



## **Myositis**

***Introduction:*** Weakness is one of the most common problems for which patients seek health care. But sometimes a common problem can be a sign of an uncommon group of diseases. What distinguishes myositis from other causes of weakness is inflammation triggered by an over-active immune system, resulting in muscle damage. The major forms of myositis treated by a rheumatologist include *polymyositis* (PM), *dermatomyositis* (DM), and *inclusion body myositis* (IBM).

Only about 5 new myositis cases per 1 million population in the United States are diagnosed every year. For PM and DM, the most common ages of onset cluster around two age groups: between 10 and 15 years of age and between 45 and 60 years of age. Childhood-onset myositis is more often DM, while adults more often develop PM. Women outnumber men for both conditions by about 2:1. IBM, on the other hand, tends to develop in patients over the age of 50, and men outnumber women 2:1. Because IBM is the rarest of the above conditions, we will focus most of our discussion on PM and DM.

The outlook for patients with myositis has improved with the discovery of effective therapies within the last several decades. Overall, 5 year survival rates are 80% for those with PM and DM, and these figures are more favorable for those with childhood-onset disease. Involvement of other organs (see below) or development of cancer (seen in DM patients) are the top causes of death. While IBM is less responsive to treatment and is associated with more long-term disability than the other two forms of myositis, this condition is associated with better survival rates due to its slow progression.

***Features of Myositis:*** The weakness of PM and DM tends to occur mostly in the large muscles of the shoulder, hip, and thigh region. Patients will often report that it is difficult for them to keep their arms above their head (to fix their hair, for example) or for them to climb stairs or get out of chairs or back seats of cars. These symptoms tend to progress gradually, and the weakness is typically not associated with pain unless the patient is experiencing an acute flare of muscle damage and inflammation. Neck muscles, abdominal muscles, and muscles further down the arms and legs tend to become affected less commonly. By contrast, IBM is more slowly progressive but can involve muscles of the forearms and hands more commonly early in the course of the disease.

In patients with DM, a rash may occur in various locations. Most typically, the skin above the eyelids develops a red or purplish discoloration (known as a *heliotrope rash*) or the skin over the knuckles of the hands develops red raised or scaly patches

(known as *Gottron's papules*). Other findings may include fissures around the fingers known as *mechanic's hands*, calcium deposits under the skin known as *calcinosis* (also seen in scleroderma), or small dilated blood vessels around the cuticles of the fingernails. In up to 10 or 20% of individuals, the rash may occur in the absence of any sign of muscle involvement (called *amyopathic DM*).

Other organs may occasionally become inflamed in patients with PM or DM. The esophagus may become weak, impairing swallowing function and potentially resulting in food or stomach contents being aspirated into the lungs. Lung inflammation can occur as a direct result of inflammation and cause difficulty breathing or scarring in the lungs. The heart muscle may also become inflamed and cause rhythm disturbances or heart failure. Both PM and DM may also be accompanied by arthritis, cold-induced color changes in the fingers (*Raynaud's phenomenon*), or may overlap with other rheumatic diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) or systemic sclerosis (SScl) (see related sections).

A final noteworthy feature of myositis is the association with cancer, mainly observed with adult-onset DM. On the average, about 25% of patients with DM are diagnosed with cancer, about a 6-fold increase over individuals of the same age in the general population. Solid tumors are most often encountered rather than leukemia, with ovarian cancer possibly being most strongly associated with DM. In about 80% of cases, cancer and DM are diagnosed with one year of each other. In spite of this association, the presence or absence of cancer and the disease activity of DM do not always go hand in hand, and removal of the tumor does not always result in improvement in signs of DM.

***Diagnosis:*** Criteria for diagnosing PM and DM were devised in the 1970's but are still in use today. They include:

- 1) History of and findings on physical examination of muscle weakness of hip and/or shoulder region
- 2) Elevation of muscle enzymes on laboratory testing
- 3) Evidence for abnormal muscle activity on *electromyography (EMG)* testing
- 4) Findings of inflammation on muscle biopsy
- 5) Typical rash of DM as described above

For a "probable" diagnosis of PM, 3 of the first 4 criteria are required, while for a "definite" diagnosis of PM, all 4 are needed. For DM, #5 is included.

The first criterion listed above is simply evaluated during physical examination by an experienced physician. Testing muscle strength is both a useful way to evaluate a patient with possible myositis and a useful way to follow a patient's progress after the diagnosis is made. A doctor may test a patient's strength directly or time them on performing an activity (arising from a chair, for example) to determine the function of the muscles.

Laboratory tests are often useful in evaluating myositis. Muscle enzyme elevations are seen in at least 90-95% of patients with PM and DM but are often less elevated in patients with IBM. The *creatinine phospho-kinase (CPK)* is the most widely used and most accurate muscle enzyme that is elevated in these conditions, but the CPK

may be elevated in other diseases as well or may be abnormal in some individuals with no apparent muscle disease. The *aldolase* is another enzyme that is often elevated in myositis, as well as the *LDH*, *SGOT*, and *SGPT*, tests that can also be elevated when liver damage is present. These enzyme levels should return to normal or near normal levels as the patient is treated, but the CPK level usually improves before a return in strength is observed, and some will remain weak even when the muscle enzyme levels improve.

Antibody testing is often abnormal in PM and DM but frequently unhelpful in patients with IBM. The *antinuclear antibody (ANA)*, also seen in SLE, is elevated in 60-75% of PM or DM patients. Other more specific studies known as *myositis-specific antibodies* may be ordered if needed to clarify the diagnosis, and many of these antibodies may predict more aggressive forms of the disease.

The EMG is a test involving needles that are applied to the muscles and which measure electrical currents in the muscles. Certain abnormal patterns are observed in 85-90% patients with myositis and can provide valuable evidence to support the diagnosis. This test is often painful but may be helpful both in diagnosing and monitoring the progress of myositis patients.

The muscle biopsy is perhaps the most useful test in diagnosing various forms of myositis and distinguishing these conditions from other causes of muscle weakness. Typically, the muscle that is most weak or that is abnormal on EMG study is chosen, and the biopsy is most commonly performed on the thigh muscles. A small incision is made under local anesthetic, and a small piece of muscle is removed and examined under a microscope. Depending on the pattern of inflammation present or the type of muscle damage that is seen, PM, DM, or IBM may be diagnosed. For IBM, abnormal proteins are found to be deposited in the muscle, which are the “inclusion bodies” for which this disease is named. While the biopsy may be nonspecific or falsely negative in a small percentage of patients, this study usually is diagnostic and allows the physician to confidently treat the patient appropriately.

While not included in the criteria, *magnetic resonance imaging (MRI)* is a tool that has gained popularity recently in the evaluation of myositis. This study is usually performed on thigh muscles and demonstrates changes suggesting inflammation that can strongly suggest the diagnosis and may help guide the muscle biopsy to increase the yield of this procedure. Moreover, the MRI can be used to assess the progress of a patient with myositis after treatment.

Because of the association of DM with cancer, all adult patients diagnosed with this form of myositis should be evaluated for cancer. Most authorities in the field simply recommend that types of cancer most common for the patient’s age group and gender be screened. While not all cancers can be detected, some patients can receive an early diagnosis and possibly better outcomes if an alert physician performs an appropriate search for the most likely malignancies expected in each individual patient.

Even with all of these studies at our disposal, many other conditions can mimic myositis. Weakness and/or elevation of muscle enzymes can be seen in other nerve or muscle disorders such as muscular dystrophy, various hormonal diseases such as thyroid dysfunction, genetic or metabolic diseases, infections, or exposure to certain medications such as cholesterol-lowering drugs, to name a few. The rash of DM may occur in sun-

exposed areas and mimic SLE, and patients with SScI often demonstrate Raynaud's and calcinosis that are seen with DM. A skin biopsy or certain laboratory tests may help distinguish between these conditions. Also, as mentioned above, other rheumatic diseases may overlap with myositis, adding to the confusion between these diseases.

As painstaking as the diagnostic workup for myositis may seem, it is necessary to go through these steps to assure it has been adequately diagnosed and differentiated from other conditions. This process helps guide therapy and avoids side effects of inappropriate medical treatment.

***Therapy:*** Major goals of therapy for myositis are reducing muscle inflammation, limiting muscle damage, and restoring muscle function. Additionally, skin involvement for DM patients and other organs affected by the disease process must be addressed, which typically can be accomplished with the same medications used to treat the muscle disease. As mentioned above, IBM patients tend to respond less dramatically to treatment but should at least be given a trial of therapy to determine the reversibility of their disease before abandoning these efforts altogether.

*Corticosteroids* are the treatment of choice for the majority of patients with myositis. The most commonly used medication in this class is oral prednisone, but intravenous forms of corticosteroids can be given to rapidly control the disease during an acute flare. Steroids work to suppress inflammation in the muscle and other parts of the body but must be given in high doses initially to control the disease. When properly administered, corticosteroids improve disease activity in 90% of patients and may be the only form of therapy required in over 1/2 of all patients with myositis. When a response is observed, the dose can be gradually reduced to minimize side effects.

Adverse effects of corticosteroids include weight gain, weakening of the bones, elevation of blood sugar or blood pressure, cataracts, and increased susceptibility to infection. Ironically, these medications that are being used to improve muscle strength and function can actually cause muscle *weakness* when given at high doses for long periods of time. Sorting out whether a patient's weakness is due to the disease or the medications given requires a careful evaluation by an experienced physician.

While few well-designed studies are available to document which medications are most effective in treating myositis, *immunosuppressive drugs* such as *methotrexate (MTX)*, *azathioprine (AZA)*, *cyclosporine*, *cyclophosphamide*, or *chlorambucil* have been reported to demonstrate efficacy in patients with myositis resistant to prednisone alone or in those unable to taper off prednisone without experiencing a relapse. Because of more favorable side effect profiles, most physicians prefer MTX or AZA as the next therapy after corticosteroids for such patients.

All of these medications work more slowly than corticosteroids but have a powerful effect on suppressing inflammation. They also suppress the immune system and may make patients more prone to developing infections. Some of these medications may also reduce the bone marrow's ability to produce white or red blood cells, cause liver enzyme elevations, or other less common side effects (see Medications section). Routine monitoring is needed to achieve the balance between safety and effectiveness of each of these drugs.

In patients with myositis resistant to these standard therapies, particularly those with DM, *intravenous immunoglobulin G (IVIgG)* has been shown in well-designed studies to have a beneficial effect on treating the muscle disease and occasionally other manifestations. IVIgG consists of antibodies taken from normal donors at the blood bank and appears to work by blocking abnormal antibodies produced by myositis patients. This therapy is expensive and must be given in high doses once per month for at least 3 months but is relatively safe, associated only with infusion reactions and volume overload in some patients.

For patients with DM in whom rashes remain active and who do not require other therapies for the muscle disease, *hydroxychloroquine (HCQ)* is a safe and often effective alternative. HCQ, under the trade name Plaquenil, suppresses inflammation in the skin without significantly suppressing the immune system and has little adverse effects on other parts of the body. Because 1 in 1,000 patients may develop changes in the eye that can impair color vision, monitoring with an eye doctor every 6 to 12 months is recommended to pick up these problems before they progress.

*Biologic response modifiers* such as the tumor necrosis factor (TNF) blocking drugs *etanercept*, *infliximab*, *adalimumab*, and *rituximab*, a medication inhibiting certain types of white blood cells, have not been well-studied but have been reported in small series of patients to produce impressive benefits. These drugs work specifically on parts of the immune system believed to be involved in myositis. The TNF blockers have been widely used in the treatment of RA and other rheumatic diseases, but all of these medications must still be considered experimental for treating myositis until better evidence surfaces that would establish their role in treating such patients.

The above therapies serve to reduce muscle inflammation and damage, but to provide optimal function, *physical therapy* for muscle strengthening has been shown to be well-tolerated and effective in myositis patients. In a way, the medications can be seen as ways to limit muscle damage, and exercise can be seen as a way to strengthen what muscle tissue is left. Even in patients with early active disease, muscle strengthening produces desirable effects if performed under the supervision of a skilled therapist.

Myositis is a challenging group of illnesses, both to treat and to experience as a patient. A coordinated team of health care practitioners is necessary to provide the proper diagnosis and treatment to maximize muscle function and improve outcomes.