



## Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency is a rare condition that prevents the body from converting certain fats to energy, particularly during periods without food (fasting).

Signs and symptoms of LCHAD deficiency typically appear during infancy or early childhood and can include feeding difficulties, lack of energy (lethargy), low blood sugar (hypoglycemia), weak muscle tone (hypotonia), liver problems, and abnormalities in the light-sensitive tissue at the back of the eye (retina). Later in childhood, people with this condition may experience muscle pain, breakdown of muscle tissue, and a loss of sensation in their arms and legs (peripheral neuropathy). Individuals with LCHAD deficiency are also at risk for serious heart problems, breathing difficulties, coma, and sudden death.

Problems related to LCHAD deficiency can be triggered when the body is under stress, for example during periods of fasting, illnesses such as viral infections, or weather extremes. This disorder is sometimes mistaken for Reye syndrome, a severe disorder that may develop in children while they appear to be recovering from viral infections such as chicken pox or flu. Most cases of Reye syndrome are associated with the use of aspirin during these viral infections.

### Frequency

The incidence of LCHAD deficiency is unknown. One estimate, based on a Finnish population, indicates that 1 in 62,000 pregnancies is affected by this disorder. In the United States, the incidence is probably much lower.

### Genetic Changes

Mutations in the *HADHA* gene cause LCHAD deficiency. The *HADHA* gene provides instructions for making part of an enzyme complex called mitochondrial trifunctional protein. This enzyme complex functions in mitochondria, the energy-producing centers within cells. As the name suggests, mitochondrial trifunctional protein contains three enzymes that each perform a different function. This enzyme complex is required to break down (metabolize) a group of fats called long-chain fatty acids. Long-chain fatty acids are found in foods such as milk and certain oils. These fatty acids are stored in the body's fat tissues. Fatty acids are a major source of energy for the heart and muscles. During periods of fasting, fatty acids are also an important energy source for the liver and other tissues.

Mutations in the *HADHA* gene that cause LCHAD deficiency disrupt one of the functions of this enzyme complex. These mutations prevent the normal processing

of long-chain fatty acids from food and body fat. As a result, these fatty acids are not converted to energy, which can lead to some features of this disorder, such as lethargy and hypoglycemia. Long-chain fatty acids or partially metabolized fatty acids may also build up and damage the liver, heart, muscles, and retina. This abnormal buildup causes the other signs and symptoms of LCHAD deficiency.

### **Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

### **Other Names for This Condition**

- 3-hydroxyacyl-CoA dehydrogenase, long chain, deficiency
- LCHAD deficiency
- long-chain 3-hydroxy acyl CoA dehydrogenase deficiency
- long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency
- long-chain 3-OH acyl-CoA dehydrogenase deficiency
- trifunctional protein deficiency, type 1

### **Diagnosis & Management**

#### Formal Diagnostic Criteria

- ACT Sheet: Elevated C16-OH +/- C18:1-OH and Other Long Chain Acylcarnitines  
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C16-OH.pdf>

#### Formal Treatment/Management Guidelines

- New England Consortium of Metabolic Programs: Acute Illness Protocol  
[http://newenglandconsortium.org/protocols/acute\\_illness/fatty-acid-oxidation-disorders/LCHADD.pdf](http://newenglandconsortium.org/protocols/acute_illness/fatty-acid-oxidation-disorders/LCHADD.pdf)

#### Genetic Testing

- Genetic Testing Registry: Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/CN074230/>

### Other Diagnosis and Management Resources

- Baby's First Test  
<http://www.babysfirsttest.org/newborn-screening/conditions/long-chain-l-3-hydroxyacyl-coa-dehydrogenase-deficiency>
- MedlinePlus Encyclopedia: Hypoglycemia  
<https://medlineplus.gov/ency/article/000386.htm>
- MedlinePlus Encyclopedia: Peripheral Neuropathy  
<https://medlineplus.gov/ency/article/000593.htm>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

### **Additional Information & Resources**

#### MedlinePlus

- Encyclopedia: Hypoglycemia  
<https://medlineplus.gov/ency/article/000386.htm>
- Encyclopedia: Peripheral Neuropathy  
<https://medlineplus.gov/ency/article/000593.htm>
- Health Topic: Lipid Metabolism Disorders  
<https://medlineplus.gov/lipidmetabolismdisorders.html>
- Health Topic: Newborn Screening  
<https://medlineplus.gov/newbornscreening.html>

#### Genetic and Rare Diseases Information Center

- LCHAD deficiency  
<https://rarediseases.info.nih.gov/diseases/6867/lchad-deficiency>

## Educational Resources

- Disease InfoSearch: LCHAD deficiency  
<http://www.diseaseinfosearch.org/LCHAD+deficiency/4126>
- Illinois Department of Public Health  
<http://www.idph.state.il.us/HealthWellness/fs/mcad.htm>
- MalaCards: lchad deficiency  
[http://www.malacards.org/card/lchad\\_deficiency](http://www.malacards.org/card/lchad_deficiency)
- Merck Manual Professional Version  
<http://www.merckmanuals.com/professional/pediatrics/inherited-disorders-of-metabolism/beta-oxidation-cycle-disorders#v25254053>
- My46 Trait Profile  
<https://www.my46.org/trait-document?trait=Long%20chain%203-Hydroxyacyl-CoA%20dehydrogenase%20deficiency&type=profile>
- New England Consortium of Metabolic Programs  
<http://newenglandconsortium.org/for-families/other-metabolic-disorders/fatty-acid-oxidation-disorders/lchadd/>
- Orphanet: Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=5](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=5)
- Screening, Technology, and Research in Genetics  
<http://www.newbornscreening.info/Parents/fattyacid disorders/LCHADD.html>
- Virginia Department of Health  
[http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet\\_LCHAD\\_English.pdf](http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_LCHAD_English.pdf)

## Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB)  
<http://www.climb.org.uk>
- Children's Mitochondrial Disease Network (UK)  
<http://www.cmdn.org.uk/>
- FOD (Fatty Oxidation Disorders) Family Support Group  
<http://www.fodsupport.org/lchad.htm>
- United Mitochondrial Disease Foundation  
<http://www.umdf.org/>

## Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28long-chain+3-hydroxyacyl-CoA+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%28LCHAD%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

## OMIM

- LONG-CHAIN 3-HYDROXYACYL-CoA DEHYDROGENASE DEFICIENCY  
<http://omim.org/entry/609016>

## **Sources for This Summary**

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