

Glycogen storage disease

TEST INFORMATION

Overview

Glycogen storage diseases (GSDs, also known as glycogenosis and dextrinosis) are a group of inherited disorders that are caused by defective glycogen metabolism in muscle, liver and other tissues. Because muscle and liver are the main sites of glycogen storage, its abnormal accumulation leads to malfunctioning of these two organs.

Overall, approximately 2.3 children per 100 000 births (1 in 43,000) have some form of glycogen storage disease. In the United States, they are estimated to occur in 1 per 20,000-25,000 births. A Dutch study estimated it to be 1 in 40,000.

There are eleven (11) distinct diseases that are commonly considered to be glycogen storage diseases (some previously thought to be distinct have been reclassified). (Although glycogen synthase deficiency does not result in storage of extra glycogen in the liver, it is often classified with the GSDs as type 0 because it is another defect of glycogen storage and can cause similar problems).

Number	Enzyme deficiency	Eponym	Incidence	Hypo-glycemia?	Hepato-megaly?	Hyperlipidemia?	Muscle symptoms	Development/ prognosis	Other symptoms
GSD type I	glucose-6-phosphatase	von Gierke's disease	1 in 50,000 ^[41] - 100,000 ^[11] births	Yes	Yes	Yes	None	Growth failure	Lactic acidosis, hyperuricemia
GSD type II	acid alpha-glucosidase	Pompe's disease	1 in 40,000 births ^[5]	No	Yes	No	Muscle weakness	*Death by age ~2 years (infantile variant)	heart failure
GSD type III	glycogen debranching enzyme	Cori's disease or Forbes' disease	1 in 100,000 births	Yes	Yes	Yes	Myopathy		
GSD type IV	glycogen branching enzyme	Andersen disease		No	Yes, also cirrhosis	No	None	Failure to thrive, death at age ~5 years	
GSD type V	muscle glycogen phosphorylase	McArdle disease	1 in 100,000 ^[12]	No	No	No	Exercise-induced cramps, Rhabdomyolysis		Renal failure by myoglobinuria
GSD type VI	liver glycogen phosphorylase	Hers' disease	1 in 65,000- 85,000 births ^[13]	Yes	Yes	No	None		
GSD type VII	muscle phosphofructokinase	Taru's disease		No	No	No	Exercise-induced muscle cramps and weakness	growth retardation	Haemolytic anaemia
GSD type IX	phosphorylase kinase, PHKA2	-		Yes	No	Yes	None	Delayed motor development, Growth retardation	
GSD type XI	glucose transporter, GLUT2	Fanconi-Bickel syndrome		Yes	Yes	No	None		
GSD type XII	Aldolase A	Red cell aldolase deficiency		?	?	?	Exercise intolerance, cramps		
GSD type XIII	β-enolase	-		?	?	?	Exercise intolerance, cramps	Increasing intensity of myalgias over decades ^[14]	Serum CK: Episodic elevations; Reduced with rest ^[14]
GSD type 0	glycogen synthase	-		Yes	No	No	Occasional muscle cramping		

http://en.wikipedia.org/wiki/Glycogen_storage_disease

Following are the 8 common types of GSD caused by a specific enzyme deficiency in liver, muscle or both:

Glycogen storage disease type I

Glycogen storage disease (GSD) type I also known as von Gierke disease is the most common type of GSDs and accounts for about 90% of all GSD cases. von Gierke described the first patient with GSD type I in 1929 under the name hepatonephromegalia glycogenica. In 1952, Cori and

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Cori demonstrated that glucose-6-phosphatase (G6Pase) deficiency was a cause of GSD type I. Subsequently, it was proposed that a transport defect of glucose-6-phosphate (G6P) into the microsomal compartment may be the underlying cause in some patients with GSD type I. Thus, GSD type I is divided into GSD type Ia caused by G6Pase deficiency and GSD type Ib resulting from deficiency of a specific translocase T1. Apart from the substrate translocation defect, patients with GSD type Ib have altered neutrophil functions predisposing them to gram-positive bacterial infections. For practical purposes, depending on the enzyme activity and the presence of mutations in the G6Pase and T genes, respectively, GSD type I may be subdivided into 2 major forms. GSD type Ia demonstrates deficient G6Pase activity in the fresh and frozen liver tissue. GSD type Ib demonstrates normal G6Pase activity in the frozen tissue samples and lowered activity in the fresh specimens. Clinical presentation GSD type I include:

- Enlarged liver and kidneys
- Low blood sugar
- High levels of lactate, fats, and uric acid in the blood
- Impaired growth and delayed puberty
- Bone thinning from osteoporosis
- Increased mouth ulcers and infection

Glycogen storage disease type II

GSD type II, also known as acid maltase deficiency or Pompe disease, is a prototypic lysosomal disease. Its clinical presentation clearly differs from other forms of GSD. Deficiency of a lysosomal enzyme, alpha-1,4-glucosidase, causes GSD type II. Pompe initially described the disease in 1932. An essential pathologic finding is the accumulation of normally structured glycogen in most tissues. Three forms of the disease exist: infantile, juvenile, and adult. In the classic infantile form, the main clinical signs are cardiomyopathy and muscular hypotonia. In the juvenile and adult forms, the involvement of skeletal muscles dominates the clinical presentation.

Glycogen storage disease type III

GSD type III is also known as Forbes-Cori disease or limit dextrinosis. In contrast to GSD type I, liver and skeletal muscles are involved in GSD type III. Glycogen deposited in these organs has an abnormal structure. Differentiating patients with GSD type III from those with GSD type I solely on the basis of physical findings is not easy. Clinical presentation includes:

- Swollen abdomen due to an enlarged liver
- Growth delay during childhood
- Low blood sugar
- Elevated fat levels in blood
- Possible muscle weakness

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Glycogen storage disease type IV

GSD type IV, also known as amylopectinosis or Andersen disease, is a rare disease that leads to early death. In 1956, Andersen reported the first patient with progressive hepatosplenomegaly and accumulation of abnormal polysaccharides. The main clinical features are liver insufficiency and abnormalities of the heart and nervous system.

Glycogen storage disease type V

GSD type V, also known as McArdle disease, affects the skeletal muscles. McArdle reported the first patient in 1951. Initial signs of the disease usually develop in adolescents or adults. Muscle phosphorylase deficiency adversely affecting the glycolytic pathway in skeletal musculature causes GSD type V. Like other forms of GSD, McArdle disease is heterogeneous. The main clinical presentations are:

- Muscle cramps during exercise
- Extreme fatigue after exercise
- Burgundy-colored urine after exercise

Glycogen storage disease type VI

GSD type VI, also known as Hers disease, belongs to the group of hepatic glycogenoses and represents a heterogeneous disease. Hepatic phosphorylase deficiency or deficiencies of other enzymes that form a cascade necessary for liver phosphorylase activation cause the disease. In 1959, Hers described the first patients with proven phosphorylase deficiency.

Glycogen storage disease type VII

GSD type VII, also known as Tarui disease, arises as a result of phosphofructokinase (PFK) deficiency. The enzyme is located in skeletal muscles and erythrocytes. Tarui reported the first patients in 1965. The clinical and laboratory features are similar to those of GSD type V.

Reason for referral

Biochemical confirmation of a clinical diagnosis

Testing of patients suspected of having glycogen storage disorder

Methods

Enzymes of glycogen metabolism and glycolysis are in the cytoplasm, either free or bound to glycogen particles. Therefore we measure their activities spectrophotometrically in 10,000 xg supernatants of 10% muscle homogenate in appropriate media.

Specimen Requirements and shipping/and handling

REQUIRED: TISSUE BIOPSIES (muscle or liver). Specimens should be flash frozen at -130 °C, and shipped on dry ice. Any delay in the initial freezing or any subsequent thawing may result in loss of activity of some or all enzymes.

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Prices and turn-around times

I. GLYCOLYTIC ENZYME DEFICIENCIES ASSOCIATED WITH: EXERCISE INTOLERANCE / MYALGIA / MYOGLOBINURIA

Test code	Description	CPT codes	Price	Turn Around Time
GSD6	Panel of 6 enzymes (PPL, PFK, PHK, PGK, PGAM, LDH)	81479	\$800	3-4 weeks
GSD3	Panel of 3 enzymes (PGK, PGAM, LDH)	81479	\$600	3-4 weeks

II. GLYCOLYTIC ENZYME DEFICIENCIES ASSOCIATED WITH WEAKNESS

Test code	Description	CPT codes	Price	Turn Around Time
GSDII	Pompe's disease Acid maltase deficiency	81479	\$800	3-4 weeks
GSDIII	Cori-Forbes' disease enzymes (debrancher deficiency)			
GSDIV	Andersen's disease (branching enzyme deficiency)			

III. DISORDERS OF LIPID METABOLISM

Test code	Description	CPT codes	Price	Turn Around Time
CPTII	Carnitine-palmitoyl transferase	81479	\$400	3-4 weeks

Required forms: GSD requisition/consent forms

References: <http://www.ncbi.nlm.nih.gov/sites/GeneTests/review>