What is Facioscapulohumeral Muscular Dystrophy?

Understanding one of the more common types of muscular dystrophy.

Facioscapulohumeral dystrophy (FSH), is the third most common of nine muscular dystrophy disorders, affecting approximately 1 in 20,000 individuals. The term Facioscapulohumeral uses three Latin words to describe the characteristic features of the disorder. Facio means face, scapula means shoulder blade, and humerous is Latin for the upper arm. Muscular dystrophy refers to muscle weakness and wasting. Thus, in FSH the muscles typically affected are those of the face, shoulder blade and upper arms.

Features of FSH

FSH affects males and females equally. Symptoms of FSH can be classified into two groups: adult-onset, which is usually mild or congenital-onset, which is typically more severe and often present from birth. As well as variability of onset and severity, there is also variability in which areas of the body are affected. The classical symptoms of FSH involve the muscles of the face, shoulder-blade, and upper arms. Some people, however, have no symptoms in the face muscles, with the lower limbs affected instead. This is known as 'Atypical FSH'.

The following features may be displayed:

- Facial weakness, causing difficulty in pronouncing words, and using facial muscles – such as in whistling, smiling or closing one's eyes.
- Weakness in the shoulder blades, preventing movements such as throwing objects and raising one's arms. Lack of strength around the shoulder blades may allow it to wing out.
- Weak lower leg muscles, causing difficulties in walking up hills, or on uneven surfaces. Foot drop may occur when the muscles weaken to such an extent the front part of the foot cannot be lifted up during walking.
- Excessive spinal curve (lordosis), due to abdominal muscle weakness.
- Weakness in the muscles surrounding the hip and those of the upper leg, causing problems when rising from a chair, climbing stairs, or running.
- The development of contractures, as scar tissue replaces normal elastic tissue. This prevents normal movement in the joint, usually the ankles.
- Eye problems are infrequent, but more severe forms of FSH are associated with Coat's disease of the retina.
- Hearing difficulties are common; complete hearing loss may occur in severe FSH.
- Epilepsy in more severe FSH cases.
- Cardiac and respiratory problems are rare in FSH, but do occur in some patients.
- Inflammation of the muscles. This can be a source of pain in FSH, as can the altered joint position resulting from muscle weakness.
- Intellectual and cognitive (understanding) difficulties are very uncommon in adults with FSH. There are many FSH people, including those in whom symptoms began in childhood, in intellectually demanding occupations.
- Learning difficulties will on occasion occur, but it is important that real cases are not confused with apparent non-responsiveness. Very bright FSH children may appear intellectually challenged due to a combination of deafness and facial immobility.

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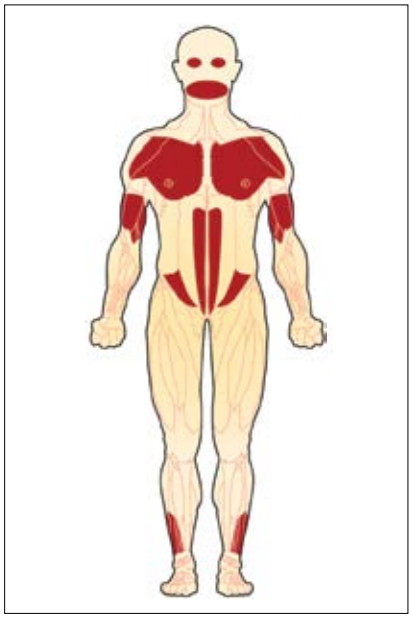

This diagram shows the muscle groups affected by FSH. Sourced from: http://mda.org/disease/fshmuscular-dystrophy/overview

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occur. It may take 30 years for serious problems to develop, if at all. Up to 20 percent of people may require a wheelchair for mobility. Life expectancy is that of the general population.

What causes FSH?

The cause of FSHD is complex. There are two main causes of facioscapulohumeral muscular dystrophy (FSHD) resulting in either FSHD type 1 or type 2. The most common is FSHD type 1 which accounts for 95 percent of cases. Although FSHD1 and FSHD2 have different processes they both result in the same end outcome, which is the switching on of the DUX4 gene. This gene is usually switched off in muscles because once activated it causes muscles to be broken down.

FSHD1

Facioscapulohumeral muscular dystrophy type 1 is mostly inherited as an autosomal dominant trait. In most cases, the affected chromosome is inherited from a parent, but sometimes the variation occurs spontaneously during early development in the womb. The genetic change affecting people with FSHD1 is located on chromosome 4 where there is normally between 11 and 110 repeat units of a genetic motif called D4Z4. In people with FSHD1 the number of repeat units is only between 1 and 10, a 'repeat contraction'. The D4Z4 units are very important because they act as a barricade, preventing DUX4 from being switched on. When there are fewer DZ4Z units, the DUX4 gene is allowed to be switched on.

FSHD2

Facioscapulohumeral muscular dystrophy type 2 is called a di-genic disorder because it requires two 'hits' or mutations in your genome. One of these mutations needs to occur in a gene called Structural Maintenance of Chromosomes Hinge Domain Containing 1 (SMCHD1) on chromosome 18 that results in reduction of the protein it produces. The SMCHD1 protein plays an important role in locking out regions of your genome, one of these regions contains DUX4. Reduced SMCHD1 protein means that not all of DUX4 can be withheld and the gene is able to be switched on.

Before DUX4 can be switched on though it requires a particular genetic sequence – a second mutation - to enable the conversion of the DUX4 gene into the destructive DUX4 protein. So, second mutation next door to DUX4, known as a pLAM sequence makes it "permissive". FHSD1 is autosomal dominant because only one copy of chromosome 4 containing both the repeat contraction and a "permissive" pLAM is required and this can be passed on from a single parent. A person with FSHD2 can inherit the mutations separately; the SMCHD1 mutation on chromosome 18 from one parent and the "permissive" pLAM on chromosome 4 from the other parent.

FSH is an autosomal dominant disorder in as many as 70-90 percent of cases, meaning only one copy of the defect is required for the FSH to develop. This is in contrast to an autosomal recessive disorder, where two copies of the defect are required for the disease to develop.

The remaining 10-30 percent of defects arise spontaneously, with the deletion occurring by chance in the egg or sperm at conception. With a spontaneous mutation, the affected person will be the first in his family to have FSH.

There is a 50 percent chance the child of a FSH parent will inherit the mutation and therefore develop the

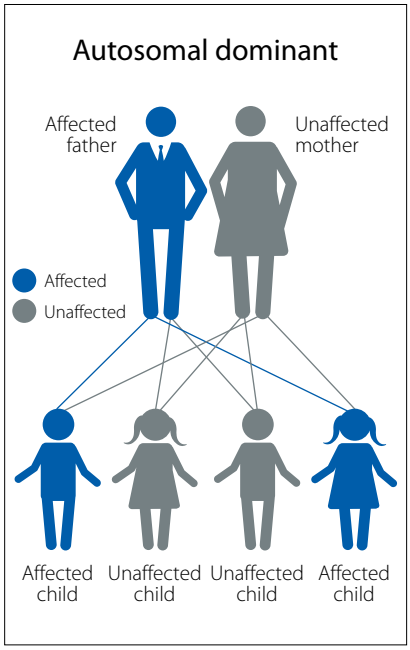
condition. Females are affected just as frequently as males, although symptoms in men are generally more severe and occur at a younger age than in women.

For further information on genetics and how disorders are inherited, please refer to the Muscular Dystrophy Association Genetics Fact Sheet.

Diagnosis of FSH

There are often difficulties in diagnosing FSH, as symptoms vary. However, once FSH is suspected, diagnostic tests will be offered to establish a definite diagnosis. These may include:

- **DNA Testing**
  There is now a reliable DNA test for FSH, which is approximately 98 percent accurate as a presumptive diagnosis. Laboratory technicians are able to extract DNA from a small amount of blood, and detect the DNA deletion responsible for the disorder. DNA testing can be done during pregnancy to determine if the fetus has inherited the deletion for FSH, but the deletion size can not be used to predict accurately the severity of the condition. The testing can raise ethical issues for parents faced with the option to terminate a pregnancy.
- **CK Testing**
  A blood test can assess the presence of an enzyme creatine kinase, also known as creatine phosphokinase. This enzyme is usually restricted to muscles cells, but when muscles are damaged as in FSH, the enzyme leaks out and into the blood serum. The CK test will show elevated amounts in the blood, but is inconclusive as elevated CK is also a feature of other forms of muscular dystrophies.
- **Electromyogram (EMG)**
  An EMG measures the electrical activity of muscles, and also measures the muscle's response to stimulation of its nerve supply. The results may be nonspecific, or show both nerve and muscle involvement, which is typical of FSH.
- **Muscle Biopsy**
  While under local anaesthetic, a small amount of muscle tissue is taken with a needle, usually from the thigh. Using special staining techniques in the laboratory, the muscle tissue is examined microscopically. This can give a lot of information on the condition of the muscle, and can help to rule out other diagnoses, or confirm the FSH diagnosis.



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Other tests include nerve conduction velocity, hearing tests and tests of cardiac function.

Soon after a diagnosis of FSH in the family, it is essential that genetic counselling is arranged, for one or both of two issues. The first is the probablility of Mum or Dad having the disorder, and the second is whether testing for FSH in pregnancy can be offered and with what degree of accuracy. Genetic counselling provides information about possible diagnostic tests, including prenatal testing. Genetic services in New Zealand are available and a referral can be made by the MDANZ.

Management of FSH

As yet, there is no known cure that can halt or reverse the symptoms and progressive muscle weakness associated with FSH. It is possible, however, to control complications by adhering to a management programme specially designed by a team of medical professionals. This team may include occupational therapists, physicians, orthopaedic surgeons, physical therapists, orthotists, dietitians, nurses and psychologists. Many other people are

there to give advice and help in any way possible, such as social workers, teachers, religious advisers, staff from the MDANZ, parents, and other persons with FSH.

- **Exercise**
  Moderate exercise, especially swimming, is generally considered to be beneficial in FSH, maintaining both muscle strength and flexibility, without undue strain. Swimming is a great source of active exercise as the water can be used for support. Passive exercise, or assisted stretching, should be established as early as possible. Physiotherapists will be able to assist in the development of an exercise programme to delay the shortening of muscles (contractures), which causes limitations in the range of motion of joints. These exercises should be undertaken on a daily basis and require assistance from parents and/ or caregivers.
- **Supportive equipment**
  Braces and splints are likely to be required to help compensate for weakened muscles. These are often worn at night to help maintain joints in a normal position. Other types of supportive equipment will be available as the need arises, and usually caters to individual need. Advice concerning these will be offered by the physiotherapist, occupational therapist, or by the MDANZ.
- **Medical treatment**
  Drugs such as albuterol, clenbuterol, and oxandrolone are being studied for their muscle building effects. These treatments seem to be moreeffective in the early stages of FSH, improving some measures of strength. Anti-inflammatory drugs may be prescribed to reduce associated inflammation.
- **Nutrition**
  Excessive weight gain leading to obesity can occur due to reduced physical activity produced by muscle weakness. Any excess weight will contribute to tiredness and weakness; hence it is important to maintain a good balanced diet incorporating plenty of fresh fruit and vegetables.
- **Surgery**
  Stabilising the shoulder blades is one of the more common surgical procedures undertaken by FSH patients. The winged scapulae are fixed to the ribs, so they don't move around. Although the 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, as the arm's leverage point is now stable. Tendons can be surgically severed to relieve contractures. This operation is most often performed at the ankle joint, but will also benefit those that have already developed severe contractures in the knees and hips. Surgery on the eyelids may be beneficial where there is incomplete closure of the lids. Incomplete closure of the lids may cause inflammation of the cornea (keratitis), so it is important not to ignore the early signs of waking up with dry and irritated eyes. Surgery may produce significant benefits, although these must be balanced against potential complications. Postoperative immobilisation can cause further muscle wasting, and extensive physiotherapy will be required after some surgeries. ®

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