Objectives

• Review decontamination techniques
• Understand indications for antidote administration
• Become familiar with proposed mechanisms of actions of both toxins and antidotes
• Recognize potential adverse effects of administration
Decontamination

• Activated charcoal (AC)
• Whole bowel irrigation (WBI)
• Gastric lavage
• Ipecac/emesis
• Dilution/neutralization
Activated Charcoal

- Adsorbs many medications, toxins
- Goal is to prevent absorption into systemic circulation
- Ideal ratio is 10:1 AC:drug
- May be hard to achieve
  - e.g., ASA 325 mg #100 tablets = 32.5 g = >300 g AC
- Pediatrics 0.5 to 1 g/kg (Adults also)
Activated Charcoal
Indications

• Potentially toxic ingestion
• Ideally if given within one hour of ingestion
• Should not be routinely employed
• Only give if patient will take AC voluntarily
Relative Contraindications

• Obtunded patients without airway protection
• Toxin with risk of seizures/obtundation
• Ileus
• Hydrocarbons
• Caustic ingestions
• Alcohols
• Metals (exception Thallium)
Activated Charcoal

Adverse Effects

• Nausea and vomiting
• Constipation
• Aspiration
• Bezoar
• Corneal abrasions
Whole Bowel Irrigation

• Iso-osmotic PEG-ELS solution (Go-Lytely®)
• Large volume => Mass effect
• No intrinsic laxative effect
• Not absorbed
• Minimal fluid/electrolyte shifts
Whole Bowel Irrigation

Indications
• Iron ingestions
• Lithium ingestions
• Sustained release
  • Potentially toxic agents
    – e.g., BB, CCB
• Enteric coated
• Body packers

Dose
• 1-2 L/hr of PEG-ELS in adults
• 500 mL/hr in children
• Consider NGT or feeding NG and pump
• Continue until clear effluent
• *Labor intensive
Whole Bowel Irrigation
Complications

- Generally well tolerated
- Nausea and vomiting
- Abdominal bloating
- Aspiration
- Rare => instilled into lungs
Gastric Lavage

- Large gastric tube is placed through mouth or nose
- Saline instilled and then removed (along with stomach contents) by gravity or active suction
- Most sustained-release too big to be removed
- May push past pylorus
- May increase solubility
Indications

• **NEVER**...almost

• Handful of agents e.g., colchicine, paraquat, hydrofluouric acid
  – The latter two NGT

• Should not be routinely used even before one hour
Ipecac/emesis

• Ipecac no longer manufactured
• Induced emesis has no role
• “Salt water”, sodium bicarbonate => deaths
• No mechanical stimulation
• What do veterinarians use?...don’t use that either
Case

- 2-year-old male found unresponsive by grandmother
- Paramedics arrived FSG 35 mg/dL
  - Dextrose 25% was given and child awoke
- In ED, vital signs and physical examination unremarkable
  - Two hours later unresponsive and a generalized seizure
  - FSG 40 mg/dL
- Grandmother has history of hypertension and diabetes
Sulfonylurea Poisoning

- Most commonly prescribed agents for treatment of Type II DM
- Sulfonylurea poisoning is associated with hypoglycemia
- The onset of hypoglycemia may be delayed for up to 12 hours
- Hypoglycemic episodes may be recurrent and prolonged
Mechanism of Action

[Diagram showing the mechanism of action involving hyperglycemia, ATP, ADP, Ca²⁺, and insulin release.]
Glucagon and Dextrose

• Both increase serum glucose levels
• Glucagon stimulates glycogenolysis and gluconeogenesis
• Resultant increase in serum glucose levels increases endogenous insulin release “vicious cycle”
• Glucagon requires glycogen stores
• May also cause nausea and vomiting
Octreotide

• Long-acting somatostatin analog
• Antagonizes insulin release
• Binds to somatostatin-2 receptors preventing influx of calcium
• Few adverse effects with short course therapy
  • Nausea and vomiting
  • Pain at injection site
  • Diarrhea
Indications and Dosage

• Sulfonylurea poisoning refractory to dextrose and feeding
• Fifty to 100 mcg subcutaneously
  – 1 to 2 mcg per kilogram for children
• Dose may be repeated every 6 to 12 hours
• Monitor for 12 to 24 hours after LAST dose of octreotide for hypoglycemia
  – Also used in quinine-induced hypoglycemia
    – Malaria, restless leg syndrome
Case

- 45-year-old chemistry professor with history of depression found unresponsive on laboratory floor
- Bystander CPR initiated
- Paramedics intubated en route
  - BP 80/palp, HR 110, O2 sat 100%
- In ED, BP 90/40 after 2 L normal saline
  - FSG 250 mg/dL
- ABG pH 7.01, pCO2 21, pO2 575, FiO2 100%
- Serum lactate 12 mmol/L
Cyanide

• Gas chamber
• Jim Jones
• Tylenol tampering
• Cyanogenic plants
• Homicide
• Artificial nail remover
• Nitroprusside
• Smoke inhalation
Cyanide Clinical Presentation

- Abrupt onset of severe effects is hallmark
- Altered mental status, headache, confusion
- Seizures, coma
- Dyspnea
- Hypertension followed by hypotension

- Myocardial depression
- Lactate > 8 mmol/L
- High venous oxygen saturation
  - “Arteriolization”
- May be delayed in nitriles or cyanogenic plant ingestions
Mechanism of Toxicity

- Most important inhibits oxidative phosphorylation
  - Binds to ferric ion of cytochrome oxidase A-A3
- Inability for tissue to utilize oxygen despite adequate oxygenation
- Shift from aerobic to anaerobic metabolism
- Resultant tissue hypoxia
- Organs with highest O2 demand most affected (Brain, Heart)
“Standard” Therapy

- Amyl nitrite
- Sodium nitrite
  - Induces MetHb
  - Cyanide has preference for ferric ion of MetHb => cyanomethemoglobin
- Hypotension side effect

- Sodium thiosulfate
  - Acts as a sulfur donor
  - Through rhodanese combines with cyanide to form thiocyanate
  - Thiocyanate excreted in urine
- Hypersensitivity and hypotension
Hydroxocobalamin

- Completely different mechanism
- Vitamin B12 precursor
- Forms cyanocobalamin (vitamin B12) in presence of cyanide
- Cyanide prefers hydroxocobalamin to ferric ion of cytochrome A-A3
Dose

- Recommended starting dose 5 grams intravenously over 15 minutes
- Additional doses of 2.5 grams may be given
- 70 mg/kg in children
- Cost $895.00 USD
- ?EMS
Adverse Effects

- Transient hypertension
- Colorimetric interference
  - e.g., Creatinine, AST, bilirubin, magnesium, iron, CK
- Co-oximetry reading interference
  - e.g., COHb, MetHb, Hb-O2
- Obtain labs including cyanide level, if possible, before hydroxocobalamin
- Red urine
- Reddening of skin
TOXICOLOGY/ORIGINAL RESEARCH

Hydroxocobalamin and Sodium Thiosulfate Versus Sodium Nitrite and Sodium Thiosulfate in the Treatment of Acute Cyanide Toxicity in a Swine (Sus scrofa) Model

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Study objective: Cyanide can cause severe hypotension with acute toxicity. To our knowledge, no study has directly compared hydroxocobalamin and sodium nitrite with sodium thiosulfate in an acute cyanide toxicity model. Our objective is to compare the return to baseline of mean arterial blood pressure between 2 groups of swine with acute cyanide toxicity and treated with hydroxocobalamin with sodium thiosulfate or sodium nitrite with sodium thiosulfate.

Methods: Twenty-four swine were intubated, anesthetized, and instrumented (continuous arterial and cardiac output monitoring) and then intoxicated with a continuous cyanide infusion until severe hypotension. The animals were divided into 2 groups and treated with intravenous hydroxocobalamin with sodium thiosulfate or sodium nitrite with sodium thiosulfate.
Case

- 73-year-old female took an unknown medication in a suicide attempt
- Found by daughter obtunded with cool extremities
- Paramedics arrived
  - 30 bpm, 80/palp, 16bpm, 98.8F, O2 sat 100% (RA)
  - FSG 350 mg/dL
- In ED, IVF 1 L NS bolus and atropine 1 mg with no response
- ECG identified third degree heart block with rate of 32
Calcium-Mediated Insulin Release
Hyperinsulinemia-Euglycemia

• Normally heart utilizes free fatty acids by oxidation
• Under stress, shifts to carbohydrates
  – Requires insulin
• Decreased cardiac function further impairs effective delivery of glucose and insulin to myocardium
• Exacerbated in CCB due to inhibition of endogenous release
  – “Induced” insulin resistance
Beneficial Effects of Insulin in CCB and Beta Blocker Poisoning

• Insulin improves myocardial carbohydrate metabolism
• Increases plasma ionized calcium
• Independent inotropic effect
• Increases lactate uptake and pyruvate formation
  – Increases ATP formation
Dosage and Administration

- Regular insulin 1 unit per kilogram IV bolus
- Infusion of 0.5 unit per kilogram per hour
- Titrate to 2 units per kilogram per hour if refractory
- Monitor serum glucose q30min until stable then hourly
- Maintain serum glucose 100-250 mg/dL
Intravenous Fat Emulsion

• Traditionally been used in parenteral nutrition
• Subsequently, as antidote for long-acting anesthetic toxicity
• More recently, used in acute poisonings
  • e.g., BB, CCB, antidepressants
• Triglycerides and phospholipids from soybean and egg
• Intralipid® 20% most common preparation studied and used
Welcome

LipidRescue™ resuscitation refers to the use of an intravascular infusion of a lipid emulsion to treat severe, systemic drug toxicity or poisoning. It was originally developed to treat local anesthetic toxicity, a potentially fatal complication of regional anesthesia that can also occur in other situations where patients receive local anesthetic injections. More recently, LipidRescue has been proposed (in articles in the ER literature and elsewhere) as a treatment modality for poisoning or overdose by lipophilic agents in general. Support for this view is provided by a most remarkable case report of its use to save a patient from overwhelming bupropion overdose. The hope is that LipidRescue will be equally effective in treating a variety of causes of toxin-induced cardiac arrest.

I established this site to serve as a source of information on LipidRescue methodology and related issues. I will provide a venue for the robust exchange of ideas on topics including the prevention of cardiac arrest due to drug intoxication.
Animal studies show efficacy of intravenous lipid emulsion in the treatment of severe cardiotoxicity associated with local anesthetics, clomipramine, and verapamil, possibly by trapping such lipophilic drugs in an expanded plasma lipid compartment ("lipid sink"). Recent case reports describe lipid infusion for the successful treatment of refractory cardiac arrest caused by parenteral administration of local anesthetics, but clinical evidence has been lacking for lipid's antidotal efficacy on toxicity caused by ingested medications. A 17-year-old girl developed seizure activity and cardiovascular collapse after intentional ingestion of up to 7.95 g of bupropion and 4 g of lamotrigine. Standard cardiopulmonary resuscitation for 70 minutes was unsuccessful in restoring sustained circulation. A 100-mL intravenous
Intralipid Outperforms Sodium Bicarbonate in a Rabbit Model of Clomipramine Toxicity

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Study objective
Previous investigators have demonstrated amelioration of lipid-soluble drug toxidromes with infusion of lipid emulsions. Clomipramine is a lipid-soluble tricyclic antidepressant with significant cardiovascular depressant activity in human overdose. We compare resuscitation with Intralipid versus sodium bicarbonate in a rabbit model of clomipramine toxicity.

Methods
Thirty sedated and mechanically ventilated New Zealand White rabbits were infused with clomipramine at 320 mg/kg per hour. At target mean arterial pressure of 50% initial mean arterial pressure, animals were resuscitated with 0.9% NaCl 12 mL/kg, 8.4% sodium bicarbonate 3 mL/kg, or 20% Intralipid 12 mL/kg. Pulse rate, mean arterial pressure, and QRS duration...
Proposed Mechanisms of Action

• “Lipid sink”
  – Most likely
  – Lipid soluble agents

• Preferred energy substrate

• Increases intramyocyte calcium by activating calcium channels

• Improves carnitine-dependent mitochondrial lipid transport
  – This results in increased ATP formation
Dosage and Administration for Cardiac Arrest

- Intralipid® 20% 1.5 mL/kg over 1 minute IV push
- Repeat bolus in 3 to 5 minutes prn
- Continuous infusion 0.5 mL/kg/min if BP declines
- MAXIMUM TOTAL DOSE 8 mL/kg
- Well tolerated at these dosages
Conclusions

• There are a number of newer antidotes that have been employed in various poisonings
• Administration of these agents may improved morbidity and mortality
• However, these agents should not replace standard supportive therapies but rather be adjuncts
"You're fired, Jack. The lab results just came back, and you tested positive for Coke."