

IIC Toxicology objectives  
Unit Chairman: Dr. Tom Pazdernik  
Chapter 9 (Mosby)  
Chapters in Katzung: 57, 58, 59

## I. General Principles of Toxicology

- Know the following definitions:
  - Toxicology: relation of hazardous effects of chemicals, including drugs, to biological systems
  - Acute toxicity: adverse effect resulting from a single, usually large, exposure to a toxin
  - Subacute toxicity: Somewhat acute, between acute and chronic (online med. dictionary)
  - Chronic toxicity: harmful effect from repeated exposures to a toxin for 3+ months
  - Therapeutic index:  $LD_{50}/ED_{50}$
  - Risk: probability that injury will result from exposure to a substance for given conditions, dose, and route
  - Threshold limit values (TLV): maximum safe ambient air concentrations of chemicals during a workweek, a 15 minute interval, and instantaneously
  
- Know the following general mechanisms by which drugs or chemicals can cause toxicity:
  - Alterations in receptor-ligand interactions
    - Nicotine, most drugs
  - Alterations in membrane function
    - Local anesthetics, hydrocarbons
  - Interference with cellular energy mechanisms
    - Cyanide, Pentachlorophenol
  - Covalent binding to biomolecules
    - Organophosphates, alkylating agents
  - Interference with calcium homeostasis
    - Oxalates
  - By causing non-lethal alterations in somatic cells
    - Carcinogens, e.g. aflatoxin
  - Alterations in ligand-activated transcription factors
    - Dioxins
  - By inducing programmed cell death (apoptosis)
    - Acetaminophen
  
- Understand the primary determinants of toxicity
  - Dose and dose rate
  - Duration of exposure: long duration: bad.
  - (Principle) routes of exposure: inhalation, transdermal, and oral
  
- Understand how the following factors modify toxicity
  - Biotransformation
    - Parathion → Paraxon
    - Methanol → Formaldehyde → Formic Acid (MeOH shares pathway with EtOH)
  - Immune function
    - Review the hypersensitivities, e.g. Mosby 1-9 or perhaps even your long term memory
    - Phototoxicity: drug intermediates accumulate in skin, exposed to UV → toxic compounds
    - Examples: tetracycline, sulfonamides
    - Age: pharmacodynamics, pharmacokinetics vary over a lifetime
    - Gender: no specifics were discussed
  
- Understand how to manage a poisoned patient - know the ABCD's
  - Airway: should be cleared of vomitus or other obstruction and an airway or ET tube inserted
  - Breathing:

Assessed by observation and measurements of arterial gases

Intubate and mechanically ventilate if necessary

#### Circulation

Monitor pulse rate, blood pressure, and urinary output

Start IV and draw blood for glucose and other labs

Dextrose: to every patient with altered mental status (thinking about hypoglycemic problems)

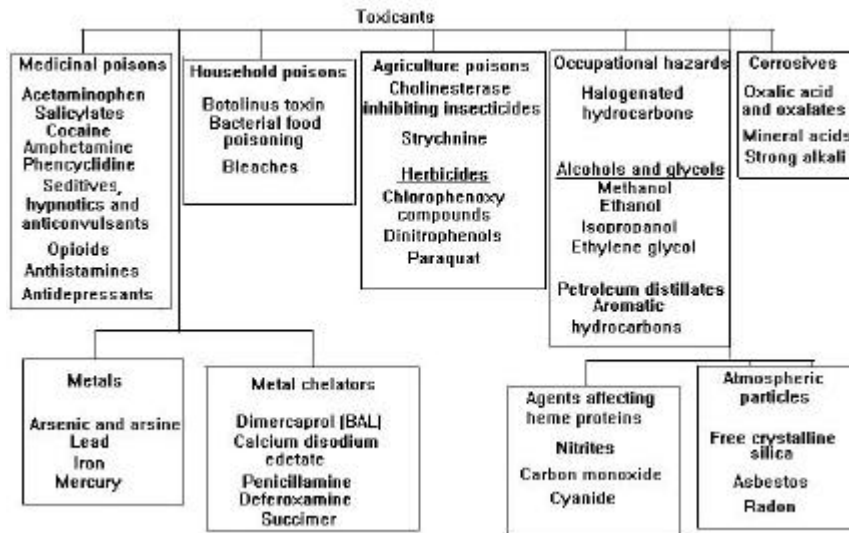
100mg thiamine to alcoholic and malnourished to prevent Wernicke-Korsakoff's

- Understand the importance of the history and physical examination in treating a poisoned patient
  - Oral history may be unreliable for a number of reasons
  - Be on the lookout for classical OD effects of common meds and poisons
  - Treat the patient, not the poison
- Understand the importance of the following laboratory analysis and procedures
  - Arterial blood gases
    - CO<sub>2</sub>: increased with hypoventilation
    - PO<sub>2</sub>: low with aspiration pneumonia or drug-induced pulmonary edema
      - Reduced with poor tissue oxygenation due to hypoxia, hypotension, or Cn poisoning
      - May appear normal in CO because dissolved O<sub>2</sub> is measured, not oxyhemoglobin
  - Electrolyte analysis (an ion gap)
    - (Na<sup>+</sup> + K<sup>+</sup>) + (HCO<sub>3</sub><sup>-</sup> + Cl<sup>-</sup>) (this is just major cations minus anions)
    - normal = 12 plus/minus 4
    - elevated by:
      - renal failure
      - diabetic ketoacidosis
      - shock-induced lactic acidosis
      - Drug-induced metabolic acidosis (salicylates, methanol, ethylene glycol, isoniazid, Fe)
  - Renal and liver function tests
    - Renal tests: In the UA look for:
      - BUN, creatinine (nitrogen load and glomerular filtration checks, respectively)
      - CK and myoglobin (muscle insults)
      - oxlate crystals: suggest ethylene glycol poisoning
    - Liver tests: transaminases, look at the PT
  - Osmolar gap: useful in alcohols poisonings; alcohols will increase the osmolar gap (K. table 59-4)
    - Calculated serum osmolality: [ 2Na<sup>+</sup> + glucose/18 + BUN/3]
    - Osmolar gap: measured osmolality – calculated osmolality
  - EKG examples:
    - Wide QRS: tricyclics, quinidine
    - Long QT: quinidine, phenothiazine, tricyclics
    - Variable AV block, screwy rhythms: dig. overdose
    - Ischemic changes: hypoxemia due to CO
- Understand how toxins can be removed or elimination can be enhanced
  - Gastric lavage
    - > 30 minutes have passed since the ingestion of a corrosive material
    - ingestion of hydrocarbons
    - coma, stupor, delirium, unconsciousness, convulsions
  - Induced emesis (know contraindications)
    - Syrup of Ipecac is often used; same contraindications as above
  - Increased rate of excretion
    - Catharsis: increased clearance of intestinal contents
      - Sorbitol is the preferred agent (hellooooo, apple juice), MgSO<sub>4</sub> can be used if kidneys are ok
    - osmotic diuretics: e.g. mannitol, urea, etc.
    - Altered urinary pH
      - Alkalinization: useful for salicylate or phenobarbital overdose
      - Acidification: not recommended b/c worsens renal effects of rhabdomyolysis

Peritoneal dialysis: simple and available, but inefficient for most drugs  
Hemodialysis: especially useful in cases where electrolyte and fluid imbalances are present  
Hemoperfusion: blood pumped from pt's vein through a cartridge filled with adsorbent material  
Especially effective for high molecular weight compounds

- Understand the importance of the following specific drugs in managing the poisoned patient
  - Activated charcoal: large surface area, suggested dose is 10:1 charcoal to est. weight of toxin
    - Good for: adsorption of many drugs and poisons
    - No good for: Fe, Li, K, Cn, alcohols, corrosive acids and alkali, methylcarbamate, tolbutamide
  - Ipecac syrup: emetic agent; use 30 ml for adults, 10-15 ml for kids, repeated q 15 minutes if necessary
    - Emetic contraindications still apply: not for corrosives, hydrocarbons, rapidly acting convulsants
  - Ammonium chloride: used to acidify the urine
    - Not used much clinically because of side effects, e.g. indirect kidney damage
    - urinary excretion of weak organic bases
  - Sodium bicarbonate: urine alkalinization
    - urinary excretion of weak organic acids
  - Magnesium sulfate: cathartic, contraindicated in renal compromise
  - Mannitol: used to renal clearance of toxins (also to intraocular and intracranial pressure)
  - Deferoxamine: use IV or IM; chelator of choice for Fe poisoning
  - Dimercaprol: single-agent therapy for arsenic and mercury, use for lead with EDTA
  - Edetate, calcium disodium (EDTA): efficient chelator of many di/trivalent metal ions, esp. lead
  - Penicillamine: chelator of Cu and Pb
    - used in Wilson's cystinuria, resistant cases of rheumatoid arthritis
  - Succimer (Dimercaptosuccinic Acid, DMSA), analog of dimercaprol,
    - prevents and reverses metal-induced inhibition of sulfhydryl-containing enzymes
    - urinary Pb excretion, protects against lethal effects of As, kidney [Hg]
  - Acetylcysteine: acetaminophen OD antidote, give within 8-10 hours of insult
  - Digoxin-specific FAb antibody: binds Dig
  - Atropine: used for cholinesterase poisonings to block ACh binding
  - Pralidoxime (2-PAM): cholinesterase reactivator, given only for organophosphates
  - Physostigmine: suggested for antimuscarinic, anticholinergic agents, but not for TCA's
  - Flumazenil: used for benzodiazepine overdoses
  - Cyanide antidote package: sodium nitrate, sodium thioisulfate, amyl nitrate
  - Glucagon: antidote for Beta-adrenoreceptor blockers, may reverse low BP, bradycardia
  - Ethanol: used in ethylene glycol poisoning to decrease kidney damage, in MeOH poisoning as well
  - Fomepizole: an alcohol dehydrogenase inhibitor used to treat MeOH and ethylene glycol accidents
  - Diazepam: used for chemical-induced convulsions
  - Pyridoxine (Vitamin B<sub>6</sub>): used for isoniazid OD
  - Methylene blue: used to convert methemoglobin to hemoglobin (nitrate poisoning)

**II. The General classification of poisons you need to know are given in the diagram on the following page.**



### III. Specific discussion of poisons

#### A. Medicinal poisons:

- Know mechanisms (M), symptoms (S) and treatment (OD) for overdoses of the following classes of medicinal agents

##### Acetaminophen

M: acetaminophen is normally glucuronidated, but with EtOH (and others) a toxic intermediate formed by induced CYP-2E1 binds covalently to sulfhydryl groups on tissue macromolecules leading to cell necrosis. Depletion of glutathione reserves leads to hepatotoxicity.

S: within 24-48 hours, PT, transaminases, hepatic necrosis

OD: acetylcysteine: It is believed that acetaminophen is hepatotoxic due to the depletion of these glutathione residues.

##### Salicylates

###### M & S:

Hyperthermia: oxidative phosphorylation uncoupling

Respiratory alkalosis: hyperpnea: O<sub>2</sub> consumption, CO<sub>2</sub> production

Metabolic acidosis: salicylic acid, ox-phos uncoupling, keto acid accumulation, bicarb, renal excretion of acids

Tinnitus from spontaneous CNVIII firing

###### OD:

Induce vomiting or perform gastric lavage

tx of hyperthermia via external cooling

sodium bicarb to acidify the urine

respiratory support

treat persisting coma with osmotic diuretics (dialysis during renal impairment)

oral or IV fluids with electrolytes, glucose

##### Cocaine

M: inhibition of Uptake I which leads to an accumulation of neurotransmitter

S: hyperthermia                      neurologic effects                      cardiac effects

Dysrhythmias                      cardiomyopathy                      hypertension

Pulmonary edema                      seizures, convulsions                      death

OD: no antidote, manage specific problems

##### Amphetamines

M: @ high doses, blocks neurotransmitter reuptake, releases serotonin, adrenergic stimulation

S: dysrhythmias, hyperthermia, cerebral bleeds, seizures, hypertension, delirium



Muscular paralysis (e.g. cranial nerves, intercostals, diaphragm)

OD:

Emesis, lavage, or cathartic depending on time elapsed since ingestion

Support vitals and draw blood for toxin determination

Administer type ABE botulinus antitoxin

### **Salmonella**

M: elaboration of toxins after ingesting bacteria

S (2-4 hr after eating):

Severe GI inflammation

mild fever

Dehydration

occasional shock

OD:

Anti-emetic (e.g. prochlorperazine) to control severe vomiting

Maintain fluid intake, supportive care

### **Bleaches**

M: corrosiveness

S: severe irritation

hypotension

delirium

coma

OD:

Rinse area with water

support vitals

Milk, melted ice cream, or beaten eggs

d/n use acid, emesis, or lavage

Antacids may be helpful

## **C. Agriculture poisons:**

- Know mechanisms, symptoms and treatment for the following agriculture poisons:

### **Organophosphates** (parathion, malathion)

M: cholinomimetic-mediated effects

S: cholinomimetic SLUD syndrome (Salivation, Lacrimation, Urination, Defecation)

Mild intoxication: anorexia, HA, dizziness, weakness, anxiety, miosis, visual acuity, tremors of tongue and eyelids

Moderate: nausea, salivation, tearing, abdominal cramps, vomiting, sweating, bradycardia, muscular fasciculations

Severe: diarrhea, pin-point, non-reactive pupils, respiratory difficulty, pulmonary edema, cyanosis, coma, heart block

OD:

Remove contaminated clothing and wash skin thoroughly

Give a small dose of atropine to block cholinergic effects, dose if necessary

2-PAM to reactivate acetylcholinesterase

gastric lavage or emesis with recent ingestion

support vitals

### **Carbamates** (Carbaryl, Aldicarb)

M: reversible cholinesterase inhibitors

S: will be very similar to those of organophosphate poisoning

OD: very similar to above, but **2-PAM is contraindicated**

### **Strychnine**

M: competitive antagonist of glycine (an important inhibitory transmitter to motor neurons and interneurons of spinal cord) which leads to blockage of nerve impulses and subsequent convulsions, rigidity of skeletal muscles

S: convulsions that are provoked by stimuli

Death from respiratory paralysis and failure

OD:

Support vitals

IV diazepam or succylcholine for convulsions

After convulsions and hyperactivity are controlled, prevent further absorption with charcoal

### **Herbicides**

Chlorphenoxy compounds:

2,4,-dichlorophenoxyacetic acid (2,4-D)  
 2,4,5- trichlorophenoxyacetic acid (2,4,5-T)  
 M: none specified  
 S: signs of neuromuscular involvement (less evident with 2,4,5-T)  
 Coma, hyperthermia, peripheral neuropathy, acidemia  
 OD: sodium bicarb, management of fluids and electrolytes  
 TCDD (tetrachlorodibenzodioxin; frequent contaminant of chlorophenoxy compounds)  
 M: p450 inducer, mechanism for death is unknown  
 S: chloracne, long-term decreased cellular immunity, carcinogenic  
 OD: none specified

#### Dinitrophenols

M: uncouple ox-phos, metabolic rate, subsequent temperature  
 S: coma, generalized muscle hypotonia  
 OD: ice baths, O<sub>2</sub>, correction of electrolyte, fluid balances

#### Paraquat

M: redox cycling leading to free radical-mediated lung injury  
 S: GI symptoms initially (hematemesis, bloody stools)  
 Eventual respiratory distress, cong. hemorrhagic pulmonary edema w/ cellular proliferation  
 Hepatic, renal, and myocardial involvement is also possible  
 OD:  
 Gastric lavage, cathartics, adsorbents  
 Prolonged observation, care

## D. Occupational hazards:

Know mechanisms, symptoms and treatment for the following classes of occupational hazards:

### Halogenated hydrocarbons:

Carbon tetrachloride	Chloroform
Methylene chloride	Chloroethylene
Trichloroethylene	Tetrachloroethylene

M: hepatotoxicity for CCl<sub>4</sub> secondary to free radical (\*CCl<sub>3</sub>) formation  
 Free radicals lead to intracellular Ca<sup>2+</sup> and subsequent cell death  
 S: CNS depressants  
 Sensitization of myocardium to catecholamines → arrhythmias at high doses  
 May cause liver and kidney damage  
 OD: remove contaminated clothing  
 Support vital signs, treat symptoms

### Alcohol and glycols

#### Methanol

M: rapid metabolic conversion to formaldehyde and formic acid (shares enzymes with EtOH)  
 S: visual disturbances, metabolic acidosis  
 Death usually results from metabolic acidosis and respiratory failure  
 OD: emesis or gastric lavage  
 Antidote is 50% alcohol (Nurse, mix 1L of 1:1 Smirnoff 100 and D5W STAT)  
 Fomepizol: synthetic aldehyde dehydrogenase inhibitor  
 Sodium bicarbonate for acidosis

#### Ethanol

M: marked CNS depression  
 S: Mild (50-150 mg%): inhibitions, visual impairment, muscular incoordination, slowed reaction time  
 Moderate (150-300 mg%): major visual impairment, slurring of speech, amplification of above effects  
 Severe (300-500 mg%): approaching stupor, severe hypoglycemia, convulsions, occasional death  
 Coma (>500 mg%): unconscious, slowed respiration, complete loss of sensation, frequent death  
 OD:  
 Acute: support vital signs, avoid depressant meds, hemodialyze if BAC > 500 mg%  
 Chronic: treat DT-associated seizures with diazepam, f/u with counseling/therapy

Disulfiram: inhibits acetaldehyde dehydrogenase → acetaldehyde dehydrogenase accumulation

Isopropyl alcohol

M: CNS depression

S: CNS depression, renal damage

OD: gastric lavage, treat symptoms

Ethylene glycol, diethylene glycol

M: similar to ethanol

S: kidney damage due to calcium oxalate crystals

OD: gastric lavage

EtOH IV; prevents conversion of glycols to oxalic acid by competing for dehydrogenase enzyme

Fomepizole; synthetic aldehyde dehydrogenase inhibitor,

Maintain vitals and treat symptoms

### Hydrocarbons

Petroleum distillates

Kerosene

Gasoline

Diesel fuel

White spirit

Polishes

Aromatic hydrocarbons

M: none specified

S: Pulmonary irritation by vapor

CNS depression by ingestion or inhalation

Severe pneumonitis after aspiration

OD: Treat symptoms and support vitals

ET tube must be placed before lavage or emesis

Aromatic hydrocarbons

Benzene, toluene, xylene

M: CNS stimulation at low dose, stimulation at high dose

S: Kidney and liver damage with high acute dose or long-term exposure

Enhanced cardiac sensitivity to catecholamines

Long-term exposure can lead to aplastic anemia and leukemia

OD: Remove ingested aromatic via lavage if aspiration can be controlled, do not induce emesis

Control excitement/convulsions with IV diazepam

### Corrosives

Oxalic acid and derivatives

M: none specified

S: local irritation and corrosion muscle weakness, convulsions, and collapse

Renal tubular damage due to calcium oxalate precipitation

OD: Precipitate oxalate by giving calcium in any form (milk, Ca antacids)

Monitor renal function and force fluids to prevent crystals from depositing in the kidney tubules

Specific antidote is calcium gluconate IV

Do not use gastric lavage or emetic compounds

Mineral Acids

Hydrochloric acid

Sulfuric acid

Acetic acid

Nitric acid

Perchloric acid

M: Irritation, inflammation, and/or necrosis to all parts of the GI tract exposed to the corrosive

S: Death is usually due to unresolved hypovolemic shock after massive hemorrhage

OD: Do not use gastric lavage or emesis after ingestion of acids

Dilute the acid with water

Give analgesics to reduce pain

Non-specific antidote is Milk of Magnesia

Treat symptomatically and support vital signs

### Strong Alkali

Sodium hydroxide

Potassium hydroxide

M: not specified

S: irritation, inflammation, and tissue damage

- Usually more penetrating than strong acids
- Death usually due to hypovolemic shock
- OD: do not use gastric enemics or emetics
- Dilute the alkali with water
- Treat symptomatically and support vital signs

**Soaps, cleansers, drain cleaners: see above**

## E. Metals

Know mechanisms, treatment and symptoms for the toxicity of the following metals:

Arsenic and arsine

- M: binds to sulfhydryl groups on enzymes and interferes with cellular metabolism
  - As<sup>5+</sup> substitutes for inorganic phosphate in production of ATP
  - As<sup>3+</sup> binds to sulfhydryls, especially lipoic acid, interfering with energy production
  - Organic <As<sup>5+</sup> <As<sup>3+</sup> <arsine (AsH<sub>3</sub>)

S: Acute:

- |                         |   |
|-------------------------|---|
| GI disturbance          | CNS effects: terminal effects are convulsion and coma |
| Ventricular arrhythmias | vasodilation, capillary permeability                  |
| Skin hyperpigmentation  | kidney tubular damage                                 |

Chronic:

- |                          |                     |
|--------------------------|---------------------|
| Polyneuritis             | Nephritis           |
| Dermatitis (Mees' lines) | Cardiac failure     |
| Cirrhosis of the liver   | Personality changes |

OD: remove ingested arsenic by lavage or emesis

- Dimercaprol** or **penicillamine** can be used to chelate
- Treat symptomatically

Lead

- M: accumulates in body, greatest degree of lead intoxication occurs in kids
- Primarily stored in bones, but symptoms are in soft tissues like bone marrow and nervous system tissue

S: Acute: GI irritation, kidney damage

Acute organic lead poisoning: much more likely to enter CNS and can cause CNS problems even in adults

Chronic (plumbism)

- Lead line on gums
- Basophilic erythrocyte stippling (RNA still in immature rbc's)
- Accumulation of delta-aminolevulinic acid (hemoglobin precursor) due to heme sythesis
- GI effects (lead colic): anorexia, constipation, abdominal pain
- CNS effects: (more prominent in kids because BBB is not as tight)
  - Hyperirritability
  - Behavior disturbances and intelluetual deficity
  - Loss of recently deveoloped skills
  - Coma and intractable convulsions
  - Neuromuscular effects: weakness, paralysis, incoordination, arthralgia, wrist and ankle drop
  - II° to periph. neuralgia

OD: remove unabsorbed lead

- Chelation produces an organic form of lead which is more likely to cross the BBB
- In severe CNS toxicity, you gotta chelate anyway
- Treat symptomatically

Iron:

- M: not specified
- S: severe G.I. irritation, inflammation
  - necrosis and hemorrhage (mucosal block is destroyed) resulting in hypotension
  - metabolic acidosis, shock
- OD: lavage only within the first hour after ingestion
  - administer **deferoxamine** parenterally

treat symptomatically and support vital signs

Mercury: all inorganic mercury (mercurous and mercuric) salts are toxic; many effects of acute poisoning are related to G.I. tract damage. Very high affinity for sulfur groups in enzymes and proteins

Inorganic mercury:

Acute effects:

- irritation and superficial corrosion
- abdominal pain
- vomiting (may be bloody)

Secondary effects:

- diarrhea
- acute renal tubular necrosis
- shock

Delayed effects:

- severe kidney damage leading to anuria
- severe G.I. damage and hemorrhage

Chronic effects:

- Early: salivation; stomatitis (swollen, bleeding gums); rarely "mercury line" on gums
- Late: "erethism" (uncontrollable blushing; emotional instability; tremor; stomatitis (more severe, may be loss of teeth)
- Continued exposure: coarse, jerky movements (arms and legs); drowsiness, depression, loss of memory; hallucinations, delusions, mania ("mad as hatter")

Organic mercury (methyl and tetraethyl mercury): predominantly CNS effects:

S: Paresthesia, muscle twitching, ataxia  
Gross constriction of visual fields

OD: lavage or induce emesis

- give milk, raw eggs or charcoal

- give **dimercaprol** parenterally for inorganic mercury, but not orally since the chelated form is more readily absorbed from the G.I. tract

- treat symptoms and support vital signs

**F. Metal Chelators:** Chelators are chemical compounds that bind metals in stable complexes to be excreted in the urine or feces.

Know appropriate pharmacology and uses of the following metal chelators:

**Dimercaprol (BAL; British Anti-Lewisite):**

Indication: used to chelate, arsenic, lead, gold and inorganic mercury

Toxic effects:

- CNS disturbance
- Cardiovascular disturbance (may produce shock due to capillary damage)
- BAL-iron complex is toxic, thus avoid medicinal iron during BAL therapy

Use:

- usual course for metal poisoning is 7-14 days by deep IM injection
- can be used with virtually complete renal shutdown

**Calcium Disodium Edetate (CaNa<sub>2</sub>EDTA):**

Indication: Used to chelate lead; zinc; alternate choice for other metals

Toxic effects:

- renal damage
- EKG abnormalities

Use:

- toxic effects can be avoided by using less than 50 mg/kg/day
- urine flow must be maintained
- therapy should not exceed 5-7 days
- do not use Na<sub>2</sub>EDTA, since it will bind calcium, causing hypocalcemia

**Penicillamine:**

Indication: used to chelate copper; alternate antidote for other metals

Toxic effects:

- nephrotic syndrome
- pyridoxine deficiency
- transient eosinophilia
- contraindicated in children with chronic renal insufficiency

**Succimer:** a lead chelator similar to dimercaprol but can be given orally; G.I disturbance most common side effect

**Deferoxamine:**

Indication: Used to chelate specifically iron (usually via ingestion)

Toxic effects:

- rapid infusion may induce shock
- long-term therapy may cause ocular damage

Use:

oral dose is effective in binding iron in the G.I. tract

**G. Agents which affect heme proteins:**

Methemoglobin-inducing agents: oxidize hemoglobin ( $\text{Fe}^{2+}$ , ferrous form) to methemoglobin ( $\text{Fe}^{3+}$ , ferric form), which is incapable of carrying oxygen.

Examples:

- Nitrites (direct)
- Aminophenols (indirect; converted to metabolites which, in vivo,  $\rightarrow$  methemoglobin)

Carboxyhemoglobin producing agents:

Carbon monoxide

Cytochrome oxidase inhibitors:

- Hydrogen cyanide
- Hydrogen sulfide

**H. Atmospheric particles**

Know the mechanisms, symptoms and treatment of exposure to atmospheric particles

**Air pollution:**

Carbon monoxide (52%)

M: binds with hemoglobin leading to carboxyhemoglobin

S: hypoxic stages

1. psychomotor impairment
2. HA, tightness in the temporal area
3. confusion and loss of mental acuity
4. deep coma, convulsions, shock, and respiratory failure

OD: 100%  $\text{O}_2$ , hyperbaric  $\text{O}_2$  at 2-3 atm is probably best

Sulfur dioxide (15%)

M:  $\text{SO}_2$  converts to sulfurous acid on contact with moist membranes

S: skin, eyes, mucus membranes, and especially the lung (where about 90% is absorbed)

Irritation, bronchial constriction, pulmonary edema after really big doses

OD: Nothing specific, it's most important to treat the airway irritation/bronchoconstriction

Hydrocarbons (12%): refer to Occupational hazards above in section D.

Particulate matter (10%)

Particles  $< 1 \mu\text{m}$ : remain suspended in air, absorbed by alveoli

1-5  $\mu\text{m}$ : may accumulate in tracheobronchial tree or be eaten by alveolar macrophages

$< 5 \mu\text{m}$ : lodge in upper respiratory tract

Nitrogen oxides (6%)

M: deep lung irritant, long term exposure leads to emphysematous changes over the long term

S: irritation of lungs, eyes, chest pain, dyspnea, can produce pulmonary edema in 1-2 h.

OD: manage symptomatically

Free crystalline silica: silicosis when silica dusts 2-3  $\mu\text{m}$  dia. are phagocytosed by alveolar macrophages

→→ silicosis over the long term; marked by SOB, susceptibility to TB  
Asbestos  
Long term: Asbestosis, which develops first in peripronchial fibrosis  
Malignant mesothelioma is a possibility, as is bronchial cancer  
Radon: Found in rocks, basements. Levels should be < 4 picocuries/L.  
Associated with lung cancer, especially in smokers

Sources:

lecture

Mosby

Katzung

Goldfrank's Toxicologic Emergencies, 6<sup>th</sup> Ed.

Prepared by John Murphy