



What is Glycine Encephalopathy, *GLDC*-related?

Glycine encephalopathy (GCE) is an inherited disease that in its typical form is characterized by seizures in infancy and other progressive nervous system problems. It is caused by an abnormally low level of an enzyme that helps to break down the amino acid glycine, which is important in brain function. Symptoms are due to a toxic build-up of glycine in the body.¹ Glycine encephalopathy is also known as non-ketotic hyperglycinemia (NKH).²

What are the symptoms of Glycine Encephalopathy, *GLDC*-related 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 present later in infancy or childhood with less severe symptoms.^{1,2}

Symptoms of all types may include^{1,2}:

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

There is no cure for GCE. Treatment includes supportive care for symptoms including medicine to help reduce levels of glycine in the blood and control seizures. A low-protein diet, feeding tube, breathing support, and physical therapy may improve symptoms in some individuals.² Without intervention, individuals with severe GCE 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, *GLDC*-related inherited?

Glycine encephalopathy is an autosomal recessive disease caused by mutations in one of three known genes. Mutations in the *GLDC* gene account for approximately 70% of cases of GCE. Mutations in the *AMT* and *GCSH* genes are responsible for the majority of the remaining cases.² Integrated Genetics' Inheritest evaluates mutations in the *GLDC* gene.

An individual who inherits one copy of a *GLDC* gene mutation is a "carrier" and is not expected to have related health problems. An individual who inherits two mutations in this gene, one from each parent, is expected to be affected with glycine encephalopathy

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 Glycine Encephalopathy, *GLDC*-related?

Glycine encephalopathy can occur in individuals of all races and ethnicities, but it appears to be most common in individuals of Finnish ancestry. In Finland, it 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

1. Hennermann JB. Clinical variability in glycine encephalopathy. *Future Neurol.* 2006; 1(5): 621-630.
2. Hamosh A *et al.* Glycine encephalopathy. *GeneReviews* Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1357/>. Accessed Mar 16, 2012.
3. National newborn screening status report: Updated 2/15/12. Available at <http://genes-r-us.uthscsa.edu/nbsdisorders.pdf> Accessed: Mar 14, 2012.

