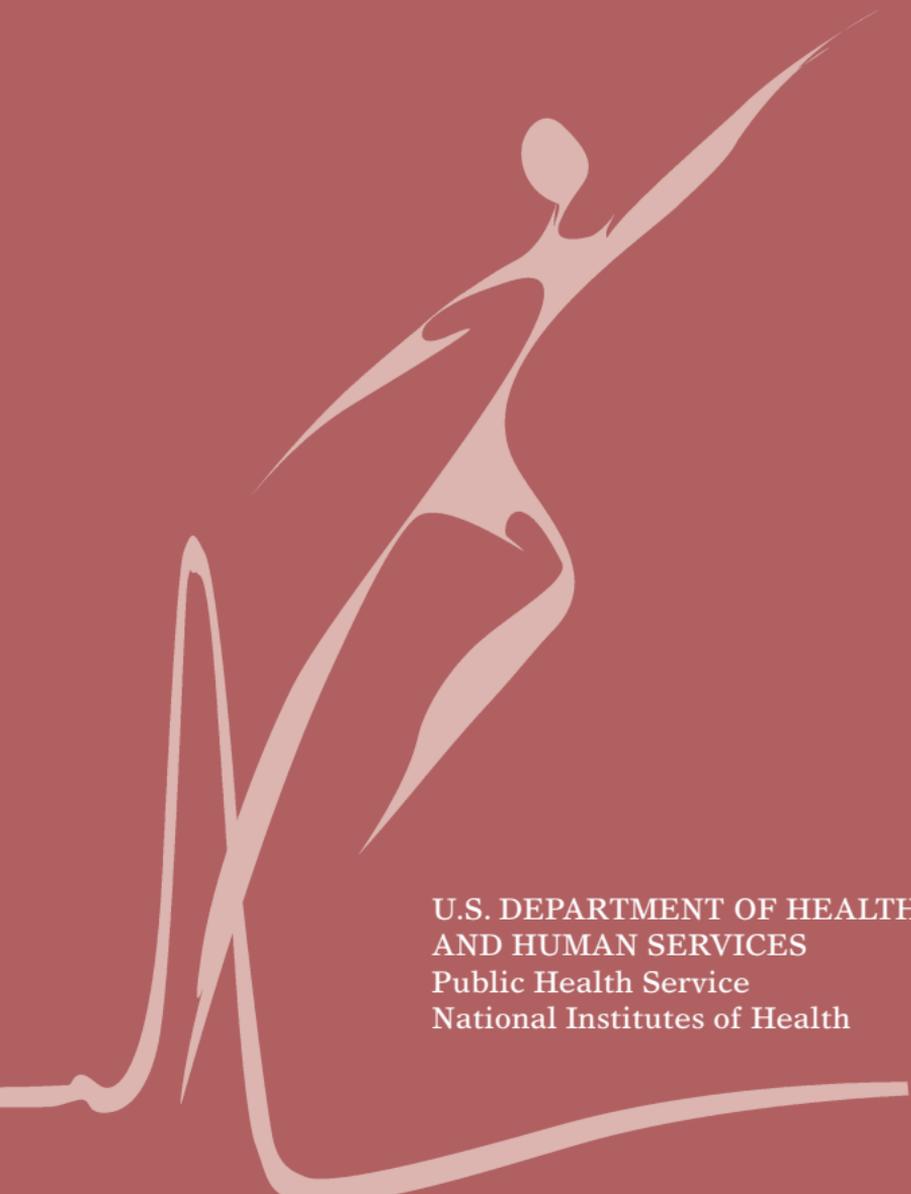


The Inflammatory Myopathies

A stylized, light-colored graphic of a person with arms raised in a gesture of triumph or health, overlaid on a pulse line. The figure is composed of smooth, flowing shapes. The pulse line starts from the left, has a small initial bump, then rises to a sharp peak before dipping and continuing as a long, low wave towards the right.

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



The Inflammatory Myopathies

What are the inflammatory myopathies?

M*yopathy* is a term used to describe muscle disease. The *inflammatory myopathies* are a group of diseases that involve chronic muscle inflammation, accompanied by muscle weakness. Another word for chronic inflammation of muscle tissue is myositis.

The three main types of chronic, or persistent, inflammatory myopathy are polymyositis, dermatomyositis, and inclusion body myositis.

What causes these disorders?

Muscle inflammation may be caused by an allergic reaction, exposure to a toxic substance or medicine, another disease such as cancer or rheumatic conditions, or a virus or other infectious agent. The chronic inflammatory myopathies are idiopathic, meaning they have no known cause. They are thought to be autoimmune disorders, in which the body's white blood cells (that normally fight disease) attack blood vessels, normal muscle fibers, and connective tissue in organs, bones, and joints.

Who is at risk?

These rare disorders may affect both adults and children, although dermatomyositis is the most common chronic form in children. Polymyositis and dermatomyositis are more common in women than in men. A rare childhood onset form of polymyositis and dermatomyositis can occur in children between the ages of 2 and 15 years. 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 that starts in the proximal muscles—those muscles closest to the trunk of the body. Inflammation damages the muscle fibers, causing weakness, and may affect the arteries and blood vessels that run through the muscle. Other symptoms include fatigue after walking or standing, tripping or falling, and difficulty swallowing or breathing. Some patients may have slight muscle pain or muscles that are tender to touch.

Polymyositis affects skeletal muscles (involved with making movement) on both sides of the body. It is rarely seen in persons under age 18; most cases are in individuals between the ages of 31 and 60. Progressive muscle weakness leads to difficulty swallowing, speaking, rising from a sitting position, climbing stairs, lifting objects, or reaching overhead. Individuals with polymyositis may also experience arthritis, shortness of breath, and irregular heart rate or rhythm.

Dermatomyositis is characterized by a skin rash that precedes or accompanies progressive muscle weakness. The rash looks 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, and there may be swelling in the affected areas. The rash sometimes occurs without obvious muscle involvement. 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 1-3 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 adults. Dermatomyositis may be associated with collagen-vascular or autoimmune diseases.

In some cases of polymyositis and dermatomyositis, distal muscles (away from the trunk 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. Polymyositis may also be associated with infectious disorders.

Inclusion body myositis (IBM) is characterized by progressive muscle weakness and wasting. The onset of muscle weakness is generally gradual (over months or years) and affects both proximal and distal muscles. Muscle weakness may affect only one side of the body. Small holes called vacuoles are sometimes seen in the cells of affected muscle fibers. Falling and tripping are usually the first noticeable symptoms of IBM. For some individuals the disorder begins with weakness in the wrists and fingers that causes difficulty with pinching, buttoning, and gripping objects. There may be weakness of the wrist and finger muscles and atrophy (thinning or loss of muscle bulk) of the forearm muscles and quadricep muscles in the legs. Difficulty swallowing occurs in approximately half of IBM cases. 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.

Juvenile myositis has some similarities to adult dermatomyositis and polymyositis. It typically affects children ages 2 to 15 years, with symptoms that 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 (chronic shortening of muscles or tendons around joints, caused by inflammation in the muscle tendons, which prevents the joints from moving freely). Children with juvenile myositis may also have difficulty swallowing and breathing, and the

heart may be affected. Approximately 20 to 30 percent of children with juvenile dermatomyositis develop calcinosis. Affected children may not show higher than normal levels of the muscle enzyme creatine kinase in their blood but have higher than normal levels of other muscle enzymes.

How are the inflammatory myopathies diagnosed?

Diagnosis is based on the person's medical history, results of a physical exam and 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 that controls muscles during contraction and at rest, ultrasound to look for muscle inflammation, and magnetic resonance imaging to reveal abnormal muscle and evaluate muscle disease. A muscle biopsy can be examined by microscopy for signs of chronic inflammation, muscle fiber death, vascular deformities, or the changes specific to the diagnosis of IBM. A skin biopsy can show changes in the skin layer in individuals with dermatomyositis.

How are these disorders treated?

The 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 (including microwave and ultrasound), orthotics and assistive devices, and rest.

Inflammatory myopathies that are caused by medicines, a virus or other infectious agent, or exposure to a toxic substance usually abate when the harmful substance is removed or the infection is treated. If left untreated, inflammatory myopathy can cause permanent disability.

Polymyositis and dermatomyositis are first treated with high doses of corticosteroid drugs. 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 people with dermatomyositis or polymyositis. Other immunosuppressive agents that may treat the inflammation associated with dermatomyositis and polymyositis include cyclosporine A, cyclophosphamide, and tacrolimus. Physical therapy is usually recommended to prevent muscle atrophy and to regain muscle strength and range of motion. Bed rest for an extended period of time should be avoided, as individuals may develop muscle atrophy, decreased muscle function, and joint contractures. A low-sodium diet may help to counter edema and cardiovascular complications.

Many individuals with dermatomyositis may need a topical ointment (such as topical corticosteroids or tacrolimus or pimecrolimus) or additional treatment for their skin disorder.

A high-protection sunscreen and protective clothing should be worn by all affected individuals, particularly those who are sensitive to light. Surgery may be required to remove calcium deposits that cause nerve pain and recurrent infections.

There is no standard course of treatment for IBM. 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?

Most cases of dermatomyositis respond to therapy. The disease is usually more severe and resistant to therapy in individuals with cardiac or pulmonary problems.

The prognosis for polymyositis varies. Most people respond fairly well to therapy, but some individuals have a more severe disease that does not respond adequately to therapies and are left with significant disability. In rare cases individuals with severe and progressive muscle weakness can have respiratory failure or pneumonia. Difficulty swallowing can lead to becoming malnourished. Falls leading to fractures (particularly of the hip) should be guarded against because of the high rate of disability or death that can result.

IBM is generally resistant to all therapies and its rate of progression appears to be unaffected by currently available treatments.

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.

What research is being done?

The National Institutes of Health (NIH), through the collaborative efforts of its National Institute of Neurological Disorders and Stroke (NINDS), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), and National Institute of Environmental Health Sciences (NIEHS), conducts and supports a wide range of research on neuromuscular disorders, including myositis and the inflammatory myopathies.

Scientists are conducting studies to determine the safety and effectiveness of alemtuzumab in improving muscle strength in individuals with IBM. This laboratory-made antibody has been used to treat people with autoimmune conditions such as rheumatoid arthritis, vasculitis, multiple sclerosis, and tissue rejection associated with transplantation.

Researchers are also studying individuals with IBM to learn how muscle inflammation destroys muscle fiber and causes weakness. Study results may lead to a new treatment for the disease.

The muscle fiber physiology of IBM is remarkably similar to protein accumulation damage

seen in the brains of people with Alzheimer's disease (AD). Both hereditary IBM and AD muscle fibers are injured by oxidative stress—the buildup of certain molecules that contributes to autoimmune diseases and inflammation. NIH-funded research is examining the mechanisms and molecular changes involved in the early buildup of harmful proteins that leads to vacuolar (involving holes in cells) muscle fiber degeneration.

The NINDS, NIAMS, and NIEHS are funding DNA analyses using microarrays to characterize patterns of muscle gene expression among adults and juveniles with distinct subtypes of inflammatory myopathies. Findings will be used to refine disease classification and provide clues to the pathology of these disorders.

Other NIH-funded research is studying prior viral infection as a precursor to inflammatory myopathy. Scientists are using a mouse model of chronic inflammatory myopathy to identify specific viral genes that are crucial to disease development.

NIH-funded researchers are also 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. Scientists are studying inflammation and how skeletal muscle degeneration leads to weakness and muscle wasting. NIEHS researchers are also studying immunogenetic and environmental risk factors for these diseases. Other research hopes to determine whether the drug infliximab, which blocks a protein that is associated with harmful inflamma-

tion, and rituximab, a monoclonal antibody directed against B cells, are safe and effective in treating dermatomyositis and polymyositis.

NIH-funded researchers are studying the effectiveness and safety of the antitumor necrosis factor drug etanercept in new-onset dermatomyositis and the safety and effectiveness of rituximab in reducing inflammation in individuals with dermatomyositis, polymyositis, or juvenile dermatomyositis.

Where can I go for more information?

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

BRAIN

P.O. Box 5801

Bethesda, MD 20824

301-496-5751

800-352-9424

www.ninds.nih.gov

Additional information about myositis and the inflammatory myopathies is available from the following organizations:

American Autoimmune Related Diseases Association

22100 Gratiot Avenue
East Detroit, MI 48021
586-776-3900
800-598-4668
www.aarda.org

The Myositis Association

1737 King Street, Suite 600
Alexandria, VA 22314
703-299-4850
800-821-7356
www.myositis.org

Arthritis Foundation

P.O. Box 7669
Atlanta, GA 30357
404-872-7100
800-283-7800
www.arthritis.org

Muscular Dystrophy Association

3300 East Sunrise Drive
Tucson, AZ 85718-3208
520-529-2000
800-572-1717
www.mdauusa.org

**National Institute of Arthritis and
Musculoskeletal and Skin Diseases
Information Clearinghouse**
National Institutes of Health/DHHS
1 AMS Circle
Bethesda, MD 20892-3675
877-226-4267
301-565-2966 (TTY)
www.niams.nih.gov

**National Institute of Environmental
Health Sciences**
National Institutes of Health/DHHS
Building 31, Room B1C03
31 Center Drive, MSC 2256
Bethesda, MD 20892-2256
301-496-3511
919-541-3345
www.niehs.nih.gov



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