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CARRIER SCREEN

Citrullinemia type I

What is citrullinemia type I?

Citrullinemia type I is an inherited disease characterized by poor growth, vomiting, spasticity, increased intracranial pressure, and neurological problems.[1] It involves defects in an enzyme called argininosuccinate synthase. This enzyme is important for breaking down nitrogen (found in proteins) so that it does not build up as ammonia. The symptoms of citrullinemia are due to the toxic accumulation of ammonia and other substances, particularly in the liver and nervous system.[2] Citrullinemia type I is also known as argininosuccinate synthetase deficiency or citrullinuria.[1,2]

What are the symptoms of citrullinemia type I and what treatment is available?

Citrullinemia type I is a disease that varies in severity and age of onset, even within families.[3] There are two forms: classic (the more common form) and late-onset. Individuals with the classic form of citrullinemia show symptoms in the newborn period, shortly after the introduction of protein into the diet. Initial symptoms of the classic form may include:[2]

- Hyperammonemia (high levels of ammonia in the blood)
- Progressive lethargy (lack of energy)
- Poor feeding
- Vomiting
- Increased intracranial pressure (swelling in the brain)
- Seizures
- Loss of consciousness

The late-onset form may be similar to or milder than the classic form, but symptoms begin later in life. Some individuals may remain asymptomatic into adulthood. There are reports of women being diagnosed during or after pregnancy after the onset of liver complications.[1]

There is no cure for citrullinemia type I. The primary treatment is a life-long, low-protein diet, and nutritional supplementation.[1] Even with treatment, however, high ammonia levels may still occur periodically. Learning disabilities, intellectual disability, liver disease, and spasticity (abnormally tight muscles) may persist despite treatment.[3] For individuals with liver failure, liver transplantation may be needed.[1]

Citrullinemia type I is included on many newborn screening panels in the United States.[4]

How is citrullinemia type I inherited?

Citrullinemia type I is an autosomal recessive disease caused by mutations in the *ASS1* gene.[2] An individual who inherits one *ASS1* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *ASS1* gene mutations, one from each parent, is expected to be affected with citrullinemia type I.

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

Who is at risk for citrullinemia type I?

Citrullinemia type I can occur in individuals of all races and ethnicities. The incidence is approximately 1 in 57,000 births,[1] with a calculated carrier frequency of 1 in 119.

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?

NIH: Office of Rare Diseases Research - Genetic and Rare Diseases Information Center: http://rarediseases.info.nih.gov/GARD/QnASelected.aspx?diseaseID=6114

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

Screening, Technology and Research in Genetics: http://www.newbornscreening.info/Parents/aminoaciddisorders/ASAS.html

References

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