



Glutaric acidemia type I

Glutaric acidemia type I is an inherited disorder in which the body is unable to process certain proteins properly. People with this disorder have inadequate levels of an enzyme that helps break down the amino acids lysine, hydroxylysine, and tryptophan, which are building blocks of protein. Excessive levels of these amino acids and their intermediate breakdown products can accumulate and cause damage to the brain, particularly the basal ganglia, which are regions that help control movement. Intellectual disability may also occur.

The severity of glutaric acidemia type I varies widely; some individuals are only mildly affected, while others have severe problems. In most cases, signs and symptoms first occur in infancy or early childhood, but in a small number of affected individuals, the disorder first becomes apparent in adolescence or adulthood.

Some babies with glutaric acidemia type I are born with unusually large heads (macrocephaly). Affected individuals may have difficulty moving and may experience spasms, jerking, rigidity, or decreased muscle tone. Some individuals with glutaric acidemia have developed bleeding in the brain or eyes that could be mistaken for the effects of child abuse. Strict dietary control may help limit progression of the neurological damage. Stress caused by infection, fever or other demands on the body may lead to worsening of the signs and symptoms, with only partial recovery.

Frequency

Glutaric acidemia type I occurs in approximately 1 of every 30,000 to 40,000 individuals. It is much more common in the Amish community and in the Ojibwa population of Canada, where up to 1 in 300 newborns may be affected.

Causes

Mutations in the *GCDH* gene cause glutaric acidemia type I.

The *GCDH* gene provides instructions for making the enzyme glutaryl-CoA dehydrogenase. This enzyme is involved in processing the amino acids lysine, hydroxylysine, and tryptophan.

Mutations in the *GCDH* gene prevent production of the enzyme or result in the production of a defective enzyme that cannot function. This enzyme deficiency allows lysine, hydroxylysine and tryptophan and their intermediate breakdown products to build up to abnormal levels, especially at times when the body is under stress.

The intermediate breakdown products resulting from incomplete processing of lysine, hydroxylysine, and tryptophan can damage the brain, particularly the basal ganglia, causing the signs and symptoms of glutaric acidemia type I.

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

- GA I
- Glutaric acidemia I
- Glutaric acidemia type 1
- Glutaric aciduria I
- Glutaryl-CoA dehydrogenase deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C5-DC Acylcarnitine
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C5-DC.pdf>

Formal Treatment/Management Guidelines

- British Inherited Metabolic Diseases Group: GA1 Clinical Management Guidelines
http://www.bimdg.org.uk/store/enbs//Final_GA1_clinical_management_guidelines_v11_Jan_2017_394224_25042017.pdf
- British Inherited Metabolic Diseases Group: GA1 Dietetic Management Guidelines
http://www.bimdg.org.uk/store/enbs//GA1_Dietetic_management_pathway_April_2015_117794_12052015.pdf

Genetic Testing Information

- What is genetic testing?
</primer/testing/genetic-testing>
- Genetic Testing Registry: Glutaric aciduria, type 1
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268595/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22glutaric+acidemia+type+1%22>

Other Diagnosis and Management Resources

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

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Amino Acid Metabolism Disorders
<https://medlineplus.gov/aminoacidmetabolismdisorders.html>
- Health Topic: Genetic Brain Disorders
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Newborn Screening
<https://medlineplus.gov/newbornscreening.html>

Genetic and Rare Diseases Information Center

- Glutaric acidemia type I
<https://rarediseases.info.nih.gov/diseases/6522/glutaric-acidemia-type-i>

Educational Resources

- Orphanet: Glutaryl-CoA dehydrogenase deficiency
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=25
- Screening, Technology and Research in Genetics
<http://www.newbornscreening.info/Parents/organicaciddisorders/GA1.html>
- Virginia Department of Health
http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_GA-I_English.pdf

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB)
<https://www.metabolicsupportuk.org/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/glutaricaciduria-i/>
- Organic Acidemia Association
<https://www.oaanews.org/ga-i.html>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28glutaric+acidemia+type+1%5BTIAB%5D%29+OR+%28glutaric+acidemia+i%5BTIAB%5D%29+OR+%28glutaric+aciduria+i%5BTIAB%5D%29+OR+%28glutaryl-coa+dehydrogenase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- GLUTARIC ACIDEMIA I
<http://omim.org/entry/231670>

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Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/glutaric-acidemia-type-i>

Reviewed: March 2007

Published: June 25, 2019

Lister Hill National Center for Biomedical Communications
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National Institutes of Health
Department of Health & Human Services