



Primary carnitine deficiency

Primary carnitine deficiency is a condition that prevents the body from using certain fats for energy, particularly during periods without food (fasting). Carnitine, a natural substance acquired mostly through the diet, is used by cells to process fats and produce energy.

Signs and symptoms of primary carnitine deficiency typically appear during infancy or early childhood and can include severe brain dysfunction (encephalopathy), a weakened and enlarged heart (cardiomyopathy), confusion, vomiting, muscle weakness, and low blood sugar (hypoglycemia). The severity of this condition varies among affected individuals. Some people with primary carnitine deficiency are asymptomatic, which means they do not have any signs or symptoms of the condition. All individuals with this disorder are at risk for heart failure, liver problems, coma, and sudden death.

Problems related to primary carnitine deficiency can be triggered by periods of fasting or by illnesses such as viral infections. 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 primary carnitine deficiency in the general population is approximately 1 in 100,000 newborns. In Japan, this disorder affects 1 in every 40,000 newborns.

Genetic Changes

Mutations in the *SLC22A5* gene cause primary carnitine deficiency. This gene provides instructions for making a protein called OCTN2 that transports carnitine into cells. Cells need carnitine to bring certain types of fats (fatty acids) into mitochondria, which are the energy-producing centers within cells. 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 *SLC22A5* gene result in an absent or dysfunctional OCTN2 protein. As a result, there is a shortage (deficiency) of carnitine within cells. Without carnitine, fatty acids cannot enter mitochondria and be used to make energy. Reduced energy production can lead to some of the features of primary carnitine deficiency, such as muscle weakness and hypoglycemia. Fatty acids may also build up in cells and damage the liver, heart, and muscles. This abnormal buildup causes the other signs and symptoms of the disorder.

Inheritance Pattern

Primary carnitine deficiency is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive disorder are carriers, which means they each carry one copy of the mutated gene. Carriers of *SLC22A5* gene mutations may have some signs and symptoms related to the condition.

Other Names for This Condition

- carnitine transporter deficiency
- carnitine uptake defect
- carnitine uptake deficiency
- CUD
- renal carnitine transport defect
- systemic carnitine deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Decreased C0 and other acylcarnitines
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C0.pdf>

Genetic Testing

- Genetic Testing Registry: Renal carnitine transport defect
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0342788/>

Other Diagnosis and Management Resources

- Baby's First Test
<http://www.babysfirsttest.org/newborn-screening/conditions/carnitine-uptake-defect>
- GeneReview: Systemic Primary Carnitine Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK84551>
- The Linus Pauling Institute: L-Carnitine
<http://lpi.oregonstate.edu/mic/dietary-factors/L-carnitine>

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

- Health Topic: Cardiomyopathy
<https://medlineplus.gov/cardiomyopathy.html>
- 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

- Primary carnitine deficiency
<https://rarediseases.info.nih.gov/diseases/5104/primary-carnitine-deficiency>

Additional NIH Resources

- NIH Office of Dietary Supplements: Carnitine
<https://ods.od.nih.gov/factsheets/Carnitine-HealthProfessional/>

Educational Resources

- Disease InfoSearch: Renal carnitine transport defect
<http://www.diseaseinfosearch.org/Renal+carnitine+transport+defect/9212>
- Orphanet: Systemic primary carnitine deficiency
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=158
- Screening, Technology, and Research in Genetics
<http://www.newbornscreening.info/Parents/fattyacid disorders/Carnitine.html>
- The Linus Pauling Institute: L-Carnitine
<http://lpi.oregonstate.edu/mic/dietary-factors/L-carnitine>
- Virginia Department of Health
http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_CUD_English.pdf

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB)
<http://www.climb.org.uk/>
- FOD (Fatty Oxidation Disorders) Family Support Group
<http://www.fodsupport.org/>

- Muscular Dystrophy Association
<https://www.mda.org/disease/metabolic-myopathies/types/carnitine-deficiency>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/systemic-primary-carnitine-deficiency/>
- United Mitochondrial Disease Foundation
<http://www.umdf.org/>

GeneReviews

- Systemic Primary Carnitine Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK84551>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22primary+carnitine+deficiency%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28carnitine+uptake+defect%5BTIAB%5D%29+OR+%28carnitine+transporter+deficiency%5BTIAB%5D%29+OR+%28primary+carnitine+deficiency%5BTIAB%5D%29+OR+%28systemic+carnitine+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- CARNITINE DEFICIENCY, SYSTEMIC PRIMARY
<http://omim.org/entry/212140>

Sources for This Summary

- Amat di San Filippo C, Pasquali M, Longo N. Pharmacological rescue of carnitine transport in primary carnitine deficiency. *Hum Mutat.* 2006 Jun;27(6):513-23.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16652335>
- El-Hattab AW, Li FY, Shen J, Powell BR, Bawle EV, Adams DJ, Wahl E, Kobori JA, Graham B, Scaglia F, Wong LJ. Maternal systemic primary carnitine deficiency uncovered by newborn screening: clinical, biochemical, and molecular aspects. *Genet Med.* 2010 Jan;12(1):19-24. doi: 10.1097/GIM.0b013e3181c5e6f7.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20027113>
- Lahjouji K, Mitchell GA, Qureshi IA. Carnitine transport by organic cation transporters and systemic carnitine deficiency. *Mol Genet Metab.* 2001 Aug;73(4):287-97. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11509010>
- Lamhonwah AM, Olpin SE, Pollitt RJ, Vianey-Saban C, Divry P, Guffon N, Besley GT, Onizuka R, De Meirleir LJ, Cvitanovic-Sojat L, Baric I, Dionisi-Vici C, Fumic K, Maradin M, Tein I. Novel OCTN2 mutations: no genotype-phenotype correlations: early carnitine therapy prevents cardiomyopathy. *Am J Med Genet.* 2002 Aug 15;111(3):271-84.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12210323>

- Li FY, El-Hattab AW, Bawle EV, Boles RG, Schmitt ES, Scaglia F, Wong LJ. Molecular spectrum of SLC22A5 (OCTN2) gene mutations detected in 143 subjects evaluated for systemic carnitine deficiency. *Hum Mutat.* 2010 Aug;31(8):E1632-51. doi: 10.1002/humu.21311.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20574985>
- Longo N, Amat di San Filippo C, Pasquali M. Disorders of carnitine transport and the carnitine cycle. *Am J Med Genet C Semin Med Genet.* 2006 May 15;142C(2):77-85. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16602102>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2557099/>
- Magoulas PL, El-Hattab AW. Systemic primary carnitine deficiency: an overview of clinical manifestations, diagnosis, and management. *Orphanet J Rare Dis.* 2012 Sep 18;7:68. doi: 10.1186/1750-1172-7-68. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22989098>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3495906/>
- Schimmenti LA, Crombez EA, Schwahn BC, Heese BA, Wood TC, Schroer RJ, Bentler K, Cederbaum S, Sarafoglou K, McCann M, Rinaldo P, Matern D, di San Filippo CA, Pasquali M, Berry SA, Longo N. Expanded newborn screening identifies maternal primary carnitine deficiency. *Mol Genet Metab.* 2007 Apr;90(4):441-5. Epub 2006 Nov 28.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17126586>
- Shibbani K, Fahed AC, Al-Shaar L, Arabi M, Nemer G, Bitar F, Majdalani M. Primary carnitine deficiency: novel mutations and insights into the cardiac phenotype. *Clin Genet.* 2014 Feb;85(2):127-37. doi: 10.1111/cge.12112. Epub 2013 Mar 12.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23379544>
- Stanley CA. Carnitine deficiency disorders in children. *Ann N Y Acad Sci.* 2004 Nov;1033:42-51. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15591002>
- Tein I. Carnitine transport: pathophysiology and metabolism of known molecular defects. *J Inherit Metab Dis.* 2003;26(2-3):147-69. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12889657>
- Wang Y, Korman SH, Ye J, Gargus JJ, Gutman A, Taroni F, Garavaglia B, Longo N. Phenotype and genotype variation in primary carnitine deficiency. *Genet Med.* 2001 Nov-Dec;3(6):387-92.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11715001>

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/primary-carnitine-deficiency>

Reviewed: September 2014

Published: June 12, 2018

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