



LMNA-related congenital muscular dystrophy

LMNA-related congenital muscular dystrophy (L-CMD) is a condition that primarily affects muscles used for movement (skeletal muscles). It is part of a group of genetic conditions called congenital muscular dystrophies, which cause weak muscle tone (hypotonia) and muscle wasting (atrophy) beginning very early in life.

In people with L-CMD, muscle weakness becomes apparent in infancy or early childhood and can worsen quickly. The most severely affected infants develop few motor skills, and they are never able to hold up their heads, roll over, or sit. Less severely affected children may learn to sit, stand, and walk before muscle weakness becomes apparent. First the neck muscles weaken, causing the head to fall forward (dropped-head syndrome). As other skeletal muscles become weaker, these children may ultimately lose the ability to sit, stand, and walk unassisted.

Other features of L-CMD often include spinal rigidity and abnormal curvature of the spine (scoliosis and lordosis); joint deformities (contractures) that restrict movement, particularly in the hips and legs; and an inward-turning foot. People with L-CMD also have an increased risk of heart rhythm abnormalities (arrhythmias).

Over time, muscle weakness causes most infants and children with L-CMD to have trouble eating and breathing. The breathing problems result from restrictive respiratory insufficiency, which occurs when muscles in the chest are weakened and the ribcage becomes increasingly rigid. This problem can be life-threatening, and many affected children require support with a machine to help them breathe (mechanical ventilation).

Frequency

L-CMD is a rare disorder. Only about 50 affected individuals have been described in the medical literature.

Causes

L-CMD is caused by mutations in the *LMNA* gene. This gene provides instructions for making very similar proteins called lamins. These proteins play an important role in determining the shape of the nucleus within cells. Lamins are an essential supporting (scaffolding) component of the nuclear envelope, which is the membrane that surrounds the nucleus. The nuclear envelope regulates the movement of molecules into and out of the nucleus, and researchers believe it may play a role in regulating the activity of certain genes.

Mutations in the *LMNA* gene lead to the production of abnormal lamins. These malfunctioning proteins alter the structure of the nuclear envelope in ways that are

not well understood. Researchers are working to determine how these changes affect muscle cells and lead to muscle weakness and atrophy in people with L-CMD.

Inheritance Pattern

L-CMD is considered an autosomal dominant disorder, which means one copy of the altered gene in each cell is sufficient to cause the condition. All known cases of L-CMD have resulted from new (de novo) mutations in the gene. These mutations occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. Affected individuals have no history of the disorder in their family.

Other Names for This Condition

- L-CMD
- LMNA-related CMD
- MDCL
- muscular dystrophy, congenital, LMNA-related

Diagnosis & Management

Formal Treatment/Management Guidelines

- American Academy of Neurology: Summary of Evidence-based Guideline for Patients and Their Families: Congenital Muscular Dystrophy
<https://www.aan.com/Guidelines/Home/GetGuidelineContent/684>
- Wang CH, Bonnemann CG, Rutkowski A, Sejersen T, Bellini J, Battista V, Florence JM, Schara U, Schuler PM, Wahbi K, Aloysius A, Bash RO, Bérout C, Bertini E, Bushby K, Cohn RD, Connolly AM, Deconinck N, Desguerre I, Eagle M, Estournet-Mathiaud B, Ferreira A, Fajak A, Goemans N, Iannaccone ST, Jouinot P, Main M, Melacini P, Mueller-Felber W, Muntoni F, Nelson LL, Rahbek J, Quijano-Roy S, Sewry C, Storhaug K, Simonds A, Tseng B, Vajsar J, Vianello A, Zeller R; International Standard of Care Committee for Congenital Muscular Dystrophy. Consensus statement on standard of care for congenital muscular dystrophies. *J Child Neurol.* 2010 Dec;25(12):1559-81. doi: 10.1177/0883073810381924. Epub 2010 Nov 15. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21078917>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5207780/>

Genetic Testing Information

- What is genetic testing?
</primer/testing/genetic-testing/>
- Genetic Testing Registry: Congenital muscular dystrophy, LMNA-related
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2750785/>

Other Diagnosis and Management Resources

- American Thoracic Society: Mechanical Ventilation
<https://www.thoracic.org/patients/patient-resources/resources/mechanical-ventilation.pdf>
- Azibani F, Brull A, Arandel L, Beuvin M, Nelson I, Jollet A, Ziat E, Prudhon B, Benkhelifa-Ziyyat S, Bitoun M, Lorain S, Bonne G, Bertrand AT. Gene Therapy via Trans-Splicing for LMNA-Related Congenital Muscular Dystrophy. *Mol Ther Nucleic Acids*. 2018 Mar 2;10:376-386. doi: 10.1016/j.omtn.2017.12.012. Epub 2017 Dec 30.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/29499949>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5862133/>
- Cure CMD: Care Guidelines
<https://www.curecmd.org/copy-of-care-guidelines>
- MedlinePlus Encyclopedia: Learning About Ventilators
<https://medlineplus.gov/ency/patientinstructions/000458.htm>
- Muscular Dystrophy Association: Medical Management of Congenital Muscular Dystrophy (CMD)
<https://www.mda.org/disease/congenital-muscular-dystrophy/medical-management>

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Learning About Ventilators
<https://medlineplus.gov/ency/patientinstructions/000458.htm>
- Encyclopedia: Muscular Dystrophy
<https://medlineplus.gov/ency/article/001190.htm>
- Health Topic: Muscular Dystrophy
<https://medlineplus.gov/musculardystrophy.html>

Genetic and Rare Diseases Information Center

- Congenital muscular dystrophy
<https://rarediseases.info.nih.gov/diseases/9138/congenital-muscular-dystrophy>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Muscular Dystrophy Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Muscular-Dystrophy-Information-Page>

Educational Resources

- Centers for Disease Control and Prevention: Muscular Dystrophy
<https://www.cdc.gov/ncbddd/musculardystrophy/index.html>
- MalaCards: muscular dystrophy, congenital, lmna-related
https://www.malacards.org/card/muscular_dystrophy_congenital_lmna_related
- Orphanet: Orphanet: Congenital muscular dystrophy due to LMNA mutation
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=157973

Patient Support and Advocacy Resources

- Cure CMD
<https://www.curecmd.org/lmna>
- Muscular Dystrophy Association
<https://www.mda.org/>
- Muscular Dystrophy Canada
<https://muscle.ca/>
- Muscular Dystrophy UK
<https://www.musculardystrophyuk.org/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/congenital-muscular-dystrophy/>
- Resource List from the University of Kansas Medical Center: Muscular Dystrophy/ Atrophy
<http://www.kumc.edu/gec/support/muscular.html>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28LMNA%5BTIAB%5D%29+AND+%28congenital+muscular+dystrophy%5BTIAB%5D%29%29+OR+%28L-CMD%5BTIAB%5D%29+OR+%28%28LMNA%5BTIAB%5D%29+AND+%28CMD%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

Catalog of Genes and Diseases from OMIM

- MUSCULAR DYSTROPHY, CONGENITAL, LMNA-RELATED
<http://omim.org/entry/613205>

Medical Genetics Database from MedGen

- Congenital muscular dystrophy, LMNA-related
<https://www.ncbi.nlm.nih.gov/medgen/413043>

Sources for This Summary

- Barateau A, Vadrot N, Vicart P, Ferreira A, Mayer M, Héron D, Vigouroux C, Buendia B. A Novel Lamin A Mutant Responsible for Congenital Muscular Dystrophy Causes Distinct Abnormalities of the Cell Nucleus. *PLoS One*. 2017 Jan 26;12(1):e0169189. doi: 10.1371/journal.pone.0169189. eCollection 2017.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/28125586>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5268432/>
- Bonati U, Bechtel N, Heinimann K, Rutz E, Schneider J, Frank S, Weber P, Fischer D. Congenital muscular dystrophy with dropped head phenotype and cognitive impairment due to a novel mutation in the LMNA gene. *Neuromuscul Disord*. 2014 Jun;24(6):529-32. doi: 10.1016/j.nmd.2014.02.004. Epub 2014 Feb 15.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24684859>
- D'Amico A, Haliloglu G, Richard P, Talim B, Maugenre S, Ferreira A, Guicheney P, Menditto I, Benedetti S, Bertini E, Bonne G, Topaloglu H. Two patients with 'Dropped head syndrome' due to mutations in LMNA or SEPN1 genes. *Neuromuscul Disord*. 2005 Aug;15(8):521-4.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15961312>
- Hattori A, Komaki H, Kawatani M, Sakuma H, Saito Y, Nakagawa E, Sugai K, Sasaki M, Hayashi YK, Nonaka I, Nishino I. A novel mutation in the LMNA gene causes congenital muscular dystrophy with dropped head and brain involvement. *Neuromuscul Disord*. 2012 Feb;22(2):149-51. doi: 10.1016/j.nmd.2011.08.009. Epub 2012 Jan 11.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22240398>
- Heller F, Dabaj I, Mah JK, Bergounioux J, Essid A, Bönnemann CG, Rutkowski A, Bonne G, Quijano-Roy S, Wahbi K. Cardiac manifestations of congenital LMNA-related muscular dystrophy in children: three case reports and recommendations for care. *Cardiol Young*. 2017 Aug;27(6):1076-1082. doi: 10.1017/S1047951116002079. Epub 2016 Dec 12.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/27938454>
- Karaoglu P, Quizon N, Pergande M, Wang H, Polat AI, Ersen A, Özer E, Willkomm L, Hiz Kurul S, Heredia R, Yis U, Selcen D, Çirak S. Dropped head congenital muscular dystrophy caused by de novo mutations in LMNA. *Brain Dev*. 2017 Apr;39(4):361-364. doi: 10.1016/j.braindev.2016.11.002. Epub 2016 Nov 19.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/27876398>
- Menezes MP, Waddell LB, Evesson FJ, Cooper S, Webster R, Jones K, Mowat D, Kiernan MC, Johnston HM, Corbett A, Harbord M, North KN, Clarke NF. Importance and challenge of making an early diagnosis in LMNA-related muscular dystrophy. *Neurology*. 2012 Apr 17;78(16):1258-63. doi: 10.1212/WNL.0b013e318250d839. Epub 2012 Apr 4.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22491857>
- Pasqualin LM, Reed UC, Costa TV, Quedas E, Albuquerque MA, Resende MB, Rutkowski A, Chadi G, Zanoteli E. Congenital muscular dystrophy with dropped head linked to the LMNA gene in a Brazilian cohort. *Pediatr Neurol*. 2014 Apr;50(4):400-6. doi: 10.1016/j.pediatrneurol.2013.11.010. Epub 2013 Nov 21.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24508248>

- Prigogine C, Richard P, Van den Bergh P, Groswasser J, Deconinck N. Novel LMNA mutation presenting as severe congenital muscular dystrophy. *Pediatr Neurol.* 2010 Oct;43(4):283-6. doi: 10.1016/j.pediatrneurol.2010.05.016.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20837309>
 - Quijano-Roy S, Mbieleu B, Bönnemann CG, Jeannot PY, Colomer J, Clarke NF, Cuisset JM, Roper H, De Meirleir L, D'Amico A, Ben Yaou R, Nascimento A, Barois A, Demay L, Bertini E, Ferreira A, Sewry CA, Romero NB, Ryan M, Muntoni F, Guicheney P, Richard P, Bonne G, Estournet B. De novo LMNA mutations cause a new form of congenital muscular dystrophy. *Ann Neurol.* 2008 Aug; 64(2):177-86. doi: 10.1002/ana.21417.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18551513>
-

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/lmna-related-congenital-muscular-dystrophy>

Reviewed: May 2018

Published: August 17, 2020

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services