



## Glutaric acidemia type II

Glutaric acidemia type II is an inherited disorder that interferes with the body's ability to break down proteins and fats to produce energy. Incompletely processed proteins and fats can build up in the body and cause the blood and tissues to become too acidic (metabolic acidosis).

Glutaric acidemia type II usually appears in infancy or early childhood as a sudden episode called a metabolic crisis, in which acidosis and low blood sugar (hypoglycemia) cause weakness, behavior changes such as poor feeding and decreased activity, and vomiting. These metabolic crises, which can be life-threatening, may be triggered by common childhood illnesses or other stresses.

In the most severe cases of glutaric acidemia type II, affected individuals may also be born with physical abnormalities. These may include brain malformations, an enlarged liver (hepatomegaly), a weakened and enlarged heart (dilated cardiomyopathy), fluid-filled cysts and other malformations of the kidneys, unusual facial features, and genital abnormalities. Glutaric acidemia type II may also cause a characteristic odor resembling that of sweaty feet.

Some affected individuals have less severe symptoms that begin later in childhood or in adulthood. In the mildest forms of glutaric acidemia type II, muscle weakness developing in adulthood may be the first sign of the disorder.

### Frequency

Glutaric acidemia type II is a very rare disorder; its precise incidence is unknown. It has been reported in several different ethnic groups.

### Causes

Mutations in any of three genes, *ETFA*, *ETFB*, and *ETFDH*, can result in glutaric acidemia type II. The *ETFA* and *ETFB* genes provide instructions for producing two protein segments, or subunits, that come together to make an enzyme called electron transfer flavoprotein. The *ETFDH* gene provides instructions for making another enzyme called electron transfer flavoprotein dehydrogenase.

Glutaric acidemia type II is caused by a deficiency in either of these two enzymes. Electron transfer flavoprotein and electron transfer flavoprotein dehydrogenase are normally active in the mitochondria, which are the energy-producing centers of cells. These enzymes help break down proteins and fats to provide energy for the body. When one of the enzymes is defective or missing, partially broken down nutrients accumulate in the cells and damage them, causing the signs and symptoms of glutaric acidemia type II.

People with mutations that result in a complete loss of either enzyme produced from the *ETFA*, *ETFB* or *ETFDH* genes are likely to experience the most severe symptoms of glutaric acidemia type II. Mutations that allow the enzyme to retain some activity may result in milder forms of the disorder.

## **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**

- electron transfer flavoprotein deficiency
- EMA
- ETFA deficiency
- ETFB deficiency
- ETFDH deficiency
- ethylmalonic-adipicaciduria
- GA II
- glutaric acidemia, type 2
- glutaric aciduria, type 2
- MAD
- MADD
- multiple acyl-CoA dehydrogenase deficiency
- multiple FAD dehydrogenase deficiency

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/genetictesting](#)
- Genetic Testing Registry: Glutaric aciduria, type 2  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268596/>

### Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22glutaric+acidemia+type+2%22>

## Other Diagnosis and Management Resources

- Baby's First Test  
<https://www.babysfirsttest.org/newborn-screening/conditions/glutaric-acidemia-type-ii>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Health Topic: Mitochondrial Diseases  
<https://medlineplus.gov/mitochondrialdiseases.html>
- Health Topic: Newborn Screening  
<https://medlineplus.gov/newbornscreening.html>

### Genetic and Rare Diseases Information Center

- Glutaric acidemia type II  
<https://rarediseases.info.nih.gov/diseases/6523/glutaric-acidemia-type-ii>

### Educational Resources

- Orphanet: Multiple acyl-CoA dehydrogenase deficiency  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=26791](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=26791)
- Screening, Technology and Research in Genetics  
<http://www.newbornscreening.info/Parents/fattyacid disorders/GA2.html>

### Patient Support and Advocacy Resources

- FOD (Fatty Oxidation Disorders) Family Support Group  
<http://www.fodsupport.org/>
- Metabolic Support UK  
<https://www.metabolicsupportuk.org/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/glutaricaciduria-ii/>
- Organic Acidemia Association  
<https://www.oaanews.org/>
- United Mitochondrial Disease Foundation  
<https://www.umdf.org/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28glutaric+acidemia+type+2%5BALL%5D%29+OR+%28glutaric+acidemia+type+II%5BALL%5D%29%29+AND+%28Metabolic+Diseases%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

## Catalog of Genes and Diseases from OMIM

- MULTIPLE ACYL-CoA DEHYDROGENASE DEFICIENCY  
<http://omim.org/entry/231680>

### **Sources for This Summary**

- Angle B, Burton BK. Risk of sudden death and acute life-threatening events in patients with glutaric acidemia type II. *Mol Genet Metab.* 2008 Jan;93(1):36-9. Epub 2007 Oct 31.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17977044>
- Cornelius N, Frerman FE, Corydon TJ, Palmfeldt J, Bross P, Gregersen N, Olsen RK. Molecular mechanisms of riboflavin responsiveness in patients with ETF-QO variations and multiple acyl-CoA dehydrogenation deficiency. *Hum Mol Genet.* 2012 Aug 1;21(15):3435-48. doi: 10.1093/hmg/dds175. Epub 2012 May 18.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/22611163>
- Curcoy A, Olsen RK, Ribes A, Trenchs V, Vilaseca MA, Campistol J, Osorio JH, Andresen BS, Gregersen N. Late-onset form of beta-electron transfer flavoprotein deficiency. *Mol Genet Metab.* 2003 Apr;78(4):247-9.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12706375>
- Goodman SI, Binard RJ, Woontner MR, Frerman FE. Glutaric acidemia type II: gene structure and mutations of the electron transfer flavoprotein:ubiquinone oxidoreductase (ETF:QO) gene. *Mol Genet Metab.* 2002 Sep-Oct;77(1-2):86-90.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12359134>
- OMIM: MULTIPLE ACYL-CoA DEHYDROGENASE DEFICIENCY  
<http://omim.org/entry/231680>
- Olsen RK, Andresen BS, Christensen E, Bross P, Skovby F, Gregersen N. Clear relationship between ETF/ETFDH genotype and phenotype in patients with multiple acyl-CoA dehydrogenation deficiency. *Hum Mutat.* 2003 Jul;22(1):12-23.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12815589>
- Olsen RK, Olpin SE, Andresen BS, Miedzybrodzka ZH, Pourfarzam M, Merinero B, Frerman FE, Beresford MW, Dean JC, Cornelius N, Andersen O, Oldfors A, Holme E, Gregersen N, Turnbull DM, Morris AA. ETFDH mutations as a major cause of riboflavin-responsive multiple acyl-CoA dehydrogenation deficiency. *Brain.* 2007 Aug;130(Pt 8):2045-54. Epub 2007 Jun 20.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17584774>
- Olsen RK, Pourfarzam M, Morris AA, Dias RC, Knudsen I, Andresen BS, Gregersen N, Olpin SE. Lipid-storage myopathy and respiratory insufficiency due to ETFQO mutations in a patient with late-onset multiple acyl-CoA dehydrogenation deficiency. *J Inher Metab Dis.* 2004;27(5):671-8.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/15669683>
- Purejav E, Kimura M, Takusa Y, Ohura T, Tsuchiya M, Hara N, Fukao T, Yamaguchi S. Molecular study of electron transfer flavoprotein alpha-subunit deficiency in two Japanese children with different phenotypes of glutaric acidemia type II. *Eur J Clin Invest.* 2002 Sep;32(9):707-12.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12486872>

- Schiff M, Froissart R, Olsen RK, Acquaviva C, Vianey-Saban C. Electron transfer flavoprotein deficiency: functional and molecular aspects. *Mol Genet Metab*. 2006 Jun;88(2):153-8. Epub 2006 Feb 28.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16510302>
  - Takken T, Custers J, Visser G, Dorland L, Helders P, de Koning T. Prolonged exercise testing in two children with a mild Multiple Acyl-CoA-Dehydrogenase deficiency. *Nutr Metab (Lond)*. 2005 May 20;2(1):12.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/15907213>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1159171/>
- 

Reprinted from Genetics Home Reference:  
<https://ghr.nlm.nih.gov/condition/glutaric-acidemia-type-ii>

Reviewed: February 2014

Published: October 16, 2018

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