INBORN ERRORS OF METABOLISM - I

GLYCOGEN STORAGE DISORDERS - DIAGNOSTIC APPROACH, MANAGEMENT AND RECENT ADVANCES

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Abstract: *Glycogen storage disorders are a group of heterogeneous inherited enzymopathies affecting glycogen metabolism, primarily in the liver and muscle. The clinical spectrum ranges from severe neonatal hypoglycemia to late-onset liver, muscle and cardiac disease. Advances in molecular genetics, including newborn screening, enable earlier and more precise diagnosis and improved genotype-phenotype correlations. Metabolic profiles (e.g. hypoglycemia with ketosis, lactic acidosis) and genetic testing guide diagnosis. Management has traditionally been primarily dietary (frequent feeding, uncooked cornstarch), but therapeutic options have now expanded considerably. Enzyme replacement (e.g. acid alpha-glucosidase for Pompe disease) and novel small-molecule or substrate-based therapies improve disease control. Emerging gene therapies and targeted agents (e.g. SGLT2 inhibitors in GSD-Ib) are transforming care. Supportive care, transplantation and emerging therapies ensure better long-term outcomes in patients with glycogen storage disorders.*

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Points to Remember

- ***GSDs are a heterogeneous group of inherited disorders affecting glycogen metabolism. The organs involved primarily are liver and muscle, however, the metabolic effect is seen in multiple systems of the body.***
- ***Hepatic forms cause fasting intolerance, hypoglycemia, hepatomegaly and growth failure; muscular forms cause exercise intolerance, cramps, rhabdomyolysis; whereas multisystemic forms (e.g., Pompe) carry cardiac and respiratory morbidity.***
- ***Advances in molecular genetics allow precise genotype-phenotype correlation, serving as the gold standard for the diagnosis of most GSDs. Biopsy is less often needed.***
- ***Core strategies for management include frequent feeds, avoidance of fasting, dietetic modification with consumption of uncooked cornstarch for sustained glucose release, high-protein diets for gluconeogenesis and complication targeted care.***
- ***Therapeutic advances include enzyme replacement therapy (ERT) for Pompe disease, novel pharmacologic options like empagliflozin for neutropenia in GSD-Ib and experimental strategies like recombinant adeno-associated viral vector (rAAV)-mediated gene therapy, genome editing, autophagy activators and glycogen synthase inhibitors.***
- ***Early diagnosis and metabolic control prevent acute crises and long-term complications such as hepatic adenomas/carcinoma, hepatic failure, renal disease, myopathy and cardiomyopathy.***

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