



Facts About
Facioscapulohumeral
Muscular Dystrophy

MDA[®]

Dear Friends:

Facioscapulohumeral muscular dystrophy (FSHD) has been a part of my family's life for many years.

My great-great-grandfather had FSHD — and lived to 102! Of the five children in my mother's family, three were affected, including my mother, who received the diagnosis in her 30s. So when I was 9 years old and my parents saw my "crooked smile," they knew.

This booklet has been prepared to give you the basic knowledge about FSHD that you'll need to make your life as enjoyable and productive as possible. With this information, you or your children can be prepared for changes to come and armed to minimize many effects of the disease.

By understanding how the disease affects me in different ways, I've been able to have a full and rewarding personal and professional life. My wife, Joy, and I have one child and three grandchildren, none of whom have FSHD. For the past six years I've been blessed with a magnificent canine companion, Randdel, a golden retriever service dog. Until recently, I had a demanding hobby building replicas of historic ships. I now focus on stamp collecting, and through my store on eBay, P&J Collectables, buy and sell sheets of U.S. mint stamps.

Like me, you'll find ways to strike a balance between doing too much and doing too little. Never think that life is over!

From this booklet you'll learn some encouraging things about FSHD: There are treatments and interventions for most of the symptoms and difficulties that arise with the disease. FSHD doesn't shorten life expectancy, and for most people it progresses very slowly, giving you time to prepare for and adjust to changes. Unlike some other forms of

muscular dystrophy, this one typically isn't threatening to heart and breathing function.

MDA's research program is constantly making strides toward better treatments and a cure. In the meantime, it's good to know that people with disabilities have more opportunities than ever before to develop and use their abilities, as well as legal rights to equal employment opportunity and access to public places. Federal law guarantees children with physical and cognitive disabilities a public education with whatever supports they need.

MDA has been a wonderful ally in my fight against this disease. "MDA Is Here to Help You" on page 10 introduces MDA's many services.

As you face the challenges ahead, please remember: You're not alone. You can have a good life with FSHD.



Paul Topkin
Lakeland, Florida



Paul Topkin

What is Facioscapulohumeral Muscular Dystrophy?

Facioscapulohumeral muscular dystrophy (FSHD) is a genetic muscle disorder in which the muscles of the face, shoulder blades and upper arms are among the most severely affected.

The long name comes from *facies*, the Latin word and medical term for face; *scapula*, the Latin word and anatomical term for shoulder blade; and *humerus*, the Latin word for upper arm and the anatomical term for the bone that goes from the shoulder to the elbow.

The term *muscular dystrophy* means progressive muscle degeneration, with increasing weakness and wasting (loss of bulk) of muscles. In FSHD, weakness first and most seriously affects the face, shoulders and upper arms, but the disease usually also causes weakness in other muscles.

Because FSHD is a disease that usually progresses very slowly and rarely affects the heart or respiratory system, it isn't considered life-threatening. Most people with the disease have a normal life span.

What causes FSHD?

FSHD is almost always associated with a genetic flaw (mutation) that leads to a shorter than usual segment of DNA on chromosome 4. The segment isn't part of any particular gene, but it nevertheless seems to interfere with the correct processing of genetic material.

A small number of people have a disorder that looks exactly like FSHD but don't have the short segment on chromosome 4. The genetic cause of their disorder has yet to be identified.

For more about how the missing chromosome 4 segment may cause FSHD, see "MDA's Search for Treatments and Cures," page 9.

Are there different forms of FSHD?

Some experts divide FSHD into adult-onset and infantile-onset forms. The adult-onset (which includes FSHD that begins in adolescence) is far more common.

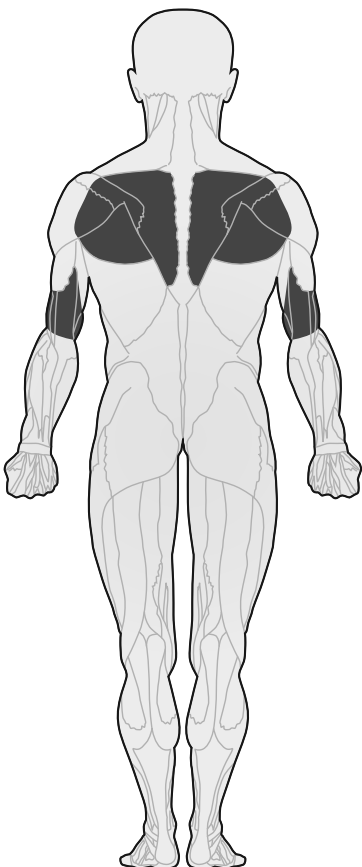
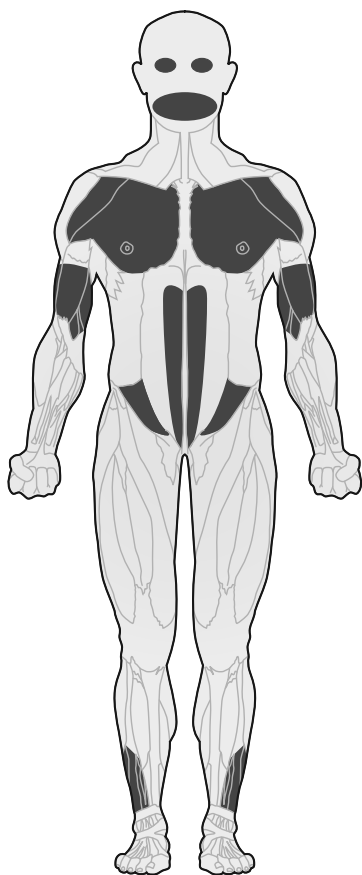
In either type of FSHD, facial weakness can start in childhood. Occasionally, other FSHD symptoms appear in early childhood. This type of FSHD, the infantile-onset form, generally runs a more severe course with regard to muscle weakness and sometimes also affects hearing and vision. Preliminary evidence suggests that the infantile-onset form is associated with a larger piece of missing DNA.

What happens to someone with FSHD?

The age of onset, progression and severity of FSHD vary a great deal.

Usually, symptoms develop during the teen years, with most people noticing some problems by age 20, although weakness in some muscles can begin as early as infancy and as late as the 50s. In some people, the disease can be so mild that no symptoms are noticed. In these cases, the disease may only be diagnosed after another, more affected member of the family comes to medical attention.

Usually, people don't go to the doctor until their shoulder or leg muscles become involved and they experience difficulty reaching over their heads or going up and down stairs. When questioned closely, many people can remember having symptoms in childhood, such as shoulder blades that stuck out or trouble throwing a ball. Very often, people say they've never been able to whistle or blow up a balloon, or that they've had trouble drinking

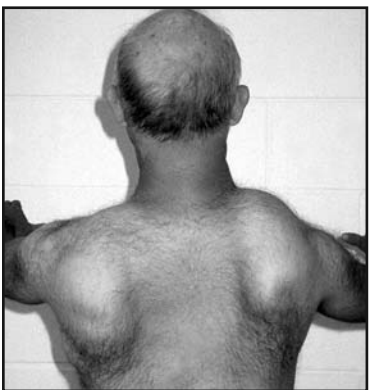
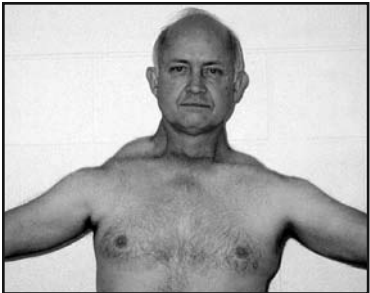




After surgery to stabilize her right shoulder blade, this woman has better use of her arm and less pain in her upper back.



Facial weakness can make it hard to use a straw or even smile.



Because of weakness in the shoulders and back, muscles that normally don't show from the front are visible in FSHD. This man also shows a typical nonsymmetrical pattern of weakness, with scapular winging and slight scoliosis.

through a straw, but they may not have associated these problems with muscular dystrophy.

In most people with FSHD, the disease progresses very slowly. It can take as long as 30 years for the disease to become seriously disabling, and that doesn't happen to everyone. Estimates are that about 20 percent of people with FSHD eventually use a wheelchair at least some of the time.

Facial weakness

Facial weakness is often the first sign of FSHD, but it may not be noticed right away by the person with the disorder. It's usually brought to his or her attention by someone else or by a doctor.

The muscles most affected are those that surround the eyes and mouth. It's hard to pucker up or to get much strength in the mouth, which is why people with the disease have trouble with balloons, straws and whistling.

Of somewhat more concern is the weakness in the eye muscles, which can keep the eyes from closing completely during the night. As the disease progresses, the eyes can sometimes dry out overnight, which can injure them. Waking up in the morning with gritty, burning or dry eyes may be a sign that eye closure isn't complete. Wearing an eye shield or patching the eyes during sleep may be necessary.

Shoulder weakness

Most people with FSHD notice weakness in the area of the shoulder blades — the *scapulae* — as the first sign that something is amiss.

The shoulder blades are normally fairly fixed in their position. They act as fulcrums that allow the arm muscles to get leverage for lifting things, including their own weight.

In FSHD, the muscles that hold the shoulder blades in place weaken, allowing these

bones to move excessively. The shoulder blades stick out and rise up toward the neck as they move, which is called *scapular winging*, because the protruding bone resembles a wing.

Leverage is at least partially lost. The weakness often isn't the same on both sides of the body.

Early on, the person with FSHD notices things like being unable to throw a ball effectively. Later, it may be hard to lift the arms over the head to do one's hair or reach a high shelf or hang something. These problems are due to weakening of the muscles around the shoulder and in the upper arm.

Lower leg weakness

As FSHD progresses, the muscles on the front and sides of the lower legs often weaken. These are the muscles that allow us to raise the front of the foot when walking so we don't trip over our toes.

When these muscles weaken, the foot stays down after pushing off during walking, sometimes tripping the walker. This condition is called *foot drop*.

The doctor may say, "Walk on your heels, like a penguin" to test the strength of these foot-lifting muscles.

When questioned, people will say, "I seem to catch my foot when I walk" or "I seem to fall over my own feet." Trouble with stairs and with uneven surfaces is common.

Not everyone with FSHD develops this lower leg problem.

Abdominal muscle weakness

In many people with FSHD, weakness develops in the muscles of the abdomen. These can weaken early in the disorder. As abdominal weakness progresses, the person develops a *lordosis*, an exaggerated curve in the lumbar (lower) region of the spine.

Hip weakness

In some people, weakness of the hip muscles that surround the pelvis (doctors call this the *pelvic girdle*) also occurs. This doesn't happen to everyone. Weakness of the hips seems to start most often in middle adulthood, if it happens at all. Hip weakness causes trouble with rising from a chair or negotiating stairs and can lead to the need for a wheelchair, especially for long distances. Upper leg muscles are sometimes also affected. Pelvic girdle weakness may result in a waddling gait and contribute to the lordosis so often seen in FSHD.

In children with FSHD, hip weakness may be the first thing parents notice, since it causes trouble with walking and running.

Unequal (nonsymmetrical) weakness

In most people with FSHD, weakness differs at least a little bit between the left and right sides of the body. In some people with FSHD, this difference between sides can be quite striking. The reason for this lack of symmetry, which is not seen in most types of muscular dystrophy, is not clear.

Does FSHD have effects other than weakness?

Yes. There are some other things to consider in FSHD besides muscle weakness.

Pain and inflammation

Inflammation of muscles — an attack by certain types of cells of the immune system — occurs in some muscular dystrophies and can be extensive in some people with FSHD.

For this reason, FSHD is sometimes misdiagnosed as another type of muscle disease, *polymyositis*, a nongenetic disorder in which the immune system attacks the muscles. An important difference is that polymyositis is treatable with prednisone

(Deltasone and other brand names), a corticosteroid drug that suppresses inflammation, while prednisone doesn't seem to change the course of FSHD. Its many side effects make it impractical to use just to relieve discomfort. (See "Are there medical treatments?" page 7.)

Pain in FSHD may also come from the way weakened muscles pull bony structures, such as the spine and shoulder blades, out of alignment.

Joint and spinal abnormalities

When muscle weakness is severe and prolonged, it can lead to freezing of joints in one position. Such freezing is called a *contracture*. In FSHD, if contractures occur at all, they're likely to be in the ankle joints.

The spinal column is actually made up of many joints between the vertebrae. The spine is designed to be flexible, somewhat like a Slinky toy, so when the muscles surrounding the spine weaken, the column is pulled out of alignment.

The misalignment often takes the form of *lordosis*, or *swayback*, but also can take the form of *scoliosis*, in which the spine curves to the side, like an S. The scoliosis that sometimes occurs in FSHD usually isn't severe.

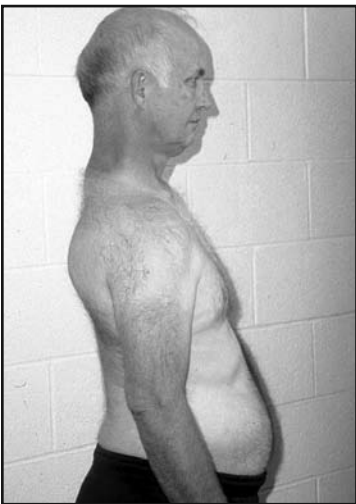
Mild hearing loss

Hearing loss sometimes occurs in FSHD, but it's usually mild and mostly affects perception of high-pitched sounds. Often, it's so minor that it isn't noticed until careful testing is done (for example, as part of a study). Some experts have even questioned whether hearing loss is really more common in adult-onset FSHD than it is in adults in general. The reason for the hearing loss, when it occurs, isn't clear.

When FSHD starts in childhood, loss of hearing in the higher pitch ranges can be more severe than in adult-onset FSHD. The reason for this is likewise unclear.



This woman can barely pull back her right foot because of FSHD.



Lordosis is typical in FSHD.

Abnormalities of the retina

Some abnormalities in the blood vessels of the retina, the “screen” on the back of the eye onto which visual images are projected, are often detected in people with FSHD. Fortunately, very few people have any problems with vision resulting from this, but it should be monitored by an eye doctor. For reasons that aren’t clear, the problem is generally more common in infantile-onset FSHD. The origin of the retinal problem isn’t well understood in either form of the disease.

Cardiac and respiratory function

As you become involved with the muscular dystrophy community, you may hear about severe cardiac or respiratory involvement, which is common in certain types of muscular dystrophy. Although cardiac involvement can sometimes be a factor in FSHD, it’s rarely severe and is often discovered only with specialized testing. Some experts have recently recommended monitoring of cardiac function in those with FSHD.

Similarly, breathing difficulties from weakened respiratory muscles aren’t as common in FSHD as they are in some other forms of muscular dystrophy. Testing of pulmonary function at intervals may be recommended for some patients.

What’s not affected?

As you read medical literature or talk with families with muscular dystrophy, you may hear about learning disabilities or other mental impairments. These don’t occur in FSHD.

You also may hear of people with spinal cord injuries or other disorders of the nervous system who experience loss of sensation, inability to control their bladder and bowels, or sexual difficulties. These problems are likewise *not* associated with FSHD.

How is FSHD diagnosed?

Today, the most reliable way to diagnose FSHD is with a test for a tiny missing section of DNA on chromosome 4. This test, which is performed on blood cells, is considered highly accurate for FSHD, even though no specific gene has been identified as being associated with the disorder.

In people who have a family history of the disease and are showing signs of it, a DNA test is generally all that need be done to confirm whether FSHD is likely to develop. (See “Does it Run in the Family?” page 9.)

In many cases, however, people with no family history are suspected of having either FSHD or some other neuromuscular disorder. In these situations, less expensive and less specific tests than the FSHD DNA test may be done first.

One test is a *creatinine kinase level*. This test, also performed on a blood sample, measures the amount of an enzyme known as creatine kinase in the blood. When muscle cells break down, as they do in muscular dystrophies and some other disorders, the creatine kinase, or CK, level is elevated. Creatine kinase was formerly called *creatinine phosphokinase*, or CPK.

Another type of diagnostic test is the *electromyogram*, or EMG. This test, which is somewhat uncomfortable, involves putting very fine needles a short way into the muscles and measuring the electrical activity in the muscles.

A *nerve conduction velocity*, or NCV, test may also be done. This involves measuring how fast signals travel from one part of a nerve to another. The nerve signals are measured with surface electrodes (similar to those used for an electrocardiogram), and the test is only slightly uncomfortable.



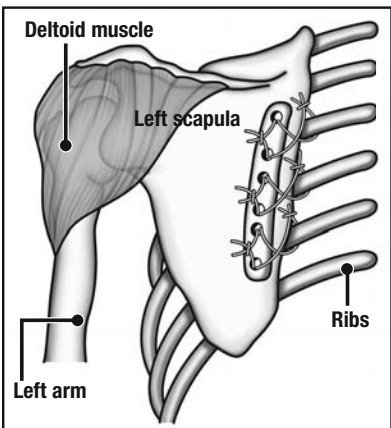
Heart function should be checked in FSHD.



Neuromuscular disease specialists at the MDA clinics are experienced in diagnosing FSHD.



Lower leg braces keep feet from flopping down and tripping the person trying to walk.



People with FSHD who have at least one strong deltoid muscle (at the top of the arm) may choose to have a surgical procedure in which the scapula (shoulder blade) is tethered to the back of the rib cage, allowing the deltoid the leverage it needs to lift the arm.

Another diagnostic procedure sometimes undertaken is the *muscle biopsy*. In this procedure, a small piece of muscle is taken, usually from the arm or leg. Doctors can tell a lot from a biopsy sample, which can be subjected to many types of biochemical tests to reveal cellular and molecular abnormalities that suggest certain muscle disorders and rule out others.

Muscle biopsies are less often performed today than in the past, especially when there's a DNA test for the disease the doctor suspects is causing the symptoms — as there is for FSHD. Muscle biopsy samples, however, are desperately needed to understand the relationship between the DNA results and what actually happens inside the muscle.

Today's muscle biopsy procedure involves a minimum of discomfort or inconvenience and is usually performed under local anesthesia. If your MDA clinic physician asks you to have a muscle biopsy for research purposes, you're certainly under no obligation to have one, but it will speed the research to find treatments for FSHD if you do!

Is FSHD ever confused with other disorders?

FSHD can be confused with *polymyositis* (see page 5), which is neither a genetic disease nor a muscular dystrophy. It can also be confused with certain conditions of the nervous system that aren't muscle disorders.

Seeing a neurologist who specializes in neuromuscular disorders at an MDA clinic or major medical center, and agreeing to a full assortment of diagnostic procedures, will increase the possibility of an accurate diagnosis.

Diagnoses made many years ago (for example, in older family members) may be worth revisiting. Many DNA tests and other diagnostic approaches became available during the 1990s.

Are there medical treatments for FSHD?

Unfortunately, these are relatively few, and none are specific to the disease. There's no treatment that can halt or reverse the effects of the disease, but there are treatments and devices to help alleviate many of the symptoms.

Anti-inflammatory drugs known as *nonsteroidal anti-inflammatories*, or NSAIDs, are often prescribed to improve comfort and mobility. These are the same drugs taken by many people with arthritis and other inflammatory conditions.

The experimental drug MYO-029 is being tested in FSHD and other MDs. It's designed to block a natural protein that limits muscle growth.

Surgical and mechanical help

Surgical procedures to stabilize the shoulder blades (scapulae) by attaching them to the ribs have helped some people with FSHD.

In this procedure, the scapulae are fixed to the ribs so that they don't move. The patient gains some leverage with the arm on the side that's had the operation, since the scapulae no longer slide around. Although this type of surgery may actually decrease the arm's range of motion (since the shoulder blade can no longer rotate normally), the ability of the arm to function may be better, since the arm's leverage point is now stable. It's important to go to a surgeon who fully understands FSHD and has had experience with this exact type of surgery.

Physical therapists often recommend devices such as back supports, corsets, girdles and special bras for people with FSHD. These supports help to compensate for weakening muscles in the upper and lower back.



Massage and physical therapy can benefit people with FSHD.



A corset-style back support worn under clothes can help keep the shoulders and lower back in better alignment.

Lower leg braces, known as *ankle-foot orthoses*, or AFOs, can compensate for weakening muscles in the lower leg that cause tripping and falling. These may be recommended by the physician or physical therapist and can be purchased as off-the-shelf or custom-made models. Some people find a lightweight, high-top shoe can be as helpful as an AFO in supporting the foot, at least in the early stages of weakness.

Physical therapists advise that those with FSHD shouldn't resist using these types of devices for fear their muscles will get "lazy." A supportive corset or AFO can help with mobility and endurance, they say, and supporting muscle in a normal position can help you use your remaining strength more effectively.

Massage or warm, moist heat (for example, from hot packs you can put in a microwave) are also good for the discomfort associated with FSHD.

Exercise

Since the precise underlying defect that causes muscle loss in FSHD isn't yet understood, it's hard to make precise recommendations about exercise.

However, physical therapists who have observed people with FSHD for many years say that moderate exercise appears to do no harm and may even be helpful, at least for muscles that haven't severely weakened.

Therapists advise that exercise shouldn't cause muscle cramping, significant muscle pain or extreme fatigue. An exercise program for someone with FSHD should be directed by a professional, such as a physical or occupational therapist, who has experience with neuromuscular disorders. The program should emphasize exercising muscles that are still relatively strong and resting those that have weakened. This can be accomplished with careful positioning and adaptation of standard exercise regimens.

Diet

There's no specific diet known to help in FSHD or any other muscular dystrophy.

Consult with your MDA clinic doctor about specific dietary recommendations for you and for advice on dietary supplements. Some doctors recommend the dietary supplement creatine for people with muscle disorders, but it should be taken with care and under medical supervision.

It only takes one mutation (from one parent) to cause the disorder.

Does it Run in the Family?

FSHD certainly can “run in families.” In this condition, a small section of the DNA on chromosome 4 that’s shorter than usual is inherited in an autosomal dominant pattern, meaning it only takes one such mutation (from one parent) to cause the disorder. This altered piece of DNA can also occur spontaneously in a child as he or she develops in the womb.

FSHD can affect either males or females. In a small number of people with FSHD, the usual chromosome 4 mutation can’t be identified. In most affected people, it can be, with genetic testing.

FSHD is one of many genetic disorders in which germ line mosaicism is believed to occur. Germ line refers to egg or sperm cells. In this phenomenon some, but not all, sperm or egg cells in a parent carry a particular mutation.

In families with more than one child with FSHD but no previous family history, it’s likely that one parent has germ line mosaicism and that affected children were conceived with egg or sperm cells carrying the FSHD mutation. In these situations, the parents have no symptoms, and, if their blood cells are tested, they don’t show the mutation.

More information can be found in MDA’s booklet, “Facts About Genetics and Neuromuscular Diseases.”

For help in understanding your family’s specific situation and planning for future children, it’s best to meet with a genetic counselor. You can obtain a referral to a counselor through your MDA clinic.

MDA's Search for Treatments and Cures

The MDA Web site is constantly updated with the latest information about the neuromuscular diseases in its program. See the latest research news at www.mda.org/whatsnew.

Researchers supported by MDA have contributed to a better understanding of the molecular basis of FSHD, and they're now applying what's been learned to the search for treatments.

In 1990, the genetic defect that underlies the disease was located on chromosome 4. Many investigators assumed that one gene would be found that, when flawed, would lead to the development of the symptoms recognized clinically as FSHD.

Mutations in the dystrophin gene on the X chromosome had recently been discovered to underlie Duchenne and Becker muscular dystrophies, and it was believed that FSHD genetics would be similar.

This, however, wasn't to be the case. No genes were found in the region of chromosome 4 which is known to be shortened in people with FSHD. Instead, the shortened strip of DNA is found in a part of the chromosome where there are no genes. The function of this type of DNA is the subject of scrutiny by research teams around the world.

Recent findings suggest that the flawed DNA on chromosome 4 may play an important role in telling the cell which genes should be processed into proteins and which shouldn't. All cells have genes that are "turned on" (available to be processed for protein production) and others that are "turned off" (not available for processing). This gene regulation is what distinguishes one type of cell from another — for example, a muscle cell from a bone cell.

In 2002, MDA-funded scientists found that the shortened DNA segment on chromosome 4 may eliminate a site where a molecular braking system normally "lands" and keeps certain genes from being inappropriately turned on.

In 2009, MDA-supported researchers found that pieces of a gene called DUX4 are abnormally activated in FSHD-affected cells, leading to production of potentially toxic proteins.

Reinstating the normal braking system or using some other method to block the erroneously activated genes or the proteins made from them seems a likely pathway for the eventual treatment of FSHD.

There may be additional factors involved in FSHD as well. The shortened stretch of DNA on chromosome 4 may, some experts say, change the shape of the chromosome and affect its interactions with distant genes or with an envelope that surrounds each cell nucleus.



MDA is Here to Help You

The Muscular Dystrophy Association offers a vast array of services to help you and your family deal with FSHD. The staff at your local MDA office is there to assist you in many ways. The Association's services include:

- nationwide network of clinics staffed by top neuromuscular disease specialists
- MDA summer camps for kids with neuromuscular diseases
- help with obtaining durable medical equipment through its national equipment loan program
- financial assistance with repairs to all types of durable medical equipment
- annual occupational, physical, respiratory and speech therapy consultations
- annual flu shots
- support groups for those affected, spouses, parents or other caregivers
- online support services through the e-community *myMDA* and through *myMuscleTeam*, a program that helps recruit and coordinate in-home help

MDA's public health education program helps you stay abreast of research news, medical findings and disability information through magazines, publications, educational speakers, seminars, videos and newsletters.

MDA's Web site at www.mda.org contains thousands of pages of valuable information, including disease specifics, research findings, clinical trials and past magazine articles.

Everyone registered with MDA automatically receives *Quest*, MDA's award-winning quarterly magazine. *Quest* publishes detailed articles about research findings, medical and day-to-day care, helpful products and devices, social and family issues, and much more. Other MDA publications can be found at www.mda.org/publications; many booklets are available in Spanish. Ask your local office for "MDA Services for the Individual, Family and Community" and for help with obtaining copies of other publications.

If you have any questions about FSHD, someone at MDA will help you find the answer. To reach your local MDA office, call (800) 572-1717.



On the cover:
Barbara Williams of Clackamas, Ore., first had FSHD symptoms in childhood. Recent surgery has given her less pain and better use of her right arm.

MDA's Purpose and Programs

The Muscular Dystrophy Association fights neuromuscular diseases through an unparalleled worldwide research effort. The following diseases are included in MDA's program:

Muscular Dystrophies

Myotonic dystrophy (*Steinert disease*)
Duchenne muscular dystrophy
Becker muscular dystrophy
Limb-girdle muscular dystrophy
Facioscapulohumeral muscular dystrophy
Congenital muscular dystrophy
Oculopharyngeal muscular dystrophy
Distal muscular dystrophy
Emery-Dreifuss muscular dystrophy

Motor Neuron Diseases

Amyotrophic lateral sclerosis (*ALS*)
Infantile progressive spinal muscular atrophy
(*Type 1, Werdnig-Hoffmann disease*)
Intermediate spinal muscular atrophy
(*Type 2*)
Juvenile spinal muscular atrophy
(*Type 3, Kugelberg-Welander disease*)
Adult spinal muscular atrophy (*Type 4*)
Spinal-bulbar muscular atrophy
(*Kennedy disease*)

Inflammatory Myopathies

Polymyositis
Dermatomyositis
Inclusion-body myositis

Diseases of Neuromuscular Junction

Myasthenia gravis
Lambert-Eaton (myasthenic) syndrome
Congenital myasthenic syndromes

Diseases of Peripheral Nerve

Charcot-Marie-Tooth disease
Friedreich's ataxia
Dejerine-Sottas disease

Metabolic Diseases of Muscle

Phosphorylase deficiency (*McArdle disease*)
Acid maltase deficiency (*Pompe disease*)
Phosphofructokinase deficiency
(*Tarui disease*)
Debrancher enzyme deficiency
(*Cori or Forbes disease*)
Mitochondrial myopathy
Carnitine deficiency
Carnitine palmityl transferase deficiency
Phosphoglycerate kinase deficiency
Phosphoglycerate mutase deficiency
Lactate dehydrogenase deficiency
Myoadenylate deaminase deficiency

Myopathies Due to Endocrine Abnormalities

Hyperthyroid myopathy
Hypothyroid myopathy

Other Myopathies

Myotonia congenita
Paramyotonia congenita
Central core disease
Nemaline myopathy
Myotubular myopathy
Periodic paralysis



MDA's Web site is constantly updated with the latest information about the diseases in its program. Go to www.mda.org.

Jerry Lewis, National Chairman
www.mda.org • (800) 572-1717

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