

Glycogen Storage Disease Type I

Subjects: Genetics & Heredity

Contributor: Camila Xu

Glycogen storage disease type I (also known as GSDI or von Gierke disease) is an inherited disorder caused by the buildup of a complex sugar called glycogen in the body's cells. The accumulation of glycogen in certain organs and tissues, especially the liver, kidneys, and small intestines, impairs their ability to function normally.

Keywords: genetic conditions

1. Introduction

Signs and symptoms of this condition typically appear around the age of 3 or 4 months, when babies start to sleep through the night and do not eat as frequently as newborns. Affected infants may have low blood sugar (hypoglycemia), which can lead to seizures. They can also have a buildup of lactic acid in the body (lactic acidosis), high blood levels of a waste product called uric acid (hyperuricemia), and excess amounts of fats in the blood (hyperlipidemia). As they get older, children with GSDI have thin arms and legs and short stature. An enlarged liver may give the appearance of a protruding abdomen. The kidneys may also be enlarged. Affected individuals may also have diarrhea and deposits of cholesterol in the skin (xanthomas).

People with GSDI may experience delayed puberty. Beginning in young to mid-adulthood, affected individuals may have thinning of the bones (osteoporosis), a form of arthritis resulting from uric acid crystals in the joints (gout), kidney disease, and high blood pressure in the blood vessels that supply the lungs (pulmonary hypertension). Females with this condition may also have abnormal development of the ovaries (polycystic ovaries). In affected teens and adults, tumors called adenomas may form in the liver. Adenomas are usually noncancerous (benign), but occasionally these tumors can become cancerous (malignant).

Researchers have described two types of GSDI, which differ in their signs and symptoms and genetic cause. These types are known as glycogen storage disease type Ia (GSDIa) and glycogen storage disease type Ib (GSDIb). Two other forms of GSDI have been described, and they were originally named types Ic and Id. However, these types are now known to be variations of GSDIb; for this reason, GSDIb is sometimes called GSD type I non-a.

Many people with GSDIb have a shortage of white blood cells (neutropenia), which can make them prone to recurrent bacterial infections. Neutropenia is usually apparent by age 1. Many affected individuals also have inflammation of the intestinal walls (inflammatory bowel disease). People with GSDIb may have oral problems including cavities, inflammation of the gums (gingivitis), chronic gum (periodontal) disease, abnormal tooth development, and open sores (ulcers) in the mouth. The neutropenia and oral problems are specific to people with GSDIb and are typically not seen in people with GSDIa.

2. Frequency

The overall incidence of GSDI is 1 in 100,000 individuals. GSDIa is more common than GSDIb, accounting for 80 percent of all GSDI cases.

3. Causes

Mutations in two genes, *G6PC* and *SLC37A4*, cause GSDI. *G6PC* gene mutations cause GSDIa, and *SLC37A4* gene mutations cause GSDIb.

The proteins produced from the *G6PC* and *SLC37A4* genes work together to break down a type of sugar molecule called glucose 6-phosphate. The breakdown of this molecule produces the simple sugar glucose, which is the primary energy source for most cells in the body.

Mutations in the *G6PC* and *SLC37A4* genes prevent the effective breakdown of glucose 6-phosphate. Glucose 6-phosphate that is not broken down to glucose is converted to glycogen and fat so it can be stored within cells. Too much glycogen and fat stored within a cell can be toxic. This buildup damages organs and tissues throughout the body, particularly the liver and kidneys, leading to the signs and symptoms of GSDI.

3.1. The genes associated with Glycogen storage disease type I

- G6PC
- SLC37A4

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- glucose-6-phosphate deficiency
- glucose-6-phosphate transport defect
- GSD I
- GSD type I
- hepatorenal form of glycogen storage disease
- hepatorenal glycogenosis
- von Gierke disease
- von Gierke's disease

References

1. Bali DS, Chen YT, Austin S, Goldstein JL. Glycogen Storage Disease Type I. 2006 Apr 19 [updated 2016 Aug 25]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1312/>
2. Chou JY, Jun HS, Mansfield BC. Neutropenia in type Ib glycogen storage disease. *Curr Opin Hematol*. 2010 Jan;17(1):36-42. doi:10.1097/MOH.0b013e328331df85. Review.
3. Chou JY, Mansfield BC. Mutations in the glucose-6-phosphatase-alpha (G6PC) gene that cause type Ia glycogen storage disease. *Hum Mutat*. 2008 Jul;29(7):921-30. doi: 10.1002/humu.20772. Review.
4. Froissart R, Piraud M, Boudjemline AM, Vianey-Saban C, Petit F, Hubert-Buron A, Eberschweiler PT, Gajdos V, Labrune P. Glucose-6-phosphatase deficiency. *Orphanet J Rare Dis*. 2011 May 20;6:27. doi: 10.1186/1750-1172-6-27. Review.
5. Kishnani PS, Austin SL, Abdenur JE, Arn P, Bali DS, Boney A, Chung WK, Dagli AI, Dale D, Koeberl D, Somers MJ, Wechsler SB, Weinstein DA, Wolfsdorf JI, Watson MS; American College of Medical Genetics and Genomics. Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics. *Genet Med*. 2014 Nov;16(11):e1.
6. Melis D, Fulceri R, Parenti G, Marcolongo P, Gatti R, Parini R, Riva E, Della Casa R, Zammarchi E, Andria G, Benedetti A. Genotype/phenotype correlation in glycogen storage disease type 1b: a multicentre study and review of the literature. *Eur J Pediatr*. 2005 Aug;164(8):501-8.