



Medium-chain acyl-CoA dehydrogenase deficiency

Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency is a condition that prevents the body from converting certain fats to energy, particularly during periods without food (fasting).

Signs and symptoms of MCAD deficiency typically appear during infancy or early childhood and can include vomiting, lack of energy (lethargy), and low blood sugar (hypoglycemia). In rare cases, symptoms of this disorder are not recognized early in life, and the condition is not diagnosed until adulthood. People with MCAD deficiency are at risk of serious complications such as seizures, breathing difficulties, liver problems, brain damage, coma, and sudden death.

Problems related to MCAD 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

In the United States, the estimated incidence of MCAD deficiency is 1 in 17,000 people. The condition is more common in people of northern European ancestry than in other ethnic groups.

Causes

Mutations in the *ACADM* gene cause MCAD deficiency. This gene provides instructions for making an enzyme called medium-chain acyl-CoA dehydrogenase, which is required to break down (metabolize) a group of fats called medium-chain fatty acids. These fatty acids are found in foods and 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 *ACADM* gene lead to a shortage (deficiency) of the MCAD enzyme within cells. Without sufficient amounts of this enzyme, medium-chain fatty acids are not metabolized properly. As a result, these fats are not converted to energy, which can lead to the characteristic signs and symptoms of this disorder such as lethargy and hypoglycemia. Medium-chain fatty acids or partially metabolized fatty acids may also build up in tissues and damage the liver and brain. This abnormal buildup causes the other signs and symptoms of MCAD 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

- ACADM deficiency
- MCAD deficiency
- MCADD
- MCADH deficiency
- medium chain acyl-CoA dehydrogenase deficiency
- medium-chain acyl-coenzyme A dehydrogenase deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C8 with Lesser Elevations of C6 and C10 Acylcarnitine
https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C8_C6_C10.pdf

Formal Treatment/Management Guidelines

- British Inherited Metabolic Disease Group: MCADD Dietary Management Guidelines
<http://www.bimdg.org.uk/store/guidelines/MCADD-dietitianguidelines-11-618345-17-05-2008.pdf>
- New England Consortium of Metabolic Programs: Acute Illness Protocol
https://newenglandconsortium.org/protocols/acute_illness/fatty-acid-oxidation-disorders/MCADD.pdf

Genetic Testing Information

- What is genetic testing?
</primer/testing/genetictesting>
- Genetic Testing Registry: Medium-chain acyl-coenzyme A dehydrogenase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0220710/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22medium-chain+acyl-coenzyme+a+dehydrogenase+deficiency%22>

Other Diagnosis and Management Resources

- Baby's First Test
<https://www.babysfirsttest.org/newborn-screening/conditions/medium-chain-acyl-coa-dehydrogenase-deficiency>
- GeneReview: Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK1424>
- MedlinePlus Encyclopedia: Newborn Screening Tests
<https://medlineplus.gov/ency/article/007257.htm>

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Newborn Screening Tests
<https://medlineplus.gov/ency/article/007257.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

- Medium-chain acyl-coenzyme A dehydrogenase deficiency
<https://rarediseases.info.nih.gov/diseases/540/medium-chain-acyl-coenzyme-a-dehydrogenase-deficiency>

Educational Resources

- Illinois Department of Public Health
<http://www.idph.state.il.us/HealthWellness/fs/mcad.htm>
- MalaCards: medium-chain acyl-coenzyme a dehydrogenase deficiency
https://www.malacards.org/card/medium_chain_acyl_coenzyme_a_dehydrogenase_deficiency
- Medical Home Portal
<https://www.medicalhomeportal.org/newborn/mcadd>
- Merck Manual Consumer Version: Overview of Cholesterol and Lipid Disorders
<https://www.merckmanuals.com/home/hormonal-and-metabolic-disorders/cholesterol-disorders/overview-of-cholesterol-and-lipid-disorders>
- Michigan Department of Community Health
https://www.michigan.gov/documents/mcad_79205_7.pdf
- Orphanet: Medium chain acyl-CoA dehydrogenase deficiency
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=42

- Screening, Technology, and Research in Genetics
<http://www.newbornscreening.info/Parents/fattyaciddisorders/MCADD.html>
- Virginia Department of Health
http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_MCAD_English.pdf
- Washington State Department of Health
<https://www.doh.wa.gov/Portals/1/Documents/5220/mcad-def-go.pdf>

Patient Support and Advocacy Resources

- FOD (Fatty Oxidation Disorders) Family Support Group
<https://www.fodsupport.org/>
- Metabolic Support UK
<https://www.metabolicsupportuk.org/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/medium-chain-acyl-coa-dehydrogenase-deficiency/>
- United Mitochondrial Disease Foundation
<https://www.umdf.org/>

Clinical Information from GeneReviews

- Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK1424>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28medium-chain+acyl-coenzyme+a+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%28MCAD+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- ACYL-CoA DEHYDROGENASE, MEDIUM-CHAIN, DEFICIENCY OF
<http://omim.org/entry/201450>

Sources for This Summary

- Derks TG, Reijngoud DJ, Waterham HR, Gerver WJ, van den Berg MP, Sauer PJ, Smit GP. The natural history of medium-chain acyl CoA dehydrogenase deficiency in the Netherlands: clinical presentation and outcome. *J Pediatr.* 2006 May;148(5):665-670.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16737882>
- Dezateux C. Newborn screening for medium chain acyl-CoA dehydrogenase deficiency: evaluating the effects on outcome. *Eur J Pediatr.* 2003 Dec;162 Suppl 1:S25-8. Epub 2003 Nov 20. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14628139>

- Grosse SD, Khoury MJ, Greene CL, Crider KS, Pollitt RJ. The epidemiology of medium chain acyl-CoA dehydrogenase deficiency: an update. *Genet Med*. 2006 Apr;8(4):205-12. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16617240>
- Hsu HW, Zytovicz TH, Comeau AM, Strauss AW, Marsden D, Shih VE, Grady GF, Eaton RB. Spectrum of medium-chain acyl-CoA dehydrogenase deficiency detected by newborn screening. *Pediatrics*. 2008 May;121(5):e1108-14. doi: 10.1542/peds.2007-1993.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18450854>
- Joy P, Black C, Rocca A, Haas M, Wilcken B. Neuropsychological functioning in children with medium chain acyl coenzyme a dehydrogenase deficiency (MCADD): the impact of early diagnosis and screening on outcome. *Child Neuropsychol*. 2009 Jan;15(1):8-20. doi: 10.1080/09297040701864570.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18608229>
- Lang TF. Adult presentations of medium-chain acyl-CoA dehydrogenase deficiency (MCADD). *J Inherit Metab Dis*. 2009 Dec;32(6):675-83. doi: 10.1007/s10545-009-1202-0. Epub 2009 Oct 11. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19821147>
- Matern D, Rinaldo P. Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency. 2000 Apr 20 [updated 2015 Mar 5]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1424/>
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20301597>
- Touw CM, Smit GP, de Vries M, de Klerk JB, Bosch AM, Visser G, Mulder MF, Rubio-Gozalbo ME, Elvers B, Niezen-Koning KE, Wanders RJ, Waterham HR, Reijngoud DJ, Derks TG. Risk stratification by residual enzyme activity after newborn screening for medium-chain acyl-CoA dehydrogenase deficiency: data from a cohort study. *Orphanet J Rare Dis*. 2012 May 25;7:30. doi: 10.1186/1750-1172-7-30.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22630369>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3543239/>

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