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Facts about Inflammatory Myopathies

Dermatomyositis (DM), Polymyositis (PM) & Inclusion-Body Myositis (IBM)

What are Inflammatory Myopathies?

The inflammatory myopathies are a group of muscle diseases that involve *inflammation* of the muscles or associated tissues, such as the blood vessels that supply the muscles. A *myopathy* is a muscle disease, and *inflammation* is a response to cell damage.

The inflammatory process leads to destruction of muscle tissue, and is accompanied by weakness and sometimes pain. Over time, there can be loss of muscle bulk (*atrophy*).

Normally, we think of inflammation, such as that following a sprained ankle or a dental procedure, as a condition that makes a part of the body hot, red and painful to touch. But inflammation can also be internal, causing tissue destruction in various organs. The common denominator in both types of inflammation is the presence of cells of the immune system in great numbers. Under a microscope, these can be seen “invading” the tissue as an army invades a city.

Another word for inflammatory myopathy is *myositis*. The *myo* root means muscle, and the *itis* root means inflammation; so a myositis is an inflammatory muscle disease.

Fortunately, for two of the three inflammatory myopathies in MDA’s program — *polymyositis (PM)* and *dermatomyositis (DM)* — effective treatments are available. New research is rapidly leading to increased understanding of these disorders and more successful treatments for them.

Although inflammatory myopathies can lead to great discomfort for at least a period of time, for the most part they aren’t life-threatening. In fact, many people recover partially or completely from PM and DM. The third inflammatory myopathy, *inclusion-body myositis (IBM)*, also isn’t life threatening.

What causes Inflammatory Myopathies?

In most cases, the cause of an inflammatory myopathy is unclear. For some reason, the body’s immune system turns against its own muscles and damages muscle tissue in an *autoimmune* response.

Viruses might be a trigger for autoimmune myositis. People with the HIV virus, which causes AIDS, can develop a myositis, as can people with a virus called HTLV-1. Some myositis cases have followed infection with the Coxsackie B virus.

There are reports of myositis following exposure to certain drugs. Among the drugs that have been suspected of contributing to myositis are carticaine (a local anesthetic), penicillamine (a drug used to lower copper levels in the body), interferon-alpha (mostly used to treat cancer and hepatitis), cimetidine (used to treat ulcers), carbimazole (to



Polymyositis and dermatomyositis mostly affect the muscles of the hips and thighs, the upper arms, the top part of the back, the shoulder area and the neck.



The first muscles affected in inclusion-body myositis are usually those of the wrists and fingers, those that lift the front of the foot, and the muscles of the front of the thigh.



treat thyroid disease), phenytoin (used to treat seizures), and growth hormone. The vaccine for hepatitis B has also been implicated in some cases.

Recent research suggests that the mixing of blood cells of a mother and a fetus during pregnancy could lead to the later development of an autoimmune disease such as myositis in the mother or the child.

Inflammatory myopathies aren't genetic disorders, although there may be genetic factors that make it more or less likely that an inflammatory myopathy will develop.

All these factors are being studied so that these diseases can someday be better understood treated or perhaps prevented entirely. In the overwhelming majority of cases, there's no clear-cut cause for the development of myositis.

What are the forms of Inflammatory Myopathy?

There are three main types of inflammatory myopathy. These are:

- **polymyositis**, a disease in which the inflammatory cells of the immune system directly attack muscle fibers
- **dermatomyositis**, a disease in which these cells attack the small blood vessels that supply muscles and skin
- **inclusion-body myositis**, a disease of older people that appears to be partly inflammatory and partly a degenerative muscle disease

People with polymyositis (PM) or dermatomyositis (DM) have a somewhat elevated risk of cancer. One theory about this is that, as the immune system tries to fight the cancer, it gets confused and attacks some of its own tissue. Adults may be asked to undergo testing for various types of cancer.

There's no apparent association of cancer with myositis in children, and inclusion-body myositis (IBM) isn't known to be associated with an increased cancer risk.

Can Inflammatory Myopathies be cured?

PM and DM are highly treatable diseases. Some people, especially children, recover completely from an inflammatory myopathy, while others experience greatly diminished symptoms for long periods of time. Several years of treatment to suppress the immune system may be necessary to achieve these results.

Those who don't recover completely may need to continue on at least a low dose of medication to control the autoimmune attack of PM or DM throughout their lives. Some permanent loss of strength and wasting of muscles sometimes occurs. In other cases, the patient recovers his or her full strength and muscle size.

New findings on the genetic and environmental factors involved in autoimmune diseases should lead to more precise and effective drugs to treat them.

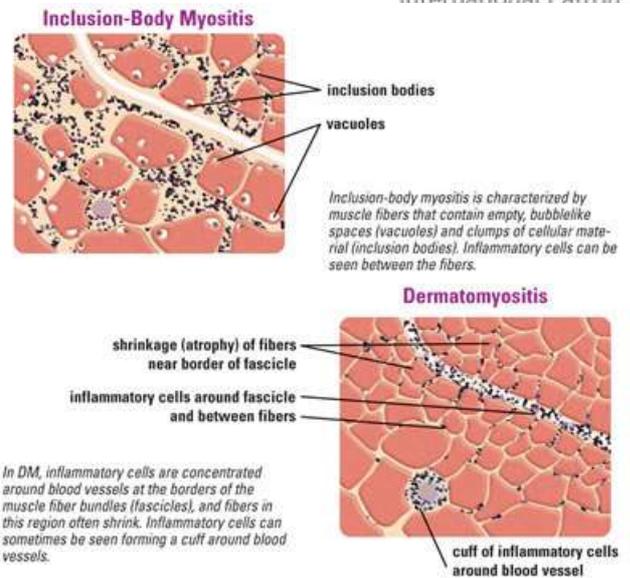
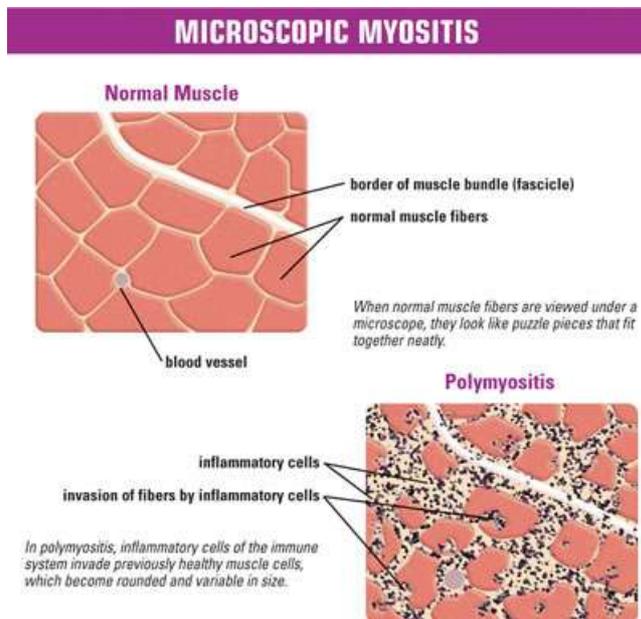
Inclusion-body myositis (IBM) isn't considered a treatable disease. Once acquired, it generally progresses slowly.



DM can cause sensitivity of the eyes, and avoidance of sunlight during peak hours is recommended.



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How are PM, DM and IBM diagnosed?

As with other muscle diseases, a doctor diagnoses an inflammatory myopathy by considering the patient's history, family medical history, and the results of a careful physical examination. This may be followed by some lab tests, perhaps of the electrical activity inside the muscles, and usually a muscle biopsy.

After a careful history and physical exam to document the pattern of weakness in the patient's muscles, a doctor who suspects myositis will likely order a blood test to check the level of *creatinine kinase (CK)*, an enzyme that leaks out of muscle fibers when the fibers are being damaged. In PM and DM, the CK level is usually very high. In IBM, it may be only mildly elevated, or even normal.

In some cases, the doctor may ask for a blood test for specific *antibodies*, proteins produced by the immune system in myositis and other autoimmune diseases.

Some of these antibodies appear to be specific to autoimmune muscle disease. One such antibody is called *Jo-1*.

The next step is sometimes an *electromyogram*, a test in which tiny needles are inserted into the muscles to test their electrical activity at rest and when the person tries to contract the muscle. Inflammatory myopathies show a distinctive pattern of electrical activity that can help differentiate them from other types of muscle disease.

A *nerve conduction velocity* test is sometimes also performed. This test measures how fast a nerve impulse travels and how strong it is.

Sometimes these tests are used to rule out disorders that aren't inflammatory myopathies.



Doctors test the strength of various muscles in determining which type of myositis a person has.



A person with a suspected inflammatory myopathy is often asked to undergo a muscle biopsy, a procedure in which a small piece of muscle is removed for examination. This biopsy can enable the physician to pinpoint the diagnosis to a type of myositis.

In PM, the biopsy generally shows the muscle fibers themselves being invaded by cells of the immune system.

In DM, the pattern of cellular invasion suggests that it's the blood vessels in the muscles, and not the muscles themselves, that are the target of the attack. Muscle cells appear smaller than normal around the edges of bundles of muscle fibers, and capillaries are scarce in these regions.

The biopsy sample from a person with IBM is unique because of its *inclusion bodies*, for which the disease is named.

These "bodies," which don't appear in normal cells, contain clumps of discarded cellular material. Inflammatory cells can be seen invading muscle tissue, although some researchers believe this invasion is secondary to the primary events in the muscle tissue, presumably those that cause the inclusion bodies to appear.

What happens to someone with Polymyositis?

Although PM, DM and IBM have certain features in common, they differ in significant ways.

PM is more common in females than males and usually begins after age 20. Over a period of weeks or months, several muscles become weak and gradually get weaker. Most affected are the muscles of the hips and thighs, the upper arms, the top part of the back, the shoulder area and the muscles that move the neck.

Many people with PM have pain or tenderness in the affected areas. The person may have trouble extending the knee, stepping down or climbing stairs. Lifting things, fixing the hair or putting things on a high shelf may be troublesome. It can be hard to raise the head off the bed from a lying-down position.

Swallowing muscles can be affected as well, leading to poor intake of food and weight loss.

PM can also affect the heart muscle, causing a condition called *inflammatory cardiomyopathy*, and the muscles involved in breathing. A few patients develop some inflammation of the lung tissues themselves, another respiratory complication. Of course, the heart, respiratory and swallowing problems are the most serious effects of PM and need close monitoring.

Treatment of PM

The first drug used in the treatment of PM is usually a corticosteroid, such as prednisone. The treatment may involve high-dose oral prednisone on a daily, every other day, or other schedule, or intermittent, short courses of intravenous corticosteroids. Sometimes, prednisone is stopped and then has to be restarted several times during the course of the disease.



Medications are usually effective at controlling the symptoms of PM.



Prednisone is usually very effective at bringing inflammation under control, restoring for the most part the person's strength, as well as swallowing, breathing and heart functions.

But prednisone has many side effects, including unwanted weight gain, redistribution of fat to the face and abdomen and away from the limbs, thinning of the skin, bone loss, cataracts and psychological problems. For this reason, if long-term treatment is necessary, most doctors (and patients) want to lower the dose of prednisone as quickly as possible. This can be accomplished by adding one or more other medications to suppress the damage being caused by the immune system.

These medications include azathioprine, methotrexate, cyclosporine, cyclophosphamide — all "traditional" immunosuppressants that have been used for many years; and some newer drugs, such as mycophenolate mofetil and tacrolimus. Although most people tolerate these medications without difficulty, they carry their own risks, such as flu-like symptoms, a lowered white blood cell count (which can predispose the patient to infection) and liver toxicity. Many are associated with an increased risk of cancer.

Some patients have responded well to intravenous infusion of antibodies culled from donors. This treatment — known as *intravenous immunoglobulins*, or *IVIg*, may seem strange in a disease that's probably caused by an immune response in the first place, but the extra antibodies seem to "confuse" the immune system and at least temporarily alleviate the attack on muscle.

Gently progressive physical therapy, such as that taken in a swimming pool, can be very helpful in maintaining strength. Range-of-motion exercise (putting a joint through its normal movement range), particularly of the shoulders, is helpful in keeping the joints supple.

Some people may need a cane, walker or even a wheelchair during acute flareups of PM. Many people eventually recover much or all of their muscle strength and function, although they may relapse and lose function if they stop taking medications.

Plasmapheresis, a "blood-cleansing" process to remove antibodies, was at one time used in PM and DM, but is seldom used in these diseases today. Immunosuppressant drugs and/or IVIg treatments are now considered more effective.

What happens to someone with Dermatomyositis?

For many decades, dermatomyositis (DM) was considered "polymyositis with a rash." It's now known that the two diseases have some fundamental differences, but for most doctors, it's still the skin ("dermato") manifestations of DM that make it a distinct disorder among the muscle diseases.

In DM, a distinctive reddish or purplish rash, presumably due to inflammation of surface blood vessels, may occur over the face, neck and chest; on the shoulders and upper back, resembling a shawl; and/or on the elbows, knees and ankles. The eyelids may appear as if eye shadow has been applied.

The skin may be scaly, dry and rough. Sometimes it looks like a sunburn.

Unfortunately, the skin involvement in DM isn't limited to rashes.



A reddish or purplish rash and scaly, rough skin are typical in DM.



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A condition called *calcinosis*, in which calcium is deposited just under the skin in hard, painful nodules, can also occur, and seems to be more common in children with DM.

Inflammation of the fat lying just under the skin, called *panniculitis*, can also occur, causing tenderness and feeling like little bumps.

The muscles of the shoulders, upper arms, hips, thighs and neck display the most weakness. As in PM, the swallowing muscles can be involved, and a few people have difficulty chewing because of muscle weakness.

The weakness usually becomes noticeable over the course of several weeks, but it can move faster (days) or more slowly (months).

Joint pain with or without true arthritis (joint inflammation) can be part of DM.

Constriction of the blood vessels around the heart and inflammation of the heart muscle tissue can lead to cardiac complications.

Inflammation of the lung tissues can also occur, as in PM.

Patients with DM can have some inflammation of the blood vessels of the intestinal tract, eyes and kidneys, and these organs can be damaged as a result.

Treatment of DM

The treatment plan in DM is very similar to that used in PM, with drugs that suppress the immune system the mainstay of therapy.

Avoidance of sun exposure during peak sunshine periods and use of sunblock and protective clothing are recommended to avoid exacerbating the skin aspects of the disease.

In children, the disease usually begins between ages 5 and 14 and is more common in girls. It often announces itself with fatigue, fever and a rash, with the muscle pain and weakness following.

DM can be systemic, with many organs involved. Muscle weakness, gastrointestinal problems, joint inflammation and calcium deposits under the skin can make life miserable for a few years. However, children are more likely than adults to eventually recover completely.

Children with DM are treated with the same medications and therapies as adults. Children may have to be kept out of physical education classes during periods of acute disease activity.



Some people with DM, when treated properly, recover completely,



In children, DM usually begins between ages 5 and 14 and is more common in girls.



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What happens to someone with Inclusion-Body Myositis?

Unlike PM and DM, IBM is a disease primarily of men instead of women, and mainly of those older than 50.

The disease also affects different muscles from the other inflammatory myopathies.

IBM usually begins with the gradual onset of slowly progressive weakness in the muscles of the wrists and fingers and those that lift the front of the foot. The muscles of the front of the thigh (quadriceps) are also commonly affected. The weakness may not be the same on both sides of the body.

Trouble with gripping a shopping bag or briefcase, and tripping, are common experiences. About a third of patients have some weakness of the swallowing muscles.

The heart and lung involvement sometimes seen in PM and DM is *not* part of the IBM picture.

IBM is generally a slowly progressive disease, and life expectancy isn't significantly affected. Most people with IBM remain able to walk, although they may require a cane or wheelchair for long distances. Some are more severely affected, becoming gradually more disabled and needing wheelchairs within 10 or 15 years of the first symptoms.

Treatment of IBM

Treatment with drugs that suppress the immune system has been tried in IBM, but in general hasn't been effective. Some physicians may try corticosteroids or other medications that alter the immune response if the patient wishes this treatment, but many feel that side effects outweigh any subtle benefits that might occur with these drugs in IBM.

There are some genetic forms of IBM, but for the most part, inflammation isn't a major part of the picture. For this reason, these forms are often called *inclusion-body myopathy* (muscle disorder), leaving out the "itis" in the disease name to reflect the relative lack of inflammation.

Genetic inclusion-body myopathies can be inherited in either a *dominant* or a *recessive* pattern. Dominant genetic disorders require only one genetic flaw to show themselves. Recessive disorders require that both parents pass on a flaw in the same gene before their offspring can show signs of the disease.

Your neuromuscular clinic physician or genetic counsellor can give you more information about the risks of inheriting or passing on inclusion-body myopathy. Also, see MDA's fact sheet, "Genetics and Neuromuscular Diseases."



Weakness caused by IBM may require modification of some activities. This man continues horseback riding but now uses a platform to mount the horse.



Many people with IBM remain able to walk but use wheelchairs for long distances.



IBM is more common in men but can also affect women.



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Search for treatments and cures

Scientists are moving ahead on several fronts with research to improve the understanding and treatment of inflammatory muscle diseases.

Studies include a search for cells persisting in the bloodstreams of mothers of patients with childhood dermatomyositis; and investigations of genetic influences in childhood DM, and patterns of gene activity in the various inflammatory myopathies, using new technologies called *gene chips*.

Other researchers are studying the mechanism of inflammation in the muscles of people with inflammatory myopathies, with the goal of deciphering the precise autoimmune target in muscle tissue. Still others are developing animal models of inflammatory myopathies.

Investigators are also studying a substance called *amyloid-beta* to understand its role in inclusion-body myositis.

Your neuromuscular clinic may provide opportunities for patients to participate in trials of experimental treatments for myositis.

