



# Diagnosing and Treating Inflammatory Myopathies (Myositis)

Once myositis is diagnosed, there are several methods for treating and managing it, as well as many ways in which patients can seek help and get involved.

**W**hile more is becoming known about inflammatory myopathies, they are still rare and making a diagnosis can often be a lengthy process. Myositis is the medical term used to describe a number of inflammatory myopathies, including dermatomyositis (DM), polymyositis (PM), inclusion-body myositis (IBM) and juvenile forms of myositis (JM).<sup>1</sup> In the U.S., myositis affects about one out of every 100,000 people. PM and DM are most common in women, with symptoms often occurring at about age 50, whereas IBM affects men more often, usually occurring around age 60.<sup>2</sup>

Myositis causes a swelling of the muscles and is believed to be an autoimmune disease, which means the body's immune system mistakenly attacks its own normal, healthy tissue through inflammation. It can be caused by injury, infection, certain medicines and even exercise. But, most forms of myositis are temporary and the swelling goes away after treating the injury or infection, after resting the muscles from exercise or after discontinuing the use of the medication.<sup>1</sup>

## Myositis Symptoms

While all forms of myositis can cause muscle weakness, all differ in their symptoms.<sup>1</sup>

DM signs include a rash on the eyelids, cheeks, nose, back, upper chest, elbows, knees and knuckles; scaly, dry or rough skin; trouble rising from a seated position or getting up after a fall; and general tiredness. Individuals who have DM often experience a painful and/or itchy rash; sudden or progressive weakness in muscles in the neck, hip, back and shoulder; difficulty swallowing or a feeling of choking; hardened lumps or sheets of calcium under the skin; and a hoarse voice.

Sudden or gradual weakness in the muscles, difficulty swallowing, falling and difficulty getting up from a fall and general feelings of tiredness all are signs of PM. Individuals who have PM often experience weakness in the muscles closest to the center of their body, such as their forearms, thighs, hips, shoulders, neck and back. Sometimes they experience weakness in their fingers and toes. And, there could also be a thickening of the skin on their hands.

Common signs of IBM include frequent falling episodes,



By Ronale Tucker Rhodes, MS

trouble climbing stairs or standing from a seated position, a foot that drops while walking, weakened hand grip and difficulty swallowing. Muscle weakness is the main symptom, and occurs in the forearm muscles, muscles below the knees, flexor muscles of the fingers, throat muscles and quadriceps. The quadriceps also noticeably shrink. And, as the muscles weaken, there is often pain and discomfort.

JM signs include a visible, reddish-purple rash over the eyelids or joints; tiredness; moodiness or irritability; stomachaches; difficulty climbing stairs, standing from a seated position or getting dressed; difficulty reaching up; and trouble lifting the head. Kids suffering from JM usually experience a rash, gradual muscle weakness, hardened lumps or sheets of calcium under the skin, trouble swallowing, a hoarse-sounding voice and stomach problems.

### **Making a Diagnosis**

While all forms of myositis are difficult to diagnose, DM is the easiest to diagnose because a skin rash often appears before muscle weakness. Both the rash, which

looks patchy, dusky and reddish or purple, and the muscle weakness are caused by inflammation in the blood vessels under the skin and in the muscles, which is also known as vasculitis. Individuals who experience the rash but not the muscle weakness have amyopathic DM (or DM sine myositis).<sup>1</sup>

When diagnosing PM, it is common for each case to be quite different from the others. Individuals who have PM often have one or more other autoimmune diseases. And, in some instances, cases originally diagnosed as PM that do not respond to treatment are later found to be IBM. With IBM, a small number of cases may be hereditary (h-IBM), but most are sporadic (s-IBM), which means there is no genetic link.<sup>1</sup>

JM may be diagnosed as either juvenile dermatomyositis (JDM) or juvenile polymyositis (JPM). The difference is that with JDM, there also is a rash.<sup>1</sup>

To diagnose myositis, a number of tests and examinations can be conducted. Conventional blood tests will be conducted to look for elevated levels of muscle enzymes in patients' blood samples. Muscle and skin biopsies will show abnormalities in muscles, including inflammation,

damage and abnormal proteins. Electro-diagnostic tests also will be conducted and include muscle resonance imaging (MRI) scans to reveal inflammation in muscles, as well as electromyograms (EMGs) to detect changes in muscles' electrical patterns that indicate muscle disease and which muscles are affected. And, last, antibody testing will confirm a myositis diagnosis and provide insight into the possible course of the disease and its potential complications.<sup>3</sup>

### Getting Treatment

Since myositis is such a rare disease, the medical community does not have a standard approach to treating the illness. And, it can be a challenge for doctors to decide how best to address the symptoms. Myositis affects individuals differently, and no one type of medication works for all patients.<sup>4</sup>

However, what is known is that there is no cure for myositis. And, it is necessary to manage the disease to reduce inflammation and to prevent muscle weakness from progressing. Managing the disease involves two approaches: medical treatment and lifestyle management changes.<sup>5</sup>

All forms of myositis are treatable, with the exception of IBM. Those with IBM get progressively weaker with time and need to prepare for the imminent limitations in their strength and mobility. While doctors sometimes prescribe prednisone (corticosteroids) for IBM, followed by methotrexate or azathioprine, if there is no improvement in their condition, the treatment is discontinued.<sup>6</sup>

Individuals with DM, PM and JM have active periods of the disease that occur as "flares," and typically respond to treatment in a month or two and generally regain strength after two to three months.<sup>5</sup> The first line of treatment, which is mandated by insurance companies, is corticosteroids or prednisone, which dampens inflammation and the immune response by interfering with the processing of antigens and with the early triggering of T cell and B cell production and, later, proliferation of B cells and T cells (cells that are produced by the immune system in autoimmune disease).<sup>7</sup> For long-term control of the disease and

to reduce the long-term side effects of prednisone, methotrexate or azathioprine is usually prescribed. Both of these drugs also interfere with the proliferation of B cells and T cells.<sup>6,7</sup>

If individuals fail to respond to prednisone or have serious side effects from the drug, intravenous immune globulin (IVIG) and other immunosuppressive medications may be prescribed. These other medications include cyclosporine (Neoral, Sandimmune); tacrolimus (Prograf) or mycophenolate (Cellcept). All of these also keep T cells from stimulating the production of more T cells and B cells.<sup>6,7</sup>

### Successful IVIG Treatment for Myositis

The use of IVIG to treat DM and PM is controversial, and myositis is not a U.S. Food and Drug Administration (FDA)-approved indication for IVIG. However, many reports have shown that IVIG has been a successful therapy in the management of this disease. In one case, a 66-year-old Caucasian female with primary idiopathic PM was admitted to the hospital. On the eighth day of hospitalization, she was started on a pulsating dose of 500 mg of intravenous methylprednisolone. The next day, she had progressive muscle weakness, hypotension and respiratory failure and was transferred to intensive care. Treatment with methylprednisolone was continued, as well as 60 mg of prednisone and pulsating treatment of cyclophosphamide — all of which were unsuccessful. On her 13th day in the hospital, she was treated with IVIG 0.04 kg/day for five days, and her clinical state started to improve with mild improvement of dysphagia and muscle strength. After five weeks in intensive care, the patient was transferred back to the internal clinic, and it was determined that IVIG was an effective therapeutic strategy.<sup>8</sup>

In a double-blind, placebo-controlled trial, 15 patients with DM were randomly selected to receive one monthly infusion of high-dose IVIG or a placebo for three months, at the end of which they had the option to cross over to the other treatment. Initially, eight were assigned to IVIG and seven to the placebo. After crossing over, a total of 12 patients had received IVIG. Nine of the patients, who were severely disabled, experienced major improvement and

*Since myositis is such a rare disease, the medical community does not have a standard approach to treating the illness.*

resumed almost normal function, two patients showed mild improvement and one had no change in condition. Of the 11 patients on the placebo, none showed a major improvement, three had mild improvement, three had no change in condition and five had a worsening of the condition. In addition, four of the patients who crossed over to the placebo after major improvement with IVIG returned to their original condition of disability, and two returned to wheelchairs. The only reported side effects to the IVIG were headaches during the course of the 12-hour infusion.<sup>9</sup>

It should be noted that while it is said that there is no treatment for IBM, there have been studies conducted to determine the effectiveness of IVIG in treating the disease. In one double-blind, placebo-controlled, cross-over study, 22 IBM patients ages 32 to 75 received IVIG or a placebo for six months each, followed by the alternative treatment. After six and 12 months, the response to treatment was evaluated using a modified Medical Research Council scale known as Neuromuscular Symptom Score (NSS), the patient's own assessment of improvement, arm outstretched time and electromyography. Overall, there was no progression of the disease in 90 percent of the patients. A mild and significant improvement (11 percent) in clinical symptoms was found using NSS, but not with the other test procedures. There was a trend in mild improvement in treated patients when using other tests. And, there were no serious side effects.<sup>10</sup>

In a second study of IVIG treatment for IBM using the same study design, 19 patients were given monthly infusions of 2g/kg IVIG or a placebo for three months. Patients crossed over to the alternate treatment after a washout period, and responses were evaluated at baseline and at the end of each treatment period using expanded (0-10) MRC scales, the Maximum Voluntary Isometric Contraction (MVIC) method, symptom and disability scores and quan-



titative swallowing studies. Of the 19 patients, nine were randomized to IVIG and 10 to the placebo. During IVIG, the patients gained a mean of 4.2 MRC points, and during the placebo, they lost 2.7 points. Similar results were obtained with the MRC and MVIC scores when the patients crossed to the alternative treatment. Six patients had a functionally important improvement by more than 10 MRC

points that declined when crossed over to the placebo. Limb-by-limb analysis demonstrated that during IVIG, the muscle strength in 39 percent of the lower-extremity limbs significantly increased compared with the placebo, while a simultaneous decrease in 28 percent of other limbs was detected. In addition, the duration of swallowing functions measured in seconds with ultrasound improved statistically in the IVIG patients compared with the placebo.<sup>11</sup>

Both of these studies determined that IVIG may be mildly effective in treating IBM by preventing disease progression or inducing mild improvement. However, whether those modest gains justify the high cost of trying IVIG remains unclear.<sup>10,11</sup>

## *Most insurance companies have medical policies outlining IVIG coverage.*

### **The Insurance Component**

The high cost of treatment is often a factor when determining whether to treat myositis with IVIG, and as stated earlier, IVIG is not an FDA-approved indication. Most insurance companies have medical policies outlining IVIG coverage. The guidelines to establish those medical policies are based upon peer-reviewed published studies, also referred to as evidenced-based medicine.<sup>12</sup>

In addition, most insurance companies have coverage guidelines for both PM and DM that determine whether IVIG will be covered. These guidelines mandate that the patient and/or their physician provide the company with a history of disease, muscle biopsy, lab results and other medications that have been tried but that failed, such as steroids and immunosuppressants. Once an insurance company agrees to cover IVIG for PM or DM, continued

coverage depends upon the patient's response, including whether symptoms diminish and/or resolve and ensuring that IVIG isn't making the condition worse. Currently, IVIG for IBM is considered investigational only; studies are not conclusive enough to warrant coverage.<sup>12</sup>

### The Lifestyle Management Component

Lifestyle management changes can help patients to restore their strength. These include exercise, rest, stress reduction and nutrition.

Once drug treatment has been started, physicians

## A Man on a Myositis Mission

When Steve Morris was diagnosed with giant cell myositis in 2006, he was determined. At first, he was determined to beat it. Then, he was determined to raise money to find treatments and raise awareness of the disease. Now, he's determined to reach out to others to help them overcome the obstacles they face.

After his diagnosis, Morris searched the Internet for any information that would help him to better understand his disease. He discovered The Myositis Association (TMA) website and its discussion board, on which he posted that, someday, he wanted to start his own foundation (Mo Beta Foundation) to help those with myositis. Since he went into remission six months after his diagnosis, he also posted that he was planning a benefit ride on his Harley motorcycle to Sturgis, S.D. In response, someone at TMA headquarters contacted him, and Morris decided to raise funds through the association's website "since they had everything in place to do that."

Morris decided to take his fundraising mission to Canada, riding 4,500 miles in 14 days to Vancouver. "This time, I had the great pleasure of meeting people along the route that actually suffered from myositis," Morris explains. "In Vancouver, we rode up on the busiest street corner in the city, and we were greeted by numerous people. They had a band playing, banners up and were doing some fundraising of their own. We felt like rock stars!" The ride raised \$10,000.

Morris has two more fundraising events planned. The first is a 90-minute endurance race at Pole Position, an indoor kart racing company, in which teams of three to five people will race as a tag team, and the team with the most laps wins. The second is a golf tournament to be held some time in 2011 or 2012. More information about both events can be found on his website at [www.riding4thosewhocant.org](http://www.riding4thosewhocant.org).

After his first fundraising event, Morris was contacted again by TMA and asked to speak on its patient panel at its 2007 National Conference in Seattle. He has continued to speak at TMA's conference annually. When he speaks, he says, "I always do about 10 to 15 minutes of humor. I always say [that] if you ain't laughing, you're crying! Most of the humor is just life stuff that might not have been funny at the time, but is now hilarious. Sometimes I think we get too caught [up] in our disease that we forget to laugh." To hear some of Morris' humor at the 2009 Charlotte, N.C., conference, go to [www.youtube.com/watch?v=5yXTXpjGWIA](http://www.youtube.com/watch?v=5yXTXpjGWIA).

According to Morris, he always ends his speeches with a couple of ideas that he takes to heart in his own life. The first is: I have myositis, but myositis does not have me. "I try not to let my disease consume me and dictate how I will live life," Morris explains. "I have a life that is truly blessed. My disease has opened my eyes to what I can do for others, instead of always thinking about what I can do for myself. I now feel more fulfilled. If not for this disease, I would not have been able to do some of the most incredible things that I have had the pleasure of doing." The second thing he always ends his speeches with: Any day you wake up on this side of the dirt is a pretty good day.



In 2007, Morris went on his first "Riding for Those Who Can't ... Yet" fundraiser, riding from his home in Southern California to Sturgis, S.D., and raising \$15,000, not to mention a great deal of awareness about myositis. In 2008,

can prescribe a program of regular stretching exercises to help maintain range of motion in weakened arms and legs. Individuals may also want to enroll in physical therapy to help prevent permanent muscle shortening. In addition, it can be beneficial to add whirlpool baths, heat and gentle massage as part of their treatment.<sup>5</sup>

Getting enough rest also can help to manage myositis. Frequent breaks should be taken throughout the day, and activity should be limited. In addition, myositis patients need to find outlets to release daily stress in their lives. Relaxation exercises, such as yoga or biofeedback, can help.<sup>5</sup>

What individuals eat also can affect their overall health. Because treatment for myositis often requires courses of steroids to fight muscle inflammation, weight gain is frequently a result, which can make symptoms even more difficult to deal with.<sup>5</sup> As such, a healthful diet is extremely important. Also, individuals with PM may be at increased risk of celiac disease. If so, a gluten-free diet may be necessary to improve signs and symptoms of celiac disease. However, a gluten-free diet will not improve signs and symptoms of polymyositis. Individuals who have PM, as well as unexplained diarrhea, may want to get tested for celiac disease.<sup>13</sup>

### Participating in Clinical Trials

Doctors can greatly benefit from additional information about medications that treat myositis, but “the ability of scientists to study effective treatments for the illness ... is limited by the small number of patients that participate in rare disease studies,” says Lawrence J. Kagan, MD, attending rheumatologist at the Hospital for Special Surgery and professor of medicine at Weill Cornell Medical College. Research studies on the effectiveness of treatments for myositis are unlike those for other diseases, such as lupus or rheumatoid arthritis, which have hundreds or even thousands of patients. Yet, for the FDA to approve a drug, such as IVIG, a proven track record clearly illustrating patient benefit must be present.<sup>4</sup>

Therefore, individuals with myositis are highly encouraged to take part in research. For information about new, ongoing and completed studies, visit The Myositis Association website at [www.myositis.org](http://www.myositis.org) or visit the U.S. National Institutes of Health's ClinicalTrials.gov website at <http://www.clinicaltrials.gov/ct/search;jsessionid=D9D2A78BB81C717131DA90D4EDBB3E54?term=inflammatory+myopathy&submit=Search>.

### Getting More Information

A host of resources are available to individuals interested in finding out more about myositis. The *IG Living* website has a list of resources at [www.igliving.com](http://www.igliving.com). And, The Myositis Association also has a list of resources at <http://www.myositis.org/template/page.cfm?id=105>.

While there are still many unknowns about diagnosing and treating myositis, it can be managed. Patients must take an active role in their own treatment, and they should get involved to improve the diagnosis and treatment options for the future. ■

**RONALE TUCKER RHODES, MS**, is the editor of *IG Living magazine*.

### References

1. The Myositis Association. About Myositis. Accessed at <http://www.myositis.org/template/page.cfm?id=2>.
2. Everyday Health. Myositis: What Is It? Accessed at <http://www.everydayhealth.com/health-information/myositis-what-is-it.aspx>.
3. The Myositis Association. About Myositis: Diagnosis. Accessed at <http://www.myositis.org/template/page.cfm?id=>.
4. Kagen, Lawrence J. A Doctor's Perspective on Treating Patients with Myositis. Accessed at [http://www.hss.edu/conditions\\_Doctor's-Perspective-Treating-Myositis-Patients.asp](http://www.hss.edu/conditions_Doctor's-Perspective-Treating-Myositis-Patients.asp).
5. Johns Hopkins Medicine. Myositis Treatment Information. Accessed at [www.hopkinsmedicine.org/myositis/differences/treatment.html](http://www.hopkinsmedicine.org/myositis/differences/treatment.html).
6. The Myositis Association. About Myositis: Frequently Asked Questions. Accessed at <http://www.myositis.org/template/page.cfm?id=13>.
7. MDA Publications. Facts About Inflammatory Myopathies (Myositis): PM and DM Treatments. Accessed at <http://www.mdaua.org/publications/fa-myosi-pmdmchart.html>.
8. Kristofova, B, Oetterova, M, Valocikova, I, Macejova, Z, Pidanicova, A, Firmont, J, Majernik, M, and Lazurova, I. Successful therapy with intravenous immunoglobulin in the management of polymyositis. *Bratisl Lek Listy*, 2008; 109(9).
9. National Institute of Neurological Disorders and Stroke. Study Shows IVIG Safe, Effective Treatment for Muscle Disease. December 29, 1993. Accessed at [www.ninds.nih.gov/news\\_and\\_events/news\\_articles/presrelease\\_dermatomyositis\\_122993.htm](http://www.ninds.nih.gov/news_and_events/news_articles/presrelease_dermatomyositis_122993.htm).
10. Walter, MC, Lochmuller, H, Toepfer, M, Schlotter, B, Reilich, P, Schroder, M, Muller-Felber, W, and Pongratz, D. High-dose immunoglobulin therapy in sporadic inclusion body myositis: a double-blind, placebo-controlled study. *Journal of Neurology*, January 2000, 247(1).
11. Dalakas, MC, Sonies, B, Dambrosia, J, Sekul, E, Cupler, E, and Sivakumar, K. Treatment of inclusion-body myositis with IVIG: a double-blind, placebo-controlled study. *Neurology*, 1997 Mar; 48(3): 712-6.
12. Vaughan, Leslie J, RPh. IVIG Therapy. Slideshow presentation. Accessed at <http://www.myositis.org/pdf/IVIG%20in%20service%20for%20TMA%20mtg.pdf>.
13. MayoClinic.com Polymyositis: Can a gluten-free diet reduce symptoms? Accessed at <http://www.mayoclinic.com/health/polymyositis/AN00572>.