Limb-girdle muscular dystrophy 1C (LGMD 1C)

LGMD 1C (also known as Caveolinopathy)
LGMD 1C is an autosomal dominant form of limb-girdle muscular dystrophy (LGMD). The age of onset of muscle weakness is variable and ranging from childhood to adulthood.

What causes it?
LGMD 1C is caused by a fault in the Caveolin3 gene, which gives instructions to produce a protein important to the muscle fibres. People with faults in the caveolin-3 gene can present with a broad spectrum of symptoms, which are classified as limb-girdle muscular dystrophy (LGMD1C), distal myopathy or Rippling muscle disease.

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 is often mildly elevated, but in a few cases, CK elevation may be much more marked. Some people may not have any weakness and show only raised serum CK levels. The diagnosis has to be confirmed by identifying the faulty gene (caveolin3) which is done on a DNA sample from a blood test. This is often done following a clue from the muscle biopsy or examination.

What symptoms are common?
LGMD1C is a rare disease and so far only few families affected by this muscular dystrophy have been reported. Because of this, the range of weakness and the progression of the condition of people with caveolin-3 deficiency are not well known.

People with LGMD1C can have initial symptoms of weakness and wasting (loss of muscle bulk) in the hip, thigh and shoulder muscles. Other people can show predominant distal muscle weakness (hand and forearm muscles in upper limbs and ankle and calf muscles in the lower limbs). This weakness is even on both sides of the body and usually is mild to moderate.

Upper leg weakness 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. Shoulder and arm weakness can lead to difficulties in raising the arms over the head and in lifting objects.

When distal muscle involvement is present, people may have difficulties in walking because of foot weakness (foot drop) which causes them to stumble frequently. People who have hand weakness may find difficulties in simple tasks (for example opening bottles).

Rippling muscle disease is a condition in which people have visible ripples which move over the muscle. These can occur spontaneously or be induced by rapid tapping of the muscles. Many people affected by caveolinopathy, regardless of their symptoms, may show muscle rippling at the onset or later stages of the condition.
It is important to mention that the individual features of muscle weakness can be different from person to person, even in the same family.

Muscle hypertrophy (large muscles), especially calf hypertrophy, is often present in people with LGMD1C. Often people complain of muscle pain and cramps, especially in the legs and after exercise. Facial and neck muscles are not usually involved and therefore swallowing problems are unlikely.

Heart and breathing problems are usually not a feature in this condition. However, heart involvement with dilated cardiomyopathy has been rarely reported.

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

**Inheritance**
LGMD1C is an autosomal dominant condition caused by a change in a gene. People affected with this condition have 1 faulty copy of the Caveolin3 gene inherited from one parent. This means that usually the parent who carries the same faulty gene is also affected but may not be aware of this because their symptoms may be very mild. However, the change in the caveolin3 gene could have begun for the first time (“new fault” or “new mutation”).

People affected by LGMD1C have 50-50 chance of passing on the faulty gene and the condition to their children (of either sex). Prenatal diagnostic testing is available and this can be discussed with your consultant or geneticist in more detail.

**Progression and complications**
LGMD1C is quite a variable condition in terms of severity and the weakness, but usually the progression is slow to moderate and people remain ambulant. Life expectancy is generally within a normal range because the heart and breathing muscles are usually not affected.

**Treatment and management**
So far there are no specific treatments for LGMD1C; 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.

Although joint contractures are not a frequent feature of Caveolinopathy, they can occur as consequence of poor mobility. Regular physiotherapy can be useful to maintain good joint mobility. This can be carried out by a physiotherapist or people can be taught to do this by themselves in their own home.
Problems with breathing are usually not associated with LGMD1C, but many clinics obtain regular breathing assessment (FVC) as part of regular follow up.

Regular cardiac assessment is usually not required because there is not strong evidence of heart muscle involvement in this condition. However, this can be discussed with your consultant on an individual basis.

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