

What is Glycogen Storage Disease type III?

Glycogen storage disease (GSD) type III, is an inherited disorder typically characterized by liver disease during childhood and slowly progressive muscle weakness in adult years. GSDIII is caused by a defect in the body's ability to completely 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) due to a deficiency of an enzyme called glycogen debranching enzyme. Symptoms associated with GSDIII are due to excessive accumulation of abnormally formed glycogen—primarily in the liver, skeletal, and heart muscles—as well as low blood glucose levels.¹

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

Glycogen storage disease type III shows wide variability in age of onset, disease progression, and severity. Most patients have both liver and muscle involvement (classified as type IIIa); however, approximately 15% of patients primarily have liver involvement (IIIb). Two other forms, GSDIIIc and GSDIIId are extremely rare, with a handful of cases reported.²

Signs and symptoms of GSDIIIa and GSDIIIb may include:^{1,2}

- Hypoglycemia (low blood sugar levels)
- Hepatomegaly (enlarged liver)
- Hyperlipidemia (high levels of fat in the blood)
- Growth retardation
- Liver adenomas (noncancerous tumors)
- Progressive liver disease (cirrhosis, liver failure and liver cancer have been reported)
- Polycystic ovary disease in female patients
- Osteoporosis

Additional GSD type IIIa symptoms may include:²

- Progressive myopathy (muscle weakness)
- Cardiomyopathy (thickened heart muscle)

There is no cure for GSDIII. Management recommendations include medical dietary treatment to ensure adequate blood sugar levels and growth, as well as cardiac, liver, and musculoskeletal monitoring.²

How is glycogen storage disease type III inherited?

GSDIII is an autosomal recessive disease caused by mutations in the *AGL* gene.¹ An individual who inherits one copy of an *AGL* 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 GSDIII.

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 glycogen storage disease type III?

GSD type III can occur in individuals of any race or ethnicity; however, it is most common in individuals of North African Jewish ancestry and individuals from the Faroe Islands. Overall, GSDIII has an incidence of 1/100,000.²



CARRIER SCREEN

Carrier Frequency in Select Ethnic Groups

Ethnicity	Carrier Rate
North African Jewish	1/37 ²
Faroese	1/30 ³
General Population	1/158 ²

Having a relative who is a carrier or is affected can also 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?

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

References

1. Glycogen Storage Disease Type III. Available at: <http://ghr.nlm.nih.gov/condition/glycogen-storage-disease-type-iii>. Accessed April 3, 2012
2. Dagli A, et al. Glycogen Storage Disease Type III. GeneReviews. <http://www.ncbi.nlm.nih.gov/books/NBK26372> Accessed: Feb 16, 2012
3. Santer, R, et al. Molecular genetic basis and prevalence of glycogen storage disease type IIIA in the Faroe Islands. *Eur J Hum Genet* 2001; 9: 388-391.

