

LIMB GIRDLE MUSCULAR DYSTROPHY

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What is Limb Girdle Muscular Dystrophy?

Limb Girdle Muscular Dystrophy (LGMD) is a group of inherited disorders that affect the voluntary muscles of the hip and shoulder areas – *the pelvic and shoulder girdles*, also known as the *limb girdles*. These muscles weaken and waste away (atrophy), and as a progressive disorder, it may involve other muscles over a period of time.



In LGMD involuntary muscles of the digestive system, bowel and bladder are not affected, and sexual function is also normal. Intellectual and cognitive abilities also remain unaltered, as do sensations such as touch, temperature and pain.

The onset of LGMD usually occurs between childhood, but symptoms may not be apparent until adolescence or adulthood. Because these disorders are so variable, an accurate incidence rate has not been calculated, though it is estimated at 5 to 70 per million people. Males and females are equally affected.

Causes of Limb Girdle Muscular Dystrophy

Most types of LGMD are autosomal recessive disorders, with approximately 10% being autosomal dominant. For further information on genetics and how disorders are inherited, please refer to the *Genetics Factsheet*.

Genes exist in chromosomes and carry the instructions for producing proteins. Several different genes that normally lead to the production of muscle proteins have been identified as mutated in LGMD. In 2005, eleven of these genes had been identified. When these proteins are not produced properly due to a faulty gene or genes, the cells in the muscles fail to function properly. As the muscles of the pelvic and shoulder girdles do in LGMD, muscles gradually weaken and waste away (atrophy) and continue to do so throughout an individual's lifetime.

Six of the genes that cause LGMD, have been found to affect the proteins in muscle cell membranes, which are protective, thin coverings. When these proteins are missing as a result of the gene mutation, the membrane cannot adequately protect the muscle cell from injury caused by normal contractions. The muscle membrane may also be "leaky" and

let substances in or out of cells that are supposed to remain on one side. Several other unidentified functions of muscle membrane proteins may also be affected in LGMD.

Not all of the muscle proteins associated with LGMD are in the membrane, however. Calpain-3 is located in the main part of the muscle cell, and myotilin and telethonin are located in the part of the muscle cell that allows it to contract and relax.

As more and more genes are identified in the cause of LGMD, there will be a greater understanding of which and how proteins are implicated in the symptoms of LGMD.

Types of Limb Girdle Muscular Dystrophy

The different types of LGMD are generally classified by its pattern of inheritance where disorders that are autosomal dominant are classified as LGMD1 and those that are autosomal recessive, as LGMD2. Subsequent letters and numbers indicate which gene is known (or suspected) to be involved in the disorder. The different types can also be classified according to the missing or deficient protein.

The following tables display the different types of LGMD, and the known proteins or genes involved:

Table 1. The different types of autosomal recessive LGMD

Alternative Names	Inheritance	Protein Involved	Characteristics
LGMD2A calpain deficiency, Calpainopathy	AR	calpain 3	Often presents aged 8-15, though may be earlier or later. Not usually very rapidly progressive.
LGMD2B dysferlin deficiency, Dysferlinopathy, Miyoshi myopathy	AR	dysferlin	Often presents in late teens. People may notice difficulty standing on toes as an early feature. Usually slow worsening of problems.
LGMD2C, 2D, 2E, 2F sarcoglycan deficiency, sarcoglycanopathy, previously called 'autosomal recessive muscular dystrophy of childhood'	AR	One of the sarcoglycan proteins (a, b, g or d)	Very variable. Usually causes problems in childhood; otherwise may be later in life. Monitoring of breathing and heart function and treatment if necessary, is important.
LGMD2G	AR	telethonin	So far only reported in Brazil
LGMD2H	AR	TRIM32	So far only reported in Canada
LGMD2I	AR	FKRP	It seems to be a relatively common form of LGMD, and can resemble Becker MD. Some patients may develop problems with their heart and breathing and should be monitored

LGMD2J	AR	FKRP	for this. So far only reported in Finland. People with one copy of the gene have a distal muscle problem
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AR = autosomal recessive

Table 2. The different types of autosomal dominant LGMD

Alternative Names	Inheritance	Protein Involved	Characteristics
LGMD1A	AD	myotilin	Not common but this gene is also involved in another muscle disease called myofibrillar myopathy. Heart and breathing problems may be a problem.
LGMD1B	AD	lamin A/C	All are at risk of heart problems as well as muscle weakness. Faults in this gene also cause AD Emery Dreifuss muscular dystrophy, neuropathy and an unusual condition called lipodystrophy, as well as other conditions. Follow up for heart complications is very important, and there may be important implications for other family members.
LGMD1C	AD	caveolin	Can present in many different ways including "rippling muscle disease" and muscle cramps. Muscle weakness seems not to be so severe in most affected people.
LGMD1D, E, F	AD	not known	Very rarely reported so far

AD = autosomal dominant

Please note, that as the causes of individual types of LGMD are better understood, the term "limb girdle muscular dystrophy" may be replaced by more specific terms.

Symptoms and Implications of Limb Girdle Muscular Dystrophy

In most cases of LGMD, the disorder starts with weakness and a loss of muscle mass in the pelvis, hips and upper legs, resulting in difficulties in getting out of chairs or climbing stairs. Individuals may compensate for this weakness by adopting an unusual walking manner, known as the waddling gait. The muscle weakness and atrophy may also result in lower back pain.

LGMD will progress to the shoulders affected which can make reaching over the head, holding the arms outstretched or carrying heavy objects difficult. It may become increasingly hard to keep the arms above the head for such activities as combing. Some individuals find it harder to type on a computer and may even have trouble feeding themselves.

Progressively, muscles of the face and distal muscles, such as the lower legs, feet, forearms and hands, may become affected and lead to considerable weakness. Calf muscles may appear unusually large

(pseudohypertrophy) as fatty deposits accumulate and replace lost muscle tissue.

Mobility may become increasingly restricted and 20-30 years from onset, individuals with LGMD may lose independent mobility and a wheelchair may become a necessity. Wheelchair options can be discussed with an occupational and/or seating therapist.

Late symptoms can also include contractures as scar tissue replaces normal elastic tissue. Contractures result in prevention of normal movement in the joint and makes the tissue resistant to stretching. These most commonly occur in the ankles and surgery may be an option to release them. For some individuals, contractures may be an early sign.

Scoliosis, an abnormal curvature of the spine, can also become an issue. Spinal bracing may be required, and in more severe cases spinal fusion surgery. An orthopaedic specialist is beneficial in monitoring the scoliosis.

Cardiac problems can arise such as weakness of the heart muscle (cardiomyopathy) or abnormal heartbeat (conduction abnormalities or arrhythmias). Arrhythmias can result in increased risk for heart palpitations (fast or irregular heartbeat) and syncope (loss of consciousness due to lack of oxygen to the brain). The heart must be monitored regularly and some problems may be controlled or treated with medication or devices (such as pacemakers), though severe forms can be fatal.

Respiratory muscles may also be affected resulting in breathing difficulties. When necessary, several options may be available to help maintain respiratory ability, ranging from exercises to the use of ventilators. Like cardiac problems, respiratory problems can be fatal and therefore need to be monitored closely.

Many researchers have noted that progression of LGMD is often faster and more severe when the onset is earlier, in comparison to individuals who develop LGMD later in adolescence or adulthood.

Additional Management of Limb Girdle Muscular Dystrophy

From an early stage, it is important to undergo regular exercise and stretching programmes, with the help of a physiotherapist, to maintain muscle strength and flexibility. Swimming is an excellent option to exercise and mobilize all muscles and joints.

A good diet with plenty of fresh fruit and vegetables is very important in ensuring excessive weight does not impede mobility. Contact with a physician and/or a nutritionist is valuable for this.

Diagnosis of Limb Girdle Muscular Dystrophy

Diagnosis usually commences after the identification of key early symptoms of LGMD:

- Muscle Biopsy – shows typical signs of damage, the presence of certain cell types, such as inflammatory cells, and can establish whether certain proteins are reduced or absent
- Electromyography (EMG) – observes the electrical activity of muscles and its consistency with activity typical of LGMD individuals.
- Blood Testing – elevated levels of creatine phosphokinase (CPK) are indicative of muscle problems
- Electrocardiogram (ECG) – which gives a graphic presentation of the electrical activity or beat pattern of the heart to look for heart abnormalities

Soon after a diagnosis of LGMD in the family, it is essential that genetic counselling is arranged, for one or both of two issues. The first is the probability of Mum or Dad having the disorder, and the second is whether testing for LGMD 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 NZ are available and a referral can be made by the MDA.

Treatment of Limb Girdle Muscular Dystrophy

As with many degenerative diseases of the nervous system, there is currently no known cure for LGMD. Treatment focuses on the prevention and management of symptoms and accompanying complications to help maintain optimal functioning as long as possible.

Research on Limb Girdle Muscular Dystrophy

Research is being carried out to better understand the exact mechanisms which cause LGMD and to make it possible to direct treatment strategies to the cause, rather than simply towards the symptoms

Clinical trials underway to find possible treatments. Two small double-blind trials have suggested that co-enzyme (vitamin) Q10 might be beneficial in this and other dystrophies, but larger trials are needed.

Support

Support is available from the MDA who can offer specialist, information, support, advocacy and referrals to other providers. There is also a nationwide Support Network for those interested in meeting with others.

There is no reason why individuals with LGMD should be disadvantaged in terms of receiving full education. For more information, request the Education Pack available from the MDA.

Disability should not hinder employment possibilities, though it is wise to choose a career that does not require physical activity. Any individual has the right to equal pay and equal rights for employment. For more information contact the Employment Relations infoline on 0800 800 863 or visit www.ers.dol.govt.nz.

The government promotes equal employment opportunities in private sector and can be contacted on (09) 525 3023 or visit www.eeotrust.org.nz

Workbridge provides a professional employment service for people with all types of disabilities and administers support funding on behalf of Work and Income. Contact on 0508 858 858 or visit www.workbridge.co.nz

More Information

Muscular Dystrophy Association can be contacted for further information, assistance, advice, support and referrals, on 0800 800 337 or by e-mail at info@mda.org.nz.

The Muscular Dystrophy Association Website also contains information on services available within NZ, our quarterly magazine, contacts, membership details, news and links to other sites - www.mda.org.nz

Additional Resources

www.nzord.org.nz – the New Zealand Organisation for Rare Disorders website provides information on a number of rare disorders, a directory of support groups, practical advice, health and disability resources, research information, news and issues.

www.mdausa.org – the MDA USA website has an extensive site with plenty of further information on any muscular dystrophy conditions as well as research news.

www.muscular-dystrophy.org – the Muscular Dystrophy Campaign UK website containing a lot of information on LGMD.

www.chb-genomics.org/hndp/ - the Harvard Neuromuscular Disease Project website with a wide range of information on several genetic and neuromuscular disorders.

Information in this fact sheet was primarily sourced from:

eMedicine (2006) Limb Girdle Muscular Dystrophy. <http://www.emedicine.com/NEURO/topic189.htm>
[cited 27 August 2006]

Muscular Dystrophy Campaign (2004) Limb Girdle Muscular Dystrophy. http://www.muscular-dystrophy.org/information_resources/factsheets/medical_conditions_factsheets/limb_girdle.html
[cited 28 August 2006]

Muscular Dystrophy Canada (2001) Limb Girdle Muscular Dystrophy.
<http://www.muscle.ca/content/index.php?id=149> [cited 28 August 2006]