

Metabolism

Carbohydrate Metabolism

Disorder	Enzyme Blockade	Accumulated Substrate(s)	Presentation	Treatment
GSD Type IIa (Pompe)	Lysosomal acid α -glucosidase	Glycogen - accumulates in skeletal and cardiac muscles	Progressive hypotonia, macroglossia, loss of motor, respiratory, and cardiac functions (cardiomyopathy). Pilot optional test on NBS	ERT (alglucosidase alfa) Heart tx for CMP
GSD Type IIIa & IIIb (Cori)	Debranching enzyme	Glycogen - accumulates in liver and muscle	Similar to Ia but may be milder; IIIb causes neutropenia	Uncooked cornstarch + continuous feeds to maintain normoglycemia, high-protein diet
GSD Type V (McArdle)	Muscle phosphorylase	Glycogen - accumulates in muscle	Exercise intolerance / cramping, "second wind" phenomenon, myoglobinuria/ rhabdomyolysis	Carbohydrate administration before exercise, high-protein diet

Fatty Acid Oxidation Disorders

PowerPlans	Metabolism Fatty Acid Ox Disorder NOS Admit Orderset, LCFAOD Admit Orderset
Biochemical Defect	Mitochondrial FA oxidation (AKA β -oxidation) = main energy (FADH ₂ / NADH for gluconeogenesis and ketogenesis) for heart, skeletal muscle, neurons when Glc is limited (starvation, exercise). Disorders occur d/t decreased carnitine uptake by cells (required for FA transport into the mitochondria), inhibiting entry of FAs into mitochondria, or by blocking β -oxidation. End result = energy-deficient state without appropriate ketosis .
Presentation	Fasting-induced vomiting, lethargy, coma, and hypoglycemic seizures, occasional hepatomegaly (may be Reye-like)
Diagnosis	Hypoketotic hypoglycemia +/- liver failure, acidosis & hyperammonemia . Acylcarnitine profile with specific findings. Confirmation w/ DNA mutation analysis (less frequently enzyme testing in cultured skin fibroblasts)

Disorder	Enzyme Blockade	Accumulated Substrate(s)	Presentation	Treatment
Medium-chain acyl-CoA DH deficiency	MCAD -- cannot degrade MC FAs to short-chain FAs and Acetyl CoA	C6, C8, and C10 acylcarnitines	Illness + poor PO \rightarrow glycogen depletion \rightarrow HKHG \rightarrow brain injury, seizures, & death if untreated; excellent prognosis if treated On NBS in most states, but may present on DOL 2-3	Avoid fasting during illnesses, give dex-containing IVF if unable to tolerate PO, carnitine supplementation if low carnitine, AVOID MCT