

Glycogen Storage Disease

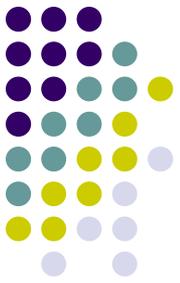


Introduction



- The food we eat is usually used for growth, tissue repair and energy. The body stores what it does not use.
- Excess sugar, or glucose, is stored as glycogen in the liver and muscle tissue.
- Between meals and during sleep (i.e. periods of fasting), or during exercise, the body breaks down glycogen and uses the stored sugar for energy.
- People who are born with GSD, are unable to properly metabolize or break down glycogen. Due to an enzyme deficiency, people with GSD have the ability to store sugar as glycogen but are unable to use the stores to provide the body with energy during fasting or exercise.

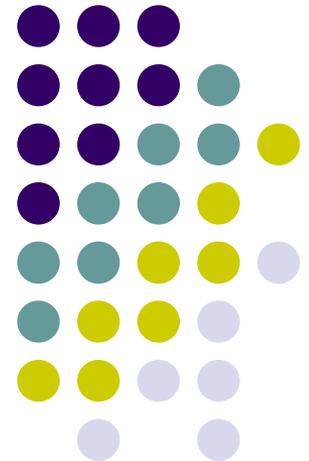
Introduction

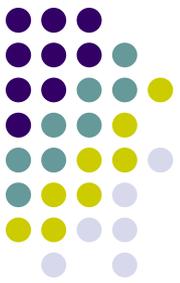


- The incidence for glycogen storage disorders is 1 case per 20,000-25,000 births.
- Because free glucose is the product of the hepatic glucose-6-phosphatase reaction, either type leads to accumulation of liver glycogen, accompanied by fasting hypoglycemia.
- Hepatomegaly, the natural consequence of glycogen accumulation, is the clinical hallmark of the disease.

What is Glycogen Storage Disease?

- Glycogen storage diseases are inborn errors of metabolism that result in the storage of abnormal amounts of glycogen in the body.

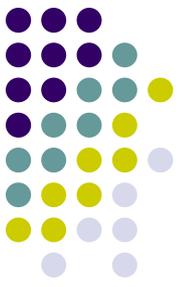




Causes

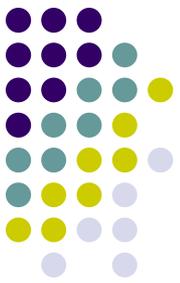
- GSD **Ia** and **Ib** are autosomal recessive genetic traits caused by mutations at loci **17q21** and **11q23**.
- GSD **Ia** is caused by deficient activity of the enzyme **glucose-6-phosphatase**, representing at least 14 distinct allelic variants.
- GSD **Ib** is caused by deficiency of glucose-6-phosphate translocase, which is responsible for importing glucose-6-phosphate from the cytosol to the interior of the microsome to bring substrate into contact with enzyme.

What is GSD 1a (von Gierke disease)?



- Glycogen storage disease type 1a was described in 1929 by von Gierke. He found that patients had frequent nosebleeds before death.
- In 1952, researchers found the missing or malfunctioning enzyme is **glucose-6-phosphatase**, found in the liver, kidneys and bowel lining.
- When the enzyme is missing, the glycogen accumulates in the liver, kidneys and lining of the bowel. People with GSD type 1a, even if treated, have enlarged livers with swollen abdomens and low blood sugar.

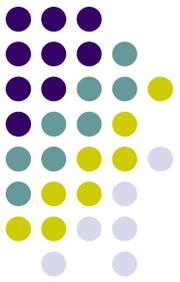
Pathophysiology



- Rapid drop in blood glucose normally occurs over the first several hours after birth.
- Within the hepatocyte, the glycogen catabolic machinery responds normally to stimuli caused by hypoglycemia (e.g., neural, hormonal).
- Glucose-6-phosphate is the substrate for glycolysis and produces lactate. Lactate exits the hepatocyte, causing significant lactic acidemia in proportion to the degree of stimulus for glycogen breakdown.
- The increase in the phosphorylated compounds of glycolysis inhibits rephosphorylation of adenine nucleotides, activating the nucleic acid degradation pathway and resulting in increased uric acid.

Pathophysiology

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- Severe hypoglycemia stimulates epinephrine secretion, which activates lipoprotein lipase and release of free fatty acids. These fatty acids are transported to the liver, where they are used for triglyceride synthesis and are exported as (VLDL).

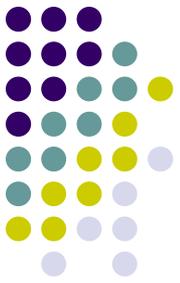
Indications



- Hypoglycemic complications include the following:
 - Twitching
 - Cyanosis
 - Seizures
 - Irritability
 - Apnea
 - Coma (may be secondary to cerebral edema from combined hypoglycemia and hypoxia secondary to hypoglycemic seizures)

Indications

(cont.)



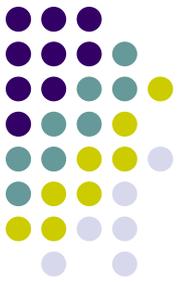
- Long-term consequences of GSD include:
 - Hepatic adenomas
 - Hepatocellular carcinoma
 - Progressive renal insufficiency
 - Hyperuricemic nephrocalcinosis
 - Short stature
- In GSD Ib, secondary consequences of neutrophilic abnormalities include multiple and recurrent infections, brain abscess.
- **Sex:** GSD occur with equal frequency in both sexes.
- **Age:** with clinical onset at birth.

Lab Studies



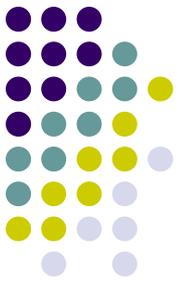
- Include blood glucose with electrolytes. If blood glucose is low, electrolyte test results an increased anion gap, which means lactic acidemia.
- Studies of liver function, plasma uric acid, and urinary creatinine clearance are essential.
- Perform a CBC and differential.
- Perform a coagulation profile to include bleeding time tests.

Imaging Studies



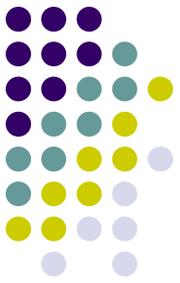
- Ultrasonography
 - Abdominal ultrasonography can provide reasonable estimates of liver and kidney size.
 - Ultrasonography may also be useful later in the clinical course to provide a baseline to evaluate nodules.

Medical Care



- Especially in infancy, diagnostic evaluation is performed most safely in a hospital because of the potential for severe hypoglycemia.
- Young infants require continuous nasogastric (NG) tube feedings to sustain blood sugars. Older children usually can eat cornstarch.
- Pay attention to the dental and oral health of patients with GSD Ib to reduce incidence of infection.

Diet



- The main point of therapy for both types of GSD I, requires close monitoring and adjustment by a highly specialized nutritionist.
- Due to the triglyceridemia characteristic in this disorder, the patient should avoid high lipid intake.
- Most biochemical parameters can be substantially normalized and liver size can be reduced by approaching glucose homeostasis through overnight feeding.

How are GSD Treated?



- The treatment for all glycogen storage diseases is aimed at prevention.
- Treatment needs to be started as soon as the disorder is diagnosed.
- The brain can only use glucose for energy. To avoid low blood sugar, it is therefore essential for the person to constantly have a source of energy that their body can use.
- People with GSD type 1a who are in good metabolic control through diet management can prevent low blood sugar. They also have fewer symptoms and long-term complications.

How are GSD Treated?

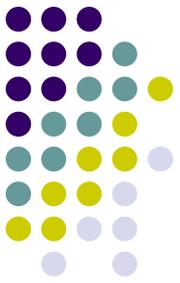
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- Since it is impossible to be eating all the time, people with GSD usually:
 - have tube feedings while they sleep, or
 - wake up in the night to take **cornstarch**, or
 - take cornstarch between meals
 - Cornstarch takes a long time for the body to break down and is therefore available as an energy source during periods of fasting.

How are GSD Treated?

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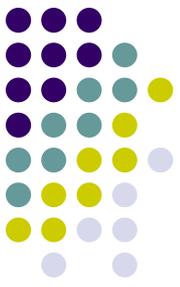


- Untreated GSD type 1a can lead to:
 - Very low blood sugar, which can be life-threatening
 - enlarged liver
 - muscle wasting
 - high levels of cholesterol
 - blood clotting problems
 - susceptibility to infections
 - stunted growth
 - bone problems (osteoporosis)
 - liver problems
 - kidney problems

What are the Long-term Complications of GSD?



- Although **GSD type 1a** mainly affects the liver, other organs are also involved.
- Possible complications include:
 - stunted growth
 - gout
 - inflammation of the pancreas
 - liver tumors that may or may not be cancerous
 - kidney disease



Other Treatments

- Because the enzyme defect is mainly in the liver, it is possible to treat GSD type 1a by doing a liver transplant.

The Balancing Act

- The challenge in treating glycogen storage disease type 1a is to provide enough glucose to avoid low blood sugar but not an excess that needs to be stored as glycogen.
- The balance can be disturbed by tough exercise, stress and illness. Special attention is needed to prevent low blood sugar.

Activity



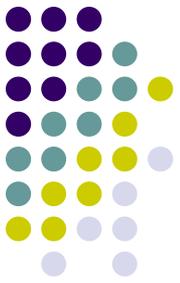
- The patient should avoid all contact sports because of the probability for bleeding and the potential for liver damage.

Patient Education



- Parents of infants should be taught how to insert a NG feeding tube.
- Family members should be taught how to test blood glucose levels.
- Family members and older children should be taught how to recognize signs of impending hypoglycemia.
- Intensive nutritional education should be provided to patients so they can assist in their own dietary control as early as possible.

Prognosis



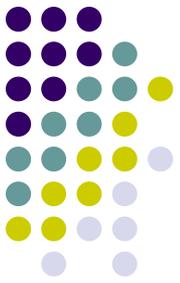
- People with well-managed, treatable types of GSD can have long, relatively normal lives.
- As the GSD type becomes more severe, a greater level of vigilance against infections and other complications is appeared.

Prevention



- Because GSD is an inherited condition, it is not preventable.
- Through chorionic villi sampling and amniocentesis, the disorder can be detected prior to birth.

How Can Friends & Family Help?



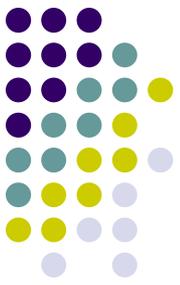
- Learn to recognize the warning signs, symptoms and treatment of low blood sugar, or **hypoglycemia**.
- Signs of mildly low blood sugar include:
 - feeling hungry
 - feeling shaky or lightheaded
 - feeling nervous or irritable
 - cold sweats
 - feeling weak
 - feeling confused
 - numbness or tingling in the tongue or lips

How Can Friends & Family Help? (cont.)



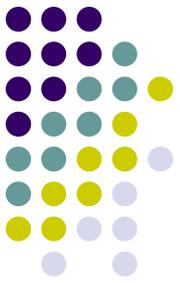
- Signs of moderately low blood sugar include:
 - complaining of feeling unusually sleepy
 - complaining of not being able to see clearly
 - acting angry or sad for no apparent reason
 - acting drunk
- Signs of severely low blood sugar include:
 - seizures
 - unconsciousness

How Can Friends & Family Help? (cont.)



- If the person with GSD is showing signs of low blood sugar, offer him or her a regular soft drink or a sugary drink. Then, make sure they have a snack.
- Help them to avoid fasting. Provide them finger foods:
 - crackers and cheese
 - bean dip
 - bread sticks
 - pita or carrot sticks with dip
 - corn chips
 - other carbohydrate-containing snacks

References



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