Devic's syndrome. These criteria emphasize that myelitis or other neurological syndromes are consistent with MS **only if there is no better diagnostic explanation**. One of the ironies and weaknesses of updated diagnostic criteria of MS is that it does not elaborate on the specific steps needed for the evaluation of alternative diagnostic explanations. In the context of this diagnostic vacuum, neurologists who are not trained in the evaluation of rheumatic disease can improperly screen patients for rheumatic disease. For example, neurologists may perform blood tests checking for ANA antibodies, which are antibodies which can be seen in lupus disease. However, these antibodies can also be seen in the general, unaffected population. Therefore, there is no specific blood test which can irreducibly establish a diagnosis of rheumatic disease. Ultimately, the diagnosis of any rheumatic syndrome tilts on the interpretation of blood tests in the context of a careful history and physical examination. This premium on patient-physician dialogue is one of the pleasures of Rheumatology. However, when blood tests are divorced from such a dialogue, then potential treatment or diagnostic workup can be misappropriated.

At this unique Clinic, my training in Rheumatology will enable me to elicit timely and crucial symptoms which might point towards a systemic auto-

immune disease.

III. Example of a "rheumatological review-of-symptoms"

In medical parlance, a "review-of-symptoms" refers to an exhaustive list of diagnostic questions poised to detect and weave seemingly discrepant symptoms into a diagnostic story. A neurologist's review of symptoms will include questions relating to decreased vision, clumsiness, confusion or cognitive impairment, motor or sensory symptoms. However, all patients with myelitis or other neurologic syndromes similarly require and deserve a *rheumatologist's review of symptoms*.

Lupus poses a formidable diagnostic challenge, as it can affect the skin, heart, lungs, kidneys, as well as the neurologic system. When I screen patients for the presence of lupus, I need to consider the potential involvement of all of these organs. This leads to an exhaustive list of questions not usually encountered in the neurologist's review of symptoms: Has there been any joint pains/joint swelling/joint warmth? Any morning stiffness? Any episodes of fingers or toes turning blue in cold weather? Any hair loss? Any rashes? Any oral or genital ulcers? Any history of shortness of breath, any pain on deep inspiration? Any history of dry eyes or dry mouth? Any problem swallowing? Any worsening of rashes or fatigue on exposure to sunlight? Any burning in the fingertip or toes?

Frequently, patients can be initially overwhelmed by the number of questions. What can difficulties with swallowing have to do with sudden paralysis and incontinence? They often demur that prior neurologist evaluations have never led to this cavalcade of questions. A critical goal is to explain the hidden unrelatedness of these questions; part of the elusiveness and complexity of any rheumatic disease is that the pathophysiologic process is as seemingly arbitrary and undiscriminating as the breadth of the rheumatologist's review of systems. *Because any organ can be attacked in rheumatic disease, questions need to comprehensively delve into the most subtle symptoms suggestive of systemic inflammation.* Without such information, any "screening" tests which are commonly performed by neurologists are incomplete. In a sense, this is the redemptive aspect of the rheumatologist's review of systems - the narrative of the patient remains the most important part of the diagnostic process. By the time I have completed a rheumatological review-of-systems, the likelihood of underlying rheumatic disease has crystallized, and awaits confirmation or repudiation by the physical examination.

IV. Example of the rheumatologist's physical examination

Any myelitis patient is familiar with the rhythm and detail of the neurologic examination. However, the rheumatological examination has a similarly meticulous sensitivity for subtle findings. Sjogren's syndrome is characterized by inflammation of the glands causing salivary production in the mouth. I therefore spend time looking under the tongue, looking for any deficiencies of salivary production. I palpate the cheeks, feeling for any swelling or nodularity of the salivary glands. All of the rheumatic disorders can cause inflammation of the smallest blood vessels. Such capillaries are clustered around the nail beds, and I often spend minutes looking at nails, looking for any corkscrewing, twisting, or other abnormalities of nail bed blood vessels. The scalp is examined for patchy hair loss. The joints are maneuvered, palpated, ranged, felt for heat, examined for structural deformities. The edge of finger tips are examined for ulcers, pitting, or loss of digital pulp, skeletal signs that can signify scarring.

V. Formulation of the diagnostic impression

Recently, I encountered a patient with myelitis, who for years had been complaining of being thirsty. Her neurologists, aware that the impaired salivary production in Sjogren's syndrome can produce symptoms of thirst, had considered this diagnosis, but improperly terminated diagnostic investigation on the basis of blood work. When I examined her, her lips were chapped, there were no saliva bubbles under the tongue. A small biopsy of the lip confirmed the diagnosis of Sjogren's syndrome, and she was started on appropriate therapy.

By the conclusion of the history and physical examination, I might have a reasonable suspicion about whether myelitis or other neurological syndromes are manifested in the context of rheumatic disease. I might then order specific blood tests to further corroborate or repudiate my diagnostic impression. A key point worth emphasizing is that such blood tests *only serve to enhance or blunt my clinical diagnostic impression, but never subvert the saliency of the history or physical examination*. In effect, **there are no blood tests for lupus, Sjogren's syndrome, or other autoimmune disease**. Any rheumatologic disease, like multiple sclerosis or Devic's syndrome, is a clinical diagnosis, imbued by the hierarchy and impact of a patient's symptoms. Therefore, any myelitis patient who undergoes blood screening tests as an exclusive diagnostic step for rheumatic disease is being shortchanged, as each symptom needs to be chronicled and rigorously investigated.

VI. The prognosis and therapeutic implications of detecting underlying rheumatic disease

When should a patient with myelitis be

concerned for underlying rheumatic disease? Here is my simple answer: Every single time. Any new diagnosis of myelitis deserves a thorough clinical and physical examination for detecting underlying rheumatic disease. Any new flare of myelitis, or any example of myelitis becoming intractable or less responsive to previous adequate therapy also deserves a more intensive evaluation for underlying rheumatic disease. Diagnoses of multiple sclerosis are unsatisfactory and invalidated in the absence of considering alternative rheumatological explanations. As illustrated above, the most seemingly mundane and seemingly incidental symptoms are often crucial in elucidating subtle symptoms of systemic inflammation.

Detection of underlying rheumatic disease is important, especially as recent work has illustrated that syndromes, such as lupus and Sjogren's syndrome are risk factors for underlying rheumatic disease. Although distinguishing myelitis occurring in demyelinating disease (i.e., multiple sclerosis, Devic's syndrome) from rheumatological syndromes can pose a diagnostic challenge, this distinction is crucial. In some cases, the treatment for multiple sclerosis (i.e., the interferons) may cause relapse of underlying rheumatic disease. Additionally, the treatment for the myelitis of rheumatic disease are immunosuppressant drugs, such as Cyclosphosphamide, Methotrexate, and Imuran, which are not usually the first-line agents for multiple sclerosis.

VII. Whom should be evaluated at the Neurological Clinic for Rheumatic Disease

In my experience, patients with potential neurological rheumatic disease are fatigued by the process of being separately evaluated by individual Neurologists and Rheumatologists. Inevitably, each specialist approaches symptoms by a restricted diagnostic lens. For the patient, this leads to the confusing and apprehensive process of reciting similar symptoms, and receiving discrepant or even conflicting interpretations. By bridging the gap between the disciplines of Neurology and Rheumatology, the convenience offered by a cross-disciplinary evaluation in a single diagnostic center will hopefully alleviate patient concerns. We anticipate evaluating the following group of patients:

(1) Patients with a diagnosis of multiple sclerosis, but who have symptoms or signs of rheumatological disease.
(2) Patients with relapsing myelitis, or a history of Devic's syndrome, since these syndromes have a higher risk of underlying rheumatological disease.
(3) Patients with possible "antiphospholipid antibody syndrome." This is a syndrome characterized by clots in the arteries or veins, and is associated with specific antibodies on blood tests. Antiphospholipid antibody syndrome can be associated with all rheumatic diseases, and can sometimes occur independently.

In the next TMA Newsletter, I will elaborate on proposed research studies which will be conducted based on the clinical experience of the Johns Hopkins Clinic for Neurological Rheumatic Disease.

In summary, I want to emphasize that my goal is to continue interacting with patients and Neurology/ Rheumatology Colleagues. As such, I welcome any inquiries or questions. Please do not hesitate to contact me by email at jbirnba2@jhmi.edu for any clinical or personal concerns.

Curbside.MD: Searching for Information about the Neuroimmunologic Disorders

It is my pleasure to bring to your attention an extremely promising search engine for those determined to find the most relevant, complete and up-to-date information on Transverse Myelitis and the other rare neuroimmunologic disorders. For years, it has been difficult to find state-of-the-art medical information on these disorders. Even experienced neurologists may not have the case experience to accurately diagnose and treat rare disorders like transverse myelitis, neuromyelitis optica and acute disseminated encephalomyelitis. The challenge, particularly for physicians, is to find the right medical information, at the right time, within the right patient context.

For the past several months, this unmet need has been tackled by The Transverse Myelitis Association in a unique partnership with Praxeon, a Boston-based healthcare startup. This month we announce the debut of Curbside.MD **(**www.curbside.md), the first medical search engine devoted exclusively to neurologic disease. "Curbside" refers to the medical practice of the *curbside consult* where physicians informally ask each other for advice on clinical questions. Praxeon set out to replicate that model online, enabling medical professionals to pose naturally phrased queries to real clinical questions, and to get an answer from the best of evidence-based medicine. Curbside.MD achieves this goal. Medical experts can get evidence-based answers to real, naturally phrased medical questions. Curbside.MD utilizes a unique semantic fingerprinting technology to enable search around complete sentences and even paragraphs of medical information. Users are guaranteed accurate and relevant results from only the best evidence-based information available.

And best of all, this is a free site open to everyone.

Curbside.MD represents a fundamental innovation within medical search and health informatics and embodies a number of unique features not found within other search engines that enables rapid identification of the right clinical answer. The core technology is an underlying model embedded within the language of medicine. This enables the search engine to specifically understand medical terms and their abbreviations, synonyms and hierarchical relationships. Results are organized intuitively into two major categories: ***Quick Consult*** with broad overviews for the novice; and ***Best Evidence*** with in-depth focus for experts. Users may also delve deeper into the literature with analytical tools that extract disease and drug terms for rapid sorting by utilizing the ***Specialize*** option. In addition, Curbside.MD provides medical images, video, and radiographic scans relevant to the questions asked.

In the coming months, Praxeon plans to supplement Curbside.MD with a physicians' forum. In the Curbside forums, doctors and patients will be able to consult on difficult cases, while simultaneously reviewing medical evidence – relevant to their conversation – in real time. This will represent a tremendous advance in information seeking for physicians treating all neurological disorders, including the rarest ones. They will have the opportunity to share their anecdotes, experiences and insights with treatment – within an evidence based context. For more details on the forum and other updates to the site, or to post your own comments, check out the curbside blog at http://blog.curbside.md.

Curbside is considered the best neurological search engine on the web. And unlike subscription-based medical search engines, Curbside.MD is a free site open to everyone.

Go to www.curbside.md and just type a question in the search box. And don't limit yourself to keywords; challenge Curbside.MD with a complete thought or question, even a paragraph of something you're interested in. We think you'll be impressed with the results and the potential for this new website. Here are some sample questions to start you off:

"Is the neuromyelitis optica IgG status of acute partial transverse myelitis predictive of longitudinally extensive transverse myelitis?" http://www.curbside.md/focus/211

"What is the diagnostic workup required to distinguish a spinal epidural abscess from transverse myelitis?" http://www.curbside.md/curbside/entry_page/758

Go ahead and give Curbside.MD a try. Curbside.MD is encouraging you to provide them with feedback during your search experience so that they can continue to enhance the effectiveness of this unique search tool. You can also find the Curbside.MD search tool on the main page of the TMA web site.

Recruiting for ACP Study: Help us to Find the Causes and Cures for TM, ADEM, NMO, MS, ON and the other Neuroimmunologic Disorders
Jana Goins

The Johns Hopkins University is working in conjunction with the Accelerated Cure Project for Multiple Sclerosis (ACP) to conduct a large-scale research study which will play an important role in determining significant causal factors and disease trends for demyelinating disorders, such as Multiple Sclerosis (MS), Transverse Myelitis (TM), Optic Neuritis (ON), Devic's Syndrome (NMO), Acute Disseminated Encephalomyelitis (ADEM) and other related diseases.

Several major academic centers located throughout the country will serve as coordinating project sites, creating a national network of collection sites. Study enrollment is targeted at 10,000 subjects over ten years. Enrolled subjects will be asked to contribute personal data (such as medical history and family information) and biological samples. The personal data collected from all subjects will be combined into a single database, while the biological samples will be processed at a central laboratory and stored. The complete anonymity of study participants will be protected. The result will be the creation of a comprehensive information system and specimen repository from which researchers can request samples to conduct in-depth analyses on various disease aspects. This study will play an important role in increasing the current knowledge of demyelinating diseases and therefore aid researchers in the development of better diagnostic techniques and cures for these diseases.

We are enrolling patients with multiple sclerosis, transverse myelitis, optic neuritis, acute disseminated encephalomyelitis, neuromyelitis optica (Devic's) or clinically isolated syndromes (one demyelinating attack, but not fulfilling the diagnostic criteria for MS). Those who are currently patients at Johns Hopkins will be able to join the study without a referral from their physician, and will just need to contact the Johns Hopkins project coordinator for study enrollment information. Johns Hopkins patients who are aware of their next scheduled clinic date may get in touch with the project coordinator *beforehand* in order to schedule a

study meeting during this clinic visit. Subjects participating at Johns Hopkins will be offered a $25 check to compensate for lunch and parking on the day of the visit, but will not be reimbursed for any travel expenses. At this time, patients receiving care outside of Johns Hopkins may be subject to additional enrollment requirements.

Please note, the enrollment requirements and participant compensation may vary by study site. If you are interested in getting involved, please contact your nearest participating center for further information regarding the enrollment process.

In addition to enrolling subjects with one of the specified demyelinating diseases, we are asking participants to refer affected and unaffected relatives as well as unaffected matched "controls" (such as a childhood friend who grew up in the same area as you or a spouse) for participation in the study.

ACP has recently obtained approval to enroll pediatric cases into the repository. If your child has one of the neuroimmunologic disorders identified above, please consider having them participate in this important study. The following centers are currently able to accept pediatric enrollment in ACP: Johns Hopkins School of Medicine, Multiple Sclerosis Research Center of New York, University of Massachusetts Medical School Multiple Sclerosis Center, University of Texas Southwestern and Barrow Neurological Institute.

This is a very exciting opportunity for both patients and researchers around the country to take part in a large-scale dynamic project that will work to improve our knowledge about demyelinating diseases. By volunteering your time and effort to this project, you will be making a significant contribution to the development of new treatments, and ultimately a cure, for these diseases.

Participating Centers

Johns Hopkins Medical Institution (Baltimore, MD)
Jana Goins
acp-study-hopkins@acceleratedcure.org
(410)502-6160

UMass Memorial (Worcester, MA)
Janice Weaver
acp-study-umass@acceleratedcure.org
(508)793-6562

Shepherd Center (Atlanta, GA)
Elizabeth Iski
acp-study-shepherd@acceleratedcure.org
(404)350-3116

University of Texas Southwestern (Dallas, TX)
Gina Remington
acp-study-utsw@acceleratedcure.org
(214)645-0560

Multiple Sclerosis Research Center of New York (New York, NY)
Lauren Puccio
acp-study-msrcny@acceleratedcure.org
(212)265-8070

Barrow Neurological Institute (Phoenix, AZ)
Breanna Bullock
acp-study-barrow@acceleratedcure.org
(602)406-3109

Study Sponsor

Accelerated Cure Project
Sara Loud, Repository Director
300 Fifth Avenue
Waltham, MA 02451
acp-study-director@acceleratedcure.org
(781)487-0032
www.acceleratedcure.org

Neuroimmunologic Disorders Sample Repository:
http://www.acceleratedcure.org/curemap/tissuebank.php

Support Groups

Sharecare4u Ghana

The Ghana Support Group for Rare Neuroimmunologic Diseases

I started thinking about a support group for people in a similar condition to mine one year after I fell ill. It's taken ten years, however, to see the beginnings of this dream, because of relapses and general weakness.

My name is Nana Yaa Agyeman and I'm from Ghana in West Africa. I am a 46 year old woman and was diagnosed with acute demyelination of the cervical cord in 1996, which was at various stages thought to be Guillain Barre Syndrome, Neuro-schistosomiasis, Multiple Sclerosis and Devic's Disease (Neuromyelitis Optica).

Over the ten year period, I have gone through symptoms of paralysis with ventilator support; I have been in a wheelchair; I have had relapses and partial blindness; and I have made a recovery of sorts. I'm now able to walk unaided indoors and with an aid outdoors. My eyesight has improved. My eyes still cloud over in hot weather, which means every afternoon since Ghana is in the tropics. My full story can be found at the sharecare4u website, which is a platform for all people with long-term illnesses to share their experiences and treatment options.

We only got an MRI scanner in Ghana last year, and after having the scan, the impression was Multiple Sclerosis, but my neurologist said it could be Devic's Disease. The diagnostic test to confirm this is not available in Ghana. From 2003 (when the only practicing neurologist returned to Ghana from specializing), 1,800 people have been diagnosed with MS and other demyelinating diseases. I discussed this and

the absence of the test for NMO with a web pal and have her permission to quote her reply to me:

I was thinking about the MS statistics. For example, it is more common in women then in men; it usually occurs in the 20-40 age group; it is more common in the white race than in the black race, and rare in the Asian race. It is more common in thin framed people. It is less common in tropical areas, and more common in cold climate areas. I have also heard of people being diagnosed in their 50's who have never had symptoms before. With Devic's I hear that it is more common in Asians and in the tropical areas. After going over all of this in my head (must be the scientist in me), I can see why research is needed on this. Many MS patients may really have Devic's. The test needs to be offered everywhere so that all MS patients can be tested to rule out Devic's.

Sharecare4u Ghana, the Ghana support group of The Transverse Myelitis Association, which is still in the formative stages, aims to create awareness about the existence of these neuroimmunologic disorders. They have only recently been found in this country giving rise to speculation about the causes, such as imported foods and additives, pesticides, chemicals in the water and environmental factors. The support group will advocate for research into these diseases and raise funds for this research.

We will also act as an advocacy group to put pressure on local and national health authorities to treat neuroimmunologic diseases with the seriousness deserved in the national health care delivery system.

One of our major aims is to join other disability groups to push for the implementation of the Disability Act of Ghana. The Act was passed in August last year, but we are yet to see any changes. It establishes a National Council on Persons with Disability, to coordinate groups such as ours. This has not yet been set up. The Act gives owners of public buildings ten years within which to make their buildings accessible to disabled people. The time frame given them could certainly be debated.

The immediate task is getting people to join the group. The neurologist who is the patron of the support group has been linking me with other patients with rare neuroimmunologic diseases that are interested in a support group. I have been paying home visits to them to share the various stages we have gone through and why we should get this group going. We are also preparing flyers so that others can contact us.

The Ghana support group would appreciate tips from established support groups. You can be sure that I will constantly learn from other groups, especially with regard to fundraising. Please feel free to get in touch with me.

Nana Yaa Agyeman
P.O. Box CT4910
Cantonments
Accra
Ghana
Tel: 233-21 220084
Cell: 233-20 815 7404
Email: sharecare4u@gmail.com
Website: www.sharecare4u.com

The ADEM Support Group

I'm a writer and former journalist. I ordinarily describe myself more by my professional accomplishments than my personal ones. That is why this communication is unusual for me. My personal perspective changed when my health did in June 2006. I lost my ability to use a computer keyboard, to tell time, to read or write, or even to draw stick figures beyond juvenile efforts. That I couldn't walk was the least of my deficits.

Ironically, I never lost my ability to spell; but I couldn't remember the birth dates of my grand kids. My sense of humor remained firmly intact; through three consecutive hospitalizations, multiple MRIs, and an unconfirmed diagnosis. The neurologist at the first hospital I went to discharged me in five days with a "brain condition" and without any medication. This was his primary diagnosis on my discharge summary. He was more interested in referring me to his sleep apnea clinic. My MRI showed that I had 13 brain lesions.

Other than a hospitalization due to a near-fatal car accident ten years ago, and for pneumonia before that, my health has been fairly uneventful, for which I am very thankful. How can one possibly imagine having this happen to them? I am interested in starting an ADEM support network. If you have ADEM or if you are a family member or caregiver, I hope that you will get involved. It is important that we find each other for the purpose of offering information and support. We also need to be there for those who will receive the ADEM diagnosis in the future. If you are interested in participating in this support network, please get in touch with me.

Barbara Kreisler
9476 Scarlet Oak Dr
Manassas, VA 20110
(Home) (703)753-4000
(Cell) (571)436-9034
bkreisler.imprint@verizon.net

The Optic Neuritis Support Group

My name is Kristin Lee. I am 32 years old and have been married for almost 11 years. I have been blessed with two beautiful kids who are now 9 and 10. I have had Optic Neuritis for more than four years. I cannot say that it all started with a dramatic episode that caused me to be rushed to the local hospital. It actually was quite by surprise that I even realized I was having problems.

I was at the local mall doing some shopping with my children. I had been having problems with my right contact lens; it seemed to have a tear or something stuck to it causing me to see a blind spot out of that eye. My optometrist's office is located in the mall, so I decided to stop in without an appointment to buy a replacement lens. My doctor insisted that she take a look at my eyes just to make sure that it was the contact lens causing the problem. After the examination, she said I needed to call someone to pick me up, because I should not be driving. She told me that my optic nerve was swelled and that I would need to have an MRI immediately. An MRI for what? I mean I just came in for a contact lens, right?

After some explaining that this was serious, my doctor told me that this was a sign of MS. Well, I felt lost, scarred, and confused. I had to keep it together; I had my kids with me. After getting more information on what was happening with my eye, the stress of the situation really started. I was told an MRI was imperative, but I had no health insurance at the time. We managed to pay cash for the first one and it was perfect; no lesions, no MS.

The doctors treated me with IV steroids at a hospital in the city. The treatment was worse than the vision problems. I had steroid induced psychosis. What a nightmare. On the second day of steroid treatment, I lost it in the hospital, removed my own IV, left the hospital, and began walking in this city with no idea of where I was or where I was going. I began having daily panic attacks and was unable to leave my bedroom for days. I lost 12 pounds. I had to start seeing a psychiatrist.

After about three months, the majority of my vision returned. Time had passed and all of the neurologists seemed to think it was just a fluke and would not happen again. Well, about 6 months later, I had a second attack on my right eye this time. It was the same drill; IV steroids again, but this time with nerve medicine to keep the anxiety in check. This cycle has continued for over 4 years, and I have had more attacks than I care to keep track of or count. I have severe bouts of fatigue and summers are long with the heat and humidity. We try to stay by the pool and avoid amusement parks, zoos or any outdoor activities during the hot months. My body does now seem to be more tolerant of the steroids. I also have a home health nurse who does the treatments at home, so it keeps things more normal for my family.

As far as other symptoms go, I also have complete heat intolerance. If I raise my core temperature, I loose my vision in my right eye completely. I often have a lot of fatigue. I get swelling in the joints of my hands and feet, as well as a burning sensation and I have severe and frequent migraines. To date, I have not received any other diagnosis other than Chronic Optic Neuritis. Sometimes I feel frustrated that no doctor, to this point, has been able to tell me why this is happening. The reality of losing a little more of my vision with each new attack sometimes seems overwhelming. Depression seems to go hand in hand with this condition for me. I have been battling ever since my first attack.

This is my journey. I have not been able to find anyone else with Optic Neuritis as their diagnosis. People with Optic Neuritis often have it in the context of MS or NMO. Finding The Transverse Myelitis Association has been great for me and hopefully I can find others who are experiencing similar circumstances. Having a good support system is the key to staying positive. I hope you will get involved in our Optic Neuritis Support Group. Please get in touch; we would love to hear from you.

Kristin Lee
115 Ridge Avenue
Beaver Falls PA 15010
(724)847-7999
kmarie1016@hotmail.com
www.onsupport.info

Jenn Nordin will be working with Kristin in the ON Support Group. We encourage you to get involved and to get in touch with both Kristin and Jenn.

Jenn Nordin
417 Yorktown Avenue #1
Huntington Beach, CA 92648
Cell: 714-231-1808
Jenn@jenndesigns.com

ADEM, NMO, ON, Recurrent TM, TM with Lupus, Sarcoidosis, Sjogren's and HIV: Finding Each Other to Share Information and Support

We are trying to assist people who have the very rare neuroimmunologic disorders find each other for the purpose of sharing information and support. We are creating the lists identified below for that purpose. If you have one of these disorders and would like to be added to the list and then receive a copy of the list, please send us your information. I only share these lists with people who are willing to be added to the lists.

1. Acute Disseminated Encephalomyelitis (ADEM);
2. Neuromyelitis Optica (NMO) or Devics disease;
3. Recurrent Transverse Myelitis;
4. Transverse Myelitis with SLE (Lupus).
5. Transverse Myelitis with Sarcoidosis;
6. Transverse Myelitis with Sjogren's syndrome
7. Transverse Myelitis or NMO with HIV; and
8. Optic Neuritis.

If you are interested in being added to one of these lists and then periodically receiving a copy of the list, you can send me your contact information either by email or through the postal service. Please send me your full name, complete postal address, phone number and email address (if you have one). Be sure you clearly identify to which list you would like to be added.

Sandy Siegel
1787 Sutter Parkway
Powell OH 43065-8806
USA
ssiegel@myelitis.org

UK TM Conference in London, Saturday 13th October 2007

Douglas A. Kerr, M.D., Ph.D., Director of the Johns Hopkins TM Center and Project RESTORE and member of The Transverse Myelitis Association Medical Advisory Board will be speaking at the first UK TM Conference on Saturday 13th October 2007. Other UK speakers will include a rehabilitation consultant who will present information about the management of TM symptoms. There are members who are already planning to attend from England, Scotland, Ireland, Germany and Australia. We hope that more of you will plan to come from across Europe. The capacity of the room is 150 people, so please make your plans as soon as possible. The Conference is FOC/gratis for members, except for a small charge (20 pounds / 30 Euros) to cover lunch and the venue. For more information and to sign up for the conference, please send an email to Lew Gray at: lewgray@blueyonder.co.uk. We are compiling questions that we will ask the speakers during the conference. If you have a question that you would like addressed by the speakers, please also send your issues or concerns to Lew Gray. We are looking forward to seeing you at this wonderful opportunity in London this October.

Transverse Myelitis Society

Southwest Symposium on Neuroimmunologic Disorders: Presentations posted on First Step Foundation and TMA Web Sites

The Cody Unser First Step Foundation, the New Mexico Governor's Commission on Disabilities and the University of New Mexico School of Medicine held the first Southwest Symposium on Neuroimmunologic Disorders, April 26-28, 2007 in Albuquerque, New Mexico. During the two and a half day symposium there were excellent presentations made on all of the neuroimmunologic disorders, the acute treatment approaches, rehabilitative therapies, the research into restorative therapies and the treatment options for the many difficult symptoms of these disorders. The presentations were videotaped in order to make this critical information available to people who were unable to attend the symposium. We urge you to watch these videos, as all of this information serves to help you become a more effective advocate for your medical care. You can view the videos at: www.myelitis.org/swnds2007 or http://cufsf.org/. The videos may be purchased by using the form included with this newsletter or by downloading the form from Cody's or the TMA Web Sites. The Transverse Myelitis Association and our membership are grateful to Cody and Shelley Unser and the First Step Foundation for working to organize an exceptional educational and support opportunity for people who have these disorders, their family members and the physicians who treat people with these disorders. We would also like to thank Dr. Leslie Morrison from the University of New Mexico for all of her efforts in putting together such an informative program agenda with outstanding speakers.

The summer family camp for kids with TM, ADEM, ON and NMO will be held from August 19 to August 24, 2007 at Victory Junction Gang Camp. The camp is for kids with these neuroimmunologic disorders who are 7 - 15 years old and their siblings and parents. The maximum capacity of the camp for our week is 32 families. We currently have about 30 families who have applied from around the world. If you have an interest in coming to camp in 2007, you will need to send in an application immediately.

There are two applications that you will need to fill out and submit to the camp:

http://www.victoryjunction.org/aa_apply/apply05_application.html

There is a medical section of the application that will need to be filled out by your doctor. Please send in your portion of the application as soon as you have it completed. Do not wait for the physician section; that portion can be sent in later. There could be cancellations, but at the present time, there may be only two openings available for the 2007 camp.

Your point of contact at Victory Junction Gang Camp regarding the application process is Kristin Wolbert. Kristin can be reached at: (336) 495-2002; her email address is kwolbert@victoryjunction.org.

Details about the application process, travel arrangements and the Victory Junction Gang Camp may be found on the VJGC web site and also in articles that have been published in previous newsletters and journals. Please refer to the TMA newsletter archives for this information.

If you are interested in coming to VJGC TMA family week, but are not able to do so in 2007, please get in touch with me (ssiegel@myelitis.org) and I will be sure to add you to our list for recruiting purposes. Victory Junction Gang Camp has committed to holding a TMA family camp every other year. Once you are added to our recruiting list, you will be contacted by the TMA as soon as the application process is initiated for the next camp.

The TMA Newsletter and Journal Archives

The TMA announced a new publication schedule and format for our newsletters and journals. A newsletter will be published each fall and spring, and a more extensive journal will be published in January of each year. When people sign up for membership in the TMA, they receive a packet of information which contains the most recently published TMA Journal. The newsletters are not included in the new membership packets.

We encourage people to read the previously published newsletters and journals. They are an excellent source of information about the neuroimmunologic disorders, both through articles written by medical professionals and by people with these disorders and their family members, which describe their personal experiences. Through these publications, you can also learn about research and clinical trials, the TMA, awareness and fundraising efforts, and the support groups around the country and around the world.

All of the newsletters and journals are archived on our web site; you can find them under the link ‘newsletters’ on the main page of our web site or you can type www.myelitis.org/newsletters/index.html into your web browser. You can view the newsletters and journals as they were published by selecting the PDF files from the column on the right, or you can view them in html format from the column on the left. The html files include an index which makes it very easy to find articles covering specific subjects. Additionally, Jim has installed a search engine for the entire TMA web site, which allows searching for specific subjects. Topics may be searched in the newsletters and journals by using the search engine.

If you have difficulty in finding information about any topic on our web site, and the search engine does not provide you with the results you were seeking, you should always feel free to contact Jim for assistance. You can send Jim a question or a request for help at jlubin@myelitis.org

Fundraising and Awareness

Helping to Fund the Work of Your TMA

The TMA does not charge membership fees. We operate exclusively on the basis of the generous and voluntary support of our members. There are numerous ways for everyone to help support the TMA, even if you are not in a position to make a financial contribution. Please consider getting involved in one of our fundraising efforts.

Donate your cell phones

You can donate your cell phones to help raise funds for The Transverse Myelitis Association. Go to http://cellphones.myelitis.org

Inkjet Recycling

The Transverse Myelitis Association has partnered with a recycling company to collect and recycle empty inkjet printer cartridges, and empty toner cartridges from laser printers and copiers. All you have to do is visit the TMA inkjet recycling page at: http://recycle.myelitis.org

Awareness Wristbands

You can show your support for The Transverse Myelitis Association and help raise awareness by ordering wristbands. To order using PayPal or by credit card, please log on to the web page at: http://www.myelitis.org/wristbands.htm You can also order the wristbands by sending an email to: wristbands@myelitis.org or call (951) 658-2689.

Reading for Rachel

If you are a teacher, a student or a parent of a student and would like to establish the Reading for Rachel Program in your school, everything you will need to get the program started can be found on the Reading for Rachel web site: http://www.readingforrachel.org. All funds received by The Transverse Myelitis Association for the Reading for Rachel Program are used exclusively for research to better understand TM, to find treatments for the symptoms of TM, and to ultimately find a cure. If you are interested in starting the Reading for Rachel program in your school, you can also contact Cathy Dorocak, Rachel's Mom and International Chair of the Reading for Rachel Program: cathy@readingforrachel.org; (440) 572-5574.

Online Shopping

There are numerous online shopping opportunities, as well as sales on eBay which can be made through the following link: http://www.myelitis.org/store.htm A percentage of the sales are donated to the TMA.

iGive.com

You can shop at more than 650 stores through iGive.com. You can find books, CDs, videos, software, office supplies, groceries, gifts, flowers, cookware, greeting cards and more at the iGive Mall and from top merchants like Barnes & Noble, Drugstore.com, Harry and David, Best Buy, Sharper Image and Dell.

Café Press

You can purchase TMA logo items through Café Press.

Amazon.com

You can shop at Amazon.com for Books, Music, DVDs, Videos, Toys and more.

eBay

Now you can sell an item on eBay and donate from 10% to 100% of the final sale price to help support the TMA.

Donations

We always welcome and are grateful for a donation to the TMA. You can download a donation form to include with your check from the link: www.myelitis.org/donation-form.htm Please make a check or money order payable to The Transverse Myelitis Association and mail it to:

The Transverse Myelitis Association
Paula Lazzeri, Treasurer
10105 167th PL NE
Redmond, WA 98052-3125

Thank you!

Support Group Leaders

ADEM SUPPORT GROUP
BARBARA KREISLER
(703)753-4000
BKREISLER.IMPRINT@VERIZON.NET

NMO SUPPORT GROUP
GAYLIA ASHBY
GAYLE@DEVIC.ORG.UK

OPTIC NEURITIS SUPPORT GROUP
KRISTIN LEE
(724)847-7999
KMARIE1016@HOTMAIL.COM

JENN NORDIN
(714)231-1808
JENN@JENNDESIGNS.COM

ALASKA
PATRICK & JENNIFER LEMAY
(907)274-4180
LEMAY@GCI.NET

CALIFORNIA
DEBORAH CAPEN
(951)658-2689
DCAPEN@MYELITIS.ORG

CINDY MCLEROY
(741)638-5493
CINDYMCLEROY@SOCAL.RR.COM

NORTHERN CALIFORNIA
JUDY MELCHER
(209)334-0771
JUDYMAE@PACBELL.COM

SAN DIEGO
CHRISTINE DAVIS
DRDAVIS@SDOPTOMETRY.COM

COLORADO
LAMAR AND DANISE BURKES
(720)851-8520
LDBURKES@HOTMAIL.COM

FLORIDA
BRAD HIGHWOOD
(772)398-3340
WHEELS1@COMCAST.NET

JAMES G JEFFRIES
(352)249-1031
MOJIMJEFF@EARTHLINK.NET

GEORGIA
CHARLENE B. DAISE
(404)289-7590
CDAISE@BELLSOUTH.NET

IDAHO
JOHN CRAVEN
(208)939-7968
JSCRAVEN@MSN.COM

ILLINOIS
NICOLETTE GARRIGAN
(773)774-6554
DUCKPRINCESS5778@AOL.COM

JEANNE & THOMAS HAMILTON
(847)670-9457
TOMBONE2@MSN.COM

KENTUCKY
ANDY JOHNSON
(859)552-5480
ANDY.JOHNSON@UKY.EDU

MAINE
COLLEEN GRAFF
CJG@KYND.NET

MARYLAND
ALAN & KELLY CONNOR
(410)766-0446
RAVENALAN@CABLESPEED.COM

MASSACHUSETTS
LESLIE CERIO
(781)740-8421
LCCERIO@AOL.COM

MICHIGAN
LYNNE MYERS
(269)789-0452
LYNNEMYERS1@YAHOO.COM

MINNESOTA
KAREN NOPOLA
(612)270-1122
NOPOLA@COMCAST.NET

DEAN H PETER
(651)492 0074
NEUAUBING1962@YAHOO.COM

DARIAN VIETZKE
(763)755-3515
VIETZKE@MYELITIS.ORG

MISSOURI
RHONDA LOGGIA
(636)537-8471
RLOGGIA@AOL.COM

NEVADA
MARY WOLAK
(702)645-3657
NOTAHORSE4@AOL.COM

NEW ENGLAND TRI-STATE AREA SUPPORT GROUP
KRISSY ZODDA
(603)589-1894
TMLADYK@YAHOO.COM

NEW YORK
PAMELA SCHECHTER
(718)762-8463
LITTLEPRINCESS900@
HOTMAIL.COM

SHANNON O'KEEFE
(585)330-1125
SHANNONJOKEEFE@
HOTMAIL.COM

NORTH CAROLINA
PAUL STEWART
(704)543-0263
BRK4YOU@BELLSOUTH.NET

OHIO
KATHLEEN KAROLY
(419)354-7316
KKAROLY@DACOR.NET

STEPHEN J. MILLER
(937)453-9832
SMILLER@MYELITIS.ORG

MARGARET MILLER
(614)486-2748
MAGMIL1336@AOL.COM

JAMES E. TOLBERT
(513)724-1940
JIMYT2@ADELPHIA.NET

LINDA GARRETT
(740) 674-4100
LIMOGA43734@YAHOO.COM

PENNSYLVANIA
MORGAN & PAMELA HOGE
(724)942-3874
HOGE5@MSN.COM

SUE MATTIS
(814)899-3539
BOBSUE6095@ADELPHIA.NET

PUERTO RICO
YVONNE LUGO DEL VALLE
(787)312-9711
MYELITISPR_YVONNE@
HOTMAIL.COM

TENNESSEE
MARY TROUP
(901)213-1698
WORK7DAYS@AOL.COM

TEXAS
ROBERT W. COOK
(281)528-8637
RCOOKHOOK@EARTHLINK.NET

COSSY HOUGH
(512)420-0904
COSSYH@YAHOO.COM

BARBARA LAMB
(817)460-2630
BABBSIE1982@YAHOO.COM

VIRGINIA
AGNES KILLOUGH
(757)422-4024
JANDAKILLOUGH@VERIZON.NET

PAMELA NEW
(757)565-6461
PNEW@MYELITIS.ORG

WASHINGTON & OREGON
BUD FEUERSTEIN
(425)398-4365
BUDFEUERSTEIN@VERIZON.NET

MIKE HAMMOND
(360)658-5878
3JMHAMMOND@CLEARWIRE.NET

WISCONSIN
LYNN SEIFERT
(715) 442-5205
TMAMNWI@YAHOO.COM

INTERNATIONAL

ARGENTINA
MARINA LOPEZ
SAUBIDET@CVTCI.COM.AR

AUSTRALIA
IAN HAWKINS
61 7 3206 4618
IHAWKINS@FUTUREWEB.COM.AU

ERROL WHITE
61 07 3886 6110
EAMJWHITE@BIGPOND.COM

CANADA
MARIEKE DUFRESNE
(514)489-0471
MARIEKE@MYELITIS.ORG

DAN KILBORN
(403)652-4347
DAN.KILBORN@SHAW.CA

DENMARK
METTE & THOMAS NYBO
JENSEN
45 76 90 50 75
METTENYBOJ@HOTMAIL.COM

GHANA SUPPORT NETWORK
NANA YAA AGYEMAN
233-21 220084
SHARECARE4U@GMAIL.COM

GERMANY
URSULA MAURO
07807 3154
UMAURO@T-ONLINE.DE

IRELAND
ANN MORAN
098-26469
ANNMORAN99@YAHOO.COM

NEW ZEALAND
STEVE & ALISON ALDERTON
64 3 3857274
SEAL4@XTRA.CO.NZ

DYLLICE EASTWOOD
649 8109807
DYLLICE@HOTMAIL.COM

JENNIFER MURRAY
09 834 5019
MURRAY_FAM@PARADISE.NET.NZ

ROMANIA
DAN BUCATARU
(021)252-5936
DAN.BUCATARU@YAHOO.COM

ALINA PARASCHIV
722 398 993
APARASCHIV@MYELITIS.ORG

SOUTH AFRICA
JENNY MOSS
082 928 3000
MOSS25@MWEB.CO.ZA

MART UYS
012-361-7671
MARTUYS@IBURST.CO.ZA

SWEDEN
ULRIKA PETTERSSON
ULPETT@GMAIL.COM

UNITED KINGDOM
LEW GRAY
020 8568 0350
LEWGRAY@BLUEYONDER.CO.UK

SALLY RODOHAN
020 8883 2721
SALLY@APINFO.CO.UK

MARGARET SHEARER
01292 476 758
MARGARET-SHEARER@HOTMAIL.COM

GEOFF TREGLOWN
01539 434 677
GEOFF.TREGLOWN@BTINTERNET.COM

Paralyzed Veterans of America: Benefits Assistance

The Paralyzed Veterans of America was founded in 1946 and is the only congressionally chartered veterans service organization dedicated solely for the benefit and representation of individuals with spinal cord injury or disease. Paralyzed Veterans is a dynamic, broad-based organization with more than 19,000 members in all 50 states, the District of Columbia and Puerto Rico.

We provide services to assist veterans in receiving both compensation and/or pension benefits (monetary in nature), and health care benefits (medical). We also assist with applications for education and home loan benefits to include assisting dependents of veterans when they have entitlement to those benefits.

The Memphis Service Office provides representation to Paralyzed Veteran members in a nine state area; Alabama, Arkansas, Western Kentucky, Northern Louisiana, Southeastern Missouri, Mississippi, Oklahoma, Tennessee and West Virginia. If you are a veteran and have TM, ADEM or NMO and you need assistance with VA healthcare or benefits issues, please contact our office for assistance. Our office is located in the Memphis VA Hospital Spinal Cord Injury Service. We can be reached at (800)795-3568 Monday through Friday from 800 a.m. to 4:00 p.m. Please fell free to call, if you have any questions concerning veteran benefits.

Clifton E. Dupree
Senior National Service Officer
1030 Jefferson Ave. Room 2B143
Memphis, TN 38104
(901)523-8990 Ext. 7795
(800)795-3568
CLIFTOND@PVA.ORG

Learning about TM and the other neuroimmunologic disorders: Bibliography and Videos on www.myelitis.org

For those of you trying to learn about Transverse Myelitis, Chitra Krishnan has compiled an excellent bibliography about TM. Chitra serves on the TMA Medical Advisory Board, is the Executive Director of Project RESTORE and is the Research Coordinator at the Johns Hopkins TM Center.

You can find the bibliography by typing this address into your web browser:

http://www.myelitis.org/Bibliography.htm

Jim has created links from the articles in the bibliography to Medline; so when you click on the article citation, you can easily get to a copy of the article to read. Additionally, when you are in Medline, you can link to other recently published articles by clicking on the authors' hotlinks.

Another tremendous resource about TM and the other neuroimmunologic disorders is the streaming video that Jim has posted on the web site. The presentations from the 2001, 2004 and 2006 symposia and from the 2002 children's workshop are available under the link 'Symposia and Workshop Information' or by typing http://www.myelitis.org/events.htm into your web browser. Jim has the presentations organized as they appeared in each of these symposia and workshop program agendas. The video presentations are also available by going through the Multimedia link from our main web page or by typing http://www.myelitis.org/multimedia.htm into your web browser. The streaming video from the Southwest Rare Neuroimmunologic Disorders Symposium, recently held in Albuquerque are now available under the symposia and workshops link, as well as the Cody Unser First Step Foundation Web Site. A link to Cody's web site can be found under our 'Additional Resources' web page.

The TMA Equipment Exchange

Darian Vietzke

Please get involved in the TMA Equipment Exchange. You will see the link to the Equipment Exchange on the column of links on the main page of the TMA web site. The program is intended to assist our community in exchanging surplus equipment with each other for the cost of shipping only. We encourage all of you to begin to list your equipment as soon as possible. The more equipment that is listed, the more individuals in our community will be helped. If you have any questions as you begin to use

the program, please use the help link on the equipment exchange web site. If you have any comments or questions regarding the TMA Equipment Exchange, please send an e-mail to exchange@myelitis.org Thank you for your support!

Contacting the TMA by Email

When writing email messages to the officers of the TMA or to support group leaders, please use TMA, Transverse Myelitis, TM, ADEM, NMO or ON in the subject header of the message. Please be sure to include a title in the subject header. The volume of emails that we receive and the way spam filters work makes it increasingly difficult to sort through emails to find legitimate messages. Also, if you would like to send an attachment, it is always a prudent approach to send an email notifying the person that you are going to follow up your message with a second email that includes the attachment; and explain the nature of the attachment. If you want to be sure that we see it, save it and open it, please include a subject header in your message and use words that will identify you as a person interested in contacting the TMA. We appreciate your help!

Please Keep Your Membership Information Current

Please keep us informed of any changes to your mailing address, your phone number and your email address. To let us know about any changes, please fill out a change of information form on the TMA web site: http://www.myelitis.org/memberform.htm – just click on the box indicating that you are changing existing information.

Medical Advisory Board

Officers and Board of Directors of The Transverse Myelitis Association

www.myelitis.org

The Transverse Myelitis Association

Sanford J. Siegel
1787 Sutter Parkway
Powell, Ohio 43065-8806

NONPROFIT ORG
U.S. POSTAGE PAID
POWELL, OH
PERMIT NO. 6
ZIP CODE 43065

Douglas A. Kerr, M.D., Ph.D. speaking at the first UK TM Conference, Saturday 13th October 2007 in London

Victory Junction Gang Camp - TMA family week , August 19 to August 24, 2007