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Ethylene Glycol and Methanol Toxicity

- Methanol, Ethylene Glycol both produce osmolar gap and can be fatal
- Osmolar Gap with acidosis: Ddx: EtOH, isopropyl alcohol, methanol, ethylene glycol, ketoacidosis (diabetic or alcoholic), lactic acidosis, chronic renal failure (although hemodialysis will normalize osmolar gap)
 - Calculated osmolality = $2\text{Na} + \text{Glucose}/18 + \text{BUN}/2.8 + \text{EtOH}/4.6$

ETHYLENE GLYCOL:

- Found in paint solvents, fire extinguishers, windshield cleaner, anti-freeze, de-icer
- Sweet taste, no odor; in anti freeze configuration it is colorful since fluorescence is added
- 100cc can be lethal
- Rapidly absorbed – peak levels @ 2 hours post ingestion
- 20% excreted unchanged in urine; other 80% is metabolized
- The metabolites, not the ethylene glycol, are toxic

Ethylene glycol -----> glycolaldehyde -----> glycolic acid -----> oxalic acid

- **Symptoms:**
 - Early (30 minutes –2 hours) –secondary to intoxication from ethylene glycol itself
Nausea, vomiting, ataxia, slurred speech, nystagmus, lethargy, coma, seizure, respiratory depression, death
may have a slightly sweet odor on breath
osmolar gap
 - Late (beginning 4-12 hours post ingestion)
 - Symptoms: tachypnea, hypotension, agitation, confusion, seizure, coma; ARDS. cyanosis, pulmonary edema, death
 - LABS: metabolic acidosis, increased anion gap, osmolar gap, lactic acidosis (secondary to hypotension or lab error as glycolic acid can cause artifactual elevation in plasma lactate concentration)
 - Acute Renal Failure: glycolic acid may be toxic to renal tubules and oxalic acid may precipitate within tubules
 - proteinuria, oliguria and anuria within 12-24 hours s/p ingestion
 - if patient survives, ARF usually resolves s/p days to weeks but it can be permanent
 - Oxalic Acid precipitates as calcium oxalate crystals in brain, heart, kidney, lung and pancreas
 - 1/3 of patients will develop hypocalcemia
- **Diagnosis:**
 - Anion gap acidosis with osmolar gap in light of altered mental status and ARF
 - calcium oxalate crystaluria – monohydrate (needle shaped –may be misread as hippurate crystals) and dihydrate (envelope shaped)
 - If patient drank anti-freeze, which contains fluorescein dye, the urine may fluoresce under a wood's lamp (found in ED) – normal urine does not fluoresce at all
 - Ethylene Glycol level – but this can take a while to come back

METHANOL:

- Found in shellac, varnish, de-icing solutions, paint remover, copy machine fluid, windshield wiper solution
- Peak serum levels 1-2 hours s/p ingestion
- Hepatic metabolism but 10% excreted unchanged in lungs and kidney
- Incidence of methanol overdose increases during times of EtOH restriction (wartime or prohibition) – typically there will be a local epidemic of people all drinking from the same distillery

- Lethal dose 50-100cc –
 - mortality >80% if patient presents with seizure, coma, pH<7.0 but mortality <6% if none of these symptoms/signs
 - In epidemics, 1/3 of people fully recover, 1/3 of people have permanent visual loss and 1/3 of people die
- Metabolites, not the methanol, are toxic

Methanol----->Formaldehyde-----> Formic Acid-----> CO2 and H2O

- **Symptoms:**

- Early: Mild inebriation, nausea, headache, weakness, abdominal pain, vertigo followed by a potentially asymptomatic period of 12-24 hours
 - Osmolar gap
- Late (after 12-24hours)
 - May have effects on liver, kidney, brain (including coma and death), lungs, GI tract, eyes
 - **Visual changes** are the classic methanol overdose symptom:
 - eye pain, blurry vision, decreased visual fields, central scotoma,
 - Eye exam: pupils dilated and sluggishly reactive, decreased light reflex, retinal sheen due to retinal edema and hyperemia of optic disk
 - blindness around 48 hours s/p ingestion –
 - Optic atrophy with demyelination may occur secondary to anoxia from the edema
 - if patient survives there is usually complete or almost complete recovery of vision over a few months
 - Metabolic acidosis. Osmolar gap
- **Diagnosis:** Osmolar gap, anion gap and visual changes

TREATMENT OF METHANOL AND ETHYLENE GLYCOL OVERDOSE:

- If pt presents to ED w/in first few hours s/p ingestion – charcoal and gastric lavage
- Sodium bicarb to treat acidosis – large amounts often needed; may also help excrete acidic metabolites by alkalinizing the urine
- Provide competition for the alcohol dehydrogenase – EtOH and Fomepizole have much more affinity for this than ethylene glycol does – remember, the toxicity from ethylene glycol is due to the metabolites not to the ethylene glycol itself – therefore, preventing metabolism allows time for it to be excreted unchanged or for it to be dialyzed off
- Treat with medications and/or hemodialysis until level of methanol or ethylene glycol is less than 20mg/dl
 - **EtOH:** 10- fold greater affinity for alcohol dehydrogenase
 - Patients who were drinking EtOH while ingesting ethylene glycol do better with fewer of the toxicities – they may present without acidosis, anion gap or symptoms **but** they will still have an osmolar gap
 - If patients arrives very late after ingestion the EtOH may not help as all of the metabolism will have occurred already – in this situation patient will have metabolic acidosis but will no longer have osmolar gap
 - Goal EtOH concentration is 100-200mg/dl – should monitor
 - Dosage: Oral or IV EtOH – if charcoal was given then double oral dosage
 - IV comes in 5 or 10% solutions (5 or 10g/100ml)
 - 20% oral solutions used (21 cc of 95% EtOH mixed in 79cc of H2O)
 - 45% EtOH is 90 proof: 95% EtOH is 190 proof
 - Non-drinkers: Load 0.6g/kg then maintenance with 66mg/kg per hour
 - Drinkers: Same load but maintenance of 154mg/kg/hour
 - Hemodialysis: 240mg/kg/hour
 - **Fomepizole:** Competitively inhibits alcohol dehydrogenase even better than EtOH; however, if patient has ingested EtOH along with ethylene glycol or methanol the half life of EtOH will also be prolonged
 - **Preferred** method of treatment rather than EtOH

- Unlike EtOH, serum fomepizole concentrations are not monitored
- Unusual side effects: Headache, nausea, bradycardia, dizziness, eosinophilia, mild elevation of liver enzymes
- Dosage: Load with 15mg/kg in 100cc D5W over 30 minutes then 10mg/kg every 12 hours for 48 hours then 15mg/kg every 12 hours (Dose increased at 48 hours because fomepizole revs up cytochrome P450 system and thus increases its own metabolism)
Give every 4 hours during hemodialysis
- \$1200 for a 1.5gm vial
- **Hemodialysis:** This is the only method that removes the toxic metabolite itself
 - Indications: Ethylene Glycol concentration >20mg/dl
Methanol concentration > 50mg/dl
Metabolic acidosis
Visual or mental status changes
- **Vitamins:**
 - Folic Acid helps metabolize formate to CO₂ and H₂O in methanol OD; 50-70mg IV q4 hours x 24 hours
 - Pyridoxine (50mg IM QID) and thiamine (100mg IM QID) help convert glyoxalate into glycine rather than oxalate in ethylene glycol OD
- **Diureses:** Fluids and mannitol diureses may prevent tubular blockade by oxalate crystals in ethylene glycol OD
- **Calcium** and other electrolytes should be replaced

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