Toxicology Review

David Donaldson, D.O.
Emergency Medicine
William Beaumont Hospital

Objectives
- Drugs of abuse
  - Benzodiazepines
  - Barbiturates
  - Hallucinogens
  - Cocaine
  - Amphetamines
  - Narcotics
  - Rave drugs

- Lithium
- Heavy metals
- Cyanide/Hydrogen sulfate
- Organophosphates
- Local anesthetics
- Mushrooms
- Plants
- Isomiazid
- Hypoglycemics
- Inhalation toxins
- Biologic hazards

Benzodiazepines
- Stimulation of the benzodiazepine receptor
- Increases the sensitivity of the GABA receptor complex
  - Leads to inhibitory effects
  - Lipid soluble

Clinical Features
- CNS
  - Drowsiness
  - Dizziness
  - Slurred speech
  - Confusion
  - Ataxia
- Paradoxical reactions
- Respiratory depression

Treatment
- Activated charcoal
- Elimination enhancement
  - Not effective
- Respiratory support
Flumazenil

- Selective antagonist
- 0.2mg IV q minute (total of 3mg)
- Seizure Activity
  - Co-ingestions
  - Physically dependent on Benzodiazepines
  - History of seizures

Barbiturates

- Lipid soluble
- Mimics ETOH intoxication
  - Lack of coordination
  - Slurred speech
  - Impaired thinking
- Skin bullae
  - 6%

Barbiturates

- Pharmacology
  - Enhances the action of GABA receptors
  - Inhibits noradrenergic excitation at neuronal junctions

Barbiturates

- Mortality
  - Early
    - Cardiovascular
  - Late
    - Pulmonary

Barbiturates

- Treatment
  - Airway
  - Activated charcoal
    - Multi-dose
  - Fluid support
  - Alkalization of urine
    - Increases the excretion rate (5 to 10 fold)
  - Hemodialysis
    - 6 to 9 times more effective than alkalization
Hallucinogens

- PCP
  - Dissociative anesthetic with brainstem preservation
  - Nystagmus, agitation, ataxia
  - Muscle rigidity, seizure, coma, dialysis, hypopyrexia
- LSD
  - Affects serotonergic and dopaminergic pathways
  - Paranoia, anxiety, psychosis
- Marijuana
- Mushrooms
  - Psilocybin
  - LSD-like
- Mescaline
  - Similar to amphetamines

Cocaine

- Onset
  - 30 sec to 2 minutes
- Peak Effect
  - 30 minutes
- Duration
  - 1 to 3 hours

Cocaine (Pathophysiology)

- Local Anesthetic
  - Inhibits conduction of nerve impulses by sodium channel blockade
- CNS Stimulant
  - Blocks presynaptic uptake of norepinephrine, dopamine, and serotonin
- Cardiac
  - Sodium channel blockade
    - QRS widening
    - QT prolongation

Clinical Features

- Cardiac
  - Arrhythmias
  - Myocarditis
  - Cardiomyopathy
  - Aortic dissection
  - Coronary artery dissection
  - Accelerated atherosclerosis
Clinical Features

- **CNS**
  - Seizures
  - Intracranial infarction and hemorrhages
- **Renal**
  - Rhabdomyolysis

- **Pulmonary**
  - Hemorrhage
  - Edema
  - Pneumomediastinum and pneumothorax
- **GI**
  - Body stuffers
  - Body packers
- **Obstetrics**
  - Uteroplacental blood flow decreased

Treatment

- Sedation
  - Benzodiazepines
- Fluid resuscitation
- Cooling
- Whole bowel lavage
- Wide complex tachyarrhythmia
  - Sodium bicarb
- Beta-blockers (contraindicated)
  - Unopposed alpha-adrenergic receptor stimulation

Amphetamines

- Competitively inhibit the reuptake of neurotransmitters
- Inhibit monoamine oxidase
  - Inhibit the breakdown of catecholamines

- Cardiac monitoring
- Benzodiazepines
- Avoid beta-blockers
Narcotics

Overdose
- Pinpoint pupils
- Midrange/dilated if CNS hypoxia
- Hypoventilation
- Pulmonary edema

Narcotics

Heroin
- 20 to 200:1 ratio of adulteration
- Quinine
- Lactose
- Sucrose
- Talc
- Mannitol
- Baking soda

Narcotics

Heroin
- Methadone
- Morphine
- Codeine
- Meperidine
- Hydromorphone
- Oxycodone

Narcotics

Acute Intoxication
- Drowsiness
- Euphoria
- Miosis
- Slowed respirations
- Nausea and vomiting
- Pruritus

Narcotics

Heroin
- 12-14 hours after last dose

Methadone
- 24-36 hours after last dose

Not life threatening
- Methadone
- Clonidine
- Inhibiting adrenergic activity at alpha-2 adrenergic receptors

Withdrawal

- Piloerection
- Lactation
- Yawning
- Rhinorrhea

Sweating
- Myalgia
- Abdominal cramping and vomiting
- Irritable and confused

Narcotic Withdrawal

- Heroin
- Methadone

Not life threatening
- Methadone
- Clonidine
- Inhibiting adrenergic activity at alpha-2 adrenergic receptors
Treatment

- **Naloxone**
  - Antagonizes opiate receptor sites in the CNS
  - Serum half-life is one hour (duration 2-3 hours)
    - 2.0mg in adults
    - 0.01mg/kg in children
  - May be given:
    - Subcutaneously
    - Intratracheally
    - Intramuscular
    - Intravenously

GHB

- Gamma-hydroxybutyric acid
- Similar in structure to GABA
- Maximal plasma concentration
  - 20-30 minutes
- Half-life 27 minutes

CNS Effects

- Binds to GABA-B receptors in the brain
- Inhibits noradrenaline release in the hypothalamus
- Mediates release of an opiate-like substance in the brain

GHB

- **Oral Dose**
  - 10mg/kg
    - Amnesia and hypotonia
  - 20-30mg/kg
    - Drowsiness and sleep
  - 50-70mg/kg
    - Deep coma
      - Usually lasts 3-6 hours
      - Accompanied by myoclonic jerks and agitation

Treatment

- Airway support
- Cardiac monitoring
- Reversal of GHB
  - Physostigmine
    - Reverse sedation in clinical trials
  - Risks
    - Bradycardia
    - Asystole
    - Seizures
### MDMA (Ecstasy)

- Amphetamine derivative
- Catecholamine release from presynaptic vesicles
  - Sympathomimetic effects
- Massive release of serotonin

### Treatment

- Supportive care
- Cooling
- Seizures
  - Benzodiazepines

### Ketamine

- Structurally similar to PCP
  - Dissociative anesthetic with brainstem preservation
  - Nystagmus, agitation, ataxia
  - Muscle rigidity, seizure, coma, rhabdomyolysis, hyperpyrexia
- Used as a dissociative anesthetic
- “Special K”

### Pathophysiology

- Competes with other similar-molecular-weight ions resulting in displacement
  - Sodium
  - Potassium
  - Magnesium
  - Calcium
- Decreases in intracellular cAMP
- Interferes with the release and reuptake of norepinephrine

### Clinical Effects

- GI symptoms
- Cardiovascular
  - Prolonged QT
  - Bradycardia
- Renal
  - Polyuria
- CNS
  - Tremor
  - Memory loss
  - Weakness
  - Ataxia
  - Seizures
- Serum levels do not predict CNS levels
Treatment

- Activated charcoal is ineffective
- Whole-bowel irrigation
- Aggressive hydration

Hemodialysis
- Levels > 3.5 mEq/L (>4.0 in an acute ingestion)
- Coma, seizures, CV collapse, renal failure
- Little or no change in levels after 6 hours of hydration
- Levels > 1.0 after 36 hours of treatment

Lead

- CNS
  - Damage to the microvascular system
    - Disruption of the blood-brain barrier
    - Cerebral edema
    - Seizures
- Kidney
  - Affects the proximal tubule
  - Toxic hepatitis

Clinical features
- Encephalopathy, seizures, parathesias, abdominal pain, peripheral neuropathy ("classic" = wrist drop)

Combination of abdominal or neurologic dysfunction with hemolytic anemia = lead toxicity

- Anemia and basophilic stippling
- PbB level > 10 microgram/dL
- X-ray

Treatment
- Whole bowel irrigation
- Chelation therapy
  - BAL
  - EDTA
  - DMSA

Arsenic

- Severe gastroenteritis, muscle twitches, delirium, hepatic/renal failure
- Diagnosis: 24 hour urine
- Treatment: chelation (BAL)

Iron

- Toxic dose 30-40 mg (elemental)/kg
  - 0-6 hours: Gastro, dehydration
  - 6-48 hours: Quiescent phase
  - 12-48 hours: Acidosis, coma, hepatic
  - 2-6 weeks: Recovery, scarring
- Serum Fe level (TIBC not reliable)
- Charcoal doesn't bind
- X-ray
- Treatment = whole-bowel irrigation and chelating agent (deferoxamine)
**Mercury**
- Interferes with enzyme activity
- CNS, GI, renal toxicity
- Metallic mercury: benign if ingested but very dangerous if inhaled or injected
- Diagnosis: 24 hour urine
- Treatment: lavage and chelation (BAL)

**Cyanide**
- Binds intracellular cytochrome oxidase
- Jewels, labs, smoke inhalation
- Abdominal pain, nausea, coma, head/neck, anoxia, CN collapse
- Bitter almond odor
- Treatment: amyl nitrite (inhaled), sodium nitrite IV, sodium thiosulfate IV
- Goal is to create a controlled state of methHb to compete for cyanide

**Hydrogen Sulfate**
- Inhalation
- Local irritant effects
- Arrest of cellular respiration = aerobic metabolism (similar to cyanide)
- Rotten egg odor
- GI, CNS, CV collapse
- Treatment: amyl nitrite, sodium nitrite, ? Hyperbaric oxygen therapy

**Organophosphates**
- Pesticides/insecticides
- Rapidly absorbed
- Garlic odor
- Muscarinic/cholinergic (SLUDGE): pinpoint pupils, salivation, lacrimation, defecation
- Irreversibly binds acetylcholinesterase
- Treatment: atropine (high dose until secretions dry) and 2-PAM (pralidoxime)
Local Anesthetics

- **Amides**
  - Lidocaine
  - Bupivacaine
  - Much less allergenic
  - methylparaben
- **Esters**
  - Tetracaine
  - Procaine

Side effects:
- CNS (seizures), CV
- Maximum lidocaine dosing
  - Plain 4mg/kg
  - with epi 7mg/kg

GI Symptoms

- **Onset < 2 hours**
  - Chlorophyllum
  - Amanita
  - Cantharellus

Treatment
- Hydration
- Antiemetics

- **Onset 6-24 hours**
  - Gyromitra
  - Amanita
  - Activated charcoal
  - High dose pen

Follow LFT’s

Muscarinic

- **Onset < 30 minutes**
- **Species**
  - Inocybe
  - Clitocybe

- **Symptoms**
  - SLUDGE

- **Treatment**
  - Atropine

CNS Excitement

- **Species**
  - Amanita

- **Symptoms**
  - Intoxication
  - Ataxia
  - Anticholinergic effects

- **Treatment**
  - Supportive sedation (benzo’s or phenobarb)
**Hallucinations**
- Onset < 30 minutes
- Species
  - Psilocybe
  - Gymnopilus
- Treatment
  - Supportive sedation

**Disulfiram**
- Onset 2-72 hours after mushroom
  - < 30 minutes after ETOH
- Species
  - Coprinus
- Symptoms
  - Headache, flushing, tachycardia, DIB
- Treatment
  - Supportive

**Plants**
- Castor bean & Jequirity bean
  - Toxalbumin that inhibits protein synthesis
  - Cytotoxic effects on multiple systems
- Oleander & Foxglove & Lily of the Valley
  - Digitalis effect
- Poison Hemlock
  - GABA antagonist
- Water Hemlock
  - GABA antagonist
- Yew
  - Cardiotoxin

**Common Plant Exposures**
- Fava beans
  - G6PD deficiency
    - Hemolytic anemia
- Jimsonweed & Deadly Nightshade
  - Hallucinatory properties
  - Anticholinergic crises

**Toxicodendron Species**
- Poison Ivy
- Poison Oak
- Sumac
**Holiday Plants**
- Holly
  - GI symptoms
- Poinsettia
  - Local irritation
- Mistletoe
  - GI symptoms
- Easter Lily
  - Non-toxic

**Isoniazid (INH)**
- Overdose
  - Seizure
  - Coma
  - Metabolic acidosis
- Consider in pediatric seizures
  - Unintentional OD
- Consider in populations likely to be on INH
- Antidote
  - Pyridoxine (Vit B-6)

**Oral Hypoglycemic Agents**
- Prolonged hypoglycemia
  - Long half life
- Treatment
  - Glucose
  - Glucagon
  - Octreotide
- Can be severe in children
- Admit for observation

**Insulin Toxicity**
- Pathognomonic of exogenous insulin
  - Hypoglycemia
  - High insulin levels
  - Suppressed C-peptide levels
- Treatment
  - Supportive care (IV glucose)
  - Depends on type of insulin
Nerve Agents
- Developed in WWII
  - Tabun, Sarin, Soman, GF, VX
  - VX-most potent
  - Sarin-most volatile
- Powerful inhibitors of acetylcholinesterase
  - SLUDGE
  - Paralysis
  - Death
- High risk of secondary contamination
- Treatment
  - Oxygen
  - Atropine
  - 2-PAM
  - Military Mark 1 auto-injector kit
- 2mg atropine
- 600g 2-PAM

Biologic Hazards
- Microorganisms or biological toxins that produce death or disease
- Usually stable, highly infectious, with no effective vaccine
- Undetectable at time of exposure
- Most likely route of transmission is respiratory

Anthrax
- "wool sorter's disease"
- Inhalation of spores
- Incubation
  - 1-6 days
- Symptoms
  - Fever
  - Cough
  - Chest pain
  - Fatigue
  - Sepsis
  - Death (within 24 hours)
- Treatment
  - Cipro or doxycycline
  - Vaccine
Ricin

- Cytotoxin
- Inhalation
- Symptoms
  - Airway necrosis
  - Fever
  - Cough
  - Sweating
  - Hemorrhagic pulmonary edema
- Treatment
  - Supportive

Random Pearls

- Drug causes of non-cardiogenic pulmonary edema
  - Opiates
  - Phenothiazines
  - Salicylates
- Cholinergic poisoning syndrome
  - Causes: organophosphates and insecticides
  - SLUDGE
  - Treatment: Atropine and 2-PAM
- The presence of hemorrhagic blisters suggests barbiturate toxicity
- Opiate overdose
  - Respiratory depression, pinpoint pupils, and decreased mental status
  - Treatment: naloxone

Random Pearls

- Over 50% of patients with PCP have nystagmus
- Heavy metal poisoning usually presents as a systemic, bizarre complex in which an occupational history is important
- X-ray is useful for iron and lead toxicity
- Disposition of a hypoglycemia induced by an oral hypoglycemic agent is admission
- The most common mistake in treating insecticide toxicity is under-atropinization

Random Pearls

- Cyanide
  - Binds to cytochrome oxidase resulting in cellular asphyxia
  - Antidote kit: works by inducing methemoglobinemia
- Pyridoxine is the antidote for INH
- The best treatment for cocaine toxicity is benzodiazepines (Beta-blockers are contraindicated)
- Charcoal is ineffective for cyanide, iron, lithium, and alcohols

Random Pearls

- Body packer vs. Body stuffer
- Anticholinergic poisoning associated with Jimson Weed
- Cholinesterase is the enzyme inhibited by organophosphates
- Nitroprusside may induce cyanide toxicity
- Arsine gas presents with the triad: abdominal pain, hematuria, and jaundice