Ornithine translocase deficiency

Ornithine translocase deficiency is an inherited disorder that causes ammonia to accumulate in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

Ornithine translocase deficiency varies widely in its severity and age of onset. An infant with ornithine translocase deficiency may be lacking in energy (lethargic) or refuse to eat, or have poorly controlled breathing or body temperature. Some babies with this disorder may experience seizures or unusual body movements, or go into a coma. Episodes of illness may coincide with the introduction of high-protein formulas or solid foods into the diet.

In most affected individuals, signs and symptoms of ornithine translocase deficiency do not appear until later in life. Later-onset forms of ornithine translocase deficiency are usually less severe than the infantile form. Some people with later-onset ornithine translocase deficiency cannot tolerate high-protein foods, such as meat. Occasionally, high-protein meals or stress caused by illness or periods without food (fasting) may cause ammonia to accumulate more quickly in the blood. This rapid increase of ammonia may lead to episodes of vomiting, lack of energy (lethargy), problems with coordination (ataxia), confusion, or blurred vision. Complications of ornithine translocase deficiency may include developmental delay, learning disabilities, and stiffness caused by abnormal tensing of the muscles (spasticity).

Frequency

Ornithine translocase deficiency is a very rare disorder. Fewer than 100 affected individuals have been reported worldwide.

Causes

Mutations in the \( SLC25A15 \) gene cause ornithine translocase deficiency. Ornithine translocase deficiency belongs to a class of genetic diseases called urea cycle disorders. The urea cycle is a sequence of reactions that occurs in liver cells. This cycle processes excess nitrogen, generated when protein is used by the body, to make a compound called urea that is excreted by the kidneys.

The \( SLC25A15 \) gene provides instructions for making a protein called a mitochondrial ornithine transporter. This protein is needed to move a molecule called ornithine within the mitochondria (the energy-producing centers in cells). Specifically, this protein transports ornithine across the inner membrane of mitochondria to the region called the mitochondrial matrix, where it participates in the urea cycle.
Mutations in the *SLC25A15* gene result in a mitochondrial ornithine transporter that is unstable or the wrong shape, and which cannot bring ornithine to the mitochondrial matrix. This failure of ornithine transport causes an interruption of the urea cycle and the accumulation of ammonia, resulting in the signs and symptoms of ornithine translocase 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**

- HHH syndrome
- hyperornithinemia-hyperammonemia-homocitrullinemia syndrome
- hyperornithinemia-hyperammonemia-homocitrullinuria syndrome
- Triple H syndrome

**Diagnosis & Management**

**Genetic Testing Information**

- What is genetic testing? /primer/testing/genetictesting
- Genetic Testing Registry: Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome

**Research Studies from ClinicalTrials.gov**

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22ornithine+translocase+deficiency %22+OR+%22Amino+Acid+Metabolism%2C+Inborn+Errors%22

**Other Diagnosis and Management Resources**

- Baby’s First Test
  https://www.babysfirsttest.org/newborn-screening/conditions/hyperornithinemia-hyperammonemia-homocitrullinuria-syndrome
- GeneReview: Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK97260
- GeneReview: Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217
• MedlinePlus Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm

• National Organization for Rare Disorders (NORD) Physician Guide: Urea Cycle Disorders
  https://rarediseases.org/physician-guide/urea-cycle-disorders/

Additional Information & Resources

Health Information from MedlinePlus
• Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm

• Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html

• Health Topic: Mitochondrial Diseases
  https://medlineplus.gov/mitochondrialdiseases.html

• Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center
• Ornithine translocase deficiency syndrome

Educational Resources
• Orphanet: Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=415

Patient Support and Advocacy Resources
• Metabolic Support UK
  https://www.metabolicsupportuk.org/

• National Urea Cycle Disorders Foundation
  http://www.nucdf.org/

• Urea Cycle Disorders Consortium
  https://www.rarediseasesnetwork.org/cms/ucdc/Learn-More/Disorder-Definitions

Clinical Information from GeneReviews
• Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK97260

• Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217
**Scientific Articles on PubMed**

- PubMed
  
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ornithine+translocase+deficiency%29+OR+%28HHH+syndrome%29+OR+%28hyperornithinemia-hyperammonemia-homocitrullinemia+syndrome%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

**Catalog of Genes and Diseases from OMIM**

- HYPERORNITHINEMIA-HYPERAMMONEMIA-HOMOCITRULLINURIA SYNDROME
  
  http://omim.org/entry/238970

**Medical Genetics Database from MedGen**

- Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome
  

**Sources for This Summary**

  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16940241

  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10369256

  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12948741

- OMIM: HYPERORNITHINEMIA-HYPERAMMONEMIA-HOMOCITRULLINURIA SYNDROME
  
  http://omim.org/entry/238970

  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14759633

  
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11814739
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11355015

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11668643

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11552031

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16376511

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10805333

Reprinted from Genetics Home Reference: 

Reviewed: November 2006 
Published: November 27, 2018

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