

What is glycogen storage disease type I?

Glycogen storage disease type I, also called von Gierke disease,¹ is an inherited disease caused by a defect in the body's ability to break down glycogen (the form in which the body stores sugar) to glucose (a free form of sugar and the body's main source of energy).⁴ Symptoms associated with glycogen storage disease type I are attributed to low blood glucose levels and excessive accumulation of glycogen and fat in the liver and kidneys.³ Glycogen storage disease type I occurs in two forms, type Ia and type Ib. In type Ia, which accounts for about 80% of all cases of glycogen storage disease, there is a deficiency of the enzyme glucose-6-phosphatase (G6Pase).^{1,3} In type Ib, there is a deficiency of the enzyme glucose-6-phosphate transporter (G6PT).⁴

What are the symptoms of glycogen storage disease type I, and what treatment is available?

Signs and symptoms of glycogen storage disease type I typically begin around three to four months of age.² Initial signs include low blood sugar and enlarged liver. Glycogen storage disease type I is characterized by:^{1,2}

- Low blood sugar levels (hypoglycemia)
- Enlarged liver and kidneys (hepatomegaly and renomegaly)
- High levels of lactic acid and uric acid in the blood (lactic acidemia and hyperuricemia)
- High levels of fat in the blood (hyperlipidemia)
- Growth retardation and short stature
- Delayed puberty
- Kidney disease (proteinuria, hypertension, kidney stones, renal failure)
- Gout
- Liver tumors (typically non-cancerous)
- Pulmonary hypertension
- Decreased bone density (osteoporosis)
- Recurrent bacterial and fungal infections
- Oral (mouth) and intestinal ulcers

There is no cure for glycogen storage disease type I, but with treatment, many affected individuals live into adulthood. Long term complications may be minimized or delayed with early intervention and ongoing care. Treatment measures include dietary therapy to maintain normal blood sugar levels and provide optimal nutrition for growth and development; prescription medications for complications such as gout, hyperlipidemia, kidney disease, and infections; dialysis for kidney disease; kidney and/or liver transplantation are options for severe disease. Normal growth and puberty may be expected in treated children.²

How is glycogen storage disease, type I inherited?

Glycogen storage disease type I is an autosomal recessive disease. Type Ia is caused by mutations in the *G6PC* gene and type Ib is caused by mutations in the *SLC37A4* gene.² An individual who inherits one mutation in either gene is a carrier of glycogen storage disease type I 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 glycogen storage disease type I.

If both members of a couple are carriers of mutations in the same gene, 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 glycogen storage disease, type I?

Glycogen storage disease type I can occur in individuals of any ethnic background. The incidence of glycogen storage disease type Ia is estimated to be 1 in 125,000 with a carrier frequency of 1 in 177.¹ Type Ia is known to be more common in individuals of Ashkenazi Jewish ancestry with a calculated incidence of 1 in 16,000 based on a carrier frequency of 1 in 64.³ The incidence of glycogen storage disease type Ib is estimated to be 1 in 500,000 with a carrier frequency of 1 in 354.^{1,2}

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 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?

Association for Glycogen Storage Disease (AGSD): www.agsdus.org

Genetics Home Reference: <http://ghr.nlm.nih.gov/condition/glycogen-storage-disease-type-i>

References

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3. Scott SA *et al.* Experience with carrier screening and prenatal diagnosis for 16 Ashkenazi Jewish genetic diseases. *Hum Mut.* 2010 Nov; 31(11):1240-1250.
4. Chen Y-T. Glycogen storage diseases. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. Childs B, Kinzler KW, Vogelstein B, assoc. eds. *The Metabolic and Molecular Bases of Inherited Disease.* 8 ed. New York: McGraw-Hill, 2001:1521–51.