

Limb Girdle Muscular Dystrophy (LGMD)

What Is Limb Girdle Muscular Dystrophy?

Limb girdle muscular dystrophy (LGMD) is a diverse group of disorders affecting the voluntary muscles, mainly around the pelvic (hip) and shoulder regions. Occasionally, the cardiac (heart) and respiratory (breathing) muscles may be involved. Different types of LGMD vary in severity, age of onset and how they are inherited. The variation seen in the LGMDs is caused by the differences in the type of gene alteration. Our genetic blueprint is made up of thousands of different genes that contain

the information needed to produce specific proteins. Genes can become altered by changes (mutations) that occur in the sequence of chemical structures known as nucleotides (represented by the four letters A,T,C, and G) that make up the gene in question. Mutations in different genes can cause different forms of LGMD, as can different changes within the same gene. These differences can lead to more severe or milder forms of LGMD. Presently, scientists have identified at least 15 different genes that can be altered to cause LGMD and are working on locating others.

How Disabling Is LGMD?

LGMD is not normally a fatal disease. The greatest danger comes from weakening heart muscles or respiratory muscles. Monitoring for heart or breathing complications is recommended for the later stages of the disorder, but these cases are rare. Affected individuals may require a wheelchair after several years but some remain mobile throughout their lives.

What Is The Age Of Onset?

Because there is so much variability in the disorder, the onset of a specific LGMD is difficult to determine. Often people with LGMD first notice problems when they begin to walk with a waddling gait because of weakness in hip and leg muscles.

What Are The Symptoms Of Limb Girdle Muscular Dystrophy?

The onset of LGMD may involve the pelvis, the shoulder area, or both. Early symptoms can include difficulty walking, running, and rising from the floor. Usually, and eventually, affected individuals will find it hard to climb stairs, stand up from a squatting position, and walk. Weak shoulder muscles can make it difficult to raise arms above the head, hold the arms outstretched, or carry heavy

objects. The brain, the intellect, and the senses are not impaired. Rarely, certain forms of LGMD can involve the heart muscle, causing symptoms of heart failure or rhythm disturbance. Uncommon forms of LGMD can also affect breathing, which can result in sleepiness, headaches, and lack of energy. As heart and breathing symptoms may be difficult to recognize, the heart and respiratory system of affected individuals should be monitored to detect changes.

How Does Limb Girdle Muscular Dystrophy Progress?

Limb girdle muscular dystrophy is progressive, which means that the affected person's muscles continue to get weaker throughout their lifetime. There is a wide range of severity for all limb girdle disorders, so the rate of progression is extremely variable. Generally, over time, a person with LGMD loses muscle bulk and strength. The muscles involved may show different levels of weakness between right and left sides (i.e. the left shoulder may be weaker than the right). Weakness can also extend to the neighbouring muscles.

When the rate of progression is slow and unnoticeable, the disorder may seem to suddenly get worse when a loss of function occurs. For example, a person may not notice the rate of progression until they find it impossible to rise from a chair, or raise an arm to brush his, or her hair. When the muscle strength falls below the minimum level needed to accomplish a task, it makes the disease appear to progress rapidly. This is called the "stair step" phenomenon in which progression seems to stop for a while, then suddenly worsen.

When the onset of LGMD begins in childhood, the increase in body weight and size from natural growth, combined with the increase in muscle weakness caused by the disease, can make the progression seem very rapid. As an adult, body growth stops. Therefore, weakness only increases as the body's muscles break down. LGMD is so variable that it is not yet possible to predict the course of the disease in most people.

How Do You Get LGMD?

LGMD is inherited when a faulty gene is passed on from one or both parents to a child. There are two ways a person can inherit the disorder: autosomal dominant and autosomal recessive. There are always two copies of a gene – one from the person's mother and one from the father. When a single copy of a gene mutation causes LGMD, it is referred to as dominant. A recessive form of LGMD occurs when it is necessary for both parents to pass on an altered gene, and thus no normal gene copy is present.

Dominant forms of LGMD can arise by a new mutation in the affected individual, or it can be

Known Types Of LGMD:

Note: Chromosomes have two arms, a short "p" and a long "q", in which genes are located.

LGMD1-Dominant

Limb Girdle Muscular Dystrophy 1A:

- Onset: young adults
- Progression: slow, late loss of ambulation
- Gene location: Chromosome 5q31
- Gene product: Myotilin

Limb Girdle Muscular Dystrophy 1B:

- Onset: 4 to 38 years
- Progression: slow
- Gene location: Chromosome 1q11-q21
- Gene product: LaminA/C

Limb Girdle Muscular Dystrophy 1C:

- Onset: usually childhood
- Progression: variable
- Gene location: Chromosome 3p25
- Gene product: Caveolin

Limb Girdle Muscular Dystrophy 1D:

- Onset: early adulthood
- Progression: slow
- Gene location: Chromosome 7q
- Gene product: unknown

Limb Girdle Muscular Dystrophy 1E:

- Onset: early adulthood
- Progression: slow
- Gene location: Chromosome 6q
- Gene product: unknown

LGMD2-Recessive

Limb Girdle Muscular Dystrophy 2A:

- Onset: 3-30 years
- Progression: the earlier the onset the more rapid the progression. Loss of walking in 20 years.
- Gene location: Chromosome 15q15-21
- Gene product: Calpain 3

Limb Girdle Muscular Dystrophy 2B:

- Onset: Late teens
- Progression: generally slow, some more rapid
- Gene location: Chromosome 2p13
- Gene product: Dysferlin. Same gene responsible for the distal Miyoshi myopathy

inherited from an affected parent. Inherited autosomal dominant traits need only one affected parent to transmit the gene mutation. There is a 50% chance that a child of either sex, born to an affected parent, will inherit the disorder.

Inherited autosomal recessive traits, on the other hand, involve children who receive the altered gene from both parents. In most cases, each parent is a carrier. This means they have one copy of the altered gene but are not affected and do not show any symptoms because the other copy of the gene in question is normal. Each child of either sex born to parents who are both carriers, has a 25% chance of having the disorder, a 50% chance of being a carrier, and a 25% chance of having two normal gene copies.

In a recessive disorder, if one parent is affected and shows the symptoms, it means that both of his or her gene copies are altered. Therefore, an affected parent has a 100% chance of passing on the gene. However, except in very rare cases, the other parent has two normal copies of the gene. Therefore, the children of these parents will be carriers (through the gene passed from the affected parent), but not affected.

How Is LGMD Diagnosed?

Better tests to diagnose LGMD are now being developed. Because the physical symptoms are similar to other neuromuscular disorders such as Becker MD, a diagnosis for LGMD is often reached after eliminating other possible causes for the weakness around the hips and shoulders. Before any laboratory tests, a medical history of the person's family and a physical exam are taken to determine the pattern of weakness in the individual. Early in the diagnostic process, a special blood test called a CK Test is performed. CK stands for creatine kinase, an enzyme that leaks out of damaged muscles. If a blood sample shows high levels of CK, it suggests that the muscles themselves are the likely cause of the weakness. This test cannot identify the specific type of disorder affecting the muscle.

To obtain more information, laboratory exams may be conducted to find evidence of general changes in muscle weakness and other muscle changes. Sometimes a special test called electromyography is done to discover the location of the weakness. This test measures the electrical activity of muscle cells. A

Limb Girdle Muscular Dystrophy 2C:

- Also known as Severe Childhood Autosomal Recessive Muscular Dystrophy
- Onset: variable, generally during first decade
- Progression: very variable, even within families
- Gene location: Chromosome 13q12-13
- Gene product: gamma-sarcoglycan

Limb Girdle Muscular Dystrophy 2D:

- Onset: most variable, generally during first decade
- Progression: very variable
- Gene location: Chromosome 17q12-21
- Gene product: alpha-sarcoglycan, formerly called adhalin

Limb Girdle Muscular Dystrophy 2E:

- Onset: variable, generally during first decade
- Progression: very variable, often in wheelchair by 10-15 years
- Gene location: Chromosome 4q12
- Gene product: beta-sarcoglycan

Limb Girdle Muscular Dystrophy 2F:

- Onset: variable, generally during first decade
- Progression: variable
- Gene location: Chromosome 5q33-34
- Gene product: delta-sarcoglycan

Limb Girdle Muscular Dystrophy 2G:

- Onset: childhood
- Progression: moderate
- Gene location: Chromosome 17q11-12
- Gene product: telethonin

Limb Girdle Muscular Dystrophy 2H:

- Onset: 8-27 years so far reported
- Progression: slow
- Chromosome 9p31-33
- Gene product: TRIM-32

Limb Girdle Muscular Dystrophy 2I:

- Onset: not known
- Progression: not confirmed
- Gene Location: Chromosome 19q13
- Gene Product: FKRP (Fukutin-related protein)

muscle biopsy may be performed by surgically removing a sample of the affected muscle for examination, to find the underlying cause of the weakness. DNA testing may be done to determine specific types of LGMD, and muscle stains may be used in some cases, to look for the precise protein that is missing.

These techniques have not yet been perfected to provide 100% accurate information about the exact type of LGMD, but progress is being made in diagnosing problems in the muscle cells.

Symptom Management

Maintaining good health is beneficial to everyone. For individuals affected by LGMD, it is a good way to preserve strength. A well-balanced diet and moderate exercise can help reduce or control weight. Intense workout is impractical and sometimes dangerous, but activities like swimming, water aerobics, and low resistance exercise may facilitate greater mobility. Physical and occupational therapy, as well as assistive devices, may also help to maintain mobility and flexibility. Affected individuals should keep walking as long as they can. This may mean using a wheelchair or scooter for long distances, thus preserving strength for short walks.

In some cases, joint deformities may be prevented through exercises, physiotherapy, orthoses, and surgery. To avoid spinal instability, proper seating and back support should be maintained. These techniques can alleviate stress from weak muscles and from joints, but they cannot reverse the symptoms of LGMD or strengthen already weakened muscles.

Research

Researchers in the US, Canada, and throughout the world are focusing on finding ways to defeat limb girdle muscular dystrophy. Currently, gene therapy is one technique being tested, as a potential treatment for LGMD. In this research, the genes of a virus are removed, and replaced by healthy human genes. They are then injected into the affected person's body. The outer shell of the virus is used as a vehicle or carrier to deliver the healthy genetic material to cells. The virus itself is disarmed, so that it is no longer infectious. Most of the virus' genes are replaced with human DNA, ensuring that the virus is unable to divide and cause harm.

There are many other areas of research in both mainstream and alternative medicine, and researchers are vigorously pursuing every potential direction.

How can I help?

Muscular Dystrophy Canada conducts year-round fund raising campaigns to support our diverse programs. Your gift will help the Association provide the dollars necessary to assist individuals living with neuromuscular disorders, and fund much needed medical research and educational information. Please make a gift through our National office or any Regional or Community Muscular Dystrophy Canada office.

**All Muscular Dystrophy Canada Information
Sheets are available on our website:**

www.muscle.ca

**Ce feuillet d'information est aussi disponible en
français.**

© Muscular Dystrophy Canada 9/07