Limb-girdle muscular dystrophy 2B (LGMD 2B)

LGMD 2B (also known as Dysferlinopathy)
LGMD 2B is an autosomal recessive form of limb-girdle muscular dystrophy (LGMD). The age of onset of muscle weakness is extremely variable; the most common being between 20 and 30 yrs.

What causes it?
LGMD 2B is caused by faults in the dysferlin gene, which contain instructions to produce a protein important to the muscle fibres. Faults in the dysferlin gene can also cause another condition, called Miyoshi myopathy which predominantly shows symptoms of distal weakness, especially involving the calf muscles in the lower limbs.

How is it diagnosed?
The diagnosis can be suspected by findings on a muscle biopsy or when a doctor experienced in muscular dystrophy examines you. A serum creatine kinase (CK) blood test may also show raised levels (up to 200 fold of the normal range) which indicate a problem in the muscles. The diagnosis has to be confirmed by identifying the faulty gene (dysferlin gene) which is done on a DNA sample from a blood test. This is often done following a clue from the muscle biopsy or examination. Because this is a very large gene, testing is very lengthy and results may not be available for many months.

What symptoms are common?
People with LGMD2B often have initial symptoms of weakness and wasting (loss of muscle bulk) in the hip, thigh and shoulder muscles. Calf muscle wasting is also a predominant feature in the majority of people, and they may complain of difficulties in standing on their tiptoes.

The weakness can be more severe on one side of the body and leg involvement is present before shoulder and arms. This can result in frequent falls, difficulty in running, climbing stairs and rising from the floor. As the condition progresses, people can have problems with walking. The distal muscles (hand and forearm muscles in upper limbs and ankle and calf muscles in the lower limbs) can also be involved and occasionally people affected by LGMD2B show both thigh and foot weakness. It is worth mentioning, however, that these symptoms can also be present in some people at the onset of the condition. When this distal muscle involvement is present,
people may have difficulties in walking because of foot drop which causes them to stumble frequently.

Shoulder and arm weakness can lead to difficulties in raising the arms over the head and in lifting objects. Some people complain of muscle pain and swelling in the legs, especially in the calves, but this is usually transient.

Facial and neck muscles are not usually involved and therefore swallowing problems are unlikely.

Whether heart problems are present in LGMD2B is under debate at the moment. Clinically significant heart problems appear to be rare. Patients with LGMD2B are at risk of developing respiratory muscle weakness and experience breathing difficulties with the progression of the condition, but this is usually a late complication.

**What are the implications of the diagnosis?**

**Inheritance**
LGMD2B is an autosomal recessive condition caused by a change in a gene. People affected with this condition have 2 faulty copies of the dysferlin gene; one inherited from each parent. This means that both parents must be carriers but remain healthy.

The exact frequency of dysferlin gene faults in the population is not known but it is a rare condition. Therefore, people with LGMD2B rarely have affected children (for the risk of meeting and having a child by a carrier of the same faulty gene will be very unlikely unless you have a partner to whom you are related). Children of people affected with LGMD2B will have inherited one faulty copy of the dysferlin gene and therefore will all be carriers but are unaffected.

Consequently, carrier testing is not generally available unless the risks are increased due to intra-familial marriage.

**Progression and complications**
LGMD2B is quite a variable condition in terms of severity and the weakness is always progressive with time although the rate of progression varies from person to person. The rate of progression is usually slow and most people remain ambulant.

Life expectancy is generally within a normal range because the heart and breathing muscles are usually not affected. In later stages of the condition, breathing difficulties can occur but are usually less severe than in other muscular dystrophies. These symptoms can include; poor sleep, nightmares, tiredness or headaches after waking up in the morning, lack of appetite and falling asleep during the day.

**Treatment and management**
So far there are no specific treatments for LGMD2B, however managing the symptoms of the condition improves a person’s quality of life.

Keeping mobile is important for all people affected with muscular dystrophy. There are not any guidelines about the type or intensity of activities however it is recommended that any exercise undertaken is done within a person’s limitation and
remains comfortable. Extreme tiredness, muscle pain and cramps during or after activities can mean that a person has pushed himself too hard and therefore should be avoided. Swimming is a good activity because it promotes movement of all muscles without increased strain.

Joint contractures (tightening) are not a frequent feature in LGMD2B however they can occur as consequence of poor mobility. Therefore regular physiotherapy is recommended. This can be carried out by a physiotherapist or people can be taught to do this by themselves in their own home. These types of exercises can include the stretching of all joints; in particular, the ankles.

Foot drop can occur in Miyoshi myopathy and less frequently in LGMD2B. An orthopaedic opinion may be indicated and orthoses are sometimes worn to help with this problem.

Breathing problems are uncommon in LGMD2B. However with progression of the muscle weakness, people with LGMD2B are at risk of developing mild breathing difficulties. Therefore regular monitoring of respiratory function (FVC) is recommended. Sometimes overnight studies are indicated (Pulse Oximetry).

Regular cardiac assessment is usually not required because to date there is no clear evidence of heart muscle involvement in this condition.

Other relevant factsheets from the Muscular Dystrophy Campaign
The Limb Girdle Muscular Dystrophies (LGMD)