Introduction to toxicology & principles of management of acute poisoning

- Poison: any agent capable of producing a deleterious response in a biological system.
- Virtually every known chemical has the potential to produce injury or death if it is present in a sufficient dose.
- Most toxic responses are usually related to dose.
- Phenomena that don't follow dose response (dose independent):
  - **Allergy:**
    An immunologically mediated adverse reaction to a chemical resulting from previous sensitization to that chemical or to a structurally similar one. Once sensitization has occurred, allergic reactions may result from exposure to relatively very low doses of chemicals. range in severity from minor skin disturbance to fatal anaphylactic shock.

  - **Idiosyncratic reactions:**
    genetically determined abnormal reactivity to a chemical. defined as adverse effects that cannot be explained by the known mechanisms of action of the offending agent, do not occur at any dose in most patients, and develop mostly unpredictably in susceptible individuals only
    Examples: G6PD, Scoline apnea, Disulfiram reactions.

  - **Drug interactions:**
    • **Additive**: the most common form. occurs due to algebraic summation of the activity of individual substance.
    Example: two CNS depressants (e.g; alcohol and tranquilizer).

    • **Synergistic**: Exposure to a chemical may drastically increase the effect of another chemical.
    Example: smoking and radon, smoking and asbestos (in the development of lung cancer), CCl4 and ethanol (in causing hepatotoxicity).

    • **Potentiation**: Occurs when a chemical that does not have a specific toxic effect makes another chemical more toxic.
    Examples:
    - isopropanol enhances hepatotoxicity of CCl4
    - drugs with extensive plasma protein binding enhance toxicity of warfarin (bleeding).

    • **Antagonist**: Occurs when two chemicals are administered together interfere with each other's actions.
      – Receptor: Occurs when two chemicals potentially bind to the same receptor, the one which occupy the receptor will dominate the action.

Examples: Naloxone and Opiates – Flumazenil and Benzodiazepine – Atropine for toxins that increase acetylcholine – Physostigmine (acetylcholine esterase inhibitor) for Atropine.

– Functional: Occurs when two chemicals counterbalance each other by producing opposite effects on the same physiologic function (tachycardia, bradycardia, hypotension, hypertension, etc..)

– Chemical: Chemical reaction between two compounds that produces a less toxic product.

Examples: Chelators for heavy metal toxicity, Protamine sulphate (basic) for Heparin (acidic).

– Dispositional: Methods that interfere with absorption, Metabolism and excretion of a chemical.

General approach to management of poisoning:

1. **Patient stabilization**
2. **Complete patient assessment**
3. **Poison decontamination**
4. **Poison enhancement of elimination**
5. **The use of antidote**
6. **Continuous patient supportive care**

- **Patient stabilization**

  Airways (A)
  Breathing (B)
  Circulatory system (C)
  Drugs induced CNS depression (D)

  Substances that can be administered for lethargic/comatose patient with possible overdose: "coma cocktail"
  • Oxygen
  • Glucose: for possible hypoglycemia.
  • Thiamine: for possible Wernicke–Korsakoff syndrome due to alcohol.
  • Naloxone: for possible opioid intoxication.
  • Atropine ??? only when the patient is stabilized because it may exacerbate hypoxia by causing tachycardia.

- **Complete patient assessment**

  Steps taken to diagnose the causative agent and to evaluate the patient's condition.

- History
- Physical examination

- Laboratory investigations LFT, KFT, CBC, Glucose…
- Toxicological analysis

Aims to Diagnose the patient, Are Antidotes needed? Know the pathophysiology of the toxic agents, Know how to direct therapy, Monitor organs functions, Protect organs functions, Supportive therapy.

- **Poison decontamination**
  Removal of unabsorbed poisons from the exposure sites to decrease absorption and damage: GI tract, Skin (irrigation), Mucous membranes.

GI tract decontamination:
The followings points should be considered: Patient status, Time since ingestion, Nature of the toxin ingested, Effectiveness of the selected procedure, Indication versus contraindication, What is the next step of management?

Methods of GI tract decontamination:
• Dilution • Emesis • Gastric lavage • Adsorbents • Cathartics

- **Dilution:** Applied only following corrosives ingestion to dilute the corrosive substance (acid, alkali). It is useful to add bulk to the stomach that may be needed for other procedures in GI decontaminations.
  It increases disintegration of drugs and enhances their absorption (unrecommended for drug intoxication).
  Dilution with water, or demulcents (milk, egg white, gelatin).
  ****Avoid using neutralizing agents.**

  Note: Most acids produce a **coagulative necrosis** by denaturing proteins, forming a coagulum (i.e. eschar) that limits the penetration of the acid. By contrast, alkali typically produces a **more severe injury** known as **liquefactive necrosis**.

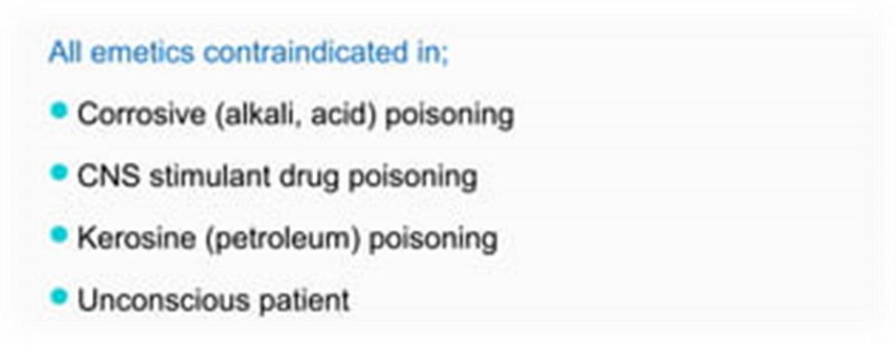
- **Emesis:**
  Induction of Emesis:
  - **Ipecac syrup**: Acts locally by direct irritation, and centrally by stimulating the vomiting center. Contains emetine and cephaline. Given orally. Response rate %90-95 within 30 minutes. **Relatively safe for children and adults**. Can be used at home and at hospitals.

- **Apomorphine**: Opiate derivative. Given by injection. Quick response 3-5 minutes. **Contraindicated for children**. Leads to CNS depression, respiratory depression, hypotension.

- **Soft liquid detergents**: Can be used at home. Effectiveness and response rate almost similar to Ipecac syrup. Dose 15-30 ml with 30 ml of water (not toxic at these doses).

- **Gag reflex**: Mechanical stimulation of pharynx. Response rate and efficiency of emesis are law. Incomplete and traumatic (injury of the pharynx, bites). Recommended with above cautions.

- **Hypertonic solution**: Concentrated sodium chloride solution. Concentration and amount are not known. Response rate and efficiency of emesis are law. Complicated by hyperosmotic dehydration. **Should be avoided**.



- **Gastric lavage:**
  Performed in hospital by experienced medical personnel in Cooperative patients. Airway protection, Patient is placed on the left lateral position to permit pooling of gastric contents and to reduce the risks of aspiration, and the patient's head should be lower than the rest of the body. The largest diameter tube should be used. Wash with 200-300 ml of warm fluids (water or NS) and the rule is to lavage until clear. There is a possibility that even if the lavage is clear there is dumps of chemicals (concretion) remaining in the Stomach (iron, aspirin, paracetamol).

  Complications: • Laryngeal spasm, Aspiration pneumonia. • Esophageal and gastric lesions (hemorrhage or perforation). • Pneumothorax, Ectopic beats. • Electrolytes disturbance.

  Contraindications: • Unprotected airways. • Ingestion of hydrocarbons, corrosive substances, Kerosene (causes Aspiration and chemical pneumonitis).

- **Adsorbents**

Activated charcoal:

Fine black powder with pores leading to tunnels, mixed with suitable amount of water or other fluids. Traps most organic, nonionized substances with molecule weight of 100 – 1000 Dalton. Dose 1-2 gm/kg.

Binds to most substances, **except:**

• Metals. • Methanol and ethanol. • Acids/bases. • Hydrocarbons.
• Inorganic salts. • Corrosives.

- **Cathartics (laxatives)**

Decrease contact time between the poison and absorption sites.

Cautions:

• Absence of bowel sounds, intestinal obstruction.
• Renal failure: Mg containing cathartics.
• Heart failure: Na containing cathartics.

- **Poison enhancement of elimination**

Get red of poisons that are present in the systemic circulation by:

1. Renal excretion: Forced diuresis and alteration of urinary pH.
   - Alkalinization of urine by Sodium bicarbonate will enhance eliminating acidic substances (Salicylates, Phenobarbital).
   - Acidification of urine by Ammonium chloride will enhance elimination of basic substances (Amphetamines, Quinidine, Phencyclidine).

   Cautions: • Pulmonary edema, cerebral edema, Electrolyte disturbance.

2. Gastrointestinal tract excretion Interrupt entero-hepatic circulation of toxins, by cholestyramine, cathartics or Repeated doses of activated charcoal.

3. Dialysis

   Only few severely poisoned patients benefit from Dialysis. The toxin must be able to pass across the dialysis membrane (small Molecular weight (<500 D), water soluble, low protein binding).
   • Hemodialysis is indicated in renal failure secondary to toxin exposure.
   • Peritoneal dialysis though it's easily performed with least complications, is less effective than Hemodialysis.

4. Plasma Exchange
5. Exchange Transfusion

- **Use of antidote**

Drug/ poison	Antidote
CO poisoning	100% O2
CN poisoning	Hydroxocobalamin, amyl nitrite, sodium thiosulphate
opioids	Naloxone
Benzodiazepines	Flumazenil
Methanol, Ethylene glycol	Fomepizole Ethanol
Paracetamol	N-acetyl cysteine
Organophosphates	Atropine Pralidoxime
Anticholinergics (atropine)	Neostigmine
Heparin	Protamine sulphate
Warfarin	FFP, vitamin K
Metals (eg. Iron)	Chelating agent (eg. Deferoxamine)

- **Continuous patient supportive care**

  Manage serious manifestations such as:
  – Hypothermia
  – Hyperthermia
  – Convulsion
  – Coma

Notes from P.P:

- ✓ In kerosine poisoning, avoid oil/fat ingestion because they will increase absorption of kerosene. (also, emesis and gastric lavage are contraindicated due to risk of aspiration. Activated charcoal is not beneficial because it does not bind kerosene).
- ✓ Hydrofluoric acid usually produces liquification necrosis (unlike other acids).
- ✓ Antidote for atropine poisoning presenting with CNS manifestations → Physostigmine (it can cross BBB)