 Glycogen branching enzyme deficiency (glycogen storage disease IV,  
 Andersen disease, APBD)

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 Glycogen  
 branching enzyme deficiency (glycogen storage disease IV,  
 Andersen disease)Authors  
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 topic last updated: May 08, 2015.INTRODUCTION — Glycogen  
 is the stored form of glucose and serves as a buffer for  
 glucose needs. It is composed of long polymers of a 1-4  
 linked glucose, interrupted by a 1-6 linked branch point  
 every 4 to 10 residues. Glycogen is formed in periods of  
 dietary carbohydrate loading and broken down when glucose  
 demand is high or dietary availability is low (figure  
 1).There are a number of inborn errors of glycogen  
 metabolism that result from mutations in genes for virtually  
 all of the proteins involved in glycogen synthesis,  
 degradation, or regulation. Those disorders that result in  
 abnormal storage of glycogen are known as glycogen storage  
 diseases (GSDs). They have largely been categorized by  
 number, according to the chronology of recognition of the  
 responsible enzyme defect (table 1). The age of onset varies  
 from in utero to adulthood.Glycogen is most abundant  
 in liver and muscle, which are most affected by these  
 disorders. The physiologic importance of a given enzyme in  
 liver and muscle determines the clinical manifestations of  
 the disease.●The  
 main role of glycogen in the liver is to store glucose for  
 release to tissues that are unable to synthesize significant  
 amounts during fasting. The major manifestations of  
 disorders of glycogen metabolism affecting the liver are  
 hypoglycemia and hepatomegaly. (See "Physiologic  
 response to hypoglycemia in normal subjects and patients  
 with diabetes mellitus".)●Glycogen  
 is the primary source of energy for high-intensity muscle  
 activity by providing substrates for the generation of  
 adenosine triphosphate (ATP). The major manifestations of  
 disorders of glycogen metabolism affecting muscle are muscle  
 cramps, exercise intolerance and easy fatigability, and  
 progressive weakness.Glycogen branching enzyme  
 (GBE) deficiency (GSD IV, MIM #232500) is also known as  
 Andersen disease. This topic will review GBE deficiency (GSD  
 IV). An overview of glycogen storage disease is presented  
 separately. (See "Overview of inherited disorders of  
 glucose and glycogen metabolism".)PATHOGENESIS — Glycogen  
 branching enzyme (GBE; amylo [1,4 to 1,6] transglucosidase)  
 catalyzes the attachment of short glucosyl chains to a naked  
 peripheral chain of nascent glycogen (figure 1). Deficiency  
 results in abnormal structure of glycogen (similar to  
 amylopectin), known as polyglucosan, with fewer branch  
 points and longer alpha-1-4-linked glucose polymers.GENETICS — Glycogen  
 acid (RNA) splicing [22].DIAGNOSIS — Liver  
 biopsy shows excessive glycogen accumulation with a  
 characteristic staining pattern. In addition to the  
 normal-appearing glycogen arranged in alpha and beta  
 particles, fibrillar aggregations of glycogen are detected  
 by electron microscopy. Fibrosis and cirrhosis are  
 invariably present in the classic form of the disease. The  
 diagnosis is confirmed by absent branching enzyme activity  
 in skin fibroblasts, muscle, or liver, and/or  
 mutation analysis of the entire coding region of the  
 glycogen branching enzyme gene (GBE1). In  
 genetically confirmed cases, prenatal diagnosis can be  
 performed accurately in subsequent pregnancies by analysis  
 of DNA from chorionic villi or cultured amniocytes [26].  
 Polyglucosan bodies (PBs) have also been detected in  
 placenta at 25 and 35 weeks of gestation in two genetically  
 confirmed cases, raising the possibility of prenatal  
 diagnosis by histologic evaluation of placental biopsies [27].In  
 patients with neuromuscular disease, the serum creatine  
 kinase level is usually elevated. Muscle biopsy reveals the  
 storage of periodic acid-Schiff (PAS) stain-positive  
 material that resists digestion with diastase. The glycogen  
 particles appear abnormal by electron microscopy, but they  
 are often associated with normal beta particles.TREATMENT — No  
 specific treatment is available. Liver transplantation has  
 been performed with evidence of reduction in glycogen  
 storage in both heart and skeletal muscle in some patients  
 [28,29],  
 but extrahepatic disease progression reported in other cases  
 [30].  
 In an in vitro study, polyglucosan neurotoxicity caused by  
 glycogen branching enzyme (GBE) enzyme deficiency was  
 reversed with rapamycin, indicating potential therapeutic  
 value of glycogen synthase inhibition for treating glycogen  
 storage disorders (GSDs) [31].SUMMARY●Glycogen  
 above.)Use of

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