PREFACE

Every day we are exposed to thousands of substances some of which may be toxic. These include both natural substances, mainly found in food, and man-made chemicals. Excessive exposure to some of these substances may cause health problems – serious illnesses, allergies, cancer, or birth defects. So it is mandatory for the medical students to have fair knowledge about commonly encountered poisons and potentially toxic substances in our locality and how to manage them.

This book is organized around the primary goal of explaining the fundamental principles of clinical toxicology that enable the future doctor to approach any toxic emergency with few problems. Every effort has been made to provide the medical students with easily accessible, but in –depth resource on toxicology.

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GENERAL TOXICOLOGY

ILOS:

- To know general factors that influence toxicity.
- To know what aspects of the physical examination and diagnostic tests are to be conducted.
- To understand steps of the initial approach to the poisoned patient in terms of setting immediate priorities.
- To know proper management of poisoned patients.

Definitions:

- A ***toxin*** is any poisonous substance of whatever origin that reacts with specific cellular components to kill cells, alter growth or development, or kill the organism.
- ***Clinical Toxicology*** is concerned with clinical manifestations associated with short or long-term exposure to toxic substances.
- ***Xeno-biotic*** is any substance, whether harmful or not, that is foreign to the body.

"All substances are poisons; there is none that is not a poison. The right dose differentiates a poison and a remedy." Paracelsus (1493-1541).

Classification of poisons according to:

I) Action
II) Origin
III) Selective organ toxicity

I) The Action may be:

1. **Local : e.g.** Inorganic Corrosive poisons (as Sulphuric, Hydrochloric and Nitric acids and Alkaline potash) and irritant mechanical poisons (e.g., glass powder).
2. **Remote:** e.g.: Plant poisons and medical Therapeutics.
3. **Both local and remote actions:** e.g.: Metallic poisons (as Arsenic, Mercury and Lead) and organic Corrosive poisons (as Carbolic and Oxalic acids).

II) The origin of a poison may be:

1. **Plant: eg.** Atropine from Datura, atropa belladonna or hyoscyamus plants.
2. **Animal: eg.** Snake and Scorpion venoms.
3. **Metallic: eg.** Lead, Mercury, Phosphorus or Iron.
4. **Synthetic: eg.** Analgesics, Antipyretics and Hypnotics.

III) Selective organ toxicity:

1. **Hepato-toxins:** Iron and Paracetamol.
2. **Nephro-toxins:** Mercury and Phenol.
3. **Cardio-toxins:** Digitalis, Quinine and Aconite.
4. **Neuro-toxins:**
   a) CNS stimulants e.g. Amphetamines, cocaine, strychnine.
   b) CNS depressants e.g. Hypnotics, narcotics, alcohol and anesthetics.
5. **Dermal toxins:** Arsenic and mercury.
6. **Ocular toxins:** Quinine and methanol.
7. **Respiratory toxins:** Kerosene and chlorine.

Factors modifying the actions of a poison in the body:

1) Factors related to the poison:

Mainly its dose (dose response relationship), form, concentration, PH and route of administration.

2) Factors related to the patient:

1. ***Stomach* of the patient:**
   a) Empty stomach allows rapid absorption.
   b) Fatty food contents help absorption of mercury.
   c) Achlorhydria ↓↓ toxicity of KCN.
2. ***State of health:***

   Some diseases increase the toxicity as in liver and renal failure due to decreased detoxification process.
3. ***Age:***

   Extremes of age are more vulnerable to toxic effects as in children the physiological functions are not well developed while in old age physiological functions are exhausted.
4. ***Tolerance:***

   It means repeated use of the same dose will not produce the same effect, as in drug addiction.

5. ***Idiosyncrasy (Toxicogenetics):***
   a) Abnormal response to drugs.
   b) Hereditary basis e.g. Sulphonamide in G6-PD deficiency →hemolytic anemia.
6. ***Hypersensitivity (Allergy):***
   a) Exaggerated response to a drug e.g. penicillin.
   b) It is an Ag- Ab reaction

3) Drug- interactions:

1. ***Augmentation:***

The chemicals enhance effects to each other, as aspirin and Paracetamol.

2. ***Synergism:***

A chemical exaggerates the effect of another as alcohol with barbiturate.

3. ***Antagonism:***

A chemical abolishes or counteract the effect of another as Chelators and metallic poisons.

Diagnosis of Poisoning

I. History and circumstantial evidence:

- Sudden illness of previously healthy person or persons after ingestion of food or drink or exposure to chemicals, gas, insect or snake bite.
- History of recent purchase of a poison or the presence of a syringe or an empty bottle nearby the patient.

II. Clinical Picture :

1) Vital signs

a. B.P: systolic 100-140 and diastolic 60-90
b. Pulse: 60 - 90 beats per minute.
c. Respiration: 12–16 breaths/minute
d. Temperature: 36.5 -37.2 C

2) Complete general and local examinations:-

a. Skin, smell of breath and pupils.
b. Chest and abdomen examination.
c. Neurological examination: -

Coma:

Coma is a state of unconsciousness in which a person cannot be awakened; fails to respond to external stimuli (sensory or verbal); lacks a normal wake-sleep cycle; and does not initiate voluntary actions.

Types of coma:

a. **Toxic coma:** CNS depressants, Anticholinergics and toxin causing cellular hypoxia e.g. HCN & CO.
b. **Pathologic coma:** hepatic failure, renal failure, metabolic e.g. hypoglycemia, hypertensive encephalopathy.
c. **Traumatic coma:** head injuries.

Coma scales:

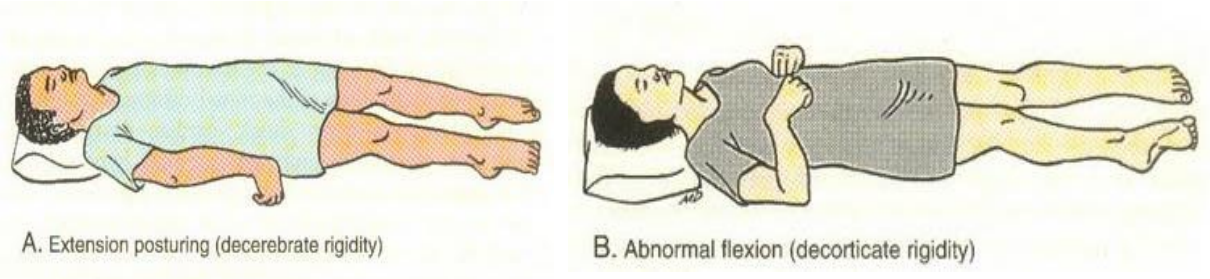
1. *Reed's coma scale*

Grade	Conscious level	Response to pain	Reflexes	Respiration	Circulation
0	Sleep	Arous-able	Intact	Normal	Normal
I	**Comatose**	Withdrawal	Intact	Normal	Normal
II	Comatose	**None**	Intact	Normal	Normal
III	Comatose	None	**Absent**	Normal	Normal
IV	Comatose	None	Absent	**Cyanosis**	**Shock**

2. *Glasgow coma scale (GCS)*

Glasgow Coma Scale	
Eye opening	
spontaneous	4
to speech	3
to pain	2
no response	1
Verbal response	
alert and oriented	5
disoriented conversation	4
speaking but nonsensical	3
moans/unintelligible sounds	2
no response	1
Motor response	
follows commands	6
localizes pain	5
withdraws from pain	4
decorticate flexion	3
decerebrate extension	2
no response	1

The maximum score is 15 & the least is 3 with bad prognosis



In the assessment of coma, Reed's coma scale is preferred to Glasgow coma scale (GCS), as GCS overestimates the degree of impairment.

3) Toxidromes:

They are the groups of signs and symptoms that consistently result from a particular toxin (group of toxins):

I. Anticholinergic Toxidrome.
II. Sympathomimetic Toxidrome (CNS stimulants).
III. Opioid toxidrome (CNS depressant).
IV. Sedative hypnotic toxidrome (CNS depressant).
V. Cholinergic Toxidrome.

III. Investigations:

1) Laboratory:

i- Routine studies: CBC, serum electrolytes, ABG, renal & hepatic function tests & serum glucose.

ii- Toxicological screening :-

a- Preliminary tests (qualitative):

1. Color tests
2. Thin layer chromatography (TLC)
3. Toxi-Lab system

b- Confirmatory tests (quantitative):

1. Immunoassay (Semi- quantitative)
2. Gas chromatography (GC) and high performance liquid chromatography (HPLC).
3. Gas mass spectrometry (GC/MS) and liquid chromatography mass spectrometry (LC/MS).

iii- Anion Assessment:

-**Anion gap:** the difference between the measured cations and anions in serum.

Anion gap = $(Na^+) – (Cl^- + HCO3^-)$ = 7±4 MMOL/L.

-Elevated values may occur in methanol, uremia, diabetic ketoacidosis, paraldehyde, iron, lactic acidosis, ethylene glycol and salicylates (MUDPILES).

N.B.:

- **Urine** is usually the **best sample** for broad **qualitative** screening while **Blood** samples should be for **quantitative** testing as Paracetamol, salicylate, iron, theophylline, cyclic antidepressants, phenothiazine, lithium, digitalis, CO, methanol and ethanol poisoning.
- Generally, metabolites in the urine can be detected as long as 2-3 days (or longer) after exposure, compared with 6-12 hours in the blood.

2) ECG:

Cardiac monitoring may be especially useful in poisoning due to sympathomimetic agents, cyclic antidepressants, digitalis, ß-blockers, etc.

3) Radiology:

1. **Chest X-ray** for chemical or aspiration pneumonitis, cardiogenic or non-cardiogenic pulmonary edema.
2. **Abdominal X-ray** for ingested radio opaque toxins {(**CHIPES)**: **C**hloral hydrate, **H**eavy metals, **I**ron, **P**henothiazine [also packets of cocaine or heroin], **E**nteric-coated and **S**ustained- release preparations}.

General Lines of Poisoning Treatment

I. **Supportive therapy (1st Aid) "**Treat the patient not the poison"
II. **Gastro-intestinal (GIT) Decontamination**
III. **Elimination of the poison from the blood**
IV. **Antidotes**

I. Supportive therapy: = (Support the ABCs)

1) Airway [keep it patent] by:

1. Optimize the airway position to force the flaccid tongue forward and to maximize the airway opening. The following techniques are useful:

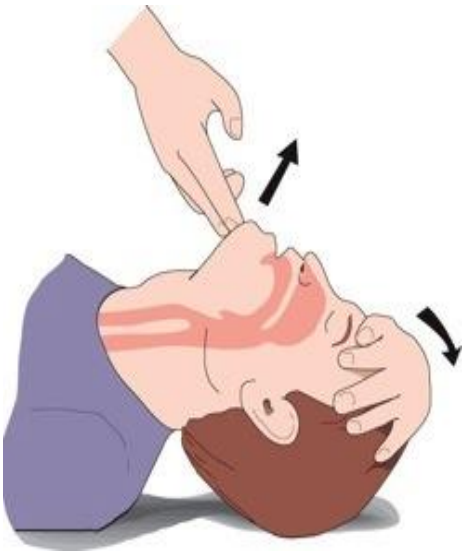
a. **Place the neck and head in the "sniffing"** position [the neck flexed forward and the head extended].

b. **Apply the "jaw thrust"** to create forward movement of the tongue without flexing or extending the neck. Pull the jaw forward by placing the fingers of each hand on the angle of the mandible just below the ears.

c. **Place the patient in a head-down, left-sided position** that allows the tongue to fall forward and secretions or vomitus to drain out of the mouth.

2. If the airway is still not patent, examine the oropharynx and remove any obstruction or secretions by suction or by a sweep with the gloved finger.

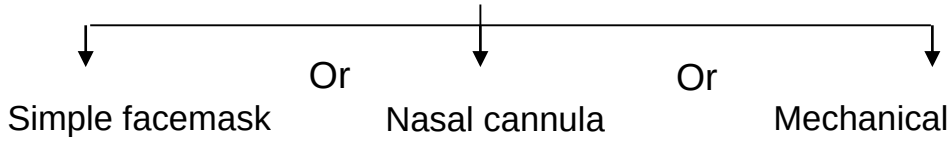
3. The airway can also be maintained with artificial airway devices.



Sniffing

Jaw thrust

2) Breathing (O2 therapy) by



N.B. Breathing difficulties are the major cause of morbidity and death in patients with poisoning or drug overdose.

3) Circulation:

- Check blood pressure and pulse rate and rhythm.
- Secure venous access.
- Begin continuous electrocardiographic (ECG) monitoring.
- Hypotensive patients→ intravenous infusion of normal saline.
- Hypertension →antihypertensive agents as ACE, CCB
- Arrhythmia →antiarrhythmic drugs (lidocaine, phenytoin, etc.).
- In seriously ill patients (e.g., those who are severely hypotensive, convulsing, or comatose), place a Foley's catheter in the bladder, obtain urine for routine and toxicological testing, and assess urine output **/** hour.

4) C.N.S: (Coma or Convulsions):

A- Treatment of Coma:

Coma cocktail should be used as diagnostic and/or therapeutic purpose.

1) ***Dextrose:*** All comatose patients should receive concentrated dextrose unless hyperglycemia is diagnosed by an immediate bedside test.

   Initial doses include the following:

   - Adults: 50% dextrose, 50 mL (25 g) IV.
   - Children: 25% dextrose, 2 mL/kg IV.

2) ***Thiamine:*** 100mg I.V. for possible **Wernicke**'s encephalopathy in patients suffering from thiamine deficiency (alcoholics and nutritionally starved patients) (Thiamine is essential for proper glucose utilization).

3) ***Naloxone (Narcan):*** All patients with respiratory depression should receive naloxone.

B- Convulsions:

- Seizures are treated with diazepam 0.2 mg/kg slowly IV (over 1-2 minutes) followed by Phenobarbital 15 mg/kg slowly IV if no response to diazepam.
- ***Caution:*** Anticonvulsants can cause hypotension, cardiac arrest, or respiratory arrest if administered too rapidly.

II. Gastro-intestinal (GIT) Decontamination

1) **Emesis**
2) **Gastric lavage**
3) **Activated charcoal**
4) **Cathartics**
5) **Whole bowel irrigation**

1) Emesis

- Syrup of ipecac–induced emesis is no longer the treatment of choice for any ingestion because of the availability of activated charcoal.
- It may be employed in rare situations when medical care is expected to be delayed more than 60 minutes and if the ipecac can be given within a few minutes of the ingestion.
- Ipecac should not be administrated more than 30–60 minutes after ingestion of the poison.
- Vomiting usually occurs within 20–30 minutes after syrup of ipecac administration.
- Severe forceful vomiting may result in hemorrhagic gastritis.

i. **Mechanism of action:**

The active principles of ipecac are ***Emetine and Cephaline***. Both of them act locally by irritating the gastric mucosa and centrally by stimulating the medullary chemoreceptor trigger zone **(CTZ)** to induce vomiting.

ii. **Administration of syrup of ipecac:**

- Dose for adults: 30 mL orally followed by 3 glasses of water.
- Dose for children < 5 years→ 15mL and children < 1 year 10 mL and it is not recommended for infants below 6 months.
- If emesis has not occurred within 20min, the dose should be repeated once.

iii. **Contra-indications of emesis:**

- **C**orrosives: for fear of perforation of esophagus or stomach.
- **C**oma: for fear of suffocation or aspiration pneumonia.
- **C**onvulsions: as vomiting and patient manipulation may stimulate convulsions.
- **K**erosene (volatile hydro**c**arbons) for fear chemical pneumonitis.
- **C**hronic poisoning.
- **C**ardiac and elderly patients and vascular insufficiency.
- Infants below the age of 6 months (immature gag and airway protective reflexes).

2) Gastric lavage

- Gastric lavage is a medical procedure only used in hospital Emergency Rooms (ER).
- Gastric lavage is probably more effective than ipecac, especially for recently ingested toxic substances (less than 2-3 h).
- **It may be valuable as long as 6 hrs. post ingestion in some poisons as:**
    - **Salicylates** make aspirin cake due to sticking to stomach mucosa.
    - **Barbiturate**, which slow down stomach motility.
    - **Morphine**, which is secreted in stomach.

i. ***Technique:***

- Place the patient on his left side with lowered head (to prevent ingested material from being pushed into the duodenum during lavage).
- Introduce gastric tube through the mouth or nose into the stomach until the mark (Gastric tubes have mark at 50 cm from distal end of the tube in adults).

- Check tube position by:
    - No cough, dyspnea or cyanosis.
    - Air insufflation while listening with a stethoscope positioned on the patient's stomach.
    - Aspiration brings up gastric contents.
    - Absence of bubbling when the end of the tube is immersed in water during expiration, but present only during inspiration.
    - No Breath sounds can be heard from the end of the tube.
- Withdraw as much of the stomach contents as possible and put it in labelled container for toxicological analysis.
- Give activated charcoal down the tube before lavage to begin adsorption of material that may enter the intestine during the lavage procedure.
- Instill slightly warm water or saline, 200 to 300 mL and remove by gravity or active suction.
- Repeat the wash for a total of 2 L or until the return are clear.
- The tube is firmly nipped (by an artery forceps) to avoid spilling of fluids during withdrawal.
- Caution: using excessive volumes of lavage fluid can result in hypothermia or electrolyte imbalance in infants and young children.

ii. Complications of gastric lavage:

- Asphyxia if the tube passes to the trachea.
- Aspiration of stomach contents leads to aspiration pneumonia.
- Esophageal perforation.
- Hypertension & tachycardia as a stress reaction.
- Electrolyte imbalance.

iii. Contraindications of gastric lavage: [are the same as for emesis] except:

- Coma & volatile hydrocarbons → Lavage is allowable after inserting a cuffed endotracheal tube to prevent aspiration pneumonia.
- Convulsions→ Lavage can be performed under general anesthesia.
- Cardiac dysrhythmias must be controlled before gastric lavage is initiated, as insertion of the tube may create vagal response →cardiac arrest.

iv. Disadvantages of gastric lavage:

- The procedure may delay administration of activated charcoal
- The procedure may hasten the movement of drugs and poisons into the small intestine, especially if the patient is supine or in the right decubitus position.

3) Activated Charcoal (AC)

This is considered **the most useful agent** for the prevention of absorption of toxins.

i. Source:

It is manufactured by pyrolysis of wood and then activation by passing hot steam to increase the pores. The final product (activated charcoal) has a large surface area of 950- 2000 m^2/g.

ii. Action:

The charcoal particles have many pores & holes, which adsorb (binds) poisons in GIT and hence decrease their absorption.

iii. Dose:

- 1 –1.5 g/kg in adults [orally, mixed with H2O].
- 15gm – 30gm in children.

iv. Contraindications:

- Paralytic ileus and Intestinal obstruction.
- Drowsy patient unless the airway is adequately protected or endotracheal intubations should be inserted

v. Activated Charcoal is ineffective (poorly adsorb) in some poisons as:

C-- Cyanide and **C**orrosives.
H--Heavy metals (Iron, Lead, Arsenic and Mercury).
A--Alcohols.
R--Rapid onset or absorption poisons (Cyanide and Strychnine).
C--Chlorine and iodine**.**
O--Others insoluble in water **(**substances in tablet form**)**.
A--**A**liphatic and poorly adsorbed hydrocarbons (petroleum distillates).
L—**L**ithium

vi. Disadvantages:

i. It may adsorb Ipecac syrup [emetic] & prevents its action so it must be given after occurrence of vomiting.
ii. It may adsorb oral antidotes (N- Acetylcysteine [antidote to Paracetamol], Penicillamine and DMSA [antidote to heavy metals] & prevent their action. Therefore, antidotes should be given 1-2 hours after charcoal administration.
iii. It may induce vomiting (gritty texture, volume administration, additives as sorbitol or a combination of them all).
iv. Mechanical obstruction of airways, if aspired into lungs (slurry is not well diluted).
v. Mechanical bowel obstruction in multiple dose manners especially with decreased gut motility.

N.B.

Cathartic agent such as sorbitol is often administered with charcoal to facilitate the removal of the toxin from the GIT.

4) Gastrointestinal Dialysis (Multiple-Dose Activated Charcoal (MDAC)):

i. Indications for poisoning that:

- Show enterohepatic circulation (TCA, Digitalis and Barbiturates)
- Stick to the stomach (Salicylate).
- Slow gut motility (Barbiturates & Morphine)

ii. Dose:

- 0.5 – 1 gm/kg every 4 hours OR
- Continuous intra-gastric flow (0.25-0.5 gm/kg/hr.) via Ryle tube.

iii. Mechanism:

MDAC facilitates the passage of toxin from plasma into intestine by creating concentration gradient between blood & intestinal lumen bowel fluid so it is called gut dialysis.

5) Cathartics

The commonly used cathartics are $MgSO_4$, Mg citrate and Sorbitol.

i. Contrindications:

1. Paralytic ileus and intestinal obstruction.
2. Sodium and magnesium containing cathartics should not be used in patients with fluid overload or renal insufficiency, respectively.
3. There is no role for oil-based cathartics (previously recommended for hydrocarbon poisoning).

ii. Adverse effects

1. Electrolyte imbalance from fluid loss and hyperosmolarity may result from repeated doses of cathartics.
2. Hypermagnesemia may occur in patients with renal failure.
3. Abdominal cramping and vomiting may occur, especially with sorbitol.

6) Whole Bowel Irrigation

i. Definition:

Irrigation of the entire GIT with non-absorbable isotonic electrolyte solution containing Polyethylene Glycol through nasogastric tube until the bowel has been cleaned rapidly from the poison.

ii. Indication:

(1) Poorly adsorbed drugs by Activated Charcoal [see A.C.]

(2) Preparations, which are slow, release e.g. Salicylates and Calcium Channel blockers.

(3) To expel the packets of illicit drugs (e.g. Cocaine or Heroin) in case of:

-Body packers: who swallow tightly sealed packets of illicit drugs or

-Body stuffers: drug sellers who swallow the evidence [i.e. just prior to detection].

iii. The rate:

The solution is given at high flow rates to force intestinal contents out: 2 L /hour in adults or 0.5L /hour (40 mL/kg/h) in children.

iv. The end point:

When the rectal effluent is clear OR ideally when radiography reveals no opacities previously visualized**.**

v. Contrindications:

1. Unprotected airway or compromised airway.
2. Bowel obstruction, ileus, or perforation.
3. Clinically significant GIT bleeding.
4. Intractable vomiting.
5. Unstable vital signs.
6. Signs of leakage of illicit drug packets (e.g. tachycardia, hypertension, hyperthermia in a patient who has ingested cocaine packets); surgical consult should be obtained in this circumstance.

III. Elimination of the poison from the blood (Enhanced Elimination Methods)

1) Forced diuresis and alteration of the urine pH (Ion Trapping):

2) Extracorporeal methods which include:

i. Dialysis: Hemo [Artificial kidney] or Peritoneal.

ii. Hemoperfusion.

iii. Plasmapheresis.

For a drug to be removed from blood, it should be located primarily within the blood stream or in the extracellular fluid. If it is extensively distributed to tissues, it is not likely to be easily removed.

Three factors are important:

1. The volume of distribution (Vd): A drug with a large Vd has a very low plasma concentration. In contrast, a drug with a small Vd is potentially quite accessible by these procedures.

Vd = D/Cp (D = dose administered, Cp = plasma concentration)

2. Protein binding:

Highly protein-bound drugs have low free-drug concentrations and are difficult to be removed by dialysis.

3. The poison should be excreted mainly by kidney

1) Forced diuresis and alteration of the urine pH:

i. Forced diuresis:

(I) Definition:

Removal of the poison from the blood through increasing the glomerular filtration rate e.g. by giving diuretics and IV fluid. The objective is to maintain a urine output of 300-500mL/hrs. or 8-14 L/day.

(II) Contraindication:

1. Electrolyte imbalance
2. Heart failure
3. Renal failure
4. If the poison is not excreted by kidney

ii. Alteration of the urine pH (Ion Trapping):

Changing PH of urine → the poison to be ionized →poison can't be reabsorbed through the cells of the renal tubule, as ionized drugs are poorly absorbable through cell membranes → increase excretion.

Types of ion trapping:

1. ***Alkalization of urine***

- For elimination of acidic drugs e.g. salicylates and barbiturates.
- **Using**: ($NaHCo_3$) 1-2 mg/ kg/ in 5% dextrose→ urine pH 7.5-8.0.

2. ***Acidification of urine***

- For elimination of alkaline drugs e.g. Amphetamine, Quinidine and PCP.
- **Using:** (NH4Cl) 75mg/kg/day in 5% dextrose → urine pH 4.5-6.0.

N.B.:

Acid diuresis is no longer used (Obsolete) owing to the complications associated with metabolic and urinary acidosis (rhabdomyolysis & myoglobinuria → renal failure).

2) Extracorporeal Methods:

Hemodialysis	Peritoneal dialysis	Hemoperfusion	Plasmapheresis
Mechanism of action			
Removal of poisons from the **blood** to the **dialysis fluid** according to **concentration gradient** (from higher to lower) through semi permeable membrane which is either ↓ Cellophan ↓ Peritoneum In hemodialysis, blood is taken from a large vein (usually a femoral vein) with a double-lumen catheter and is pumped through the hemodialysis system. The patient must be anti-coagulated to prevent clotting of blood in the dialyzer. Drugs and toxins flow passively across the semipermeable membrane down a concentration gradient into a dialysate solution.		The blood is pumped directly through a column containing an adsorbent material (either charcoal or exchange resins). Then blood returns via a venous catheter free from poisons.	A volume of blood is removed, and all **blood components** except the **plasma** are returned to the circulation. The plasma is replaced with a **crystalloid** solution **or fresh frozen plasma from another donor.**
Indication			
1) Renal failure and the poison is excreted by kidneys **2) Liver failure,** & the poison is metabolized by the liver **3) prolonged coma** **N.B.** the drug must be dialyzable i.e. Low molecular weight, Low lipid solubility, Low protein binding and Water-soluble.		For clearing toxic substances that are poorly eliminated by dialysis **[Non-dialyzable]** i.e. High molecular weight, High lipid solubility, High protein binding and Low water solubility.	Useful for removing protein-bound toxins, such as **phenytoin,** those are not removed by hemodialysis and are inefficiently removed by hemoperfusion.
Complications			
1) Hemorrhage 2) Venous thrombosis 3) Hypotension 4) Infection 5) Hepatitis	1)**P**eritonitis 2)**P**erforation of abdominal organs	1) Hemorrhage(may be due to heparin) 2) Hypotension 3) Hypoglycemia 4) Hypocalcemia	1) Hypervolemia or hypovolemia 2) Anaphylactic shock 3) thrombocytopenia

IV. Antidotes

Antidotes are substances, which oppose the effects of poisons without causing damage to body.

Types of Antidotes:

1) Local:

i. **Physico-mechanical Antidotes**

ii. **Chemical Antidotes**

i. Physico-mechanical Antidotes	
Adsorbents	Used to adsorb the toxic agents **e.g. Activated charcoal**
Demulcents	Protect the stomach mucosa by coating it **e.g. Milk & egg white**
Entanglers	Catch the sharp solid objects e.g. **cotton** for pins
Dissolvent	Dissolve the poisons e.g. **Ethanol 10%** used to dissolve phenol
ii. Chemical Antidotes	
Neutralization	**Weak alkalis/**acids used to neutralize **acidic/**alkaline corrosives respectively. Obsolete due to:- **(1) Exothermic** reaction increases tissue destruction **(2) Co_2 release** when $NaHCo_3$ is used gastric perforation occurs.
Precipitation	▪ **Skimmed milk** precipitate **mercury** ▪ **Tannic acid** (strong tea) precipitates **plant toxins.**
Reduction	**Mercuric chloride** [divalent, toxic] is reduced by **Na formaldehyde sulfoxylate** **Mercurous chloride [**Monovalent, non-toxic].
Oxidation	Oxidation using **H_2O_2** or **$KmnO_4$**1/5000, used for **Plants and Cyanide.**

2) Systemic:

i. Physiological or pharmacological antidotes:

These produce effects opposite to that of poison e.g.:

- **Atropine and oxime** for Organophosphorus poison**,**
- **Naloxone** for Morphine,
- **N-Acetylcysteine** for Acetaminophen

ii. Chelating agents:

These substances combine with **metals** forming nontoxic compounds that are easily excreted in urine:-

1- **BAL (British anti-lewisite) Dimercaprol.**
2- **EDTA (Ethylene Diamine Tetra Acetic acid):**
   a) Ca disodium EDTA.
   b) Disodium EDTA.
   c) Dicobalt EDTA.
3- **Deferrioxamine (Desferal).**
4- **D-Penicillamine (Cuprimine).**
5- **DMSA [2,3-Dimercapto succinic acid] (Succimer).**

BAL (British anti-lewisite) (Dimercaprol)	EDTA [Ethylene diamine tetra acetic acid]	Deferrioxamine (Desferal)	D-Penicillamine (Cuprimine)
Preparations			
• Oil • Ointment • Eye drops	Ampoules	Ampoules	Capsules
Mechanism of action			
• BAL has **2- SH** groups that can attract **metals (**have a great affinity for SH group) → nontoxic compounds rapidly excreted in urine. • **Metals** + SH containing resp. enzymes → Inactive enzymes • **BAL** [2SH] +**Metals** → Non-toxic rapidly excreted compound.	• **Ca disodium EDTA** combines with **metal** → non-toxic and rapidly excreted compound **[the metal replace calcium].**	• It has high affinity for ferric iron. • It competes for iron of ferritin and hemosiderin, while iron of cytochromes and Hb is not affected.	• It is hydrolytic product of penicillin, • It contains one SH group.
Dose			
2.5mg/kg/6hrs for 2 days **2.5 mg**/kg/12hrs for 1week **[I.M oily]**	1 gm / 250 ml saline-twice daily for 5 days [**IV infusion]**	**I.M.:** 1gm I.M. injection then 500mg / 4 hours / 2 days	1-2 **capsules** (250mg) / 6 hrs. on empty stomach, to preserve dietary minerals
Uses			
• Lead • Arsenic • Mercury • Gold • Bismuth	• Calcium disodium EDTA is used in Lead & cadmium • Disodium EDTA is used in digitalis • Dicobalt EDTA is used in cyanide poisoning	• Iron	• Lead • Mercury • Arsenic
Disadvantages			
Contraindicated in: **- Iron toxicity,** as the iron – BAL complex is more toxic than iron. **- G6-PD deficient** patients leading to Hemolysis. **- High B.P** and **fever.**	**Nephrotoxicity**		

DMSA An analogue of ***BAL***, which is **less toxic.**
Uses: Lead, Arsenic & Mercury.

Dose: 10mg/kg/eight hrs. for 5 days then**10mg**/kg/12 hrs. for 2 weeks [orally].

Advantages:
1) It can be used in **iron** toxicity.
2) No Hemolysis in **G-6 PD deficient** patients.
3) Has minimal effect on **essential body minerals.**

TOXIDROMES

They are the groups of signs and symptoms that consistently result from a particular toxin (group of toxins).

I. **Anticholinergic Toxidrome**
II. **Sympathomimetic Toxidrome (CNS stimulants)**
III. **Opioid toxidrome (CNS depressant)**
IV. **Sedative hypnotic toxidrome (CNS depressant)**
V. **Cholinergic Toxidrome**

I. Anticholinergic Toxidrome

1- Atropine.
2- Antihistaminic.
3- Tricyclic antidepressants.
4- Phenothiazine.

1- Atropine, Hyoscyamine and Hyoscine

Source:

All parts of the following plants:

- Datura (Fastiosa and Stramonium) "Thorn apple".
- Atropa Belladonna.
- Hyoscyamus muticus.

Uses of Atropine:

1) Pre-anesthetic as it prevents vagal inhibition of the heart, secretions in air passages and vomiting.
2) Antispasmodic for treating abdominal colic.
3) Bronchodilator for treating asthma
4) Heart stimulant following cardiac arrest.
5) Mydriatic.
6) In Toxicology → antagonist in: Morphine, Digitalis and Organophosphorus insecticides.

Uses of Hyoscine:

Mania, motion sickness and as “Truth serum“(it depresses CNS without initial stimulation).

Conditions of Poisoning:

- **Accidental:**

In children, therapeutic overdose or eating manzool [aphrodisiac mixture of cannabis, nutmeg, datura, honey and spices).

- **Homicidal:**

To facilitate rape and robbery.

Mechanism of action:

1. Atropine and hyoscyamine:

They are isomers having the same action

a. Peripheral: antagonize the muscarinic action of acetylcholine.
b. Central: stimulation of central nervous system followed by depression.

2. Hyoscine:

a. Peripheral action is week
b. Central action: depression from the start, without initial stimulation.

Clinical presentation:

1. Signs and symptoms due to peripheral action:

- Dry secretions as saliva, sweat and bronchial secretions.
- Dilated fixed pupils.
- Rapid weak pulse and rapid shallow respiration.
- Dilated vessels→ Flushed skin "atropine flush".
- Decreased GIT & UT motility (due to relaxation of the smooth muscles) → constipation and urine retention.
- Inhibition of sweating → Atropine fever.

2. Signs and symptoms due to central action:

i. Stimulation stage:

- Occupational delirium (Purposeless movements as catching flies or rolling cigarettes).
- Staggering gait.
- Restlessness and euphoria.

iii. Depression stage:

- Drowsiness passing to coma.
- Central asphyxia (Respiratory Center (R.C.) depression).

Cause of death:

Central asphyxia.

Investigations:

1. Routine laboratory investigation.
2. Toxicological screening.
3. ECG shows sinus tachycardia.

Differential diagnosis:

1- Other Anticholinergic drugs e.g. Antihistamines, TCA, Phenothiazines, & Antiparkinson
2- Alcohol.

	Atropine	**Alcohol**
Characteristic smell	-ve	+ve
Temperature	Atropine fever	Subnormal
Pupils	Dilated fixed	McEwen's sign
Flushed skin	+ve	+ve
Staggering gait	+ve	+ve

Treatment:

1. **Supportive: ABC**
2. **GIT decontamination:**

- Gastric lavage can be done a long time after ingestion due to diminished gastric motility → prolonged emptying.
- Local antidote:
  Using one of following antidotes.
  - Charcoal [Adsorption].
  - Hydrogen peroxide (H_2O_2) or potassium permanganate ($KmnO_4$) 1/5000 [oxidation].
  - Tannic acid [precipitation].

3. **Antidote:**

- **Pilocarpine:** a Parasympathomimetic that acts peripherally only.
- **Physostigmine (Eserine):** a Parasympathomimetic that crosses the blood brain barrier, acting centrally and peripherally. Cardiac monitoring during administration is mandatory to avoid bradyarrhythmias.

4. **Symptomatic:**

- Urinary catheterization.
- Active cooling.
- Diazepam (for seizures).

2- Antihistaminics

Classification:

- Histamine H_1-receptor antagonists**:**
  - First-generation: crosses BBB → CNS effects e.g. diphenhydramine.
  - Second-generation: peripherally selective e.g. Ketotifen.
  - Third-generation: are the active metabolic derivatives of second-generation drugs have increased efficacy with fewer adverse drug reactions.
- Histamine H_2-receptor antagonists e.g**.** Cimetidine.

Therapeutic uses:

- Histamine H_1-receptor antagonists**:**
  Anaphylaxis, allergic rhinitis, urticarial & motion sickness.
- Histamine H_2-receptor antagonists**:**
  Peptic ulcer and acid reflux.

Condition of poisoning:

- **Accidental:**
  - Children.
  - Medical overdose.
- **Suicidal**.

Mechanism of action:

- **H1 receptor antagonists:**
  - Antagonize effects of histamine on H1 receptor.
  - **Anticholinergic action** (except second-generation).
- **H2 receptor antagonists:**
  - Antagonize effects of histamine on H2 receptor in the stomach →decreasing the production of acid.

Clinical Manifestations:

- **H1 Receptor Antagonists**:
  - CNS depression.
  - **Anticholinergic syndrome.**
  - Second-generation antihistamines: no significant CNS depression or anticholinergic effects.
  - Large diphenhydramine overdose: Prolongation of QRS (sodium channel blockade).
  - In severe cases, seizures may occur →rhabdomyolysis → myoglobinuria → renal failure.
- **H2 Receptor Antagonists:**
  - Acute toxic effects are extremely rare.

Investigations:

Routine laboratory investigation +CPK.

Treatment:

1. **Supportive: ABC**
2. **GIT decontamination:**
   a. Gastric lavage.
   b. Activated charcoal
3. **Elimination of the poison from blood:**
   Diuresis, dialysis & hemoperfusion are largely ineffective due to:
   - Large volume of distribution.
   - Tight binding of the drug to plasma proteins.
4. **Antidote:**
   - No specific antidote.
   - Physostigmine:
     - It reverses the peripheral or central anticholinergic effects.
     - It is indicated in severe cases.
     - Should be given under cardiac monitoring & should not be given as a constant infusion for a long time.
     - It is contraindicated with wide QRS complex, bradycardia, asthma and bowel or bladder obstruction.
5. **Symptomatic:**
   - Hypotension: I.V saline & vasopressors.
   - Seizure: diazepam.
   - Hyperthermia: cold foments.
   - Conduction abnormalities (diphenhydramine): sodium bicarbonate.
   - Rhabdomyolysis: alkalinization of urine (Na bicarbonate) & diuretics.

3- ***Tricyclic Antidepressants (TCA)***

Therapeutic uses:

- Depression, and panic disorders.
- Nocturnal enuresis.
- Prophylaxis of migraine.

Conditions of poisoning:

- **Accidental**:
  - Children.
  - Medical overdoses.
- **Suicidal**

Mechanism of action:

1) **Neurotransmitter reuptake inhibition:**
   Norepinephrine, Dopamine and Serotonin.
2) **Receptor blockade:**
   Cholinergic receptors**,** Alpha adrenergic receptors and Histaminic receptors**.**
3) **Cardiovascular effects:**
   - **Myocardial effects:** Direct **Quinidine like** effect on the heart–(block sodium channels) →conduction defects and arrhythmias.
   - **Hypotension** due to: direct myocardial depression, peripheral vasodilatation and increased capillary permeability.

Clinical picture:

1-CVS:

- Hypotension.
- Sinus tachycardia due to hypotension and anticholinergic toxicity.
- Arrhythmias and conduction defects. ECG may show widened QRS complex, prolonged PR & QT intervals and atrioventricular (AV) block. Torsade's de pointes may occur.

2-CNS:

- Delirium and convulsion followed by coma.

3-Anticholinergic effects:

- Dry skin, dilated pupil, sinus tachycardia, urinary retention, decreased bowel sounds, constipation, and hyperthermia.

Investigations:

1. Routine lab investigations.
2. Toxicological screening.
3. ECG & continuous cardiac monitoring.

Treatment:

1- **Supportive measures:** ABC.

2- **GIT decontamination:**

- Emesis is contraindicated since rapid neurologic and hemodynamic deterioration may occur.
- Gastric Lavage is effective many hours after overdose.
- Multiple dose activated charcoal (MDAC) is indicated due to enterohepatic circulation.

3- Elimination of the poison from blood: Diuresis, dialysis, and hemoperfusion are ineffective due to:

- Large volume of distribution.
- Tight binding of the drug to plasma proteins.

4- The specific antidote:

Sodium bicarbonate for:

- Conduction defects. - Arrhythmias.
- Metabolic acidosis.

Mechanism:

***Alkalinization:** promotes dissociation of the tricyclic antidepressant from sodium channels.

***Increased plasma sodium:** helps to drive sodium through sodium channels.

Dose:

1-2 mEq/kg bolus dose, followed by continuous IV infusion (100-150 mEq $NaHCo_3$/1L dextrose) to maintain alkalinization. Serum pH should be maintained between 7.45 and 7.55.

5- Symptomatic treatment:

a) CVS toxicity:

a- Arrhythmia → sodium bicarbonate. If no response, conventional antidysrhythmic drugs are used.

b- Torsade's de pointes**:**

- Hemodynamically unstable patients → electrical cardioversion.
- Hemodynamically stable patients → Mg SO_4 & correct electrolyte abnormalities.

c- Hypotension: Normal saline + vasopressor agent.

b) CNS toxicity:

- Seizures → diazepam.
- Coma → Care of the coma.

c) Metabolic acidosis: sodium bicarbonate.

d) Hyperthermia: cold fomentation.

e) Correct electrolyte disturbances.

Remember:

- No flumazenil if benzodiazepines are known coingestants (induce seizures).
- No Physostigmine (induce seizures and fatal dysrhythmias).

N.B. Antidepressants are classified as:

1) Monoamine Oxidase (MAO) Inhibitors
2) Alpha $_2$ Blockers
3) Amine Reuptake Blockers:

a) ***Selective:***

- Selective Serotonin Reuptake Inhibitors (SSRI)
- Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
- Dopamine Norepinephrine Inhibitors.

b) ***Non selective:*** Bicyclic, Tricyclic & Tetracyclic Antidepressants.

4- Phenothiazines(Antipsychotics)

Therapeutic uses:

1. Psychotic illness as schizophrenia.
2. Antiemetic (chlorpromazine).

Conditions of poisoning:

- **Accidental**
  -Children.
  -Medical overdoses.
- **Suicidal**

Mechanism of action:

1. ***Receptor blockade:***
   - Cholinergic, Alpha adrenergic, Histamine and **Dopamine** receptors**.**
   - Blockade of **Dopamine** receptors → **Extrapyramidal manifestations**& increased Prolactin (amenorrhea galactorrhea syndrome).
2. ***CVS effects:***
   - ***Myocardial effects:*** *direct* ***"Quinidine like"*** *effect on the heart → conduction defects and arrhythmias.*
   - ***Hypotension:*** *due to direct myocardial depression, peripheral vasodilatation and increased capillary permeability.*
3. ***CNS effects: Depression of:***
   - *Cerebral cortex → Coma. Seizures may occur.*
   - *Respiratory center → Respiratory failure.*
   - *Chemoreceptor trigger zone (CTZ) → Antiemetic action.*
   - *Heat regulatory center (HRC) → → Hyperthermia or Hypothermia.*

Clinical picture:

1- CNS manifestations:

- CNS depression: Ataxia, Stupor and Coma.
- Hypothermia is common in the elderly. Occasionally hyperthermia.

2- Anticholinergic Effects:

Sinus tachycardia, blurred vision, dry mouth, decreased intestinal motility and urinary retention.

3- CVS manifestations:

- Hypotension.
- Tachycardia: due to hypotension and anticholinergic toxicity.
- Conduction abnormalities and arrhythmias: tachycardia, ventricular fibrillation. ECG may show prolongation of PR and QT interval, widening of QRS complex, AV block and Torsade's de pointes.

4- Extrapyramidal manifestations:

- **Acute dystonia:** Spasm of muscles of tongue, face and neck (spastic torticollis).
- **Akathesia:** Restlessness (inability to sit still).
- **Parkinsonism:** mask face, rigidity and tremors at rest.

- **Tardive dyskinesia** (long term use):
  - Involuntary, repetitive movements of the face, tongue & lips and chorea of extremities. Movements disappear during sleep.
  - Mechanism: Chronic blockade of dopamine receptors →↑dopamine secretion & hypersensitivity of the receptors.
- **Neuroleptic malignant syndrome (NMS):**

-NMS is caused by sudden, marked reduction in dopamine activity.

-It is characterized by 4 cardinal features:

- Muscle rigidity (lead-pipe rigidity).
- Hyperpyrexia (temperature 38 to 42^{o}c)
- Mental status changes (confusion, delirium, stupor, and coma)
- Autonomic instability (tachycardia, hypertension, diaphoresis & incontinence).

-Complications:

- Rhabdomyolysis with myoglobinuria →acute renal failure.
- Cardiovascular collapse, respiratory failure & death may occur.

-Differential diagnosis:

Serotonin syndrome cause by excess serotonin on the CNS e.g Selective Serotonin Reuptake Inhibitors (SSRI) and treated by serotonin antagonists such as Cyproheptadine.

Investigations:

1. Routine lab investigations +CPK
2. Toxicological screening.
3. ECG & continuous cardiac monitoring:
4. X-ray abdomen: phenothiazine tablets are radio-opaque.

Treatment:

1- Supportive measures: ABC (see general toxicology).

2- GIT decontamination:

- Emesis is contraindicated (↓CTZ and dystonic reaction →aspiration).
- Gastric lavage.
- Activated charcoal.

3- Elimination of the poison from blood:

Forced diuresis, hemodialysis and hemoperfusion are ineffective due to:

1. Large volume of distribution.
2. Tight binding of the drug to plasma proteins.

4- Symptomatic:

- Coma: supportive care

- **Seizures:** diazepam.

- CVS toxicity: See TCAs.

- Acute dystonic reaction: Benztropine (Cogentin), and Diphenhydramine if < 3 years.

- Tardive dyskinesia: Increase the dose and shift to another neuroleptic with less anticholinergic effects.

- Parkinsonism: Anti-parkinsonian drugs.

- **Neuroleptic malignant syndrome**: Dantrolene sodium, Bromocriptine and other supportive care.
- **Rhabdomyolysis:** alkalinization of urine (Na bicarbonate) & diuretics.

N.B. Antipsychotics are classified as:

I-Typical Antipsychotics: phenothiazines

II-Atypical Antipsychotics: more selective dopamine D2 antagonists (Clozapine, Risperidone, Olanzapine, Ziprasidone) so they in general, have minimal **extrapyramidal** effects.

II. Sympathomimetic Toxidrome
Central Nervous System (CNS) Stimulants

Classification:

- **Amphetamines:** Amphetamine, Dexamphetamine, Methamphetamine, Benzphetamine.
- **Hallucinogenic amphetamines**: e.g. MDMA: 3,4 Methylenedioxy-methamphetamine (Ecstasy).
- **Analeptics:** Strychnine, Nikethemide, Picrotoxin, Doxapram.
- **Local anesthetics**: Cocaine, Camphor.
- **Xanthines**: Caffeine, Theophylline, Theobromine.

1- Amphetamine

Therapeutic uses:

- Treatment of obesity.
- Treatment of narcolepsy in adults.
- Attention deficit hyperactivity disorder (ADHD) in children.

Conditions of poisoning:

- **Accidental:**
  - Over dose in addicts.
  - Medical over dose.
  - Children.

Mechanism of action:

- Amphetamines are **sympathomimetic**.
- They increase the **release, inhibit the reuptake, and slow down metabolism** of catecholamines (epinephrine, norepinephrine & dopamine) leading to marked central and peripheral α- and β-adrenergic receptor stimulation, together with CNS stimulation.

Clinical manifestations:

System	Minor/ moderate intoxication	Severe intoxication
CVS	• Tachycardia • Hypertension	• Cardiogenic shock • Cerebral hemorrhage • Circulatory collapse
CNS	• Confusion • Severe agitation • Hyperreflexia • Tremor	• Amphetamine psychosis (delusions and paranoia) • Serotonin syndrome • Sympathomimetic Toxidrome
Musculoskeletal	• Muscle pain	• Rhabdomyolysis
Respiratory	• Rapid breathing	• Pulmonary edema • Pulmonary hypertension • Respiratory alkalosis
Urinary	• Painful urination • Urinary retention	• No urine production • Kidney failure
Others	• Mild hyperthermia	• Hyperpyrexia • Metabolic acidosis

Investigations:

1- Routine investigations.
2- Toxicological screening.
3- Creatine phospho-kinase (CPK), urine myoglobin (hyperthermia & rhabdomyolysis).
4- ECG & continuous cardiac monitoring.
5- Chest X-ray.
6- CT of the head.

Treatment:

1- Supportive treatment: ABC (see general toxicology).

2- GIT decontamination:

- Do not induce emesis since rapid neurologic and hemodynamic deterioration is known to occur.
- Gastric lavage (in the absence of seizures).
- Activated charcoal.
- Whole bowel irrigation: In body stuffers and packers.

3- Elimination of the poison from blood:

- Forced acid diuresis increases urine execration of the drug, but carries the risk of metabolic acidosis and worsens myoglobin precipitation in the renal tubules.
- Hemodialysis used only in renal failure.

4- Symptomatic:

- Convulsions: Benzodiazepines.
- Hypertension:
  - Benzodiazepines.
  - Sodium nitroprusside (potent peripheral vasodilator).
  - Avoid beta-blocker for treatment of tachycardia or hypertension as it leaves Alfa receptors unopposed → V.C → severe hypertension. If a β-adrenergic receptor antagonist is selected, it should be short-acting (e.g., esmolol), and coupled with α-adrenergic receptor antagonist such as phentolamine.
- Psychosis:
  - Benzodiazepines.
  - Haloperidol (antipsychotic) may be considered in patients unresponsive to benzodiazepines.
  - Avoid chlorpromazine as it may produce hypotension and may induce convulsion.
- Delirium: Benzodiazepines.
- Hyperthermia: Benzodiazepines and external cooling.
- Ventricular arrhythmias:
  - Lidocaine is generally the first line agent.
  - Unstable rhythms require immediate cardioversion.
- Rhabdomyolysis: alkalinization of urine (Na bicarbonate) & diuretics.

Remeber:

- No beta-blocker for treatment of tachycardia or hypertension as it leaves Alfa receptors unopposed → V.C → severe hypertension.
- No chlorpromazine as it may induce convulsion.

2- Cocaine

Source:

Whitish crystalline powder produced from the dried juice extracted from the leaves of the coca plant (Erythroxylon coca).

Uses:

- Local anesthetic (Marcaine)
- Antiarrhythmic (Xylocaine)
- Sports doping.
- Anorexigenic

Conditions of poisoning:

- **Accidental:**
  - Over dose in addicts.
  - Therapeutic over dose (anesthetic).

Routes of intake:

- Sniffing the powder.
- Smoking (crack).
- Intra-venous injection.

Mechanism of action:

- Sympathomimetic and a strong C.N.S stimulant (Blocks the *reuptake* of catecholamine).
- Local anesthetic (Blocks the fast inward sodium channels).

Clinical presentations:

1. CNS:

(CNS stimulation followed by depression)

- Euphoria, agitation and insomnia.
- Mental confusion, hallucinations and headache.
- Exaggerated reflexes and convulsions, which may cause rhabdomyolysis.
- Hyperthermia due to:
  - Heat gain (increased muscle contractility).
  - Decreased heat loss due to vasoconstriction (V.C.).
  - Disturbances of heat regulatory center (HRC).
- Drowsiness, confusion up to coma.
- Circulatory collapse due to depression of vasomotor center (VMC).
- Cyanosis and death from central asphyxia due to depression of R.C.

2. CVS:

- Hypertension and intracranial hemorrhage.
- Tachyarrhythmias.
- Coronary artery spasm and myocardial infarction.

3. Other manifestations:

- Renal failure may result from:
- Shock and decreased renal perfusion or
- Rhabdomyolysis and myoglobinuria.
- Accidental subcutaneous injection of cocaine may cause localized necrotic ulcers "*coke burns*".

Causes of death:

- Hyperthermia → rhabdomyolysis (myoglobinuric renal failure), coagulopathy, and multiple organ failure.
- Central asphyxia.
- Circulatory collapse.

Investigations:

1. Routine laboratory investigation:
2. Toxicological screening: Urinary Benzoylecgonine (main metabolite), detected up to 3 days.
3. Serum enzymes: Creatine Phosphokinase (CPK), to indicate rhabdomyolysis.

Treatment:

1- **Supportive: (ABCs)**
2- **GIT decontamination:**
Emesis and gastric lavage are performed only in the absence of seizures.
3- **Symptomatic:**
- Anti-convulsant (Diazepam).
- Anti-hypertensive (Sodium nitroprusside).

3- *Theophylline (Bronchodialtors)*

Therapeutic uses:

- Bronchial asthma and chronic obstructive pulmonary diseases (COPD).
- Neonatal apnea.

Mechanism of action:

- Release of catecholamines→ stimulation of B1- and B2- adrenergic receptors.
- Phosphodiesterase inhibitors→ increase cAMP (second messenger system of B-adrenergic stimulation).
- Adenosine antagonist.

Clinical manifestations:

1. GIT:

- **Nausea and severe vomiting due to:**
  - Direct effects on vomiting center.
  - Local effects on gastric acidity.

2. CVS:

- Tachyarrhythmias, especially supraventricular tachycardias (SVTs),
- Hypotension with wide pulse pressure (peripheral vasodilation).

3. CNS:

- Anxiety, agitation, insomnia, tremors and irritability.
- **Seizures** are severe, recurrent and refractory to standard treatment →Rhabdomyolysis may occur.

***4.* Metabolic:**

- Hypokalemia, hypomagnesaemia, and hypophosphatemia.
- Hyperglycemia and metabolic acidosis.

Chronic Theophylline Toxicity:

1-Minimal GIT symptoms.
2-Seizures at lower blood level.
3-Dysrhythmias more common than in acute toxicity.
4-Hypokalemiaand metabolic acidosis **are absent** in chronic cases as a result of tolerance to B2 effects.

Investigations:

1- Routine lab investigations + CPK.
2- Toxicological screening:
   Serum theophylline levels:
   - Every 2–4 hours (sustained-release preparations)
   - 90–100 mg/L in acute intoxication.
   - 40–60 mg/L in chronic intoxication.
3- ECG & continuous cardiac monitoring

Treatment:

1- Supportive measures: ABC.
2- GIT decontamination:
- Gastric lavage.
- Activated charcoal
- Multiple dose activated charcoal (MDAC) is indicated in sustained-release pill.
- Whole-bowel irrigation (WBI) is indicated in sustained-release pills.

3- Enhanced elimination:
Charcoal hemoperfusion and hemodialysis are effective as it has small volume of distribution.

4- Symptomatic:
i. Vomiting: Metoclopramide or more potent serotonin antagonist.
ii. Hypotension:
- Saline and vasopressors.
- Refractory hypotension: cautious administration of a B-adrenergic antagonist.

iii. supraventricular tachycardia:
- Benzodiazepines
- Calcium channel blockers preferred than B-adrenergic antagonists because of the risk of provoking bronchospasm with B- antagonists. Correction of hypokalemia and hypomagnesaemia.

iv. Seizure: usually resistant to treatment so benzodiazepines (IV) and phenobarbital may be used to treat seizures.

Remember:

- No B-adrenergic antagonist in asthmatic patients (induce bronchospasm).

III. Opioid toxidrome (CNS depressants)

1- Opium [Morphine]

- **Opium** is a naturally occurring substance derived from the green unripe capsule of papaver somniferum “poppy " plants.
- **Opium** contains more than 20 alkaloids such as morphine, papaverine and codeine.
- **Opium** is ingested or smoked & has a characteristic smell while **morphine** is injected only & has no smell.

Classification of Opoiods:

1. **Natural:** Morphine, Codeine, Thebaine & Papaverine.
2. **Semi synthetic:** Heroin.
3. **Synthetic:** Fentanyl, Meperidine, Methadone & Buterphanol.

Therapeutic Uses:

- Morphine is a potent painkiller.
- Codeine is used as antitussive (suppress the cough reflex).

Heroin:

- Heroin is a semisynthetic derivative of morphine, with analgesic properties superior to morphine and cough-suppressant properties superior to codeine.
- Heroin is six times more addictive than morphine; it is not used medically and not manufactured legally.

Route of intake of heroin and morphine:

a. Injection (SC or IV). b. Sniffing of powder.
c. Transdermal opioid patches.

Conditions of poisoning:

- **Accidental:**

- Children. - Therapeutic [overdose]. - Addicts [overdose].

- **Suicidal:**

- In addicts.

Mechanism of action:

The opioids exert their effects by interacting with specific opioid receptors [mu, kappa, **s**igma and delta receptors] → a mixture of stimulations and depressions but **mainly depressions.**

I. Stimulation of:

1. Vagal center →slow full pulse and slow deep respiration.
2. Vomiting center →vomiting.
3. Pupillo-constrictor center → pinpoint (non-reactive) pupil.

II. Depression of:

1. Cough center →anti-tussive effect.
2. Sensory cortex →analgesia.
3. Consciousness →coma.
4. Respiratory center →central asphyxia.
5. Vasomotor center →circulatory collapse.

Types of opiate receptors:

Receptor Type	Effects	
Mu receptor	**De**pendence, **R**espiratory depression, **E**uphoria, **A**nalgesia and **M**iosis	**DREAM**
Kappa receptor	**M**iosis, **A**nalgesia, **R**espiratory depression, and **S**edation	**MARS**
Sigma receptor	**P**sychosis, **H**allucinations, and **D**ysphoria	**PHD**
Delta receptors	**S**eizures, **E**uphoria and **A**nalgesia	**SEA**

Clinical presentation:

1. The patient feels euphoria (sense of wellbeing and relief of pains) followed by dysphoria (distress, anxiety and fear).
2. Gradual deterioration of consciousness (drowsy, stupor then comatose).
3. Slow full pulse,
4. Slow deep respiration.
5. **Non-cardiogenic pulmonary edema**.
6. The pupils are constricted pin pointed pupil **(ppp)** and non-reactive.
7. Constipation and diminished bowel sounds.
8. Vomiting.
9. Cyanosis (depression of R.C.).
10. Circulatory collapse.

Causes of death:

- Central asphyxia
- Pulmonary edema.
- Arrhythmias.

Investigations:

1. Routine laboratory investigation.
2. Toxicological screening.
3. Chest X-ray: pulmonary edema.
4. ECG: arrhythmias.

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D.D.:

Patients with classic opioid Toxi-drome [3C] coma, cyanosis and constricted pupil. May be due to:

	Opium	Phenol	OPP	Pontine Hge
History	Intake	intake	intake	trauma or hypertension
Smell	Meconic	Characteristic	Garlic	-
Temperature	Subnormal	Normal	Normal	Hyperthermia
Limbs	Normal	convulsions	convulsions	quadriplegia
Special manifestations	Sluggish reflexes	Green urine	Increased secretions	Exaggerated reflexes
Chemical Analysis	+ ve	+ ve	+ ve	- ve

Treatment:

1. **Supportive measures: ABCs.**
2. **GIT Decontamination:**

i. Gastric lavage:

a) Using cuffed endotracheal tube even if alert (rapid CNS depression).

b) Even in case of injected morphine (morphine is re-excreted in the stomach).

ii. Local antidotes:

Using one of following antidotes.

a) Charcoal [Adsorption].

b) Hydrogen peroxide (H_2O_2) or potassium permanganate ($KmnO_4$) 1/5000 [oxidation].

c) Tannic acid [precipitation].

3. **Antidote:**

i. Atropine

Block vagal stimulation and ↑heart rate (HR.).

ii. Antagonists:

1- Naloxone [Narcan] [Short half-life = 1 hr.].

Uses: acute opioid intoxication and treatment of coma of unknown etiology.

Administration: not effective orally but may be given subcutaneously, intramuscularly, intravenously, or even endotracheal. After intravenous administration, opioid antagonism occurs within 1–2 minutes and persists for approximately 1–4 hours.

2- Nalmefene [Revex] [long half-life = 8hrs].

It is a newer opioid antagonist with long duration of action.

3- Naltrexone [Trexan] [longer half-life = 72hrs].

It is used in treatment of opiates addiction.

2- Tramadol Hydrochloride

Tramadol is a centrally acting **synthetic analgesic** with **opioid-like effects**.

Preparations:

- Immediate release capsules 50 mg.
- Sustained release tablets 50 mg, 100 mg, 150 mg or 200 mg.
- Solution as oral drops 100 mg/mL.
- Injection 50 mg/mL, 100 mg/2mL.

Therapeutic Uses:

Analgesic for moderate to severe pain.

Mechanism of action:

- Tramadol is a centrally acting synthetic analgesic with opioid-like effects. It is not derived from natural sources, nor is it chemically related to opiates.
- It binds to μ−opioid receptors and inhibits the reuptake of noradrenaline and serotonin.

Clinical presentation:

- Manifestations of over dosage with tramadol are similar to those of opioids.
- Convulsions & serotonin syndrome may occur due to its serotonergic effect.

Investigations:

1- Routine investigations:

2- Toxicological screening.

Treatment:

1. **Supportive measures: ABCs.**
2. **GIT Decontamination:**
   - **Gastric lavage.**
   - **Local antidotes:** Activated charcoal.
3. **Physiological Antidote:**

Naloxone will reverse respiratory depression, but not all symptoms caused by over dosage with tramadol.

4. **Symptomatic:**

Convulsions: diazepam.

IV. Sedative hypnotic toxidrome (CNS depressant)

1- Barbiturates

Classification:

Class	Duration of action	Drugs
Long-acting	6-12 hours	Phenobarbital & Barbital
Intermediate-acting	3-6 hours	Amobarbital & Butabarbital
Short- acting	3hours	Secobarbital & Pentobarbital
Ultra-short acting	few minutes	Thiopental

Therapeutic uses:

Sedatives, hypnotics, anticonvulsants, anesthetic agents.

Conditions of poisoning:

- **Accidental:**
  - Children
  - Addicts (over dose).
  - Synergistic action (with ethanol).
- **Suicidal:**
  - Common (painless death).
- **Homicidal:**
  - To facilitate rape & robbery.

Mechanism of action:

- Barbiturates have dose-related CNS depressant effects.
- Enhance the binding of γ-aminobutyric acid (GABA) to GABA receptors causing GABA dependent chloride channel to remain opened for longer time with subsequent inhibition of post-synaptic nerve impulse transmission.

Clinical presentations:

1- CNS manifestations:

- Mild drowsiness up to **coma** which characterized by:
  - **Deep & prolonged (may last for days).**
  - Cyanosis, clammy skin & bullae in pressure areas.
  - Muscle flaccidity with diminished reflexes.
  - Slow weak pulse & slow shallow respiration.
  - Hypotension and hypothermia.
- Confusion, memory deficit and poor judgment.
- Vertigo, slurred speech, and ataxia.
- Hypothermia (depression of heat regulatory center).
- Respiratory failure (central asphyxia).

2- <u>CVS manifestations:</u>
- **Hypotension**: due to
    - Depression of vasomotor center (VMC).
    - Direct myocardial depression.
    - Vasodilatation.

3- <u>Respiratory manifestations:</u>
- **R.C. depression**, which results in hypoventilation & apnea.
- **Pneumonia** due to:
    - Prolonged coma.
    - Inhibition of the protective reflexes (cough reflex).
    - Aspiration pneumonia following vomiting of gastric contents.
- **Non-cardiogenic pulmonary edema**.

4- <u>Renal manifestations</u>: renal failure due to:
- Hypotension → decreased perfusion.
- Rhabdomyolysis (due to prolonged coma).

5- <u>Skin manifestations:</u>
- Barbiturate blisters “bullae” over pressure points (hands & feet).

6- <u>GIT manifestations:</u> Diminished bowel sounds.

<u>D.D:</u>

Medications associated with coma and blisters:
-Barbiturates.
-Benzodiazepine (Nitrazepam, Oxazepam & Temazepam).
-Carbon monoxide.
-Opioid (Heroin, Morphine, Methadone & Hydrocodone).
-TCA (Amitriptyline & Imipramine)

<u>Causes of death:</u>

Early: central asphyxia or cardiovascular collapse.
Late: pneumonias or renal failure.

<u>Investigations:</u>

1- Routine investigations.
2- Toxicological screen.
3- Monitor urine myoglobin with significant intoxication (rhabdomyolysis).
4- Chest X-ray: pneumonia and non-cardiogenic pulmonary edema.

<u>Treatment:</u>

1-Supportive treatment: ABC.
2-GIT decontamination:
- *Emesis:* not recommended since rapid neurologic deterioration is known to occur.
- *Gastric Lavage*: with cuffed endotracheal tube up to several hours after the overdose due to decreased GIT motility.
- *Activated charcoal.*
- *MDAC:* in phenobarbital toxicity (enterohepatic circulation).
- *Cathartics:* Sorbitol or MgSO4.

3-Elimination of the poison from blood:

- *Forced alkaline diuresis:* for long acting barbiturates only (less bound to plasma proteins than short acing and mainly excreted in the urine).
- *Hemodialysis and hemoperfusion* have been successfully utilized in all types of barbiturate overdoses (most effective for long-acting barbiturates) and considered in patients with refractory hypotension and severe prolonged coma.
- Charcoal hemoperfusion is more effective than hemodialysis.

4- Symptomatic treatment (especially for coma, hypothermia and pneumonia).

2- Benzodiazepines

Benzodiazepines have replaced barbiturates as first-line anoxiolytics and hypnotics due to higher safety margins.

Common preparations:

- Diazepam
- Flunitrazepam (Rohypnol date rape drug)
- Flurazepam
- Lorazepam
- Midazolam
- Nitrazepam

Mechanism of action:

- Benzodiazepines exert their effects through high affinity binding to Benzodiazepine (BZ) receptors that are located at the alpha subunit of the GABA receptors.
- This result in increasing the frequency of prolonged opening of the GABA chloride channel with subsequent increase in the inhibitory synaptic transmission.

Clinical presentations:

1-CNS manifestations:

- Drowsiness, **low-grade coma** (most comatose patients become arousal within 12-36 hrs. following an acute overdose).
- **Memory loss**, confusion, and difficult concentration.
- **Ataxia, slurred speech**, lethargy.

2-CVS manifestations:

Hypotension and bradycardia (particularly with Flunitrazepam).

3-Respiratory manifestations:

Respiratory arrest has been reported following rapid IV administration.

3-Gastrointestinal manifestations: Nausea and vomiting.

4-Dermatologic manifestations: Bullae have been reported with Nitrazepam, Oxazepam and Temazepam.

N.B. Profound coma, significant respiratory depression, significant hypotension or hypothermia is ***extremely uncommon in isolated* BZ** overdose cases.

Investigations:

1. Routine investigations.
2. Toxicological screening.

Treatment:

The **same lines of treatment as in barbiturate** toxicity except:

1. Multiple dose activated charcoal is not indicated.
2. Forced diuresis and hemodialysis are ineffective (high protein binding & large volume of distribution).
3. **Specific antidote:**

Flumazenil (Anexate):

Action: Flumazenil is a competitive BZ receptor antagonist.

Dose:

- Adults: 0.2 – 0.5 mg IV, over 30 sec, may be repeated at 1-min. interval up to a maximum total dose of 3 mg.

Contra-indications:

- Hypersensitivity to flumazenil or BZ.
- Co-ingestions especially BZ+ drugs causing seizures.
- Chronic use of BZ as it may induce withdrawal syndromes.
- Patients given BZ for control of a potentially life-threatening condition as status epilepticus.
- History of convulsions.
- Head trauma (seizures may occur).

Advantages:

- Effective within minutes in treating **isolated** BZ overdose (It is highly lipid-soluble and crosses the blood brain barrier quickly).

Disadvantages and precautions:

- Its half-life is 57 min (which is much shorter than most of oral BZ), and re-sedation commonly occurs after a single dose.

V.Cholinergic Toxidrome

1- Organophosphorus Compounds: see insecticides.

2- Carbamates: see insecticides.

TOXIDROMES

Toxidrome	Mental status	Pupils	Vital signs	Other manifestations	Examples of toxic agents
Sympathomimetic	Hyperalert agitation, hallucinations, paranoia	Mydriasis	Fever, tachycardia, hypertension, tachypnea	Diaphoresis, tremors, seizures	Cocaine, amphetamines, ephedrine, theophylline, caffeine
Anticholinergic	Agitation, Hallucinati-ons, delirium, coma	Mydriasis	Fever, tachycardia, hypertension& tachypnea	Dry flushed skin, Dry mucous membrane, ↓bowel sounds, Urinary retention & seizures (rare)	Atropine Antihistamines, TCA, phenothiazines, antiparkinsonian agents
Opioid	CNS depression coma	Miosis	Hypothermia bradycardia, hypotension, bradypnea	Hyporeflexia, pulmonary edema, needle marks	Opiates (eg. heroin, morphine, methadone), diphenoxylate
Sedative hypnotic	CNS depression coma	Miosis	Hypothermia bradycardia, hypotension, bradypnea	Hyporeflexia, pulmonary edema	Barbiturate Benzodiazepine
Cholinergic	Confusion coma	Miosis	Bradycardia, hypertension or hypotension, tachypnea or bradypnea	SLUD, diaphoresis, GI cramps, Bronchoconstriction, muscle weakness, seizures	Organophosphate (insecticides) and carbamate, nerve agents, nicotine, pilocarpine, physostigmine

CORROSIVES

Corrosive materials: (Caustics) are substances that cause local and rapid damage on contacting tissue surfaces.

Classification:

Class	Inorganic corrosive	Organic corrosive
Effect	Strong	Mild
Action	Local only	Local and remote
Examples	-Acids: as sulphuric acid, Hydrofluoric acid and Nitric acid. -Alkalis: as NH4OH, NaOH and KOH (Potash)	-Carbolic acid (phenol) -Oxalic acid

Inorganic Corrosive

Caustics in commercial products:

1) **Alkali containing products are:**
   - Drain Cleaner.
   - Soap manufacturing.
   - Oven cleaning products.
   - Swimming pool cleaning products.
   - Automatic dishwasher detergent.
   - Hair relaxers.
   - Bleaches.

2) **Acid containing products are:**
   - Toilet bowl cleaning products.
   - Automotive battery liquid.
   - Rust removal products.
   - Metal cleaning products.
   - Drain cleaning products.

Conditions of poisoning:

- **Accidental:**
  - Occupational workers.
  - Children.
- **Homicidal:** throwing H_2SO_4 on face.

Factors Determining severity of action:

- Physical form: Solid/liquid.
- Concentration.
- Quantity.
- PH: pH <2 and >11 are more corrosive.
- Duration of contact
- Food: Presence or absence of food in stomach.

Mechanism of Action:

	Acids	Alkali
Action	**Coagulative** necrosis → Eschars formation→ Limits penetration.	**Liquefactive** necrosis→ Saponification → continue to penetrate.
Main affected site	Stomach.	Oropharynx & Esophagus
Complications	Perforation can occur when eschar sloughs.	-Stricture formation -Fistula -Cancer Esophagus

Clinical Presentation

1. **GIT:**
   - Severe pain of lips, mouth and stomach.
   - Excessive salivation.
   - Dysphagia and odynophagia.
   - Vomiting.
   - Symptoms and signs of GIT perforation.
2. **Respiratory system:**
   - Cough.
   - Dyspnea.
   - Hoarseness, stridor and respiratory distress due to edema of vocal cords.
   - Bronchoconstriction.
   - Pulmonary edema.
   - Chemical pneumonitis.
3. **Skin:**
   - Chemical burns and eschars.
4. **Eye:**
   - Corneal ulcers.
   - Conjunctival irritation with lacrimation.
   - Photophobia and severe burning pain.
5. **Significant exposures:**

May also result in gastrointestinal absorption of the acidic substances leading to:

- Significant metabolic acidosis.
- Acute renal failure.

Complications (causes of death):

1) **Acute:**
   - Airway obstruction
   - Shock (due to pain)
   - Vomiting→ dehydration
   - GIT perforation.
2) **Late:**
   - Stricture leading to cachexia.
3) **Remote:**
   - Carcinoma of esophagus.

Investigations:

1) **Laboratory Tests:**
   - Routine lab investigation.
2) **Radiology:**
   - Chest X-ray: pneumothorax, pneumomediastinum and pleural effusion.
   - Abdominal X-ray: pneumoperitoneum
3) **Endoscopy:**
   - Should be done within 12 hours.
   - Done for grading the esophageal and gastric lesions to guide therapy.
   - Contraindicated in airway obstruction and in cases of perforation.
   - It reveals different grades of severity:
     a) **Grade I:** erythema of mucosa.
     b) **Grade II:** destruction of mucosa (IIa: discrete ulcers, IIb: circumferential ulcers).
     c) **Grade III:** destruction of all layers of the gut beyond the mucosa.

Management:

1) **Prophylactic:**

Safety goggles, protective gloves, and a coat shall always be worn when working with corrosive chemicals.

2) **Curative:**

a. **Asymptomatic patient**: only observation in the Emergency Room.
b. **Symptomatic patient**:

1- Supportive care:

- ABC
- Strong analgesic for pain: 10mg morphine IV.

2- GIT Decontamination:

It is **CONTRAINDICATED** to do the following:

- **Induced emesis:** causes reintroduction of the caustic to the upper gastrointestinal tract and airway.

- **Activated charcoal:**
  - It interferes with tissue evaluation by endoscopy.
  - Most caustics are not adsorbed to activated charcoal.
- **Gastric lavage:** carries the risk of perforation.
- **Neutralization and dilution:**
  - It has the potential to form gas.
  - Generate an exothermic reaction leading to more tissue damage.

3- *Decontamination of the skin and eyes:*

Irrigation with copious amount of normal Saline for a minimum of 15 minutes, to remove any residual caustic agent.

4- Local antidote:

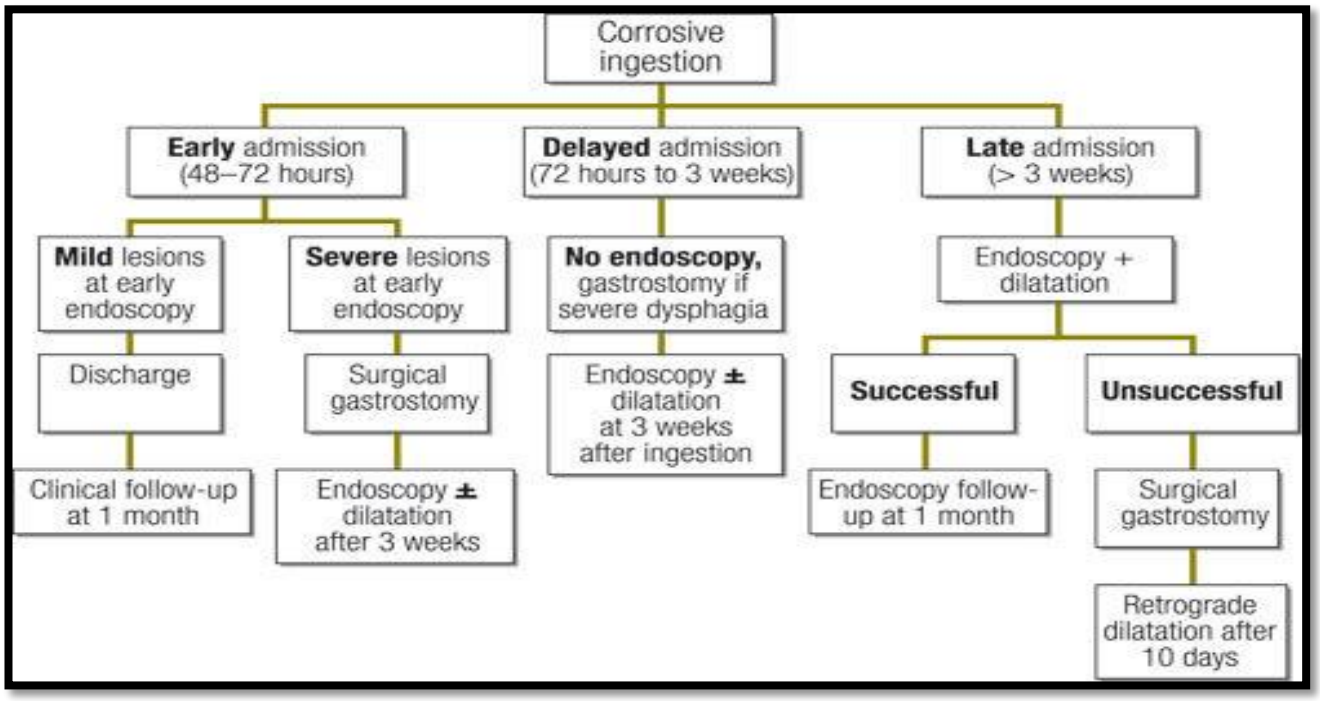
Milk to attenuate the heat generated by a caustic.

5- Symptomatic:

- **Corticosteroids:** Intralesional steroids may be given but systemic steroids has no role in the management of caustic ingestion.
- **Antibiotics:** Antibiotics are not recommended prophylactically in corrosive poisoning. They are recommended in GIT perforation.
- **Proton pump inhibitors (PPIs) and H2-blockers.**
- **Nutrition:** Endoscopic grade of lesions needs to be assessed for planning nutritional support (either orally or through gastrostomy).

6- Surgical procedures:

- Tracheotomy in case of laryngeal edema.
- Gastrostomy, gastrectomy or esophagotectomy with colon interposition.



Organic Corrosive

1- Carbolic acid (phenol)

It is a coal tar derivative, with characteristic smell.
Present in Dettol, Lysol, phenol detergent (Disinfectant).

Condition of poisoning:

- **Suicidal:** common because it is easily obtained, cheap, rapidly fatal and painless.
- **Accidental:** common among children and workers exposed to skin contamination as it is readily absorbed through intact skin.

Action:

1) Local:

a. **Weak corrosives:** leading to superficial ulcers.
b. **Coagulative necrosis:** leading to thickening of gastric mucosa.
c. **Local anesthetic action:** leading to transient pain & vomiting.
d. **Skin:** eschars and it may cause gangrene if applied for a long period.

2) Systemic:

a. **CNS**: stimulation followed by depression.
b. **CVS:** have direct myocardial depressant effect.
c. **Acid Base imbalance:**
   - Respiratory alkalosis due to respiratory center stimulation.
   - Metabolic acidosis follows due to uncompensated renal loss of base during stage of alkalosis because of renal damage.
d. **Methemoglobinemia.**
e. **Kidney:** Acute glomerulonephritis.

Clinical presentation:

1) Local:

a. **Stomach:** temporary pain and vomiting (due to local anesthetic effect). Vomitus has characteristic phenolic smell.
b. **Skin:** white eschars with smell of phenol around the mouth or skin, which turns brown on exposure to air due to oxidation.

2) Systemic effect:

a. **CNS**: constricted pupil and convulsions rapidly followed by coma.
b. **CVS:** hypotension, tachycardia and arrhythmias.
c. **Kidney:** oliguria with albumin, blood and casts in urine passing to anuria. The urine turns **green** on exposure to air due to oxidation of the excretory products of phenol (hydroquinone).

Causes of death:

1- **Early:** respiratory failure due to respiratory center depression.
2- **Late:** renal failure.

Investigations:

1- Routine lab investigation.
2- Met-hemoglobin level.

Treatment:

1) Supportive measures: ABCs

2) GIT Decontamination:

- **Emesis** is not recommended due to rapid onset of coma and seizures (within half an hour for significant ingestion).
- **Gastric lavage** is indicated and essential due to:-
  - Vomiting is temporary (local anesthetic action).
  - Thickening of gastric wall (coagulative necrosis) and superficial ulcers (no expected perforation).
  - Carbolic acid has a systemic effect so lavage is indicated to decrease absorption.
- **Local antidote is:**
  - Milk & egg white: as phenol will coagulate their protein instead of stomach protein.
  - Ethanol 10%: it dissolves phenol then rapidly removed by gastric lavage.
- **Eye decontamination:**
  - Flush exposed or irritated eyes with copious amounts of water or saline for at least 15 minutes.

3) Elimination of the absorbed poison:

- Dialysis (peritoneal & hemodialysis)
- Charcoal hemoperfusion
- Exchange transfusion.

4) No specific antidotes.

5) Symptomatic:

- Care of kidneys.
- Met-hemoglobinemia: If more than, 30% give methylene blue (1-2 mg/kg).
- Correct acid-base disorders.
- Seizures: Diazepam if no response, Phenytoin or Phenobarbitone may be given.

NB: Dettol is an aromatic chemical compound that has mild corrosive action. Its ingestion or inhalation may lead to vomiting, throat pain, laryngeal edema, abdominal pain, dizziness and coma.

2- Oxalic acid

It is used for metal polish and removing ink stains.

Action:

1) Local:

a. **Stomach:** mild corrosive (superficial ulcers).
b. **Skin:** eschars.

2) Systemic:

Oxalic acid combines with ionized blood calcium, forming insoluble calcium oxalate resulting in:

a. **Obstruction of collecting tubules** by Ca oxalate crystals, which may lead to renal failure.
b. **Hypocalcemia** that give rise to:

- **CVS**: Arrhythmias or cardiac arrest in diastole.
- **Nervous system**: Tetany and convulsions.

Clinical presentation:

1) Local:

- Pain, vomiting and diarrhea.
- Superficial ulcers on the lips and mouth.
- White eschars.

2) Systemic:

i. Hypocalcemia:

a. Twitches of the face muscles and extremities with carpopedal spasm.
b. Convulsions.
c. Contraction of respiratory muscles (Respiratory failure).

ii. CVS:

Arrhythmias or cardiac asystole.

iii. Renal failure:

Oliguria with **calcium oxalate crystals** in urine (detected microscopically), then anuria (uremia).

Investigations:

1) Routine lab investigation.
2) Urine analysis [white calcium oxalate crystals**].**
3) Ca level in blood.
4) ECG monitoring.

Treatment:

Antidote "Calcium" is lifesaving by every route.

1) **Supportive measures [ABCs]**
2) **GIT Decontamination.**
   - **Gastric Lavage.**
   - **Local antidote** (milk) or $CaCO_3$ to precipitate oxalic acid as calcium oxalate and decrease its absorption.
3) **Elimination of the absorbed poison:**
   - **Dialysis.**
4) **Antidote:**
   - **Calcium gluconate 10% IV slowly or orally to treat hypocalcaemia.**
5) **Symptomatic:**
   - Convulsions: Diazepam.
   - IV fluids to prevent calcium oxalate precipitation in the kidney.

3-Hydrofluoric acid

Although it is one of the strongest **inorganic** acids, it has both local and remote action

Uses: in glass etching, metal cleaning, electronics manufacturing and rust removers.

Action:

1- **Local corrosive action:** severe burn (Burns may involve underlying bone).
2- **Remote action**: form insoluble salts with calcium and magnesium.

Causes of death:

Cardiac arrhythmias that were precipitated by hypocalcaemia and hypomagnesaemia.

MEDICAL TOXICOLOGY
CARDIOVASCULAR MEDICATIONS
1- *Beta Adrenergic Blockers*

Classification:

According to lipid solubility:

1- High lipid soluble e.g., Propranolol and Penbutolol.
2- Moderate lipid soluble e.g., Labetalol and Pindolol.
3- Low lipid soluble e.g., Atenolol and Sotalol.

Therapeutic uses:

1- **Cardiovascular diseases as**:
Hypertension, ischemic heart disease, congestive heart failure, and certain arrhythmias.

2- **Non-cardiovascular diseases as:**
Essential tremors, pheochromocytoma, glaucoma, and migraine.

Mechanism of toxicity:

They induce blockage of beta-receptors → block effects of catecholamines (metabolic, chronotropic and inotropic).

Clinical picture:

1- Cardiovascular manifestations:

- Two cardinal signs: **Hypotension** and **bradycardia**.
- A-V block and asystole may occur in severe cases.
- Prolonged QRS & QT and Torsade's de pointes may occur.

2- Other manifestations:

- CNS manifestations: seizures and coma.
- Hypoglycemia.
- Hyperkalemia.
- Pulmonary edema.
- Bronchospasm occurs only in susceptible patients.

Investigations:

1- Routine lab investigations.
2- Toxicological screening.
3- ECG & continuous cardiac monitoring.

Treatment:

1- Supportive measures: ABC (see general toxicology).

2- GIT decontamination:

- Gastric Lavage.
- Activated charcoal
- Multiple dose activated charcoal (MDAC) is indicated in sustained-release pills.
- Whole-bowel irrigation (WBI) is indicated in sustained-release pills.

3- Specific treatment:

Atropine is given in mild cases. Patients who fail to respond to **it require specific antidotes:**

1) **Glucagon:**
   - Glucagon provides significant inotropic and chronotropic effects.
   - 3–5 mg given slowly I.V.
2) **Catecholamines.**
3) **Phosphodiesterase Inhibitors:** e.g. Amrinone

   Increases cAMP levels→ increases inotropic & chronotropic effects.
4) **Calcium:**

   Calcium reverses the negative inotropic effect, impaired conduction and hypotension.
5) **Insulin and Glucose**: Positive inotropic effects.
6) **Cardiac pacing:**
   - Patients unresponsive to pharmacological therapy.
   - Torsade de pointes

4- Enhanced elimination:

1) It is ineffective for high lipid-soluble beta antagonists because:
   - Large volume of distribution.
   - Tight binding of the drug to plasma proteins.
2) It is effective for low lipid-soluble beta antagonists because:
   - Low volume of distribution.
   - Low binding of the drug to plasma proteins.

2- Calcium Channel Antagonists

Examples:

Verapamil, Nefidipine, Amlodipine, Diltiazem, etc.

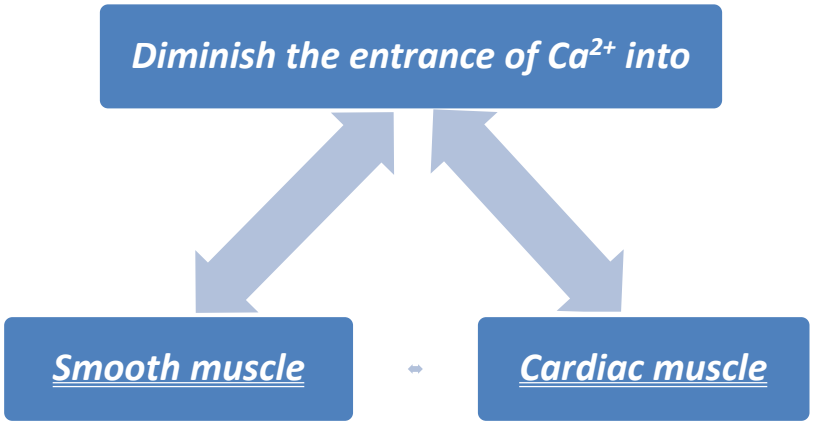
Therapeutic uses:

Hypertension, angina pectoris, myocardial infarction and cardiac arrhythmias.

Condition of poisoning:

- **Accidental:**
  - Children.
  - Medical overdose.
- **Suicidal.**

Mechanism of action:



- Relaxation of vascular smooth muscle
- Vasodilation (peripheral and coronary)
- Negative inotropic effect
- Depress the rate of sinus node and slow AV conduction.

Clinical manifestations:

1- **CVS manifestations:**

a- Two cardinal signs: **Hypotension** and **bradycardia.**

b- Prolonged PR & QT intervals, ventricular arrhythmia & Torsade's de pointes may occur.

2- **Other manifestations:**

a- CNS: depression and coma.

b- GIT: nausea and vomiting.

c- Respiratory: pulmonary edema.

d- Metabolic acidosis.

e- Hyperglycemia: due to suppression of insulin release coupled with body insulin resistance.

Differential diagnosis:

Toxins-inducing bradycardia with hypotension:

- Ca channel blockers.
- B-Adrenergic antagonists.
- Digitalis.
- Opioids.
- Organophosphate and Carbamate.
- Cyanide, hydrogen sulfide.
- TCA (in severe cases).

Investigations:

1- Routine lab investigations.

2- Toxicological screening.

3- ECG & continuous cardiac monitoring.

Treatment:

1- **Supportive measures:** ABC (see general toxicology).
2- **GIT decontamination:**
   - Gastric Lavage.
   - Activated charcoal
   - Multiple dose activated charcoal (MDAC) is indicated in sustained-release pills.
   - Whole-bowel irrigation (WBI) is indicated in sustained-release pills.
3- **Specific treatment:**
   1- **Calcium(**10% solution)
      - Calcium reverses the CVS effects: negative inotropic effect, impaired conduction and hypotension.
      - 10 mL of calcium chloride or 20 mL of calcium gluconate repeated every 15–20 minutes up to 4 doses.
   2- **Catecholamine.**
   3- **Glucagon**:
      - Has significant inotropic and chronotropic effects.
   4- **Phosphodiesterase Inhibitors**: e.g., Amrinone
      - Increases cAMP levels→ increases inotropic & chronotropic effects.
   5- **Insulin and Glucose**:
      - Positive inotropic effects.
   6- **Cardiac pacing:**
      - Patients unresponsive to pharmacological therapy.
      - Torsade de pointes.
4- **Enhanced elimination**: Diuresis, dialysis, and hemoperfusion are largely **ineffective** due to:
   - Large volume of distribution.
   - Tight binding of the drug to plasma proteins.

3- *Digitalis*

Source:

The cardiac glycosides, of which digitalis is the most commonly known, are the active principles in many plants as: Digitalis purpurea (Purple foxglove), Digitalis lanata (White foxglove) and Oleander.

Uses:

Digoxin is used in the treatment of congestive heart disease and in certain cardiac arrhythmias.

Condition of poisoning:-

- **Accidental:** Therapeutic overdose and in Children.
- **Suicidal:** rare.

Mechanism of action:

1) Therapeutic dose:

- Stimulation of the Vagus nerve which → **–ve chronotropic** (↓ H.R.) i.e. Elongation of the diastolic phase and improved filling of the heart due to bradycardia.
- It inhibits Na^+–Ka^+ ATPase in the cardiac muscle fibers → increased intracellular Na^+ and Ca^{+2} and increased extracellular Ka^+ →improved cardiac contractility (+ve Inotropic).

2) Toxic dose:

Inhibition of Na^+–Ka^+ATPase together with the electrolyte imbalance especially hyperkalemia → arrhythmias and worsening of heart failure.

Clinical presentation:

Toxicity may be acute or chronic (due to cumulative effect).

1. **Cardiac (the most frequent):**
   - Acute Toxicity: bradyarrhythmias (due to vagal stimulation).
   - Chronic Toxicity:

   - Ventricular tachyarrhythmias are more common in chronic or late acute poisoning.

   - Bradyarrhythmias (due to direct actions on the heart and so minimally responsive to atropine).
2. **GIT:** (the first to occur) nausea, vomiting, colic and diarrhea.
3. **Visual:** blurring, halos (yellow / green halos) due to cones and rods affection.
4. **CNS:** headache, drowsiness and disorientation.
5. **Hyperkalemia** may occur (in acute digitalis toxicity), but hypokalemia may be seen in chromic patients due to concomitant intake of potassium losing diuretics.

Investigations:

1. Routine laboratory investigation:

- Hyperkalemia in acute toxicity and it is a primary predictor of need for antidotal therapy.
- Hypokalemia in chronic toxicity.
- Hypercalcemia.
- Kidney function tests (renal impairment alters elimination of glycosides).

2. Toxicological screening (Digoxin level):

- Therapeutic blood level is 1- 2 ng/ml.
- Toxic blood level is 2.5 - 4 ng/ml.
- Concentrations exceeding 12 ng/ml carry serious prognosis.

3. ECG and continuous cardiac monitor.

Treatment:

1. Prevention of further exposure.

***2.* Supportive measures: ABC + symptomatic:**

i. For electrolytes disturbance:

1. Insulin in 5% glucose to avoid hypoglycemia → ↑K (Acute toxicity).
2. KCl → ↓K (chronic toxicity).
3. Disodium EDTA →↑Ca.

ii. Anti arrhythmic drugs:

1. Lidocaine → Atrial or ventricular arrhythmias.
2. Atropine → Bradycardia or heart block.

3. G. I. T. decontamination:

- **Gastric lavage.**
- **Local antidotes:** Activated charcoal.

4. Antidote:

Digi bind [Fab] (Digoxin-specific antibody fragments)

i- Preparation:

- Sheep immunized by digoxin–albumin conjugate produce antibodies.
- Antibodies are fragmented to be less immunogenic and easily excreted though kidney.

ii- Dose:

- Each vial of Digi bind binds 0.5 mg of digoxin.
- The dose is adjusted according to the amount of digitalis taken and the body weight.

iii- Indications:

1-Serum digoxin level above 10ng/ml in adults and >5 ng/ml in children.
2- Severe cardiac arrhythmias.
3- Severe hyperkalemia (> 5.5 mEq/L).
4- Heart block even 1st degree.

5. Elimination of the poison from blood:

- Forced diuresis, hemoperfusion, and hemodialysis are ineffective because of its large volume of distribution and its high affinity for plasma proteins.
- Plasmapheresis may have a role for removing retained Fab-digoxin complexes to prevent rebound toxicity.

ANALGESIC AND ANTIPYRETIC POISONING

1- Salicylates

Common preparations:

1. **Tablets:**
   - Aspirin (acetyl salicylic acid)
   - Integrated in various cold preparations.
2. **Vials:**
   - Aspegic.
3. **Topical preparations:**
   - Methyl salicylate "oil of wintergreen"→ (counter irritant).
   - Salicylic acid → (Keratolytic).

Clinical Uses:

- Anti-inflammatory, antipyretic and analgesic drug.
- Platelet-aggregation inhibitor.

Conditions of poisoning:

- **Accidental:**
  - **In children,** accidental intoxication may occur during treatment because pyrexia due to aspirin overdose may be mistaken for fever of infection with further administration of aspirin.
  - **Coadministration** of more than one salicylate-containing medication.
  - **The elderly** patient may suffer chronic toxicity due to gradual alteration in the patient's metabolic elimination process.
- **Suicidal:**
  By young adolescents.

Toxic dose:

Acute overdose: >150 mg/kg (in a single ingestion).
Chronic overdose: >100 mg/kg/d over 2 days.

Fatal dose:

400 mg/kg. (Children's tablets contain 81 mg & Adult tablets contain 325 mg or 500 mg).

Mechanism of action:

At therapeutic doses:

Antipyretic, anti-inflammatory and analgesic effects primarily through inhibition of prostaglandin biosynthesis.

At toxic doses:

Salicylates impair cellular respiration by **uncoupling oxidative phosphorylation** resulting in **fever, acid-base, fluid and electrolyte abnormalities** that are observed in three broad phases:

Phase I: (respiratory alkalosis): respiratory center stimulation → hyperventilation →**respiratory alkalosis** and compensatory alkaluria (potassium and sodium bicarbonate are excreted in the urine). This phase may last as long as 12 hours (in a young infant respiratory alkalosis may be short lived or not occur at all).

Phase II: Characterized by **aciduria** in the presence of continued respiratory alkalosis. This phase may begin within hours and may last 12–24 hours.

Phase III: (metabolic acidosis): Characterized by **dehydration, hypokalemia**, and **progressive metabolic acidosis**. This phase may begin 4–6 hours after ingestion or 24 hours or more after ingestion.

Progressive metabolic acidosis is explained as; the cells try to compensate the decrease in ATP production by:

- Increasing glycolysis (accumulation of lactic and pyruvic acids).
- Stimulation of lipid metabolism → accumulation of ketone bodies.
- Inhibition of amino-acid metabolism (accumulation of amino acids).
- Renal compensation through urinary excretion of HCO_3.
- Renal dysfunction → accumulation of salicylic acid metabolites

Clinical presentation:

1. **Gastrointestinal (GIT):**
   - Nausea, vomiting and abdominal pain.
   - GIT bleeding & ulceration.

   Due to Gastric irritation and stimulation of chemoreceptor trigger zone.
2. **Neurologic:**
   - Irritability, agitation, and confusion are early signs of severe toxicity.
   - Coma, seizures, and cerebral edema are late signs of severe toxicity and result from:
     - Direct toxic effect,
     - Decreased brain glucose concentration.
     - Accumulation of co2 in the brain.

3. **Cardiovascular system:**
   - Tachycardia in mild toxicity.

- Hypotension and dysrhythmias in severe toxicity.

4. Respiratory system:

Non-cardiogenic pulmonary edema resulting from adrenergic over activity→ shift of blood from systemic to the pulmonary circulation → pulmonary hypertension and edema.

5. Urinary system:

- Direct nephrotoxicity →renal tubular necrosis → renal failure.
- Indirect effect due to:
  - Decreased renal flow caused by dehydration
  - Inhibition of prostaglandins necessary to maintain renal blood flow.
  - Rhabdomyolysis.

6. Hepatic:

- Chronic toxicity → elevated liver enzymes.
- Reye's syndrome in children (Reye syndrome is acute brain damage and liver dysfunction, which occur in children who were given aspirin when they had chickenpox or flu).

7. Hematologic:

Bleeding tendencies is common in chronic intoxication due to inhibition of prothrombin synthesis & platelet aggregation.

8. Hyperthermia:

Mild hyperthermia due to:

- Uncoupling of oxidative phosphorylation with subsequent increase in cellular metabolic rate.
- Dehydration.

9. Hypersensitivity reaction (Allergy):

- Urticaria, skin rash and angioneurotic edema.
- Precipitation of bronchial asthma.

10. Salicylism:

- Tinnitus, vertigo, deafness may occur with therapeutic and toxic doses.
- This effect is due to 8^{th} cranial nerve involvement. It is reversible.

11. Fluid and electrolyte disturbances:

- Dehydration due to:
  - Increased metabolic rate and hyperthermia (sweating).
  - Vomiting and
  - Hyperventilation.
- Hypokalemia.

12. Metabolic disorders:

- Initially there is short period of hyperglycemia (due to ↑glycolysis).
- Hypoglycemia occurs either late in acute toxicity or in chronic toxicity

(due to depletion of glycogen stores).

- Hypoglycemia is more common in children.

Causes of death:

- Early (12-24hrs): central respiratory failure, pulmonary edema and/or cardiac arrhythmias (acidosis).
- Delayed (few days): renal failure and hemorrhage.

Investigations:

1- Routine lab investigations:
2- Coagulation profiles: prothrombin time (PT), prothrombin concentration, PTT (partial thromboplastin time), bleeding time and INR (International Normalized ratio).
3- Serum salicylate levels (mg/dl):
   - Therapeutic: 3-30
   - Toxic: > 40.
   - Lethal: > 100.
4- Abdominal X-Ray: radiopaque concretions of enteric coated aspirin.
5- Chest X-Ray: pulmonary edema.

Treatment:

1- Supportive measures: ABCs

2- GIT decontamination:

- Gastric lavage using sodium bicarbonate.
- Activated charcoal.
- MDAC appears to be superior to single doses.
- Whole bowel irrigation: helpful with sustained-release preparations and enteric-coated forms.

3- Elimination of the poison from the blood:

- Forced alkaline diuresis:
  Effective in moderate toxicity (>40mg/dL in acute toxicity & >30mg/dL in chronic toxicity).
- Hemodialysis:
  Effective in salicylate poisoning (small volume of distribution) and indicated in the following conditions:
  - Serum salicylate levels > 80 mg/dL after acute overdose or > 50 mg/dL with chronic intoxication).
  - Renal failure or congestive heart failure.
  - Refractory acidosis.
  - Pulmonary edema.
  - Seizures, coma & cerebral edema.

4- Symptomatic treatment:

- Dehydration →normal saline
- Hypokalemia → potassium.

- Hypoglycemia →glucose.
- Seizures → diazepam.
- Metabolic acidosis → IV. Na HCO3.
- Pulmonary edema→ oxygen and hemodialysis.
- Cerebral edema → mannitol, oxygenation & hemodialysis.
- Hyperthermia → cold foments and ice enema.
- Bleeding tendencies → Vit. K or blood transfusion.
- GIT irritation → demulcent.

2- Acetaminophen (Paracetamol)

Common preparations:

1. **Tablets:**
   - Panadol, Paracetamol, Paramol, Pyral.
   - Integrated in various cold preparations.
2. **Vials:**
   - Perphalgan.

Pharmacokinetics:

- Rapidly absorbed from the GIT.
- Peak plasma levels usually occur within 4 hours.
- 5-20% bounds to plasma protein & may increase to 50% in overdose.

Metabolism:

1. **At therapeutic doses:**
   - 94% of Paracetamol is metabolized in the liver through conjugation with glucuronide (42%) and sulfate (52%) → nontoxic conjugate that are then excreted in the urine.
   - 2% is excreted unchanged in the urine.
   - -The remaining 4% is metabolized via the cytochrome P450 to a toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI). NAPQI is rapidly conjugated with hepatic glutathione, forming a nontoxic compound that is excreted in urine.
2. **At toxic doses:**
   - The sulfate and glucuronide pathways become saturated, resulting in increased fraction of the toxic metabolite (NAPQI) that overwhelms the glutathione detoxification mechanism (depletion of glutathione stores).

Conditions of poisoning:

- **Accidental:** Most common especially in children.
- **Suicidal:** common

Toxic dose:

- Acute toxicity (single dose): > 150 mg/kg (Adults) and > 200 mg/kg

(children).

- Chronic toxicity: > 150 mg/kg/ d over 2 days.

N.B children appear to be more resistant to Paracetamol toxicity (most probably due to more ability for sulphation than adults).

Mechanism of action:

- **Therapeutic action:** potent inhibitory effect on synthesis of **central** prostaglandin (PG). However, the anti-inflammatory action is very weak due to its weak inhibitory action on synthesis of peripheral PG.
- **Toxic action:** The toxic metabolite acetyl-p-benzoquinone imine (NAPQI) will bind to (–SH) group of hepatic cellular protein → centri-lobular necrosis.

Clinical presentations:

Stage	Time Following Ingestion	Characteristics
I	**0.5 to 24 hr.**	Asymptomatic, anorexia, nausea, vomiting, malaise & pallor.
II	**24 to 48 hr.**	-Resolution of the above characteristics. -Right upper quadrant abdominal pain and tenderness. -Elevated bilirubin, prothrombin time, INR, hepatic enzymes.
III	**72 to 96 hr.**	-Stage I symptoms reappear. -Signs of liver failure (jaundice, marked elevation in hepatic enzymes, coagulation defects, encephalopathy and altered conscious level). -Metabolic acidosis, hypoglycemia, and acute renal failure may be apparent
IV	**4 d to 2 wk.**	-Resolution of hepatic dysfunction in survivors. -Death may occur in patients with fulminant hepatic failure (FHF) or due to multi-organ failure.

Investigations:

1- Routine investigation.

2- Serum Paracetamol levels (4hr post ingestion) (mcg/mL):

- Therapeutic: 5-20;
- Toxic: 120-300;
- Lethal: > 300.

Treatment:

1- Supportive measures: ABCs.

2- GIT decontamination:

- Gastric lavage **not recommended** as it is rapidly absorbed from the GIT.
- Activated charcoal is **not recommended** to be administered in conjunction with ***N- Acetyl Cysteine*** (NAC) as charcoal may adsorb NAC.
- Ipecac is **not recommended** as it may interfere with oral NAC.

3- Specific antidotes:

- ***N- Acetyl Cysteine (NAC):***

Mechanism:

- It is metabolized by the hepatocytes to a glutathione precursor (cysteine) that provides protective levels of glutathione to detoxify the hepatotoxic metabolite NAPQI by providing (–SH) group (minor pathway).
- It enhances sulphation conjugation by providing sulfur (major pathway).
- NAC should be given within 8h after Paracetamol ingestion.
- If time of ingestion is unknown or hepatotoxicity is evident immediate initiation of NAC treatment.

Forms of NAC:

-Oral (Mucomyst):

- *Initial loading dose* (140 mg/kg), followed by *maintenance doses* (70 mg/kg/4hours for 3 days).
- Any vomited dose should be repeated + antiemetic.
- If recurrent vomiting develops, switch to the intravenous formulation.

-Intravenous (Parvolex):

- *Two situations in which IV NAC is undoubtedly preferable to oral:*
  1. Fulminant hepatic failure (FHF) 2. Inability to tolerate oral NAC.
- *Dosage: 150 mg/kg IV infusion over 15 minutes, 50 mg/kg IV infusion over 4 hours, then 100 mg/kg IV over 16 hours.*
- *It is very important that NAC be given slowly. A fast rate of infusion may cause rash, flushing, and itching.*

4- Elimination of the poison from the blood:

Hemodialysis may be indicated if renal failure, refractory acidosis, or fluid and electrolyte changes occur.

ORAL HYPOGLYCEMIC

Common preparations:

- **Sulfonylureas** e.g. Tolazamide, Chlorpropamide
- **Biguanides** e.g. Metformin.

Mechanism of action:

- **Sulfonylureas**: increase insulin level through stimulation of Beta-receptors in pancreas.
- **Biguanides**:
  - Decrease amount of glucose produced by liver.
  - Decrease intestinal absorption of glucose.
  - Decrease the body need to insulin & Improve insulin sensitivity by increasing peripheral glucose uptake and utilization.

Conditions of poisoning:

- Accidental overdose.
- Suicidal.
- Homicidal.

Clinical presentation:

1- **General symptoms and signs of hypoglycemia (adrenergic hyperactivity)** anxiety, nervousness, palpitation, tachycardia, sweating, pallor, coldness & dilated pupils.

2- **CNS manifestation:**

i. Mental status ranged from normal up to coma (according to serum glucose level).
ii. Increase muscle activity up to seizures.

3- **Respiratory manifestation**

i. Rapid shallow respiration due to **adrenergic** hyperactivity.
ii. Rapid deep respiration (Kussmaul respiration) if metabolic acidosis (increased lactic acid) occurred.

Investigations:

Routine investigation.

Treatment:

1. **Supportive measures: ABC**
2. **GIT decontamination**
   a. Gastric lavage with airway protection.
   b. Activated charcoal.
3. **Enhance elimination**
   a. Alkalinization of urine enhances excretion of Chlorpropamide.
   b. Dialysis is not effective in sulfonylurea (most of them):
      - Large volume of distribution.
      - Tight binding of the drug to plasma proteins.

4. **Specific antidotes**
   a. Glucose: 1-2 ml/Kg of 50% Dextrose. Continue with 10% Dextrose to keep normal serum glucose
   b. Octreotide (somatostatin): inhibits release of insulin from beta cells. It acts as specific antidote of sulfonylurea.
5. **Symptomatic:**
   - Seizures: Diazepam.
   - Acidosis: NaHCO3

LITHIUM (Li)

Lithium is a monovalent cation, chemically similar to Na+ and K+.

Uses:

- *Lithium metal:* manufacture of storage batteries.
- *Lithium salts:* manic-depressive disorders.

Mechanism of action:

- Lithium competes with Na+ and K+ altering their transport at the level of cell membrane and neuronal synapses.
- **Inhibits** the release of **dopamine** and norepinephrine.
- I**ncreases** the release of **serotonin**.

Clinical picture of acute Toxicity:

1. **GIT:** Anorexia, nausea, vomiting, abdominal pain and diarrhea.
2. **Respiratory:** Acute respiratory distress syndrome (ARDS) in severe cases.
3. **CNS:**
   - Mild to moderate toxicity: Mental confusion, lethargy, tremors, hyperreflexia, ataxia, slurred speech and cogwheel rigidity.
   - Severe toxicity: seizures and coma.
4. **Renal:**
   - Chronic toxicity: nephrogenic diabetes insipidus with polyuria, polydipsia and resulting hypernatremia.
   - Acute toxicity: acute renal failure.
5. **CVS:**
   - Conduction disturbances, arrhythmias and ECG changes.
6. **Endocrine:**
   - Hypothyroidism.
   - Hyperparathyroidism.
   - In long-term therapy osteoporosis may occur.
7. **Fluid-electrolyte balance:**
   - Dehydration (chronic toxicity).
   - Severe hypernatremia in patients with diabetes insipidus.

- Decreased anion gap.

N.B. Increase in unmeasured cations (lithium) →decreased anion gap while increase in measured cations (Na & K)→ increased anion gap.

Investigations:

1- Routine investigations + Anion gap measurement.
2- Toxicological screening.
3- ECG.

Treatment:

1-Supportive: ABC (see general toxicology).

2-GIT decontamination:

- Emesis.
- Gastric Lavage.
- Activated charcoal **does not** adsorb lithium.
- Whole bowel irrigation.

3-Elimination of the poison from blood:

- Hemodialysis is very effective as lithium is a small ion, non-protein-bound and having small volume of distribution (Vd).
- Diuretics: should be avoided as it worsens intoxication.

4-Symptomatic:

- Dehydration: IV normal saline
- Dysrhythmias: antiarrhythmic drugs and magnesium sulfate in refractory tachycardia.

5-Antidote therapy:

Sodium polystyrene sulfonate (SPS):

- **Mechanism of Action:**
  - SPS is a cation-exchange resin that acts by exchanging its sodium for potassium in the large intestine.
  - It may delay but not prevent absorption of lithium.
  - Routine use for lithium toxicity is not recommended.
  - Hemodialysis is more effective.
- **Indications:** Hyperkalemia & lithium toxicity.
- **Contraindications:**
  - Hypersensitivity to SPS.
  - Hypokalemia.
  - Obstructive bowel disease.
- **Adverse Reactions:**
  - Constipation, nausea & vomiting.
  - Fecal impaction in the elderly.
  - Colonic necrosis (rectal administration)
  - Electrolytes abnormalities: Sodium retention, and hypokalemia.
- **Dosage: (Adults):**
  - 15 g orally, 1 to 4 times daily, as slurry solution.
  - 30 to 50 g rectally every 6 hr as a warm emulsion in 100 mL sorbitol, retain 30-60 min and follow with a cleansing enema.

PESTICIDES

Definition:

Pesticides are compounds that are designed to eradicate undesirable pests (plants or animals).

Classification:

- **Insecticides:** which include:
  - ♦ Organophosphorus.
  - ♦ Carbamate.
  - ♦ Organochlorine (rarely used nowadays).
  - ♦ Pyrethroids.
  - ♦ Naphthalene.
  - ♦ Inorganic insecticides; e.g. Lead hydrogen arsenate.
- **Rodenticides:** which include:
  - ♦ Anticoagulants.
  - ♦ Zinc phosphide.
  - ♦ Strychnine.
  - ♦ Naphthylthiourea agents.
  - ♦ Fluorinated agents.
- **Herbicide.**
- **Fungicide.**

Conditions of exposure:

- **Accidental:**
  - Children: accidental ingestion of insecticides.
  - Eating food contaminated by pesticides.
  - Intoxication may also occur during lice control.
  - Occupational exposure may occur during fumigation, or manufacturing of pesticides.
- **Suicidal:** common.
- **Homicidal:** rare.

INSECTICIDE

1- *Organophosphorus Compounds*

(Cholinergic Toxidrome)

Mechanism of action:

- Organophosphates inhibit cholinesterase → accumulation of acetylcholine → stimulation followed by depression of:
    - Nicotinic receptors.
    - Muscarinic receptors.
    - CNS.
- They act by **irreversible** binding of their phosphate radicals to the cholinesterase enzyme forming phosphorylated enzymes.
- Within 48 hours after phosphorylation, the enzyme complex loses an alkyl group in a process called “aging”.
- Aged enzymes cannot regenerate spontaneously.

Fatal dose: 0.02-0.1 g of parathion orally.

Clinical picture:

1. Muscarinic receptors effects: (DUMBBLES)

- **D**iarrhea, **U**rine incontinence, **M**iosis, **B**ronchospasm, **B**radycardia, Lacrimation, **E**mesis and **S**alivation.

2. Nicotinic receptors effects:

- Musculoskeletal: Fasciculation → paralysis.
- Cardiovascular (Sympathetic ganglia): tachycardia & hypertension followed by bradycardia & hypotension.

3. CNS effects

- Stage of stimulation: anxiety, irritability, and convulsions.
- Stage of depression: coma, and depression of both respiratory & cardio-vascular centers.

4. Other effects:

- Metabolic acidosis.
- Hyperglycemia.
- Non-cardiogenic pulmonary edema.

Late sequelae:

1- Intermediate syndrome:

- Begins after 3 days and lasts for 30 days.
- Characterized by: paralysis of proximal muscles of the limbs, neck flexor muscles, and respiratory muscles.
- The condition is not responsive to Atropine or Pralidoximes, but early & adequate treatment of toxicity with Pralidoximes may prevent the syndrome.

2- Delayed peripheral neuropathy:

- Begins after 3 weeks.
- The neuropathy begins by paresthesia (glove & stocking), and pain in the calves followed by weakness “toe drop” that rapidly progresses to flaccid paresis.
- The condition may be ascending as seen in Guillain-Barre syndrome.
- Treatment is difficult & no role of antidotes.

Differential diagnosis:

- Carbamate (rapid onset, short duration, and absent CNS toxicity).
- Other causes of Miosis such as opioids and sedative-hypnotics.
- Medical conditions e.g. gastro-enteritis & Guillain-Barre syndrome.

Cause of death:

Respiratory failure due to peripheral and central actions:

- **Peripheral:** bronchospasm; increased bronchial secretion; and paralysis of respiratory muscles.
- **Central:** depression of R.C.

Investigations:

1. Routine lab investigation.
2. Cholinesterase levels:
   - **True** cholinesterase present mainly in erythrocytes and nervous tissues (good for non-acute exposure monitoring).
   - **Pseudo**-cholinesterase found in plasma and liver (quick fall and quick recovery after exposure so it is good for acute exposure monitoring).
3. Detection of **para-nitrophenol** (metabolite of organophosphate) in urine.
4. Chest X-ray: pneumonia, non-cardiogenic pulmonary edema.
5. ECG: arrhythmia.

Treatment:

I- Prophylactic for workers:

- Periodic examinations with monitoring of the cholinesterase level.
- Protective clothing, masks, gloves & boots.
- Frequent washing of hands and body.

II- Curative:

1-Supportive treatment: ABC.

2- Decontamination:

GIT:

- Emesis should be avoided (CNS depression and seizures).
- Gastric lavage
  - Using a large-bore orogastric tube.
  - Cuffed endotracheal tube to prevent aspiration (petroleum distillate vehicle).
- Activated charcoal.
- Cathartics.

Skin: Skin wash with copious water.

Eyes: Irrigation of the eyes with copious amount of tape water for at least 15 minutes.

3- Antidote:

- **Atropine**

  Action: it antagonizes muscarinic action only.

  Dose: IV injection of 2 mg (for adults) or and 0.05 mg/kg (for children), every 15 minutes, till **full atropinization** (dilated pupil, dry mouth, cleared bronchi from secretions & tachycardia).

- **Oximes (cholinesterase reactivators)**

  Action:

  - They antagonize both muscarinic & nicotinic actions.
  - Pralidoxime may also act as a scavenger for the remaining organophosphates molecules.

  Dose: 1 gm (adult) or 25 mg/kg (children) to be followed by IV infusion of 5% solution over 60 min.

  Time of administration: in the first 24-48 hrs. (before enzyme aging).

4-Symptomatic treatment:

- Convulsions: diazepam or phenobarbital if seizures persist.
- Care of coma.
- Arrhythmias: antiarrhythmic.
- Pulmonary edema: oxygen - mechanical ventilation.

2-Carbamates

(Cholinergic Toxidrome)

Mechanism of action:

Carbamates are **reversible** cholinesterase inhibitors → accumulation of acetylcholine → clinical picture similar to that of organophosphates.

Difference between carbamates & organophosphates:

- They are **reversible** cholinesterase inhibitors so they are **less toxic** & of **shorter duration** than organophosphates.
- Carbamate has a **rapid onset** (15 – 120 minutes).
- Carbamate poorly cross the blood brain barrier, so **no CNS** effects.
- Carbamates have **no long-term sequelae**.
- Serum and red cells **cholinesterase values are not reliable** in the diagnosis of Carbamate poisoning. The enzyme activity with Carbamate poisoning return to normal within few hours.
- **Oximes are not indicated** in the treatment of carbonates since aging of the enzyme does not occur.

3-Organo-Chlorine Insecticides *(rarely used)*

Types:

- *Dichlorodiphenyltrichloroethane (DDT).*
- *Hexachlorocyclohexane.*
- *Cyclodienes.*
- *Chlordecone, Kelevan, and Mirex.*
- *Toxaphene.*

Mechanism of toxicity:

- **CNS stimulation:** by disturbing the neuronal membrane causing hyperexcitability of the nervous system.
- **Cardiac effects:** due to sensitization of the myocardium to catecholamines.
- **Air way irritation** (inhalation of toxic vapors).
- **Hemolysis of RBC's.**
- **Degenerative changes of liver & kidney.**

Clinical presentations:

1- CNS stimulation followed by depression.
2- Cardiac dysrhythmias.
3- Cough, wheezing, shortness of breath or may be respiratory distress in severe cases.
4- Jaundice & hepatic coma.
5- Hematuria, oliguria& anuria.
6- Nausea, vomiting, diarrhea, or abdominal pain.
7- Skin rash.

Investigations:

1- Routine lab investigation.
2- ECG.
3- Chest X-ray.
4- Abdominal X-ray: radiopaque chlorinated pesticides.

Treatment:

1-Supportive treatment: ABC (see general toxicology).

2- Decontamination:

GIT:

- Emesis should be avoided (CNS depression and seizures).
- Gastric lavage with care to prevent aspiration.
- Activated charcoal.

Skin: Skin wash with copious water.

Eyes: Irrigation of the eyes with copious amount of tape water for at least 15 minutes.

3- Symptomatic treatment:

- Convulsions: diazepam or phenobarbital if seizures persist.
- Care of coma.
- Arrhythmias: antiarrhythmic.
- Liver support.
- Hemodialysis for kidney failure.

4-Pyrethrins /Pyrethroids (plant origin)

Types:

- Pyrethrins *(Pyrethrum)*

Pyrethrins are a natural compound extracted from the dried flowers of pyrethrums.

- *Pyrethroids*

They are synthetic derivatives similar to the natural pyrethrum.

They are two types:

Type I Pyrethroids: (no systemic toxicity).

Type II Pyrethroids: (systemic toxicity).

Uses:

- Household pesticides.
- Repellant: applied only on the outer surface of clothes.

Action:

- Local irritation of the skin, respiratory, and gastro-intestinal systems.
- In severe toxicity, CNS effects can occur.

Clinical picture:

1- Skin (most common):
   - Erythema, vesiculations, and mild paresthesia.

2- Respiratory system:
   - Upper airway irritation such as rhinitis, throat irritation, and oral & laryngeal edema.
   - Lower airway reactions such as cough, wheezes, dyspnea, and chest pain.
   - Chronic exposure can produce hypersensitivity pneumonitis.

3- Gastro-intestinal system: Nausea, vomiting, diarrhea, and abdominal cramps.

4- Eye: Corneal irritation.

5- Central nervous system: Excitation, tremors, incoordination, paralysis, or seizures.

Treatment:

1- Generally no treatment is required for acute ingestion of Pyrethrins.

2- Decontamination:

- Emesis or gastric lavage.
- Copious irrigation of the skin and the eyes with water.

3- Symptomatic treatment:

- Seizures: diazepam or barbiturates.
- Allergy & bronchospasm: epinephrine, anti-histaminic, and steroids.

5- Naphthalene
(Mothballs)

Uses:

- Moth repellents.
- Toilet bowl deodorizers.

Mechanism of action:

Naphthalene toxic metabolites combine with:

- Hemoglobin→ met-hemoglobin.
- Cell wall structures → hemolysis.

Toxic dose:

- 250 – 500 mg pure naphthalene (mothball = 0.5 – 3.5 gm) may cause hemolysis in patients with G6PD deficiency. Patients without G6PD deficiency require several grams to produce toxicity.
- 1 – 2 gm may produce seizures.

Clinical picture:

1) Blood:

-**Hemolysis**→ hemoglobinurea.

- Starts after 1 – 3 days of exposure to naphthalene.
- Persons with G6PD deficiency are more prone to develop hemolysis after exposure to naphthalene.

-**Met-Hemoglobinemia** may occur.

2) Other manifestations:

i. GIT:

- Nausea, vomiting, and diarrhea.

ii. CNS:

- Coma and convulsions.

iii. Kidneys

- Dark urine (hemoglobinurea, and naphthalene excretion in urine).
- Renal failure that may.

Investigations:

Routine lab investigation.

Treatment:

1- Supportive treatment: ABC.

2- GIT decontamination

- Emesis.
- Gastric lavage is not effective to remove large mothballs.
- Activated charcoal
- Cathartics.

3- Symptomatic treatment

- Blood transfusion in severe hemolysis.
- Corticosteroids are helpful in limiting the hemolysis.
- Methylene blue for Met-Hemoglobinemia.
- Care of the kidneys
  - Monitoring the urine output.
  - Hemoglobinurea: alkalinization of urine and diuresis.

RODENTICIDE

1- Zinc Phosphide

Mechanism of Action:

- Zinc Phosphide is changed to phosphine gas (in the presence of moisture and acid in the stomach).
- phosphine gas has the following actions:
  - Cytochrome C oxidase inhibitor (responsible for cellular respiration).
  - Gastrointestinal and pulmonary irritant.

Clinical picture:

1- Gastrointestinal: Nausea & vomiting.
2- Respiratory: Pulmonary edema, cough & dyspnea.
3- Hepatic: Centrilobular necrosis.
4- Metabolic: Metabolic acidosis & hypocalcemia.
5- Central nervous system: Headache, fatigue, ataxia
6- Neuromuscular: Paresthesia & kinetic tremors.
7- Ocular: Diplopia.

Investigations:

1- Routine lab investigation.
2- Detection of zinc phosphide.
3- Ca^{+2} level.

Treatment:

1-Supportive treatment: ABC (see general toxicology).

2-Decontamination:

GIT:

- Emesis should be avoided (vomiting).
- Gastric lavage
- Activated charcoal.

Skin: Skin wash with copious water.

Inhalation: 100% humidified oxygen.

3-Symptomatic treatment:

- Acidosis: sodium bicarbonate.
- Pulmonary edema: Oxygen & mechanical ventilation.
- Hypocalcemia: Ca^{+2}.

2- ORAL ANTICOAGULANTS (Warfarin)

The mechanism of action:

It acts as vitamin K antagonist → inhibits the biosynthesis of vitamin K-dependent coagulant factors II, VII, IX and X. These effects are gradually developed over several days.

Clinical picture:

Bleeding:

- Hematuria, blood in stool, epistaxis, bruising and menorrhagia.
- Hemorrhage into the airway with resultant airway obstruction.
- Intracranial hemorrhage.

Investigations:

Prothrombin time (PT), (International Normalized ratio) (INR), partial thromboplastin time (PTT), thrombin time & and fibrinogen concentration.

Treatment:

1-Supportive treatment: ABC (see general toxicology).

2-GIT decontamination:

- Gastric lavage.
- Activated charcoal.

3- Antidote: Vitamin K1

- It takes several hours to activate enough factors and reverse the coagulopathy.
- Severe cases: 10–25 mg SC (I.V. may induce anaphylaxis) or
  100mg orally.
- Stable cases: 100mg orally in 3 - 4 divided doses daily.

4-Symptomatic: Bleeding:

- Blood transfusion,
- Vitamin k–dependent factors,
- Packed red blood cells or
- Fresh-frozen plasma (FFP).

TOXIC GASES

1- Carbon Monoxide (CO) Poisoning

It is a colorless, odorless and nonirritant toxic gas 'Silent Killer'.

Sources:

Endogenous:

Normal heme catabolism.

Exogenous:

It is a product of incomplete combustion of carbon compounds or organic matter.

Conditions of Poisoning:

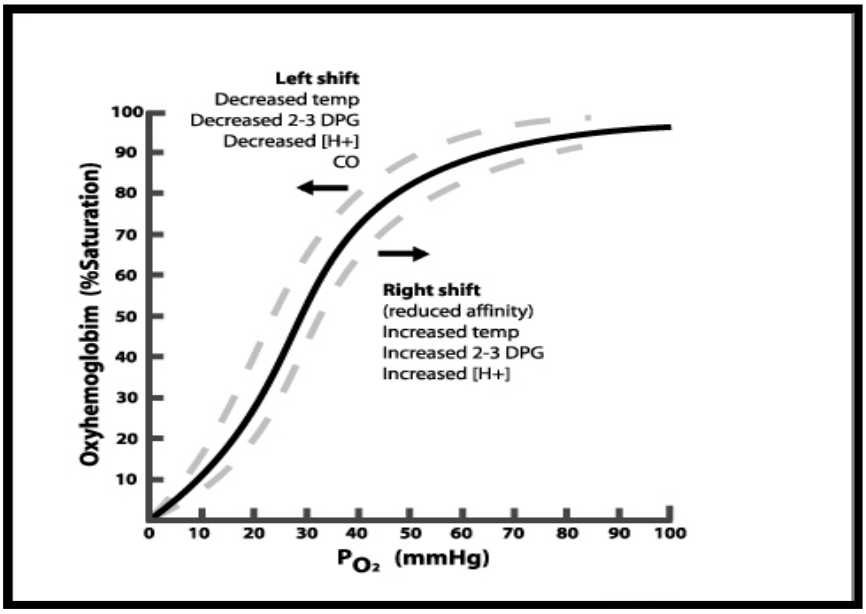
- **Accidental:**
  - **1- Household:**

    Any fuel-burning appliance that is not vented properly, such as:
    - Charcoal grills,
    - Wood burning chimneys or
    - Gas heaters and stoves.
  - **2- Environmental**
    - Automobile exhaust gas or
    - Cigarette smoke.
  - **3- Occupational**
    - Firemen or
    - Coal miners.
- **Suicidal:**
  - Painless death due to inhalation of automobile exhaust in a closed garage.
- **Homicidal:**
  - Rare.

Mechanism of action:

A) The affinity of binding of CO to hemoglobin is about 200 to 250 times greater than that of oxygen, this result in:

- Formation of carboxyhemoglobin (COHb) → Red coloration of body **(Red asphyxia).**
- Decreased association of oxygen and hemoglobin i.e. decreased O_2-carrying capacity of blood, which leads to **anemic anoxia.**
- Decreased dissociation of O_2 from unaltered oxyhemoglobin to the cells→ shifting of oxyhemoglobin-dissociation curve to the left.



B) CO binds to other iron-containing proteins:

- **Myoglobin**: causing myocardial (reduced cardiac output and hypotension) and skeletal muscle dysfunction.
- **Cytochrome oxidase, which** responsible for allowing cells to utilize oxygen.

C) Brain lipid peroxidation → neuronal dysfunction.

Clinical presentations:

Depends upon carboxyhemoglobin level:

- **Mild (<15 - 20% COHb):**
- Headache, dizziness and blurred vision
- Nausea & vomiting.
- **Moderate (> 20 - 40% COHb):**
- Confusion.
- Syncope, chest pain & tachycardia.
- Tachypnea & dyspnea.
- Weakness *(unable to escape or call for help)*
- Rhabdomyolysis.
- **Severe (> 40 - 60% COHb**):
- Palpitations, dysrhythmias, hypotension, myocardial ischemia & cardiac arrest.
- Pulmonary edema & respiratory arrest.
- Seizures and coma.
- **Fatal (> 60% COHb**).

Neurological sequelae:

They may occur at the onset of intoxication or days to weeks later after a period of apparent total recovery. The severity of these symptoms depends on the duration of hypoxia of brain tissue and the neurological structures affected.

They include:

- Amnesia.
- Parkinsonism & paralysis.
- Confusion.
- Disorientation.
- Encephalopathy.
- Mental retardation.
- Psychosis and manic depression.

Causes of death:

Respiratory and circulatory failure.

Investigations:

1) To detect COHB level in blood:

The blood is collected under a layer of liquid paraffin to avoid exposure to air. The following investigations are done:

- Spectroscopic Examination.
- CO-oximeter.
- Gas chromatography.

2) To detect effects of CO:

- Routine lab.
- Chest x- ray.
- ECG.
- MRI.

Treatment:

I. Prophylactic:

- Workers exposed to CO poisoning should have an instrument for early detection of CO concentration in air.
- The maximum allowable concentration (MAC) is 50 parts / million (50 ppm).

II. Curative:

1. Oxygen

- COHb < 15% → Fresh air.
- COHb > 15% → 100% O2
- COHb ≥ 40% → Hyperbaric O_2 (2 atmospheric pressure O_2).

Role of hyperbaric oxygen in the ttt:

- Hastens dissociation of CO from carboxyhemoglobin and cytochrome oxidase.
- Reduces the half-life of carbon monoxide.
- Enhances oxygen transport to the tissues by plasma.

2. ***Bed rest & warmth:***
   to decrease muscle O_2 demands.
3. ***Symptomatic treatment:***
   - Convulsions→ Diazepam.
   - Arrhythmias→ Antiarrhythmic drugs.
   - Pneumonia→ Antibiotics.
   - Hypotension→ intravenous fluids &vasopressors.
   - Metabolic acidosis→ sodium bicarbonate.

2- Hydrocyanic Acid Poisoning

(Prussic Acid)

A volatile colorless liquid with bitter almond smell.

Chemical forms

a. Salts: sodium, potassium, or calcium cyanide.
b. Volatile liquids: hydrocyanic acid.
c. Gas: released from combustion of plastics, petrochemicals & wool.
d. Cyanogenic glycoside (Amygdalin): in the seeds of unripe fruits as peaches, cherry, apple, pear, plum. It is converted to cyanide in the small intestine by enzymes & bacteria, and then cyanide is detoxified by endogenous detoxifying systems.

Uses:

1- Industrial uses:
- Cyanide salts are used in industries of photography, electroplating and coating silver.

2- Agricultural:
- Cyanide gas [HCN] is used as insecticide and rodenticide.
- Cyanide salts are used as fertilizer.

3-Medical uses:
- Na nitroprusside: Antihypertensive, which is converted to cyanide if exposed to light.
- Laetrile: Antineoplastic.

4- Household uses:
- **Acetonitrite** (a component of some nail glue removers).

Condition of poisoning:

- **Accidental:**
  Industrial, agricultural or household exposure.
- **Suicidal:**
  As being rapid potent killer, it is used by people who can get it (spies, laboratory worker, etc…).
- **Homicidal:**

- Rare [characteristic smell and taste of bitter almond oil].
- Execution by the gas chamber in some states of U.S.A.

Mechanism of action:

- **Cyanide:** blocks **cytochrome oxidase** enzymes (terminal enzyme involved in aerobic metabolism) as it unites with ferric ions of the enzyme leading to their paralysis. This will lead to:
  1. Cellular asphyxia (histotoxic anoxia) with no cyanosis (Red asphyxia) as the tissues cannot utilize oxygen (no O_2 consumption by the tissues) i.e. O_2 in Arterial blood = O_2 in venous blood.
  2. Anaerobic metabolism→ increased lactic acid production→ metabolic acidosis.
  3. Reduced ATP stores.
- **Cyanide salts:**
  1. Corrosive effect.
  2. Liberate HCN after reacting with gastric HCL.

Fatal dose:

- One drop of pure hydrocyanic acid.
- 300 mg of potassium cyanide.

Fatal period:

- 2 **-** 10 minutes.
- 4 hours in case of cyanide salts (time needed for conversion to HCN by the action of gastric HCL).

Clinical picture:

I. **Large dose:** Sudden death within 1 – 2 minutes.

II. Small dose:

1. **CNS:** headache, anxiety, agitation, confusion, lethargy, seizures, and coma.
2. **CVS:** initial bradycardia and hypertension followed by hypotension with reflex tachycardia, but the terminal event is bradycardia and hypotension.
3. **Respiratory:** initial tachypnea followed by bradypnea and pulmonary edema. Cyanosis not apparent, since blood is adequately oxygenated.
4. **Metabolic acidosis.**

D.D. red asphyxia:

- CO poisoning (carboxyhemoglobin).
- Cyanide poisoning ((Histotoxic anoxia).
- Cold (Hypothermia lowers dissociation of oxyhemoglobin).

Treatment:

Emergent interference is lifesaving.

1- Physiological Antidotes:

a) Cyanide Kit

Consists of:

1- Amyl nitrite: 1 capsule up to 8 capsules crushed in front of nose (inhalation).

2- Sodium nitrite: 10 ml of 3% solution IV over a period of 3-5 minutes.

3- Sodium thiosulfate: 50 ml IV over 10-20 minutes following administration of sodium nitrite.

4- Reducing agents: Vitamin C or methylene blue.

Mechanism of action:

- **Nitrite** therapy coverts Oxyhemoglobin to Methemoglobin which has higher affinity to HCN than cytochrome oxidase, thus forming Cyano-Methemoglobin complex and cytochrome oxidase sets free.
- **Sodium thiosulfate** reacts with cyan-met-Hb to form nontoxic thiocyanate, which is excreted in urine.
- **Reducing agents** convert met-hemoglobin to oxyhemoglobin.

Side effects:

- Hypotension.
- Met-Hemoglobinemia.

b) Dicobalt EDTA (Kelocyanor): *300 – 600 mg IV*

It chelates cyanide in circulation but it does not bind to intracellular cyanide.

c) Hydroxycobalamin (Vit B_{12}a):

Hydroxycobalamin binds to cyanide and form cyanocobalamin (Vit B_{12}) which can be excreted in urine leaving free enzymes.

d) Dimethyl-4-aminophenol (DMAP): *A newly introduced drug that produces a rapid met-hemoglobinemia.*

N.B. Repeat physiological antidote after 24-48 hrs. if the toxicity signs recur uses half the dose.

2- Care of respiration:

Artificial respiration using 100% oxygen.

3- GIT Decontamination:

Gastric lavage (if ingested) by Sodium Thiosulphate 5% solution or H_2O_2 (oxidation) → nontoxic thiocyanate.

3- Hydrogen Sulfide (H2S)

It is a colorless gas with the characteristic foul odor of rotten eggs.

Sources of exposure:

Produced and collected in sewage systems by the decomposition of organic household or industrial wastes.

Mechanism of action:

As cyanide.

Treatment:

As cyanide.

VOLATILES

Ethyl Alcohol (Ethanol)

Ethanol is a clear, colorless liquid having a slight pleasant odor.

Source:

From fermentation of sugar using living yeast.

Uses:

It is used as antiseptic, organic solvent, in cosmetic lotions and in beverages.

Conditions of Poisoning:

- **Accidental:**
  - Children (drink cosmetic preparations containing ethanol).
  - Addicts (acute on top of chronic).
- **Homicidal:** To facilitate rape and robbery.

Pharmacokinetics:

Absorption:

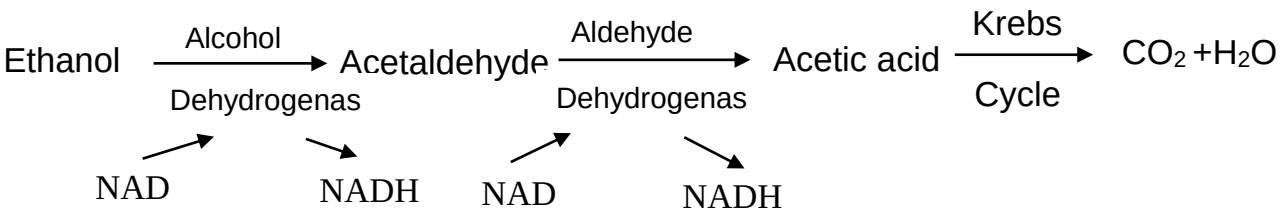
- Major part (80%) from small intestine.
- Minor part (20%) from stomach & large intestine.

Distribution:

- To all tissues and body fluids, parallels the water content of each.
- Crosses the alveolar membrane, the blood brain barrier as well as the placenta.

Metabolism:

90-98% is metabolized in liver.



Excretion:

2-10% is excreted as unchanged ethanol through:

- Urine.
- Breath.
- Small amounts can be detected in sweat, tears, bile, gastric juice and other secretions.

Fatal dose:

- 300-400 ml of pure alcohol.

Fatal period:

- Within 10 hours.

Mechanism of Action:

1. Central:

- Ethyl alcohol depresses the central nervous system in descending order, from cortex to medulla, depending on the ingested amount.
- The effect of alcohol is potentiated by concomitant ingestion of depressant drugs as barbiturates.

2. Peripheral:

- Vasodilatation ➔ false sensation of heat (heat regulating center is inhibited, so temperature is low).
- Ethanol metabolism ➔significant decrease in NAD/NADH ratio in the liver results in:
    - Reduction in the metabolism of glycerol, resulting in accumulation of fat in the liver ➔fatty liver.
    - Accumulation of lactic acid & ketoacids ➔metabolic acidosis.
    - Inhibition of gluconeogenesis ➔Hypoglycemia.

Clinical Picture:

(According to blood alcohol concentration)

1. **Mild intoxication:** (stage of excitation)**:** Up to 150 mg %:
   - Alcoholic euphoria (CNS depression).
   - Abnormal behavior and sexual crimes (Depression of the mental brake).
2. **Moderate intoxication: (**stage of incoordination**):**150 – 300 mg %:
   - Staggering gait *(drunkard gait)*, slurred speech with tremors of the hands and lips (Muscle incoordination).
   -Vomiting (local gastric irritation and irritation of CTZ. by acetaldehyde).
   -Hiccough (myoclonic contractions of the diaphragm).
   -Blurring of the vision, diplopia and nystagmus.
   -Flushing (Cutaneous VD.).
3. **Severe intoxication:** (Alcoholic coma): more than 300 mg %:
   -Vital signs: weak and rapid pulse, low B.P., subnormal temperature, slow and shallow respiration with alcoholic smell & pale moist skin.
   -Inhibited reflexes.
   -Convulsion due to brain edema.
   -McEwen's sign pupils (changeable pupils): contracted but dilate on pinching the skin of face or neck.
4. **Fatal intoxication:** more than 500 mg%:
   Death occurs due to R.C. inhibition → central asphyxia.

Investigations:

1. **Routine laboratory investigation.**
2. **Toxicological screening:**

   i. ***Rapid tests :***

   - Finger to nose test.
   - Heel to shin of tibia.
   - Arrange eight matches in square.
   - Walking along a straight line.
   - Buttoning and unbuttoning.

   ii. ***Chemical analysis:***

   - **Blood:** maximum blood level occurs within 1- 1 ½ hours.
   - **Urine:** maximum urine level occurs 20 minutes after that of blood.
   - **Expired air:** is estimated by breath analyzer or drunk meter.

N.B. A blood ethanol concentration higher than **150 mg %** is considered a **legal evidence of drunkenness**.

Treatment:

1. **Supportive measures: ABC**
2. **GIT Decontamination:**
   Gastric lavage with NaHCO3 then leave strong coffee or tea in the stomach.
3. **Elimination of the absorbed poison:**
   - Forced alkaline diuresis using NaHCO3.
   - Hemodialysis is very effective (ethanol has small volume of distribution & low molecular weight). It is indicated if:
     - Blood alcohol level >350 mg%.
     - Acid-base and/or electrolyte disturbance.
4. **Antidotes:**

No specific antidote.

5. **Symptomatic:**
   - Metabolic acidosis: NaHCo3.
   - Hypoglycemia: 10-50% dextrose solution IV.
   - Hypothermia: warming the patient.
   - Shock: fluid expansion and inotropic agent.

Methyl Alcohol (Methanol)

(Wood Alcohol)

Source:

From distillation of wood.

Uses:

- Antifreeze solvent, fuel, paints remover and household cleaners.
- It is used to adulterate ethyl alcohol (cheap).

Conditions of Poisoning:

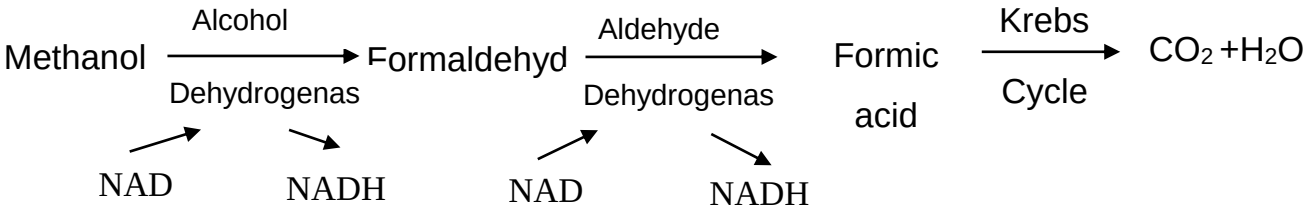
- **Accidental:**
  - Ingestions of adulterated beverages.
  - Less commonly by inhalation of fumes, or through percutaneous absorption.

Pharmacokinetics:

Absorption: inhalation, ingestion and skin contact.

Distribution: to all of the body but mainly distributed to optic nerve.

Metabolism: (90% in liver) slower than that of ethanol



N.B. Formaldehyde & Formic acid are more toxic metabolites than methanol itself.

Excretion:

Through kidneys and lungs.

Fatal dose:

- 60 – 100 mL of pure methanol. 15 mL produce blindness.

Fatal period:

- Few hours.

Mechanism of Action:

- CNS depression (more than Ethanol).
- G.I.T. irritation.
- Metabolic acidosis due to:
  1- Accumulation of formic acid.
  2- Accumulation lactic acid, which is generated by lowering of hepatic NAD/NADH ratios.
- Ocular toxicity as formic acid inhibits cytochrome oxidase enzyme in the optic nerve resulting in cellular ischemia, optic degeneration and optic atrophy.

Clinical Picture:

1. GIT: nausea, vomiting, colic, and back pain (pancreatitis).
2. CNS depression: convulsions then coma, with weak rapid pulse, low blood pressure, subnormal temperature and slow shallow respiration.
3. Eyes: pain in the eyes, photophobia, blurring of vision and dilated fixed pupils.
4. Metabolic acidosis: tachypnea (air hunger) and confusion.

Cause of death:

Central asphyxia

Investigations:

1- Routine laboratory investigation.
2- Toxicological screening.
3- Fundus Examination: Initial and serial examinations are essential to assess optic nerve affection.

Treatment:

1. **Supportive measures: ABC**
2. **GIT Decontamination:**
   Gastric lavage with NaHCO3 then leave strong coffee or tea in the stomach.
3. **Elimination of the absorbed poison:**
   - Forced alkaline diuresis.
   - Hemodialysis is indicated if:
     - Methanol blood level >50 mg/dl.
     - Visual symptoms.
     - Severe metabolic acidosis.
     - Renal failure.
     - Failure of treatment
4. **Antidotes:**
   a) **Ethanol:**
   Competes with methanol for alcohol dehydrogenase enzyme. Therefore, it reduces the metabolism of methanol to its toxic metabolites.
   b) **4-methyl pyrazole (fomepizole):**
     - Inhabits alcohol dehydrogenase enzyme.
     - Advantage: It does not cause CNS depression like ethanol.
   c) **Folinic acid (leucovorin calcium):**
   Converts formic acid to $Co_2 + H_2O$.
5. **Symptomatic:**
   - Metabolic acidosis: NaHCo3
   - Hypoglycemia: 10-50% dextrose solution IV.
   - Hypothermia: warming the patient.
   - Shock: fluid expansion and dobutamine.
   - Care of eyes.

Hydrocarbons

Hydrocarbons are the simplest organic compounds contain only carbon and hydrogen.

Source:

Petroleum distillation.

Uses:

Hydrocarbons are one of the most important energy resources.

Main types of hydrocarbons:

1- **Aliphatic:** gasoline, naphtha, kerosene and turpentine.
2- **Aromatic:** benzene, toluene and xylene.
3- **Halogenated:** methylene chloride, carbon tetrachloride trichloroethylene and tetrachloroethylene.

Kerosene Poisoning

Source:

It is a petroleum product.

Uses:

It is used as fuel, solvent, paint remover and lubricant.

Condition of poisoning:

- **Accidental:** in children.
- **Suicidal:** in young females.

Fatal dose:

- 20 ml.

Fatal period:

- 24 hours (central asphyxia).
- Few days (pneumonia).

Mechanism of Action:

1. Local:

- Skin irritation.
- Mucus membranes irritation.

2. Remote:

CNS depression due to:

-Direct effect (large amount).

-Hypoxia due to chemical pneumonitis.

-Acidosis.

Clinical picture:

1. Acute:

(Ingestion or inhalation)

- G.I.T irritation: nausea, vomiting, colic and diarrhea.

- C.N.S. depression: coma with cyanosis ➔ death in 24 hours.

- Lung: aspiration pneumonitis due to its aspiration during vomiting or ingestion.

2. Chronic:

(Inhalation)

Anemia, weight loss, weakness, numbness and paresthesia.

Treatment:

1) Supportive measures: ABC

2) GIT Decontamination:

- **Emesis** is contraindicated (aspiration pneumonitis).
- **Gastric lavage** (with cuffed endotracheal tube) is indicated in:
    1. Ingestion of large amounts.
    2. Other toxic additives.

3) Decontamination:

1. Remove contaminated clothes.
2. Wash skin with soap and water.
3. Irrigate exposed eyes with copious water.

4) Symptomatic: (aspiration pneumonitis)

1. Antipyretics for fever.
2. Antibiotics for bronchopneumonia.
3. Bronchodilators for bronchospasm.
4. Corticosteroids for preventing pneumonitis, but some authors claimed to be ineffective.

FOOD AND ANIMAL POISONING

Definition:

It refers to the onset of **similar** symptoms and signs in **one person** or a **group of people** sharing **the same food**

Types of food poisoning:

- Chemical food poisoning:
  Food contaminated with chemicals as metals & insecticides.
- Microbial food poisoning
  - Bacterial:
    - Organisms (Salmonella, Shigella, Streptococci).
    - Exotoxins (Botulism, Cholera).
  - Viral: retrovirus.
  - Protozoal: ameba and giardia lamblia.
- Toxic food stuff
  - Poisonous mushrooms.
  - Poisonous berries.
  - Poisonous fishes.

Botulism

Causative agent:

- Exotoxin that is produced by Clostridium Botulinum.
- It has many antigenic types as A, B and E.
- It is the most powerful & lethal toxin known 0.5 µg is lethal.
- The toxin is **heat labile** (destroyed by boiling at 100°C for 1 minute).

Source:

- Improperly processed canned food.

Incubation period:

- 12-72 hours.

Mechanism of action:

- Binds to presynaptic receptors→ **block acetylcholine** release→ progressive descending bulbar and skeletal paralysis.

Clinical picture: (Mainly paralysis)

1. **Initial GIT symptoms:** (-ve in 1/3 of patients)
   Nausea, vomiting, abdominal distension, pain, and diarrhea,
2. **Occular**: blurred vision, diplopia, photophobia & dilated fixed pupil.
3. **Bulbar**: dysphonia, dysarthria & dysphagia.
4. **Skeletal:** bilateral limb paralysis as well as respiratory muscles.

Treatment:

I. Prophylactic:

Proper preservation of canned food (by acidifying it to a pH < 4.5).

II. Curative:

1- Supportive measures: ABC.

2- GIT decontamination:

- Gastric Lavage with cuffed endotracheal intubation.
- Activated charcoal.

3- Antitoxin:

- Trivalent (A, B & E) 1 vial IV repeated after 4 hrs. then 1 vial/day according to C/P.
- Should be given to all patients (symptomatic as well as asymptomatic).
- Should be given as early as possible as (≤ 2 days after onset of symptoms).

Animal Envenomation

Types:

- Snake bites and scorpion stings.
- Jellyfish sting → local allergic reaction, rarely systemic.
- Spider bites → some spiders contain neurotoxin (black widow) and are dangerous.

1-Snake Bites

- **98%** of snakes are non-poisonous.
- Common venomous snakes in Egypt:
  - **Cobra:** found mainly in Nile valley.
  - **Viper**: found mainly in desert.
- Snake venom contains **Cytotoxins, Neurotoxins, Coagulants, Hemorrhagins, Hemolytics, Myotoxins,** and **Nephrotoxins.**

Action & Clinical picture:

I. Local:

1. **Cytotoxins: (mainly in Viber)** break down of tissue →swelling, pain & bruising at the site of bite.
2. Two punctured wound.

II. Systemic:

1. **Neurotoxins: (mainly in cobra)** competitive antagonist of acetylcholine (ACh) at neuromuscular junction→ produce neuromuscular paralysis →Ptosis, ophthalmoplegia, facial muscle paralysis, inability to swallow and finally paralysis of respiratory muscles and death.

2. **Cardiotoxins**: **(mainly in cobra)** cardiac systolic arrest.
3. **Coagulants:** inhibit normal clotting cascade and platelet aggregation→ bleeding from nose or gums, bite site and in urine and stools.
4. **Hemorrhagins:** affect mainly lungs → hemorrhagic edema of lung.
5. **Myotoxins**: rhabdomyolysis → myoglobinuria and hyperkalemia.
6. **Nephrotoxins:** renal failure.
7. **Hemolytics**: hemolysis of red blood cells.

Causes of death:

1. Asphyxia (mainly in cobra).
2. Cardiac arrest (mainly in cobra).
3. Renal failure.
4. Neurogenic shock (sudden fear)
5. Tetanus (secondary infection).

Investigations:

1. Routine lab investigations.
2. Coagulation studies.
3. Urine analysis: myoglobinuria and hemoglobinurea.
4. Toxin detection: enzyme-linked immunosorbent assay.
5. Chest X-Ray: pulmonary edema.
6. ECG.

Treatment:

I. Before arrival to the hospital:

1. Reassurance.
2. Immobilization of the limb.
3. Application of a tourniquet is no longer recommended.
4. Suction of venom is no longer recommended.

II. After arrival to the hospital:

1. Supportive measures: ABC
2. Tetanus toxoid, antibiotics, analgesics.
3. **Specific anti-snake venom (antivenins):**
   - Administered within 4-5hrs, useful till 24 hrs.
   - Neutralize the venom, but do not reverse local injury.
   - May cause severe allergic reaction, so hypersensitivity intra-dermal test should be done first.
   - Prior to administration: Diphenhydramine or epinephrine should be given (to avoid allergic reaction).
   - **Dose:** loading dose of 4-6 vials diluted in 250ml saline and infused slowly at 20-50 ml/h for the 1st 10min. If no adverse reactions, the remainder is infused over the next hour.

2- Scorpion Stings

Mechanism of action:

Scorpion venom act on sodium and potassium channels→ sodium channel remains open→action potential turned into an abnormally long signal →massive release of neurotransmitters on skeletal and other muscles → hyperexcitability, convulsions, paralysis and death.

Clinical picture:

I. Local:

1. One punctured wound.
2. Local pain that becomes generalized.
3. No swelling, ecchymosis, or erythema.

II. Systemic:

1. Central nervous system

- Agitation, tremors, fasciculations, and cranial nerve dysfunction in severe cases.
- Coma and convulsions.
- Malignant hyperthermia.
- Hypertensive encephalopathy.

2. Cardio-vascular system

- Tachycardia and hypertension.
- Shock and cardiac arrest.

3. Respiratory system

- Tachypnea, stridor & respiratory distress.
- Acute pulmonary edema: cardiogenic or non-cardiogenic.

4. Gastro-intestinal system

- Vomiting and diarrhea.
- Acute gastric erosions, hematemesis and melena.

5. Metabolic

- Acidosis, hyperkalemia, and hyperglycemia.

Treatment:

I. Before arrival to the hospital:

Similar to snake bite.

II. After arrival to the hospital:

1- Supportive measures: ABC.

2- Specific anti-scorpion antivenin:

- Can reverse neurologic symptoms within minutes to hours.
- Given after intradermal sensitivity test.
- Dose is 1 ampoule (2ml) IM.

3- Symptomatic treatment:

- Pain: non-SAID (avoid narcotics → respiratory arrest).
- Stridor and non-cardiogenic pulmonary edema: Corticosteroids.
- Acidosis: NaHCO3.
- Convulsion: diazepam.
- Shock: I.V. fluid & inotropic agents.

HEAVY METALS

General characters:

1- Toxicity by metals can occur by any route.

2- All have double actions:

a) Local direct irritant action on mucous membranes:

GIT irritation → Nausea, vomiting and diarrhea, **except Lead** → constipation.

b) Systemic action:

- Metals generate free radicals, which may result in membrane and organelle degradation.
- They are also combine with normally occurring molecules, such as proteins (SH- group on protein), and inhibit or alter their activity.

3- Selective organ toxicity:

Lead	→	Blood, Brain, Peripheral nerves & kidneys.
Mercury	→	Kidney
Arsenic	→	Liver, Heart, kidney & Skin.
Iron	→	Liver.
Cadmium	→	Kidney and Lung.
Phosphorus	→	Liver.
Antimony	→	Heart.

4- All have metallic taste except arsenic.

5- Gastric lavage can be done safely in acute poisoning.

6- Their antidotes are called Chelators (react with metals → chelates) which is not toxic and H2O soluble → renal excretion. e.g. EDTA, BAL, Penicillamine DMSA & Deferrioxamine.

7- There is a general antidote (Sodium Thiosulphate) used to help excretion.

8- Vitamin E & C: has protective effect probably due to their ability to support the detoxification and scavenge free radicals (antioxidant action).

9- They can be detected by Reinsch test and atomic absorption spectrometer.

Lead Poisoning (Plumbism)

[Plumbum] Pb

Route of exposure:

1) Oral:

- Children: ***Pica*** (i.e. craving to non-nutritional substances e.g. paint, pencils & licking of toys).
- Water: supplied via leaded pipes.
- Ceramic food containers (Pb containing glazers).

2) Inhalation:

- Pb fumes → Battery, Insecticide, Missiles industries, Plumbers & painters.
- Leaded gasoline (Tetra-Ethyl Lead (TEL) used as antiknock agent).

3) Dermal:

- Organic lead compounds (Petroleum additive).
- Cosmetics.

4) Intravenous:

- I.V. Methamphetamine users (common method of illegal methamphetamine production uses lead acetate as a reagent).

Conditions of poisoning:

- **Accidental (mainly):**
  - Ingestion of ***lead acetate*** (for bruises treatment).
  - The use of ***lead oleate*** in criminal abortion.
  - During ***deleading*** (treatment of chronic lead toxicity) with sudden release of lead to the blood.
  - Occupational and environmental exposures in chronic poisoning
- **Suicidal and homicidal**
  - Intake of insecticides (rare).

Pharmacokinetics:

1. Absorption:

- Children absorb more Pb than adults (Children absorb 40% to 50% of ingested lead; adults absorb10% to 15%).
- Organic lead → skin & CNS
- Ca, Fe & Zn → ↓ Pb absorption so, their deficiencies → ↑absorption & storage.
- Vitamin D → ↑ Pb deposition in bone.
- Parathyroid hormone → ↑Pb release from bone.

2. **Distribution:**
   - Blood → Parynchymatous organs (lung, kidneys, liver & spleen).
   - Deposited in teeth, bones near joints & hair as insoluble tertiary lead phosphate.
   - Bones are comprising 90% of the total body lead burden.
3. **Excretion:**
   - Kidney accounts for 75% of the daily Pb. Loss.
   - Bile, exfoliated epithelium & sweat.
   - ½ life = 30 years in bone & 7years in kidney.

Mechanism of action:

- Combine with SH- group of proteins. The primary organs of attack are the brain, peripheral nervous system, blood and kidneys.
- Combine with SH- group on enzymes →
  - -↓↓ Several enzymes in heme synthesis pathway → anemia.
  - -↓↓ Pyrimidine -5- nucleotidase (responsible for breakdown of RNA) → clumping of ribosomal RNA *(**basophilic stippling**).*

Clinical presentation:

1. **GIT:**
   - Oral → **blue line at gingival margin** (H2S from decay of food in carious tooth → PbS).
   - Intestine → **Colic** (paroxysmal, relieved by pressure).
     Constipation with dark stool (PbS).
   - In acute poisoning: metallic taste, nausea & vomiting may occur.
2. **Blood & vascular system:**
   - Microcytic **hypochromic anemia** due to:
     1-↑ Fragility of RBCs → interferes with Na-K pump & attaches to membrane → fragility.
     2-↓ Heme synthesis.
     3- Defect in erythropoietin function secondary to associated renal damage.
   - Circum **oral pallor** → V.C.
   - Punctate **basophilia** (stippling) due to inhibition of pyrimidine-5-nucleotidase.
   - Reticulocytosis (early release of immature RBCs).
3. **Nervous:**
   - Lead **palsy**: Wrist & foot drop (demyelination and axonal degeneration → inhibition of muscle contractions of the **extensor** group).
   - Encephalopathy (stupor, ataxia, coma & convulsion, which is more in children).
   - **Cognitive deficits** and IQ decline.

4. **Renal:**
   - **Fanconi like syndrome** → aminoaciduria, phosphaturia and glucosuria.
5. **Other organs:**
   - Myocarditis.
   - Abortion (Ecbolic action).
   - Bone aches & arthritic pain
   - Sterility & impotence in males.
   - Reduced thyroid.

Investigations:

1- **Blood lead level** (BLL) the most reliable indicator:
   BLL > **55 μg/dl** → toxicity.
   BLL > **70 μg /dl** → constitutes a medical emergency.
2- **Renal function tests.**
3- **Blood Picture:** hypochromic microcytic anemia, reticulocytosis and basophilic stippling.
4- **Urine analysis**: ↑aminolevulinic (ALA) acid owing to lead inhibition of gamma aminolevulinic acid dehydratase enzyme (enzymes involved in heme synthesis).
5- **X-ray on long bones:**
   - Lead lines at the distal ends of growing bones.
   - The width and density increase with duration of exposure.
   - Multiple lead lines → repeated episodes of toxicity.
   - Most commonly seen between 2-5 yrs. (bone is growing rapidly).

Treatment:

Treatment is based on BLL, age of the patient, and severity of symptoms.

I- Prophylactic:
- Periodic medical examinations of the exposed workers.
- Proper exhaust ventilation, dust filters, protective clothing, masks, gloves & boots.
- Intake of proper amounts of Ca, Zn & Fe.

II- Curative:

a. **Asymptomatic patient**: Prevent further exposure & no treatment is needed.
b. **Symptomatic patient**:
   1. **Prevent further exposure.**
   2. **GIT Decontamination:**
      Gastric lavage using MgSo4 (in acute poisoning)
   3. **Chelating agents:**
      - **DMSA** is the Chelators of choice unless the patient presents with protracted vomiting and severe toxicity.
      - **Calcium disodium EDTA ($CaNa_2$ – EDTA).**
      - **Dimercaprol (BAL).**
      - **D-Penicillamine.**
      - **Patients with encephalopathy** are treated with BAL plus Ca Na_2 EDTA started 4 hrs. after the BAL for 3–5 days.

4. **Gradual mobilization of lead from bones (deleading):**
   Decreasing alkalinity of blood with ammonium chloride together with starting EDTA then followed by oral Penicillamine.
5. **Symptomatic treatment.**
   - $MgSO_4$ → constipation.
   - Fe → anemia.
   - Diazepam → convulsion.
   - Splint & massage → wrist drop.
   - Care of the kidneys.

Mercury Poisoning

[Hydrargyrum]."Hg"

Sources:

1. **Elemental (metallic) mercury:**
   - Hg vapor, dental amalgam and Hg of thermometers.
   - Toxicity occurs after inhalation only.
   - If swallowed it is poorly absorbed from GIT.
2. **Inorganic salts → corrosive:**
   - **Mercurous chloride** (Calomel):
     - Used as purgatives, teething lotions and diaper powders.
     - Insoluble → not absorbed from GIT.
     - repeated topical absorption in children → chronic mercury poisoning→ **pink disease *(Acrodynia)*** which is manifested by:
       Insomnia, hypertension, peeling of skin, alopecia, pink & painful hands & feet. Acute renal failure within 24 hrs.
   - **Mercuric chloride** (absorbed from GIT) → disinfectant.
3. **Organic salts → diuretics & fungicidal:**
   Methyl mercury and ethyl mercury are environmental contaminants that have been incorporated and concentrated in the aquatic food chain.

Condition of poisoning:

- **Accidental [most common]:**
  - Ingestion **Mercuric Chloride** as a result of eating contaminated fish and food polluted with industrial wastes.
  - Inhalation of mercury vapor is the principle route of uptake in industry.
- **Suicidal & homicidal [Rare].**

Mechanism of action:

1- Mercury reacts with sulfhydryl (SH) group resulting in depression of the cellular enzymatic mechanisms.
2- Elemental mercury vapor and organic mercurial compound are particularly toxic to the CNS.
3- Inorganic mercuric salts are corrosive and nephrotoxic.

Clinical presentation:

1- GIT:

- Oral:
  - Salivation **(**early sign).
  - Grey line on the gum.
  - Gingivitis (swollen, painful, bleeding gingiva) loose teeth.
  - Gangrene (Cancrum Oris).
- Intestinal
  - Mercurial dysentery (diarrhea, mucus & blood)
- Metallic taste, burning sensation, nausea & blood tinged vomiting (**corrosive action**) & dehydration may occur in acute poisoning.

2- Renal:

- Albuminuria and hematuria with casts in urine.
- Oliguria & **renal failure**.

3- Nervous:

- **Kinetic tremors** (cerebellar affection).

4- Psychic:

- **Hg erethism**: shyness, loss of confidence, vague fears, and depression (neurosis).

5- Skin:

- **Dermatitis.**

6- Eye:

- **Mercurialentis** (discoloration of anterior capsule of eye lens).

7- Respiratory

- Respiratory failure (Inhalation of elemental mercury vapors).

Treatment:

I. Prophylactic treatment:

a. Periodic medical examinations of the exposed workers.
b. Proper exhaust ventilation, dust filters, protective clothing, masks, gloves & boots.

II. Curative treatment:

1- **Prevent further exposure.**

2- **GIT Decontamination:**

- **Gastric lavage:** (in acute poisoning) using one of the local antidotes:
  - Egg white and skimmed milk → precipitation of Hg albuminate.
  - Sodium formaldehyde sulphoxylate → reducing agent ($HgCl_2$ → HgCl insoluble).
- Upper GIT endoscopy should be considered before lavage due to its corrosive action.

3- **Physiological antidotes (chelation therapy):**

- D-Penicillamine.
- BAL and its oral analogues DMSA.

4- **Symptomatic**

- Mouth hygiene.
- Tranquilizers.
- Atropine → salivation.
- Na hyposulphite for dermatitis.
- Care of kidneys & I.V. fluids for dehydration.
- Selenium: It is competitive inhibitor of mercury absorption, also increases metal excretion.

Arsenic Poisoning

(As)

Sources:

- It is commonly used as pesticides, rodenticides, herbicides, wood preservatives, and manufacturing of glass.
- **Arsine gas (AsH_3)** is a byproduct of ore smelting and has been used in the semiconductor industry.
- **Arsenic** occurs in both inorganic and organic forms. Inorganic arsenic occurs as pentavalent (As_5 or **arsenate)** and trivalent (As_3 or **arsenite**). In general, the higher valence compounds are less toxic.

Conditions of Poisoning:

- **Homicidal:**

Commonly used in the past, because it was:

a) Easily obtained.
b) Has no characteristic smell or taste →Easily mixed with flower; milk, rice, or eggs and cakes.
c) It produces signs and symptoms very similar to gastroenteritis after a latent period (1-4 hours) sufficient to change the place of intake.

- **Accidental:**
  a) *Household:* drinking of contaminated water or eating of contaminated fish or seafood (mainly from occupational waste products).
  b) *Occupational:* Accidental liberation of arsine gas in workers dealing with paints, wallpaper, insecticides and wood preservatives.
- **Suicidal:**
  Rare, as it causes very painful death.

Mechanism of Action:

As is a general protoplasmic poison. It combines to SH-containing enzymes essential for tissue oxidation-reduction processes→ uncoupling of oxidative phosphorylation → Energy block.

Clinical presentation:

1- GIT disorder:
- Nausea, vomiting, colic and diarrhea with **rice-water stools** (due to toxic capillaritis) (D.D. cholera). Dehydration may occur.

2- Skin lesions:
- Melanosis (increased pigmentation).
- Hyperkeratosis (thickening of palms and soles).
- Alopecia (fall of hairs).
- Warts that may turn malignant.

3- Mucous membrane:
- Coryza-like manifestations: Cough lacrimation, addiction and chronic chromium poisoning.

4- Peripheral neuritis:
- Mixed (motor and sensory) but more sensory [D.D. alcohol (mixed more motor), lead (purely motor)].

5- Parenchymatous degeneration:
- Fatty liver and Jaundice, heart failure or renal failure.

6- Aplastic anemia:
- With occasional basophilic stippling.

7- Arsine gas:
- Inhalation of arsine gas results in appearance of symptoms after **latent period** of 2-24 hrs.
- **Manifestations** include; severe abdominal pain, nausea, vomiting, shortness of breath and hemolysis of RBCs → ***Hemolytic anemia***, hemoglobinurea and ***renal failure***.
- **Treatment**: hemodialysis and exchange transfusion.

Treatment:

I. Prophylactic treatment:

(As in mercury)

II. Curative treatment:

1. ***Gastric lavage: (in acute poisoning)***
   - Using freshly prepared ***ferric hydroxide ($FeOH_3$)*** which precipitate arsenic as ferric arsenite and then leave olive oil or milk as demulcent.
2. ***Chelating agents:***
   - BAL.
   - Penicillamine-BAL combined therapy.
   - DMSA
3. ***Symptomatic:***
   - I.V. fluid for dehydration.
   - Morphine for colicky pain and diarrhea.
   - Glucose and vitamins to support the liver.
   - Artificial kidney (hemodialysis) or peritoneal dialyses.

Cadmium Poisoning

Sources of exposure:

- **Industrial:** electroplating, photography, silver (Ag) alloy, fireworks, paints, plastics such as polyvinyl chloride, fungicides and fertilizers.
- **Environmental:** Zink (Zn) & lead (Pb) smelting, cigarette smoking and coal.

Condition of Poisoning:

Accidental: occupational exposure.

Mechanism of Action:

- Binds with SH-containing enzymes especially alpha-1 anti-trypsin whose deficiency is claimed to induce emphysema & pulmonary symptoms.
- Competes with cellular uptake of Cu & Zn.
- Cadmium stored in **liver & kidney** due to high level of Metallothionein (low molecular weight protein rich in sulfhydryl group), forming cadmium Metallothionein complex (CdMT) which have paradoxical effect as it protects liver from toxicity but enhances nephrotoxicity.

Clinical presentation:

Cadmium is more toxic if inhaled than if swallowed owing to its poor absorption from GIT.

1- Acute poisoning:

a) Ingestion: abdominal pain, nausea, vomiting & diarrhea. These symptoms are usually self-limited with no long-term consequences. However, fatal outcome have been described.

b) Inhalation: Sore throat, cough, dyspnea, followed by fever, rigors and chest pain. Death occurs due to pulmonary edema and respiratory failure. Bilateral cortical kidney necrosis has been described as well.

2- Chronic poisoning:

Kidneys & lungs are the main targets.

a) Kidney:

- Tubular necrosis (Fanconi syndrome) → increase protein, glucose & amino acids in urine.
- Renal failure & hypertension.
- Osteomalacia occurred due to decreased phosphate reabsorption.

b) Lung:

- Chronic obstructive airway disease and increased risk of developing lung cancer.

c) Others:

- Carcinogenicity, decrease growth, yellow coloration of teeth & testicular damage.

Treatment:

I. Prophylactic treatment: (as in mercury)

II. Curative treatment:

1- GIT decontamination (acute cases):

Gastric lavage followed by demulcent.

2- Chelation:

- EDTA
- DMSA
- BAL should ***not*** be used, as the combination of BAL and cadmium is nephrotoxic.

3- Hemodialysis: for renal failure.

Acute Iron Poisoning

Iron is essential for synthesis of hemoglobin, myoglobin, cytochromes and other enzymes. It is widely used for treatment of anemia and as a common daily vitamin supplement.

Conditions of Poisoning:

Accidental (mainly), especially in children due to:-

- Iron preparations are attractive and similar to candies.
- They are available at home.

F.D. → 200 mg/ Kg elemental iron.

Mechanism of action:

I. Local:

GIT → Corrosive effect on mucosal tissue and may cause hemorrhagic necrosis and perforation.

II. Remote:

Iron causes oxidative stress and inhibits several key metabolic enzymes. Reactive oxygen species (ROS) oxidize membrane-bound lipids and cause loss of cellular integrity and tissue injury.

- **Liver:**

  Free iron accumulates first in the Kuppfer cells then hepatocytes localizing in mitochondria producing periportal necrosis.

- **Cardiovascular system:**
  - Iron produces hypotension and shock (iron or ferritin causing massive post arteriolar dilatation leading to venous pooling).
  - Iron has direct myocardial depressant effect.
- **Metabolism:**

Iron produces metabolic acidosis due to:

- Conversion of ferrous iron to ferric iron with subsequent release of hydrogen ions (major role).
- Disruption of mitochondrial function forcing anaerobic respiration (lactic acids & other organic acids).

Clinical presentation:

- **Stage I:** 1- 6 hrs. post ingestion (local corrosive effect on GIT).
  - Abdominal pain.
  - Nausea, vomiting, hematemesis and melena
  - Shock and dehydration from fluid loss.
- **Stage II:** 6- 24 hrs. post ingestion (latent or quiescent stage)
  - Apparent recovery of the patient
  - It is due to redistribution of free iron from blood to (RES).

- **Stage III:** 24-48 hrs. post ingestion.
  - Metabolic acidosis.
  - Fever and leukocytosis.
  - Lethargy and coma.
  - Mortality is highly recorded during this stage.
- **Stage IV:** 2- 3 days post ingestion (Hepatic manifestations).
  - Elevated liver enzymes and bilirubin levels.
  - Defective coagulation.
  - Hypoglycemia may occur.
- **Stage V:** 4-6 weeks after ingestion
  - Gastro-intestinal scarring with or without obstruction (pylorostenosis, gastric fibrosis or small bowel strictures).

Investigations:

1- Serum iron levels:

The most suitable time for assessing serum iron is 4-6 hrs. post-ingestion due to delayed absorption:

- Mild toxicity: 300 µg/dL
- Serious toxicity: 500 µg/dL
- Fatal toxicity: 1000 µg/dL

2- Liver function tests.

3- Deferoxamine challenge test

- (Change urine color after single IM Deferrioxamine dose indicates presence of iron in urine, which is chelated by Deferrioxamine).

4- Abdominal x-ray

- (Radiopaque iron tablets could be detected).

Treatment:

1- Supportive: ABC

2- GIT Decontamination:-

- Gastric lavage using the **local antidote (**$NaHCO_3$) to convert free ferrous salt → ferrous carbonate, which is poorly absorbable.
- Whole bowel irrigation.

3- Physiological antidote:

- Deferrioxamine (see general toxicology).

4- Symptomatic:

- Care of liver.
- I.V. $NaHCO_3$→Metabolic acidosis.
- Care of kidneys.
- H2 antagonists or antacids → GIT irritation.
- I.V. fluids → hypovolemia.

Chronic Iron Toxicity (Haemosiderosis)

Haemosiderosis is a state of deposition of excess iron within tissues that results in cellular damage & dysfunction by free radical formation [oxidative stress].

Causes:

1- **Multiple blood transfusions** [e.g. Thalassemia].
2- **Genetic iron overload** [defects in iron transport from intracellular stores into plasma due to deficiency in Ceruloplasmin].
3- **Liver diseases as** in Alcoholism or chronic hepatitis [infection increase iron storage].
4- **Increased Iron in take** [medicinal tablets].

Clinical presentation:

1- Heart :

- Cardiomyopathy [direct effect of free iron on myocytes].
- Arrhythmia

2- Liver failure:

[It is the body's major site of Fe storage].

3- Endocrine system :

- Pancreatic dysfunction leads to D.M.
- Pituitary dysfunction leads to delayed sexual maturation & infertility.
- Parathyroid dysfunction leads to hypocalcemia & skeletomuscular complication.

4- Skeletomuscular system:

Osteoporosis & muscle cramps.

5- Immune system:

Frequent infections due (to ↑ transferrin).

6- Skin:

↑ Melanin production [Bronze pigmentation] [almond – colored hue].

Investigations:

1- Invasive tests:
- Liver and cardiac biopsies.

2- Lab tests:
- Serum iron

Treatment:

- Prevent further exposure.
- Oral irons Chelators include ***Deferiprone and Deferasirox***. They have better distribution than Deferrioxamine, but more side effects

Lifestyle management for reducing metal toxicity Risk

I. Reduce General Exposure:

- Establish worker and workplace health surveillance guidelines.
- Understand the sources of metal exposure and reduce contact with them.
- Avoid mercury amalgam dental fillings to reduce mercury exposure.

II. Maintain Nutrient Sufficiency:

- Adequate intake of essential trace minerals may reduce toxic metal uptake.
- Choose fish oil supplements over high-mercury fish by checking the label to ensure your fish oil supplement achieves the rigorous IFOS 5-star rating.
- Folic acid is a cofactor in sulfur-containing amino acid which is precursor to heavy metal chelator (glutathione).
- **N-Acetyl Cysteine:** provides a source of sulfur for glutathione production and is effective at reducing oxidative stress due to heavy metal toxicity.

Plant poisons

"Alkaloids"

Some plants contain active toxic substances which behave like alkalies, as they unite with acids to form salts (e.g. atropine sulfate). Hence, they are known as alkaloids. They have ***remote action only.***

1. **Atropine, Hyoscyamine and Hyoscine**
2. **Opium [Morphine]**
3. **Digitalis**
4. **Cocaine**
5. **Cannabis**
6. **Nutmeg**
7. **Khat**

Cannabis

Source:

- Cannabis sativa plant.
- Cannabis indica plant.

It is present as:

1. **Hashish:** dried resin from the flowering tops.
2. **Bango:** from dried leaves.
3. **Marijuana:** Mixed [Flower and leaves].

Active principle:

Δ^9Tetra-hydrocannabinol [delta -9-Tetra hydro cannabinol] (THC).

Medical uses:

Marinol or dronabinol tablets used as stomachic or antiemetic in cancer patients.

Routes of intake:

1. Smoked with tobacco in pipe, goza and cigarettes.
2. Eaten mixed with sweets, nut-meg, datura seeds and spices (Manzool).
3. Drunk with coffee or tea.

Condition of poisoning:

Accidental: overdose.

Mechanism of action:

1- It acts on two specific cannabinoid receptors:

CB1: distributed mainly in CNS →regulation of cognition, memory, motor activities, analgesia, nausea and vomiting.

CB2: distributed mainly in immune system → affect immune system.

2- No physical dependence occurs with repeated use, only habituation and craving.

Clinical presentation:-

I) Mental:

1. Euphoria, later replaced by dysphoria.
2. Hallucinations (visual, auditory and sexual).
3. Accentuation of special senses → increased perception of music, colors and patterns.
4. Disorientation of:
   -Time→ false prolongation of sexual intercourse.
   -Distance→ car accidents.
   -Body image → depersonalization.

II) Physical :-

1. **Eyes:** Dilated pupil & conjunctival congestion.
2. **CVS:** Tachycardia & orthostatic hypotension.
3. **Respiration:** Depression of R.C.
4. **GIT:** Increase appetite to sugars & dry mouth.
5. **Bladder:** urinary frequency.

Cause of death:

- Central asphyxia
- Car accidents.

Chronic toxicity leads to:-

1. Habituation: not addiction.
2. Amotivational syndrome (Lack of interest in school, work and life).
3. Sterility :
   - ↓ Testosterone.
   - ↓ Sperm count and
   - ↓ Ovulation.

4. Long-term use produces lethargy, apathy, and passiveness.

Investigation:

1. Routine laboratory investigations.
2. Toxicological screening for THC.

Treatment:

1. Mainly symptomatic and supportive.
2. Psychiatric counseling.

Nutmeg

- Nutmeg has been used as an abortifacient and abused as a hallucinogen.
- Its main active ingredient is **myristicin.**
- Toxicity manifests after ingestion of 1–3 whole nuts or 1–2 tablespoons of freshly ground nutmeg.

Action:

CNS toxicity (increased serotonin in the brain).

Clinical picture:

- Nutmeg toxicity may mimic **anticholinergic toxicity**, with flushing, dryness, tachycardia, hypertension, agitation, and altered mental status.
- One feature that may help differentiate anticholinergic toxicity from nutmeg ingestion is that the pupils are constricted.

Khat

- Its fresh leaves and tops are chewed.
- Khat contains an alkaloid called cathinone (amphetamine-like stimulant).

DRUG DEPENDENCE

Drug abuse:

The misuse of illicit drugs such as marijuana, cocaine or amphetamines.

The 4 main classes of abused drugs are:

1. Depressants (Opiates, alcohol, barbiturates & benzodiazepines)
2. Stimulants (cocaine & amphetamines).
3. Hallucinogens (LSD, mescaline & nutmeg).
4. Others (coffee, hashish, cigarettes & volatile solvents).

Addiction or Drug Dependence:

A state of chronic intoxication characterized by:-

- Physical dependence (withdrawal symptoms "abstinence syndrome" on stopping).
- Tolerance (the dose must be increasing to produce the same effect).
- Detrimental effects to the individual and community.

Habituation:

It results from continued consumption of a drug or substance; eg. Coffee, hashish, cigarettes, resulting in:

- Psychological dependence (A desire is present but ***without*** compulsion to take the drug for sense of well-being).
- No physical dependence (no withdrawal symptoms).
- No tolerance.
- There may be detrimental effects to the individual.

Alcohol

Clinical picture:

1) Physical:

- Anorexia → malnutrition
- Inflammations of mucous membranes due to lack of Vit. A.
  - Conjunctivitis.
  - Rhinitis with Red drunkard nose (VD of blood vessels).
  - Laryngitis.
- Fatty liver & cirrhosis due to malnutrition and absorption of toxic products from intestine.
- Cardiomyopathy.

2) Nervous:

- Peripheral neuritis (Mixed but more motor) due to Vit. B deficiency leading to:-
  - Optic atrophy.
  - Impotence.
- Chronic subdural Hematomata.

3) Mental:

- Dementia: Decrease intellectual power & lack of concentration.
- Dipsomania: Overpowering desire to drink alcohol.
- Delusions of jealousy: jealous husband syndrome or Othello syndrome (Increase sexual desire & impotence due to neuritis).
- Delirium tremens (Alcohol withdrawal syndrome)
  - Which appears on withdrawal, or after taking large amounts of alcohol.
  - Manifested by fearful hallucinations, e.g. seeing snakes surround him, in addition to tremors and tachycardia.
- Auditory hallucinations.
- Korsakoff psychosis: "Alcohol amnestic disorder"
  - Impaired memory for recent events.
  - Confabulation.
- Wernicke's encephalopathy: (Vitamin B1 deficiency)
  - Tremors.
  - Ataxia.
  - Ocular palsy.

4) Withdrawal symptoms: Delirium tremens.

Fetal alcohol syndrome (FAS):

- Fetal alcohol syndrome is the most common preventable cause of mental retardation.
- Diagnostic criteria for FAS include:
  - Heavy maternal alcohol consumption during gestation.
  - Pre and postnatal growth retardation.
  - Craniofacial malformations including microcephaly.
  - Mental retardation.

Treatment:

1. Hospitalization (Gradual withdrawal is preferable to avoid delirium tremens).

2. Antabuse [Disulfiram]:

Action: cause acetaldehyde syndrome, i.e. prevent metabolism of acetaldehyde; the metabolic product of alcohol→ accumulation, causing [when patient return drinking alcohol]:

- Flushed face.
- Vomiting.
- Palpitation & extra systoles.

Therefore, the patient hates alcohol & refuses drinking.

3. Barbiturates or Diazepam to treat anxiety or convulsions.

4. Antipsychotic drugs.

5. Good nutrition & vitamins especially vitamin B1, vitamin B2, folic acid & ascorbic acid with glucose [liver support].

6. Psychological and religious rehabilitation.

Opiates

Clinical picture:

1. Physical:

- Anorexia & constipation.
- Loss of sexual desire and impotence.
- Injection marks (Tattoos are frequent to conceal injection marks).
- Complications of injections.

2. Mental:

Amnesia, decreased mental powers and mood swings (periods of depression, anger and irritability alternating with euphoria).

3. Withdrawal manifestations:

- Due to appearance of clinical effects **opposite** to those of intoxication.
- Withdrawal typically starts 15 hours after stopping the drug, peaks at 48 hours and subsides over 7 days.
- Withdrawal manifestations are:
  - **Craving for the drug.**
  - **Generalized aches:** Pains and cramps in the back, legs and abdomen.
  - **Irritability and insomnia.**
  - **Nausea & vomiting.**
  - **Increased secretions** (Diarrhea, lacrimation & cold sweating).
  - **Yawning.**
  - **Dilated pupils.**
  - **Tachycardia & hypertension.**

N.B.

- No tolerance occurs for miosis or constipation.
- Heroin is more euphoric and less constipating than morphine.

Treatment:

1) Hospitalization.

2) Gradual withdrawal:

Treatment programs are aimed at gradual reduction of opiate & substitution by either Methadone or Buprenorphine.

a. Methadone: oral opiate preparation.

- It is taken **once daily**
- Has longer duration of action, thus keeping the individual free of withdrawal symptoms for up to **24 hours**.

b. Buprenorphine: sublingually

- A partial opioid agonist and potent antagonist
- Has long duration of action.

3) **Rapid withdrawal**:
   a. **Ultra Rapid detoxification (5-30 minute period):** Naltrexone is given under general anesthesia, which blocks all endorphin receptors.
   b. **Rapid Detoxification (4 to 8 hours):** Naltrexone, Naloxone or Nalmephine is given under general anesthesia as well as other medications that reduce the withdrawal symptoms such as muscle relaxants or anti-nausea medications.

N.B. Many serious adverse effects associated with anesthesia assisted detoxification: pulmonary (aspiration pneumonia), psychiatric complications, metabolic complication of diabetes and death may occur.

   c. **Stepped Rapid detoxification** (**2 to 3 days):** naltrexone with high doses of clonidine and benzodiazepines before and after the naltrexone to ameliorate the symptoms.
   d. **Outpatient detoxification:** buprenorphine-naloxone or clonidine alone or combined with naltrexone.

4) **Clonidine:** Alpha-adrenergic receptor stimulant; it causes release of endogenous opioid and decreases all manifestations of abstinence.
5) **Diazepam** is often necessary.
6) **Naltrexone:** in addicts who stopped opiates, a long acting antagonist is given as an outpatient treatment for 3 months, so if the addict return to opiates, it will have no effect.
7) **Good nutrition**, vitamins and physical exercise.
8) **Psychological** and religious rehabilitation.

Barbiturates

Clinical Picture:

1. **Physical:**

Loss of weight, hypersomnia, drowsiness.

2. **Mental:**

Amnesia, dementia and depression.

3. **Withdrawal Manifestations:**

Anxiety, insomnia, restlessness, tremors, twitches, convulsions, weakness, nausea & vomiting.

Treatment:

1) **Hospitalization:** Gradual withdrawal over a period of 3 weeks.
2) **Diazepam** is often necessary.
3) **Good nutrition**, vitamins and physical exercise.
4) **Psychological** and religious rehabilitation.

Benzodiazepines

Tolerance: develops rapidly to its sedative effect

Dependence: if the benzodiazepine is continuously administered in large doses for more than four months

Clinical picture:

Similar to barbiturates.

Treatment:

Withdrawal and substitution of short acting benzodiazepine by long acting one, then gradual withdrawal of the long acting one.

Cocaine

Clinical picture:

1. **Physical:**
   - Tachycardia, hypertension, tachypnea and increased temperature.
   - Weight loss.
   - Facial pallor due to vasoconstriction.
   - Dilated pupils and "**crack keratitis**" due to the local anesthetic effect allows excessive rubbing of the eyes.
   - Nasal septum may become **perforated** due to:
     - Blood vessel spasm with ischemia.
     - Cocaine anesthesia (patient does not feel pain of necrosis).
     - Adulteration with salicylic acid powder.
   - Teeth may show acid erosion of the surface enamel.
2. **Mental:**
   - Euphoria & well-being.
   - Hallucinations.
   - **Cocaine bugs:** feeling of insects crawling under the skin due to the chronic effects on the sensory nerve endings.
3. **Withdrawal symptoms:**
   - Withdrawal symptoms are not serious as opiates.
   - It includes irritability, neurological pain in arms and legs and tendency to violence.

Treatment:

1) Hospitalization: Sudden withdrawal

2) Barbiturates or Diazepam to treat anxiety or convulsions.

3) Good nutrition, vitamins and physical exercise.

4) Psychological and religious rehabilitation.

Amphetamines

Clinical picture:

1. **Physical:**

- Tremors, tachycardia, hypertension, dilated reactive pupil.
- Anorexia and loss of weight.
- Euphoria, increased self-confidence, alertness & delayed fatigue.

2. **Mental:**

- Amphetamine psychosis (paranoid): psychosis resembling paranoid schizophrenia.
- Hallucinations (visual, auditory, olfactory or tactile).
- Tendency to violence.

3. **Withdrawal manifestations:**

Fatigue, somnolence, confusion, apathy & depression.

Treatment:

1) Hospitalization: Sudden withdrawal.

2) Barbiturates or Diazepam to treat anxiety or convulsions.

3) Good nutrition, vitamins and physical exercise.

4) Psychological and religious rehabilitation.

Tramadol

Clinical picture:

1. **Physical:**

Similar to opiate with higher incidence of nausea, dizziness, loss of appetite and convulsions.

2. **Mental:**

Aggressive behavior, suicidal thoughts and mood swings

3. **Withdrawal manifestations:**

- Symptoms of opiate withdrawal: see before.
- Symptoms of SSRI withdrawal: numbness, tingling, paresthesia and tinnitus. Hallucinations, paranoia, extreme anxiety, panic attacks, and confusion.

Treatment:

1-Hospitalisation.

2-Gradual withdrawal: decrease the dose of tramadol until no more is being taken.

3-Clonidine: alpha-adrenergic receptor stimulant, it causes release of endogenous opioid and decreases all withdrawal symptoms.

4-Diazepam: seizures.

5-Selective serotonin reuptake inhibitors (SSRI): withdrawal symptoms.

6-Good nutrition, vitamins and physical exercise.

7-Psyhcological and religious rehabilitation.

Drugs Schedule

GRADE	CHARACTERS	DRUGS
Schedule I:	-Drugs with high potential for abuse and addiction, -**NO medical value**	- Heroin, - LSD, - Ecstasy, - Marijuana, - Methaqualone.
Schedule II:	-Drugs with high potential for abuse and addiction, -have **some medical value** with restrictions	- PCP, - Cocaine, - Amphetamines, - Most Opiates, - Some Barbiturates.
Schedule III	-Drugs with less potential for abuse and addiction, -currently acceptable for **medical use.**	- Some Barbiturates, - Codeine, - Steroids.
Schedule IV	-Drugs with low potential for abuse and addiction, -Currently acceptable for **medical use.**	Tranquilizers like Valium, Xanax, and Librium.

Common Street Names for Some Drugs of Abuse

Drug		
Opiates: **Opium** **Heroin**	*Big O* *Junk, smack, china white*	
Barbiturates : **Seconal**	*Barbies, barb*	**الفراولة أم لمعه**
Benzodiazepines : **Rohypnol** **Clonazepam (Revotril)**	*Date rape drug-Roofies*	**الروش، أبو صليبة** **صليبه –ريفو-أبوزمبة**
Amphetamines	*uppers, speed black bombers*	**الماكس (حقن)** **أبو مسحة أبو ملف(حبوب)**
Cocaine	*crack, coke, snow, rock, blow*	
LSD	*Blue Heaven*	**الطوابع والبرق الأبيض**
Marijuana **Cannabis**	*weed, grass, Mary Jane*	**جوب و بهجة والهبو والصدام حشيش**
Parkinol (antiparkinsonien)		**الصراصير**

APPENDIX

Toxins affecting the skin:

Red skin (red asphyxia):

- CO
- Cyanide
- Cold

Blue skin (cyanosis):

CNS depressants:

- Opioid
- Sedative hypnotics
- Alcohol
- Cholinergics such as organophosphates, Carbamate including Physostigmine.
- Anticholinergics & Sympathomimetic in severe cases
- Others (salicylates, Lead, lithium, hypoglycemic agents)

Yellow skin (jaundice):

- Iron
- Paracetamol
- Arsenic
- Organochlorine insecticides
- Salicylates
- Ethanol
- Zinc phosphide

Brown skin (methemoglobinemia):

- Phenol
- Naphthalene
- Nitrites

Coma with skin blisters:

- Barbiturates.
- Benzodiazepine (Nitrazepam, Oxazepam & Temazepam).
- Carbon monoxide
- Opioid (heroin, morphine, methadone & hydrocodone)
- TCA (amitriptyline & imipramine).

Ophthalmotoxic toxins

Miosis:

- Organophosphates & Carbamate
- Opioids
- Carbolic acid
- Sedative – hypnotics (barbiturates, benzodiazepines)
- Ethanol
- Phenothiazines
- Parasympathomimetic drugs (Physostigmine- Pilocarpine)

Mydriasis

- Drugs with Anticholinergic action (atropine, TCAs)
- Sympathomimetic (amphetamines- cocaine- theophylline)
- Hallucinogens (phencyclidine)
- Serotonin syndrome (MAOI + SSRI)
- Cyanide
- Withdrawal of opiates

Others Ophthalmotoxic toxins:

- Methanol
- Mercury
- Digitalis
- Corrosives

Toxins with characteristic odors:

- Alcohol: Acetone.
- Cyanide: Bitter almonds (genetically determined).
- Arsenic, Organophosphates: Garlic
- Hydrogen sulfide: Rotten eggs
- Moth Balls
- Phenol
- Kerosene
- Opium

Hepatotoxic toxins

- Iron
- Paracetamol
- Arsenic
- Organochlorine insecticides
- Salicylates
- Ethanol
- Zinc phosphide

Nephrotoxic toxins

- Phenol
- Oxalic acid
- Lead
- Mercury
- Cadmium
- Salicylates
- Lithium
- Organochlorine insecticides
- Snake venom

Cardiotoxic toxins

- Carbolic acid (direct myocardial depression)
- CCBs (bradycardia & hypotension)
- BBS (bradycardia & hypotension)
- Scorpion venom
- Drugs causing ECG changes such as:
  - **Widened QRS**: TCAs, Phenothiazines & Antihistaminic (diphenhydramine)
  - Drugs causing **prolonged QT** interval: TCAs, Phenothiazines
  - **Tachyarrhythmia**: Anticholinergics & sympathomimetic

Toxins causing bradycardia & hypotension:

- Calcium channel antagonists
- B-Adrenergic antagonists
- Digitalis
- Opioids
- Organophosphates and Carbamate
- Cyanide, hydrogen sulfide
- Tricyclic anti-depressants (in severe cases)

Toxins causing Non-cardiogenic pulmonary edema:

- Morphine
- Salicylates
- Barbiturates
- Hydrocarbons
- Carbon monoxide

Toxins causing hyperglycemia

- Salicylates: hyperglycemia (followed by hypoglycemia)
- Calcium channel blocking agents (due to blockage of insulin release)
- Theophylline & amphetamine
- Organophosphates
- Chronic iron toxicity (bronzed diabetes)

Toxins causing hypoglycemia

- Hypoglycemic drugs
- Beta-adrenergic blocking agents.
- Ethanol
- Salicylates: hyperglycemia (followed by hypoglycemia)
- Paracetamol (3rd stage)
- Acute Iron toxicity (4th stage)
- Barbiturates

Toxins causing hyperkalemia

- Beta-adrenergic blocking agents.
- Digitalis Toxicity (Acute Poisoning)
- Amphetamines in late stage
- Potassium-sparing diuretics

Toxins causing hypokalemia

- Beta-adrenergic agonists such as amphetamines & theophylline
- Digitalis in chronic toxicity
- Salicylates
- Laxatives
- Diuretics (except potassium sparer)

Toxins causing rhabdomyolysis

- Toxins causing **prolonged convulsion** such as CNS stimulants (amphetamines, theophylline, cocaine), strychnine, TCAs, Phenothiazines, antihistamines, Salicylates, etc.
- Toxins causing **prolonged coma** such as barbiturates, severe benzodiazepine toxicity, etc.
- **Calcium channel blockers & beta blockers** due to coma &/or convulsion secondary to shock)
- **Direct causes** such as snake & severe animal bites

Toxins causing Paralysis

- Botulism
- Lead (purely motor)
- Ethanol (more motor than sensory)
- Arsenic (more sensory than motor)
- Organophosphates

Toxins causing Seizure

- Sympathomimetic (Amphetamine- Cocaine- Theophylline)
- Hypoglycemic drugs
- Anticholinergics
- Carbon monoxide, cyanide
- Organophosphorus & Carbamate insecticides
- Calcium channel blocking agents & beta blockers due to convulsion secondary to shock)
- Others (salicylates, Lead, lithium)

Antidotes that should be readily Available in an Emergency Department

ANTIDOTE	TOXIN
Naloxone, Nalmefene	Opiates
Ethanol	Methanol
Oxygen± hyperbaric therapy	Carbon monoxide
Flumazenil	Benzodiazepines
Atropine, Pralidoxime	Organophosphates, Carbamate
Sodium bicarbonate	Cyclic antidepressants
Physostigmine	Anticholinergics (atropine & antihistamines only)
Methylene blue	Methemoglobinemia
N-Acetylcysteine	Acetaminophen
Cyanide kit	Cyanide
Digoxin-specific antibody fragment	Digitalis
Calcium preparations	Calcium channel blockers
Glucagon	Beta blockers Calcium channel blockers
Deferrioxamine	Iron