Fatty Acid Oxidation Disorders

Disorder	Enzyme Blockade	Accumulated Substrate(s)	Presentation	Treatment
Long-chain / Very long-chain acyl-CoA DH deficiency	LCHAD/VLCAD	**LCHAD/TFP**: 3-hydroxy-acyl-carnitines (C16-OH) **VLCAD**: unsat. long-chain acylcarnitines (C14:1)	More severe than MCAD -- rhabdo, CMP, liver failure, and HKHG even w/ rx LCHAD may have peripheral neuropathy + retinopathy On NBS in all states	Dietary fat restriction MCT oil supplementation Avoid fasting; give dex-containing IVF Serial cardiac evaluations, check CK with illnesses
Primary Carnitine Deficiency	Defective carnitine transporter (OCTN2) -- dec GI absorption / renal reabs.	Elevated urine carnitine, low blood carnitine	CMP + recurrent HKHG, may progress to Reye-like picture **Blood**: low free carnitine **Urine**: elevated carnitine excretion	High-dose oral carnitine, avoidance of fasting, dex-containing IVF if unable to tolerate PO

Organic Acidemias

PowerPlans	Metabolism IVA, MMA, PA, Glutaric Acidemia Type I Admit Orderset (one for each)
Biochemical Defect	Defect in AA breakdown → accumulation of organic acid byproducts
Presentation	Neonatal lethargy, poor perfusion, vomiting, coma, CVAs, death
Diagnosis	Definitive: quant plasma AAs. Often on NBS (elevated C3 / C5 acylcarnitines). Usu p/w severe high AG metabolic acidosis, +/- hyperammonemia, hypoglycemia, liver dysfunction, ketosis, and secondary carnitine deficiency
Treatment	Stop all protein intake, high-dose carnitine, promote anabolism with D10NS + IL +/- insulin, +/- $NaHCO_3$ for severe acidosis, dialysis for life-threatening acidosis or hyperammonemia

Disorder	Enzyme Blockade	Accumulated Substrate(s)	Presentation	Treatment
Methylmalonic acidemia	methylmalonyl-CoA mutase deficiency (MM-CoA → succinyl CoA)	Products of BCAAs (Ile, Val, Met) - MMA, methylcitrate, C3 acylcarnitine	Stressor (illness, excess protein intake) → metabolic crisis (high-AG metabolic acidosis, basal ganglia stroke, pancreatitis). Complications: renal dz, intellectual disability. Variable age of onset.	As above, plus Vitamin B12, liver or liver/kidney transplantation, avoid Ile, Val, Met, Thr in diet

Organic Acidemias continued on next page →

Organic Acidemias

Disorder	Enzyme Blockade	Accumulated Substrate(s)	Presentation	Treatment
Propionic acidemia	propionyl-CoA carboxylase deficiency (propionyl CoA → MM-CoA)	Products of BCAAs (Ile, Val, Met) - 3-OH propionic acid, methylcitrate, C3 acylcarnitine	Newborn period - profound metabolic acidosis w/ high AG and **prominent ketosis** → multiorgan dysfunction (cardiac, respiratory, pancytopenia, basal ganglia stroke, pancreatitis), hyperammonemia Later - cardiomyopathy and dysrhythmias	As above, plus liver transplant, avoid Ile, Val, Met, Thr in diet
Isovaleric acidemia	isovaleryl-CoA dehydrogenase (isovaleryl-CoA → → acetoacetate and Ac-CoA)	Products of Leu metabolism (Isovaleric acid and metabolites), C5 acylcarnitine	Neonatal: severe lethargy and obtundation, +AG metabolic acidosis, hypoglycemia, ketonuria, hyperammonemia, odor of IVA in urine, pancreatitis Infantile/late-onset: FTT, DD, seizures	As above, avoid Leu
Glutaric acidemia type I (GA1)	Glutaryl CoA DH deficiency	Products of Trp and Lys metab (plasma C5 dicarboxylic (C5DC) acylcarnitine)	Macrocephaly (risk of tearing of bridging veins → subdural hemorrhage), isolated **cerebral** acidosis -- may **not** have metabolic acidosis/ ketosis/hyperammonemia Catabolic stress → devastating neurologic injury (dystonia, movement disorders)	As above, restrict Trp and Lys in diet Aggressive sick day management