MDA Muscular Dystrophy Association

# Limb-Girdle Muscular Dystrophy (LGMD)

**Limb-girdle muscular dystrophies (LGMD)** are a diverse group of rare progressive genetic disorders. Subtypes of LGMD are categorized by disease gene and inheritance. (Learn more about subtypes on the next page.)

LGMD is characterized by **muscle wasting (atrophy) and weakness** of the voluntary muscles. It primarily affects muscles around the hips and shoulders. This group of disorders gets its name from the observed weakness and wasting of the muscles connected to the limb girdles. The shoulder girdle is the bony structure that surrounds the shoulder area, and the pelvic girdle is the bony structure surrounding the hips.

Progression of LGMD may cause muscle wasting to spread to other areas, such as the arms, legs, and respiratory muscles. In some cases, people with LGMD may need mobility aids such as canes, walkers, or wheelchairs.

**LGMD can begin in childhood, adolescence, or adulthood**, depending on the specific type. Both males and females can be affected. LGMD is typically inherited in either an autosomal dominant or autosomal recessive pattern.

Together, the group of disorders that constitute LGMD is the fourth most common genetic cause of muscle weakness, with an estimated worldwide prevalence ranging from **2.27 to 6.89 per 100,000 individuals**. It is estimated that 20,000 to 30,000 people are currently living with LGMD in the United States.

While there are no approved drugs for LGMD, access to multidisciplinary care and other supportive treatments can help manage symptoms and improve quality of life.

# LGMD Subtypes

LGMD is not one single disease, but a group of related conditions caused by different **genetic mutations**. There are many subtypes of LGMD, each caused by mutations in different genes. The progression and severity of symptoms can vary widely between people and subtypes.

Each subtype can differ in age of onset, progression, symptoms, and which muscles or organs are affected. Knowing your LGMD subtype can guide treatment planning, predict complications, and help identify appropriate clinical trials.

**Genetic testing** is the most accurate way to identify your subtype. To learn more about genetic testing, speak with your healthcare provider or contact MDA's Resource Center as there may be free or low-cost genetic testing options. The following resources may also be helpful:

- **Access Workshop: Genetic Testing**
- **Genetics-and-NMD.pdf**

As of now, there are more than **30 identified subtypes** of LGMD, classified based on the specific gene and mode of inheritance:

- **Autosomal recessive (LGMD R):** The most common form; the genetic mutation is inherited from both parents.
- **Autosomal dominant (LGMD D):** Less common; inheriting one copy of the genetic mutation is enough to cause the condition.

Researchers continue to discover new subtypes as genetic testing advances.

## Recessive LGMD subtypes

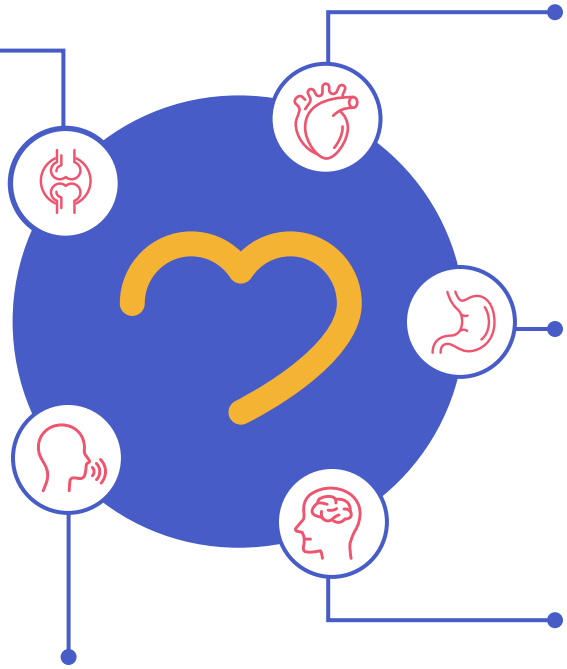
| Name | Gene |
|---|---|
| LGMD R1 | *CAPN3* |
| LGMD R2 | *DYSF* |
| LGMD R3 | *SGCG* |
| LGMD R4 | *SGCA* |
| LGMD R5 | *SGCB* |
| LGMD R6 | *SGCD* |
| LGMD R7 | *TCAP* |
| LGMD R8 | *TRIM32* |
| LGMD R9 | *FKRP* |
| LGMD R10 | *TTN* |
| LGMD R11 | *POMT1* |
| LGMD R12 | *ANO5* |
| LGMD R13 | *FCMD* |
| LGMD R14 | *POMT2* |
| LGMD R15 | *POMGNT1* |
| LGMD R16 | *DAG1* |
| LGMD R17 | *PLEC1* |
| LGMD R18 | *TRAPPC11* |
| LGMD R19 | *GMPPB* |
| LGMD R20 | *ISPD* |
| LGMD R21 | *POGLUT1* |
| LGMD R22 | *COL6A2* |
| LGMD R23 | *LAMA2* |
| LGMD R24 | *POMGNT2* |
| LGMD R25 | *POPDC1* |
| LGMD R26 | *POPDC3* |
| LGMD R27 | *JAG2* |
| LGMD R28 | *MYPLG* |
| LGMD R29 | *SNUPN* |

## Dominant LGMD subtypes

| Name | Gene |
|---|---|
| LGMD D1 | *DNAJB6* |
| LGMD D2 | *TNPO3* |
| LGMD D3 | *HNRNPDL* |
| LGMD D4 | *CAPN3* |
| LGMD D5 | *COL6A1, COL6A2, COL6A3* |

# What Are the Signs and Symptoms of LGMD?

**Skeleton and muscle:**
- Muscle wasting
- Muscle cramps
- Muscle weakness, particularly in hip, thigh, and shoulder muscles
- Decreased muscle mass over time
- Abnormal walking gait or frequent falls
- Enlarged calf muscles (in specific subtypes)
- Difficulty climbing stairs, standing from a seated position, or lifting arms
- Scoliosis
- Myalgia (Muscle pain)
- Elevated creatine kinase levels



**Heart:**
- Cardiomyopathy (in specific subtypes)
- Abnormal heart rhythms or conduction issues (in specific subtypes)

**Gastrointestinal:**
- Swallowing difficulties (in specific subtypes)
- Digestive issues are not common but may happen if muscle weakness affects swallowing

**Cognition:**
- Potential developmental delay or intellectual disability (in some subtypes)

**Breathing:**
- Weakness of the diaphragm and breathing muscles (in later stages)
- Shortness of breath, especially when lying flat
- Increased risk of respiratory infections





To learn more about LGMD and MDA's programs, visit **MDA.org** or contact the MDA Resource Center at **833-ASK-MDA1 (275-6321)** or **ResourceCenter@mdausa.org**.

# What Should I Know About LGMD?

**1.** Disease progression in each type of LGMD cannot be predicted with certainty, although knowing the underlying genetic mutation can be helpful. Some forms of the disorder progress to loss of walking ability within a few years and cause serious disability, while others progress very slowly over many years and cause minimal disability.

**2.** MDA-supported scientists are pursuing several exciting strategies in muscular dystrophy research that have implications for LGMD. These strategies include genetic therapy (replacement or editing), antisense oligonucleotides, stop codon readthrough, and small molecule drugs. For more information, visit **Limb-Girdle Muscular Dystrophy (LGMD) Research**.

**3.** LGMD can significantly impact mobility and daily activities over time. Some people find activities like holding arms outstretched or carrying heavy objects difficult. It may become increasingly challenging to keep the arm muscles engaged, such as combing one's hair, cleaning dishes, arranging things on a shelf, etc.

**4.** The condition is progressive, meaning symptoms worsen over time. Early signs may be mild and go unnoticed until weakness becomes more apparent.

**5.** Pain isn't a major symptom of LGMD, although limited mobility sometimes leads to muscle soreness and aching joints.

**6.** The emotional and social impact of LGMD symptoms can be significant. Mental health support is important.

**7.** Genetic counseling is recommended for affected individuals and family members.

**8.** Participation in clinical trials may be an option and may provide access to experimental therapies. To find clinical trial opportunities, visit **Muscular Dystrophy Clinical Trials**.

# How Is LGMD Treated?

There are currently no approved drugs to treat LGMD, but several are in clinical testing for different subtypes. Current treatment options focus on managing symptoms and maintaining mobility. A multidisciplinary care team (neurologist, physical therapist, cardiologist, etc.) is essential for best outcomes. Connect with your local MDA Care Center at **mda.org/CareCenters**.

- Physical therapy can help maintain and improve range of motion as well as prevent contractures. Occupational therapy can help with maintaining abilities related to work, recreation, or daily living.
- Orthopedic care may include the use of supportive aids such as railings, braces, orthotics, walkers, or wheelchairs that may help prevent falls, alleviate fatigue, and preserve mobility, and surgical interventions for scoliosis or joint issues.
- Respiratory care may include breathing exercises, cough assistance devices, or ventilatory support if needed.
- Cardiac monitoring and treatment for heart issues may be necessary for certain subtypes. A pacemaker can be used to stimulate a normal heartbeat in individuals who experience arrhythmia.
- Genetic counseling helps families understand inheritance and risk.
- Regular follow-ups with a neuromuscular specialist are important to monitor progression.
- Clinical trials and research studies may offer opportunities for new therapies.

Although no FDA-approved disease-modifying drugs exist specifically for LGMD, medical treatment focuses on managing symptoms and preventing complications. Cardiac involvement in certain subtypes is treated with standard heart failure drugs, such as ACE inhibitors, beta blockers, and mineralocorticoid receptor antagonists (e.g., eplerenone). Respiratory management may include cough assist devices and noninvasive ventilation when muscle weakness compromises airway clearance or nocturnal breathing. Corticosteroids are generally not part of routine LGMD care, but they can be considered in inflammatory or borderline presentations.

Meanwhile, multiple clinical trials are exploring gene therapies and other molecular approaches tailored to specific LGMD subtypes, offering the prospect of targeted treatments in the near future.

# MDA Glossary

**Cardiac arrhythmia**
Abnormal heartbeat

**Cardiomyopathy**
A condition in which the heart muscle is weakened, making it harder for the heart to pump blood to the body

**Conduction defect**
Irregular electrical control of the heartbeat

**Contracture**
A shortening of muscles or tendons around joints that can limit mobility

**Dysarthria**
Difficulty speaking or forming words

**Dysphagia**
Difficulty swallowing

**Gene mutation**
A flaw in the DNA code

**Gene therapy**
A treatment approach that involves altering genes inside the body's cells to treat or stop disease. It is an emerging area of research for LGMD.

**Genetic testing**
A medical test that identifies mutations in DNA that can confirm an LGMD diagnosis and determine the subtype

**Hypertrophy**
Overgrowth of muscle

**Limb girdle**
The shoulder girdle is the bony structure that surrounds the shoulder area, and the pelvic girdle is the bony structure surrounding the hips. Collectively these are called the limb girdles.

**Muscular dystrophy**
A number of diseases that cause progressive loss of muscle mass, resulting in weakness and, sometimes, loss of mobility

**Myalgia**
Muscle pain

**Voluntary muscles**
Muscles that are under conscious control, such as those used for walking or lifting. These are primarily affected in LGMD.



Images: iStock.com/Lisa5201; peterschreiber.media