

N-acetylglutamate synthase deficiency

Description

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.

[Learn more about the gene associated with N-acetylglutamate synthase deficiency](#)

- NAGS

Inheritance

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

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hyperammonemia, type III (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268543/>)

Genetic and Rare Diseases Information Center

- Hyperammonemia due to N-acetylglutamate synthase deficiency (<https://rarediseases.info.nih.gov/diseases/7158/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22N-acetylglutamate synthase deficiency%22](https://clinicaltrials.gov/search?cond=%22N-acetylglutamate%20synthase%20deficiency%22))

Catalog of Genes and Diseases from OMIM

- N-ACETYLGLUTAMATE SYNTHASE DEFICIENCY; NAGSD (<https://omim.org/entry/237310>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?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>)

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