N-acetylglutamate synthase deficiency

N-acetylglutamate synthase deficiency is a disorder that causes abnormally high levels of 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 brain is especially sensitive to the effects of excess ammonia.

The signs and symptoms of N-acetylglutamate synthase deficiency often become evident in the first few days of life. An infant with this condition may be lacking in energy (lethargic) or unwilling to eat, and have difficulty controlling his or her breathing rate or body temperature. Severely affected babies may experience seizures or unusual body movements, or go into a coma. Complications of N-acetylglutamate synthase deficiency may include developmental delay and intellectual disability.

In some affected individuals, signs and symptoms of N-acetylglutamate synthase deficiency do not appear until later in life. Some people with this form of the disorder notice that eating high-protein foods, such as meat, affects how they feel, although they may not know why. In many affected adults, illness or other stress can trigger episodes of vomiting, lack of coordination, headaches, confusion, behavioral changes, or coma.

Frequency

N-acetylglutamate synthase deficiency is a very rare disorder. It is estimated to affect fewer than 1 in 2 million people worldwide.

Causes

Mutations in the NAGS gene cause N-acetylglutamate synthase deficiency. This condition belongs to a class of genetic diseases called urea cycle disorders because they are caused by problems with a process in the body called the urea cycle. The urea cycle is a sequence of reactions that occurs in liver cells. This cycle breaks down excess nitrogen, which is made when protein is used by the body, to make a compound called urea. Urea is removed from the body in urine.

The NAGS gene provides instructions for making the enzyme N-acetylglutamate synthase, which is integral to the first step of the urea cycle.

In people with N-acetylglutamate synthase deficiency, N-acetylglutamate synthase is not available in sufficient quantities, or is not present at all. As a result, the urea cycle is impaired, and nitrogen is not broken down efficiently. The excess nitrogen accumulates in the blood in the form of ammonia. This buildup of ammonia damages tissues in the brain and causes neurological problems and other signs and symptoms of N-acetylglutamate synthase 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

• hyperammonemia, type III
• N-acetylglutamate synthetase deficiency
• NAGS deficiency

Diagnosis & Management

Genetic Testing Information

• What is genetic testing?
  https://primer/testing/genetictesting

• Genetic Testing Registry: Hyperammonemia, type III

Research Studies from ClinicalTrials.gov

• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22N-acetylglutamate+synthase+deficiency%22+OR+%22Urea+Cycle+Disorders%2C+Inborn%22

Other Diagnosis and Management Resources

• 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

• MedlinePlus Medical Tests: Ammonia Levels
  https://medlineplus.gov/lab-tests/ammonia-levels/

• 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: Metabolic Disorders
  https://medlineplus.gov/metabolicdisorders.html
- Medical Tests: Ammonia Levels
  https://medlineplus.gov/lab-tests/ammonia-levels/

Genetic and Rare Diseases Information Center

- N-acetylglutamate synthase deficiency
  https://rarediseases.info.nih.gov/diseases/7158/n-acetylglutamate-synthase-deficiency

Educational Resources

- MalaCards: n-acetylglutamate synthase deficiency
  https://www.malacards.org/card/n_acetylglutamate_synthase_deficiency
- Orphanet: Hyperammonemia due to N-acetylglutamate synthase deficiency
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=927
- Screening, Technology and Research in Genetics
  https://www.newbornscreening.info/

Patient Support and Advocacy Resources

- Metabolic Support UK
  https://www.metabolicsupportuk.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/n-acetylglutamate-synthetase-deficiency/
- 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

- 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%28n-acetylglutamate+synthase+deficiency%5BTIAB%5D%29+OR+%28n-acetylglutamate+synthetase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- N-ACETYLGLUTAMATE SYNTHASE DEFICIENCY
  http://omim.org/entry/237310

Sources for This Summary


- OMIM: N-ACETYLGLUTAMATE SYNTHASE DEFICIENCY
  http://omim.org/entry/237310
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27037498

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15878741

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