

The limb girdle muscular dystrophies (LGMDs)

This factsheet is for all people for whom a diagnosis of limb girdle muscular dystrophy (LGMD) has been suggested. This is a complicated subject since there are many different types of limb girdle muscular dystrophy. Not all of the things that we talk about in this factsheet will be relevant to everybody with the diagnosis.

What is limb girdle muscular dystrophy?

Muscular dystrophy is the name given to a group of inherited conditions where there is a progressive wasting and weakening of muscle. There are many different types of muscular dystrophy. One of the ways in which the different types of muscular dystrophy are distinguished is by noting the groups of muscle that are involved first. The limb girdle group of muscular dystrophies is so called because generally they cause weakness in the shoulder and pelvic girdle, for example the big muscles around the top (proximal) part of arms and legs (hip, thigh and shoulder muscles). Usually weakness of the legs is noticed before that of the arms and usually the muscles of the face are unaffected.

Specialised tests for LGMD are now available through a national scheme for specialised diagnosis, the National Specialised Commissioning Team (NSCT). Further information can be found at the end of this factsheet.

What are the causes of limb girdle muscular dystrophy?

There are many different genetic mutations associated with LGMD and these are listed in the table below. These genes contain the blueprints for proteins which are needed to make muscles function properly. When a person has a mutation in a LGMD gene, the muscles cannot work properly and weakness occurs.

Quite often, complex tests may be needed to work out the causes of LGMD in an individual, which may include examination of a muscle biopsy and a blood sample for DNA testing.

How is limb girdle muscular dystrophy diagnosed?

The first clue towards the diagnosis of LGMD is usually obtained when your doctor takes your medical history and examines you. Your family history can help to identify the pattern of inheritance and to distinguish between autosomal dominant and autosomal recessive forms.

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A physical examination, particularly a neurological evaluation including a muscle strength assessment, can help the doctor determine the pattern of the muscle involvement. Occasionally this may suggest a particular form of muscular dystrophy but usually a number of different tests will be needed to make the diagnosis. These may include a selection of blood tests, electrical tests, radiological investigations and, most importantly, a muscle biopsy.

Blood tests can show raised creatine kinase (CK) levels which suggest there may be a problem in the muscles. CK is a muscle enzyme, which is released into the bloodstream at high levels when there is muscle fibre damage. In addition to elevated CK serum levels, some people often have elevated transaminates levels. These enzymes are also referred to as liver enzymes and people with muscular dystrophy can therefore, sometimes, be wrongly diagnosed as having liver disease.

Electromyography (EMG) is a test that measures the muscle's response to stimulation of its nerve supply and the electrical activity in the muscle. EMG and radiological investigations (MRI scan) can help to identify the pattern of the muscle involvement, which may suggest a particular form of muscular dystrophy.

Each of the tests, on its own, can indicate that LGMD may be a likely diagnosis. It is, however, usually by studying a muscle biopsy that we can be most clear about what type of LGMD someone might have. This is because we are now able to look directly at the proteins which may be reduced or absent in different types of LGMD. In most situations, the muscle biopsy gives the best chance of reaching a precise diagnosis. However, even today, the muscle biopsy alone is sometimes not enough to distinguish between the exact types of LGMD and therefore genetic tests may be needed to confirm or identify a precise diagnosis.

In approximately 25 percent of all LGMD patients, a precise diagnosis cannot be found in spite of all the testing that is available.

Is there a treatment or cure?

To date there is no specific treatment or cure for the muscle weakness that arises in LGMD. Promising research, however, has been developed over the last few years. Additionally there are supportive interventions which can help with managing symptoms and complications. Your consultant and the Muscular Dystrophy Campaign can give you up-to-date and scientific information about clinical trials and potential suitable treatments for patients.

Appropriate management of symptoms and complications is essential and may vary from type to type. Therefore knowing exactly which type of LGMD someone has helps to ensure that the affected person is receiving the best follow-up and care.

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Regular exercise to maintain good mobility is important for all patients affected by muscular dystrophy. There are no precise guidelines about the type or intensity of activities however it is recommended that any exercise undertaken is done within your limitations and ensuring you remain comfortable. Extreme tiredness, muscle pain and cramps during or after activities can mean that you have pushed yourself too hard and therefore those activities should be avoided. Swimming is a beneficial activity because it promotes movement of all muscles without increased strain. Physiotherapy may also be very important to keep you mobile and to keep your joints supple.

Regular monitoring of breathing and heart function is necessary. Early detection of any problems can lead to starting treatments promptly, which can be life-saving. It is therefore very important that all affected persons have access to this kind of regular follow-up.

What is the prognosis?

LGMDs are rare conditions and they present differently in people, even within the same family, with regard to age of onset, areas of muscle weakness, heart and respiratory involvement, rate of progression and severity.

The different types of LGMD may have different features associated with them and some of these are described in the table below. However, the common features to all people in this group will be weakness of the big muscles of the legs and/or arms. This may result in frequent falls, difficulty in running, climbing stairs and rising from the floor. As the condition progresses, people can have problems with walking and may need to use a wheelchair over time.

The involvement of shoulder and arm muscles can lead to difficulty in raising arms above the head, and in lifting objects. In some types of LGMD, the heart and breathing muscles may be involved. Consequently regular checks of heart and breathing function may be needed in order to identify any changes and treat them as necessary.

What are the different types of limb girdle muscular dystrophy?

The different types of LGMD have all gone through various name changes and reclassifications over the last few years. They are listed in the table below. All forms of LGMD have a genetic basis.

The LGMDs are divided into two main groups, depending on the way they are passed on in families. On this basis, they are grouped into autosomal recessive (or type 2 LGMD) and the much rarer group of autosomal dominant (or type 1 LGMD). They can now be further sub-divided on the basis of the gene with a mutation or the muscle protein deficiency, which may tell us exactly where the problem lies.

Autosomal recessive conditions become apparent only if both parents carry a faulty gene but the parents themselves do not manifest any symptoms. **Autosomal dominant**

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conditions become apparent even though the affected person has only one abnormal gene.

You can read more about the inheritance of these types of LGMD's in the Muscular Dystrophy UK's Inheritance factsheet.

Names	Inheritance	Protein involved	Clinical features	CK level	Genetic test available
LGMD2A calpainopathy Calpain-3 deficiency	Autosomal recessive	Calpain 3	<ul style="list-style-type: none"> - A common form of LGMD worldwide. - Onset of muscle symptoms: eight to 15 years (may be earlier or later). - Weakness and wasting in the hip, thigh and shoulder muscles. - Not usually very rapidly progressive. - Joint contractures may be present. - Heart and breathing involvement is not a common feature of the condition. 	Elevated	Yes

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Names	Inheritance	Protein involved	Clinical features	CK level	Genetic test available
LGMD2B dysferlinopathy Dysferlin deficiency Miyoshi myopathy	Autosomal recessive	Dysferlin	<ul style="list-style-type: none"> - Onset of muscle symptoms: 20 years (may be earlier or later). - Same people with a typical hip and shoulder muscle weakness (LGMD2B); other people with difficulty standing on toes and hand weakness (Miyoshi myopathy or distal myopathy). - Usually slow progression. - Muscle pain and swelling in calves can be present. - Heart and breathing involvement is not a common feature of the condition. 	Markedly elevated	Yes
LGMD2C, 2D, 2E, 2F sarcoglycanopathies Sarcoglycan deficiency	Autosomal recessive	One of the sarcoglycan proteins (alpha, beta, gamma and delta)	<ul style="list-style-type: none"> - Onset of muscle symptoms: usually in childhood. - Weakness and wasting in the hip, thigh and shoulder muscles. - Rate of progression of the condition is extremely variable. - Joint contractures may be present. - Heart and breathing muscles may be involved. 	Elevated	Yes
LGMD2G	Autosomal recessive	Telethonin	So far only reported in Brazil.	Elevated	No
LGMD2H	Autosomal recessive	TRIM32	So far only reported in Canada.	Elevated	No

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LGMD2I	Autosomal recessive	FKRP (Fukutin related protein)	<ul style="list-style-type: none"> - A common form of LGMD in the UK and in the North of Europe. - Onset of muscle symptoms: 10 to 20 years (may be earlier or later, with a range from two to 40 years). - Rate of progression of the condition is extremely variable. - Joint contractures may be present. - Heart and breathing muscles may be involved. 	Elevated	Yes
LGMD2J	Autosomal recessive	Titin	<ul style="list-style-type: none"> - So far only reported in Finland. - People with one copy of the mutated gene have a distal muscle myopathy. 	Elevated	No
LGMD2K	Autosomal recessive	POMT1	<ul style="list-style-type: none"> - Onset of muscle symptoms: childhood. - Weakness and wasting in the hip, thigh and shoulder muscles. - Severe learning difficulties. - The gene is also involved in a severe congenital muscular dystrophy. - Few cases described. 	Elevated	Yes

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LGMD2L	Autosomal recessive	Anoctamin 5	<ul style="list-style-type: none"> - Onset of muscle weakness: adulthood. - Weakness and wasting in the hip, thigh and calf muscles. - Possible predominantly distal onset. Symptoms often asymmetrical. - Usually slow progression. - No cardiac or respiratory involvement. 	Elevated	Yes
LGMD2M	Autosomal recessive	Fukutin	<ul style="list-style-type: none"> - Onset of muscle symptoms: childhood. - Weakness and wasting in the hip, thigh and shoulder muscles. - The gene is also involved in a severe congenital muscular dystrophy. - Few cases described. - Deterioration of weakness with viral infections. - Heart and breathing muscles may be involved. 	Elevated	Yes
LGMD2N	Autosomal recessive	POMT2	<ul style="list-style-type: none"> - Recently described. - Mutations in this gene are responsible for a wide spectrum of symptoms, ranging from severe muscle weakness and wasting, learning difficulties and eye problems at birth, to a milder form of LGMD. 	Elevated	Yes

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Names	Inheritance	Protein involved	Clinical features	CK level	Genetic test available
LGMD2O	Autosomal recessive	POMGN T1	<ul style="list-style-type: none"> - Recently described. - Mutations in this gene are responsible for a wide spectrum of symptoms, ranging from severe muscle weakness and wasting, learning difficulties and eye problems at birth, to a milder form of LGMD, 	Elevated	Yes
LGMD2Q	Autosomal recessive	Plectin	<ul style="list-style-type: none"> - So far only few cases described. - Early childhood onset. - Muscle weakness and atrophy. 	Elevated	No
LGMD1A	Autosomal dominant	Myotilin	<ul style="list-style-type: none"> - So far only few families described. - Mutations in this gene also cause another autosomal dominant muscular disease, called Myofibrillar myopathy. - Onset of muscle symptoms: adulthood. - Some affected individuals can have a particular nasal pattern of speech (dysarthria). - Heart and breathing muscles may be involved. 	Normal or mildly elevated	Yes

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Names	Inheritance	Protein involved	Clinical features	CK level	Genetic test available
LGMD1B	Autosomal dominant	Lamin A/C	<ul style="list-style-type: none"> - Mutations in this gene also cause AD and AR Emery-Dreifuss muscular dystrophy, a congenital muscular dystrophy, an isolated cardiomyopathy, a peripheral neuropathy and other rare conditions with no major muscle involvement. - Onset of muscle symptoms: five to 20 years. - Usually slow progression. - Heart involvement is frequent and can sometimes be the only manifestation of the muscular condition. - Breathing problems are not common. 	Normal or mildly elevated	Yes
LGMD1C	Autosomal dominant	Caveolin 3	<ul style="list-style-type: none"> - Onset of muscle symptoms: from childhood to adulthood. - People can present weakness and wasting in the hip, thigh and shoulder muscles, a distal muscle weakness and 'rippling muscle disease'. - Cramps and muscle pain after exercise are common. - Usually slow progression. - Heart and breathing involvement is not a common feature of the condition. 	Mildly elevated	Yes

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Names	Inheritance	Protein involved	Clinical features	CK level	Genetic test available
LGMD1D	Autosomal dominant	DNAJB6	- So far only a few cases described. - Onset of muscle symptoms: in adulthood. - People can present proximal weakness in the lower limbs and later in shoulder muscles as well. Possible prevalently distal phenotype at onset. - No heart and respiratory involvement.	Normal or mildly elevated	Yes
LGMD1E, 1F, 1G and 1H	Autosomal dominant	Not known	- Very rarely reported to date.	Normal or mildly elevated	No

Other relevant factsheets from the Muscular Dystrophy UK

- ▶ LGMB1B
- ▶ LGMB1C
- ▶ LGMB2A
- ▶ LGMB2B
- ▶ Sarcoglycanopathies: LGMB2C, LGMD2D, LGMD2E and LGMD2F
- ▶ LGMB2I
- ▶ LGMD2L
- ▶ Inheritance



If you have feedback about this factsheet please email info@muscular dystrophyuk.org.

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Here for you

The friendly staff in the care and support team at the Muscular Dystrophy UK's London office are available on **0800 652 6352** or **info@muscular dystrophyuk.org** from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

If they can't help you, they are more than happy to signpost you to specialist services close to you, or to other people who can help.

www.muscular dystrophyuk.org

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