Differential Diagnosis by Clinical Manifestations

Later Onset
About 50% of patients with IEMs present beyond the immediate neonatal period (even as adults!)

History	*Episodic illness* precipitated by mild intercurrent illness, fasting, or change of diet, specific dietary preferences (e.g., autovegetarianism seen in conditions predisposing to hyperammonemia), behavioral issues such as ADHD (partially treated PKU)
Presentation	Can be classified into 2 patterns which may overlap: • **Acute**, presenting in a **metabolic crisis** w/ emesis, lethargy, seizures, tachypnea

Encephalopathy	**Without focal findings** look for predominant acidosis, hyperammonemia or hypoglycemia & work up as outlined below **With focal findings**: homocystinuria with thromboembolic event, mitochondrial disorders with CVA, biotin-responsive basal ganglia disease, some OA (striatal necrosis inorganic acidemias); cerebral edema in UCDs
Recurrent ataxia	MSUD, OTC, pyruvate dehydrogenase (associated peripheral neuropathy)
Psychiatric symptoms	UCD's, porphyrias, homocystinuria, cobalamin C disease, late-onset Tay Sachs
Dehydration	**Polyuria**: RTA, nephrogenic Diabetes Insipidus **Diarrhea**: glucose or galactose malabsorption, acrodermatitis enteropathica (Zn deficiency), sucrase isomaltase deficiency, congenital chloride diarrhea **Ketoacidosis**: MMA, IVA, PA, DM **Salt losing**: CAH, hypoaldosteronism
Reye syndrome-	UCD's and OA's, disorders of mitochondrial fatty acid oxidation and

• **Indolent**: **FTT, myopathies, neurological sequelae** (DD, ID, micro/microcephaly), dysmorphisms

Management of Metabolic Crises

General Principles

0. Consult metabolism!
1. ABCs: ? need for airway protection, intubation, mechanical ventilation, rehydration, inotropic support
2. Consider alternate dx: electrolyte imbalance, sepsis
3. Established dx: acute illness protocols above, family should have home / ED illness protocol

Acute Metabolic Encephalopathy

Definition	Acute **global cerebral dysfunction** → altered mentation w/ or w/o seizures NOT due to primary structural brain disease (e.g., tumor or hemorrhage) or infection (though some IEMs may cause strokes)
Etiologies	Hyperammonemia, metabolic acidosis-hyperlactatemia or ketosis, hypoglycemia, recurrent seizures ('excitotoxic' damage), specific toxins, e.g., copper deposition in Wilson's, electrolyte imbalances
Presentation	• Precipitated by high protein intake, catabolic state (fever/illness/GIB/fast), present w/ lethargy, AMS, seizures, tachypnea 2/2 metabolic acidosis or central stimulation by inc NH3 • FND, presentation @ older age, sudden onset, no PMHx, do NOT rule out IEMs