Toxicology

Decontamination

Focus on activated charcoal and whole bowel irrigation. NO gastric lavage, ipecac, or dilution!

Activated Charcoal (AC)

- How: increased surface area to absorb many toxins (prevents toxin from going into systemic circulation → prevents toxicity)
- How much: ideal is 10:1 (activated charcoal:drug)
  - Example: 100 aspirin tablets (325mg each) = 32.5g aspirin = >300g AC
- Contraindications:
  - Obtunded with no airway protection (risk AC vomited/aspirated)
  - Toxin with risk of seizure or obtundation (risk AC vomited/aspirated)
  - Ileus (AC will sit in the intestines and not move)
  - Hydrocarbons (AC does not bind them well)
  - Caustic ingestions (goal is for endoscopy to evaluate the esophagus for burns; AC will blacken the entire passage and make viewing impossible)
  - Alcohols
  - Metals

Whole Bowel Irrigation (WBI)

- How: iso-osmotic solution taken in LARGE volume → mass effect and will push everything through; no intrinsic laxative effect
- Example: polyethylene glycol (Go-Lytely)
  - Use with ingestions of iron, lithium, sustained release medications (beta-blockers, calcium channel blockers), enteric-coated tablets, body packers (e.g. body packers)
  - Give: 1-2L per hour (adults) or 500mL per hour (children)
  - Consider placing a nasogastric tube (NGT) with a pump to get the max volume in rapidly; continue until what comes out the other end is clear and effluent
  - Labor intensive for the patient and the staff

Gastric Lavage (stomach pumping)

- No longer used in the Emergency Department, but may show up on exam
- Consider use in a test question if **ingestion WITHIN ONE HOUR**
- Large gastric tube is placed via mouth/nose and saline is instilled into the tube and removed by either gravity or active suction
- Why this a method is NEVER used:
  - Most sustained-release too big to be removed
  - May push drugs past pylorus
  - May increase drug solubility

Ipecac/Emesis

- No longer manufactured
- Induced emesis has no role and is NOT used in the Emergency Department

Acetaminophen

- The key to understanding acetaminophen toxicity is to understand its breakdown pathways
- Normally, the CYP450 pathway breaks down acetaminophen to its toxic metabolite NAPQI, which is conjugated with glutathione and inactivated
- In overdose, glutathione stores are overwhelmed and depleted → NAPQI accumulates → toxicity in the liver, pancreas, and kidneys
- N-acetylcysteine (NAC) replenishes the liver's stores of glutathione, allowing for NAPQI to be metabolized safely

N-acetylcysteine (NAC)

- **PO & IV dose are EQUIVALENT efficacy**
- PO dose: 140mg/kg load; then 70mg/kg q4hr
- IV dose: 150mg/kg load; then 50mg/kg over 4 hrs; then 100mg/kg over 16 hrs
    - Possible anaphylactoid reactions so infuse the initial load over one hour

Acetaminophen Nomogram

- **ACUTE single ingestion poisonings ONLY**
- Serum acetaminophen levels at **≥4 hours** (<4 hours NOT useful, unless ZERO)
- Other useful lab tests: PT/INR, AST/ALT, bilirubin, albumin, lipase
- Numbers to know:
    - **Acute single ingestion overdose: >150mg/kg**
    - Chronic dose is variable: >4g per day

Fun fact: there is NO reported case of death in the United States of a child (<6 years) from an acute single ingestion of acetaminophen

NSAIDs

- COX inhibitor decreases prostaglandin (anti-inflammatory, analgesic, antipyretic)
- Generally well tolerated in acute poisonings
- GI upset common, **acute GI bleed uncommon**
- Large ingestions: somnolence, ataxia, and disorientation
- Massive ingestions: coma, metabolic acidosis, seizure
- Chronic use: peptic ulcer disease, analgesic nephropathy, and agranulocytosis
- Tx: supportive care

Opioids

- Analgesia, antitussive, adjunct to anesthesia
- Toxicity: respiratory depression, pinpoint pupils
- Reversal agent: **naloxone**
- Withdrawal: nausea/vomiting, diarrhea, abdominal pain, piloerection; not life-threatening except in neonates
- Meperidine: can cause seizure from the metabolite
- Tramadol: can cause seizure and has a NARROW therapeutic index
- Methadone: QT prolongation, torsade de pointes
- What you DO see on the urine tox screen: natural derivatives
    - e.g. heroin, morphine, codeine, hydrocodone, oxycodone
- What you DO NOT see on the urine tox screen: synthetic derivatives
    - e.g. fentanyl, hydromorphone, buprenorphine, methadone, meperidine
- Drug interactions: risk of serotonin syndrome (especially meperidine, tramadol, dextromethorphan) when used with antidepressants

Alcohols

- Methanol toxicity: metabolized to formic acid and causes blindness
- Ethylene glycol toxicity: metabolized to oxalic acid, which binds calcium and precipitates in the kidneys → renal failure
- Isopropyl alcohol toxicity: makes you clinically intoxicated; you get better because it is metabolized to acetone, which you breathe out
- Methanol, ethanol, fomepizole all metabolized by **alcohol dehydrogenase**
- Treatments for acute toxic alcohol ingestions:
    - Ethanol or fomepizole (for alcohol dehydrogenase inhibition)
    - Hemodiaylsis for methanol, ethylene glycol, propylene glycol
    - Supportive care alone possible for ethanol, isopropyl alcohol

Serum Osmolal Gap

- Serum osmolal is both measured and calculated; a large difference between the two indicates the presence of an osmotically active substrate (in the appropriate clinical context, this could be a toxic alcohol)

Serum Osm Gap* = Osm calculated – Osm measured (normal -14 to +14)
Osm calculated = 2*Na +Glucose/18 + BUN/2.8 + BAL/4.6

**Osm measured and serum chemistry must be sampled simultaneously*

- The serum osmolal gap only helps you if it is large (specific but not sensitive)

Fun fact: Pediatric patients with acute alcohol ingestion may present with hypoglycemia

Lidocaine

- Mechanism: blocks Na channels in nerve fibers, impairing nerve conduction (at higher doses can affect CNS and cardiovascular systems)

	ESTERS	AMIDES
Differentiate by	ONE "I" in the name	TWO or more "I"s
Examples	cocaine, procaine, benzocaine	lidocaine, mepivacaine, bupivacaine
Duration of action	SHORT	LONG
Metabolized by	cholinesterase	liver
Other facts	more allergic reactions due to PABA metabolite or preservative	can accumulate in the liver (dysfunction or large doses)

Fun fact: as a local anesthetic, if a patient has an allergy to lidocaine, you can use the crash cart lidocaine (preservative free!) or use diphenhydramine IV solution (also has Na channel blockade)

- CNS toxicity: perioral numbness, slurred speech, seizure
  - Stop the seizure (benzodiazepine) and let the patient metabolize
- Cardiovascular toxicity: ventricular tachycardia (VT), ventricular fibrillation (VF), reentrant arrhythmias, AV block
  - VT/VF tx: sodium bicarbonate IV push
- Methemoglobinemia (cyanosis, not responsive to O2, tx with methylene blue)
- Allergic reaction: epinephrine, steroids, H1 and H2 blockers
- MAX dose lidocaine: plain = 4mg/kg; lidoacine with epinephrine = 7mg/kg
- New antidote = lipid rescue

Anticholinergics

- Cholinergic mnemonic (SLUDGE or DUMBELLS):
  - Diarrhea, urination, miosis, brady, emesis, lacrimation, lethargy, salivation
- Anticholinergic mnemonic
  - Blind as a bat, mad as a hatter, red as a beet, hot as a hare, dry as a bone
- **Peripheral effects**
  - Mydriasis, hot/dry skin (no sweat) and flushing (vasodilation), HYPERthermia, dry mucous membranes, ileus, urinary retention (put in a foley)
- **Central effects**
  - Agitation (passive), delirium, somnolence, coma, seizure
- Examples: atropine, antihistamines (diphenhydramine), Jimson weed, cyclic antidepressants (variable), phenothiazines
- Tx: supportive care and benzodiazepines
- **Physostigmine** (acetylcholinesterase inhibitor)
  - AVOID if known cyclic agent, wide QRS, seizure, reactive airway disease

- Crosses the blood-brain-barrier
- Usually NOT the answer on the exam unless there is no other option
- Consult toxicology or poison control before using this

Anticoagulants

Warfarin

- Mechanism**:** inhibit vitamin K dependent clotting factors: II, VII, IX, X (follow INR)
- Duration: 2-7 days
- Indications for reversal
  - Asymptomatic: HOLD warfarin
  - Active bleeding (if INR severely elevated): FFP, Vitamin K
- Unusual to eat enough "super" warfarin to get symptomatic
- Skin necrosis (early protein C inhibition → hypercoagulable state): rare, seen in 2-5 days; tx with FFP/vitamin K and discontinue warfarin

Heparin

- Mechanism**:** inactivate thrombin and activated factor X (Xa)
- Low molecular weight heparin (LMWH): measure anti-factor Xa activity
- **Protamine sulfate**
  - Reverses heparin, somewhat reverses LMWH
  - Derived from fish sperm
  - Dose: 1mg protamine for every 100units heparin
  - Clinically often unnecessary as heparin has short half-life
  - Adverse effects: allergic reactions and anticoagulant if overshoot dose
- **Heparin-induced thrombocytopenia (HIT) and thrombosis**
  - Abnormal antibodies that activate platelets
  - Up to 5% patients treated with heparin
  - Develops in 5 days in naïve patients; minutes-hours with prior exposure
  - Diagnosis: clinically if platelets decrease by >50% or confirm with antibodies
  - Alternative agent: argatroban
  - HIT associated with THROMBOSIS

Clopidogrel

- Mechanism: anti-platelet agent
- Adverse events: hemorrhage, TTP, neutropenia
- Tx: platelets

Newer Anticoagulants

Dabigatran

- Mechanism: direct thrombin inhibitor (inhibits thrombus formation)

- Thrombin allows conversion of fibrinogen to fibrin
- Tx: dialysis, albumin (questionable role for prothrombin complex concentrate)

Rivaroxaban

- Mechanism: direct Factor Xa inhibitor, does not require cofactors for its anticoagulant effect
- Tx: supportive (no known reversal agent)

Antiemetics

	Phenothiazines	5HT3 (serotonin) antagonists
Mechanism	Block dopamine receptors	Block 5HT3 receptors
Indications	N/V, antipsychotic, intractable hiccups	N/V
Adverse Drug Reactions	Sedation, dystonia, parkinsonism, local tissue injury (parenteral)	Well-tolerated
Toxicity	TCA-like, seizure, VT, hypotension, pinpoint pupils	QT prolonged and torsades
Agents	Prochlorperazine (compazine), Promethazine (phenergan), Chlorpromazine (thorazine)	Ondansetron (zofran)

- **Torsades de pointes**
  - Polymorphic ventricular tachycardia (associated with prolonged QT)
  - Anything that can increase your QT can increase your risk for torsades
  - Many meds can cause torsades: phenothiazines, antidysrhythmics, butyrophenones (Haldol), macrolides, fluoroquinolones, methadone, ondansetron
  - **Tx**: **Magnesium 2g IV over 60 sec**; overdrive pacing (get capture and control rate at 100bpm); isoproterenol (beta-agonist increases heart rate → "chemical pacing")

Bronchodilators

- Mechanism: beta2 agonists
- Adverse effects: tachycardia, palpitations, anxiety, tremors, hyperkalemia

Corticosteroids

- Mechanism: complex (inhibits all inflammatory mediators)
- Indications: anti-inflammatory, immune suppressant
- Adverse drug reactions: moon face, buffalo hump, striae, hyperglycemia, fluid retention, infection, psychosis, adrenal suppression
- Agents: prednisone, dexamethasone, methylprednisolone

Cocaine

- Mechanism: inhibit neuronal uptake of catecholamine, Na channel blockade (anesthetic)
- Use: local anesthetic, hemostasis
- Toxicity: hypertension, hyperthermia, rhabdomyolysis, MI, seizure, VT
- Tx: benzodiazepine, cooling, nitrates, CCB (e.g. nicardipine)
- **Avoid beta-blocker (do not want unopposed alpha activity)**
    - If you give a beta-blocker (BB, there is unopposed alpha effect

Amphetamines

- Mechanism: catecholamine release
- Indication: ADHD, weight loss
- Toxicity: HTN, tachycardia, hyperthermia, intracranial hemorrhage, rhabdomyolysis
- Tx: benzodiazepine, cooling, nitrates, CCB (AVOID BB)

Fun fact: Pinpoint pupils can be caused by select opiates, cholinergics, phenothiazines, barbiturates

Drugs of Abuse

K2 Spice/Synthetic cannabinoids

- Plant and herbal ingredients that are smoked
- Marketed as incense or potpourri with statement “not for human consumption”
- Presentation: anxiety, paranoia, tachycardia, agitation, diaphoresis
- “Herbal Marijuana alternatives”
- Agonists at endogenous cannabinoid receptors
- Herbal components may contribute to high

Hallucinogenic amphetamines

- Substituted amphetamine structure with serotonergic properties
- Popular in the 1960s; example MDMA (ecstacy)
- Tx: supportive care, benzodiazepine (for agitation), IV fluids (hydration), cooling measures (hyperthermia), possible intubation and paralysis
    - No acidification of urine (does not reverse toxicity, may worsen rhabdo)

Fun fact: Hyperthermia is a common cause of death in amphetamine overdose

GHB

- "Date rape drug"; rapid onset; hard to trace
- Onset 15min and duration 2-6 hours
- Side effects: euphoria, decreased inhibitions, "prosexual" properties, increased tactile sensation, muscle relaxation
- Toxicity**: bradycardia, bradypnea, coma, rapid awakening,** disorientation, loss of coordination, hypotension, lethargy, and deep sleep
- Dx: Made clinically or by history
  - Drug is so rapidly cleared from the body that checking a lab value is NOT usually helpful
  - Serum levels last 6 hours, urine levels last 12 hours
- Tx: Intubation may be required
- **GHB withdrawal**
  - Chronic use: hypertension, tachycardia, agitation/anxiety/confusion, diaphoresis, hallucinations/delusions, tremor, insomnia, seizure
  - Tx: supportive, benzodiazepine, barbiturate, consider baclofen

Bath salts

- Powder snorted, ingested, injected, or smoked
- Inexpensive, easily manufactured; marketed as "bath salts" and "not for human consumption"; also sold as "insect repellant" or "plant food"
- Similar to other sympathomimetic poisoning although adrenergic effects may be less prevalent (similar to MDMA)
- Hallucinations, tremors, hyperreflexia, tachycardia, hypertension
- CNS stimulation (agitation, delirium, acute psychosis), mydriasis, diaphoresis, hyperthermia, bruxism
- Users report need to "redose often", which can lead to hours-days of abuse
- Tx:
  - Agitation: benzodiazepine, large doses
  - Hypertension: benzodiazepine, AVOID BB including labetalol (unopposed alpha effect), consider nitroglycerin or nicardipine infusions
  - Hyperthermia: benzodiazepine (sedation), aggressive active cooling measures, RSI with neuromuscular blockade in severe cases (do NOT use succinylcholine)

Fun fact: make sure your get a core temp with cocaine, amphetamine, and bath salt abuse. It is the HYPERthermia that can kill you!

Snake Envemonation

North American Snake Classification

- Crotalinae (Crotalids): rattle snakes, copperheads, cottonmouths
- Elapidae: coral snakes

Crotalinae (Crotalid)

- Physical characteristics
  - Triangular or diamond shaped head
  - Elliptical or "cat like" pupils
  - Single row of scales behind the anal plate (if you flip the snake over)
  - Facial pits located anteriorly below eyes, heat sensing organ
  - Not all crotalinae have rattles
- Clinical presentation
  - Pain at the site
  - Metallic taste
  - Lightheaded, perioral numbness, N/V, diaphoresis
  - Local edema, progressive swelling, bleeding at the site, fasciculations, hemorrhagic blisters, thrombocytopenia, hypofibrinogenemia
- Tx: CroFab (antivenom) – the **ONLY indications for ANTIVENOM** are:
  - **Progression of swelling**
  - **Low platelets or low fibrin**

Fun Fact: just because you were bit by a snake does NOT mean you need antivenom!

Black widow spider (Latrodectus)

- Large black widow spider with **hourglass on ABDOMEN**
- Only FEMALE envenomates humans
- Found in woodpiles, out-house, hidden spaces
- Not aggressive (they feel threatened when you come in contact with them)

Exam question: you are in a hidden space (outhouse or a wood pile) and are bitten by a spider - what kind of spider most likely bit you? Black widow spider

- Bite characteristics: painful bite
- **Bulls eye lesion with central bite site**
  - **Venom: causes release of norepinephrine and epinephrine** (like injecting epi) and releases acetylcholine (vasodilation = red and wet)
- Tx: Pain control (opioids), benzodiazepine, antivenom (monitor for allergic rxn)
- Disposition: may require admission for pain control (can last 48-72 hours), can be discharged home if pain controlled; observe for 6 hours if anti-venom given

Fun Fact: there are NO reported deaths (even in children and elderly) of a black widow bite in the United States. BUT there are deaths from antivenom!

Brown Recluse Spider (Loxosceles)

- Small spider, violin-shape on the head
- **Three pairs of eyes** NOT four (may show up on exam)
- Southeast and Midwest United States
- Not aggressive
- Can cause "necrotic arachnidism"
- **Painless bite** leads to misdiagnosis
- Local reaction: erythema, induration, central ulcer may develop, may progress to necrosis, poor wound healing (can take weeks – months to heal)
- RARE: hemolysis, DIC, shock (the appearance of the wound is NOT related to the reaction)
- Tx: supportive only; tetanus update
    - Antibiotics only if secondary infection
    - Not supported but may see this on an exam: dapsone (problem is methemoglobinemia), hyperbaric oxygen, surgical excision
    - Skin grafting RARE

Scorpion (Centruroides)

- Arizona (United States) predominately
- Small, light to dark brown, two pincers and tail with telson (venom apparatus)
- Nocturnal feeding on insects (so envenomation occurs at night)
- **Neurotoxic venom**:
    - **Acetylcholine and catecholamine release**
    - Causes hypertension, tachycardia, diaphoresis, N/V, hypersalivation, bronchoconstriction
- CNS effects: opsoclonus, blurry vision, difficulty swallowing, slurred speech
- Somatic effects: fasciculations, jerking of extremities, paralysis (rare), respiratory arrest (rare)
- Tx: largely supportive care – NSAIDs, opioids, benzodiazepine, intubation (rare), and antivenom

Marine Toxins

Ciguatera

- Toxins from dinoflagellates
- Common fish: grouper, barracuda, Red snapper
- Mechanism: affects Na channels and cholinergic receptors
- Location: Hawaii, Florida
- Presentation: **onset within 6 hours**, gastroenteritis, **"hot/cold" reversal**, paresthesia, myalgia, weakness, "loose teeth," bradycardia, respiratory arrest
- Tx: **mannitol** (in fluid-repleted patients with significant neurologic symptoms)

Scombroid

- Results from poor refrigeration of fish
- Histidine in fish flesh broken down to **histamine** and histamine like compounds
- Fish: tuna, mahi mahi, blue fish, mackerel
- **Meal described as "peppery"**
- Presentation: rapid onset, skin flushing (skin/torso), gastroenteritis
- Tx: supportive, antihistamines, bronchodilators
- Must consider true allergy in differential diagnosis!
- Can see multiple affected in scombroid but NOT in allergy

Paralytic Shellfish poisoning

- Dinoflagettates in "red tide"
- Toxin blocks Na conductance and neuronal transmission in skeletal muscle
- Presentation: rapid onset <30min, gastroenteritis, headache, paresthesia, weak
- Tx: supportive

Jellyfish and Cnidaria

- Different species (sea nettle, anemone, fire coral)
- Nematocysts open by changes in pressure or physical contact → venom
- Effects: burning pain, pruritis, muscle pain, arrhythmia
- Tx: ABCs, analgesia, specific antidote for Box jellyfish
- For exams: **Acetic acid for 30min,** NOT urine/water

Lionfish, stonefish (Scorpaenidae)

- Divers, home aquariums
- Envenomation via contact with dorsal spines
- Immediate onset of pain lasts 1-2 days

- Rarely fatal (more common with stonefish)
- Stonefish antivenom available
- **Heat labile toxin → hot water** deactivates

Stingrays *(Scorpaenidae)*

- Stepped on while walking into water
- Usually strike in the lower extremity or foot
- **Heat labile toxin → hot water** deactivates, analgesics
- Barb sometimes retained → explore well
- Cover with **antibiotics for Vibrio**

Irritant Gases

- Multiple chemicals (chlorine, ammonia, hydrogen chloride)
- Common scenario: mixing bleach with ammonia
- Toxic effects depend upon properties of gas formed (water solubility and ability to get to safety)
- Effects: respiratory tract irritation, cough, dyspnea, conjunctivitis, prolonged exposure skin and respiratory burns, pulmonary edema
- Tx: remove from area and ABCs (humidified oxygen, bronchodilators, $NaHCO_3$)
- Stridor worrisome → may need intubation

Alkaline Ingestions

- **LIQUEFACTION necrosis** (like making soap)
- Cell death occurs from emulsification and disruption of cellular membranes
- Injury occurs within minutes of contact
- Risk for **PERFORATION or stricture formation**
- After 4-7 days, early granulation tissue after necrotic tissue sloughs off → perforation risk

Acid ingestions

- **COAGULATION NECROSIS**
- Pharynx and esophagus relatively resistant; **stomach most common**
- Emesis common
- Perforation risk (after 3-4 days); gastric outlet obstruction risk (over 2-4 weeks)
- Large exposures may → metabolic acidosis, hemolysis, acute renal failure, death

Disc Batteries

- Small, coin shaped batteries
- **PERFORATION risk**; may rupture → burn (can generate electrical current)
- Need for endoscopic retrieval is a function of size (smaller may pass) – usually >15mm diameter may pass

Chemical warfare agents

- Organophosphorus compounds (sarin, soman, tabun, VX)
  - Tx: high does of **ATROPINE**, 2-PAM, Diazepam (can give at the same time)
- Vesicants: nitrogen and sulfur mustard (skin blistering)

Botulism

- Infants: associated with **RAW HONEY** (exam question), ingest C. botulinum (in vivo) which then replicates → produces the toxin → gives them the botulism
- Adults
  - Ingest toxins directly
  - Wound: associated with **BLACK TAR HEROIN** use
  - Iatrogenic: **botox**
- Mechanism: inhibits your ability to release acetylcholine (unlike Guillain-Barre which is an ascending paralysis, this is a **DESCENDING paralysis)**
- Dysphagia, ptosis, blurred/double vision, respiratory failure, descending paralysis
- Floppy baby, constipation
- Tx: supportive care, ventilator support, antitoxins, contact the CDC

Beta Blockers (BB)

- Bradycardia (may be relative)
- Hypotension
- **HYPOglycemia** (may be normal)
- AV conduction blockade
- Tx: atropine, glucagon, epinephrine, calcium, high dose insulin (new technique)
- Other: GI decontamination (AC, WBI), IV crystalloid fluids, pacing, ECMO

Calcium Channel Blockers (CCB)

- Bradycardia, hypotension, **HYPERglycemia** (may be normal), AV conduction blockage, ileus
- TX: same as BB tx

HYPERglycemia distinguishes CCB toxicity from BB toxicity (HYPOglycemia)

Cardiac Glycosides

Digitalis (digoxin, digitoxin, foxglove, oleander)

- Mechanism: poisons the Na-K-ATPase pump (potassium cannot enter cell → hyperkalemia)
- Allows increased Ca2+ into the cell → increasing contractility
- Cardiac: bradycardia, PVCs (most common dysrhythmias), bi-directional VT
- CNS: agitation, lethargy, psychosis
- Visual: yellow-green vision (RARE but may show up on exam)
- GI: N/V, abdominal pain
- Metabolic: hyperkalemia (ACUTE only)
- Tx: decontamination (AC), Fab fragments, supportive care (IV fluids, atropine), pacemaker (avoid transvenous), **AVOID CALCIUM** on exam

For the exam: if a person is HYPERkalemia with dig toxicity – do NOT treat with calcium

Fun Fact: THE "BRADY bunch" causes bradycardia and HYPOTENSION and include: CCB, BB, digoxin, clonidine

Antidepressants

- Mechanism: breakdown of catecholamines
- TCA: inhibits reuptake of 5HT3, norepinephrine, dopamine
- SSRI: work on 5HT3 only

Cyclic antidepressants

- Antimuscarinic/anticholinergic
- Alpha-adrenergic blockage; Na channel blockage (QRS widening); GABA antagonism (seizures)
- CNS: lethargy, obtunded, seizure
- CV: QRS widening, QT prolongation, tachycardia, VT/VF, hypotension

Na channel blockade

- Causes: cyclic antidepressants, Benadryl, propranolol, procainamide, cocaine
- Sinus tachycardia, rightward axis, VT/VF, seizure
- Tx: $NaHCO_3$, alpha agonists (NE, phenylephrine), supportive care (IVF)

If a patient presents with a new widened QRS from drug ingestion, treat with sodium bicarbonate and then worry about the cause later

Carbon monoxide

- Incomplete combustion of fuels, gas heaters, **closed space fires**
- Mechanism: CO moves the oxygen dissociation curve to the LEFT
- Presentation: FLU-like, except the whole family comes in with the SAME symptoms
- Tx: oxygen (high flow with NRB mask), hyperbaric oxygen (HBO)
- Fetus is at increased risk of toxicity

Half-life of CO: on RA 4-6 hours; on 15L NRB 1 hour; on HBO (20-30min)

Clonidine (imidazolines)

- Example: clonidine, afrin, visine, naphcon
- Toxicity: opioid mimic (lethargy, obtundation, miosis, respiratory depression)
- CV: Bradycardia, hypotension, may see hypertension early
- Tx: supportive care (tactile stimulation for lethargy and respiratory depression)

Cellular Asphyxiant

Cyanide (CN)

- Mechanism: **inhibition** of oxidative phosphorylation (NOT uncoupling); blocks aerobic ATP production
- Shift to anaerobic metabolism → SEVERE lactic acidosis
- **Bitter almond smell**
- Combustion of wool, polyurethanes, silk: can all liberate CN
- Clinical presentation: syncope, seizure, coma, CV collapse, sudden death
- Tx: amyl nitrite or Na nitrite (both induce methemoglobinemia); Na thiosulfate (helps excrete CN)
    - Hydroxocobalamin (newer antidote), forms vitamin B12 when it conjugates CN

Hydrogen sulfide

- Decay of sulfur containing material (e.g. sewage); **"rotten egg smell"**
- Industrial source, volcanoes, sulfur springs
- Tx: remove from the source

Classic exam question: A man who is working underground with a septic tank becomes unconscious. Two men go down to check who also become unconscious. Police go down and become unconscious. What is it? Hydrogen sulfide

Disulfiram

- Inhibition of aldehyde dehydrogenase
- Disulfiram-Ethanol reaction: flushing, headache, N/V, chest pain, tachycardia
- With acute poisoning can become HYPOtensive (inhibits norepinephrine production)
- Tx: AC, IVF, pressors

Hydrocarbons

- **Sniffing** from container; **Huffing** from impregnated cloth; **Bagging** from plastic bag
    - Sudden sniffing death due to VT/VF
    - Tx: Beta antagonists
- **Ingestion**: typically not dangerous unless aspirated
- Accidental pediatric poisoning most common
- Tx: supportive care; **do NOT induce emesis;** NO activated charcoal
- Aspiration = ARDS

Hydrofluoric Acid

- Sources: glass etching, brick cleaner, wheel cleaner, rust remover
- Clinical presentation: **pain out of proportion**, delayed onset, dysrhythmias
- Toxicity: **hypocalcemia, hyperkalemia,** hypomagnesemia, QT prolongation, VT
- Tx: topical or SQ injection of Ca gluconate for small body surface area (BSA), IV calcium for large BSA or oral ingestion; consider Bier block

*For the exam: hydrofluoric acid presentation will focus on **HYPOcalcemia** (even though hyperkalemia kills you)*

HEAVY METALS

Iron

- Many different formulations
- Ferrous sulfate: most common, 20% elemental
- Lethal dose: >20mg/kg toxic, >60mg/kg potentially lethal

Fun fact: chewable iron has NEVER caused a death in a child…except on exams

- Mechanism: corrosive, inhibits oxidative phosphorylation, inhibits thrombin
- Stages of toxicity
  - Stage I: GI effects (<6 hours)
  - Stage II: Quiescent period (6-12 hours)
  - Stage III: Systemic
  - Stage IV: Resolution (possible GI scarring → gastric outlet obstruction)
- Workup: CBC, Chem7, lactate, Fe level, KUB (only helpful if positive)
- Tx: WBI, IV fluids, deferoxamine (do not give PO; administer if serum Fe level >500, or if serum Fe level >300 and symptomatic)

Lead

- Found in: old households from paint, old batteries, fishing weights, ceramic glaze
- Acute: abdominal pain, encephalopathy, seizure, death
- Chronic: malaise, weight loss, arthralgia, anemia (basophilic stippling of RBC)
- GI: abdominal pain
- CNS: acute headache, encephalopathy, seizure, **wrist drop**
- Dx: whole blood lead level
- Tx: supportive for seizure; chelators (BAL, EDTA, DMSA)

Isoniazid (INH)

- Mechanism: inhibition of pyridoxine co-factor necessary for GABA
- Presentation: sudden convulsions, status epilepticus
- Tx: pyridoxine IV (1gram for each 1gram INH; otherwise 5g IV empirically if unknown INH dose)

Lithium

- Mechanism: often secondary to drug interactions
  - do NOT give NSAID, ACEi or diuretic
- Presentation: GI (nausea/vomiting/diarrhea), tremors, T-wave inversions on EKG
- Tx: **IV fluid hydration**; WBI (no AC)
  - Lithium is renally eliminated: if patient is ESRD must dialyze

Monoamine oxidase inhibitor (MAOI)

- Mechanism: inhibit breakdown of biogenic amines (norepinephrine, epinephrine, dopamine, 5HT3)
- Food interactions: tyramine, aged cheeses, red wine (normally you have MAO in your gut to break this down but if you are taking MAOI you cannot break it down)

- Drug interactions: meperidine, sympathomimetics, dextromethorphan, SSRIs, lithium
- You need to ADMIT these patients
- Toxicity: tachycardia, hypertension (maybe delayed), hypotension (after the hypertension), HYPERthermia, agitation, seizure
- Tx: supportive care, nitroprusside (HTN), IV fluids (for hypotension)

Metal Fume Fever

- Welding history, flu like illness, tachyphylaxis occurs throughout week and symptoms improve, tolerance lost over the weekend, "Monday morning fever"
- **Normal CXR**

For the exam: welder who comes in every Monday with flu-like illness and improves during the week with a normal CXR = metal fume fever

Methemoglobinemia

- Oxidation of Fe2+ to Fe3+ on hemoglobin
- Methemoglobin cannot transport O2 → left shift of O2 dissociation curve with low O2 saturation
- Causes: nitrites, aniline dyes, medications, well water, hereditary
- Tx: Methylene blue; avoid use in G6PD deficiency (can cause hemolysis)

Mushrooms

- Amanita: hallucinogenic, not hepatotoxic
- Emesis: most common symptom
- **The 6-hour rule** (for exam)
  - If symptomatic **<6 hours** from ingestion; generally **LESS toxic**
  - If symptomatic **>6 hours** from ingestion; **hepatotoxicity concern**
- Muscarinic: DUMBELLS/SLUDGE
- Tx: atropine, IV fluids

Pesticides

- Organophosphates (OP): Acetylcholinesterase inhibitors, irreversible after-aging
- Carbamates: Acetylcholinesterase inhibitor, short acting, reversible; includes medications (physostigmine, pyridostigmine)
- Tx: **DECONTAMINATION** (dermal, nasogastric lavage, AC)
  - **Atropine (titrate until DRY secretions)**
  - Pralidoxime (2-PAM): used in OP poisonings (avoid in known carbamate)

Antiepileptics

Phenytoin

- Oral toxicity (gingival hyperplasia)
- No cardiac toxicity
- Seizure extremely uncommon
- IV toxicity: hypotension from propylene glycol diluent, NOT from phenytoin
    - Tx: give fosphenyotin (not phenytoin)
- Low therapeutic index
- Anticholinergic effects
- Na channel blockade

Carbamazepine

- Mechanism: similar to TCAs; Na channel blockade
- Low therapeutic index
- Clinical: anticholinergic, ataxic, nystagmus, GI upset, QRS widening
- One of few antiepileptics that paradoxically cause seizures at high doses
- Tx: sodium bicarbonate if QRS widened

Aspirin (salicylates)

- Mechanism: **UNCOUPLES** oxidative phosphorylation (cannot make ATP but have all the electrons trying to make it → generate LOTs of heat → HYPERthermia)
- Primary respiratory alkalosis (stimulation of respiratory center)
- Presentation: tachypnea, HYPERthermia, tachycardia, seizure, lethargy, primary respiratory alkalosis, mixed metabolic acidosis + respiratory alkalosis, ketosis (can mimic DKA)
- Treatment
    - Decontamination: AC or WBI
    - Alkalinization: NaHCO3 infusion
        - For exam: alkalinize URINE to enhance excretion
        - For practice: alkalinize SERUM to prevent CNS distribution
    - Dialysis indications: renal failure, severe academia, pulmonary/cerebral edema

For exam: dialyze salicylate toxicity if serum salicylate level >100mg/dL (acute) and >60mg/dL (chronic)

Sedatives

Benzodiazepines

- Mechanism: GABA agonist → decreases neuronal activity
- Indications: anxiolytic, hypnotic, seizure, alcohol withdrawal
- Toxicity: reversal agent = flumazenil (**do NOT use** → precipitate withdrawal)

Barbiturates

- Mechanism: similar to benzodiazepine, GABA agonist
- Indications: anesthesia, seizure
- Can cause: hypotension, bradycardia, decreased respiratory drive
- Can get "barb blisters" when down a long time (rhabdomyolysis concern)

Chloral hydrate (sedative hypnotic)

- Halogenated hydrocarbon
- Think about chloral hydrate in "sudden sniffing death"
- May sensitize myocardium to catecholamines causing VT
  - Tx: BB
- Synergistic effect with ethanol
- Radio-opaque on x-ray (however not reliable)

CHIPES mnemonic (radio-opaque on xray): Chloral hydrate, Heavy metals, Iron/Iodide, Phenothiazine, Enteric-coated, Solvents

Serotonin syndrome

- MUST have exposure to serotonerigc agent
- Usually exposed to 2 agents (e.g. MAOI, lithium, SSRI, antidepressant, ecstasy)
- Presentation: altered mental status, rigidity (lower extremity > upper extremity), hyperthermia, **CLONUS**, tremor, but a diagnosis of exclusion

Strychnine

- Used as rodenticide for gophers; adulterant in heroin
- Pathophysiology similar to Tetanus (inhibits glycine)
- Presentation: agitation, myoclonus, opisthotonus, seizure, mental status appropriate
- Tx: benzodiazepine, airway protection, neuromuscular blockade, monitor for rhabdomyolysis

Diabetic Medications

Sulfonylureas

- Block potassium channels on beta islet cells → stimulates release of insulin
- **LONG acting** → recurrent, severe hypoglycemia
- Requires **ADMISSION** (especially for exam purposes)
- Tx: dextrose IVP +/- IV infusion
    - **OCTREOTIDE** blocks Ca channel → INHIBITS release of insulin

For exam: Toxic causes of HYPOglycemia:
ethanol (kids), insulin, beta-blockers (kids), salicyltes (central), quinine

Insulin

- Mechanism: exogenous protein mimics endogenous
- Indication: diabetes, hyperkalemia
- Adverse drug reactions: hypoglycemia, lipodystrophy, allergic reaction
- Toxicity: hypoglycemia → Tx: glucagon and dextrose

Metformin (biguanide)

- Mechanism: decrease hepatic glucose output, inhibit gluconeogenesis, converts intestinal glucose to LACTIC ACID
- Indications: diabetes type II, polycystic ovarian syndrome
- **Toxicity: LACTIC ACIDOSIS**

Theophylline

- Methylxanthine derivative (like caffeine)
- Adenosine antagonist (makes you feel more awake)
- Beta agonist (dilates the airways, why once used with asthma exacerbation)
- Metabolism: CYP450 so multiple drug interactions possible
- Tx: Decontamination multiple-dose AC
    - Avoid phenothiazines for vomiting (may decrease seizure threshold)
    - Seizures: benzodiazepines, phenobarbital
- **Classic dysrhythmia: multi-focal atrial tachycardia common**
    - Tx: BB
- Hypotension: IV fluids, BB (hypotension due to over beta-stimulation)

Diaylsis indications: Acute serum theophylline level >100 mg/dL; Chronic serum theophylline level >40mg/dL

Nutritional supplements

- Water-soluble vitamins usually very safe
- The fat-soluble vitamins (Vitamins ADEK)
  - Vitamin A → pseudotumor cerebri
  - Vitamin C → hypercalcemia
- Anabolic steroids: testosterone agonist (many side effects)

Sympathomimetics

- Amphetamines, ephedrine, pseudoephedrine, ma huang
- Mask fatigue and pain
- Weight loss agent
- Does not decrease lactic acid production (does not benefit athletic performance)

Creatine

- Safe
- Adverse effects: weight gain, increases serum CK and creatinine urinary excretion
- Acute tubular necrosis never reported

EPO and blood doping

- Why: increases O2 carrying capacity in blood can increase aerobic endurance
- Done “naturally” by living/training at altitude
- Increases hemoglobin by 7%
- Stimulates RBC production
- Increases risk for sludging → CVA

Energy Drinks

- Contain various ingredients; many considered stimulants such as caffeine and caffeine containing agents
- Not FDA regulated (classified as dietary supplement)
- Side effects: difficulty sleeping, chest pain, anxiety, seizure (all due to caffeine like substances)