THE MYOSITIS ASSOCIATION

OUTLOOK EXTRA

FALL 2007

Conference Report

In this issue

Those at The Myositis Association's 2007 Annual Conference attended dozens of sessions with valuable information on topics ranging from research trends to coping skills. This issue of *The Outlook* summarizes some of the important points from the medical panel and some of the sessions related to myositis research, diagnosis and treatment. Many of the Conference presentations can be viewed in their entirety on the TMA website at www.myositis.org. Click on "Updates from Seattle" under "In the Spotlight."

The Outlook's Winter issue will have information on complementary therapies, including acupuncture, Tai Chi and Yoga, from Conference presentations on these topics as well as interviews with additional experts in these fields. There will also be a special section on skin care, and advice on how those with physical limitations can prepare for a disaster emergency.

Because many of the topics covered at the Conference – such as medication side effects, exercise, research and autoimmunity – apply to both adult and juvenile forms of the disease, *The Outlook* and the *JM Companion* publications are combined into this one report. The "Answers for Families" section that begins on page 10 contains highlights of the four-hour interactive session with JM families and medical professionals.

Experts discuss progress in myositis and related research

Animal models suggest complex causes

Kanneboyina Nagaraju, DVM, PhD, *a veterinarian and veterinary immunologist, trained at the National Institutes of Health in Dr. Paul Plotz's laboratory and established an independent laboratory at the Johns Hopkins University School of Medicine. He directs a pre-clinical mouse functional drug testing facility for muscular dystrophy funded by the Department of Defense. His research is supported in part by The Myositis Association.*

It's not hard to see the changes myositis causes in human cells when you see a biopsy in the lab. You'll see an infiltration, an invasion "akin to an army," said Dr. Kanneboyina Nagaraju, with cells flocking to the muscle fibers and the fibers changing shape and becoming larger and smaller than normal. The cells invading the muscle are inflammatory cells, extremely powerful cells able to enter the cells and communicate with each other. Stopping the communication between the cells is one of the keys to solving myositis. It's no easy task because there doesn't seem to be a main communicator in myositis.

Nagaraju said people from so many different backgrounds, environments, genetic types and ages are myositis patients that it becomes very difficult to find any common threads. He found himself with the difficult job of creating a mouse model for myositis that would be consistent and that would develop the disease in a predictable manner under controlled conditions.

How do you create a disease in mice when you don't know its cause? This was Nagaraju's dilemma. With multiple genetic weaknesses and multiple environmental causes, hitting upon the right combination of factors would be close to impossible. Instead, his team looked at slides of people already affected by myositis and found a molecule called MSC present in excessive amounts in the muscle. They decided to create an excess of that molecule and see what happened. To their surprise, the mice displayed both muscle weakness and ongoing damage.

When researchers stopped the overexpression, though, the disease did not, telling them the disease at some point becomes self-sustaining. They also found that immunity accounted for only a little more than half of the disease activity.

"We don't know what else is going on inside the fibers," Nagaraju said. He predicted that therapies developed to address myositis will be very sophisticated, addressing immunity, inflammation and the muscle function itself. He also said that myositis is a disease that will eventually have extremely personalized treatment, changing depending on the duration of the disease and the extent of present damage as well as the symptoms and type of myositis. "The disease in

Continued on page 3

Published by: TMA, Inc.
THE MYOSITIS ASSOCIATION
1233 20th Street, NW, Suite 402
Washington, DC 20036

P: 202-887-0088
P: 800-821-7356
F: 202-466-8940
Email: tma@myositis.org
Web: www.myositis.org

Executive Director: Bob Goldberg
Editors: Theresa Reynolds Curry
Kathryn Spooner

Patient panel offers inspiration

Hearing the trials and tribulations of those who live with myositis but continue to strive to achieve their personal goals can be very moving. Among the patients invited to be on the Patient Panel and share their experiences at the Annual Conference were three remarkable individuals living with myositis:

In Oregon, Shannon Young, a dermatomyositis patient and Portland television news anchorwoman, tried and abandoned her dream of running a 10-mile race before coming to the Annual Conference. Young told the audience that "winning doesn't always mean finishing the race." Sometimes, she said, just training for it is a victory. Training for the race is one of her many victories since being diagnosed: She's also now learning to play the banjo when not paddling her kayak as much as she can.

Last summer, Steve Morris, a giant-cell myositis patient and middle-school teacher, set out on a 3,000-mile journey on the Harley he thought he'd never ride again. He raised thousands of dollars for myositis patients and research. Morris recounted in a unique and very entertaining style his experiences, personal setbacks and achievements during a trying and difficult first year. The lesson he learned and imparted to the audience: "Don't focus on myositis when you think about your dreams. Find a way to do what gives you strength and satisfaction."

Madge Franklin, an inclusion-body myositis patient and mother of a large family, shared the many ways her children have helped her deal with the disease and raise money to help all those with myositis. In addition, she continues to pursue her personal interests, including hosting an annual bridge tournament that raises a significant amount of money for myositis research and support.

Among her children, Madge's son Willie ran the Baltimore Marathon to raise money for TMA on behalf of his mother, and involves friends in other fun and successful fundraising events.

"The bottom line is that my friends and I have put forth our efforts to raise money for TMA in order to show my mother how much she means to all of us," Franklin said.

He says his mother's illness has had a major impact on everyone in her large family. "She was and still is a very generous and giving person, but myositis forced her to change her mindset and actually accept help from us. You would be surprised just how many people are willing to help if asked."

The Myositis Association is a participant in the Combined Federal Campaign; #11526 in the CFC brochure.

Progress and research, continued from cover.

day one, or month one; year one or year 10 is not the same," he said. "The disease is dynamic, very different in every case. I want to be able to reverse it while it is still reversible – and that may mean finding it when it is still asymptomatic." With science now being able to take a look at 30,000 genes in a couple of hours, there's reason for optimism, he said.

The promise of stem cells

"Along with the controversy surrounding stem cells, there's a lot of hope," Nagaraju said. These are cells with an enormous ability to proliferate and the capacity to form any organ or any tissue. They also repair and regenerate damaged tissue.

"This is what we need for myositis," Nagaraju said. There are embryonic stem cells, but also those that exist in adult form. He explained: Every tissue has a small pool of cells that helps when tissue is damaged. While embryonic stem cells can form any tissue, the adult form of stem cells is limited to a precise form of tissue or organs, whether it be skeletal muscle or new hair follicles.

Adult stem cell therapy is used quite extensively for cancer, and continues to be used to replace and reset the overly aggressive immune system.

There are still a lot of problems in figuring out how best to use adult stem cells: There are graft failures, a limit to the numbers that can be made, and some forms are limited in survival. "They are ideal for a condition such as myositis," Nagaraju said, "but outside the lab they have a tendency to grow into tumors." There are also problems with distribution and delivery as well as complications. Speaking both of his work with mice in the lab and work with stem cell therapy, he cited a need for support for research into rare disease. "Pharmaceutical companies aren't going to do it," he said.

In answering a question, he noted that there is presently no DNA test for myositis. "It's multi-genetic, involving a subtle weakness in 12-18 genes," he said. "One defect in one gene wouldn't mean anything, but if there's 12-18, that's when you show symptoms."

What research tells us about polymyositis and inclusion-body myositis

Andrew Mammen, MD, PhD, *is an Assistant Professor of Neurology at Johns Hopkins University in Baltimore and Co-Director, with Dr. Lisa Christopher-Stine, of The Johns Hopkins Myositis Center. Dr. Mammen has a special interest in myositis and cancer and in the relationship between statins and myositis.*

Looking back a couple of years, you'll find several hundred research studies examining polymyositis and inclusion-body myositis. "This seems like a lot," says Dr. Andrew Mammen, "but if you look for Alzheimer's Disease studies published in the same time period, you'll find more than 7,000 papers, so the amount of research going on in myositis is really quite small when compared to other, more common diseases."

In his summary of selected recent research, Dr. Mammen reviewed studies having to do with muscle regeneration as well as with disease progression and treatment in myositis.

Two of the recent studies were of possible therapies. One, a pilot study of etanercept (Enbrel) for inclusion-body myositis by Barohn et al, was published in *Neurology* in 2006. The drug, a tumor necrosis alpha inhibitor, was given to nine patients who were treated for an average of 17 months. Researchers tested hand strength and elbow flexion in treated patients and compared these two measures of strength with the same measures in untreated patients. Although they found no difference at six months, handgrip at 12 months was improved in the patients taking etanercept. "This tells us a couple of things," Mammen said. "We need larger trials and it appears we really need *longer* trials to test the efficacy of drugs for IBM."

Another study – Rituximab for Refractory Polymyositis: An Open-label Prospective Study – was published by the *Journal of Rheumatology* in 2007. Rituximab, an antibody that binds to CD20 on B-cells, was studied in four patients who had not responded to steroids plus two other medications. Of the four, two of the patients had clinically meaningful improvements in strength. "This just gives us more reason to be hopeful about the large rituximab study led by Dr. Oddis," Mammen said.

Dr. Mammen reported on a 2007 study of an intensive exercise program published by Alexandersson et al in *Arthritis & Rheumatism*. In this small study, five DM and three PM patients on prednisone and other medications exercised three days a week according to a prescribed program. Their routine included a warm-up and 45 minutes of exercise, ending with five minutes of stretching. Over seven weeks, they gradually increased the intensity of exercise, adjusting the weights at the third and fifth weeks. Biopsies at the beginning and end of the program found that exercising did not increase inflammation in any of the patients, even in patients with active disease.

Researchers in Britain and Sweden conducted another study to see if taking creatine supplements with exercise was more effective than exercise alone in improving muscle function in people with dermatomyositis or polymyositis who had weakness as a symptom. In a six-month trial, 37 patients were randomly assigned to one of two groups, either the group taking creatine supplements or the group taking a placebo. All of them did home exercises. The researchers found that taking creatine supple-

Continued on page 4

Progress and research,

continued from page 3.

-ments combined with home exercise improved muscle function without significant adverse effects. They were tested by walking, climbing stairs, and getting up quickly, Mammen said. "These functional outcomes are very important." Mammen often recommends creatine for his patients. "We also need to test this in IBM," he said.

Statins and myositis

"We see an awful lot of people who are put on statins and then develop myositis," Mammen said. He cited a recent paper, a study done at Kaiser Permanente in Colorado.

The Kaiser study looked at people from the ages of 40 to 89, and included more than 187,000 patients. Researchers identified myositis by a blood test that showed inflammation at ten times the normal level and by claims submitted by patients who identified themselves as myositis patients. The two-fold increase (compared to those not taking statins) in alleged myositis and the nine-fold increase in those taking fibrates and statins were significant.

"When you see that one out of 1,000 developed myositis, this is a large number," Mammen said. The two statins appearing most often in the increased muscle disease were lovastatin and simvastatin.

There's a disclaimer, Mammen said: "Statins are also very useful drugs. It's estimated that for every 40 people who take them, a significant heart attack is prevented in one of them."

This research may actually underestimate people who develop muscle disease, Mammen said, since myositis patients, particularly IBM patients, often do not have ten times the normal limit of inflammation as measured by the blood test. "More research is needed," he said. "The real question for most people here: Is it safe to use statins if you already have myositis? Clearly, more study is needed."

Polymyositis misdiagnosed

It's clear to all of us that polymyositis is often misdiagnosed as another disease, Mammen said. He was interested in a study that showed that a number of people with dysferlin gene mutations – 10 out of 40 in a 2007 study – were originally diagnosed with polymyositis. "We often talk about how hard it is to get a correct diagnosis of PM," he said. "It appears there's also a chance that you may have a different disease."

Drugs in the pipeline

Any drug that promotes muscle regeneration is also of interest for possible use for myositis, Mammen said. He cited some recent papers looking at a fairly common medication called Losartin.

This drug, normally prescribed for high blood pressure, has been used with some success in patients with Marfan's syndrome, a condition that prevents patients from increasing muscle mass despite physical exercise and causes serious artery problems. The 2007 study showed that Losartin normalizes muscles in mouse models of Marfan's. In mice with a genetic form of muscular dystrophy, Losartin also increased strength. "There's a great deal of interest in this," Mammen said, "but we don't even know yet if it will work in humans with muscular dystrophy."

Other work of interest is being done in what's called the "TGF Beta Pathway." It's already known that a substance called myostatin limits skeletal muscle growth. The "super" animals that appear from time to time in the media are those who have no myostatin to limit growth. Animals and humans lacking myostatin have a twofold increase in muscle mass. Another substance, follistatin, binds myostatin. Animals and humans producing greater amounts of follistatin have even greater muscle mass – about four times normal – so scientists theorize that it may bind not only to myostatin, but to other substances that suppress muscle growth.

This may be relevant to myositis, Mammen said, because we know that TGF is present in dermatomyositis. "Turning it down might be helpful," he said. TGF is also found with beta amyloid in the muscle fibers of IBM patients.

Disposing of beta amyloid

Beta amyloid is very important in the pathogenesis of IBM, Mammen said. Usually, cells get rid of it when they accumulate too much, either by way of the ubiquitin-proteasome system or by lysosomal degradation, a term for the process whereby intracellular proteins are carried to lysosomes by autophagosomes. A 2007 paper points to the possibility that harnessing the autophagic pathway could be a helpful treatment for IBM.

IBM and PM questions and answers

In the IBM question-and-answer session, Dr. Mammen fielded questions about Losartin and statins:

- Should IBM patients ask their doctors for Losartin? Patients with IBM who are on blood pressure medication might ask for Losartin in place of their current medication, Mammen said.
- Are statins a possible "trigger" for IBM? The role of statins is still unclear, Mammen said. It is possible that statins, especially statins and fibrates together, cause a low level of muscle damage that might begin the disease process in people who are genetically predisposed.

Dr. Chester Oddis of The Myositis Association Board of Directors answered patient questions about polymyositis:

Rituximab danger, success. Dr. Oddis, who leads the study, doesn't know how patients in the multi-center trials of rituximab are doing because it's crucial to the design of the trial that he not know. Keeping track of adverse effects is part of a collaborative effort, said Oddis; and so far,

there have not been major ill effects from the drug. A neurological disease called progressive multifocal leukoencephalopathy (PML) has been reported in some patients with SLE (lupus) who take rituximab. "The onset of PML seems to be associated with long-time suppression of the immune system," Oddis said. The trial, which will enroll 76 adult PM patients; 76 DM patients; and 50 JM patients, is about a quarter of the way through enrollment.

Celiac disease and myositis. Like other diseases that overlap with myositis, celiac disease is of autoimmune origin and is more common in people with myositis than in the general population. "It's more of a problem in DM than in other forms of myositis," Oddis said.

PM and Jo-1 antibody. It's a classic cluster, Oddis told patients: PM, lung disease, fevers, Raynaud's Syndrome. "If you have all of these, take a look and you may very well find out that you have the Jo-1 antibody." Oddis tests for the antibody: "It may not make any difference in your treatment," he said, "but it kind of helps me know what to expect and plan for."

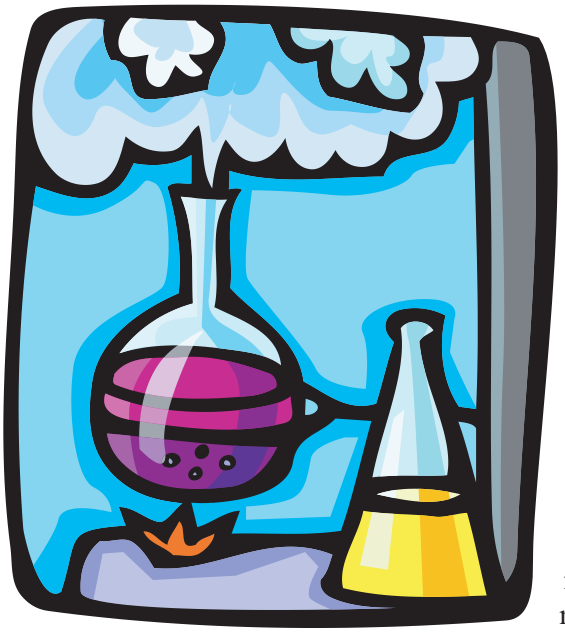
Long-time methotrexate use. "You can't just bang away with prednisone as your treatment forever," Oddis said. "Methotrexate not only helps suppress myositis symptoms; it also reduces the amount of prednisone needed for treatment." Oddis said some people have been on methotrexate for decades, with no ill effects.

The importance of exercise. "It used to be we said, 'go to bed;' now we say, 'exercise.' Even if the disease is active, we say to get up and do what you can." Obviously, if the disease is extremely active or you are in pain, you make an exception, Oddis said. In a recent study of exercise and myositis patients, researchers confirmed by biopsy that no harm was done by exercise, even with active disease.

Progress in treating dermatomyositis

Richard Sontheimer, MD, *is Professor and Vice-Chair, Department of Dermatology, and Richard and Adeline Fleischaker Chair in Dermatology Research at the University of Oklahoma Health Sciences Center. He is a former member of the research committee of TMA's Medical Advisory Board and has a special interest in amyopathic dermatomyositis as well as classic DM.*

When you think of dermatomyositis, with its unmistakable skin signs, the first question to solve is how the immune system works in the skin to cause rashes.



Other autoimmune diseases – as well as diseases and injuries that are not autoimmune – include a rash. There are literally thousands of skin diseases, but some special characteristics allow physicians to make the DM diagnosis.

The first characteristic of the rash is its red color. Why is it red? Increased blood flow tells us that the skin is inflamed. In Caucasian and other people with light complexions, it's very easy to see. In people with heavily pigmented skin, it's sometimes hard to see the redness, especially at first.

Inflammation is the skin's attempt to show that it's been injured, or (in the case of DM, at least) it *perceives* that it's been injured. The other property of a rash – that it itches – is part of the way that skin expresses what might be pain in another organ. Our skin is likely to itch rather than feel pain.

As in other autoimmune diseases, inflammation is the attempt by our immune system to protect our skin. In the case of DM, it's gone haywire and is attacking its own tissues.

There's a common example of this reaction caused by an outside substance. We're all familiar with the red rash caused by poison ivy. The oil from poison ivy gets on the skin and injures it, and the immune system responds by producing a rash, trying to protect the skin. In bad cases, it will even cause the skin to blister. That blistering is seen in DM occasionally, too. There are so many cells coming to the aid of the skin that the skin actually forms blisters.

When scientists look for answers for human diseases, they look first to animal models, but there is no animal model for skin inflammations. Researchers study the skin by taking little pieces of skin (this is called a "punch biopsy") to be studied by a dermapathologist. Under the microscope, the punch biopsy of DM clearly shows the army of cells accumulating in the muscle, creating damage to the muscle fibers. The skin responds by getting red.

This is not an army we want to wipe out: We need this army of cells – and substances made by cells – every day to help us ward off cancer and other disease. The new approach to treating many autoimmune diseases is to look at the signaling patterns.

Continued on page 15

DIAGNOSIS AND BEYOND

What your physician learns in the lab

Michael D. Weiss, MD, *is Director, EMG Laboratory, and Co-Director, MDA/ALS Center, at the University of Washington Medical Center and also serves as Assistant Professor at the University of Washington School of Medicine. He sub-specializes in neuromuscular disorders in a new clinic at UWM treating patients with a variety of neuromuscular disorders including peripheral neuropathy, myopathy, ALS, and myasthenia gravis.*

Once diagnosed, myositis patients sometimes wonder why their physicians continue to refer them for tests. "I know I'm weak and I believe that my doctor is right and that I do have myositis," said one Seattle-area patient at the Annual Conference. "Why does it matter which kind I have, and why does my doctor keep ordering additional tests?"

Dr. Weiss says the exact nature of the diagnosis is vitally important, not only for patients to get the best possible treatment, but also to suggest other health risks and avoid treatment that could be both pointless and harmful.

For instance, if you have dermatomyositis or polymyositis, chances are you'll respond to corticosteroids, chemotherapies like azathioprine and methotrexate, and sometimes IVIG. If your physician determines you have DM, you may have a malignancy workup that includes CT scans of the body, a mammogram for women, a colonoscopy, and other tests to find malignancies.

If you have inclusion-body myositis, which is often confused with PM, your doctor may have asked for more than one biopsy to be sure of the diagnosis. The distinction, although sometimes difficult, is important, says Weiss. IBM patients do not ordinarily respond to corticosteroids or chemotherapies, so it makes sense not to expose them to the potential side effects. More IBM patients than PM patients report trouble swallowing, so your physician will want to monitor your swallowing carefully. The risk of malignancy is not elevated much, so your cancer screenings will be close to what's recommended for other people your age.

Most likely you've had at least a blood test and an electromyograph (EMG) if you've been diagnosed with myositis. Weiss describes how these tests and others help your physician identify and monitor your disease.

Blood testing

Creatine kinase (CK) leaks from damaged muscle and its elevation – typical in all forms of myositis – shows up on this test, often called simply a CK test, or part of a blood enzyme test. Here are some things the test will show about your disease type:

- In DM and PM, the CK may be two to 100 times the normal reading.
- In IBM, the elevation is less, between two and 10 times normal.

Aldolase, another enzyme that leaks from damaged muscle, and **alanine aminotransferase** and **aspartate aminotransferase**, enzymes that are found in both muscle and liver, may also be elevated. These markers are not as reliable, since they could also indicate liver disease.

Erythrocyte sedimentation rate indicates inflammation and is elevated in about half of PM and DM patients, less in IBM patients.

Antibodies, substances generated by the immune system to fight infection, are elevated in the majority of PM and DM patients, but not in IBM patients. The antibodies elevated in myositis patients are **antinuclear antibodies**, meaning they target the cell's nucleus and suggest a self-directed immune response. This elevation is not seen in IBM. There are **myositis-specific antibodies (MSAs)** that are normally seen only with a form of myositis and not with any other disease. About half of PM and DM patients (not usually IBM patients) have these in their blood, and they are associated with certain disease types:

- **Jo-1** and other **amino-acyl tRNA synthetases antibodies** are seen with "anti-synthetase syndrome," which includes myositis, often interstitial lung disease, mechanic's hands (rough, hardened hands) and fever.
- **Signal recognition particle (SRP) antibodies** are associated with rapidly progressing PM, severe weakness and cardiac involvement.
- **Mi-2 antibodies** are associated with "classic DM" (shawl sign, heliotrope rash, cuticular signs).
- **P155 antibodies** are associated with the juvenile form of DM.

There are also **myositis-associated antibodies (MAAs)** seen in other diseases and also in the blood of up to half of myositis patients:

- **PM/Scl antibodies** are associated with PM overlapping with scleroderma.
- **Ku antibodies** are also seen with PM-scleroderma overlap.
- **Antibodies to small nuclear ribonuclear protein** are seen with PM overlapping with mixed connective tissue disease.
- **Antibodies to cytoplasmic ribonuclear protein**, including **Ro/SSA** and **La/SSB**, are seen with PM overlapping with Sjogren's disease.

Electromyography (EMG)

In an EMG, a needle electrode is inserted into a muscle and information relayed to a computer that's connected

to a video screen and loudspeaker. In all forms of myositis, needle movements in resting muscle show abnormalities, called **fibrillation potentials** and **positive sharp waves**. With contraction of the muscle, waveforms called **motor unit action potentials** appear. They are smaller in amplitude and shorter in duration than normal. It's rare for a myositis patient to have a normal EMG, and less than 10 percent do.

Muscle MRI

Magnetic resonance imaging (MRI) uses a tube-like machine with strong magnets to visualize muscle and other tissue. Your physician might order an MRI to detect signs of inflammation or damage to muscle, or check involvement of specific muscles like the quadriceps to distinguish IBM from PM/DM.

Weiss referred to a 2002 study that showed how an MRI helped diagnosticians distinguish between PM and IBM. They chose 220 patients, each with a diagnosis of either disease confirmed by muscle biopsy. They found the PM patients showed inflammation only; the IBM patients also showed fatty infiltration and atrophy; and that lower arm and leg involvement was more prominent in IBM. Asymmetry (greater weakness on one side than on the other) was also more common in IBM patients.

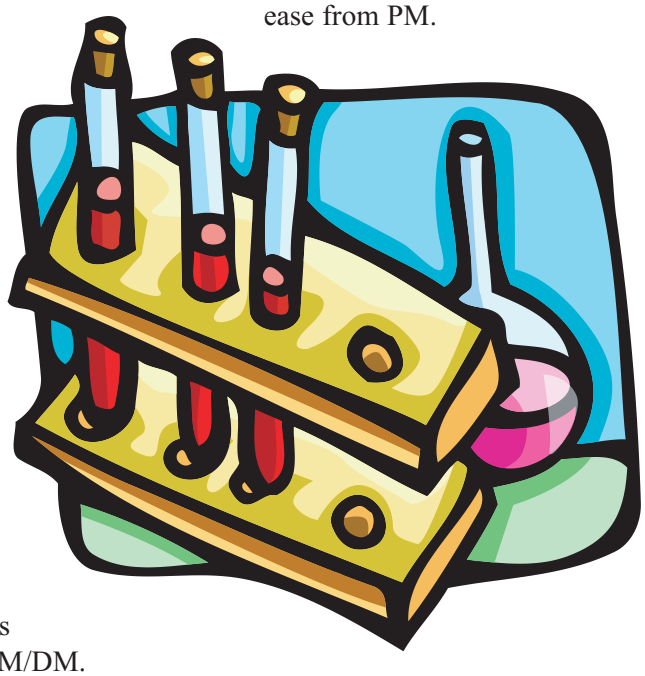
Physicians sometimes order an MRI to pinpoint the best muscle to target before a muscle biopsy.

Muscle biopsy

In a muscle biopsy, a small piece of muscle tissue is removed. Usually, local anesthesia is used and the patient is awake. The muscle tissue is examined under a microscope to identify the changes caused by myositis.

In PM and IBM, the biopsy normally shows evidence of inflammatory cells invading normal muscle fibers, causing damage.

In IBM, the biopsy will also show muscle fibers with small holes in them. These are called **rimmed vacuoles** (the "inclusion bodies" that give IBM its name) and distinguish the disease from PM.



In DM, the inflammatory cells are more likely to be found surrounding or invading **blood vessels** in the muscle rather than the muscle fibers.

Skin biopsy

Sometimes a skin biopsy in the right setting will allow a physician to diagnose DM and avoid a muscle biopsy, which is a more invasive and lengthy procedure. Or it may be used to confirm a diagnosis, showing inflammation around blood vessels within the skin. This kind of inflammation is also found in other rheumatologic disorders that do not affect the muscle.

The diagnostician's dilemma

While IBM and DM have unique characteristics that emerge during screening, PM is a more difficult disease to nail down, Weiss said. It's often a disease that's diagnosed simply by ruling out IBM or DM. A 2003 study published in Neurology examined 165 patients diagnosed with PM between 1977 and 1998. The authors reevaluated all muscle biopsies, as well as the initial clinical examinations and follow-up visits.

After eliminating the patients who had obvious IBM or muscular dystrophy based on the reevaluation, the authors used the criteria of clinical appearance combined with at least twice the normal level of creatine kinase and the inflammatory invasion of normal muscle fibers to confirm the remaining cases. Only nine of the 165 cases (5 percent) fit these criteria. Those cases with the elevated CK but little or no inflammation were considered "possible myositis," and the majority of initial and follow-up patients fit in this category. The study concluded that PM is over-diagnosed and that the majority of patients may have a type of unspecified or undifferentiated myositis. In the future, discovery of additional autoantibodies and better screening techniques may allow physicians to find clusters of patients with unspecified myositis who have features and disease outcomes in common.

Other predictions for the future of myositis diagnosis from Weiss:

- Physicians will be able to make better distinctions between IBM and PM by patterns of muscle injury on MRI.
- New antibodies will be used to increase detection of amyloid (IBM) in muscle biopsies.
- Researchers will find new genetic markers in patients that will predict a predisposition to a specific form of myositis.

Slides of disease signs as well as diagnostic tests are included in Weiss's presentation, on The Myositis Association web site at www.myositis.org.

IMMUNITY, SUSCEPTIBILITY AND IVIG

***Tahseen Mozaffar, MD, FAAN**, completed his undergraduate and medical education in his native Pakistan. After training in neurology at Barnes Hospital in St. Louis and Washington University, he joined the faculty at University of California Irvine in 2000, assuming the directorship of the neuromuscular program, and is the director of the MDA clinics at UC Irvine and director of the ALS center.*

The same system that leads the charge against foreign proteins, viruses, bacteria and toxins, providing us with immunity, can turn on our own body, a condition we call "autoimmunity."

The normal development of our immune system allows it to recognize the difference between the normal parts of ourselves and those that are foreign and likely to cause harm. This recognition is stored in memory cells, and our body "remembers" to recognize and tolerate itself, and to launch attacks against the substances seen as harmful.

In autoimmunity, this response is confused. "All of a sudden our own proteins are perceived as foreign, and the body mounts an immune response," Dr. Mozaffar said. All kinds of chronic diseases result, affecting every bodily system: nerves and muscle, skin and organs.

The causes of autoimmunity are complex. Sometimes it's an infection where foreign proteins are similar to the body's own proteins. A form of Guillan-Barre syndrome is an example of this type, where some of the proteins on the surface of the bacteria are exactly like the proteins in human nerves. The cells – programmed to recognize and destroy the protein – begin attacking human nerves.

Sometimes an infection or inflammation causes the body to lose control of the regulatory process. There may be a "clonal" expansion of one type of cell, or a loss of memory cells that tell the body what's foreign. Sometimes there's an expression of protein in the cells promoting immunity.

Scientists agree that before any of this happens there's already a situation where people are susceptible. There are definitely some groups more likely to develop autoimmune diseases. There's a unique genetic signature in certain people that causes a predisposition. Who are these people?

- **Women**. Women are much more likely to have autoimmune diseases: In some diseases the ratio is more than nine women for each man. Scientists speculate that female hormones have a role, although pregnancy often provides protection.

- **People in northern latitudes.** Autoimmunity occurs more in colder climates, in areas farthest away from the equator and usually in areas once populated by Vikings. One theory is that less exposure to sunlight (and thus reduced levels of oxidized vitamin D) may have a positive influence on the development of autoimmunity, but other environmental factors may play a role.
- **Developed countries.** Developed countries with highly successful childhood immunization programs and the subsequent elimination of infectious childhood illness have higher incidences of autoimmune disorders. Developing countries that have infectious childhood illnesses have fewer autoimmune disorders.
- **The Western diet,** rich in fat and sugar, may also play a part in the development of autoimmunity.

Intravenous immunoglobulin

Many autoimmune diseases are treated with intravenous immunoglobulin (IVIG), from the pooled blood of a large number of healthy human volunteers. The human immunoglobulin is screened for known viruses, bacteria and other pathogens; undergoes a rigorous filtration and purification process; and is formulated into a powder or liquid.

In myositis, the use of IVIG has never been officially approved. Like other drugs commonly prescribed for myositis, it is considered an "off-label" medication. There are a number of reasons that it works in some cases:

- It "floods the system" with good antibodies.
- It causes less space to be available for bad antibodies to bind.
- It increases the destruction of bad antibodies.
- It increases the internalization of bad antibodies.
- It slows down the production of bad antibodies.

IVIG doses used in myositis are not a cure for the disease; rather, they are a way to control symptoms. Here's how it's used to control myositis symptoms:

- IVIG is used primarily in DM, and especially in juvenile dermatomyositis that doesn't respond to prednisone or where side effects prohibit the use of prednisone.
- It can be used as the first line of treatment in young adults with DM.
- It has been particularly useful in alleviating the swallowing problems that often occur with myositis.
- It has been used successfully, but to a lesser extent, in PM patients.
- It has been used in the kinds of myositis described as "autoantibody-associated myositis" (see page 6), often in conjunction with prednisone and mycophenolate mofetil.

Usually, IVIG is chosen because of the absence of side effects compared to other drugs, but IVIG also has some possible side effects:

- Fever, chills, rash
- Allergic reactions
- Kidney and cardiac problems

Complications in IVIG treatment can often be avoided if liquid formulations or formulations with less sucrose content and lower concentrations are used.

There are some at-risk patient groups where IVIG use is prescribed only if it's absolutely needed: diabetics, people with known kidney failure, patients with a tendency to form blood clots, patients with a high level of immune antibodies, and patients with "thick" blood.

Find Dr. Mozaffar's full presentation on TMA's web site, www.myositis.org.

A quick look at prednisone

Many people diagnosed with myositis have at least considered corticosteroids for treatment. Medications like prednisone produce fast results by reducing inflammation, thus decreasing disease symptoms. In fact, says Dr. Chester Oddis, they may be the strongest anti-inflammatory agents available.

Yet these wonder drugs come with well-documented side effects: Weight gain, bone loss, cataracts, increased susceptibility to infection, stomach problems, and water retention are some of the side effects. Doctors and patients carefully consider the options to decide if the benefits outweigh the risks.

How well this medicine works depends partly on how the medicine is administered. It can be taken orally, intravenously or topically. The timing of the medication is also important. Alternate-day dosing, for instance, tends to cause fewer side effects but is also less beneficial than other regimens. Taking divided daily doses (half the dose in the morning, half in the evening) controls inflammation quickly but is more likely to have unwanted effects. In general, the degree to which you experience side effects increases with higher doses taken for longer periods. How your doctor prescribes prednisone depends on how serious your disease is as well as your health history.

Tapering prednisone (gradually lowering the dose) is an important process as your body needs adequate time to adjust. Once a patient is ready to taper, Oddis recommends a 20-25 percent dose reduction each month, with careful monitoring for signs of relapse. Patients sometimes experience withdrawal symptoms such as fatigue, swollen joints, mood changes, and muscle weakness.

Set goals for treatment and reassessment

Dr. John Ravits, the director of the Clinical Neurophysiology Laboratory and a neurologist at Virginia Mason Medical Center in Seattle, speaking on "Treatment choices, options and goals," reminded patients and their families to work with their physician to set their own care plan. "It's important to have a timeline," he said. "Discuss this with your doctor and make sure to set a time to take a look at your progress. If your treatment is not showing results, there needs to be a definite time where your case is reviewed and a decision made about whether to continue or change it." Other items to discuss: a do-able exercise plan and a practical way to measure your progress.

Ravits is in a position to work with the lab so he can effectively monitor the progress of his patients. "Sometimes your doctor has to help the physicians in the labs understand what you're trying to do," he said. "They're geared to focus on one muscle, at one moment in time." In chronic disease, the tests – whether they be blood tests, electro-diagnostic tests or biopsies – should let the specialist know the trend of the disease. This, combined with his clinical exam and observations together with conversations with you, identifies the way your disease is going. This is more important than any single snapshot.

Also important, especially as physicians become more concerned about disease duration: "Establish whether the disease is long-standing or just beginning." Physicians now know that it's important to distinguish disease damage from disease activity. This also helps specialists choose the medications they use to manage your disease.

Find the presentation by Dr. Ravits at www.myositis.org.

ANSWERS FOR FAMILIES

The 2007 Annual Conference in Bellevue, Washington, incorporated a special extended session devoted entirely to the unique issues facing families living with juvenile myositis. Families and children took advantage of the knowledge and expertise of a variety of specialists working with patients who have chronic diseases. The following speakers met with families and children:

Helen Emery, MD, MBBS, *is Section Chief and Fellowship Program Director in Pediatric Rheumatology at Seattle Children's Hospital and Regional Medical Center. She is also Section Head of Rheumatology and Professor of Pediatrics in the Division of Infectious Diseases, Immunology, and Rheumatology at the University of Washington School of Medicine. Her team at Seattle Children's diagnoses and manages children with rheumatic diseases, including juvenile dermatomyositis. She has 30 years of experience treating JM and currently sees about 60 children diagnosed with JM.*

Wendy Baer, PhD, *is a psychiatrist at Swedish Medical Center in Seattle. She went to medical school at the University of North Carolina at Chapel Hill and completed her residency at the University of Pennsylvania. Her specialty is working with patients with chronic conditions and terminal disease.*

Cate Brummett, DPT, *is a Doctor of Physical Therapy, practicing at Swedish Medical Center in Seattle. She has been a therapist for 22 years in a variety of settings including acute inpatient care and outpatient orthopedics, and currently works as a liaison to the Swedish Pain Clinic. Special interests include rehabilitation regarding osteoporosis, hand therapy and manual therapy.*

Tahseen Mozaffar, MD, FAAN, *is the director of the MDA clinics and of the ALS center at UC Irvine. He is recognized for his research on immune-mediated myopathies, critical care myopathies and animal models of chronic compression neuropathies.* *See page 8 for more on Dr. Mozaffar.*

The informal session allowed for interactive discussions among the speakers and families, bringing up issues from when to taper medicines to how to deal with anxiety.

Emotional issues and challenges

Can you ever have enough information to be prepared for your child's diagnosis of juvenile myositis? That is the question one parent asked in this year's special JM session at the Annual Conference.

The answer was a resounding "no." Parents scour the Internet, talk to doctors, find parents in similar situations, join The Myositis Association, and discuss things with families and friends. Yet they still hunger for more. There is both comforting and alarming information available. It becomes a balance, said Dr. Wendy Baer, and it takes time to come to grips with your new situation, both emotionally and practically.

"There is tremendous value in peer-to-peer support," she said, and this was a major focus in her presentation on the emotional challenges and family dynamics related to a chronic illness like JM. In fact, she said that one of the greatest benefits in getting together at events like the Annual Conference is the chance to talk with other families about how everyone has dealt with the various challenges and situations.

Depression, anxiety and sleep disturbance are just a few of the possible emotional manifestations of living with a chronic disease. Myositis patients, like those with other chronic illnesses, go through different phases – diagnosis, adjustment, disease exacerbation. Relationship issues crop up; anxiety over upcoming shots or treatments takes over. You will progress through some stages more smoothly than others, Baer said. Something that works one time might not work the next. A lot depends on what other stressors come into play at that point in your lives.

Getting appropriate help – both for caregivers and patients – is essential to everyone's emotional well-being.

Dr. Baer, along with other presenters and families, discussed specific issues:

Treatment anxiety

Anticipation is often worse than the actuality, said one parent whose 15-year-old son has juvenile myositis. Her son's anxiety over upcoming methotrexate injections led to headaches and upset stomachs. "Those to me seem to hurt more than if I were getting a blood draw or my port access," he said.

Other parents in the room shared that they had similar ordeals with their children.

"Anxiety comes from a lot of different places," Baer said. It might be the pain, being tired of dealing with the discomfort or treatments, or wanting to be your own person, she said. And the mental energy it takes to worry can in fact make you physically ill. Whatever is causing your particular anxiety needs to be addressed, so the steps will be different for each individual. The goal is to stay as healthy as possible, to avoid the battles.

Finding help for your family's emotional needs

Dr. Helen Emery noted that most children's hospitals make child life specialists available to families. These specialists are trained to help children deal with various situations and procedures. The specialists use visualization, guided imagery and storytelling to mentally take the children away from their treatment process. Social workers fill similar roles in other hospital or clinic settings. If your doctor has not initiated a session with a child life specialist or social worker, ask what services are available to your family.

Introducing these therapists early in the diagnosis is helpful to every family member. Nurses are also adept at keeping in tune with families and helping with communication between doctors and families. With a new diagnosis, Emery said, you feel as if you've been hit by a truck – and it takes time to wrap your brain around the situation. Pediatric specialists are there to provide support and information as you come to grips with the changes you now face.

Family-doctor relationship

Our culture and the media insinuate that doctors fix things, Emery said, but in reality, doctors have different options and do rely somewhat on trial and error, even with good science behind it all. Still, parents understandably want to know the right path for their own child. When medicines don't work as anticipated, emotional distress surfaces.

Discovering the right diagnosis is often a difficult and lengthy process; finding a doctor to care for your child is equally difficult – and equally important.

There is a delicate balance between the parent being an expert on the child and the doctor being the expert on the disease and its treatment, Emery said. Parents and doctors must work together, respecting one another as important decisions are made on the child's behalf. As a parent, you want to believe in the person who is treating your child. If you're not comfortable, she said, you have the right to look around. Ask for a second opinion if you feel this is the right step for your child and your family.

Remember that doctors are people too, she added, and don't necessarily have all the answers up front, especially for a disease as complicated, rare and individual as JM. Keep an open mind. "(Doctors) have good and bad days, too," she said.

Dr. Emery stressed the importance of not just being heard but of proactively speaking up. "Explain what you see," she said. "Question things." Doctors may not recognize something in a single office visit, so parents need to freely share their thoughts and observations. If you feel intimidated, she suggests writing it down. Reading from a list often lessens your anxiety. "Once you start," said one parent, "it gets much easier." Recognize it's a two-way street, Emery added. Doctors don't enjoy sharing bad news or the often lengthy list of medicine's side effects. An honest and open relationship between doctors and families is necessary to give your child the most complete care possible.

What's normal and what's not

Parents regularly ask whether a child's behavior is caused by normal transitions or is a reaction to having JM or to the medicines. There's no simple answer, but Dr. Baer lists what is NOT normal:

- To not enjoy anything
- To be irritable all day long for several days
- To not sleep or eat
- To feel guilty or hopeless
- To worry to the point of obsession

This holds true both for parents caring for their children and for the children who have JM. Dr. Emery prepares her own patients and families by letting them know that they are likely to experience strong feelings, questions and worries. Therefore, families may not feel so disrupted by their intense emotions. "If it gets in the way of your functioning," she said, "it's a problem." Remain keenly aware of your child's as well as your own energy level and emotional balance.

Dr. Baer reiterated the importance of addressing both the physical and emotional elements of chronic disease – for everyone: "The goal is sort of a balanced life where you're dealing with the stressors that are there and the realities that are there but also feeling like you're getting some fulfillment out of your day."

Friends and family

When explaining to friends and family what your child can or cannot do, parents commented that even close relatives and friends often don't understand. They don't appreciate the importance of protecting your child from the common cold. "Blame it on the doctors," said one mother. Tell them you are following the doctor's orders and leave it at that. This often alleviates your own feelings of guilt – of feeling like the "neurotic mom," as one parent put it – and avoids the inevitable barrage of questions. Sometimes, she said, you just need to educate family and friends again and again.

This process becomes exhausting over time, draining you of the energy

Continued on page 12

Answers from families, continued from page 11.

you need to have focused on your family and health issues, another parent said. Find other families facing similar frustrations and learn what they have found useful.

In the end, juvenile myositis affects every member of your family. Don't shy away from seeking help for yourself, your child or any member of your family if anyone is feeling depressed, overwhelmed or anxious.

That help might be in the form of a new-found hobby or activity that provides distraction and comfort. Or it may be in consulting a therapist to discuss your concerns.

The medical side of things

"It's the drug I love to hate," said Dr. Helen Emery. Anyone who has experience with it knows right away she's talking about prednisone.

That said, doctors and parents alike are thankful to have this treatment available to anyone suffering from juvenile myositis. As a long-term solution, it has its downside, but it is fast acting and effective at controlling the symptoms of JM. Prednisone works by mimicking cortisol, a hormone naturally produced by the body. In effect, taking prednisone signals your adrenal glands to shut down, so they cannot "kick in" when needed. Therefore, it is imperative that patients do NOT stop taking prednisone "cold turkey." Lowering the dose gradually gives your body time to adjust so that the adrenal glands can once again start producing cortisol on their own.

Quitting prednisone all at once leads to life-threatening situations. Signs include fever, diarrhea and high blood pressure. "Even missing a day," said Emery, "is not a great thing."

One thing to consider is that the body will normally produce extra cortisol in response to a stressful situation. While on prednisone, your child does not have the ability to produce the cortisol, so the amount of this hormone available may not be enough to deal with the stressors.

[See page 9 for more on prednisone.]

Biologics. Biologics are increasingly being studied in conjunction with myositis treatment. These medicines include rituximab, infliximab and etanercept. Biologics, unlike prednisone, are "smart drugs" – aimed at targeting a specific problem rather than the entire immune system.

Studies have mainly looked at rituximab (Rituxan) in adult myositis patients. This biologic agent shows promise in anecdotal reports of its use to treat children with JM, and new studies are being started to better test this treatment in both children and adults.

Adults have a particular antibody that seems to correlate with a positive response to rituximab, Emery said. Children do not tend to have this antibody. Rituximab works by targeting CD20, a type of white blood cell that produces antibodies. There are downsides:

- Rituximab can keep the body from producing any antibodies, begging the question as to whether children will respond to new immunizations in the absence of these antibodies.
- Rituximab is a long-acting medicine, so once someone takes this medicine it remains in the system for a long time.

A recent paper reviewed the cases of four pediatric patients treated with rituximab, noting strength, muscle enzymes and rash one to two years after treatment. All four patients tolerated rituximab well and were able to reduce prednisone six months after the treatment began. Three children improved clinically while the fourth experienced a progression of her disease. This review supports the further study of anti-B cell therapies for the treatment of JM, especially for those children with myositis-specific autoantibodies and/or those with refractory cases of JM. [Find this study online at www.myositis.org, in the Juvenile Myositis section of Published Research under the Research tab.]

The Food and Drug Administration (FDA) has become more interested in the medicine's long-term effects, so there is now a formal registry to collect follow-up data.

IVIG. Intravenous immunoglobulin (IVIG) is often considered an option only after trying prednisone as well as other medicines. However, neurologists like Dr. Tahseen Mozaffar (see page 8) tend to rely more on IVIG earlier in the treatment regimen. There are simply stylistic differences between doctors, he said.

Mozaffar believes introducing IVIG earlier in the disease process spares his patients from the side effects of other medicines. Rheumatologists have traditionally looked to prednisone first, sometimes adding methotrexate quickly in the treatment plan, followed by Plaquenil and other medications as dictated by the individual patient's response. IVIG is considered only after other options are exhausted.

Simply put, Mozaffar said, IVIG works by saturating the system with good antibodies so that bad disease-causing antibodies have no place to

go and are unable to bind to the tissue they are trying to destroy. So IVIG is not only preventing these antibodies from causing the disease symptoms but also increasing the destruction of the "bad" antibodies.

It is not routine to use IVIG alone or as a first-line treatment, though it is done. If you need infusions frequently – every month or less – then this treatment is not the right one for your situation, he said.

Coming off medicines

When your child is symptom free, when should you consider weaning the medications? Original studies suggest that children should show no symptoms of the disease for two years before coming off medicines completely, Emery said. Doctors will look at how individuals respond to the tapering process to determine the best plan for each child. It's important to watch carefully, as flares can be more difficult to control than the original disease course, she said.

Exercise and physical therapy

If there is good control of the inflammation but no physical therapy, Dr. Emery said, then your child's treatment plan is incomplete. At most children's hospitals and other centers, doctors and physical therapists are aggressive with stretching, since inflamed muscle tends to shorten and tighten. Physical therapy can effectively prevent contractures or, once established, can help stretch them out. Muscles most often affected by tightening are those that cross two joints – shoulders and hips, for example.

In principle, then, exercise is good, said Dr. Cate Brummett. However, with higher CPK readings, resistive exercise is not recommended. "The best way is to incorporate therapy into what kids want to do, into their lives," she said. Ballet provides appropriate stretching and strengthening without the resistive component. Swimming and playing are also good options, with the additional benefit of being positive socially.

A home program is possible once you have seen a licensed therapist for a detailed plan. It's important for families to be consistent in this program. "Find structure," Brummett said. "Children and teenagers tend not to be long-term thinkers, so they need parents as the enforcers."

It's important to understand the precautions your child must take, especially in sports. Explain to coaches, therapists, and even teammates what limitations your child might face. Allowing them to participate in sports, when appropriate, gives them a sense of normalcy. It also allows them to experience the "fun-ness" of exercise in a sports setting, said one parent.

When in remission, your child will benefit from visiting a therapist to target the weaker muscle groups that need more attention. A pediatric specialist works with parents and children to develop the best plan for everyone, a plan that both parent and child will stick to over time. However, you won't necessarily find someone with myositis experience, Brummett said. Doctors and hospitals can send your child's records to a therapist and work with them to find the right routine for each child and in each stage.

Short notes on JM from the conference

Supplements. Dr. Emery encourages children to take a calcium supplement, noting that Viactiv chewables (or the generic brand) have 500 milligrams of calcium along with enough vitamin D to help the body properly absorb the calcium. With the different flavors, most children find these chewables more of a treat than yet another medicine to add to the daily routine. Aldora is another good alternative. She also recommends a multi-vitamin for children. Whether you choose gummies or chewables, whatever your child will regularly – and without fuss – take is appropriate.

Sunscreen. Should you remain vigilant about sunscreen use for life? It is her hope, Emery said, that children do "outgrow" any sensitivity to the sun. However, with long-term prognosis still unknown, it is best to keep at it.

Bone density. Bone density scans (known as DEXA scans) need to be done annually. These scans are painless, similar to X-rays. Newer studies are now determining a better baseline figure with which to compare children's standard scores as they grow. "You need to have this [scan] done by a center with knowledge of children's standards," Emery said.

As to whether bone-building medicines are indicated, recommendations are based on an educated guess and not yet supported by solid data. If a child has a Z-score of -2.5 or less, or has had a bone fracture, she said, she will start the medicines. The downside to bone-building medicines is that they can inhibit remodeling of the bone: to just what extent is still not fully understood.

Growth hormone. On a related topic, growth hormone has been suggested to some children as having a positive effect on bone density. "But does it make you grow more," she asked, "or just grow sooner?" Again, any supportive or contradictory data are missing.

Muscle biopsy. Neurologists and rheumatologists, as a general rule, treat muscle biopsies differently. "If I'm subjecting someone to a long immunosuppressive treatment," said Dr. Mozaffar, "then it's useful for me to know what I'm treating." Therefore, he relies on muscle biopsies. Pediatric rheumatologists have a tendency to weigh other tests more heavily in an effort to avoid the more invasive muscle biopsy.

Swallowing problems. Emery uses the "nancy-paper-jug" test for potential swallowing issues in her patients. If her patients sound nasally when saying any of these words, she looks

Continued on page 14

Answers from families,

continued from page 13.

into a possible problem – and potential solutions.

Research studies. A good drug study is costly, so multi-center trials are becoming more common, especially with the help of groups like PRINTO (Paediatric Rheumatology International Trials Organisation) and CARRA (Childhood Arthritis and Rheumatology Research Alliance) to "collect" children for the studies. Trials involving children have strict rules to follow so that children are not put at risk. If children flare when taken off of a medicine under study, for example, they are immediately put back on the treatment, even if this disqualifies them from the study. Even when the researchers and subjects are unaware of which group they are in (those receiving the medicine versus those receiving placebo), an administrator is aware of each subject's group as well as all medical visits and notes.

Insurance and social security disability issues. Insurance companies often have advocates, sometimes called case managers, to help families deal with more complicated and costly diseases like JM. If you don't already have a relationship with a case manager, ask if one is available. There may also be advocates through your employer, if you are covered through your own company's policy, who help navigate your health care policy and any coverage issues that arise.

In terms of social security disability, it is tough to categorize children as disabled, Emery said. You typically have to be fairly impaired to receive the benefits. That said, she encourages families to apply on behalf of their children. The way the system is set up, she admits, most applications are denied the first time so you must appeal the decision. Social workers can help with this process.

Physical therapy in the schools. "There's nothing better than a squeaky wheel," Emery said. So when your child needs physical therapy or other adaptations, talk to the school and develop a formal Individualized Education Plan (IEP) or Section 504. Schools are required to work with you to determine what they can do to make your child's schooling experience a positive one.

When you have a plan on paper, don't sign it on the spot, she said. Take some time to think about it and to be sure it meets your child's needs – both current and anticipated needs. "Take the opportunity to get it right in the first go-round," she said.

GLOSSARY OF COMMON TERMS

See TMA's website at www.myositis.org under "Resources" for more terms related to myositis.

Antibody: protein produced by the body that acts against antigens in the immune response.

Antigen: foreign protein that stimulates an immune response in the body. [See antibody.]

Asymptomatic: having no symptoms of the disease.

Beta amyloid: amyloid, primarily protein, derived from amyloid precursor protein that is the primary component of plaques characteristic of Alzheimer's disease (in the brain) and inclusion-body myositis (in the muscle).

Biologic medicines: products made by cells in the body or in the laboratory that are directed toward specific targets in the body.

Contractures: shortening of the muscles or tendons causing the joint to remain stiff or bent, limiting its movement.

Dendritic cells: specialized (antigen-presenting) cells of the immune system that recognize and break down special types of antigens.

Disease activity: changes or problems that are a direct result of current, ongoing inflammation.

Disease damage: long-lasting changes that result from previous disease activity but are not caused by current inflammation.

Placebo: inactive treatment, like a sugar pill, given in clinical trials to test the effectiveness of a proposed treatment without researcher or patient bias.

Systemic: affecting the entire body, not just a single area. (Local refers to something that affects a single body part, organ or area.)

Taper: the controlled process of lowering the dose of medicine over time. It is essential to adhere to the prescribed tapering schedule for prednisone and other corticosteroids to avoid serious, life-threatening side effects.

Transgenic: an organism or cell of one species into which one or more genes of other species have been incorporated. Transgenic mice, for example, are used as models for myositis to determine pathways of and potential treatments for the disease.

Tumor necrosis factor alpha: immune cell protein that kills cells that appear abnormal and stimulates autoimmune reactions like inflammation. TNF blockers include infliximab (Remicade) and etanercept (Enbrel).

Progress and research,

continued from page 5.

There are special cells that act like sentinels. They're out there sitting in the tissues. Those tissues that are exposed to the environment are especially subject to autoimmune reaction, and there's a reason for this. The skin is exposed to all kinds of foreign substances that might cause injury, the gastrointestinal system is exposed to food and drink that could potentially cause harm, and the lungs are always taking in outside air, so these tissues have a lot of sentinels.

When there's a threat, or a perceived threat, the sentinels start signaling the rest of the immune army. The "T cells" and "B cells" are mobilized to ward off the threat. This is a communication channel that's active all the time. If we can block the communication, maybe we can turn down the mobilization. Recent work in Europe has confirmed the idea that interferon alpha is a signaling element in DM and lupus, and there's a certain type of dendritic cell that's really good at turning it off. Research using this is showing results in lupus. This kind of work shows promise, and there are other biologic drugs that don't wipe out the army, just turn off one abnormal pathway. These drugs are used every day in other autoimmune diseases, and we need to test them in myositis. We're very excited about the rituximab study led by Dr. Oddis.

New drugs are more selective

In poison ivy, our internal army helps us: In autoimmune disease it really hurts us. Drugs that suppress all of the elements of our immune system help us, but they knock down everything; while the biologic drugs go in and do one thing, target one little molecule, turn off one abnormal pathway. Several drugs that block the signaling mechanism in psoriasis, for example, look like they might work in DM skin disease. We're also looking at anti-fibrosis type drugs, since they may give us ways to prevent permanent damage.

From patient questions:

■ **Where the rash is present but no muscle weakness.** The usual course of the disease is either skin rash or muscle weakness first, followed in a fairly short time by the other symptom. There are those who do not get the

muscle weakness, but the rash is exactly the same. These are people with "amyopathic dermatomyositis."

■ **Treatment for skin rash.** In those with both symptoms, the dermatologist will work with the rheumatologist. If the muscles have improved, or if there is no muscle involvement, dermatologists now prefer to use a "skin only" approach, avoiding overtreatment. Dermatologists use what are called "anti-malarials" like Plaquenil to target the skin. The doctor may also prescribe topical treatments that combine steroids for the inflammation with anti-itch compounds. Rarely, the dermatologist will prescribe corticosteroids or immunosuppressive drugs because of the systemic consequences. New biologics that target only the disease are working well in some dermatomyositis patients. It is important to aggressively and adequately treat burning and itching because of quality-of-life issues.

■ **Finding a dermatologist to treat the rash.** Chances are, a practice that does mostly cosmetic procedures will not have any experience with dermatomyositis. Ask for a "medical dermatologist." Find a way to see a specialist who is familiar with the disease, probably at a medical school-based group practice.

■ **Swelling (edema) in the face and fingers.** This can be part of the disease process as well. "Sausage" fingers may signal an overlap with scleroderma or "sclerodermatomyositis."

■ **The role of the sun.** Sun and, in some cases, fluorescent lights act as a trigger for a skin flare in half of all DM patients; in others, it plays a subtler role. Patients should wear a sunscreen even in the shade, where rays reflect off the grass and ground. Since vitamin D is so crucial to health, it's important to take a good vitamin D supplement for protection against other diseases.

Detailed instructions of skin care by Dr. Sontheimer are available on TMA's website at www.myositis.org and will be in the Winter OutLook.

■ ■ ■

Create your own fundraising campaign from home!

TMA now has available a new online fundraising tool, "Campaign Builder", that allows you to join the fight against myositis right from your home. Campaign Builder enables members to create a personalized online fundraising campaign. It is quick and easy to build your campaign and email it to friends, family members, co-workers and others. It is also a very effective way for those who care about you to show support for you and the battle against myositis.

Please take a look at how easy this is to do. To get started, go to www.myositis.org and click on "Community" and then "My TMA". You will find a link titled "Start a campaign" toward the bottom of the page. Click there and you will be directed to a new page and prompted to enter the necessary information:

- Name your campaign
- Upload a photo or any other image (optional)
- Tell your story and why raising money in the battle against myositis is important to you
- Set a fundraising goal
- Designate how the funds will be used

Once finished, click on "submit" to see what your campaign page will look like to others. If the page looks just as you like it and you're ready to share it with others, click the email link on the lower left of the page. You will be taken to a page where you can enter multiple email addresses (separated by commas) and type an email message encouraging your friends to read your campaign page and donate.

At any time you can edit your campaign page, by going to "My TMA" and click "Edit campaign." However, once donations are received, you cannot change the restrictions on use of the funds. As people begin contributing to your campaign, you will be able to see who has donated by viewing the Campaign Reports that will appear in My TMA for your campaign.

This is a very efficient way to raise funds for our worthy cause.

Please consider starting your campaign now as friends and relatives are beginning to think about end-of-the-year charitable giving. Each person donating will receive a written acknowledgment from The Myositis Association that they can use for tax purposes.

If you have questions or need assistance, do not hesitate to call TMA at 1-800-821-7356.

The Myositis Association

1233 20th Street, NW, Suite 402
Washington, DC 20036