Management of Metabolic Crises

Acute Metabolic Encephalopathy

Management

- Reverse catabolism ASAP and prevent sequelae, do frequent neuro checks
- **Hydration**: 10 mL/kg NS bolus if dehydrated, then D10 NS + 20 mEq/L of KCl (add after ruling out hyperkalemia or after voiding) @ 1-1.5x M, avoid hyponatremia (predisposes to cerebral edema; minimum of 4-5 meq/kg/day of sodium in fluids)
- **Nutrition**: give calories via carbs + IL alone (unless FA ox d/o is on ddx, then no IL) to provide 1 -1.5x TEE (120-150 kcal/kg/day), preferably enteral nutrition (enteral carbs → portal vein → maximize insulin release); can give TPN if enteral feeds are not tolerated, start protein w/in 48h
- **Promote anabolism**: nutrition, ↓ counter-regulatory hormones → ensure adequate volume, ondansetron for vomiting, treat infxn/fever/pain, correct hypoglycemia (bolus of 2 or 5 mL of 25 or 10% Dextrose → rule of 50 (i.e., vol*%dex = 50), then infusion to maintain a GIR of 8-12 mg/kg/min [GIR in mg/kg/min = dextrose% x Vol (ml/kg/day) / 144]), maintain normoglycemia if needed with insulin @ 0.1mcg/kg/hr, titrating to maintain glucose between 100-120mg/dL (goal of high GIR = get glucose (i.e., calories), into the cells rather than add to Sosm by causing hyperglycemia)
- **Cofactor therapy**: try the vitamins below even empirically, but esp if these disorders are on ddx

Suspected Enzyme Deficiency	Cofactor
Propionyl-CoA carboxylase Beta-methylcrotonyl-CoA carboxylase Holocarboxylase synthase Pyruvate carboxylase Biotinidase deficiency	Biotin (dose depends on disorder)
Methylmalonyl-CoA mutase	Hydroxycobalamin 1 mg/day IM
BCAA DH (MSUD) Pyruvate DH Alpha-ketoglutarate DH	Thiamine (B1) 100 mg/day
Glutaryl-CoA dehydrogenase Medium acyl-CoA DH	Riboflavin (B2) 200 mg/day

- **L-carnitine**: inc urinary excretion of carnitine-bound organic acids → secondary deficiency; carnitine is neuroprotective and non-toxic, give 100mg/kg/day, max 6 g/d, 1st via IV bolus of daily dose, then divide q4-6h, IV or enteral; carnitine controversial in FAOD
- **Toxin removal**: CVVH ideal; can consider PLEX or peritoneal dialysis in neonates (less effective); extracorporeal toxin removal if severe
- **Specific rx**: Address underlying acidosis, hyperammonemia, metabolic pathway block

Risks of rx

Overhydration, cerebral edema / herniation (may need ventilation + other modes to control ICP while maintaining cerebral perfusion w/ mannitol, hypothermia), protein malnutrition (if no protein >48h)

Hyperammonemia

PowerPlan	Metabolism Hyperammonemia Admit Orderset
Definition	Normal ammonia levels vary w/ prematurity, age, and catabolic state; usu 15-35 µmol/L (up to 100 µmol/L in neonates), nl <50 µmol/L. Most IEMs >500, while ↑ NH_3 in liver failure, sepsis usually <500
Etiology / DDx	UCDs (OTC most common), hyperammonemia-hyperornithine-hypercitrulline (HHH) syndrome, organic acidemias (PA, IVA, MMA), FAODs (MCAD, LCAD, LCHAD), systemic carnitine deficiency, PC deficiency, THAN (esp in preemies), liver failure from any cause, VPA toxicity, infection with urease-positive organism (e.g., *Proteus*, *H pylori*), post-transplant idiopathic HA

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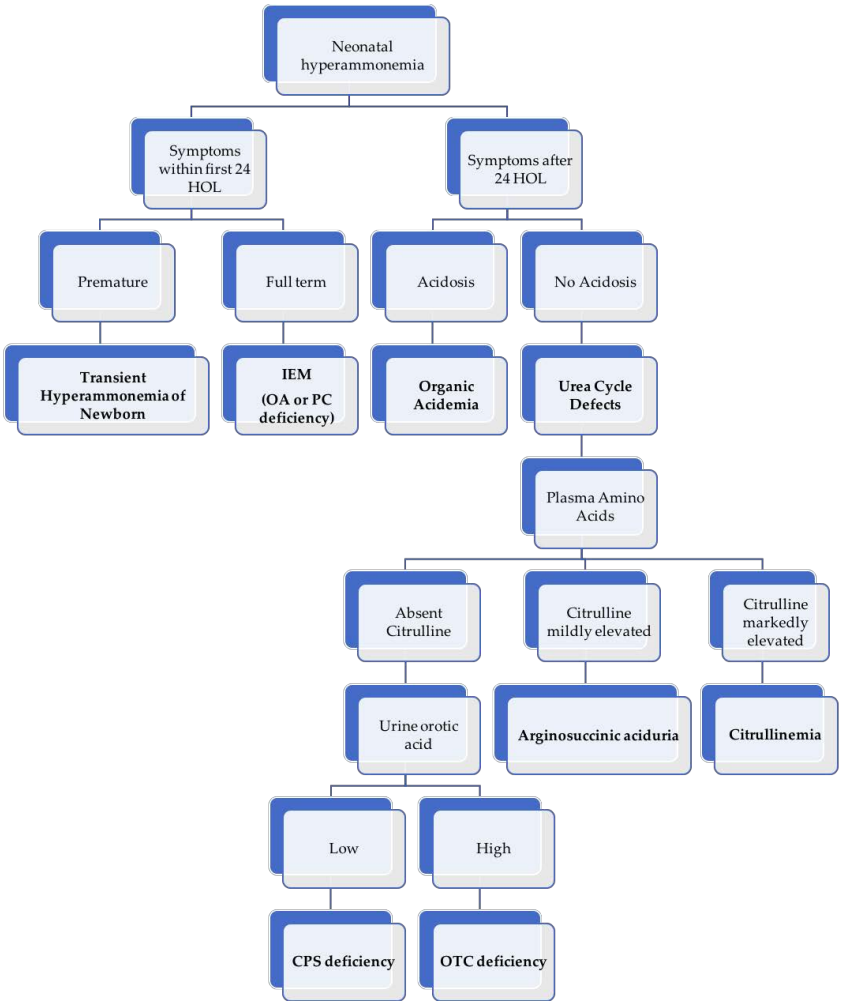
Hyperammonemia

Pathophys

Inc NH_3 in brain → astrocytes turn NH_3 into Gln → inc intracellular osmolality → cerebral edema. NH_3 inhibits α-KG DH → TCA cycle blocked → pyruvate ⇒ lactate, α-KG ⇒ Glu → excitotox/sz → cerebral edema, possible herniation. Even **brief** periods of hyperammonemia in infants may have chronic sequelae

Approach to DDx[3]



Presentation

Lethargy/delirium + vomiting → coma, sz, opisthotonic posturing; central hyperventilation/resp alkalosis; cerebral edema → inc ICP → HTN + bradycardia, CN VI palsy, encephalopathy

Workup

free-flowing sample in Na heparin tube w/o tourniquet, send to lab **on ice STAT** w/ chem 10, VBG, CBC/diff, plasma AAs, urine OAs, repeat NH_3 at least q6-8h alongside daily chem and others PRN

Treatment

General measures/ABCs as above.

Stop protein intake: start hydration and nutrition as described above for goal GIR of 10-12 mg/kg/min, aiming to provide 120-150 kcal/kg/day

Give ammonia scavengers: sodium benzoate 250 mg/kg + sodium phenylacetate 250 mg/kg + 10% Arginine HCl (600 mg/kg) - avoid in Arginase deficiency

Mix the above in 35 ml/kg of 10% dextrose (no additional sodium) and give over 90 min

Repeat the same solution over 24 hours

Consider **dialysis** for NH3 >175 mcmol/L (preferably ECMO-based, requiring NICU transfer)

Reintroduce protein w/in 48h to prevent endogenous protein from breaking down