

Facioscapulohumeral muscular dystrophy

What is it?

It is a muscle wasting condition, caused by a genetic fault, which may be affecting the regulation of the level of many of the different proteins in muscles.

Why this name, and are there others?

The name describes the usual distribution of weakened muscles: 'facio'=facial; 'scapulo'=shoulder blade; 'humeral'= upper arm. Landouzy-Dejerine and facioscapulooperoneal muscular dystrophy are two previously used terms. Also, some people with a diagnosis of scapulohumeral or scapulooperoneal syndromes may have this condition. However, the legs can also be affected.

How rare is it?

It is probably the third most common muscular dystrophy (after Duchenne and myotonic dystrophies), although its frequency may vary in different places and quite possibly in different racial groups. Estimates of frequency have varied from one in about 400,000 to one in 20,000. In Britain, the frequency is at least one person in every 50,000, and probably closer to one in 20,000, accounting for between about 1200 and 3000 cases in all.

What causes it?

It is a genetic condition, present from when or soon after egg and sperm come together at conception. Normally, at a particular site on the gene map, each of us has many copies of a particular sequence of genetic instruction (DNA), arranged like a train of identical carriages. FSHD is caused when the number of copies is reduced below a certain level, like a train having too few carriages. In some way this seems to influence the production or assembly of several of the protein components of the affected muscles.

How severe or mild is it?

The degree of weakness or disability can vary quite widely between different affected members in a family, but can show even greater variation between people in different families. For some, it can result in weakness not only of facial muscles and shoulders/upper arms, but also of additional combinations from the neck, forearms, wrists, fingers, hips, legs, ankles and the back muscles. Around 10-20% of people eventually require a wheelchair, but by contrast, up to one third remain unaware of symptoms at least into old age, although may well have subtle detectable clinical signs. The majority of people come between these two extremes. The average severity of presentation in a family, or in a single case, seems to correlate with the smallness of the number of copies of the DNA repeat sequence which remain (i.e. the fewer copies left, the greater is the severity).

In general, the most severely affected people tend to be the ones who have the altered genetic instruction for the first time in the family, and where the symptoms of weakness are evident from early childhood.

Are men and women affected equally?

We now know that, on average, men do tend to show more weakness and from a slightly earlier age than women (see also question 16). The reason for this is not yet clear. Within large families, and therefore excluding the most severe cases, women are more likely to be less severely affected and so could be unaware that they have inherited the condition.

What are the mildest signs that someone is affected?

Within the context of a family history of FSHD, weakness of facial muscles can be suspected if the eyes remain slightly open when asleep, particularly in young children, or if the eyelids cannot be screwed tightly enough to bury the eyelashes. Difficulties in pursing the lips to whistle or to play a woodwind or brass instrument, or in blowing up balloons, are also suggestive of the condition. During the teenage years or in adulthood, excessive aching around the shoulders, rounded shoulders and thin upper arms may be the first presenting signs or symptoms.

Does FSHD affect lifespan?

Generally speaking, lifespan is not affected, except perhaps in the most severe cases with greatly impaired mobility and consequent greater risk of chest infections. There are some recent reports suggesting an increased association with heart rhythm disorders, but only in a few cases, and these are responsive to appropriate medication. Because of these reports, adults with FSHD would be advised to see their GP (or hospital doctor) every few years for a simple heart check.

Will I become disabled?

The earlier in life the weakness appears the greater its eventual severity. Nevertheless, the progression of either arm or leg weakness in the individual can be hard to predict. Although the legs are affected to some degree in over 50% of people, for those in whom this does not become evident until early adulthood, even an eventual requirement for a wheelchair is unlikely.

To some extent, knowledge of the size of the DNA rearrangement (i.e. the number of repeat units remaining) in a person with FSHD can give a broad guide as to whether the course of the condition would be expected to be relatively mild or more severe.

One fairly common feature of FSHD is an asymmetry of weakness: an uneven distribution of muscle weakness where one side of the body is more affected than the other (particularly early on). This is often evident in the shoulders, usually with the right side to be the first one involved in right-handed people.

In what way are the legs affected?

Early weakness at the ankles causing 'foot drop' is not uncommon. Some degree of weakness at the knees or hips develops by middle age in over 50% of people. Together with weakness in the back muscles, this can result in a typical backward-leaning and high-stepping gait, although only 10-20% ever requires a wheelchair.

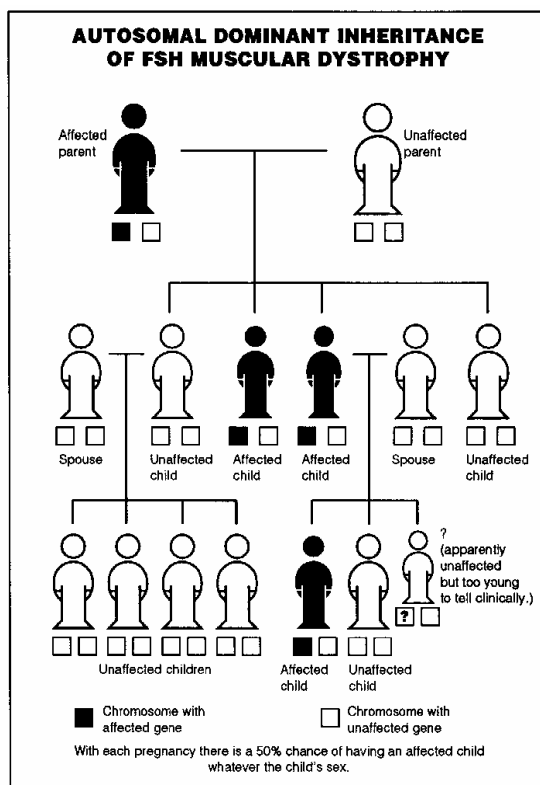
Can any other problems be anticipated?

In some of the earliest childhood onset cases, learning difficulties and epilepsy have been reported. Hearing loss and specific problems with blood vessels at the back of the eye have been found, and although this rarely causes visual problems, a periodic eye check may be useful. It is still uncertain whether these rare features are generally associated in mild degree with FSHD, or are limited to a few more severe cases.

Muscle pain is unfortunately a quite frequent complaint accompanying FSHD, often in the early stages. This may relate to inflammation within the muscles, which seems to occur more in FSHD than other muscular dystrophies. Treatment with simple analgesia combined with anti-inflammatory agents is usually tried, but the effectiveness for relief can vary. Further studies are needed.

How is it inherited?

A separate gene determines each hereditary characteristic or function. These genes are packed together into chromosomes like beads on a string. There are two copies of each chromosome (excepting the X and Y chromosomes in males), and hence two copies of each gene (a pair), coming one from each parent. The 'gene' for FSHD is at one end of each copy of chromosome 4. In FSHD, one copy of this particular pair is faulty (part of it is missing, which is referred to as a 'deletion'). Hence there is a 50:50 (1 in 2) chance for each of the offspring of an affected parent to inherit the faulty copy, resulting in FSHD. They also have an equal chance of inheriting the good copy (resulting in no risk for these individuals or their descendants of being affected by FSHD). This pattern of inheritance is called 'autosomal dominant'.



With completion of the ‘human genome project’ has the gene causing FSHD been identified?

Unfortunately the situation is a little more complex than as discussed (in answer 12.) above. Amongst genetic conditions, FSHD seems so far to be unique in that the genetic fault (‘mutation’) is the reduction (‘deletion’ at one end of chromosome 4) of multiple copies of a repeated sequence of DNA (likened to reducing the number of carriages in a train). This DNA change, which is the dominantly inherited factor, is probably exerting an effect on the way that the function of many genes is regulated in muscle, and particularly in the muscles of the face and shoulder girdle. Hence, there may be many ‘genes’ which are involved in causing FSHD, but for which the controlling dominantly inherited mutation always occurs at the same place on chromosome 4. Much current research in FSHD is aimed at trying to define this link.

Can FSHD be diagnosed from a blood sample?

The DNA mutation causing FSHD can indeed be recognised from a blood sample in most people with this condition. However, interpretation of the test is not always easy, and the DNA sample will need to be forwarded to one of a few molecular genetic laboratories able to offer this. In individual cases it can be harder to exclude the diagnosis than to confirm it, although both are usually made easier if blood samples are also taken from both parents of a possible affected person.

In families where there are several people known to be affected, confirmation of diagnosis, or genetic prediction for an individual family member, will almost always be possible if blood samples are collected from several of the affected people.

Is there always a family history?

A person diagnosed with FSHD, particularly if this is in early childhood, may have a fresh mutation (i.e. they have not inherited it from either of their parents). More often, however, a person diagnosed with FSHD will have inherited the faulty gene from one of his or her parents. It may be that a newly diagnosed person finds that there is a family history, but that this had not been recognised before because the symptoms of other family members had been very mild, or had been misdiagnosed. We now also know that in a significant proportion of even quite early onset cases in children, who appear to be the first ones in a family, one of the parents can show the same FSHD mutation in some of their cells but not in others. This ‘mosaic’ situation in the parent may not give any symptoms in them, but does mean that further children of theirs would have a risk of being affected. We would therefore always recommend that both parents be invited to provide blood samples for DNA study if they wish to know about potential risk to future children.

In other cases genetic testing may help resolve any uncertainty over the affected status of a young adult. Family members or couples seeking further information should refer to their local Clinical Genetics Service.

How severely affected would my sons and daughters be?

The age at onset of symptoms, and hence the severity of FSHD, seems to correlate broadly with the extent of the DNA rearrangement on chromosome 4, which, once it has arisen, remains

a fixed size in a family. Thus there will be some families where FSHD will always tend to be quite severe, and others where it will always be relatively mild. However, there can still be considerable variation within a family for severity and age at onset. Partly, this is due to differences between men and women. Although men and women develop the same symptoms, males tend to develop these earlier, and be more severe at a given age than females. By age 30 years, just about all males with FSHD exhibit symptoms, but only two-thirds of females do. We now know that some people (particularly men) with average or mild presentations of FSHD, may, if they are the first cases in a family, have a mixture of normal and FSHD-type cells and their offspring, who have inherited the FSHD mutation, would do so in all their cells, and therefore present earlier and more severely.

Data from many families suggests that offspring inheriting the faulty gene are likely to be affected from a similar young age and at least as severely as occurred in their affected parent, although in large families affected daughters with FSH might be milder than their fathers.

At what age does it usually start?

This is dependent on the extent of the DNA rearrangement. In large families with several affected members, an affected person usually first becomes aware of muscle weakness in teenage years or early adulthood, when he or she experiences difficulty in raising one or both arms, or notices prominent shoulder blades or wasting of upper arm muscles.

In the more severe cases, which are often the first ones in a family and arising from a new mutation giving a small residual DNA repeat length, impaired movement of facial muscles, particularly around the mouth, can be evident by early childhood, followed by the shoulder girdle and upper arm weakness. In these children progressive weakness of the legs can start to develop by teenage years and lead to the need for a wheelchair.

By contrast, in the mildest families, with the largest residual DNA repeat lengths, people inheriting the condition may remain unaware of symptoms until even late in adulthood.

If I have no symptoms can I still carry the gene and pass it on to my children?

If the person with FSHD has been affected from childhood, it is very unlikely that an adult relative (say a brother or sister) who is unaware of any symptoms, could 'carry' the faulty gene or pass on FSHD to their children. The parents of the affected child are an exception, as they could be 'carrying' the mutation but in only some of their cells, and hence pass this on to more than one child.

For people from families where several relatives or a parent have FSHD, one cannot give the same level of reassurance except following DNA testing. In these situations, many people 'at risk' may be affected only mildly, and are unaware of the abnormal signs that are present. Although some degree of reassurance may be possible if examined by a doctor well familiar with the condition, we now know that up to one-third of adult women carrying the milder mutations for FSHD, and a probably much smaller proportion of men, may not be showing any definite sign of the condition. Therefore, the answer to this question can only be given reliably following DNA testing.

If one of my children is affected, but another seems clear, is he or she likely to have 'escaped' inheriting FSHD?

If the apparently unaffected child is several years beyond the age at which the affected one first presented with symptoms, it becomes very likely that they have not inherited the condition. This is particularly so if the affected child is the first-presenting person in the family, and if DNA testing has shown that their condition has arisen from a new DNA rearrangement (a new mutation) not present in a DNA sample from either parent. However, if either parent is clinically affected or carries the mutation, only DNA testing can give reassurance. If a child has no signs of FSHD, requests for DNA testing would normally be refused until the child is of an age to choose this for themselves.

Can I avoid passing the faulty gene on to my children?

Accurate pre-natal testing, performed by chorion villus biopsy (CVS), usually at 11 weeks gestation, is now available to most couples who would wish this, and whose offspring would be at risk of FSHD. It is essential that genetic (DNA) tests be performed first on blood samples from the affected parent or child to define the DNA mutation in that family. Blood samples would usually be required from both parents, and in some cases from other affected relatives. The CVS procedure is now widely available, although the tissue sample obtained would be forwarded to one of a few specialist genetic laboratories. Couples considering this should consult with their local genetic service that would advise accordingly, preferably prior to becoming pregnant.

Treatment

Can I improve muscle strength?

There are no cures or specific drug treatments. Regular gentle exercise (especially swimming) is beneficial. It is essential to keep your weight down (through diet if necessary) in order to reduce stress on already weakened muscles. If exercises are undertaken to increase muscle strength any build-up should be done gradually.

Can surgery help?

The scapular muscles, which attach the shoulder blades to the chest, are often very weak and this leads to difficulty in lifting the arms. The operation of scapular fixation (fixing the shoulder blades to the ribs at the back) has enabled some people to regain more use of their arms. Because prolonged immobilisation of limbs could increase the weakness of disused muscles, combined assessment from a neurologist and an orthopaedic surgeon prior to operation is advised. For people who have troublesome inflammation of the eyes as a result of them if they are remaining open at night, surgery to bring the eyelids closer can be offered if artificial tears alone are insufficient.

Are anaesthetics a risk?

There is no known risk, but you should be sure that the anaesthetist is aware of your diagnosis prior to operation.

Should I declare it on insurance forms?

Once the diagnosis has been made you have an obligation to declare it when requested. As there is no significant effect on life span, you should ask your doctor for a letter of support if you run into problems. When applying for a driving licence, especially HGV or PSV, this may be issued for a limited duration, with renewal subject to satisfactory medical examination.

The FSH Support Group offers support and encouragement to families and individuals that have FSHD. For further details please contact:

FSH Support Group
C/O Muscular Dystrophy Campaign
61 Southwark Street
London SE1 0HL
Tel: **0800 652 6352**
Fax: **020 7401 3495**
Web: www.fsh-group.org

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Author: Dr.P.W.Lunt, Consultant Clinical Geneticist

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