

# FSHD

## Facioscapulohumeral Disease

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fa•cio•scap•u•lo•hum•er•al

(fā-shē-ō-skap-ye-lō-hūm-e-ral) adj.

relating to or affecting the muscles of the face, scapula, and arm (~muscular dystrophies)

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Facioscapulohumeral muscular dystrophy (Landouzy-Déjérine disease) is an inheritable muscle disease commonly called FSH or FSHD.

Facioscapulohumeral muscular dystrophy is the second most prevalent inheritable adult dystrophy.

Progressive weakening and loss of skeletal muscle are its major effects. It has significant medical and health impacts on individuals, families and society. Details about the nature of the disease and some basic knowledge of inheritance of genetic diseases are important to better understand FSH Muscular Dystrophy.

The **FSH Society** hopes this brochure more widely circulates understanding of FSHD, and that better understanding will help those who are living with, and concerned about, this unique disease.

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FSH Society, Inc.,  
A 501(c)(3)  
non-profit corporation*  
**[www.fshsociety.org](http://www.fshsociety.org)**



## **What is FSHD?**

FSHD is a common form of muscular dystrophy defined by a specific set of symptoms that collectively characterize the disease. Its major symptom is the progressive weakening and loss of skeletal muscles. The usual location of these weaknesses at onset is the origin of the name: face (facio), shoulder girdle (scapulo) and upper arms (humeral). Early weaknesses of the muscles of the eye (open and close) and mouth (smile, pucker, whistle) are distinctive for FSHD. These symptoms, in combination with weaknesses in the muscles that stabilize the scapulae (shoulder blades), are often the basis of the physician's diagnosis of FSHD.

Although the progression of FSHD is quite variable, it is usually slow. Other skeletal muscles invariably weaken. Involvement of muscles of the foot, hip girdle and abdomen is common. With FSHD, most affected people develop unbalanced (side-to-side) weaknesses. The reason for this asymmetry is unknown.

In most cases, FSHD muscle involvement starts in the face and slowly progresses to the shoulder and upper-arm muscles and then down to the abdominal and foot-extensor muscles. Foot drop and foot weakness are early manifestations.

Initial signs of FSHD include difficulty reaching above the shoulder level, foot drop, scapular winging and facial weakness. Weakness in the abdominal muscles can cause a protuberant abdomen and lumbar lordosis. The lower abdominal muscles are usually weaker than the upper abdominal muscles. This distribution of weakness causes a positive Beever's sign that is not seen in many other diseases and is a physical characteristic very specific to FSHD.

In more than half of FSHD cases, there are other symptoms like high-frequency hearing loss and/or abnormalities of blood vessels in the back of the eye. The vascular abnormalities in the

back of the eye lead to visual problems in only about 1% of the cases. Since these abnormalities are not exclusive to FSHD, one must be cautious of the fact that their presence alone, in an FSHD at-risk individual, is insufficient for a diagnosis of FSHD.

## ***What causes FSHD?***

By going from the large (muscle cells) to the small (DNA), one can partially understand the cause and origin of FSHD. DNA, short for deoxyribonucleic acid, is a long molecule found in the cells of our body. In association with some proteins, DNA makes up our chromosomes. It holds the genetic instructions for our hereditary traits. Discrete segments of DNA, called genes, determine specific traits. Taken together, the combination of an estimated 100,000 genes makes each of us “an original.”

A sudden structural change in DNA – a mutation – causes FSHD. The FSHD gene(s) is still unknown, but its approximate location is toward the end of the DNA of the long arm of chromosome 4. The specific genetic location of the FSHD deletion is 4q35 in the D4Z4 DNA region.

Researchers are investigating the molecular connection of this deletion and FSHD. The size of the deletion may have a relationship to the severity of the disease. It is not yet certain whether the deleted DNA contains an active gene or changes the regulation or activity of a nearby FSHD gene (a position effect). DNA, RNA, and protein research is ongoing in this area.

Perhaps 2% of FSHD cases are not linked to chromosome 4. Their linkage to any other chromosome or genetic feature is under investigation.

## ***How does a person inherit FSHD?***

Most individuals with FSHD inherit the mutation from a parent with the disease. DNA is the means of transmission of inheritable traits

from parent to child. Chromosomes are the vehicles for these DNA transfers from one generation to the next. Each chromosome contains a long, thread-like strand of DNA. Human cells usually contain 46 chromosomes, 23 from each parent. Forty-four of the chromosomes, also called autosomes, are homologous pairs (numbered 1 through 22) with each strand of the pair having the same size, order and arrangement with genes for the same traits in the same position on the chromosome. Children inherit one member of each of the 23 pairs of chromosomes from each parent. The remaining chromosome pair consists of the nonhomologous sex chromosomes X and Y. A mother donates an X chromosome, and a father donates either an X or Y chromosome.

FSHD is the result of a DNA mutation on one member of the chromosome 4 pair. FSHD is highly penetrant. This means that when a person inherits a chromosome 4 with the FSHD mutation, there is a high probability that discernible muscle weaknesses will develop. Since weakness still occurs in the presence of the normal member of the chromosome 4 pair, the disease is considered dominant. FSHD is, therefore, a dominant inherited disease meaning only one parent has to have the disease gene or deletion to inherit FSHD. Since each parent donates only one member of each chromosome pair to a child, the probability of passing the disease to an offspring is 50%. However, the 50% means that in a population of 1,000 people this will happen about 50% of the time. In an individual family this can happen 100%, 0%, or anything in between.

## ***What are sporadic cases of FSHD?***

Sporadic FSHD cases are those resulting from a new mutation. Studies report from 10% to as high as 33% of FSHD cases as sporadic (de novo mutation). Approximately 20% of reported sporadic cases are those inherited from a seemingly unaffected parent who is a “germline mosaic” meaning that only the mother’s or father’s germ cells (the egg or sperm) is affected. When a germline mosaic is involved, the parent appears unaffected but the children are at risk.

In the remaining 80% of sporadic cases, a new spontaneous mutation results in a chromosome 4 deletion that causes FSHD. When the 4q35 deletion fragment appears in a sporadic FSHD case, it is transmitted in an autosomal dominant (only one parent needs to be affected) manner to succeeding generations. The probability, then, of passing the disease to an offspring is 50%.

## ***How many people have FSHD?***

It is difficult to calculate the exact incidence of FSHD. It may be under reported, but an accepted estimate of its occurrence in the general population is one in 20,000. A recent publication reports FSHD as the most prevalent dystrophy: one in 14,286. FSHD occurs in all racial groups and with equal frequency in both sexes.

## ***When do symptoms appear?***

Although the FSHD gene is present at birth, weaknesses are generally not noticeable until the second decade. Sometimes muscle weaknesses are slight throughout adulthood. A physician can usually recognize and diagnose FSHD beyond the age of 20. However, it is important to realize that the onset of FSHD is variable.

In perhaps 5% to 10% of cases of FSHD, a young child or an infant develops symptoms. In infantile FSHD (IFSHD) there are facial weaknesses during the first two years of life in addition to other typical muscle weaknesses of FSHD. Some of these children also experience early hearing losses and retinal abnormalities.

Early onset and infantile cases of FSHD often pose special challenges arising from severity of the symptoms and schooling issues. The FSH Society provides helpful information that includes contact with a network of families with similar concerns.

## ***What is the prognosis of FSHD?***

Predicting the course and outcome of the disease (i.e., the prognosis) has its clinical certainties and uncertainties. There is certainty that some skeletal muscles will weaken and waste throughout life and that this can, and often does, cause limitations on personal and occupational activities. FSHD appears not to diminish the intellect. The heart and internal (smooth) muscles seem spared and, with rare exceptions, those with FSHD have a normal life span.

There are uncertainties. The rapidity and extent of muscle loss differ considerably among FSHD patients – even among members of the same family. Some report few difficulties throughout life, while others may need a wheelchair as walking becomes too difficult or impossible. The degree of severity in an FSHD

parent cannot accurately predict the extent of disability that may develop in that parent's child.

As a group, people with FSHD are well adjusted, educated and motivated. They cope with a legion of adaptations. Muscle and motion are an important part of the full expression of much of life. Often, there are losses difficult to define in clinical terms. Interactions with family, friends and associates may become limited. The accompanying losses often eclipse the clinical certainties and are an unspoken and significant part of the FSHD prognosis.

### ***If a family member has FSHD, could I have the FSHD mutation?***

Yes. If one has a blood parent, sibling or other relative who has the FSHD mutation, there may be a risk of carrying that mutation. Often, when a person is diagnosed, the disease is discovered to be throughout the extended family tree and many generations. It is important to be aware that there may be other family members who are affected but unaware that they may have FSHD or may be at risk for FSHD. Professionals with knowledge of genetics and inheritance of FSHD can advise them regarding that risk in individual circumstances. The FSH Society can also provide answers and referrals about questions of risk.

### ***Can a physician diagnose FSHD?***

Yes. Even an adult at risk, with no obvious symptoms, should avail themselves of a clinical diagnosis if they wish reassurance. Examinations by clinicians familiar with the disease are quite dependable when there are symptoms that follow an expected location and pattern of weakening muscles. By the age of 20, muscle weakness can be found approximately 95% of the time in affected individuals.

Often the physician will supplement a physical examination with inquiries about a

possible family history of FSHD, measurement of specific enzyme levels in the blood, an electromyograph (EMG), and/or a muscle biopsy. An EMG records abnormal electrical activity of a functioning skeletal muscle. A biopsy consists of a small piece of muscle tissue analyzed for visible abnormalities.

A thorough examination will detect the disease in approximately 95% of affected individuals beyond the age of 20. However, the diagnosis may still be equivocal at younger ages and with some at-risk adults with mild or asymptomatic cases. This uncertainty can occur during years when there are important vocational, marital and family planning choices at issue. This has created a real need in the FSHD population for a DNA test for the disease.

### ***Is a DNA test for FSHD possible?***

Yes. There is now a DNA test for FSHD in the clinical arsenal. It is highly reliable for many cases where diagnosis of FSHD is uncertain or impossible. The test detects the 4q35 DNA deletion described earlier. Although several factors may occasionally complicate the test, confirmation of the 4q35 deletion is 98% reliable as a presumptive diagnosis of FSHD. The test requires no more than a small amount of blood that one's physician sends to a testing laboratory. The laboratory extracts sufficient DNA for the test from the cells present in the blood. The FSH Society can provide information regarding the test and laboratories that currently offer it. It does not, however, endorse any test or laboratory. An individual should consult their own physician and the laboratories about the DNA diagnostic test.

Currently, there is no DNA test available for those few cases where there is no linkage between FSHD and chromosome 4.

## ***Is there a prenatal test for FSHD?***

Yes. Using the same technology of the DNA test described above, prenatal testing is possible. An individual who is interested in a prenatal test for FSHD should consult with their physician or contact the FSH Society. The Society can provide further information about this subject.

## ***Are treatments and aids available for FSHD?***

There is no treatment or cure yet for FSHD. There are, however, things that can be done to alleviate its effects including meeting with the appropriate health practitioners.

Neurologists are often the primary physicians in muscle disease clinics since muscles do their work through stimulation by nerves. Physiatrists are physicians who work with chronic neuromuscular conditions. Periodic visits with a neurologist or physiatrist are useful to monitor the progress of FSHD and to obtain referrals to other professionals and services. An orthopedist (one concerned with the skeletal system and associated muscles, joints and ligaments) can offer advice about mobility issues and other functional problems of the muscular/skeletal system.

Physical therapy, including light exercise, helps preserve flexibility. Swimming is especially helpful in this regard by making many movements easier. One should stay as active as possible, with rest breaks as needed during exercise and activities.

Occupational therapy can help with suggestions for adaptations and physical aids that can often partially free an FSHD patient from some constrictions of the disease. Foot drop can be managed with ankle-foot orthotics (AFOs) and knee-ankle-foot orthotics (KAFOs).

Dietitians can help maintain a good diet and avoid unnecessary weight to reduce stress

on already weakened muscles. In addition, speech and hearing therapists can help with limitations imposed by hearing loss and weakened facial musculature to improve speech and communication.

Sometimes a surgeon attaches the scapulae (shoulder blades) to the back to improve motion of the arms. An individual who is considering such surgery should consult with their neurologist or physiatrist and an orthopedic surgeon. Discussion of this procedure with individuals who have undergone the surgery is important.

Pain is part of FSHD in many patients. No specific treatments are available. Pain medication and mild physiotherapy are often prescribed with moderate results.

The FSH Society provides referrals to physicians and other professionals.

## ***Can respiratory insufficiency occur in FSHD?***

Yes. Respiratory involvement can be seen. Evaluation of the symptoms and signs of respiratory insufficiency should be sought during routine clinic visits in patients with moderate to severe FSHD. Regular monitoring of respiratory function is suggested as one might experience insufficiency over a long period of time without presenting signs.

Symptomatic respiratory insufficiency can be initially managed with nighttime non-invasive pressure support (e.g., a BiPAP machine). In very severe cases, patients may require the use of a ventilator. In standard practice, trauma (ER, ICU), surgery and anesthesiology settings, care should be taken not to suppress respiratory drive with narcotics unless it is a situation of palliative care.

Oxygen supplementation can be detrimental to patients with hypercarbic (high CO<sub>2</sub>) respiratory failure and lead to worsening CO<sub>2</sub> levels. Oxygen should generally not be

administered unless BiPAP or similar ventilatory support is also being used. Your physician and a pulmonologist can help you periodically monitor CO<sub>2</sub> levels in the office or pulmonary function lab in the hospital.

## **What is the FSH Society?**

The **FSH Society** is a 501(c)(3) nonprofit, tax-exempt U.S. corporation established in 1991 by Daniel P. Perez. The **Society** solely addresses specific issues and needs regarding facioscapulohumeral muscular dystrophy (FSHD).

It actively promotes research toward the prevention, cause and treatment of FSHD. It also helps facilitate support groups where individuals with like concerns have an opportunity to interact and receive helpful information concerning day-to-day life with FSHD.

The **Society** publishes a newsletter with information about advances in research, political action effecting FSHD research and profiles of people living successful lives. The newsletter is one of several benefits of membership in the **Society**.

Other services provided by the **Society** include additional written information about FSHD; genetic and prenatal testing; physical, occupational, speech and hearing therapy; and dietary concerns. The **Society** also offers assistance and materials to physicians and other professionals interested in FSHD.

Anyone with questions about FSHD should contact his or her physician(s), the **FSH Society** or their local muscular dystrophy association office.

