Inheritest®
CARRIER SCREEN

Glutaric acidemia type 1

What is glutaric acidemia type 1?

Glutaric acidemia type 1 is an inherited disease characterized by episodes of severe brain dysfunction that result in spasticity, low muscle tone, and seizures.[1,2] Individuals with glutaric acidemia type 1 have defects in the glutaryl-CoA dehydrogenase enzyme, which breaks down the amino acids lysine, hydroxylysine, and tryptophan. The symptoms of glutaric acidemia type 1 are due to the build-up of these amino acids and their metabolites in the body, primarily affecting the brain.[1] Glutaric acidemia type 1 is also known as glutaric aciduria type 1.[2]

What are the symptoms of glutaric acidemia type 1 and what treatment is available?

The severity of symptoms of glutaric acidemia type 1 can vary widely, even within families. Newborns may have macrocephaly (large head size) with no other signs or symptoms. Symptoms typically begin within months after birth and are often triggered by illness or fasting. Symptoms may include[2]:

- Hypotonia (low muscle tone)
- Feeding difficulties
- Poor growth
- Swelling of the brain
- Spasticity (abnormally tight muscles)
- Dystonia (sustained muscle contractions causing twisting movements and abnormal posture)
- Seizures
- Developmental delays
- Coma, and possibly death, especially if untreated

Individuals tend to have a reduced life expectancy. Approximately 10% of individuals die within the first decade; more than half do not survive past 35 years of age.[3] There is no cure for glutaric acidemia type 1, and treatment is aimed at preventing episodes of brain dysfunction and seizures. Treatment generally includes a low protein diet and nutrition supplements, and a feeding tube may be required for some individuals. The avoidance of fasting is typically recommended.[2,4]

Glutaric acidemia type 1 is included on all newborn screening panels in the United States.[5]

How is glutaric acidemia type 1 inherited?

Glutaric acidemia type 1 is an autosomal recessive disease caused by mutations in the *GCDH* gene.[1] An individual who inherits one copy of a *GCDH* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *GCDH* mutations, one from each parent, is expected to be affected with glutaric acidemia type 1.

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.

Who is at risk for glutaric acidemia type 1?

Glutaric acidemia type 1 can occur in individuals of all races and ethnicities. It appears to be most common in individuals of certain ancestry, including Old Order Amish ancestry in Pennsylvania, affecting approximately 1 in 300 individuals with a carrier frequency of 1 in 9[6]. In the German population it is estimated to affect 1 in 100,000 individuals, with a calculated carrier frequency of 1 in 158.[6]

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?

Screening, Technology and Research in Genetics:
http://www.newbornscreening.info/Parents/organicaciddisorders/GA1.html

Organic Acidemia Association: www.oaanews.org

References

1. Genetics Home Reference: Glutaric acidemia type I and GCDH. Available at http://ghr.nlm.nih.gov/condition/glutaric-acidemia-type-i. Accessed: March 16, 2012.
2. STAR-G-Screening, Technology and Research in Genetics http://www.newbornscreening.info/Parents/organicaciddisorders/GA1.html. Accessed: March 16, 2012
3. Kyllerman, M *et al*. Long-term follow-up, neurological outcome and survival rate in 28 Nordic patients with glutaric aciduria type 1. *Eur J Paediatr Neurol* 2004; 8(3):121-9.
4. Kolker S *et al.* Diagnosis and management of glutaric academia type I – revised recommendations. *J Inherit Metab Dis* 2011; 34:677-694.
5. National Newborn Screening Status Report. November 2, 2014. Available at: http://genes-r-us.uthscsa.edu/ sites/genes-r-us/files/nbsdisorders.pdf . Accessed January 6, 2016.
6. Hedlund, G *et al*. Glutaric Acidemia Type 1. *Am J Med Genet C Semin Med Genet*. 2006: 142C(2):86-94.