Arginase deficiency

Arginase deficiency is an inherited disorder that causes the amino acid arginine (a building block of proteins) and ammonia to accumulate gradually in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

Arginase deficiency usually becomes evident by about the age of 3. It most often appears as stiffness, especially in the legs, caused by abnormal tensing of the muscles (spasticity). Other symptoms may include slower than normal growth, developmental delay and eventual loss of developmental milestones, intellectual disability, seizures, tremor, and difficulty with balance and coordination (ataxia). 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 in ammonia may lead to episodes of irritability, refusal to eat, and vomiting.

In some affected individuals, signs and symptoms of arginase deficiency may be less severe, and may not appear until later in life.

Frequency

Arginase deficiency is a very rare disorder; it has been estimated to occur once in every 300,000 to 1,000,000 individuals.

Causes

Mutations in the ARG1 gene cause arginase deficiency.

Arginase 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 ARG1 gene provides instructions for making an enzyme called arginase. This enzyme controls the final step of the urea cycle, which produces urea by removing nitrogen from arginine. In people with arginase deficiency, arginase is damaged or missing, and arginine is not broken down properly. As a result, urea cannot be produced normally, and excess nitrogen accumulates in the blood in the form of ammonia. The accumulation of ammonia and arginine are believed to cause the neurological problems and other signs and symptoms of arginase 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

• ARG1 deficiency
• Arginase Deficiency Disease
• Argininemia
• Hyperargininemia

Diagnosis & Management

Formal Diagnostic Criteria

• ACT Sheet: Increased Arginine
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Arginine.pdf

Genetic Testing Information

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

• Genetic Testing Registry: Arginase deficiency

Research Studies from ClinicalTrials.gov

• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22arginase+deficiency%22+OR+%22Hyperargininemia%22

Other Diagnosis and Management Resources

• Baby's First Test
  https://www.babysfirsttest.org/newborn-screening/conditions/argininemia

• GeneReview: Arginase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1159

• 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: Amino Acid Metabolism Disorders
  https://medlineplus.gov/aminacidmetabolismdisorders.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**

• Arginase deficiency
  https://rarediseases.info.nih.gov/diseases/5840/arginase-deficiency

**Educational Resources**

• Cincinnati Children’s Hospital
  https://www.cincinnatichildrens.org/health/u/ucd

• Connecticut Department of Public Health

• MalaCards: argininemia
  https://www.malacards.org/card/argininemia

• Orphanet: Argininemia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=90

• Screening, Technology and Research in Genetics
  http://www.newbornscreening.info/Parents/aminaciddisorders/argininemia.html

**Patient Support and Advocacy Resources**

• Metabolic Support UK
  https://www.metabolicsupportuk.org/

• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/arginase-deficiency/
Clinical Information from GeneReviews

- Arginase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1159
- 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=%28arginase+deficiency%5BTIAB %5D%29+AND+english%5BLa%5D+AND+human%5Bmh%5D+AND+%22last +3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ARGININEMIA
  http://omim.org/entry/207800

Sources for This Summary

- OMIM: ARGININEMIA
  http://omim.org/entry/207800
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301396
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15694174
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15173438
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15465784

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301338

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