Disease	Deficiency	Type	Clinical Manifestation	Notes
FA Oxidation Disorder				
MCAD Deficient (most common AR enzyme deficiency)	Decreased ability to oxidize Medium Chain FA	6-24 Months	- Sever Hypoglycemia - Hypoketonemia	Medium Chain Acyl Carnitines found in Urine *In disorders where B-oxidation is defective (i.e. MCAD Deficiency), ***Dicarboxylic Acids*** may be found in Serum & Urine
Systemic Carnitine Deficiency	Transport of Long Chain FA into Mitochondria is impaired	Early Age	- Hypoglycemia - Hypoketosis	
Myopathic Carnitine Deficiency	B-oxidation is decreased	Later Age	- Muscle Weakness - Cardiomyopathy	Lipid Droplets in muscle biopsy CK-MM & Myoglobinuria (indicates skeletal m. damage)
CPT-I Deficiency	CPT-I		- Hypoglycemia - Hypoketosis	Affects Primarily the Liver
CPT-II Deficiency	CPT-II		- Muscle Weakness - Cardiomyopathy	Lipid Droplets in muscle biopsy CK-MM & Myoglobinuria (indicates skeletal m. damage)
Jamaican Vomiting Sickness	Unripe *Ackee Fruit* *Hypoglycin A* (MCAD inhibitor)		- Vomiting - Drowsiness (due to hypoglycemia) - Coma → Death	Medium Chain Acyl Carnitines found in Urine
Zellweger Syndrome	Defective Peroxisomal oxidation of *Very Long Chain FA* (22-26C)	Fatal Infancy	- Hepatomegaly & Hepatic failure - Neurological Manifestations	Increased serum 26C FA
Refsum Disease	Defective Peroxisome alpha oxidation (Phytanic Acid accumulation) [branched chain FA]		- Visual defects - Ataxia - Polyneuropathy	Treatment: dietary restriction of branched chain FA
Nitrogren Disorders				
Cystinuria	Defective AA transporter that prevents reabsorption of **COLA** (**C**ystine, **O**rnithine, **L**ysine, **A**rginine)	AR	Hexagonal Cystine stones in urine	
Hartnup Disease	Neutral AA absorption transporters (tryptophan)	AR	**Pellagra**	Decreased Tryptophan for conversion to Niacin (Vit. B3), and thus decreased conversion of Niacin to NAD+
Pellagra	Vit. B3 (Niacin) Deficiency		- **D**iarrhea - **D**ementia - **D**ermatitis (C3/4 dermatome)	**3 D's** of B3
Urea Cycle Disorders (UCDs) - Increased serum Ammonia & Glutamine levels & decreased/absent Urea formation; deficiency of an enzyme leads to accumulation of that enzymes' substrate				
Hyperammonemia Type I	CPS I		- Hyperammonemia	Treatment: - Arginine (Arginine stimulates the formation of NAG, & high levels of NAG may stimulate deficient CPSI) - Benzoate, Phenylacetate, Phenylbutyrate
Hyperammonemia Type II (most common UCD)	OTC (Ornathine Transcarbamoylase)	X-Linked (usually male)	- Hyperammonemia - Increased ***Orotic Acid*** in urine	

Disease	Deficiency	Type	Clinical Manifestation	Notes
Citrullinemia	ASS (Argininosuccinate Synthetase)		- Hyperammonemia - Increased Citrulline levels (serum, urine)	Treatment: Arginine
Argininosuccinic Aciduria	ASL (Argininosuccinate Lyase)		- Hyperammonemia - Increased Argininosuccinate levels (serum, urine, CSF)	Treatment: Arginine
Argininemia	Arginase		- Increased Arginine levels (serum NH3 levels not as elevated as other UCDs)	Treatment: Essential AA ***except Arginine***
Pyruvate Dehydrogenase (PDH) Complex Disorders				
Wernicke-Korsakoff Syndrome	Thiamine (TPP) (Vit. B1) Deficiency (Decreased PDH Complex Activity)	- Ataxia (lack of voluntary movement) - Opthalmolplagia (paralysis of eye muscle) - Memory Loss - ***Wet Beri Beri*** (cardiac failure & edema)		- Impaired breakdown of glucose → ATP depletion (worsened by glucose infusion) - Highly aerobic structures affected first (Brain & Heart) - Alcoholics & Malnourished more at risk [Vit. B1 is also a cofactor for: *Pyruvate DH, alpha-KG, Transketolase (from PPP)*]
PDH Complex Deficiency	Leads to a buildup of pyruvate that gets shunted to Lactate (via LDH) & Alanine (via ALT) Decreased Acetyl CoA production; *Decreased ATP Production*	Fatal Early Age X-Linked	- Neurologic defects (corpus callosum agenesis, basal ganglia cats) - Lactic Acidosis - Increased serum Alanine (starting in infancy)	Treatment: Increase intake of ketogenic nutrients (high fat content or increase Leucine & Lycine) Leucine & Lycine - the onLy pureLy ketogenic AAs
Heavy Metal Poisoning	Arsenate, Mercury & Lead bind to Lipoic Acid			Treatment: Lipoic Acid
Mitochondrial Diseases - transmitted only through the mother; Variable expression due to Heteroplasmy				
LHON (Leber's Hereditary Optic Neuropathy)	Mitochondrial Genome Mutation (not nuclear) [defect in NADH DH]	25-35 y/o (late onset)	- Retinal degeneration - Optic nerve atrophy (most common cause of optic n. damage)	Critical threshold 90% (mutation in mtDNA must exceed 90% before disease appears)
Kearns-Sayer	mtDNA Deletion (common deletion #)	Before 20 y/o	- Retina degeneration/Ocular paralysis - Ataxia/Skeletal weakness - Congestive heart failure - Diabetes - Mental illness	Affects systems with high energy requirements (Brain & Heart) *progressive nature helps to identify it*
MELAS (Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis, Stroke-like episodes) *(most common Mitochondrial Disease)*	OxPhos Defect (mtRNA mutation)	Presents ~15 w/ stroke-like episode	- Stroke-like episodes (*not actual stroke*) - Myopathy & Muscle twitching - Deafness - Dementia	Excess Pyruvate → Lactic Acid (accumulates)
MERRF (Myoclonic Epilepsy Ragged Red Fibers)	mtRNA mutation *(most common mtRNA mutation)*	Presents 6-16 w/ myoclonus	- Seizures - Ataxia & Muscle weakness - Declining eye sight & hearing	
Aminoglycoside (antibiotic) Induced Deafness	Mitochondrial rRNA		- Bilateral hearing loss (moderate to severe)	

Disease	Deficiency	Type	Clinical Manifestation	Notes
Cholesterol Disease				
SLOS (Smith-Lemli-Optiz Syndrome)	DHCR7 Mutation (Loss of Function)	AR	- Heart defects - Limb malformation - Growth retardation - Microcephaly - Mental disabilities	- 7 DHCR is last enzyme needed to synthesize cholesterol - Buildup of 7-DHC (dehydrocholesterol) Treatment: Cholesterol administration (won't help with CNS problems, though)
Cholelithiasis (Cholesterol Gallstone Disease)				
Glycogen Storage Disorders				
I - Von Gierke Disease	Glucose 6-Phosphatase	AR	- Severe fasting hypoglycemia - Glycogen accumulation in Liver & Kidney - *Hepatonephromegaly* - Increased Serum Lactate - Increased Uric Acid (Gout)	Glycogen: Normal Structure; ***High*** *Amount* Treatment: **Uncooked Corn Starch** (frequently) ***Important the patient doesn't encounter fasting metabolism***
II - Pompe Disease **Infantile** - Death in 1st year from Heart Failure **Late Onset** - breathing problems (less severe)	Lysosomal Acid alpha-1,4-glucosidase (Maltase)	AR	- Cardiomegaly - Hypotonia / Exercise Intolerance	- Glycogen: Normal Structure; Normal Amount (normal Blood Glucose Levels) - Lysosomal Glycogen accumulation - Liver & Striated Muscle Treatment: Enzyme replacement therapy
III - Cori Disease **"Forbes Disease" "Limit Dextrinosis"**	Debranching Enzyme	AR	Mild version of Von Gierke - Normal Serum Lactate	- Glycogen: ***Abnormal*** *Structure*; ***High*** *Amount* - Accumulation of Limit Dextrins in Cytosol - Gluconeogenesis is intact
IV - Anderson Disease	Branching Enzymer	Death by 5 y/o	- Infantile Hypotonia - Infantile Cirrhosis → Hepatomegaly	- Glycogen: ***Abnormal*** *Structure*; ***Low*** *Amount* - Long unbranched glucose chains attacked by Immune System → Scarring → Cirrhosis
V - McArdle Disease	Glycogen Phosphorylase **Skeletal Muscle**	AR	- Weakness & Muscle Cramping - **No** increase in serum lactate post-exercise → ATP deficiency - Elevated CK-MM - Myoglobinuria	- Glycogen: Normal Structure; ***High*** *Amount (in muscle)* (normal Blood Glucose Levels) - **Often goes undiagnosed** (child just appears unmotivated) **McArdle = Muscle**
VI - Hers Disease	Glycogen Phosphorylase **Liver**		- Mild Hypoglycemia - Hepatomegaly - Growth Retardation	- Glycogen: Normal Structure; ***High*** *Amount (in Liver)*
VII - Tarui Disease	PFK-1 **Muscle & RBC**		Muscle: lack of ATP → Muscle Cramp **(no rise in lactate)** RBC: lack of ATP → Hemolysis	- Glycogen: Normal Structure; ***High*** *Amount (in muscle)* (normal Blood Glucose Levels) - Deficient Glycolysis in Muscle & RBC