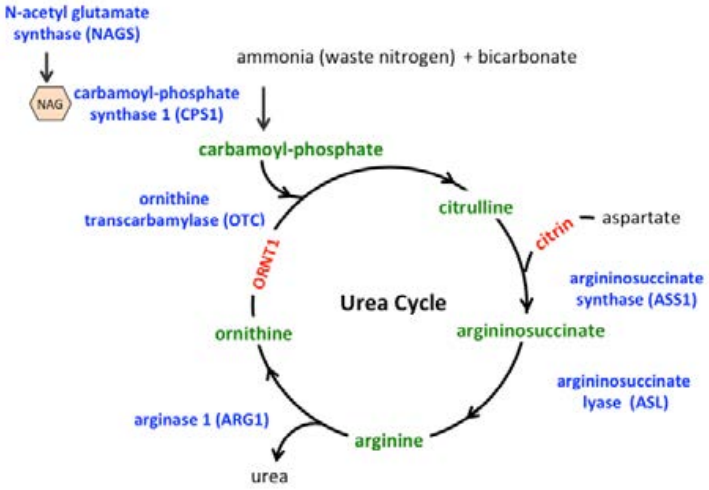
Urea Cycle Defects

PowerPlans	Several, including for known defects and unknown; search "metabolism urea" in PC for full list
Biochemical Defect	Deficiency in any of the 6 UC enzymes, which converting toxic nitrogenous metabolites from protein turnover to non-toxic urea for urinary excretion → NH_3 accumulation. 
Presentation	Interim healthy period → **catabolic stressor** (stress, infection, surgery, or starvation) → vomiting, feeding intolerance, tachypnea (due to central hyperventilation) → encephalopathy and coma, with potentially irreversible brain damage if untreated.
Diagnosis	Labs w/ **hyperammonemia** and **respiratory alkalosis** → metabolic acidosis. Send plasma/urine levels of UCD metabolites and confirm with enzyme testing
Treatment	**Acutely**: immediate treatment of hyperammonemia (see full details in section below): Stop all protein intake (but no longer than 36-48h), give dex-containing IVF (10-25% @ 1.5xM) and IL (1-3 g/kg/d) through central line, NH3 scavengers (Ammonul = Na benzoate and Na phenylacetate) usually with IV arginine, avoid hypoNa (would exacerbate cerebral edema), prepare for HD (absolute if NH3 > 300 µmol/L) **Long term**: Low-protein diet, avoid catabolism, include missing UC intermediates, liver tplt

Disorder	Enzyme Blockade	Accumulated Substrate(s)	Presentation	Treatment
Ornithine Transcarbamylase Deficiency	OTC (carbamoyl phosphate + ornithine → citrulline) - **most common**, XLR	NH_3 → cerebral edema Glutamine elevation Low arginine and citrulline as cycle is blocked proximally Elevated **orotic acid** in urine	**Hyperammonemic crisis**, typically early on, p/w poor feeding, lethargy, tachypnea, hypothermia, irritability, vomiting, ataxia, seizures, hepatomegaly, coma **NOT** always evident on NBS, may flag for low citrulline	As above, alongside: citrulline/ arginine, ± carnitine, ammonia scavengers such as glycerol phenylbutyrate. **Consider ammonul for acute hyperammonemia**

Urea Cycle Defects continued on next page →