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What is Glutathione Synthetase Deficiency?
Glutathione synthetase (GS) deficiency is an inherited disease characterized by anemia with or without neurological problems. It is caused by defects in the enzyme glutathione synthetase, which is important in the production of an antioxidant called glutathione. Glutathione helps to protect cells from damage. Symptoms associated with GS deficiency are due to low levels of glutathione in cells. GS deficiency is also known as 5-oxoprolinuria or pyroglutamic aciduria. [1]

What are the symptoms of Glutathione Synthetase Deficiency and what treatment is available?
Glutathione synthetase deficiency is a disease that varies in severity and age of onset, even within families.[2] Individuals with the mild form of GS deficiency typically have only mild anemia (fewer than normal red blood cells.)[1] Individuals with moderate and severe GS deficiency may present with additional symptoms:

The moderate form includes[1,3]:
- Mild/moderate anemia
- Metabolic acidosis (high levels of acid in the blood)

The severe form includes symptoms found in the moderate form plus[1,3]:
- Motor skills delays
- Mental retardation
- Seizures
- Spasticity (abnormally tight muscles)
- Ataxia (difficulty coordinating movements)
- Intention tremor (shaking of hand(s)/fingers when moving toward something)
- Frequent bacterial infections

There is no cure for GS deficiency. For all types, some long-term complications may be minimized or delayed with early identification and treatment, including medications and vitamins C and E. Certain medications should also be avoided, including acetylsalicylic acid (aspirin) and some seizure medications. Affected individuals may live to adulthood, although they may have mental retardation. There are reports of early death, especially in individuals with moderate to severe GS deficiency types. [3,4]

A few states offer newborn screening for glutathione synthetase deficiency.[5]

How is Glutathione Synthetase Deficiency inherited?
Glutathione synthetase deficiency is an autosomal recessive disease caused by mutations in the *GSS* gene.[1] An individual who inherits one *GSS* gene mutation is a "carrier" of GS deficiency and is not expected to have related health problems. An individual who inherits two *GSS* gene mutations, one from each parent, is expected to be affected with GS deficiency.

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 GS deficiency?
Glutathione synthetase deficiency can occur in individuals of all races and ethnicities. The overall incidence of GS deficiency is unknown, because it is rare.[1,2]

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Having a relative who is a carrier or is affected can increase an individual's risk to be 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?

- Children Living with Inherited Metabolic Disease (CLIMB): http://www.climb.org.uk/IMD/Golf/GlutathioneSynthetaseDeficiency-Generalised.pdf
- National Organization of Rare Disorders (NORD): http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/522/viewAbstract

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