**Toxicology Overview**

1. Toxidromes
   1. Dry skin and mouth, hyperthermic, mydriasis, agitation, urinary retention, tachycardia, hypertension
      1. = Anticholinergic toxidrome
      2. Inciting exposures relevant to pediatrics:
         1. Diphenhydramine
         2. Promethazine
         3. Scopolamine
         4. Cyproheptidine
         5. Quetiapine
         6. Some mushrooms
         7. “Night shade” (belladonna) family of flowering plants.
   2. Diarrhea, urinary incontinence, miosis, bronchospasm, bradycardia, emesis, salivation
      1. = Cholinergic toxidrome
      2. Inciting exposures relevant to pediatrics:
         1. Organosphosphate or carbamate containing insecticides
   3. Drowsiness (to obtundation), bradypnea/apnea, bradycardia, hypotension
      1. = Opioid toxidrome (also can be seen with clonidine ingestion)
      2. Inciting exposures relevant to pediatrics:
         1. Opiate containing pain medications
   4. Agitation, tremor, tachycardia, hypertension, mydriasis, sweating
      1. = Sympathomimetic toxidrome
      2. Inciting exposures relevant to pediatrics:
         1. Pseudoephedrine
         2. Cocaine
         3. Amphetamines
2. Antidotes
   1. Opiates: Naloxone (for severe respiratory depression, may precipitate withdrawal in the context of chronic use/abuse)
   2. Clonidine: Atropine (for bradycardia)
   3. Physostigmine: anticholinergic agents **other than TCAs**.
      1. Has a short half-life, so usually only used for severe agitation or to confirm diagnosis.
      2. Can cause seizures or life-threatening arrhythmias if given in context of TCA overdose.
   4. Methanol: fomepizole
   5. Ethylene glycol: used to be ethanol, but now fomepizile
   6. Organophosphates: atropine **and** pralidoxime
   7. Serotonin: cyproheptidine
3. Specific ingestions
   1. Acetaminophen
      1. Clinical presentation: Nausea vomiting progressing over 24 hours to abdominal pain and laboratory evidence of liver injury and disfunction, then followed (around 48-72 hours) by coagulopathy, liver failure, multi-organ failure, and death.
      2. Workup: Acetaminophen level (as well as checking for co-ingestions), PT, INR, liver enzymes. (Note: Rumack-Matthew nomogram begins at 4 hours post-exposure. Earlier acetaminophen levels are not useful).
         1. 4 hour cutoff for treatment is 150ug/mL
         2. 10 hour cutoff for treatment is ~50ug/ml (53.03 to be exact)
      3. Treatment:
         1. If presents within 1 hour of exposure, give activated charcoal for ingestions > 150mg/kg (or 7.5 g if 12 years or older)
         2. N-acetyl cysteine if indicated by Rumack-Matthew nomogram.
            1. Early presenter protocol: 150mg/kg over 60 minutes, 50 mg/kg over 4 hours (~12.5 mg/kg/hour), 100 mg/kg over 16 hours (~6.25 mg/kg/hour).
            2. Late presenter protocol: 150mg/kg over 60 minutes followed by 15mg/kg/hour for 44 hours. (???)
            3. Response to anaphylactoid reactions

Flushing: continue NAC

Hives: Stop infusion, give diphenhydramine, epinephrine, and steroids, and resume infusion when rash has resolved.

Angioedema and/or wheezing: Stop infusion, give diphenhydramine, epinephrine, and steroids, and resume infusion when symptoms resolve (but at least 1 hour after epinephrine).

Hypotension or persistent symptoms: treat anaphylaxis, do not resume infusion, give oral NAC instead. **(This is Danielle’s favorite option).**

* + - * 1. Continue NAC after 22 hour protocol if ALT is still elevated or acetaminophen level has not dropped below limit of detection.
      1. Monitor AST/ALT and PT/INR
         1. Note: NAC and acetaminophen can elevate INR even in the absence of impaired hepatic synthetic capacity, up to 1.5.
      2. Hepatic failure requiring transplantation as a result of acetaminophen overdose is exceedingly rare in children. Indications for transplant include:
         1. Acidosis (ph < 7.3) **by itself OR**
         2. Encephalopathy **and**
         3. Creatinine > 3.4 **and**
         4. Prothrombin time > 100 seconds
  1. Aspirin
     1. Clinical presentation: Tinnitus, nausea, vomiting, possibly agitation and confusion or coma, combined with a mixed acid/base disturbance (respiratory alkalosis with metabolic acidosis), hypokalemia, and hyper- or hypo-glycemia.
        1. Typically, symptoms are apparent with ingestions > 300mg/kg and serum levels > 30mg/dL.
     2. Workup: Monitor blood gas, electrolytes, coags, and salicylate levels every 2 hours until stable.
     3. Treatment:
        1. Activated charcoal if exposure < 1 hour prior to presentation
        2. Maintain K levels > 4 (to minimize excretion of H+ into urine)
        3. Alkalinize if salicylate level > 30 mg/dL, with target urine pH > 8.5 (and serum pH up to 7.55)
           1. Sodium bicarb dosing

Initial: 1 to 2 mEq/kg (maximum 100 mEq) IV push over 3 to 5 minutes and/or

Maintenance: 100 to 150 mEq sodium bicarbonate in 1 L of D5W, at 1.5 to 2 times maintenance rate

* + - 1. If altered mental status, supplemental glucose **regardless of serum level** (as CSF levels may be paradoxically low).
      2. Consider preparations for hemodialysis.
  1. Anti-hypertensives
     1. Clinical presentation: hypotension, bradycardia, hypoglycemia (beta-blockers) or hyperglycemia (calcium channel blockers).
     2. Workup: Cardiac monitoring, blood glucose monitoring
     3. Treatment:
        1. Activated charcoal (if less than 1hour since ingestion)
        2. Fluids
        3. Dextrose if hypoglycemic
        4. Atropine and/or naloxone (for clonidine ingestion)
        5. Glucagon (especially for beta-blocker ingestion)
        6. IV Calcium (for calcium channel blocker)
        7. High dose insulin + glucose (presumably in the ICU)
        8. Vasopressors (definitely in the ICU)
  2. Iron
     1. Clinical presentation: multiphase syndrome evolving over days featuring GI symptoms for first few hours, followed by up to a day of apparent recovery, followed by cardiovascular collapse, acidosis, hepatic failure, GI bleeding, coma and death. Bowel obstruction from GI scarring is a long-term complication.
     2. Workup: Abdominal films, iron level 4-6 hours after ingestion, and monitoring of electrolytes, blood gas, and liver enzymes and function (coags).
        1. Toxicity is apparent with levels >350ug/dL (somewhere around 20-40mg/kg of elemental iron—note that commonly available supplements are 12-30% elemental iron as a percent of total iron salt)
     3. Treatment
        1. Supportive care
        2. Chelation with deferoxamine
           1. If iron level >500ug/dL, or ingestion of >60mg/kg **elemental** iron, or “significant” number of radioopaque pills on xray.
           2. Initial dose: 5-15mg/kg/hour, titrating up every couple of hours

Details of starting dose and duration of therapy remain controversial so get help from a toxicologist.

Note: chelation therapy will turn urine orange/red as iron is chelated and cleared.

* 1. Methemoglobinemia
     1. Clinical presentation: Headache, dyspnea, syncope, confusion, chest pain, seizures, acidosis, coma, death.
        1. May be hereditary or secondary to dapsone, benzocaine, hydroxychloroquine,
     2. Workup: Pulse oximetry, blood gas (desaturation—typically 85%—unresponsive to increased FiO2 combined with normal PaO2 is the classic finding), chocolate brown blood, co-oximetry. (Note that many blood gas machines can measure methemoglobin directly).
     3. Treatment: remove offending agent, give oxygen and methylene blue (**unless** patient has G6PD deficiency!)
  2. Lead
     1. Presentation: anemia, abdominal pain, fatigue, declining school performance, encephalopathy, blue-black lines along gums and at edge of teeth
     2. Workup: Lead level, CBC. Consider abdominal xray if PICA to identify intraintestinal load of lead containing material. If moderate to severe intoxication, add CMP, calcium, magnesium, iron studies, and UA. If encephalopathic, add head CT.
     3. Treatment:
        1. Asymptomatic Mild intoxication (<45ug/dL): removal of exposure, whole bowel irrigation if intraintestinal lead found on xray, repeat testing in 1-12 weeks (depending on level)
        2. Asymptomatic Moderate intoxication (45-69ug/dL): above, plus oral succimer chelation (admit to hospital and ensure removal of exposure).
        3. Asymptomatic Severe intoxication: (>70ug/dL): above, plus calcium disodium edetate started 48 hours after succimer.
        4. **Symptomatic** patients should receive BAL and, once urine output is demonstrated, calcium disodium edetate.
           1. These patients also require management of encephalopathy, which may include CNS imaging and even LP (**Note: lead poisoning can elevate ICP**. Try to avoid LP, and take small volume if performed).
        5. It is **essential** that the child be discharged to a lead-free environment, and ongoing lead monitoring is arranged.
  3. Alcohols (Ethanol / Methanol / Ethylene Glycol)
     1. Presentation: intoxication, nausea/vomiting, vision changes (methanol), hypoglycemia (ethanol), renal failure (ethylene glycol).
     2. Workup: blood levels, blood gas and lactate (high anion gap without lactate without elevated lactate or ketonuria), blood sugar.
     3. Treatment
        1. Ethanol intoxication: supportive care, dextrose (with concurrent administration of thiamine if comatose)
        2. Methanol:
           1. **Immediate hemodialysis if acidotic**, end organ damage, and/or serum level > 50 mg/dL with pH < 7.3
           2. Bicarb (1-2 meq/kg load, then 133 meq of sodium bicarbonate per liter of D5W at 1-2x maintenance rate)
           3. Fomepizole (15 mg/kg IV, followed by 10 mg/kg every 12 hours)
           4. Folate
           5. Early treatment is essential to prevent irreversible vision loss and CNS injury from formation of formic acid.
        3. Ethylene glycol: same as methanol, except give plus thaimin and pyridoxine instead of folate (shunts metabolism to less toxic metabolites).
           1. Again, **immediate hemodialysis if acidotic**, end organ damage, and/or serum levels > 8.1 mmol/L with pH < 7.3
  4. Selective serotonin reuptake inhibitors (Serotonin syndrome)
     1. Presentation: Tremor, hyper-reflexia, clonus, diaphoresis, mydriasis, continuous horizontal eye movements, agitation, hyperthermia, autonomic instability, seizures.
     2. Workup: CK, screen for co-ingestions, standard workup for altered mental status if indicated.
     3. Treatment:
        1. Supportive care focused on normalization of vital signs
           1. Autonomic instability can be lead to rapidly changing vital signs and thus short acting agents should be used
        2. Benzodiazepines for agitation
        3. Cyproheptidine for severe symptoms
        4. **Note:** severe symptoms, including hyperthermia and/or marked agitation or significant vital sign abnormalities are indications for ICU management.