Toxicology course

Part 2:

General approaches to the management of poisoned patients

- Poisonings and drug overdoses can cause quick physical and mental changes in a person.

- Bystanders usually are the ones who must initiate care and call a poison control center or emergency number.

Chemical agents that cause toxicity include:

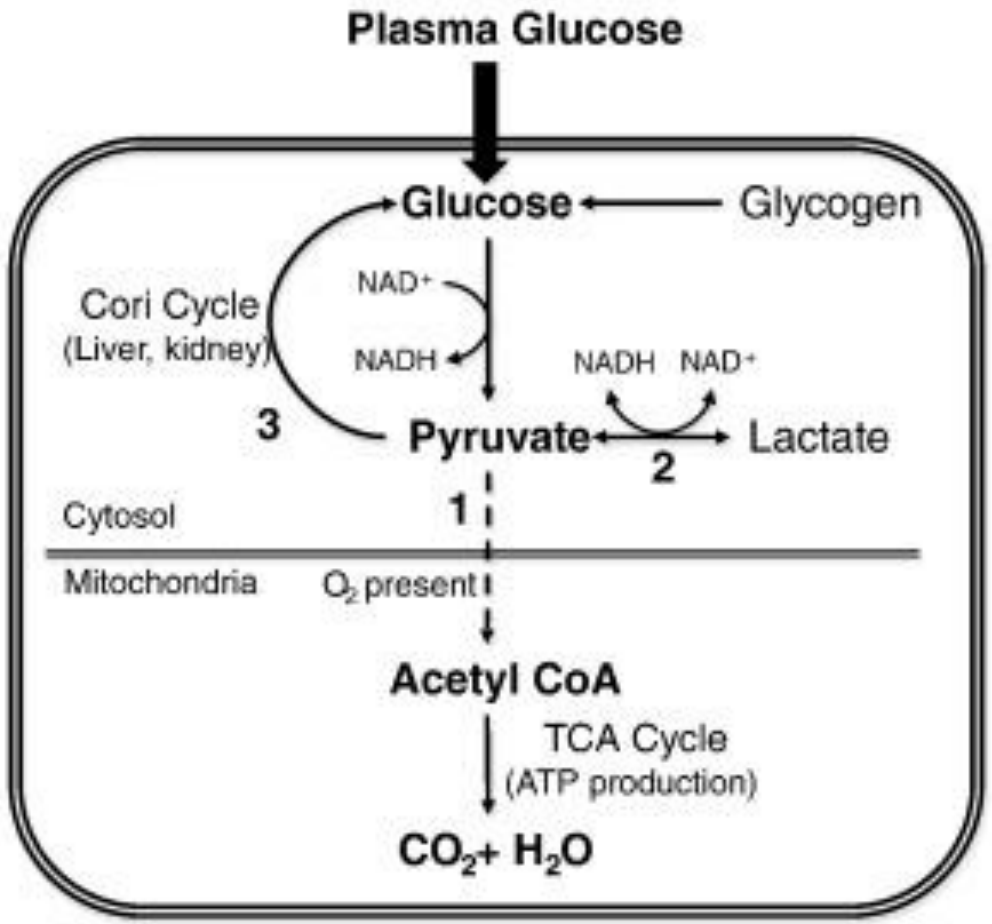
- Drugs.
- Insecticides/herbicides.
- Plant toxins, animal toxins.
- Chemical weapons.
- Radioactive elements.

- Most exposures to toxic fumes occur in the home. Burning wood, gas, oil, coal, or kerosene produces carbon monoxide (CO).

- CO gas is colorless, odorless, tasteless, and non-irritating, which makes it especially dangerous.

- Cellular **hypoxia** may occur in spite of adequate ventilation and oxygen administration when poisoning is due to carbon monoxide, cyanide, hydrogen sulfide, and other poisons that interfere with transport or utilization of oxygen.

LACTIC ACIDOSIS



Causes of Lactic Acidosis

Type A (tissue underperfusion or hypoxia)
- Cardiogenic shock
- Septic shock
- Hemorrhagic shock
- Acute hypoxia
- Carbon monoxide poisoning
- Anemia

Type B (absence of hypotension and hypoxia)
- Hereditary enzyme deficiency (glucose 6-phosphatase)
- Drugs or toxins
  - Phenformin, metformin
  - Cyanide
  - Salicylate, ethylene glycol, methanol
  - Propylene glycol[25]
  - Linezolid[22]
  - Propofol[24]
  - Nucleoside reverse transcriptase inhibitors: stavudine, didanosine[23]
  - Clenbuterol[26]
  - Isoniazid
- Systemic disease
  - Liver failure
  - Malignancy

APPROACHES OF TREATMENT

- In such patients, **cellular hypoxia is evident by** the development of tachycardia, hypotension, severe lactic acidosis, and ischemia.

- **Commonly observed poisonings** or drug overdoses are caused by (but certainly not limited to) carbon monoxide, salicylates, acetaminophen, nicotine, alcohol, heroin, marijuana, narcotic analgesics, benzodiazepines, tricyclic antidepressants, amphetamines, and cocaine.

Approach to the poisoned patient

- How does the poisoned patient die?
- Many toxins depress the Central Nervous System(CNS), resulting in coma.
- Patients under the influence of hallucinogens such as LSD may die in fights or falls from high places.

- Comatose patients frequently lose their airway protective reflexes and their respiratory drive. Thus they may die as a result of airway obstruction by the flaccid tongue, aspiration of gastric contents into the tracheobronchial tree, or respiratory arrest .

- These are the most common causes of death due to overdose of narcotics and sedative-hypnotic drugs.

- Cardiovascular toxicity is also frequently encountered in poisoning. Hypotension may be due to depression of cardiac contractility; peripheral vascular collapse due to blockade of alpha adrenoceptor-mediated vascular tone or cardiac arrhythmias.

- Lethal arrhythmias such as ventricular tachycardia and fibrillation can occur with overdoses of many **cardioactive drugs** such as epinephrine, amphetamines, cocaine, digitalis and theophylline; and drugs **not usually considered cardioactive**, such as tricyclic antidepressants, antihistamines, and some opioid analogs.

- Hypothermia or hyperthermia due to exposure as well as the temperature dysregulating effects of many drugs can also produce hypotension.

- Hyperthermia may result from sustained muscular hyperreactivity and can lead to muscle breakdown and myoglobinuria, renal failure, lactic acidosis, and hyperkalemia.

- Seizures, muscular hyperactivity, and rigidity may result in death.
- Seizures may cause pulmonary aspiration,hypoxia, and brain damage.
- Drugs and poisons that often cause seizures include antidepressants, isoniazid, diphenhydramine, cocaine, and amphetamines.

- Some organ system damage may occur after poisoning and is sometimes delayed in onset.
- Pulmonary fibrosis may begin several days after ingestion.
- Massive hepatic necrosis due to poisoning by acetaminophen or certain mushrooms result in hepatic encephalopathy and death 48-72 hours or longer ingestion.

Ox – multifocal coagulative necrosis of the liver due to embolism of *Fusobacterium necrophorum* from the rumen following lactic acidosis

CLINICAL STRATEGY FOR THE TREATMENT OF THE POISONED PATIENT

- Important elements of the initial clinical encounter for a poisoned patient include:

1. Clinical stabilization of the patient
2. Clinical evaluation (history, physical, laboratory, radiology)
3. Prevention of further toxicant absorption
4. Enhancement of toxicant elimination
5. Administration of antidote (if available)
6. Supportive care, close monitoring, and clinical follow-up

Clinical Stabilization (Resuscitation)

1. **Assessment of ABC's:**

- The patient's **Airway** (ability to move air into and out of the lungs) should be cleared of any obstruction, oral airway or nasotracheal or endotracheal **intubation** may be necessary to adequately maintain and protect the patient's airway.

- For many patients is sufficient to move the tongue out of the airway.

- **Breathing (the presence of spontaneous respirations), measuring arterial blood gases, Mechanical ventilation may be necessary to support the patient (ex: heroin depress the respiratory system)**

- **Circulation** (adequate blood pressure and perfusion of vital organs) is the initial step of emergency treatment, monitoring of pulse rate, and urinary output.

- In these cases, fluid balance needs to be carefully controlled.

- Invasive monitoring (e.g., central venous pressure, pulmonary artery catheter, Foley catheter with urometer) and drug therapy may be necessary to prevent or minimize complications such as pulmonary edema.

2. Vital signs and hypoglycemia;

- Giving dextrose to correct hypoglycemia

- Most poisoned patients, with a toxic exposure, will exhibit symptoms early in their presentation…. Some don't show significant symptoms for a period of time.

- Ex: Some drugs, such as a benzodiazepine, can cause significant sedation early after exposure but often have a comparatively mild clinical course, whereas camphor, show little clinical effects initially but can produce a fatal outcome.

Clinical evaluation (history, physical, laboratory, radiology)

History:

- Determine the substance, dose, route
- The extent of exposure
- Timing of exposure. (most difficult)

- Difficulty in obtaining history appeared if the patient is unresponsive and unable to provide the history, suicide or patient who has taken illegal substances is not willing to provide an accurate history.

Informative clinical history can be obtained by:

1. interviewing with family members
2. emergency medical technicians who were at the scene
3. a pharmacist who can sometimes provide a listing of prescriptions recently filled
4. An employer who can provide a list of chemicals found in the work environment for an occupational exposure.

- ❑ Check for empty bottles or containers, smells or unusual containers, or suicide not

Physical Examination

- Check clothing for objects or substances.
- Assess the general appearance of the patient.
  - Agitation, confusion…..
- Exam skin for bruising, cyanosis, flushing.

✓ Ex: Excessive sweeting occurs with organophosphates, nicotine and sympathomimetic drugs

- Exam eyes for pupils size, reactivity, increased lacrimation…..

✓Miosis is typical of opioids, cholinesterase inhibitors (e.g. Organophosphate insecticides), and deep coma due to sedative drugs.

✓Mydriasis is common with amphetamines, cocaine, atropine and other anticholinergic drugs.

✓Horizontal nystagmus is characteristic of intoxication with alcohol and other sedative drugs.

❖Vital signs: BP, HR,RR, Temperature

✓Hyperthermia may be associated with sympathomimetics, anticholinergic, salicylates, and drugs producing seizures.

✓Hypothermia can be caused by any CNS depressant drug.

✓Cyanosis may be caused by hypoxemia or by methemoglobinemia.

- Oropharynx : increase salivation or excessive dryness, Typical odors of alcohol or ammonia.
- Cardiovascular: rhythm, and regularity

✓Ex: Hypertension and tachycardia are typical with amphetamines, cocain and anticholinergic drugs.

✓Hypotension and bradycardia are characteristic features of overdose with calcium channel blockers, beta blockers, clonidine, and sedative hypnotics.

✓Hypotension with tachycardia is common with tricyclic antidepressants, vasodilators and beta agonists.

- **Lungs**: rate, wheezing…..

✓Ex: Rapid respirations are typical of salicylates, CO poisoning.

- **Abdomin**: bowel sounds, tenderness or rigidity…

✓Hyperactive bowel sounds, tenderness abdominal cramping and diarrhea are common in poisoning with organophosphatase, iron, arsenic

- **Extremities**: tremors…..

- **Neurological**: reflexes, muscle tone coordination….

✓Physiologic excitation – anticholinergic, sympathomimetic, drug withdrawal

✓Physiologic depression – cholinergic (parasympathomimetic), opiate, or sedative-hypnotic agents, or alcohols

✓Muscular rigidity can be caused by anti-psychotic agents, serotonin syndrome

- Many factors can affect the patient's mental status.
- Hypoglycemia and hypoxemia; that can be life-threatening but easily addressed by administering oxygen and IV dextrose until laboratory results are available.

- **Toxidrome**: is a group of signs and symptoms associated with overdose or exposure to a particular category of drugs and toxins

- The major toxic syndromes include narcotic, cholinergic, sympathomimetic, and anticholinergic.

- For example, if a patient presents with altered mental status, mydriasis (dilated pupils), mild hypertension, tachycardia, warm skin, dry mucous membranes, and diminished bowel sounds in the abdomen, the clinical toxicologist can characterize the patient's presentation as consistent with the anticholinergic toxic syndrome

TABLE 3.7 Common Toxidromes and Their Clinical Features

Common toxidromes	Features
Anticholinergic	Dry mucous membranes, flushed skin, urinary retention, decreased bowel sounds, altered mental status, dilated pupils, cycloplegia
Sympathomimetic	Psychomotor and physical agitation, hypertension, tachycardia, hyperpyrexia, diaphoresis, dilated pupils, tremors, seizures (if severe)
Cholinergic	SLUDGE, BBB, muscle weakness, intractable seizures
Opioid	CNS depression, miosis, respiratory depression, bradycardia, hypotension, coma
Benzodiazepine	Mild sedation, unresponsive or comatose with stable vital signs, transient hypotension, respiratory depression

Abbreviations: SLUDGE, sialorrhea, lacrimation, urination, diaphoresis, gastric emptying; BBB, bradycardia, bronchorrhea, brochospasms; CNS, central nervous system.

- **Characteristic odor can be detected on the poisoned patient's breath or clothing**

Table 33-2

Characteristic Odors Associated With Poisonings

ODOR	POTENTIAL POISON
Bitter almonds	Cyanide
Eggs	Hydrogen sulfide, mercaptans
Garlic	As, organophosphates, DMSO, thallium
Mothballs	Naphthalene, camphor
Vinyl	Ethchlorvynol
Wintergreen	Methylsalicylate

DMSO, dimethyl sulfoxide.

Laboratory Evaluation

Tests that provide clues to the agent(s) taken by the patient include:

1. Arterial blood gases (ABGs).
2. Electrolytes.
3. Serum osmolality tests.
4. Urinalysis.
5. Complete blood count.
6. Electrocardiography.
7. Toxicology screens.

1. Arterial Blood Gases (ABGs)

- Hypoventilation will result in an elevated PCO2 (hypercapnia) and a low PO2(hypoxia).
- The PO2 may also be low with aspiration pneumonia or drug induced pulmonary edema.

- Signs of inadequate ventilation or oxygenation include cyanosis, tachycardia, hypoventilation, intercostal muscle retractions, and altered mental status.

2. Electrolytes

- Acute poisoning can cause an imbalance in a patient's electrolyte levels, including sodium, potassium, chloride, bicarbonate, carbon dioxide, magnesium, and calcium.

- Serum level measurements are also available for carbamazepine, iron, ethanol, lithium, aspirin, and valproic acid and may be obtained if these agents are suspected in an overdose

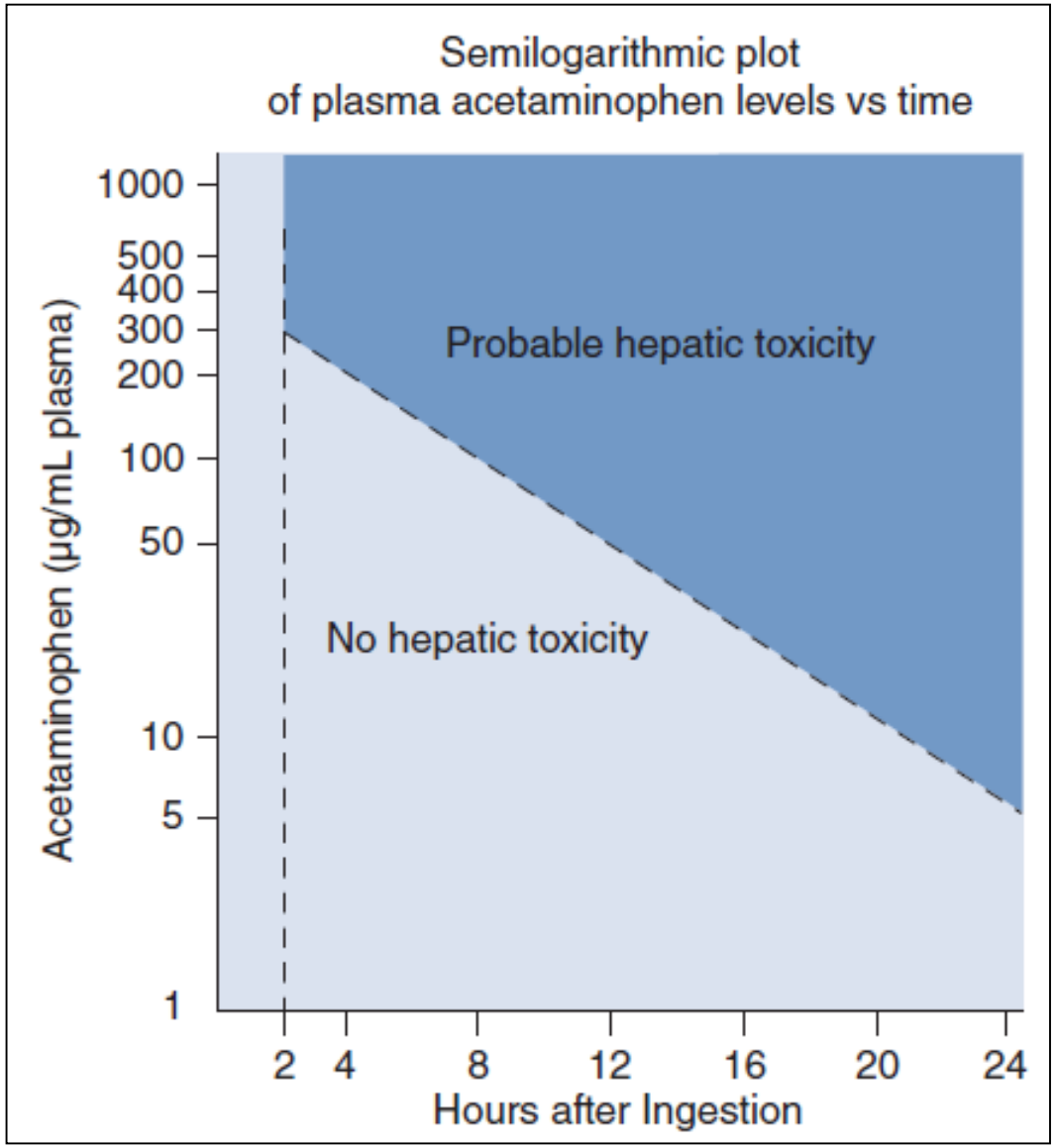
Table 33-3

List of Tests That are Commonly Measured in a Hospital Setting on a STAT Basis

Acetaminophen	Osmolality
Acetone	Phenobarbital
Carbamazepine	Phenytoin
Carboxyhemoglobin	Procainamide/NAPA
Digoxin	Quinidine
Ethanol	Salicylates
Gentamicin	Theophylline
Iron	Tobramycin
Lithium	Valproic Acid
Methemoglobin	

NAPA, N-acetylprocainamide.

- In 1975, Rumack and Mathews published a nomogram for acetaminophen poisoning.
- This nomogram predicts clinical outcome and is also valuable to guide the clinician in the decision as to whether or not to administer N -acetylcysteine (NAC), an antidote for significant acetaminophen ingestion.
- several other drugs including lithium, salicylates, digoxin, iron, phenobarbital, and theophylline.



Calculated clinical parameters:

- The anion gap (AG) calculations
- The osmol gap calculations.

- The patient's condition is consistent with exposure to chemicals known to cause elevations of these parameters (i.e., metabolic acidosis, altered mental status, etc).

$$AG = [Na\ mEq/L - (Cl\ mEq/L + HCO_3\ mEq/L)]$$

Normal $AG \leq 12$

- Elevated AG; metabolic acidosis (low blood pH and low serum HCO3)

Table 33-4

Differential Diagnosis of Metabolic Acidosis With Elevated Anion Gap: "AT MUD PILES"

A	Alcohol (ethanol ketoacidosis)
T	Toluene
M	Methanol
U	Uremia
D	Diabetic ketoacidosis
P	Paraldehyde
I	Iron, isoniazid
L	Lactic acid
E	Ethylene glycol
S	Salicylate

The osmolal gap is the difference between the measured osmolality and the calculated osmolality

Osmol gap = measured serum osmolality (mOsm) − calculated serum osmolarity (mOsm)

where calculated serum osmolarity = 2 × Na mEq/L + glucose mg/dL /18 + BUN mg/dL /2.8

Normal osmol gap < 10 mOsm

An elevated **osmol** gap in the setting of a poisoned patient suggests the presence of an osmotically active substance in the plasma that is not accounted for by the Na, glucose, or BUN concentrations

Table 33-5

Differential Diagnosis of Elevated Osmol Gap

Methanol
Ethanol
Ethylene glycol
Isopropanol

3. Electrocardiography:

- Provide evidence of drugs causing arrhythmias or conduction delays (e.g., tricyclic antidepressants).

4. Renal function tests:

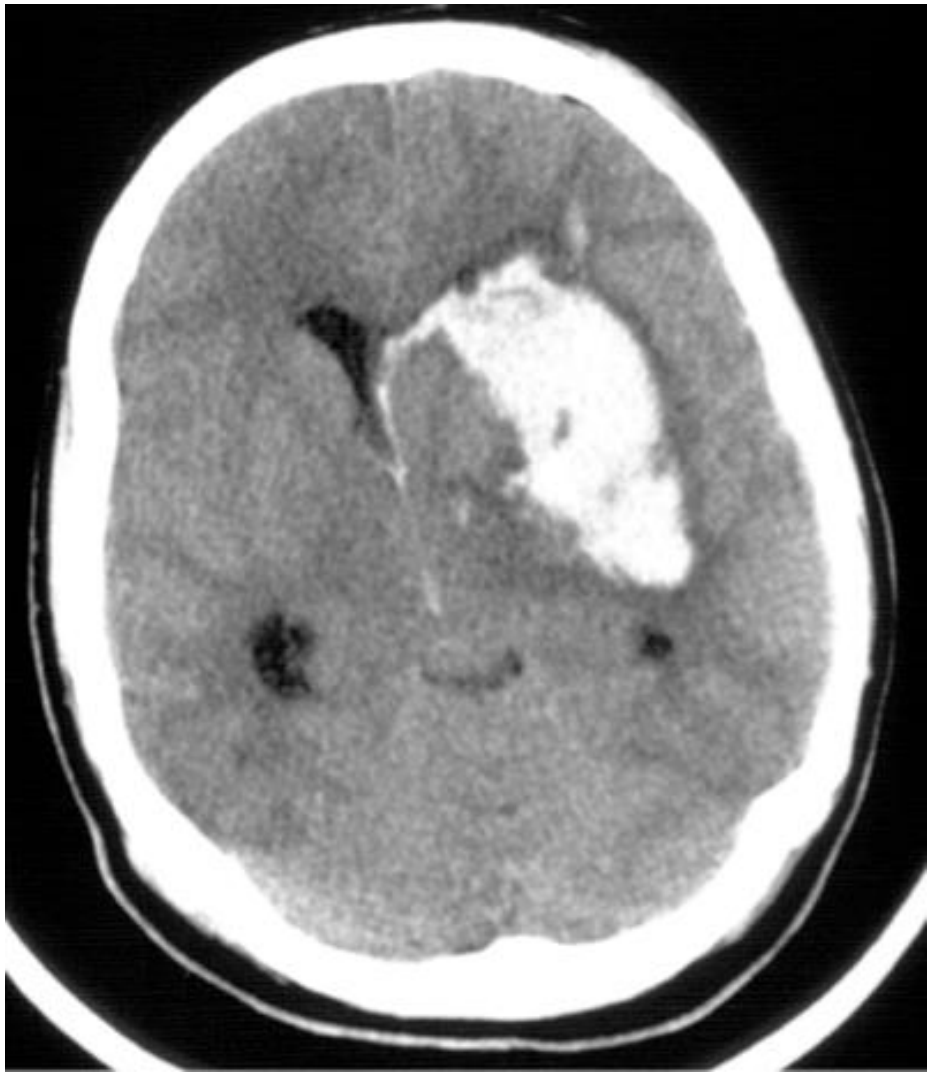
- Some toxines have direct nephrotoxic, in other cases renal failure is due to shock.
- BUN and creatinine levels should be measured and urinanalysis performed.

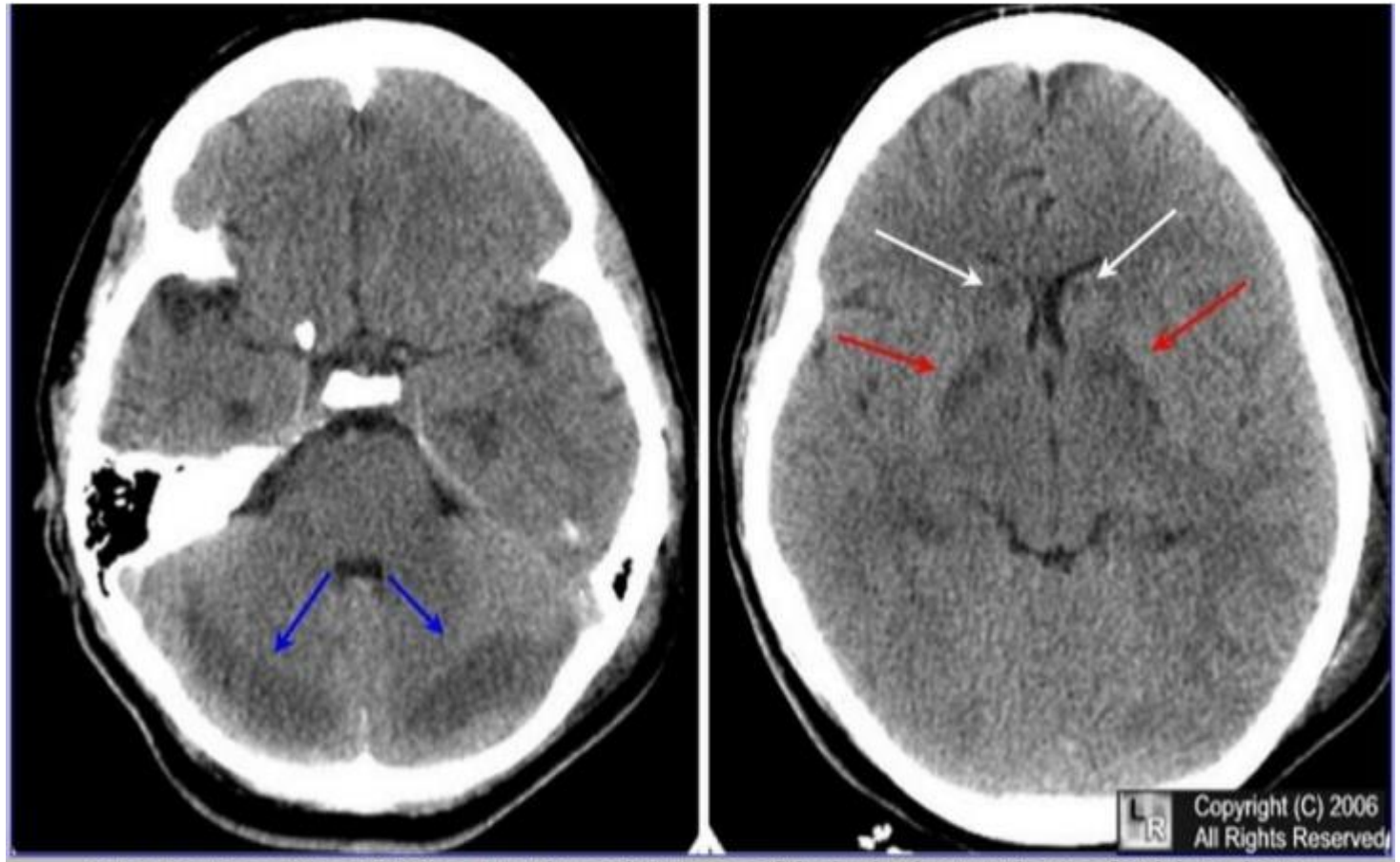
5. Radiographic Examination

- Is relatively limited. This is due primarily to the lack of radiopacity of many oral forms of medication.

1. Chest radiographs: drug-induced noncardiac pulmonary edema is associated with serious intoxication with salicylates and opioid agonists.
2. Abdominal radiographs: foreign Bodies, batteries, lead, halogenated hydrocarbon (chloroform), cocaine or heroin containers.
3. The computed head tomography [CT]: carbon monoxide has been associated with lesions of the brain consisting of low-density areas in the cerebral white matter and in the basal ganglia

Computer tomography (CT) scan





Carbon monoxide poisoning. Unenhanced CT scan of the brain about 16 hours after injury shows bilaterally symmetricl low attenuation lesions in the cerebellum (blue arrows), globus pallidus (red arrows) and caudate nuclei (white arrows). The patient was in a house fire.

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6. Renal function tests

- Some toxins have direct nephrotoxic, in other cases renal failure is due to shock or myoglobinuria.
- BUN and creatinine levels should be measured and urinanalysis performed.

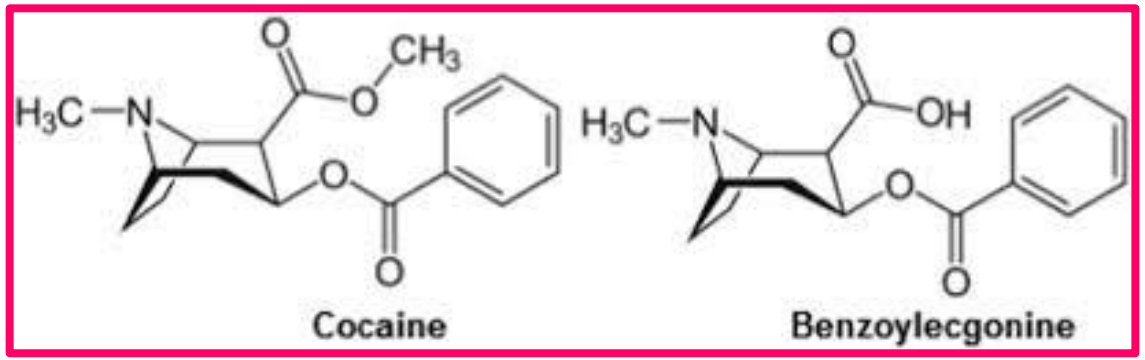
7. Toxicology screens

- Toxicology screen is a laboratory analysis of a body fluid or tissue to identify drugs or toxins. Saliva, spinal fluid, and hair may be analyzed, blood or urine samples are used more frequently.Each screen tests for specific drugs or agents.

- The sample must also be properly collected, and there must be a laboratory near enough to obtain results quickly.

- The test sample must be collected while the drug or toxin is in the body fluid or tissue used for testing.

- For example, cocaine is a rapidly metabolized drug; however, its metabolite, benzoylecgonine, can be detected in the urine for several hours after cocaine use.



Management

- Prevention of the absorption and further the exposure to the agent.
- Treatment begins with first aid at the scene and continues in the emergency department and often the intensive care unit (ICU).
- Advanced management involves further steps to prevent absorption and enhance elimination of the agent.
- For instance, antidotes, antivenins (the treatment of venomous bites or stings

GENERAL- MANAGEMENT:

1. Provision of supportive care.
2. Prevention of poison absorption.
3. Enhancement of elimination of poison.
4. Administration of antidotes.

1. Supportive care

- Vital signs, mental status, and pupil size
- Cardiac monitoring, ECG
- Protection of the airways
- Intravenous access.
- Cervical immobilization if suspect trauma
- Rule out hypoglycaemia

2. Prevention of Further Poison Absorption

Decontamination

- To minimize the total amount of chemical that reaches the systemic circulation.

1. Inhalation route: remove the patient from the environment where the toxin is found and to provide adequate ventilation and oxygenation for the patient.

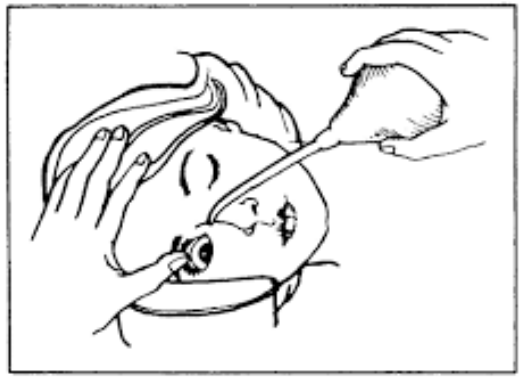
- Further evaluation is needed if the patient experiences respiratory irritation or shortness of breath.

2. Topical route: patient clothing containing the chemical must be removed and properly disposed in airtight wrappings or containers to ensure that the rescuers and healthcare providers are adequately protected from secondary exposure.

- Require gentle washing of the skin with water and mild soap taking care not to cause cutaneous abrasions of the skin that may enhance dermal absorption.

- Some toxins may require further decontamination. For example, three separate soap and water washings or showers are recommended to decontaminate **organophosphate pesticides** (e.g., Malathion or Diazinon).

- Protective clothing should be worn to reduce the risk for toxicity while handling contaminated clothing or assisting with skin decontamination.



Eyes

- Many substances can accidentally splash into the eyes. When this happens, the eyes must be flushed to remove the agent.
- Immediate irrigation with lukewarm water or normal saline is recommended.
- Continuous flooding of the eyes with a large glass of water or low-pressure shower should be done for 15 minutes.

- The patient should blink the eyes open and closed during the irrigation.
- If necessary, the pH of the eyes can be tested. If the pH is abnormal, irrigation should continue until the pH normalizes.
- An ophthalmologic examination is needed when ocular irritation or visual disturbance persists after irrigation.

Eye pH measurement

- Then the **pH** of the injured **eye** should be tested with litmus paper that is touched to the conjunctival fornix (the area between the eyelid and globe) inside the lower eyelid.
- Irrigation should be continued until a neutral **pH** level (7.0) is achieved and maintained for at least 30 minutes.

4. Oral route: Four general methods involve removing toxin from stomach.

❖Induction of emesis with syrup of ipecac, gastric lavage, oral administration of activated charcoal, and whole-bowel irrigation.

- Many clinical toxicologists believe that there remains a limited role for the clinical use of syrup of ipecac.

- **The accepted contraindications for use of syrup of ipecac are:**

(1) Children less than six months of age.

(2) In the ingestion of a caustic agent (acid or alkali).

(3) In a patient with a depressed level of consciousness or gag reflex.

(4) When there is a significant risk of aspiration of gastric contents such as for ingestion of a liquid hydrocarbon with high aspiration potential.

- Dosing: 15 ml for 1-12 years old and 30 ml for adults; may repeat once if no emesis in 12 hr.
- 90% vomit within 20 minutes of first dose and 97% vomit with second dose.
- The American Academy of Pediatrics no longer recommends the use of emetics (such as syrup of ipecac) for GI decontamination.

- **Milk** or **water** dilutes ingested irritants such as bleach or caustics such as drain cleaner.
- After such an ingestion, adults or children should drink milk or water (children based on their size).
- Because of the risk of aspiration, ingestions should not be diluted when they are accompanied by **seizures**, **depressed mental status**, or **loss of the gag reflex.**
- Again, neutralization is not used because of the risk of thermal burn.

The use of gastric lavage:

- The technique of placing an orogastric tube into the stomach then cyclically instilling fluid and aspirating until the effluent is clear

- Contraindications:
  - Unconscious patient unless intubated (risk aspiration)
  - Caustic ingestion or hydrocarbons with a high aspiration potential
  - Airway integrity not secured, more toxic to lung than GI.

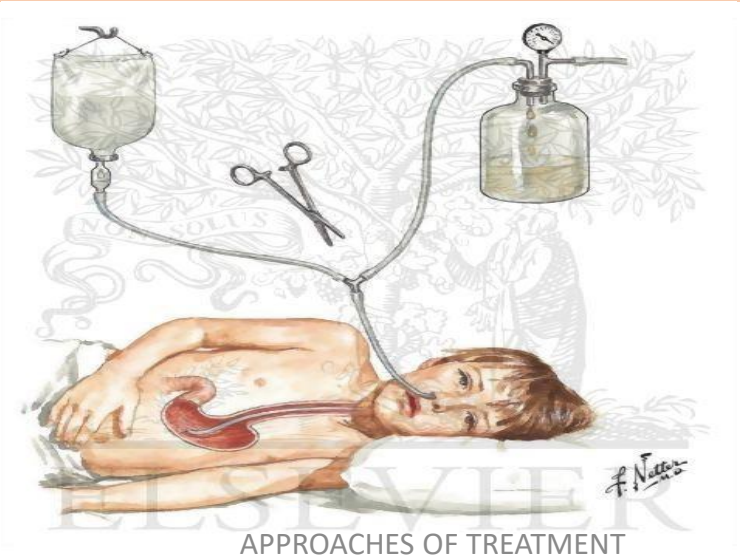
Complications:

- ❖Insertion into trachea.
- ❖Esophageal or gastric perforation.
- ❖Decreased O2.
- ❖Pulmonary aspiration.
- ❖Electrolyte imbalance.
- ❖Tension pneumothorax, and
- ❖Hypothermia (when cold lavage solutions are used).

- Gastric lavage should be used **only** if the patient has ingested [1] a life-threatening amount of a substance and [2] the procedure is undertaken within **an hour** of the ingestion.

- Orogastric lavage may only be useful to attempt removal of liquid toxins or possibly dissolved tablets or capsules

- For the lavage, the patient is positioned in the left lateral position, with the head lower than the feet.



USE OF “ACTIVATED” CHARCOAL:

- Activated charcoal is a fine, black powder that is given as a slurry with water, either orally or by nasogastric or orogastric tube, as soon as possible after the ingestion.

- Commercially available activated charcoal products may be mixed with 70% sorbitol to decrease grittiness The usual dose that is given is one 50-g bottle.

- Low molecular weight and polar compounds such as ethanol, and substances such as lithium, iron, and certain inorganic salts tend to be less well bound to activated charcoal.
- Is typically administered at a dosage of 1.0 to 1.5 g/kg.
- Orally or is placed into the stomach via orogastric or nasogastric tube

- The most consistent efficacy and best safety profile.

- Activated charcoal is used cautiously in patients **with diminished bowel sounds** and is contraindicated in patients with bowel obstruction.

- Should not be given if esophageal or gastric perforation suspected or emergent endoscopy possibly needed.

- Complications rare; aspiration or impaction possible.

Drugs/Toxins **Well** Adsorbed by Activated Charcoal	Drugs/Toxins **Not Well** Adsorbed by Activated Charcoal
■Acetaminophen ■ Amphetamines ■ Antihistamines ■ Aspirin ■ Barbiturates ■ Benzodiazepines ■ Beta blockers ■ Calcium channel blockers ■ Cocaine ■ Opioids ■ Phenytoin ■ Theophylline ■ Valproic acid	■Acids ■ caustic alkalis ■ Alcohols ■ Iron ■ Lithium ■ Metals cyanide ■ Mineral acids, organic solvents.

CATHARTICS

- A cathartic is a substance that causes or promotes bowel movements.
- In theory, cathartics decrease the absorption of drugs and toxins by speeding their passage through the GI tract, thereby limiting their contact with mucosal surfaces.
- 70% sorbitol (1 g/kg) or 10% Mg citrate

The whole bowel irrigation:

- It is a procedure that cleanses the lumen of the gastrointestinal tract.
- Poorly absorbed, osmotically neutral polyethylene glycol electrolyte solution.
- Is administered orally to expel the contents of the intestines via the rectal route.
- Remove of ingested packets of illegal drugs
- Whole-bowel irrigation is contraindicated in the patient with bowel obstruction or perforation.

- Common indications: Heavy metals, Iron, Lithium, Sustained or delayed release formulations
- Contraindications: absent bowel sounds or obstruction
- Complications: bloating, cramping, rectal irritation
- As a result, absorption is delayed, and

  the development of toxic effects may not be observed for several hours.

3. Enhancement of Poison Elimination

1. Alkalinization of the urine.
2. Chelation.
3. Hemodialysis.
4. Hemoperfusion.
5. Hemofiltration.
6. Plasma exchange or exchange transfusion
7. Multiple-dose activated charcoal:-

- The administration of oral activated charcoal serially during the treatment time course.

1. Urinary alkalinization

- Enhancement of the renal clearance of certain weak acids.
- Increase urinary filtrate pH to a level sufficient to ionize the weak acid and prevent renal tubule reabsorption of the molecule.
- Requires adequate urine flow and close clinical monitoring including that of the pH of the urine.

- The procedure is accomplished by adding sterile **sodium bicarbonate** to sterile water with 5% dextrose for intravenous (IV) infusion and administering the mixture intravenously to titrate the urine pH to 7.5 to 8.5.

- Used for moderately severe salicylate compounds and phenobarbital.

- Complications of alkalinization include cerebral or pulmonary edema and electrolyte imbalances.

ACIDIFICATION OF THE URINE:

- ✓Enhancement of clearance of drugs such as amphetamine and phencyclidine.
- ✓ Adverse effects: acute renal failure and acid-base and electrolyte disturbances.
- ✓Urine acidification is no longer recommended because of low drug clearance and the risk of complications such as rhabdomyolysis.

2. Chelation

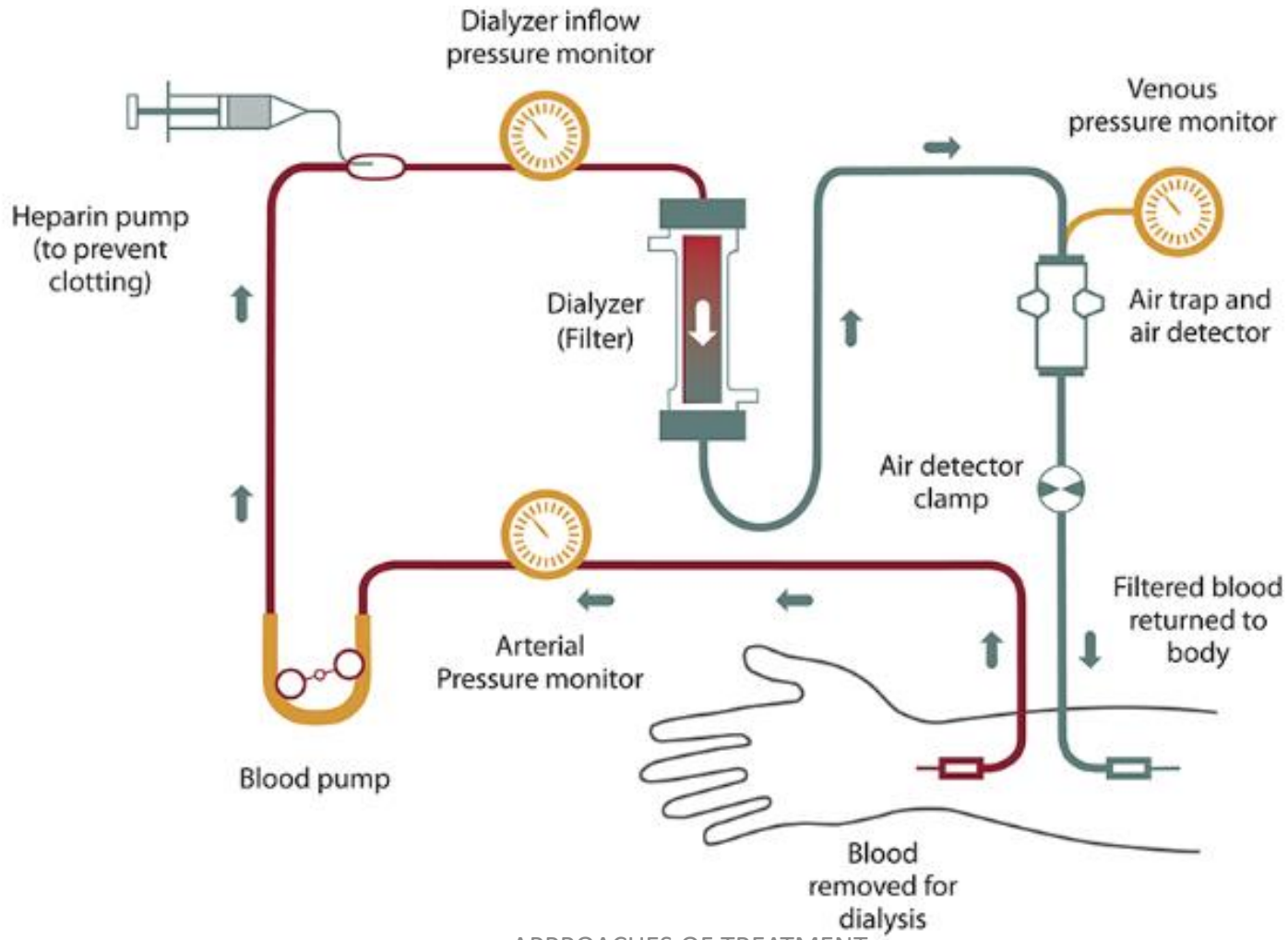
- Chelation involves the use of binding agents to remove toxic levels of metals from the body, such as mercury, lead, iron, and arsenic.

- Examples of chelating agents are dimercaprol (BAL), calcium disodium edetate (EDTA), and deferoxamine.

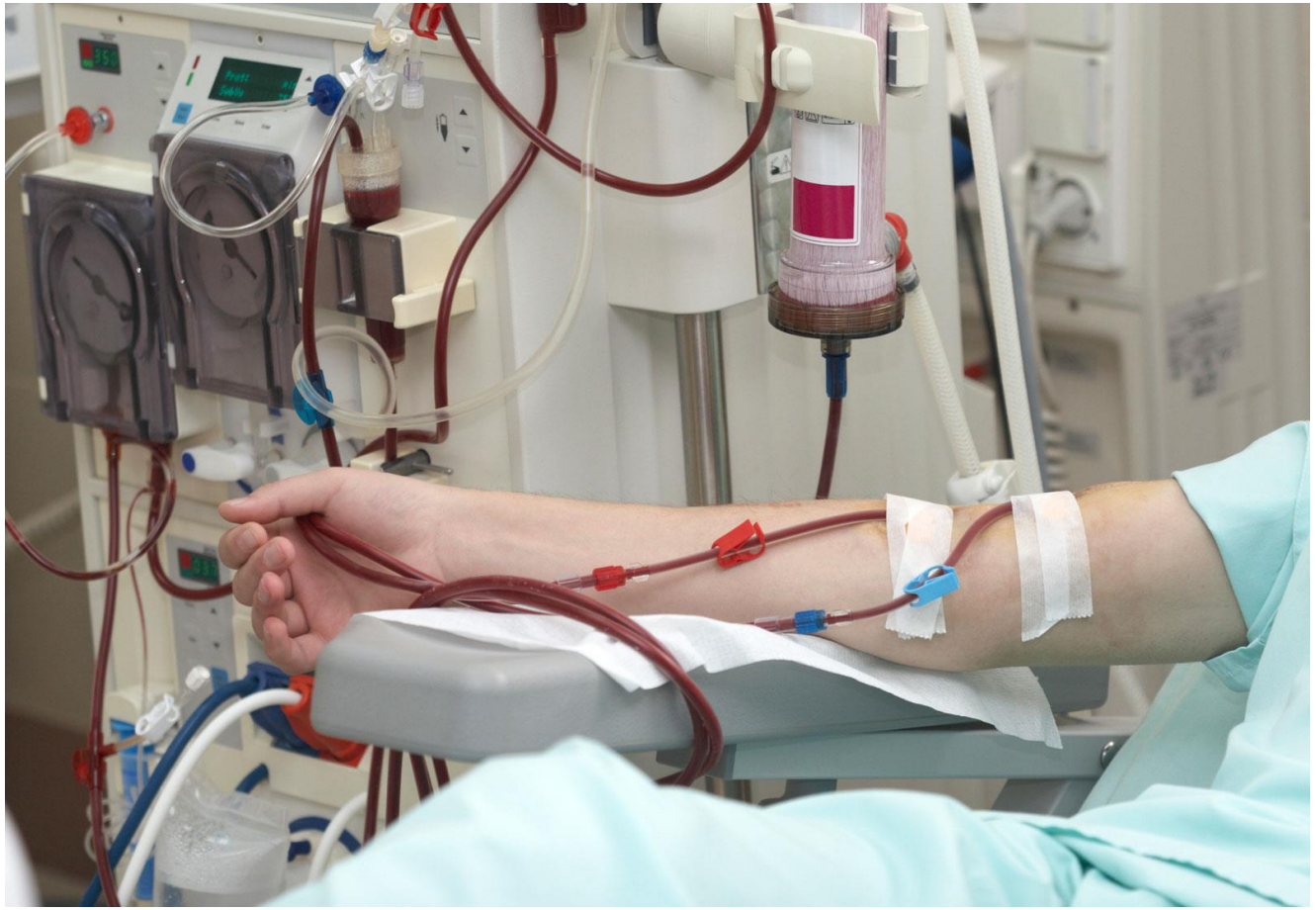
3. Dialysis techniques

- Hemodialysis, continuous venous filtration, or peritoneal dialysis.
- Passage of the toxic chemical through a **semipermeable dialysis membrane** like peritoneal membrane.
- The chemical must have a relatively **low volume of distribution**, **low protein binding**, a **relatively high degree of water solubility**, and **low molecular weight.**

Hemodialysis:



Hemodialysis:



- It is used in moderate to severe intoxications to remove a drug or toxin rapidly when more conservative methods (e.g., gastric lavage, activated charcoal, antidotes) have failed or in patients with decreased renal function.

- Hemodialysis requires consultation with a nephrologist and specially trained nurses to perform the procedure and monitor the patient.

- Dialysis reserved for specific toxins: **salicylates**, **methanol**, **lithium**, **theophylline**, **amanita** (mushrooms)
- No dialysis for small children, exchange transfusion should be considered.

Table 33-6

Chemicals for Which Hemodialysis Has Been Shown Effective as a Treatment Modality for Poisoning

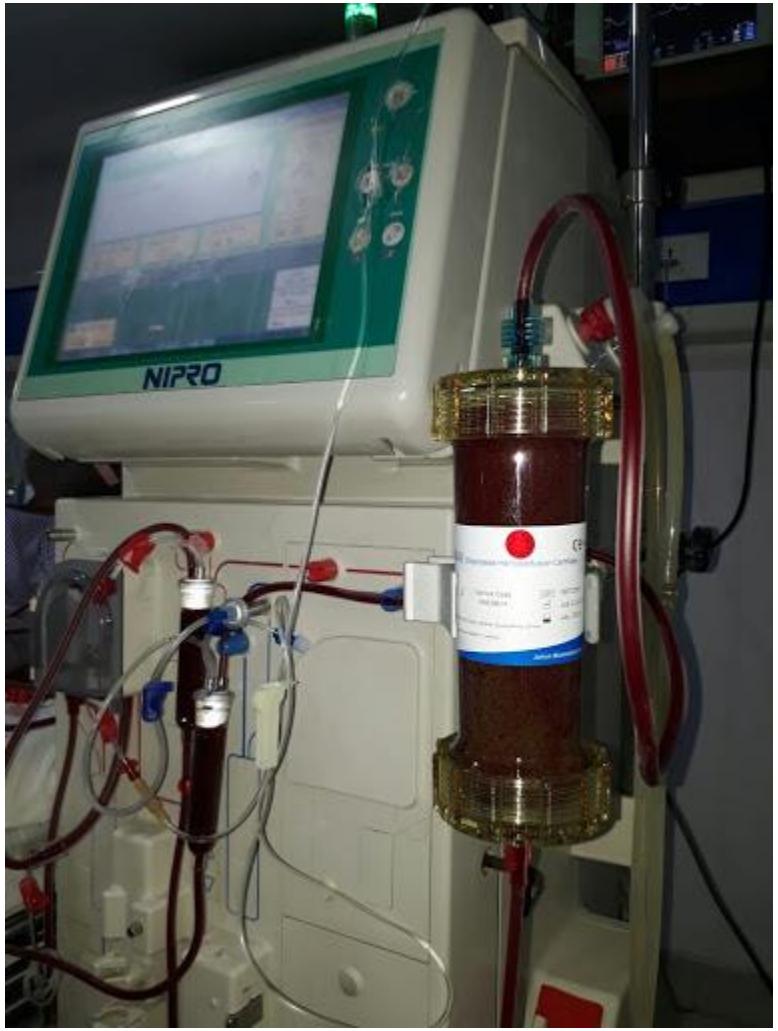
Alcohols	Meprobamate
Antibiotics	Metformin
Boric acid	Paraldehyde
Bromide	Phenobarbital
Calcium	Potassium
Chloral hydrate	Salicylates
Fluorides	Strychnine
Iodides	Theophylline
Isoniazid	Thiocynates
Lithium	Valproic acid

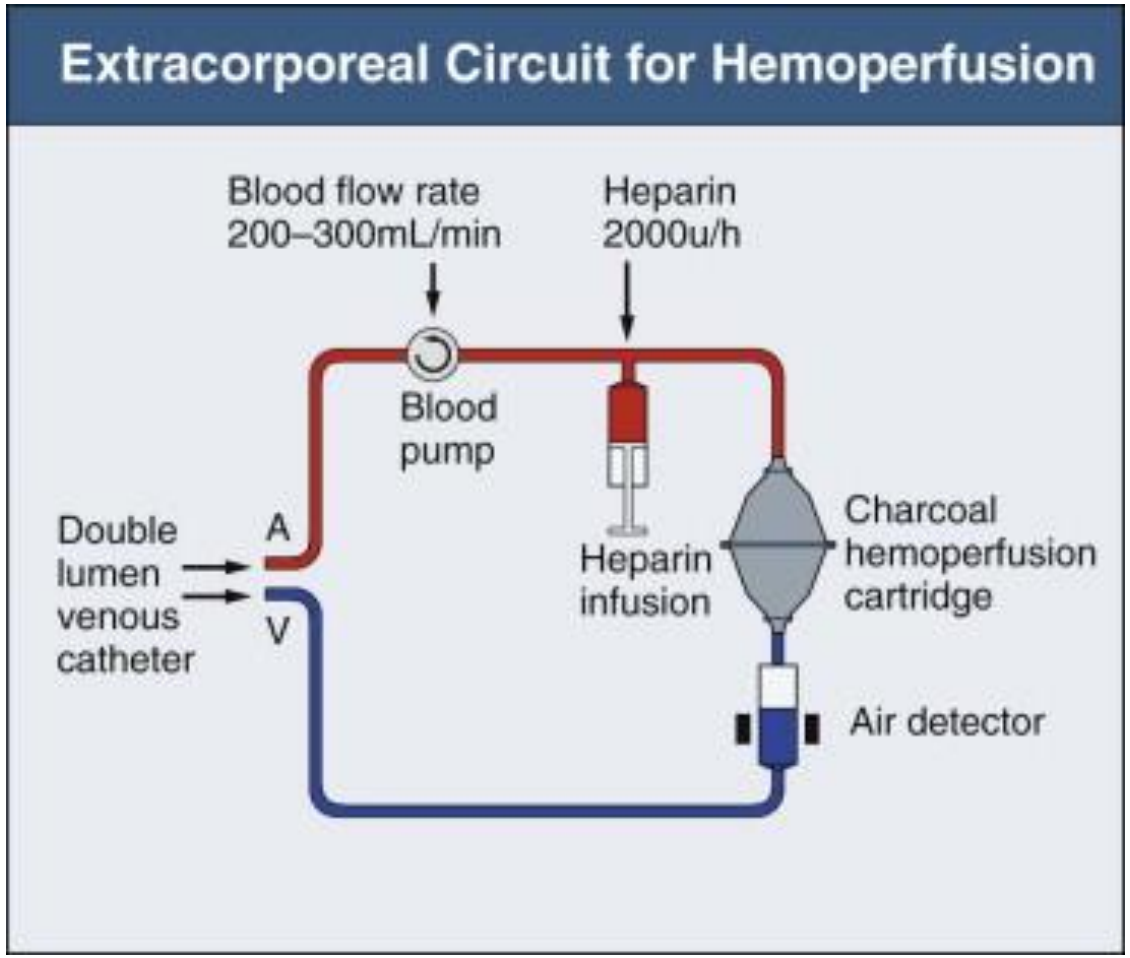
4. Hemoperfusion:

- It is similar to hemodialysis except there is no dialysis membrane or dialysate involved in the procedure.
- **Dialysate:** is the fluid that is used in dialysis to adjust the extracellular fluid composition and to maintain body homeostasis.
- SIMPLY, **hemoperfusion** is an extracorporeal (outside the body) blood purification modality that consists of the passage of anticoagulated whole blood through a device, usually a column, that contains adsorbent particles.

- The patient's blood is pumped through a perfusion cartridge where it is in direct contact with adsorptive material (usually activated charcoal) that has a coating of material such as cellulose or a heparin-containing gel to prevent the adsorptive material from being carried back to the patient's circulation.

Hemoperfusion:





Substance should have low volume of distribution and adsorption by activated charcoal.

- Can be used with lipid soluble compounds and with higher molecular weight compounds than for hemodialysis.
- Protein binding does not significantly interfere with removal by hemoperfusion.
- Primarily used for the treatment of serious **theophylline** overdose, as well as **paraquat** [herbicide] poisoning.

- An advantage of hemoperfusion over hemodialysis is that the total surface area of the hemoperfusion cartridges is much greater then with the dialyzing membrane in hemodialysis.
- Medical risks include thrombocytopenia, hypocalcemia, and leukopenia.
- Limited use because of the need to access to the sterile hemoperfusion cartridge

5. Hemofiltration

- **Two types:**

1. Arteriovenous hemofiltration.
2. Venovenous hemofiltration.

- The patient's blood is delivered through filters that take the shape of **hollow fiber tubes** and an ultrafiltrate (waste products and water) of plasma is removed by hydrostatic pressure from the blood side of the membrane.
- **Hemofiltration**: is a renal replacement therapy which is used in the intensive care setting. It is usually used to treat acute kidney injury (AKI), but may be of benefit in multiple organ dysfunction syndrome or sepsis.
- During hemofiltration, a patient's blood is passed through a set of tubing (a filtration circuit) via a machine to a semipermeable membrane (the filter) where waste products and water (collectively called **ultrafiltrate**) are removed.

- Different membrane pore sizes.

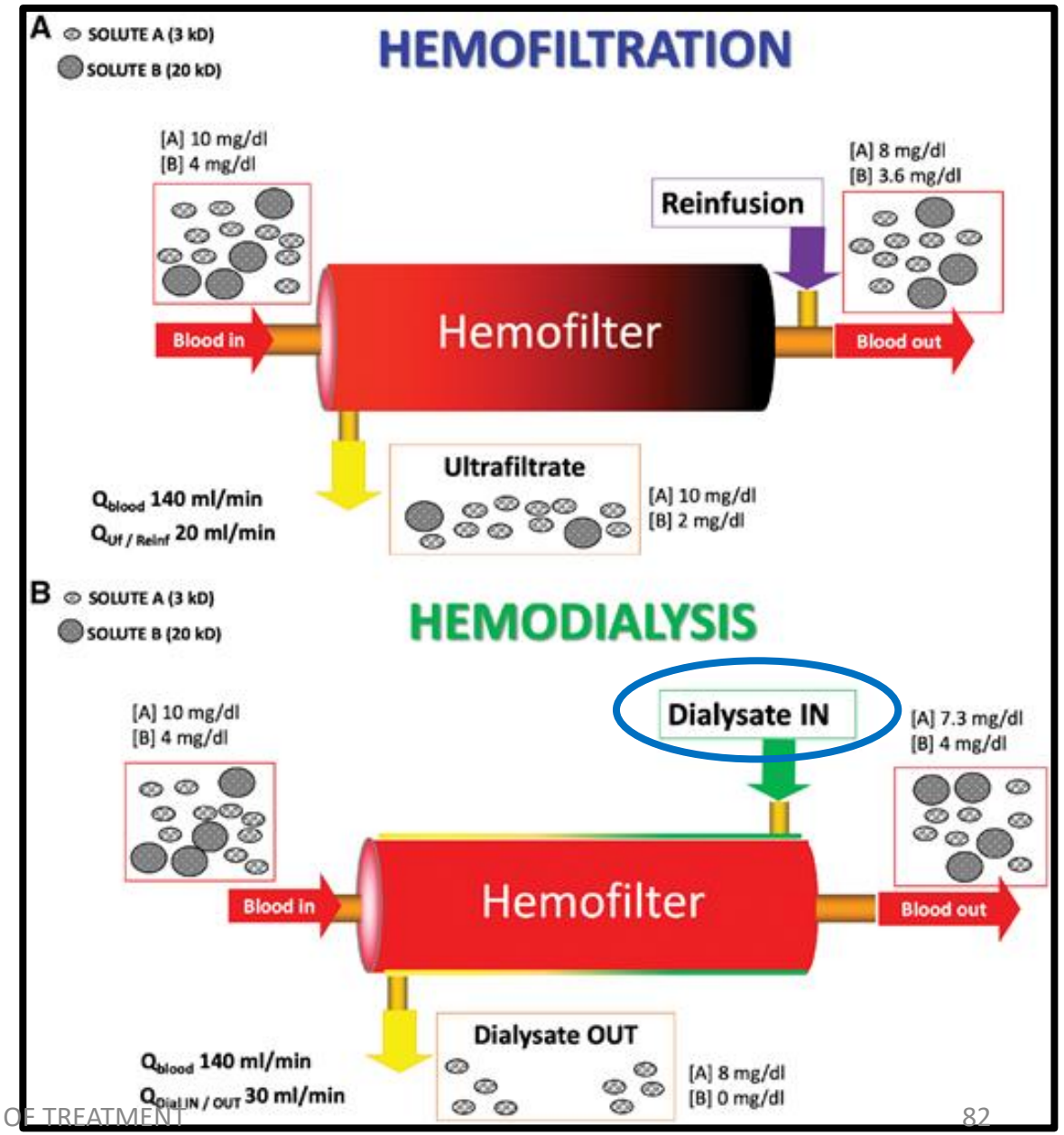
- The perfusion pressure for the technique is either generated by the patient's blood pressure (for arteriovenous hemofiltration) or by a blood pump (for venovenous hemofiltration).

- One potential advantage of continuous filtration versus intermittent hemodialysis is that the rebound phenomenon (increase in plasma toxin concentration shortly after hemodialysis is terminated—due to redistribution of the toxicant from the nonvascular, tissue, compartment to the vascular space) is not seen with hemofiltration due to the continuous nature of the procedure.

- This rebound is commonly seen during hemodialysis for lithium overdose

Difference between hemofiltration and dialysis?

- As in **dialysis**, in **hemofiltration** one achieves movement of solutes across a **semi-permeable** membrane.
- With **hemofiltration**, **dialysate {the fluid that is used in dialysis to adjust the extracellular fluid composition and to maintain body homeostasis} is not used**.
- Instead, a positive hydrostatic pressure drives water and solutes across the filter membrane from the blood compartment to the filtrate compartment, from which it is drained.



6. plasma exchange

- Limited use.
- **Advantage:** removing high molecular weight and/or plasma protein-bound toxicants.
- **Procedure:** involves removal of plasma and replacement with frozen donor plasma {blood product made from the liquid portion of whole blood}, albumin, or both with **IV** fluid.
- **The risks and complications** include allergic-type reactions, infectious complications, and hypotension.

- **Technique:** continuing oral administration of activated charcoal beyond the initial dosage, every two to four hours with approximately one-half the initial dose, or 0.5 g/kg.

Multi-dose activated charcoal

Table 33-7

Drugs for Which Multiple Dose Activated Charcoal Has Been Shown Effective as a Treatment Modality for Poisoning

Carbamazepine	Nadolol
Dapsone	Phenobarbital
Digoxin	Salicylates
Digitoxin	Theophylline

4.
Use of Antidotes in Poisoning

- In pharmacology, an antagonist is a substance that counteracts the action of another drug.

- Antitoxins neutralize toxins.
- Antivenins are antitoxins that neutralize the venom of the animal like a snake or spider.

- Although the general public often believes there is an antidote for every drug or toxin, the opposite is closer to the truth.

- There are, in fact, very few antidotes.

Mechanism of action

1. **Chelating** agent ex: heavy metal poisoning.

Antagonizing the effects of the toxicant ex: Atropine antagonizes the effect of organophosphate insecticides.

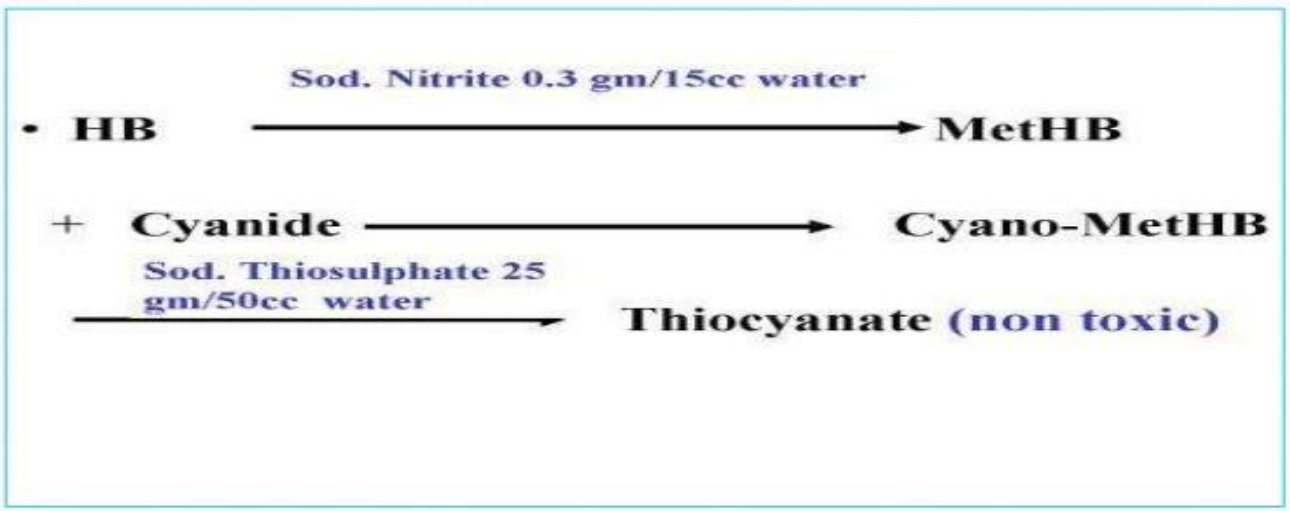
1. **Chemical** reacting with biological systems to increase detoxifying capacity for the toxicant.

Ex: sodium nitrite with cyanide poisoning ….formation of methemoglobin… alternative binding site for the cyanide ion, thereby making it less toxic to the body. {see the next slide}

Cyanide toxicity

Second step :

use **sodium thiosulfate** : which is administered IV. The sodium thiosulfate and cyano-methemoglobin become thiocyanate, releasing the hemoglobin, and the thiocyanate excreted by the kidneys .



- Many antidotes have a relatively narrow safety margin or low therapeutic index.

- Ex: physostigmine (a cholinergic agent) is given at an excessive dose or dosing rate to a patient with mild-to-moderate anticholinergic poisoning.
- Physostigmine is the antidote of choice for *Datura stramonium* poisoning. It is also an antidote for *Atropa belladonna* poisoning, the same as for atropine.
- The antidote can cause a potentially fatal bradycardia that can progress to a fatal cardiac arrest.

TABLE 3.10 Classification of Toxins and Their Specific Antidotes

Classification of toxins	Examples of specific toxic agents	Antidote
Alcohols	Ethylene glycol	Ethanol, fomepizol, pyridoxine
	Methanol	Ethanol, fomepizol, folic acid, leucovorin
Analgesics	Acetaminophen	*N*-acetylcysteine
	Aspirin	Sodium bicarbonate, ipecac
Anticholinergics	Cholinergic blockers	Physostigmine
	Tricyclic antidepressants	Sodium bicarbonate
Anticoagulants	Heparin	Protamine
	Warfarin	Vitamin K_1 (phytonadione)
Arthropod bites and stings	Black widow spider bite	*Latrodectus* antivenom
	Brown recluse spider bite	*Loxosceles* antivenom
	Rattlesnake bite	*Crotalidae* antivenom
	Scorpion sting	Antivenin
Benzodiazepines	Diazepam, alprazolam	Flumazenil
Cardiovascular drugs	Digitalis glycosides	Digoxin immune FAB
	β-Blockers	Glucagon
	Calcium channel blockers	Calcium, glucagon

B6

Folinic acid, also known as leucovorin, is a medication used to decrease the toxic effects of methotrexate and pyrimethamine

Warfarin decreases blood clotting by blocking an enzyme called **vitamin K** epo xide reductase that reactivates **vitamin K** 1.

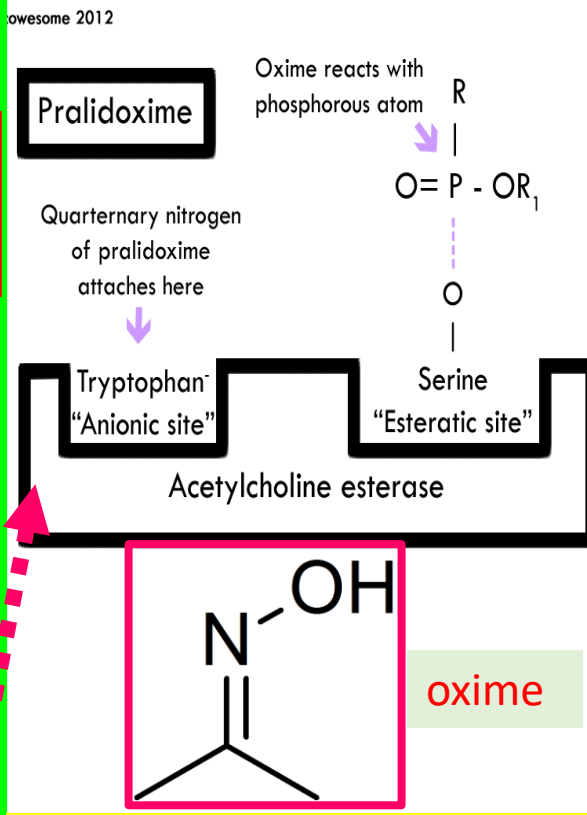
It does so by competitively antagonizing the benzodiazepine at the receptor site level.

Fragment-antigen binding

Gases	Chlorine gas	Sodium bicarbonate[a]
	Hydrogen sulfide gas	Sodium nitrite
	Carbon monoxide	100% oxygen
	Cyanide	Amyl nitrite, sodium nitrite, sodium thiosulfate
Infectious agents	Clostridium botulinuum (botulism)	*Botulinuum* antitoxin
Metals	Arsenic	BAL
	Copper	D-Penicillamine
	Mercury	BAL, DMSA
	Iron	Deferoxamine
	Lead	Calium-Na_2-EDTA, dimercaprol, DMSA, BAL, D-penicillamine
Methemoglobinemia-inducing agents	Nitrites, nitrates	Methylene blue
Opiates	Narcotic analgesics and heroin	Naloxone, natrexone, nalmefene
Pesticides	Organophosphate insecticides	Atropine followed by pralidoxime
	Carbamate insecticides	Atropine

[a] For treatment of accompanying metabolic acidosis.

Abbreviations: BAL, British antilewisite; DMSA, 2,3-dimercaptosuccinic acid; EDTA, ethylenediamine tetraacetate; FAB, fragment antigen binding.



Methylene blue accelerates the conversion of **methemoglobin** to **hemo globin** effectively **reversing** the functional **anemia** caused by **methemoglobinemia**.

HYPERBARIC OXYGENATION THERAPY (HBO)

- In **HBO therapy**, oxygen is administered to a patient in an enclosed chamber at a pressure greater than the pressure at sea level (e.g., 1 atmosphere absolute).
- This therapy has been used in **carbon monoxide** and **methylene chloride** poisonings (methylene chloride is metabolized to carbon monoxide in the body).

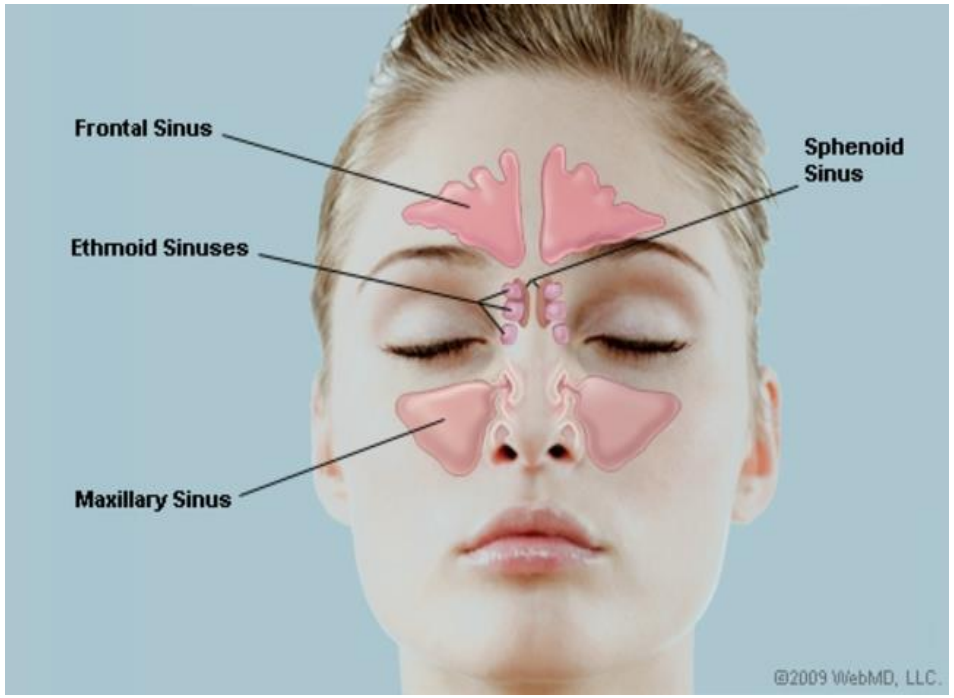
Complications of HBO therapy include:

1. Pressure-related otalgia (ear pain).
2. Sinus pain.
3. Tooth pain.
4. Tympanic membrane [ear-drum] rupture.
5. Anxiety.
6. Convulsions.
7. Tension pneumothorax also have been observed in patients receiving HBO therapy.

❖**Pneumothorax:**

❖An abnormal collection of air in the pleural space between the lung and the chest wall.

❖Symptoms typically include sudden onset of sharp, one-sided chest pain and shortness of breath.



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- Clinical toxicology , principles and mechanisms, 2 ed , Frank A. Barile,2010,chapter3