

Toxicology



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Recourses:

- Simpson's Forensic Medicine By Richard Shepherd -12th edition*
- Doctor's slide*
- Lecture notes*
- 424 lecture notes*

Toxicology is the science of medicine which deal with poisoning, its diagnosis and management.

-The branches of toxicology are environmental, industrial, radiation and military.

-The poison is any product substance that can harms someone if used in the wrong way by wrong person, or in the wrong amount. The harmful effect varies, and can cause death.

- **Examples of possible poisons:**

1- Some of household product, e.g. flash, Clorox, corrosives

2- Chemicals at work or in the environment.

3- Snake, spider and scorpion bites.

Classification of Poisons:

A. According to their mode of action (The Best Classification):

- ❖ Poisons with local action only.
- ❖ Poisons with remote actions; they act after absorption, e.g. morphine, atropine
- ❖ Poison with both local and remote action, e.g. irritant (heavy) metals as arsenic.

B. According to the organs affected:

- ❖ Hepatotoxic, e.g. alcohol, barbiturate, phosphorus, paracetamol, anesthetic.
- ❖ Cardiotoxic, e.g. atropine, beta blockers, digitalis.

- ❖ Nephrotoxic, e.g. antibiotic, amino glycosides, cyclosporine, digitalis.

C. According to the chemical nature:

- ❖ Acidic.
- ❖ Organic.
- ❖ Inorganic.

Arsenic most common in crimes because:

- It's available.
- Takes 12-38 hours to produce its effect.
- Death is due to gastroenteritis, i.e. dehydration.

Factors Affecting the Action of Poisons:

- ❖ Age: children die in little amount due to their lesser body weight.
- ❖ Personal hypersensitivity: (allergy or anaphylaxis), e.g. aspirin, penicillin, iodine.
- ❖ Tolerance: tolerated people need large dose
- ❖ Idiosyncrasy: abnormal response to drugs, i.e. opposite to their action
- ❖ State of health: physically ill patients e.g. having hepatic or renal diseases, get affected by small doses.
- ❖ Condition of the stomach: The action of a poison is very rapid in an empty stomach and vice versa.
- ❖ The type of food:
 1. Arsenic (fat insoluble poison) effect is delayed or even absent if taken with fatty meal. Conversely, a fat soluble poison (phosphorus) gives rapid effect.
 2. Acidity: combination of cyanide and achlorhydria gives no effect (no absorption)
- ❖ Synergism, e.g. alcohol and barbiturates.
- ❖ State of the poison: gases produce the fastest effect, then liquid then solid poisons.

- ❖ Method of administration: the most rapid is inhalation, then IV, then IM pump.
- ❖ Dose of poison: (the most important factor): the more the dose, the higher the effect, but very high doses lead to vomiting, which decrease their effect (antiemetic are contraindicated in poisoning)

Diagnosis of poisoning:

1. History and circumstantial evidences:

- ❖ Suicidal: bottle of a drug, suicidal note, history of depression.
- ❖ Accidental: food poisoning.
- ❖ Homicidal.

2. Clinical picture:

- ❖ Contracted pupils in morphine, organophosphorous,
- ❖ Dilated pupils in atropine, cocaine and antidepressant that have atropine like effect.
- ❖ Red skin in carbon monoxide (forming carboxyhemoglobin) and cyanide poisoning (a cytochrome oxidase inhibitor).
- ❖ Flushed face and red mouth in atropine and alcohol poisoning
- ❖ Patches around the mouth in corrosives.
- ❖ Characteristic smell of the mouth in case of opium, cyanide (bitter almond), arsenic, kerosene, alcohol, phenol.
- ❖ Fever: atropine (antispasmodic), salicylates (antipyretics), Kerosene and tricyclic antidepressants.

- ❖ Convulsions: oxalic acid (causing hypocalcemia), strychnine (used to increase the appetite), egorts (common after labor) and in insecticides.
- ❖ Slow pulse occurs with morphine and digitalis poisoning-while rabid pulse with atropine, nicotine.

3. *Radiopacity of poisons:*

- ❖ There are a number of tablets with different chemical compositions that exhibit varying degrees of Radio-opacity. E.g. Barium Enteric coated tablets, Tricyclics antidepressants, Antihistamines , Heavy metals.

4. *Chemical analysis:* The most important evidence of poisoning.

A- *In the living:*

Samples are taken from vomit, gastric lavage, blood, urine and stool.

B- *In the dead :*

- ❖ Blood from the heart or femoral vein.
- ❖ Stomach and its contents and parts of the intestines
- ❖ Parts of the liver, kidney, brain, lung

5. *Autopsy in suspected poisoning (PM).*

6. *Screening test (rapid):*

- ❖ These are various tests to evaluate the type (and roughly measure the amount) of legal and illegal drugs a person has taken, which done by special machines.
- ❖ Each country has its own medical report about the most common used drugs.

- ❖ These drugs undergoing special tests (KETS) or color test.
- ❖ putting a reagent on a sample of urine or blood results in a special color if the drug exists, e.g. salicylate and ferric chloride gives the urine a blue color.

General Lines For Treatment Of Poisoning

- *All or some of these essential lines may be used for the patient according to his clinical state:*

- 1- Decontamination: washing out the poison.
- 2- Supportive care: stabilizing the vital signs, i.e. ABC.
- 3- Prevent further exposure to the poison, e.g. lead poisoning in lead factory.
- 4- Removal of the unabsorbed poison from the stomach.
- 5- Inactivation of the poison remaining in the stomach, i.e. adsorption.
- 6- Enhancement of excretion through the lung, kidney, or the liver.
- 7- Administration of an antidote: only in 2-35% of cases.
- 8- Symptomatic treatment.

Decontamination:

Skin, e.g. corrosives, acids, insecticide (farmers):

- ❖ Wear protective clothes and gloves.
- ❖ Remove the patient's contaminated cloths because it is a source of absorption.
- ❖ Flush the exposed area by copious quantities of lukewarm water or saline; use soap with liquid substances.

- ❖ Do not use neutralization because it may generate heat, which can potentially worsen the injury.

Eye, e.g. corrosive agents (like spray which is used by ladies or polices) and solvents:

- ❖ Toxins that are readily absorbed through the skin can also be absorbed through the cornea.
- ❖ Flush by copious quantities of tepid (cold) water or saline; use at least 1 liter to irrigate each eye.
- ❖ Wash carefully the upper and lower conjunctival fornices.
- ❖ Check the pH of the tears to know the irritant substance, and wash until the pH returns to normal.
- ❖ Don't use neutralizing agents due to heat and salt formation.

Inhalers, e.g. irritant gases, fumes, and toxins that are absorbed through the respiratory tract (CO₂, cyanide, hydrogen sulphate, organophosphorus, and insecticides):

- ❖ Ensure adequate respiratory protection for yourself and other health providers.
- ❖ Remove the victim from exposure.
- ❖ Administer humidified O₂ and assist ventilation of necessary.
- ❖ Observe for evidence of upper respiratory edema (manifests as stridor and hoarseness) or noncardiogenic pulmonary edema (manifests as dyspnea, tachypnea, cyanosis, and hypoxemia)
- ❖ Use carbogen, which is a combination of O₂ (95%) and CO₂ (5%) to stimulate respiration and increase the removal of poisons.

Supportive Care:

- ❖ Commonly, patients detoxify the poison as the ingested compound is metabolized by normal body processes (when the amount of poison is small)
- ❖ Supporting the vital signs and good pulmonary hygiene enhance any of the other more specific methods.
- ❖ The patient should be observed on a cardiac monitor until medically cleared.
- ❖ 30-40% of poisoned patients can be treated with supportive care.
- ❖ The drug will be progressively eliminated over the next 12-36 hours in most patients, and usually this is all the care that is necessary.

Prevent Further Exposure to Poisons:

- Suicidal cases must be hospitalized and kept under supervision to prevent another attempt.
- In industrial or agriculture exposure, the poisoned worker should be removed from the polluted area.
- In cases of toxic inhalation, the first priority of treatment is removal of the patient from poisoned environment to fresh air and giving oxygen.

Removal of the Unabsorbed Poison:

Emesis:

- **Methods:**
 - A. *Mechanical:* irritate the pharynx, using the index finger, the handle of a spoon or a tongue depressor.
 - B. *Central:* ibuprofen injection (SC or IM)

C. Chemical: syrup of ipecac is a natural substance that causes vomiting after 10-20 minutes:

- ❖ The emetic of choice in both children over the age of 6 months and adult.
- ❖ The dose is 30 ml for adults and 15 ml for children, and repeated if vomiting does not occur.
- ❖ Gastric lavage should be done to remove ipecac from the stomach (as it is toxic) if it didn't work.
- ❖ Contraindicated in comatose patient and those with peptic ulcer.

• **Contraindication of emesis:**

- ❖ A corrosive poison because it may lead to perforation.
 - ❖ Antiemetic poisoning.
 - ❖ Volatile poison due to the risk of aspiration pneumonia.
 - ❖ Chronic poisoning for more than 6 hours.
 - ❖ Esophageal varices as it will cause bleeding.
 - ❖ Unconscious patients.
 - ❖ Recent gastric operation.
 - ❖ Don't give salt and water ; it may lead to hypernatremia which will cause fatal arrhythmia.
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Gastric Lavage:

- Recently it is considered only if life threatening amount of poison is ingested within one hour.

■ **Contraindication:**

- ❖ Corrosive poisons.
- ❖ Poisoning with mineral acids and alkaline.
- ❖ Chronic poisoning for more than 6 hours, because it is already absorbed except salicylate and antiemetic poisons which stick on the stomach, mucosa and drugs that decrease gastric motility.
- ❖ Kerosene and related petroleum distillate poisoning as they are volatile in the stomach.
- ❖ Varices

■ **Complication:**

- ❖ Aspiration pneumonia the most frequent; cough and cyanosis indicate that the tube is in the trachea.
- ❖ Perforation of the esophagus.
- ❖ Chemical pneumonia.

Technique:

- ❖ The patient is placed on the left lateral position with the head lower than the level of the feet to prevent regurgitated material from the entering the respiratory tract; dentures should be removed if present.
- ❖ Open the mouth by gag to prevent the rubber gastric tube from being bitten.
- ❖ Pull the tongue forwards while introducing the tube, and ask the patient to swallow if he is conscious.

- ❖ The lower end of the tube should be lubricated with paraffin oil to prevent trauma.
- ❖ The tube is introduced in the stomach and not in the air passage. If the patient is conscious, sudden spasmodic cough, dyspnea or cyanosis will develop when the tube passes into the air passage, but if he/she is semiconscious or in a coma, the following tests should be done before lavage:
 - a. Put the ear near the funnel end of the tube; a hissing sound of the air is heard when the tube is in the trachea.
 - b. Proper location of the tube on the stomach can be assessed by auscultating the stomach meanwhile injecting air into the tube.
 - c. Aspiration of the stomach contents confirms its proper location.
- ❖ After testing, a sucker is connected to the tube and aspirate as much as possible.
- ❖ The first aspirated sample is considered a concentrated poison, and should be sent for laboratory diagnosis.
- ❖ Disconnect the sucker and attach the funnel, then pour 200-300cc (50-100cc for children) of water, which enters the stomach by gravity.
- ❖ Lower the funnel below the level of the patient stomach and let the content regurgitate into a container.
- ❖ Washing is the repeated with warm water or with specific antidote until the returning fluid is clear.
- ❖ Before extraction of the tube, magnesium or sodium sulphate (15mg) is left in the stomach to confirm purgation of any poison that has passed to the intestine.
- ❖ Tightly close the external end of the tube by a finger before withdrawal to prevent the escape of any fluid from the lower end into the air passage, and then remove the mouth gag.

NOTE:

- The stomach (orogastric) tube is 150 cm long and .25 cm wide, marked at 50 cm from the lower end; when this mark is at the level of the lips, this denotes that the lower tip has reached the stomach.
- The tube is made of soft rubber with a number of lateral holes at the blunt lower end. Large-bore oral tubes increase the return of pill remains; decrease the chance for tube occlusion, and increase the rapidity with which gastric lavage is performed.

Inactivation Of The Poison Remaining In The Stomach:

- ❖ Local antidotes are substances which stop or neutralize the poison of its harmful effect on the stomach.
- ❖ Toxins will remain in the stomach but become intoxicant.

Physical Antidotes:

- ❖ They interfere with the ingested poisons through physical means only, and do not change the chemical nature. They include:

1. Demulcents with corrosives, e.g. flash. They coat (soothing) the gastric mucosa, e.g. milk, row egg white and olive oil.

2. Diluents e.g. water.

3. Adsorbents (activated charcoal):

➤ A residue from the distillation of various organic materials such as wood, paper and bone. It is activated by heating with steam, oxygen and acids at temperatures in excess of 600 C in the absence of air. It must be homogenous.

➤ It has large surface area, safe, effective, inexpensive and universally used for adsorbing a wide range of chemicals.

- In general, most drugs and household products are adsorbed well enough to make the administration of activated charcoal clinically useful.
- A dose of activated charcoal that provides a charcoal to poison ratio of 10:1 ensure optimal binding. Since the estimates of ingested doses of toxins are often inaccurate, a suggested dose is usually used, i.e. 1-2gm/kg.
- It should be mixed with 60-90 ml of water and should be stirred constantly to ensure uniform slurry, and activated charcoal tablets are ineffective.

Chemical antidotes:

- ❖ These change the chemical nature of the poison by chemical reaction producing less or nontoxic form.

1. Precipitating antidotes:

- Tannin (tannic acid) produced by strong decoction of tea, will precipitate the alkaloids as tannates, morphine, salicylates, barbiturates and codeine. It is not used due to its corrosive nature.
- Sodium bicarbonate is used also to precipitate alkaloids.

2. Oxidizing antidotes:

- Potassium permanganate, 1/5000 solution in a dose of 150ml orally, is used in plant and insecticides poisonings. It acts locally in the stomach..

3. Reducing antidotes:

➤ Sodium formaldehyde sulphoxalate is given in cases of mercury poisoning to reduce it to less toxic insoluble mercurous form.

Household antidotes:

- ❖ Substances that are available in house and can be used as a first aid treatment of poisoning.
- ❖ Examples of these local antidotes are lemon or orange juice, vinegar , milk, egg white, water and strong decoction of tea or coffee(tannin).

Enhancement Of Excretion:

- Poisons or their metabolite are excreted from the body through different ways. Hence, the methods used to help the elimination of the poison will differ accordingly.
- Poisons eliminated through the lung (in expired air)e.g. alcohol inhalation of carbogen (95% O₂ and 5% CO₂) to increase the depth and rate in respiration.
- Those, which excreted by bile, e.g. morphine enhanced by multiple doses activated charcoal.
- Poisons eliminated by intestine: treated by laxatives.
- Poisons excreted by the kidney, e.g. barbiturates and salicylate :depend on the kidney function, however, the following methods may be used:

1- Fluid diuresis: IV saline and 5% dextrose or glucose.

2- Forced diuresis:

- Forced osmotic diuretics, e.g. Lasix, dextrose 50%

- Forced acid diuretics used in alkaline poison: changing the urinary pH.

Alkaline Diuresis:

- ❖ By promoting alkaline urine (pH7-8)
- ❖ Both salicylate (aspirin) and phenobarbital are weak acids. These drugs will become more ionized in the distal tubular lumen, which will slow tubular reabsorption and allow a larger fraction of the drug to be excreted without being reabsorbed back into the body.
- ❖ This can be done by infusing the following:
 - ✓ 500 cc 5% dextrose.
 - ✓ 500 cc 0.9% saline
 - ✓ 500 cc 1.26% sodium bicarbonate.

Acid Diuresis:

- ❖ Treat alkaline poisons, e.g. amphetamine, kinin, phencyclidine.
- ❖ Because the excretion of myoglobin is decreased in acid urine, there is a greater likelihood of causing an acute tubular necrosis.
- ❖ It contains saline 0.9%, dextrose 5% and acidified by vitamin C and ammonium chloride:
 - ✓ 1 gm of ascorbic acid to each liter of normal saline. oral or IV preparations were suggested.
 - ✓ Ammonium chloride 75mg/kg IV or orally per day, has been suggested, but caution is advised for patients with kidney or liver disease.
 - ✓ The pH should be kept below 5.

Hemodialysis (artificial kidney):

- ❖ Use in nephrotoxic poisoning.
- ❖ The rate of removal of a dialyzable poison is usually 5-10 times greater with hemodialysis than with peritoneal dialysis .
- ❖ Indication for dialysis:
 - Immediately indicated for only two drugs; methanol (caused blindness) and ethylene glycol.
 - Dialysis on the basis of patient condition, e.g. renal failure, acid base disorders, hypothermia, and electrolyte disorders.

Hemoperfusion:

- ❖ The blood is passed through various adsorbent materials. Such as activated charcoal or a resin that has an affinity for lipid soluble organic molecules. It is essentially dialysis against an adsorbent.
- ❖ It is indicated for a massive intoxication when the extracellular distribution of the poison is significant.

Peritoneal Dialysis:

- ❖ A simple method based on the fact that the peritoneum is a semi-permeable membrane, which permits the movement of water and dissolved substances in both directions, so the dialysate solution in peritoneal cavity will exchange the body fluids (that contain the poison) across the peritoneal membrane until equilibrium occurs.
- ❖ Hence, the poison concentrated in the body fluid will be reduced.
- ❖ **Technique:**
 - A catheter is inserted midway between the umbilicus and symphysis pubis, and a solution is injected.

- The sterile solution (dialysate) consists of electrolytes dextrose, heparin, and gentamycin (5mg/L).

❖ **Complications:**

- ✓ Peritonitis (sepsis), the most important.
- ✓ Injury of perforation of intestine or bladder.
- ✓ Intaperitoneal bleeding.
- ✓ Electrolyte disturbances.

Administration of physiological antidote if available (counteraction):

Antagonist:

- ❖ Strychnine poisoning causes convulsions, which is best, treated by IV diazepam 10mg.
- ❖ Atropine antagonizes muscarinic action in Organ phosphorus poisoning.
- ❖ Pilocarpine antagonizes the peripheral action of atropine

Chelators:

- ❖ Antidotes that unite with the absorbed poisons forming chelates, which are less toxic and easily excreted through the kidney.
- ❖ BAL(British antilewisite): in arsenic poisoning.
- ❖ EDTA (ethylene diamine tetracetate): in heavy metal poison

- ❖ Naloxone: in morphine poisoning. It also antagonizes most of the narcotics.
- ❖ DSMA (DIMERCAPTOSUCCINIC ACID) is similar to , but is water soluble and given orally in the treatment of chronic lead and arsenic poisonings.
- ❖ DMPS(2,3-dimercapto-1-propane sulfonic acid): like DSMA
- ❖ Desferrioxamine : iron poisoning.

Competitors:

- ❖ Naloxone: morphine poisoning
- ❖ Ethyl alcohol: methanol poisoning (decrease the rate of metabolism and destroys alcohol dehydrogenase)

Symptomatic Treatment:

Shock (SBP is less than 90, and DBP is less than 60):

- ❖ The first and easiest thing to do is elevation of the bed foot.
- ❖ IV fluids, and plasma expanders e.g. dextran.
- ❖ Vasopressor drugs are given till the BP reach 100 mmHg, and the stopped since the may cause oliguria.
- ❖ Hydrocortisone 100 mg if no improvement.
- ❖ Correct arrhythmias, acidosis, hypoxia, and other manifestations.

Coma:

**An Altered mental status (unconsciousness), but there is no description that is universally accepted.*

Stage 1

- Drowsiness.
- Respond to spoken Stimuli.
- Normal response to pain.
- Intact Superficial and deep Reflexes.

Stage 3:

- Unconsciousness.
- No respond to spoken Stimuli.
- No respond to minimal painful stimuli.
- Respond to maximal (deep) painful stimuli.
- No superficial reflexes.
- Sluggish deep reflexes.

Stage 2:

- Unconsciousness.
- No respond to spoken stimuli.
- Respond to painful stimuli.
- PaO₂ is more than 60mmHg, and PaCO₂ is 40 mmHg or less, (measured in the arterial blood).

Stage 4:

-Most Dangerous stage

- The patient is in coma.
- PaO₂ is less than 60, and PaCO₂ is less than 50.
- No superficial or deep reflexes.
- Doesn't withdraw from pain.
- There is cyanosis and circulatory and/or respiratory depression; endotracheal intubation is required

-Causes And Types:

- 1- Toxic
- 2-Traumatic
- 3-Pathological
- 4-Functional (hysterical): no organic cause, normal vital signs, incomplete coma, and negative investigations.

-Management:

- 1- ABC
- 2- Special care of respiration: endotracheal intubation (for maximum 48 hours since it causes ischemia and necrosis), then tracheostomy, suction of secretion, oxygen inhalation, and mechanical ventilation.
- 3- Change the position of the patient to prevent bedsores.
- 4-Prophylactic antibiotics against respiratory infections.

5-Feeding by Ryle's tube or IV fluids.

6-Catheterization to prevent urine retention.

7-Monitoring of pulse, BP, ECG, temperature and reflexes.

8- NEVER give analeptic.

9-If the patient enters the ER with an altered mental status, give therapeutic agents that are considered safe i.e DONT; Dextrose, Oxygen, naloxone, thiamine. since naloxone is a pure narcotic antagonist, it will not cause any deterioration of the patient condition, and dextrose and thiamine will not harm the Hyperglycemic patient.

Convulsions (CNS stimulation by Atropine):

- Differential diagnosis includes epilepsy.
- Poisons can cause convulsions through different mechanisms, mainly by affecting the CNS, or by decalcification of blood as in Oxalic acid poisoning, which changes the ionized calcium to non ionized one, leading to Hypocalcemia.

• Treatment:

- 1- Put the patient in a dark quiet room.
- 2- Control convulsions by 10 mg of diazepam (the drug of choice), barbiturate, or succinylcholine.

Disturbance In Body Temperature:

1- Hypothermia:

- Rectal temperature is more than 36C e.g barbiturate overdose
- Treat the patient in a warm room while wrapping the patient with blankets.

2-Hyperthermia:

- Rectal temperature greater than 38C e.g. Anticholinergics, salicylates, kerosene, cocaine, amphetamine, and other sympathomimetics.

- Can lead to extensive muscle breakdown and renal failure as well as direct brain injury.
- Keep the patient in a cool, well ventilated room.
- Ice bags (the best treatment), antipyretic, and antibiotic may be needed.

Acid Base Disorders:

- Salicylate, iron, methanol, and Ethanol are poisons which cause acidosis.
- Severe metabolic acidosis may require infusion of sodium bicarbonate.

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