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CARRIER SCREEN

Argininosuccinic aciduria

What is argininosuccinic aciduria?

Argininosuccinic aciduria is an inherited disease characterized by vomiting, liver disease, and intellectual disabilities. It involves defects in an enzyme called argininosuccinate lyase (ASL).[1] This enzyme is important for breaking down nitrogen (found in proteins) so that it does not build up as ammonia. The symptoms of argininosuccinic aciduria are due to the toxic accumulation of ammonia, particularly in the liver and nervous system. Argininosuccinic aciduria is also known as argininosuccinate lyase (ASL) deficiency.[2]

What are the symptoms of argininosuccinic aciduria and what treatment is available?

Argininosuccinic aciduria is a disease that varies in severity and age at onset. There are two forms: neonatal-onset argininosuccinic aciduria and late-onset argininosuccinic aciduria. Symptoms of the neonatal-onset form are seen in the newborn period shortly after the introduction of protein into the diet, and symptoms of the late-onset form may be seen during the first few months of life or during childhood.[1,3]

Initial symptoms may include:[1]

- Hyperammonemia (excess ammonia in the blood)
- Poor feeding and vomiting
- Lethargy (lack of energy)
- Hypothermia (low body temperature)
- Tachypnea (rapid breathing)
- If untreated, symptoms can lead to seizures, coma, and possible death

Long term symptoms may include:[1,3]

- Poor growth
- Hepatomegaly (enlarged liver)
- Coarse and brittle hair
- Learning disabilities
- Behavioral problems
- Hypertension

There is no cure for argininosuccinic aciduria. The primary treatment is a life-long, low protein diet and nutritional supplementation. Even with treatment, however, high ammonia levels may still occur periodically. Learning disabilities, behavior problems, liver disease, coarse hair, and high blood pressure may persist despite treatment. Additional treatment includes supportive care for symptoms, avoidance of fasting, and in some cases liver transplantation.[1]

Argininosuccinic aciduria is included on all newborn screening panels in the United States.[4]

How is argininosuccinic aciduria inherited?

Argininosuccinic aciduria is an autosomal recessive disease caused by mutations in the *ASL* gene.[2] An individual who inherits one copy of an *ASL* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *ASL* mutations, one from each parent, is expected to be affected with argininosuccinic aciduria.

If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

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Who is at risk for argininosuccinic aciduria?

Argininosuccinic aciduria can occur in individuals of all races and ethnicities. It is estimated to affect 1 in 70,000 live births with a calculated carrier frequency of 1 in 132.[2] In the Finnish population, the carrier frequency is 1 in 190.[5]

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

National Organization for Rare Diseases:
https://rarediseases.org/rare-diseases/argininosuccinic-aciduria/

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

References

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