

What is glycine encephalopathy?

Glycine encephalopathy is an inherited metabolic disease that, in its typical form, is characterized by seizures in infancy and other progressive nervous system problems. Individuals with glycine encephalopathy have an abnormally low level of an enzyme that helps to break down the amino acid glycine. Symptoms are due to a toxic build-up of glycine, especially in the brain.¹ Glycine encephalopathy is also known as non-ketotic hyperglycinemia.²

What are the symptoms of glycine encephalopathy and what treatment is available?

Glycine encephalopathy is a disease that varies in severity and age at presentation. The majority of individuals with glycine encephalopathy show symptoms within the first few days of life, and a subset of individuals with early onset may also have birth defects (such as cleft lip/palate or club feet). Some individuals may show less severe symptoms later in infancy or childhood.^{1,2}

Symptoms may include:^{1,2}

- Seizures that may not respond to treatment
- Lethargy
- Hypotonia (low muscle tone)
- Difficulty breathing
- Hiccups
- Feeding difficulties
- Intellectual disability and possible behavior problems
- Coma and possible death

There is no cure for glycine encephalopathy. Treatment includes supportive care for symptoms including medicine to help reduce levels of glycine in the blood and control seizures. A ketogenic diet, feeding and respiratory support, and physical therapy may improve symptoms in some individuals.² Without intervention, individuals with severe glycine encephalopathy often do not survive past infancy.¹

Glycine encephalopathy is included on newborn screening profiles in some states in the US.³

How is glycine encephalopathy inherited?

Glycine encephalopathy is an autosomal recessive disease caused by mutations in one of three different genes. Mutations in the *GLDC* and *AMT* genes account for approximately 70% and 20% of glycine encephalopathy cases, respectively. Mutations in the *GCSH* gene are responsible for <1% of the cases.²

An individual who inherits one copy of a mutation in any of these genes is a carrier and is not expected to have related health problems. An individual who inherits two mutations in the same gene, one from each parent, is expected to be affected with glycine encephalopathy. For example, a child with two *GLDC* mutations is expected to be affected, and a child with one *GLDC* mutation and one *AMT* mutation is a carrier.

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 glycine encephalopathy?

Glycine encephalopathy can occur in individuals of all races and ethnicities. Mutations in the *GLDC* gene appear to be most common in individuals of Finnish ancestry. In Finland, glycine encephalopathy is estimated to affect 1 in 55,000 individuals, with a calculated carrier frequency of 1 in 117.²

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?

NKH International Family Network: www.nkh-network.org

Genetic and Rare Diseases Information Center (GARD):
<http://rarediseases.info.nih.gov/GARD/Disease.aspx?PageID=4&diseaseID=7219>

Children Living with Inherited Metabolic Diseases (CLIMB): <http://www.climb.org.uk/>

References

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3. 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.