The Inflammatory Myopathies

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
National Institutes of Health

The Inflammatory Myopathies

What are the inflammatory myopathies?

The *inflammatory myopathies* are a group of diseases that involve chronic (long-standing) muscle inflammation, muscle weakness, and, in some cases, muscle pain. *Myopathy* is a general medical term used to describe a number of conditions affecting the muscles. All myopathies cause muscle weakness.

The four main types of chronic, or long-term, inflammatory myopathies are:

- polymyositis
- dermatomyositis
- inclusion body myositis
- necrotizing autoimmune myopathy.

What causes these disorders?

Myositis, or general muscle inflammation, may be caused by:

- autoimmune disorders in which the immune system attacks muscle
- an allergic reaction following exposure to a toxic substance or medicine
- a virus or other infectious organism such as bacteria or fungi.

Although the cause of many inflammatory myopathies is unknown, the majority are considered to be autoimmune disorders, in which the body's immune response system that normally defends against infection and disease attacks its own muscle fibers, blood vessels, connective tissue, organs, or joints.

Who is at risk?

The inflammatory myopathies are rare and can affect both adults and children. Dermatomyositis is the most common chronic form in children. Polymyositis and dermatomyositis are more common in females while inclusion body myositis affects more men. Inclusion body myositis usually affects individuals over age 50.

What are the signs and symptoms?

General symptoms of chronic inflammatory myopathy include slow but progressive muscle weakness. Inflammation damages the muscle fibers, which causes weakness, and may affect the arteries and blood vessels that pass through muscle. Other symptoms include fatigue after walking or standing, frequent episodes of tripping or falling, and difficulty swallowing or breathing. Some individuals may have muscle pain or muscles that are tender to touch.

- **Polymyositis** affects skeletal muscles (the type involved in body movement) on both sides of the body. It is rarely seen in persons younger than age 20. Generally, the onset occurs between age 30 and 60.

Signs and symptoms of polymyositis vary considerably from person to person, which can make it difficult to diagnose. Untreated progressive muscle weakness may lead to difficulty swallowing, speaking, rising from a sitting position, climbing stairs, lifting objects, or reaching overhead. Some people with polymyositis may also develop arthritis, shortness of breath, heart arrhythmias (irregular heartbeats), or congestive heart failure (when the heart is no longer able to pump out enough oxygen-rich blood).

- **Dermatomyositis** is characterized by a skin rash that precedes or accompanies progressive muscle weakness. The rash appears patchy, with purple or red discolorations, and characteristically develops on the eyelids and on muscles used to extend or straighten joints, including knuckles, elbows, knees, and toes. Red rashes may also occur on the face, neck, shoulders, upper chest, back, and other locations. There may be swelling in the affected areas. The rash sometimes occurs without obvious muscle involvement and often becomes more evident with sun exposure.

  Adults with dermatomyositis may experience weight loss or a low-grade fever, have inflamed lungs, and be sensitive to light. Adult dermatomyositis, unlike polymyositis, may accompany tumors of the breast, lung, female genitalia, or bowel. Children and adults with dermatomyositis may develop calcium deposits, which appear as hard bumps under the skin or in the muscle

(called calcinosis). Calcinosis most often occurs one to three years after disease onset but may occur many years later. These deposits are seen more often in childhood dermatomyositis than in dermatomyositis that begins in adulthood.

In some cases of polymyositis and dermatomyositis, distal muscles (which are the muscles away from the center of the body, such as those in the forearms and around the ankles and wrists), may be affected as the disease progresses. Polymyositis and dermatomyositis may be associated with collagen-vascular or autoimmune diseases such as lupus. Polymyositis may also be associated with infectious disorders such as HIV, which causes AIDS.

- **Inclusion body myositis (IBM)** is the most common form of inflammatory myopathy in people age 50 years and older and is characterized by slow, progressive muscle weakness and wasting over the course of months or years. IBM affects both proximal and distal muscles, typically in the thighs and forearms, and is often occurs on both sides of the body, although muscle weakness may affect only one side of the body. It also includes features of muscle degeneration with multi-protein aggregates (clumps) in the muscle that can contain toxins seen in Alzheimer's disease and other neurodegenerative diseases.

Falling and tripping are usually the first noticeable symptoms. The disorder often begins with weakness in the wrists and fingers that causes difficulty with pinching, buttoning, and gripping objects. People may experience weakness in their wrist and finger muscles and atrophy (thinning or loss of muscle bulk) in their forearm muscles and quadriceps muscles in the thighs. Difficulty swallowing occurs in approximately half of IBM cases due to involvement of the throat muscles.

Symptoms of the disease usually begin after the age of 50, although the disease can occur earlier. Unlike polymyositis and dermatomyositis, IBM occurs more frequently in men than in women.

- **Necrotizing autoimmune myopathy (NAM)** is a rare and relatively newly recognized subgroup of inflammatory myopathies. NAM can occur at any age but usually affects adults. Its symptoms are similar to polymyositis and dermatomyositis, with weakness in both the upper and lower body, difficulty rising from low chairs, climbing stairs, or lifting objects. However, the onset of these symptoms can be more severe and sudden, reaching their peak over a period of days or weeks. Other symptoms include fatigue, weight loss, and muscle pain.

NAM occurs alone or after viral infections, in association with cancer, in people with connective-tissue disorders such as scleroderma, or, rarely, in people taking cholesterol lowering medications (statins). Muscle weakness and pain may continue to worsen even after individuals stop taking the drugs.

- **Childhood inflammatory myopathies** have some similarities to adult dermatomyositis and polymyositis. They typically affect children ages 2 to 15 years. Symptoms include proximal muscle weakness and inflammation, edema (an abnormal collection of fluids within body tissues that causes swelling), muscle pain, fatigue, skin rashes, abdominal pain, fever, and contractures. Contractures result from shortening of muscles or tendons around joints, are caused by inflammation in the muscle tendons, and prevent the joints from moving freely.

  Children with inflammatory myopathies may have difficulty swallowing and breathing. The heart may also be affected. Between 20 to 40 percent of children with juvenile dermatomyositis develop calcinosis, which can cause significant muscle weakness and pain, joint contracture, skin ulcers, and decreased muscle bulk.

How are the inflammatory myopathies diagnosed?

Diagnosis is based on medical history, results of a physical examination that includes tests of muscle strength, and blood samples that show elevated levels of various muscle enzymes and autoantibodies. Diagnostic tools include:

- electromyography to record the electrical activity generated by muscles during contraction and at rest
- ultrasound to look for muscle inflammation
- magnetic resonance imaging to reveal abnormal muscle anatomy.

A biopsy sample of muscle tissue should be examined for signs of chronic inflammation, muscle fiber death, vascular deformities, or other changes specific to the diagnosis of a particular type of inflammatory myopathy. A skin biopsy can show changes in the skin associated with dermatomyositis.

How are these disorders treated?

Chronic inflammatory myopathies cannot be cured in most adults but many of the symptoms can be treated. Options include:

- medication
- physical therapy
- exercise
- heat therapy
- orthotics and assistive devices
- rest.

Dermatomyositis, polymyositis, and necrotizing autoimmune myopathy are first treated with high doses of corticosteroid drugs, such as prednisone. This is most often given as an oral medication but can be delivered intravenously.

Immunosuppressant drugs, such as azathioprine and methotrexate, may reduce inflammation in individuals who do not respond well to prednisone. Periodic treatment using intravenous immunoglobulin can increase the chance for recovery in individuals with dermatomyositis, polymyositis, or NAM. Other immunosuppressive agents that may treat the inflammation associated with dermatomyositis and polymyositis include cyclosporine A, cyclophosphamide, mycophenolate mofetil, and tacrolimus.

Injections of adrenocorticotropic hormone gel may be another option for people who do not respond to or cannot tolerate other drug treatment options. Biologic therapies such as rituximab or tumor necrosis factor (TNF) inhibitors such as infliximab or etanercept may be used in severe cases where other treatment options have failed. However, there are very few studies that have shown how well these agents treat polymyositis and dermatomyositis.

Physical therapy is usually recommended to prevent muscle atrophy as well as to maintain muscle strength and range of motion. Bed rest for an extended period of time should be avoided, as people may develop muscle atrophy, decreased muscle function, and joint contractures. A low-sodium diet may help to reduce edema (swelling) and cardiovascular (heart and blood vessel) complications.

Many individuals with dermatomyositis may need a topical ointment such as corticosteroids, tacrolimus, or pimecrolimus for their skin disorder. They should wear a high-protection sunscreen and protective clothing, particularly those who are light-sensitive. In rare instances, surgery may be required to remove calcium deposits that cause nerve pain and recurrent infections.

There is no standard, evidence-based course of treatment for inclusion body myositis. The disease is generally unresponsive to corticosteroids and immunosuppressive drugs. Some evidence suggests that immunosuppressive medications or intravenous immunoglobulin may have a slight, but short-lasting, beneficial effect in a small number of cases. Physical therapy may be helpful in maintaining mobility. Other therapy is symptomatic and supportive.

What is the prognosis for these diseases?

In most cases, the symptoms of dermatomyositis resolve with therapy. The disease is usually more severe and resistant to therapy in individuals with heart problems. Approximately one-third of individuals with juvenile-onset dermatomyositis recover from their illness, one-third have a relapsing-remitting course of disease, and the other third have a more chronic course of illness.

The prognosis for polymyositis varies. Most individuals respond fairly well to therapy, but some people have a more severe disease that does not. These individuals may have significant disability. Since polymyositis can cause difficulty swallowing, people can become malnourished. They are also at increased risk for falling, which can lead to hip and other bone fractures, disability, or death. In rare cases people with severe and progressive muscle weakness can develop respiratory failure or pneumonia.

Although necrotizing autoimmune myopathy is more difficult to treat than polymyositis and dermatomyositis, it generally responds well to long-term combination immunosuppressive therapies.

IBM is generally resistant to all therapies and currently available treatments do little to slow its progression.

What research is being done?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge of the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world.

NINDS, along with other agencies within the NIH, conducts and supports a wide range of research on neuromuscular disorders, including myositis and the inflammatory myopathies. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) is the primary funding institute for these efforts.

One challenge in treating inflammatory myopathies is that, for some individuals, there is little direct relationship between muscle inflammation and the degree of weakness and disability. While inflammation can be slowed or reversed, muscle weakness may not respond to treatments. NIH researchers are working to identify the causes of muscle weakness in order to discover effective treatments. In addition, researchers are working to develop objective, imaging-based methods for describing the muscle damage associated with inflammatory muscle disease.

Additionally, NIH-funded researchers are studying childhood-onset polymyositis and dermatomyositis to learn more about their causes, immune system changes throughout the course of the disease, and associated medical problems. For example, scientists are studying the role of genetics in the development of juvenile dermatomyositis. Researchers are examining the genetic differences between sets of twins in order to identify the relationship between genes and dermatomyositis that may lead to potential new treatment methods for the condition.

Currently, there are no therapies approved by the U.S. Food and Drug Administration for diagnosing inflammatory myopathies. NIH-funded researchers are looking for better, less invasive ways of diagnosing these disorders. For example, researchers are developing a non-invasive test that diagnoses IBM using circulating RNA molecules in the blood or urine. Researchers hope that this test will help clinicians identify individuals with IBM and assist them in monitoring their responses to clinical therapeutic trials.

Scientists are testing if the drug sodium thiosulfate can treat calcium buildup seen in people with juvenile and adult dermatomyositis. Other NIH-funded researchers are studying the genetic diversity disease susceptibility in the inflammatory myopathies. Researchers from the National Institute of Environmental Health Sciences (NIEHS) are evaluating possible contributing causes, including dietary supplements, tobacco smoke, and infectious agents. Other researchers are also investigating

the impact of certain drugs on muscle inflammation. For example, NIH researchers are exploring the impact of autoimmune muscle disease triggered by statins.

More information about research on myositis and the inflammatory myopathies supported by NINDS and other NIH Institutes and Centers may be found using NIH RePORTER (projectreporter.nih.gov), a searchable database of current and past research projects supported by NIH and other Federal agencies. RePORTER also includes links to publications and resources from these projects.

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
800-352-9424
www.ninds.nih.gov

Information also is available from the following organizations:

American Autoimmune Related Diseases Association
22100 Gratiot Avenue
Eastpointe, MI 48021
586-776-3900
800-598-4668
www.aarda.org

Arthritis Foundation
1355 Peachtree Street, NE
Sixth Floor
Atlanta, GA 30309
404-872-7100
844-571-5357
www.arthritis.org

Myositis Association
2000 Duke Street, Suite 300
Alexandria, VA 22314
703-553-2632
800-821-7356
www.myositis.org

Muscular Dystrophy Association
161 N. Clarke, Suite 3550
Chicago, IL 60601
800-572-1717
www.mda.org

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Information Clearinghouse
National Institutes of Health, DHHS
Bethesda, MD 20892-3675
877-226-4267
www.niams.nih.gov

National Institute of Environmental Health Sciences (NIEHS)
National Institutes of Health
105 T.W. Alexander Drive
Research Triangle Park, NC 27709
919-541-3345
www.niehs.nih.gov

U.S. National Library of Medicine
National Institutes of Health/DHHS
8600 Rockville Pike
Bethesda, MD 20894
301-594-5983
888-346-3656
www.nlm.nih.gov

National Institute of
Neurological Disorders
and Stroke

NIH . . . Turning Discovery Into Health

Prepared by:
Office of Communications and Public Liaison
National Institute of Neurological
Disorders and Stroke
National Institutes of Health
Department of Health and Human Services
Bethesda, Maryland 20892-2540

NIH Publication No. 20-NS-5321 March 2020