THE MYOSITIS ASSOCIATION

OUTLOOK EXTRA

WINTER 2008

Conference Report

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Members share stories of challenge and courage

Marianne's story

Marianne Moyer spent 30 years in corporate America and has the battle scars to prove it. "I was driven," she told the group gathered for the TMA Conference patient panel. "I think I probably also drove everyone crazy." She found retirement slow after the formerly frantic pace of her daily life and worked as a consultant. Marianne lives in Bradenton where her new profession – a volunteer position – is leading the Southwest Florida support (KIT) group.

Her path between the two parts of her life was sometimes scary but always inspiring. She spent some time wondering why she couldn't lift her hands to blow-dry her hair. There were other signs of weakness, too, before she was diagnosed with polymyositis. Things were to get a whole lot worse before they got better. For many months, she wasn't able to move her arms and legs at all. "That was awful," she said. Even worse was the growing realization that she'd have to depend on her husband, John, for everything. Even worse, from their joint point of view, was accepting help from friends and family.

"John turned down the church ladies for a while when they came forth with meals," she recalled. "There was a time, though, when that home-cooked meal sounded pretty good." Here's how the "church ladies" turned it around: "They approached us," she said, "with a request that we help another member of our church who was struggling." Busy and overwhelmed as they were with their own lives, the couple jumped at the chance. That's when they found out that the request was a kind of parable, a lesson in humility. "That was their way of pointing out that people sincerely wanted to help," she said.

Moyer learned to accept help as she fought her way back to normal life with occupational therapy and physical therapy. Crucial to her recovery was her "standing chair," a device that stood her up so she could "practice" for the day when she would walk again.

More setbacks: a cough (interstitial lung disease); a flare at 18 months; but she returned again. Two years ago, she turned her considerable organizational talents to forming a new KIT group, beginning with three people and building to 90 at their last meeting. The Southwest Florida KIT has raised $9,000 this year. "Even

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Ask an expert

Environment and myositis: what's the connection?

The Myositis Association offers live discussions on the TMA website as a benefit of membership. If you haven't participated in our live discussions as yet, it's easy! Submit questions in advance by going to the "Live Discussion" page and clicking on the link that says "Click here to learn how to participate." You will find easy-to-follow instructions for submitting questions in advance and also as the discussion progresses.

Experts known internationally for their experience have answered hundreds of your questions about cancer, interstitial lung disease, dysphagia, exercise, statins and other topics.

Dr. Fred Miller led November's live discussion on possible environmental connections with myositis and other autoimmune diseases, and some excerpts follow. For the full transcript, go to TMA's website, www.myositis.org. His full presentation on this topic at TMA's 2008 Annual Conference is also featured on the website.

Fred Miller, M.D., Ph.D. currently leads the Environmental Autoimmunity Group at the National Institute of Environmental Health Sciences in the National Institutes of Health, Bethesda, MD. He has studied the inflammatory myopathies for more than 25 years.

Question: I was diagnosed with polymyositis seven years ago. Around the same time, two of my co-workers were also diagnosed with serious autoimmune diseases -- sarcoidosis and Sjogren's syndrome. We are centrally located within a triangle of three coal-fired generating stations. Might the air quality here be the cause of, or exacerbate, our conditions?

Dr. Miller: You raise an interesting question, and I hear stories like this all the time – unfortunately small numbers of anecdotal cases like yours cannot be easily studied to answer if there is a relationship or not. That is why very large studies of hundreds or thousands of cases and controls are usually needed to address if a particular exposure is related to a disease. This has been difficult to do with rare diseases like myositis. There have not been any studies of the role of coal-fired plants in autoimmunity so we don't really know about them.

Question: Six months before I was diagnosed with dermatomyositis, the factory I work in cleaned the entire plant with chemicals and then painted walls, ceiling and all machinery. A month before this project was started I had a complete physical and was given a 100% clean bill of health. Any connection?

Dr. Miller: You and I both wish we knew – again there have been too few studies of any specific chemicals (that might be associated) with autoimmune disease and virtually none with myositis to answer this question. Careful animal studies are often the first step in trying to understand possible associations but even then, they are usually done with pure chemicals rather than the complex mixtures that make up most cleaners and industrial compounds.

Question: I am the only member on both sides of my family to suffer from IBM. What kind of environmental issues would affect only one member out of so many when all belong pretty much to the same socio-economic level, were raised with similar diet, physical activity, and education? I had one uncle who who used to fall often, had trouble going up and down stairs and was diagnosed with muscle

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Challenges, *from cover*

more important," she said, "is that when people find us, they know they're not alone."

Peter's story

Peter Rebovich had a life that centered on sailing and racing, a passion that he was able to pursue in his summers off. Peter, who has IBM, was a schoolteacher for 40 years before retirement. In 1973 he bought his present boat, the Sinn Fein, and began entering distance races every other year.

Rebovich passed on his enthusiasm for open water and facing the elements to his two sons. They looked forward to the Massachusetts to Bermuda races held every other year, and the Sinn Fein became a contender to take seriously. "We took a trophy every now and then," Rebovich said. One year, the whole family raced to Bermuda, winning first in the "family" class. Rebovich and his boys were hooked. Every other year, they'd commission a crew, and spend days on the water.

Rebovich calls himself the "navaguesser," trusting his instincts as well as his maps. His intuition paid off in 2002, 2004 and 2006, as the Sinn Fein placed higher and higher in competition. Earlier this year, he won the coveted Centennial race, with a trophy awarded by Britain's Princess Ann, a sailing enthusiast. As his crew prepared to hoist him on their shoulders for a trip up the steep steps to the stage, the Princess stopped them. "I shall come down," she said.

Just as important as recognition from the world sailing community is the example he's been able to show his sons, who have learned the importance of holding onto their dreams. Rebovich wasn't hampered by his disease; in fact all of his highest honors came after his diagnosis with IBM. "Some dreams really do come true," he said.

Rosemary's story

It took three years and 12 doctors for Rosemary Istre to find out what was wrong with her. At one dark hour she suspected she must be mentally ill, since no one could find out what was wrong with her. It was a stunning reversal for the dermatomyositis patient. "I was going to go to medical school, I'd married the man of my dreams," she said. "I had big plans. Suddenly, my world got smaller. My biggest ambition was to be able to go the grocery store."

Istre became so weak she feared she would die during several hospitalizations. Intravenous immunoglobulin turned her around in more ways than one. It made her stronger, and it also put her in the proximity of another dermatomyositis patient, Sue Fehl. Looking back, Istre remembers the encounter as a humorous one. They were both being infused when Fehl remarked that Istre didn't look so good. "

"You don't look so good yourself," Istre countered. They hatched a plan for a golf tournament. "Do you play golf?" Fehl asked. It turns out, Fehl didn't play either. So the two sickly, non-golfers teamed up with healthy golfer Sande Dunphe for the first Texas KIT golf tournament, an event that has now become TMA's largest annual fundraiser, bringing in over $60,000 in 2008. Raising the money was wonderful for TMA; but also for Istre, who was slowly feeling better. "For the first time in years, I felt like I mattered," she said. Her confidence partly restored, she believed she could take on medical school, course by course, lying down in the conference room until she was strong enough to go home.

Istre is the Houston KIT leader, and was a presenter at the Conference on the research she's done on myositis and an anti-inflammatory diet. Her determination, she said, comes from a lesson she keeps on learning. "You don't have to be perfect to make a positive difference," she said. "All you need is a big heart."

Steve's story

Steve Morris thanked the other panel members and said his presence on the panel signaled the need for comic relief. Morris, a long-time teacher, said he realized he had a limited vocabulary when he heard the medical panel speak Saturday.

"'Rhabdomyolysis,'" he repeated; "now that sounds terrible. And I don't think 'intra-cellular messaging' has anything to do with texting or cell phones."

Morris talked about his 4,500-mile "Riding for those who can't, yet" trip last summer, raising money for myositis patients. He rode his Harley up into Canada from Southern California, "Riding for those who can't yet." He noted the help he had along the way, illustrated by a slide show of the myositis patients, friends and family who turned out to wish him well: Mike and Marlene Coates of Kelowna, British Columbia, who provided media notice of the ride, organized a breakfast gathering where Morris spoke, and arranged a police motorcycle escort to and from town.

In Seattle, Ann Robertson and the Washington KIT group organized a barbecue and gave the crew a place to stay for the night. He also met Gracie, a JM patient, and gave her a ride around the parking lot.

On to the next stop, where Rita Albano put together a reception on the busiest street corner in Vancouver. Morris described rolling into Starbucks: "She had the press out there. She had a folk band playing as we rode up. She had a raffle going on with the proceeds going to TMA. There was a banner welcoming us to Vancouver and she set up an interview for me with the local radio station. "We felt like rock stars!" Morris presented photos of his journey with music for a moving presentation that has been sent to KIT leaders.

MANAGING YOUR DISEASE

Inclusion-body myositis

Todd Levine, MD, is the co-director of Samaritan Peripheral Neuropathy Center, director of Samaritan Stroke Clinic, Director of Samaritan ALS Clinic and Director of Neurophysiology at Good Samaritan Hospital, as well as Assistant Professor of Clinical Neurology at the University of Arizona. Dr. Levine is a member of TMA's medical advisory board.

It's essential to properly diagnose inclusion-body myositis, said Dr. Levine, both to avoid drugs that might have unpleasant side effects and to plan an appropriate course of disease management. A typical patient might be a 69-year old man (the disease is more frequent in men, and in those over 50) who has complained of a weakening grip and weakness in his legs and forearm muscles.

The laboratory measurement of inflammation, creatine kinase levels or CK, (a blood test that shows muscle enzymes released by inflammation) might show mild elevation or normal levels, and an electromyogram, or EMG, reveals both muscle and nerve abnormality. Normally, said Levine, the weakness will have been developing over a course of years. There's apt to be an incorrect diagnosis in the patient's past, he said, with the most common being polymyositis or ALS. Other clues for the diagnostician are mild facial weakness (in 30-40 percent) and difficulty swallowing (40 percent). Often ankles are affected, which complicates the balance problems of IBM patients.

When a patient has received a diagnosis of IBM, he or she doesn't have the additional risk of malignancy or heart or lung disease that other myositis patients experience. IBM patients frequently (20 percent) do have other autoimmune disorders, such as lupus, Sjogrens's syndrome, scleroderma, sarcoidosis and diabetes. Nineteen percent of IBM patients will have a peripheral neuropathy, or nerve damage.

"It's a common misconception among physicians that IBM patients don't experience pain," Dr. Levine said. "As many of you know, your muscles can hurt like crazy." In fact, he said, patients describe their aches as "flu-like." "That's because a similar process is happening in your body," he explained. "Your body, trying to stop the disease process, becomes inflamed, and inflammation causes pain."

Appropriate exercise not only helps the pain, but it improves your overall function, he said. "In general, we know that people with IBM who are more active do better." When IBM patients become less active, or there are muscles they do not use, they should receive therapy to reduce contractures. Patients should avoid becoming overweight, as that puts added stress on already compromised muscles, and they should also strive to get the best nutrition possible.

With no consistently effective treatment yet for inclusion-body myositis, which progresses slowly, Levine advised patients to address some of the practical challenges of the disease. An occupational therapist can introduce patients to adaptive therapy, devices to improve mobility like wheelchairs and scooters as they are needed; and other devices that solve practical everyday problems like picking things up off the floor, climbing stairs, or steadying the patient as he or she walks. Splints and braces can help with the common "foot drop" experienced by IBM patients, allow the knee to bend while taking a step, and immobilize the knee when standing to avoid falls caused by muscles too weak to stabilize the knee.

The prevention of aspiration caused by weak swallowing muscles is important, Levine said, as this is an ongoing and potentially life-threatening problem. Poor swallowing and subsequent poor nutrition can lead to a host of ailments, including digestive and respiratory emergencies. Patients may ask their physicians for exercises that help them swallow, may find that different positions make swallowing easier, and can try adjustments in their position. Levine recommends working with a speech therapist.

Many dysphasia patients are able to modify their diet to eliminate the food consistency that seems to be causing problems. Dr. Levine advises those with swallowing problems that are beginning to cause significant impact on comfort, respiration or nourishment to ask about a feeding tube, also called a PEG or G tube, an aid that doesn't rule out eating by conventional means and is invisible and easy to use.

The arsenal of drugs available to other myositis patients just isn't effective in IBM, Levine said. Neither prednisone, nor methotrexate nor IVIG have much effect, although doctors often prescribe a short trial. One drug, Alemtuzumab (Campath) has been tested but results haven't been released.

Levine talked about Lithium, a drug that has resulted in improved

muscle strength in animal studies. He is conducting an open label pilot trial of Lithium in IBM. To enroll, patients will need muscle biopsies before and after entering the trial, which will consist of six months of oral therapy. Anyone interested in joining the trial is encouraged to email Dr. Levine at Levine865@aol.com.

Polymyositis

Lisa Christopher-Stine, MD, MPH, is assistant professor of medicine at Johns Hopkins University and co-director of the myositis center there. Her research work, funded by the National Institutes of Health, is on the development of a database of patients evaluated at NIH with autoimmune myositis and related diseases. Her other research includes statin-associated myotoxicity, for which she has written medical reviews. This past summer, she led a web-based live discussion on the subject for The Myositis Association. She is the president of The Maryland Society for Rheumatic Diseases.

Once your physician has diagnosed polymyositis, he or she is likely to prescribe a course of steroids, usually prednisone. Because of the side effects of these drugs (see box), you may quickly be put on another drug or combination of drugs called "steroid-sparing therapies," so-called because their purpose is to allow you to proceed to a lower dose of prednisone. Many of these drugs themselves have potential side effects, so alert your physician if you experience any of those listed. Some reactions are mild and resolve after a few days; others are potentially serious.

Intravenous immunoglobulin (IVIG), given through IV: Side effects may be fever, chills, excessive sweating, aseptic meningitis, headache, low blood pressure, and decrease in white blood count. Your physician should monitor your blood pressure, heart rate, blood urea nitrogen and creatine.

Methotrexate, given orally or through IV: Side effects may be liver damage, decrease in white blood count, loss of hair, sores in the mouth or throat and unusual cell growth. Your physician should monitor liver function and complete blood count.

Azathioprine, given orally: Side effects may be liver damage, decrease in white blood count, anemia (low blood iron count), and allergic reaction. Your physician should monitor liver function and complete blood count.

Cyclosporine, given orally: Side effects may be kidney damage, high blood pressure, unusual hair growth, liver damage, infection, unusual growth of cells in the gums. Your physician should monitor blood pressure, blood urea nitrogen, creatine, liver function and drug levels.

Mycophenylate mofetil, given orally: Side effects may be diarrhea, cramps, liver damage, and decrease in white blood count. Your physician should monitor your complete blood count and liver function.

Tacrolimus, given orally: Side effects may be kidney damage, high blood pressure, unusual cell growth in the gums, diabetes. Your physician should monitor blood pressure, blood urea nitrogen, creatine and liver function.

Cyclophosphamide, given orally and through IV: Side effects may be low white blood count, cystitis, hair

THE GOOD, THE BAD, THE UGLY

That's how Dr. Christopher-Stine describes **prednisone**, a "necessary evil" that works very well to reduce inflammation in most cases, but has a long list of side effects: such as weight gain, swelling, diabetes, emotional ups and downs, and fatigue.

These are just the major side effects, said Christopher-Stine. Minor side effects are: stretch marks, nervousness, acne, rash, increased appetite, frequent urination, diarrhea, depletion of intestinal flora and hyperactivity.

Most myositis patients become familiar with the routine of "tapering," gradually cutting down on the size of the steroid dose over a period of time. Generally, Dr. Christopher-Stine recommends tapering by 10 mgs. a day every 1-2 weeks for those on 60 mgs. or more a day; 5 mgs. every 1-2 weeks for those on 20-60 mgs. a day; 2.5 mgs. a day for those on 10-19 mgs. a day; and 1 mg. a day every 1-2 weeks for those on less than 5 mgs. a day.

If symptoms are well controlled as tapering progresses, physicians usually continue with the tapering. If symptoms flare, they may increase prednisone by 10 to 15 percent and maintain that dosage for 2-4 weeks. If symptoms are then well controlled, they'll resume tapering with dosage decreasing every 2-4 weeks. If symptoms continue to flare, they may double the dose until symptoms subside, then taper more slowly.

There are things you can do to help yourself avoid the worst effects of steroids, Dr. Christopher-Stine said:

- Taper down steroids as fast as possible, but only when advised by physician. Alternate-day dosing may be helpful in some cases, she said: for example, alternating 10 mg with 7.5 mg every other day for two weeks before dropping to a daily dose of 7.5 mg for two to four weeks
- For weight gain, be very conscious of food choices. Limit carbohydrates and make reasonable snack choices
- Unusual joint pain – especially in the hips – or any nocturnal pain needs to be reported in order to rule out osteonecrosis or avascular necrosis.

loss, infections, unusual cell growth. Your physician should order a complete blood count and urinalysis. When given intravenously, cyclophosphamide can also cause nausea and vomiting.

Chlorambucil, given orally: Side effects may be liver damage, decrease in white blood cells, nausea and vomiting. Your physician should monitor liver function and complete blood count.

Dr. Christopher-Stine also talked about newer drugs, drugs that target the disease process of dermatomyositis and polymyositis more specifically, instead of affecting the entire immune system. These tend to have fewer side effects when tested in the small trials presently available.

Infliximab is being studied in a randomized control trial at the National Institutes of Health after scattered case reports demonstrated benefit in polymyositis and dermatomyositis. Muscle strength in both diseases improved; the rash of dermatomyositis improved; and the blood tests that measured inflammation confirmed that improvement. Other reports showed increased muscle inflammation in patients taking infliximab.

Etanercept has been tried in scattered cases, and one case report demonstrated clinical benefit in one patient with polymyositis who did not respond to treatment. Although there is a trial of etanercept and myositis underway, there are no reports yet.

Rituximab showed success in a small trial of 7 patients with long-standing illness who received four infusions each one week apart. All of them experienced increased muscle strength, some as early as four weeks after the first infusion. All patients, showed decrease in blood markers of inflammation. A multi-center trial is now underway for adults and children with PM and DM, where patients are randomly assigned to one of two groups, each of which receives the drug at some point.

Medi-545, a fully human anti-interferon alpha monoclonal antibody is now being studied for safety in adult DM and PM patients.

Dermatomyositis

Chester Oddis, MD, a rheumatologist, received his M.D. and residency training from Pennsylvania State University. He is currently director of clinical services, Clinical Immunology, Division of Rheumatology, and Professor of Rheumatology at the University of Pittsburgh School Of Medicine. His investigative efforts have focused on the idiopathic inflammatory myopathies, and he has been involved with experimental clinical trials using new and novel agents in the treatment of polymyositis and dermatomyositis, including being the lead investigator for the Rituximab in Myositis study, a multi-center trial. He is a member of the International Myositis Assessment and Clinical Studies Group (IMACS), and a long-time member of TMA's Medical Advisory Board.

Twenty years ago or so, physicians learned that dermatomyositis was "polymyositis with a rash," Dr. Oddis told TMA members at the TMA Conference. "Now we know this isn't so," he said. "The two diseases look different under a microscope, and the diseases have different targets. Knowing this helps us treat them."

The targets Dr. Oddis is talking about are the muscle fibers in polymyositis and the blood vessels in dermatomyositis. "Even the cells involved are different," he said. "There are T-cells involved in both diseases, but you'll also see the characteristic B-cells in dermatomyositis, not in polymyositis."

He gave an example of the whole-body implications of dermatomyositis, one from his own practice. "We had a woman with the classic rashes and she said she felt fine, didn't complain of muscle weakness at all." The blood tests bore this out: The creatine kinase test, which measures the enzymes inflamed muscles are causing to circulate in the blood, showed the levels were barely elevated. When she had a muscle biopsy, though, the picture changed. "She clearly had dermatomyositis, and a clinical exam did reveal some weakness in her neck and hips," he said.

He treated her with a small dose (10-15 mg. twice daily) of prednisone. "In retrospect, she felt stronger, probably just didn't realize she had gotten gradually weaker, and never needed a stronger dose," Dr. Oddis said. "We're not sure if she would have gotten many more muscle symptoms if she hadn't been treated, or if she would have stayed at that level."

The point, said Dr. Oddis is "this is a systemic disease. If it were just the skin or just the muscle, it would be a lot simpler." Because DM, like PM, involves the whole body, it's important to treat it even when individual symptoms are not severe. He noted that we can now identify markers associated with cancer, with the possibility of overlap disease, with greater risk of organ involvement, and with the classic skin symptoms that respond well to treatment. "We're working at getting down into even smaller subgroups as we look for genetic predisposition that predict a certain disease course, even how well they'll respond to certain treatments," he said.

Dr. Oddis went over the medications for muscle weakness, the same array as those prescribed for polymyositis (see "Polymyositis" above). One treatment more often prescribed for dermatomyositis than polymyositis is IVIG, and Dr. Oddis discussed it at length.

"This is not a completely benign treatment," he said. "I've had patients who have had blood clots and strokes – and there's a kind of meningitis you can get from these infusions. I've seen those, too." For the most part, though, he said, IVIG produces few

side effects and can be a life saver.

He described some of the skin problems, particularly the itchy scalp – "this can be one of the worst things to deal with," he said. "It just drives people crazy." He mentioned one case where IVIG helped a patient with this very uncomfortable problem. When your skin problems are really interfering with the quality of your life, it's time to work with a dermatologist," he said. "There are topical creams, steroid shampoos, many kinds of ointments and medications that can be monitored by a dermatologist." (Dr. David Fiorentino's Conference session on skin care is available now on TMA's website).

Finally, watch exposure to light, Dr. Oddis warned. "For some patients, just sticking an arm out the window will bring on a flare, and not just of skin but muscle weakness. Other patients are sensitive to other forms of light: some actually are more sensitive to industrial lighting than to the sun. "You have to know your body, protect yourself," he said.

Juvenile Myositis

Dr. Ann Reed is professor of pediatrics and the chair of pediatric rheumatology at the Mayo Clinic Medical School in Rochester, Minnesota. She's a long-time member of TMA's medical advisory board and the co-director of the rituximab in myositis (RIM) study.

Juvenile myositis has some differences as well as similarities, when compared to adult dermatomyositis, Dr. Reed told parents at TMA's Annual Conference in Denver. It does not have an association with cancer, but it has complications, including serious stomach problems and hardened calcifications, called calcinosis, that are seen more rarely in adults.

The good news is that growing use of multiple medications instead of solely relying on prednisone to treat juvenile myositis is helping children reach remission sooner as well as reducing the side effects of prednisone, said Dr. Reed. Some examples:

- Adding methotrexate to prednisone showed improved disease outcomes in 21% of JM patients in a study. 53% reached remission, and the total doses of prednisone were reduced.
- Adding cyclosporine lowered the prednisone needed, while improving the strength of 100% of those who participated in a study.
- Using pulse steroids instead of oral prednisone may decrease the length of time the drug is needed, while achieving the same outcome.
- Using IVIG (intravenous immunoglobulin) in disease that doesn't respond to prednisone caused 30% of children in a study to normalize and 63% to improve strength.
- Rituximab has shown improvement in children as well as adults in small studies, and is now being studied in a large, multi-center trial.

The family just receiving the diagnosis of juvenile myositis can expect one of three outcomes. These are partly determined by the severity of the disease, said Dr. Reed; but might also be affected by the speed of diagnosis and appropriate treatment:

- Monocyclic (30% of JM children are in this category) describes a limited disease, with quick response to treatment and an excellent outcome. These children will have only a mild flare after treatment, or none at all.
- Chronic non-ulcerative (40% of JM children are in this category) describes a more extensive disease, with a good initial response, but a number of relapses and occasional disabilities before remission.
- Chronic ulcerative (30% of JM children are in this category) describes an active disease that can last for multiple years and which includes ulcerations, little response to medications, and may include calcinosis.

Dr. Reed said new diagnostic features help physicians track the various stages and complications of JM:

- P-31 magnetic resonance spectroscopy can examine abnormal mitochondria, the energy sources within the cells.
- Physicians use bone scans or ultrasound to follow calcinosis as it grows under the skin. They can also track bone density loss caused by prednisone.
- MRI images show physicians if there's edema (fluid beneath the skin) in muscle and soft tissue.

Also important in managing JM, said Dr. Reed, are hydroxychloroquine for the rash, plenty of calcium and Vitamin D for bone health, sun screen, and exercise to keep muscles strong and flexible. Exercise led by someone trained in childhood muscle disease is extremely important in order to keep muscles from growing small, weak and contracted. If children are bedridden or in a wheelchair, passive range of motion activities can keep them flexible. As children feel better and are active, their normal exercise and play should keep them fit, and parents should encourage them to pursue active pastimes rather than sedentary ones. Good nutrition and avoiding weight gain due to prednisone are both important.

What's ahead? Diagnosis and treatment have come a long way since JM was first described, Dr. Reed said, but research into possible causes and better treatments will improve the situation still more. Fully 75 % of JM children diagnosed now will live normal lives; and most of the rest will have minimal disability.

STATINS AND MYOSITIS: WHAT WE KNOW

The connection between statins – the most commonly prescribed cholesterol-lowering drugs – is clouded by incomplete understanding and misconception, said Dr. Lisa Christopher-Stine at TMA's 2008 Annual Conference. She has published several studies on this subject and answered questions from TMA members in an online TMA "live discussion" last spring. Dr. Christopher-Stine also made a presentation on myositis and statins at TMA's 2008 Annual Conference in Denver.

Myositis patients continue to have many questions about statins, and Dr. Christopher-Stine continues to study their role in the disease. Following are some of her answers to common patient questions during the online chat and the conference session. The answers have been edited and condensed.

Do statin drugs cause inclusion-body myositis, polymyositis, and dermatomyositis?

This is the most commonly-asked question from TMA members, and one that's hard to answer definitively. There is what's called "an association" between PM, DM and IBM and statins, but no evidence as yet that they actually cause these diseases. Truthfully, no one is entirely sure how statins cause toxic effects on the muscle, so there are many grey areas when it comes to evaluation and treatment.

When Dr. Christopher-Stine has stopped statins in myositis patients who believed statin use was a factor in their disease, the myositis has not gone away. The problem is that statins are so widely prescribed, making it difficult to discern whether there is a true link here.

Only 1 percent of patients have had a reaction to statins, but because of the huge number of patients involved, this amounts to many thousands. Had so many patients taken a drug that was very rarely prescribed, the association would be much clearer. Many patients have made the connection between the fact that they were taking a statin at the time they developed DM, PM, or IBM. It is now the job in the medical community to determine whether there really is a causal link here, Dr. Christopher-Stine said, but this will be difficult to do.

There is a condition called "statin-induced myopathy." If statins don't cause IBM, PM and DM, then what is this disease?

"Statin-induced myositis" or "statin-induced myopathy" technically refers to a direct toxic effect to the muscle caused by statins - not to a potential link between statins and myositis such as PM, DM, or IBM. Most mild muscle weakness and pain that's caused by statins is resolved when the statins are discontinued; but this is not always the case: there are examples of the weakness and pain continuing. Dr. Christopher-Stine said that muscle changes in this disease differ from IBM, PM and DM when seen under the microscope, but that the possible connection still intrigues her and is worthy of study.

Why do so many myositis patients report statin use immediately before symptoms appear?

Statin drugs are now a multi-billion dollar industry, and represent 87 percent of all lipid-lowering drugs. One of the statins, Lovastatin, is being considered for availability without prescription. By sheer numbers alone, it would stand to reason that many myositis patients will have taken statins. However, because statins do affect the muscles, physicians and researchers don't rule out a possible role for statins in the development of myositis.

Labeling of statin drugs always warns of possible "severe and life-threatening muscle disease." If this is not myositis, what is it?

Statins can cause a severe type of muscle destruction called rhabdomyolysis, especially when combined with certain drugs, including fibrates and high-dose niacin, which are also often used to control cholesterol; and cyclosporine, which is sometimes used by myositis patients. Dr. Christopher-Stine notes that when there's an effect on the muscles, it is believed to be a direct one, not a result of lowering the cholesterol. Rhabdomyolysis is a massive breakdown of muscle, can cause kidney failure, is very dangerous, and is very clearly linked with statin drugs. In fact, Baycol, a certain kind of statin, was taken off the market in the United States because it appeared to be more likely than other statins to cause rhabdomyolysis.

I have myositis and high cholesterol. Should I take a statin drug?

There is debate in the medical community about the safety of statin drugs in patients who have an established (or suspected) diagnosis of dermatomyositis or polymyositis, and possibly IBM. Dr. Christopher-Stine allows patients to start or continue a statin if the benefit seems to outweigh the risks. She tries the statin in full dose first with careful monitoring of CPK - weekly for the first 4 weeks and then generally monthly thereafter. If muscle symptoms develop, she may go to every other day dosing.

She generally does not alter the dose during disease flares if the statin was tolerated in times when the disease was stable.

However, she said, she's noticed that patients are too often placed on a statin in the absence of significantly elevated cholesterol; a strong family history of high cholesterol or early coronary artery disease; or any other primary risk factor. She's also seen

some patients who probably could have avoided taking statins with diet and exercise modifications. Statins do have their role, and if used in patients with PM, DM, or IBM, they should be used with care, with careful monitoring for worsening of muscle-related symptoms or elevation in CPK that can be attributed to the statin.

Is there a statin or statin alternative less likely to affect the muscles?

Of the statins, Pravachol is water-soluble (as opposed to lipid or fat soluble) and therefore seems to have slightly less chance of inducing muscle-related side effects. Dr. Christopher-Stine also mentioned Welchol, which has been tolerated in myositis patients who could not tolerate other statins. Zetia may be tried, but has caused similar problems and may not lower cholesterol as effectively.

Omega-3 (found in supplements and in fatty fish like salmon and tuna) and Niacin are also alternatives. Fibrates (like gemfibrozil) may be tried but they, too, can be direct muscle toxins, although they probably act in a different manner to do so. Serious adverse reactions to fibrates (myositis, myopathy, or rhabdomyolysis) occur in approximately 1% of patients who take them; these events are more likely to occur in patients with decreased kidney function. In major clinical trials, the rates of these complications were low.

The risk for rhabdomyolysis seems to be increased when a fibrate is combined with a statin, but the risk seems to be specific to gemfibrozil, whereas fenofibrate is probably safe when used in combination. Nevertheless, fenofibrate can cause a myopathy when used alone.

There is at least one naturally occurring statin: red yeast rice. Its chemical structure is identical to lovastatin. Dr. Christopher-Stine does not recommend that her patients try this: she has seen it cause the same side effects in patients who have previously experienced statin toxicities with the man-made statins.

What could doctors do to prevent or treat muscle symptoms caused by statins?

Most doctors are well aware of the side effects of statins - including liver toxicity and myopathy. While most physicians would recognize rhabdomyolysis, the most severe form of statin myopathy, there is little consensus on what to do for patients with elevated CK or myalgias (muscle pain) in the absence of an elevated CPK. In an ideal world, said Dr. Christopher-Stine, doctors would measure a CK prior to initiating a statin. This would at least serve as a baseline, or perhaps serve as a warning that muscle inflammation was already present.

As we learn more about muscles and statins, is there anything doctors could do to screen out people who might be affected?

Exciting research in this regard is being done by Dr. Vladutiu at the University of Buffalo, and those at the Johns Hopkins Myositis Center are collaborating with her on this project, evaluating patients who have developed statin-related muscle symptoms, elevated CPK, or rhabdomyolysis.

Dr. Vladutiu has an NIH-funded study of the genetic risk factors associated with statin myopathies. While there is almost certainly a genetic predisposition for developing statin myopathy in some, finding those candidate genes is in the very early stages. Information about statin myopathy susceptibility will be available in the near future. To date, Dr. Vladutiu and her colleagues have noted that patients with statin myopathies had a greater chance of having a metabolic myopathy or being a carrier for one - such as CPT II deficiency or McArdle's disease.

Study: myositis-affected muscles respond to exercise

In a recent article, "Molecular effects of exercise in patients with inflammatory rheumatic disease," Ingrid E. Lundberg and GA Nader examined the molecular effects of exercise on people with systemic inflammatory disease. Dr. Lundberg is a Professor of Rheumatology at Karolinska University Hospital, Solna, and a member of TMA's medical advisory board. The report summarizes:

Exercise is now known to be beneficial for patients with inflammatory rheumatic disease. In patients with rheumatoid arthritis, exercise can improve physical performance, cardiorespiratory fitness and muscle strength, and reduce disease activity and systemic inflammation, as evidenced by reductions in erythrocyte sedimentation rate and other systemic markers of inflammation. Similar effects on physical performance and cardiorespiratory fitness have been observed in patients with PM and DM. Improved muscle performance in these patients is associated with an increased ratio of type I to type II muscle fibers and increased cross-sectional area of type II muscle fibers, suggesting that myositis-affected muscle retains the ability to respond to exercise.

In addition, resistance exercise training can reduce the expression of genes involved in inflammation and fibrosis in patients with myositis, and in vitro mechanical loading of chondrocytes can suppress the expression of proinflammatory cytokines, indicating that exercise can also reduce inflammation in the local tissue environment. Further studies of the systemic and local responses underlying exercise-associated improvement in muscle performance, soft tissue integrity and health outcomes are warranted.

GETTING YOUR CHILD THROUGH THE WINTER...

Help your child avoid common winter colds and illnesses

Avoiding exposure to germs is very important to children whose immune systems are suppressed, Dr. Ann Reed said at TMA's 2008 Annual Conference. Dr. Reed, a pediatric rheumatologist, is professor of Pediatrics and Medicine and Chairperson of Pediatric Rheumatology at the Mayo Clinic in Rochester, Minnesota. It's important for obvious reasons: children with suppressed immune systems don't have the same ability to fight invading virus and flu bugs.

It's also important to keep from adding more unpleasant symptoms to children who already have plenty, and it's not impossible to teach even the youngest children to protect themselves, Dr. Reed said: "Kids are actually pretty much in tune with this, especially if you reinforce it while you're with them. " Teach them to wash their hands, avoid children with colds and other diseases, and avoid putting objects in their mouths.

While on prednisone and other myositis medications, your child may not display the typical signs of infection, so keep a careful watch for even the mildest sign of colds, fever, headaches, sore throat and digestive complaints. Your child may require medical treatment for these common childhood maladies beyond what other children might need. If another member of the household becomes ill, be very careful not to infect the child with JM by avoiding sharing food, drink, utensils, cups and dishes. In fact, since family members may be contagious before they show symptoms, you may want to observe these practices whenever your child is taking medication.

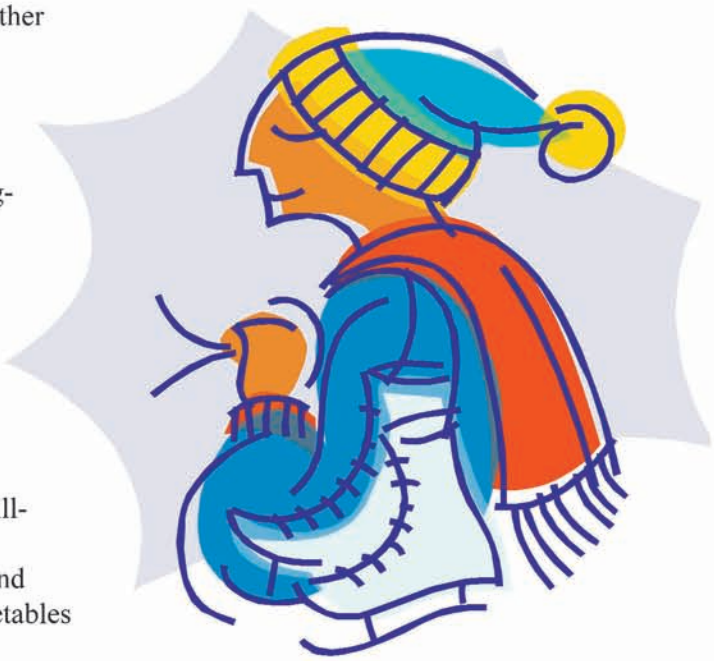
In "Myositis and You" Drs. Laura Mirkinson, Judy Beeler and Ildy Katona say that children being treated for JM may get more minor infections, like ear and sinus infections, than other children who are exposed. It's important, the authors say, to treat strep throat and infections around the nails as soon as they appear. Children sometimes develop a cheesy white layer in their mouths or in the vaginal area, and these may be yeast infections. There are antibiotics that can relieve these diseases, so report them promptly.

There are also infections related to a lower level of immunoglobulin rather than to myositis medications, say the authors. In addition to avoiding germs, they suggest having your child avoid unpasteurized dairy products, undercooked meat, raw eggs and shellfish, all of which may cause bacterial and viral illness. Well water should be boiled, and fresh fruit and vegetables carefully washed.

JM parents, who spent a couple of days in conversation with Dr. Reed, had a lot of questions on this topic. They also had a number of suggestions for other parents based on years of experience with their JM child during cold and flu season:

Don't bring germs home from your job. Parents – especially those who deal with a lot of children each day in their line of work – realize that they may be the most likely source of infection. At the Conference, parents said they wiped off surfaces of shopping carts, cleaned telephones and door handles, and asked those with colds not to get near them, especially if they were actively coughing and sneezing.

One mother who works with prisoners worried about HIV and Hepatitis C in that population. "These are blood-borne diseases," Dr. Reed said. "If there's an open cut, stay away from it. Within the blood, these viruses can hang around for a while." Other diseases, like lung and fungus diseases sometimes found in prisons, are easy to catch and can be devastating to a child with a suppressed immune system.



One father said he showers and changes as soon as he walks in the door to avoid spreading the minor diseases he's exposed to during his day working with school-age children. A mother, who works part-time photographing families, including babies, asks parents to take any used diapers with them when they leave so she doesn't have to handle contaminated trash. Others scrub chairs where babies have sat, wash hands constantly, and use masks when they can't avoid dealing with people with colds and flu. "Simply washing your hands all the time is one of your best defenses," Dr. Reed said. "I wash and use alcohol wipes all day and at the end of the day, wash my hands for

about five minutes." She cautioned those who wear gloves to touch possibly contaminated surfaces to remember to take the gloves off before touching their own face or the eating utensils they use.

Respond to local health emergencies. One father reported a flu epidemic in his community where even the schools were closed because so many teachers and children were sick. "We stayed home, ate what we had in the pantry, used a lot of alcohol for cleaning," said his wife. They avoided crowds and waited until the local public health picture was a lot better before venturing out. Their self-imposed quarantine applied to the whole family and ended up being a bit of an adventure, they reported.

Dr. Reed said she had the flu last year for the first time in many years and wore a mask for a month afterwards to see her patients. "Don't be afraid to take some measures to protect your child," she said. "We don't really know how long some of these things hang around." Don't worry that you'll offend someone with gloves or a mask. If appropriate, explain that you have a chronically ill child and must be especially careful not to become infected yourself.

Immunizations pose a challenge for JM children

Juvenile myositis families and Dr. Ann Reed discussed strategies for helping families decide when to immunize (vaccinate) children who are receiving immune-system-suppressing drugs. This is an important issue in families where a child has active disease and, in the case of live-virus vaccines, involves every member of the household.

Approach the issue with some common sense, advised Reed. First, make sure you're aware of immunizations your child has already received and which ones may be due while he or she is under treatment. If your child is being seen by a specialist, make sure he or she has a copy of the immunizations already given your child by another doctor. The recommended immunization schedule for children is published by the Centers for Disease Control and Prevention every year, and is available online at www.cdc.gov/nip. Another good source is the website of the American Academy of Family Physicians (www.aafp.org).

If you do not have a computer or a way to find this information online, go to your health department and get a printed copy of an immunization schedule. The schedule below, currently published by the American Academy of Family Physicians, may help, but keep in mind that the recommended vaccinations change from time to time.

- **Hepatitis B vaccine, an inactive virus,** at birth, prior to hospital discharge, or may be delayed with proof of mother's negative lab report. Three doses are generally given, finishing no sooner than 24 weeks.
- **Diphtheria, Tetanus, Pertussis, an inactive virus**, no sooner than six weeks, four separate doses, final dose at 4-6 years.
- **Haemophilus influenzae type b, an inactive virus**, no sooner than six weeks.
- **Pneumococcal vaccine, an inactive virus**, various schedules according to health and family issues.
- **Influenza vaccine (both inactive virus and active virus forms)** is administered annually to children from six months to five years. Many different schedules exist according to the health and age of the patient, so discuss with your doctor.
- **Measles, mumps, and rubella vaccine, an active virus**, no sooner than one year, with second dose 4-6 years.

See Winter, page 13

JUST FOR ME...

Ah Choo! I'm staying away from you!

Germs aren't cooties, bugs or soldiers in a germ army, but they fly through the air in sneezes, coughs, or even breaths. Germs can also spread in sweat, saliva, and blood. Some pass from person to person through something else, like shaking hands with someone with a cold and then touching your own nose.

The best way to protect yourself from germs is to steer clear of the things that can spread them:

Cover your nose and mouth when you sneeze and cover your mouth when you cough to keep from spreading germs.

Remember the two words germs fear — soap and water. Washing your hands well and often is the best way to beat these invisible invaders. Wash your hands every time you cough or sneeze, before you eat or prepare foods, after you use the bathroom, after you touch animals and pets, after you play outside, and after you visit a sick relative or friend.

Using tissues for your sneezes and sniffles is another great weapon against germs. But don't just throw tissues on the floor to pick up later. Toss them in the trash and, again, wash your hands!

Now that you know the facts about germs, you may still pick up a cough or a cold once in a while, but you'll be ready to keep most of those invading germs from moving in.

PARENTS ASK ABOUT FLARES, IMPROVEMENT

Informal questions raised at TMA's Annual Conference show parents often feel uncertain about how to measure improvement in their child's illness as well as how to recognize a flare. They spent many hours in informal conversations with Dr. Ann Reed and shared common-sense strategies with each other.

When improvement seems slow

Parents watching their children struggle to improve, getting only a little stronger over a long time, often feel discouraged. Part of it is watching their children themselves get discouraged: "I tell her she'll feel better if she takes her medication and goes to physical therapy. She gets frustrated if she does everything she's supposed to and doesn't feel much better," one mother said.

"We try to look at the big picture over a long time when deciding if something is working," Dr. Reed said. "You may find that even in a course of general improvement, there will be times when things look worse for a while." One family reported it took their daughter nearly a year and a half to see any improvement in her rash. Several people suggested keeping a diary so they could look back with some objectivity on the disease course.

Setting standards for measuring improvement

Measuring improvement in a complex chronic disease is something that challenges medical professionals as well as parents. Dr. Reed told the group about the international community of juvenile myositis specialists who work together to establish guidelines for deciding whether or not a treatment is working. This is tremendously important, not only for individual decisions, but also in drug trials, where it's crucial to have accepted standards to determine if a treatment is working. "We meet for a few days, and one of us will explain what he uses as an indicator of improvement, then someone else will have another measurement. We try to stay at it until we agree," Dr. Reed said.

The same process is used to come up with standardized treatment. "It shocked us all to see how much variability there was in the way we treated things," Dr. Reed said. "Getting together and hammering these things out has really helped us advance."

This type of collaborative effort has resulted in tremendous improvement in the outlook for childhood cancer. "This is what the pediatric oncologists did," she said. "They shared information in a systematic way until they learned enough from each other, to the point where childhood leukemia is considered completely curable." The old attitude towards treating diseases, which tended to be a little territorial, has changed, Dr. Reed said.

What to expect from a flare

Families questioned the definition of a flare. "If my child has a flare, will it be pretty much the same as the initial disease, or might it affect her differently?" a mother asked.

Usually, flares will reflect the same pattern as the original illness – for instance, if the skin was the main problem, the flare will probably be similar, Dr. Reed said. But this is not always the case. Although the initial disease onset usually has the most severe symptoms of the JM disease course, there are exceptions, Dr. Reed said. "There are also cases where perhaps the disease wasn't so bad at the beginning and responded to treatment. Then, later, the flare seemed much worse than the original episode."

Most children will have the "polycyclic" course of disease, meaning they will go up and down a bit after initial treatment. "If there's just a slight difference – a little weakness, say, or a more pronounced rash, we might wait a bit before bumping up or resuming the treatment," she said. If there are new symptoms, like a new ulcer or lung involvement, the physician will probably order a higher dose or add another drug."

Flares can also be relative, she said. "I had a young woman come in and I saw she was bright red. She was so strong normally (she worked on the family farm) that it was hard for her family to see she was experiencing a flare." She did not want steroids – she'd had them before and hated the side effects -- but she was getting weaker fast. Dr. Reed decided to give her oral prednisone for a short time – six weeks – and it worked out well. Another way of making a quick, early impact on the disease is to use solumedrol, an intravenous steroid drug. "This might hit the disease hard enough that we can buy some time for the other medications to work," Dr. Reed said.

In assessing treatment options, doctors try to use the minimum dose of steroids. "Sometimes we'll start with a high dose and just wait until something else – a medicine with fewer side effects – kicks in," she said. If the initial disease responded well, the flare will usually respond to the same course of treatment, but there are cases that don't, Dr. Reed said.

Finding support

Parents asked how they could find other juvenile myositis patients in their area. "We can't ask our doctor for phone numbers, obviously, since they're confidential," one mother said. "And I don't think it's appropriate to ask the doctor to have other people call us."

Dr. Reed said she thought it was perfectly appropriate for parents to make this request of their physician. "I know I'd be glad to do this," she said. "I see it as part of my job to

make sure that my patients have what they need."

Day to day tips from conference parents

Families have ingenious approaches to some of the realities of living with JM. Some of their tips:

- One family sets watch or phone alarms to go off when it's time for medication. "It's surprising, but with all the hustle and bustle of a school day morning, it's not unusual for us to all get in the car and realize we've forgotten to give her medication," said a father.
- All the members of a family take vitamins at the same time that the JM patient take his or her medications. "This makes her feel normal and the other kids feel important," a mother said.
- Families use video activity games, dancing and musical instruments to introduce gentle movement into the routine of their children.
- One family plans their IVIG schedule around their child's favorite nurse. If she's out, they'll wait a day or two.
- Families ask doctors to address their children rather than talking over them to the adult. "Our doctor is great about this," a mother said. "She knows that our daughter is going to be in the room and that we want her to ask questions."
- Teenagers are included in the decision process as much as they can be, especially when making the decision to change or increase medications. Parents mentioned a case where a teenage boy balked at steroids when his parents discussed the need for them but, after a private interview with his physician, felt reassured that they were necessary. He and his doctor reached a compromise that involved a shortened, but very intense, course of steroids that worked in his case.

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Winter, *from page 11.*

- **Varicella vaccine, an active virus**, minimum age: 12 months for first dose, second dose at 4-6 years.
- **Hepatitis A vaccine, an inactive virus**, no sooner than 12 months, with doses at other ages.
- **Meningococcal vaccine, an inactive virus**, no sooner than 2 years.
- **Polio (inactive virus)** various schedules. There is also a form with active virus.

It's very important to know whether a vaccine uses active or inactive viruses if you have a child currently under medications that suppress the immune system. Here's why: live-virus vaccines have live viral or bacterial parts that produce mild infection, which stimulates immunity to a virus or bacteria. Not only may the vaccine not produce the desired immune reaction that confers protection on your child; but it may cause an unexpected reaction, with symptoms exceeding those in a child whose immune system is working well. Live vaccines include the nasal influenza vaccine called FluMist, varicella (chicken pox); smallpox; yellow fever; measles, mumps and rubella, and some oral polio and tuberculosis vaccines, primarily given in countries outside the U.S.

Most vaccines are routinely given to children between birth and five years. At every stage of myositis, you should weigh the risks and benefits with your child's doctor.

Here's where the common sense comes in. If your child has active disease, it's not a good time to either catch up on missing vaccines or to administer the scheduled ones. Most physicians prefer to wait – even with the inactive virus vaccines -- until the myositis is well controlled. "Just wait until everything is settled down," said Dr. Reed. "One of the purposes of the immunization is to provoke an immune reaction," she said. "Obviously, if your child has very active disease and taking an immunosuppressant, he or she will not have the desired response." Family members are also advised not to get vaccines with live viruses because of the possibility of transmitting the viral infection to the child with myositis. The exception is the MMRII (measles, mumps, rubella) vaccine, which includes three strains of viruses but has little risk of transmission.

Resources

Besides the vaccine recommendations at www.aafp.org, there are other resources specifically addressing juvenile myositis patients. In "Myositis and You, "(available from TMA), Drs. Laura Mirkinson, Judy Beeler and Ildy Katona recommend that family members in a household with a susceptible child make sure they are up to date with immunizations using inactive viruses. This should include making sure everyone has a recent TB skin test and an inactivated influenza vaccine each year, the authors say.

Your doctor will be able to help you understand the various vaccines and their possible relationship to the drugs your child is taking. Exceptions to the warnings for avoiding vaccines with active viruses are those children taking the drugs hydroxychloroquine (plaquenil) and IVIG, both common treatments for JM.

Chapter 29 of "Myositis and You" also includes important information on dealing with the onset of childhood diseases in JM patients, particularly chicken pox and the flu.

At www.cdc.gov/vaccines/pubs/ACIP-list.htm, the CDC gives recommendations for immunizations for children with many different health problems.

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RESEARCH UPDATES

Current research reports

More research – sponsored by TMA and also by other private and public agencies – is being done in myositis than ever before. Members of TMA's medical advisory board spoke about exciting research in biologic medicine, gene therapy, juvenile myositis and the involvement of skin in autoimmune diseases. The presentations on research into skin and autoimmunity and progress in juvenile myositis will be presented in the winter issue of the OutLook.

Dr. Jerry Mendell, of the Columbus Children's Research Institute, spoke of the work he and Dr. Brian Kaspar have completed, successfully enlarging and strengthening the quadriceps muscle in mice and monkeys by using a common virus (AAV- the same virus that's so effective in carrying a common cold) to carry a follistatin gene into the quadriceps muscle. Follistatin blocks myostatin, which inhibits muscle growth, so Drs. Kaspar and Mendell are testing whether this particular gene therapy might be used to help promote muscle growth and increased strength in humans who have lost muscle mass and strength.

So far, the safety data is good. Dr. Mendell reports no clinical adverse effects in mice or monkeys; normal reproductive ability in mice and monkeys; and no organ damage in test animals. Phase two of the study will test the safety of the vector, or the virus that carries the follistatin gene into the muscle. This phase of the trial will also establish the best dose of the virus, confirm improved muscle strength in the thigh muscles, and measure the immune response to the vector.

The trial moves closer to human participation. In July, the researchers reviewed the trial with the FDA, which approved their protocol pending a toxicology safety study. Drs. Mendell and Kaspar are preparing this next step, which will take about six months and cost about $350,000.

The Myositis Association will let members know immediately when the trial has moved to Phase 3, or human research.

Dr. Todd Levine of Phoenix Neurology Associates showed two cartoons: one of a nuclear bomb destroying everything for miles; and one of a personified bomb in thick glasses studying in a library. "Here we have a nuclear bomb and a "smart bomb," he said. "Drugs that wipe out your immune system to treat myositis are like the nuclear bomb; biologic drugs that target specific sites are the smart bombs."

One very specifid target is a certain type of cell, B cells that are players in polymyositis, dermatomyositis and juvenile dermatomyositis. In the Rituximab in Myositis (RIM) study, researchers are conducting the largest controlled trial ever done of these diseases, to see if B cells are successfully depleted and muscle strength improved. The trial has targeted 225 patients, and 155 have enrolled so far through multiple international centers.

Another drug, called MEDI-545, targets Interferon-a, a substance that's over-expressed in polymyositis and dermatomyositis patients. The study of this drug, now in Phase I B, is to test for tolerability, but will also look at muscle strength improvement.

Etanercept (Enbrel) has been successful in treating rheumatoid arthritis patients, and researchers are studying it in dermatomyositis patients in a multi-center trial. It blocks TNF alpha, a factor at play in these diseases.

Finally, said Dr. Levine, it's important to realize that we are not always able to predict how people will react to drugs in human trials. "The immune system still confounds us," he said.

TMA Resources: to find out what trials are currently enrolling patients, go to the TMA website and click on Research.

■ ■ ■

TMA going forward with international, treatment-oriented research

The Myositis Association works in international collaborations and funds researchers all over the world, Dr. Fred Miller told members at TMA's Conference in Denver. Presently, the TMA Board of Directors is concentrating on treatment, Dr. Miller said, although past funding of studies of disease mechanisms has helped move TMA to this point.

Recent funding focused on improving therapies include studying if a new high-tech "smart brace"

device is effective for knee instability in IBM; investigating if a drug that improves cognition and reduces amyloid beta in Alzheimer's patients will also work to reduce the effects of amyloid-beta in the IBM-experimental human muscle culture mode; and to see if diet and exercise can prevent, halt, or reverse the disease process of IBM.

To make sure TMA's resources are used in the wisest way possible, the Medical Advisory Board looks not only for treatments, but ways to predict which patients will benefit from specific treatments. Since myositis is not a simple hereditary disease, there are a number of genes as well as other factors involved in the disease process. Subgroups emerge that have certain characteristics in common, and future researchers will try to identify -- based on genetic and environmental risk factors – how many myositis subgroups comprise these syndromes. Finally, said Dr. Miller, we may be able to turn some of this insight to the prevention of some forms of myositis in the future.

Tools for the future will emerge:

- New environmental and genetic risk and protective factors
- Mechanisms for some forms of myositis defined
- Better animal models and drug development
- Better ways to measure myositis activity and damage
- Better treatments for muscles, skin, lungs, GI, heart
- New, more personalized therapies to induce remission and reverse damage – drugs, biologics, cell and alternative gene therapies, medicines
- More international collaborations and coordination in basic and clinical myositis research.

Environment, *from page 2.*

atrophy many years ago. I have two twin male cousins with MS. I also have Sjogren's syndrome and cutaneous lupus.

Others on both sides of my family have had thyroid issues. I would like to know if I am more predisposed to environmental factors than these relatives and, if so, what these might be.

Dr. Miller: This is a good example of why we think there are genes in some families that predispose to many different autoimmune diseases. These genes are the keys to enter the theater of autoimmunity.

Other genes and environmental exposures define the particular disease that develops (they help escort a person to their individual seat in the theater of autoimmunity). The idea here is that a particular genetic make-up may be more susceptible to a particular exposure – so in reality, it is the gene and environment interaction that is most important. So to answer your question, while we have identified some of these genes, we don't yet know which particular genes interact with which environmental exposures to cause disease and therefore we can't give advice about preventing disease – which is our ultimate goal here.

Question: Are we any closer to knowing what causes myositis?

Dr. Miller: YES! Each year we learn about new genes and some hints at possible environmental causes (ultraviolet radiation, certain viral infections, certain drugs, excessive stress) and we learn more about the mechanisms going on in the muscle and other tissues that are affected. Still we have a long way to go, and the studies are expensive and take a long time.

Question: Is myositis definitely an autoimmune disease?

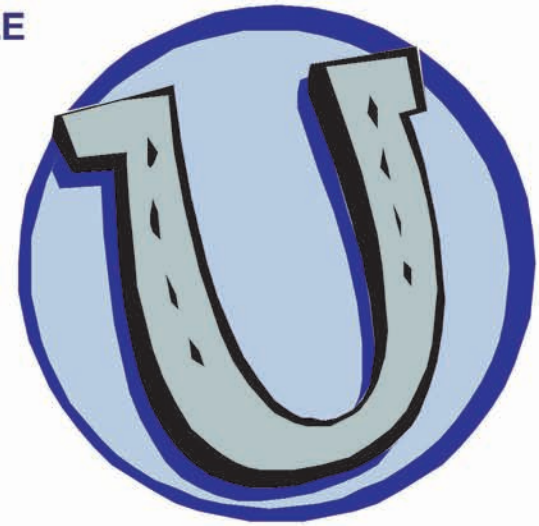
Dr. Miller: Most researchers think that polymyositis and dermatomyositis are autoimmune diseases but there remains some controversy about inclusion body myositis. This is because there are two basic forms of diseases with the abbreviation IBM.

Inclusion body myositis – the kind that has inflammation in the muscle biopsy and higher CK levels – is probably an autoimmune disease, but inclusion body myopathy – the disease that does not have inflammation in the biopsy and lower CK levels and more often runs in families – is not an autoimmune disease but likely a form of dystrophy. IBM is probably many different diseases. Some of them are probably mostly genetic and others involve gene-environment interactions. Some researchers hypothesize that a virus or other environmental agent may be involved but there is no good evidence for this yet.

Question: How great a part does the environment play in myositis?

Dr. Miller: Ah – the million dollar question! Well, I think it has a lot to do with it, but most of my suspicions are based on anecdotal single cases. These include cases of a patient developing myositis after taking a drug or supplement and then getting better when it is stopped and then the myositis starting up again after the drug or supplement is started again; or a young woman developing dermatomyositis just after her first severe sunburn; or a child in a large family, who has an identical twin, developing JDM after being the only one in the family to get a severe strep throat, and many more examples. These individual cases suggest to me that the environment is important and that each person (or each set of genes) may have a particularly dangerous exposure that should be avoided, but more research is needed to prove this and understand what each individual needs to avoid.

AND WE HAVE A WINNER – MYOSITIS MIRACLE



Nearly 100 TMA members submitted suggestions for the name of the "myositis racehorse" and we are pleased to announce that Myositis Miracle is the name Spendthrift Farm chose from the names suggested. Spendthrift will be selecting one of their horses early in 2009 to race as Myositis Miracle, and we will all be cheering him or her on as the first $50,000 earned by the horse will be donated to TMA. Two TMA members suggested this name and they will each be receiving lifetime memberships to TMA. Thanks to all who sent in names and let's hope that our horse lives up to its name and delivers a myositis miracle in the near future!

THE MYOSITIS ASSOCIATION

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