**1…INTRODUCTION / IMPORTANT DEFINITIONS**

**Toxicology** is the study of the harmful effects of chemical compounds on biologic systems, including their properties, actions, and effects. The toxic agent is referred to as a toxicant or poison.

**Toxin** refers to poisons produced by a biologic source (eg, venoms, plant toxins); the redundant term biotoxin is occasionally used. They usually produce effects via chemical mechanism.

**Toxicant** refers to those agents, which are produced by synthetic or semisynthetic source and give effects via physical destruction. (alpha, beta, gamma, uv radiations)

**Poison** is the agent (toxin or toxicant) that is severely dangerous to the living body even at low dose for rapid action.

**Toxicity** is the indicating parameter to judge potential/degree of harmfulness.

**Poisoning** is the process of unintentional/accidental exposure and subsequent effects that are produced by the poison.

**Overdose** is the intentional exposure to relatively higher dose and production of associated adverse effects by any agent. (Suicidal attempt)

**Toxic effects** may be either lethal or toxic. toxic effects may either be local or systemic or both.

Toxicity may be expressed either by dose or concentration.

**Toxic Dose=** known strength and route of administration

**Toxic Concentration**= Unknown strength and route of administration, just related with available contents in the body.

**2…TOXICOLOGICAL EXPOSURE**

Based on duration and frequency of exposure, we can divide into 4 categories.

1. Acute Toxicity= Frequency is for once and effects observed within 24 hours.
2. Sub-acute= Frequency is more than one, and effects are produced from 1 day ---1 month.
3. Sub-chronic= Frequency is more than one, and effects are seen from 1---3 months.
4. Chronic= Frequency is high, and effects are seen beyond 3 months.

**3….GENERAL MANAGEMENT OF INTOXICATED PATIENTS**

Principle of treatment will be:

**“TREAT THE PATIENT (regarding symptoms), NOT THE POISON.”**

The approach to poisoned patients must be systematic. The range of symptoms and clinical findings in the physical examination are wide in drug poisoning patients; initial management is focused on stabilization of life-threatening conditions. The approach for the poisoned patients in emergency includes: resuscitation, history, physical examination, and management. Initial screening examination should be done on all patients to find out immediate abnormal measures which need to be stabilized starting with vital signs, conscious level and pupil size, skin temperature, pulse oximetry, and electrocardiogram. Patients who are hemodynamically unstable must be kept in continuous cardiac monitoring. Intravenous access should be done and the blood glucose must be checked especially if the patients have a decreased level of consciousness.

**3. Resuscitation (Restoration)**

3.1 Airway and ventilation

Step-1 is to stabilize

A=Airway Obstruction

B=Breathing

C=Circulatory system

The initial priorities for a poisoned patient presented to the emergency department are: securing the airway and breathing and stabilizing the circulation. Adequate ventilation and intubation with mechanical ventilation must be done early in the intoxicated patients with depressed mental status, except in cases of easy reversible causes of coma like opioid intoxication or hypoglycemia to prevent complications of intubation like aspiration. Other indications for intubation include severe acid-base disturbances or acute respiratory failure. In intubated patients, development of a respiratory acidosis must be prevented by adequate ventilation; in some cases like high-grade physiologic stimulation, the patient may need sedation and paralysis to prevent complications such as hyperthermia, acidosis, and rhabdomyolysis.

3.2 Hypotension

Drugs cause hypotension by four major mechanisms: decreased peripheral vascular resistance, decreased myocardial contractility, dysrhythmias, and depletion of intravascular volume. First-line treatment of hypotension is IV fluid bolus (10 to 20 mL/kg); if hypotension is not responding to fluid, it may be necessary to add vasopressors such norepinephrine. Norepinephrine is better than dopamine.

3.3 Hypertension

Elevated blood pursues caused by CNS sympathetic overactivity, increased myocardial contractility or increased peripheral vascular resistance, or a combination. The treatment of hypertension and agitated patients starts with sedatives such as benzodiazepines; if not responding for initial treatment and there is evidence of endorgan dysfunction, calcium-channel blocker is preferred treatment. The use of betablockers is not recommended in the case of sympathetic hyperactivity because it may cause unopposed alpha-adrenergic stimulation and intensified vasoconstriction. Ventricular tachycardia occurs because of tricyclic antidepressant toxicity. Sodium bicarbonate is first line therapy. antiarrhythmic agents may worsen cardiac conduction; hence, they are not recommended; also, using these agents could be potentially dangerous. Magnesium sulfate can also be used in the case of drug-induced torsade de pointes and prolonged QT intervals on ECG. Digoxin toxicity with life-threatening tachyarrhythmias or bradyarrhythmias should be treated with specific Fab fragments (Digibind).

3.4 Bradyarrhythmias

Treatment of bradyarrhythmias with hypotension starts with atropine and/or temporary pacing. Calcium, glucagon, or high-dose insulin are used in the case of calcium channel blocker or beta blocker intoxication.

3.5 Seizures

The best treatment of intoxicated patients with seizures is benzodiazepines; we may add barbiturates if necessary. Phenytoin is not recommended to control seizures in poisoned patients.

3.6 Severe hyperthermia

Elevated temperature (hyperthermia) due to drug toxicity (e.g., sympathomimetic overdose, serotonin syndrome, or neuroleptic malignant syndrome) must be treated aggressively to prevent complications like rhabdomyolysis, organ failure, and disseminated intravascular coagulation. Treatment of hyperthermia includes active cooling like ice water immersion; if active cooling is ineffective, the patient may need sedation, neuromuscular paralysis, and intubation. Patients presenting with signs of opioid overdose (low Glasgow coma scale-GCS respiratory depression, meiosis) must be given naloxone (0.1–2.0 mg I.V) as soon as possible.

**4. History**

History of the present illness is very important and can be obtained from the patients if they are alert and conscious; although the history following intentional ingestion is often unreliable, which makes history taking very challenging especially if the patients are comatose or cannot give their history, in such situations, history can be taken from collateral information from family, friends, ambulance crew, or medical records looking for past psychiatry illness, previous history of suicide or drug abuse, chronic medication, etc. History must include time, route of entry, quantity, intentional or accidental exposure, availability of drugs at home, and if any member of the family has chronic diseases (hypertension, diabetic, etc.) and missing tablets or any empty pill bottles or other material was found around him . It is very important to ask specifically about the use of traditional or herbal remedies and dietary supplements.

**5. Physical Examination**

Physical examination of poisoned patients may give clues regarding the substance which has been abused and toxidromes. Physical examination includes: general appearance,

• Mental status (agitated or confused) Some drugs or substances affect the central nervous system either causing agitation or depression.

• Skin (cyanosis, flashing, and physical signs of intravenous drug abuse (track marks) Red and flushed skin occurs.

• Eye examination: (pupil size reactivity lacrimation and nystagmus)

5.1 Toxidromes

Toxidromes are a group of abnormal physical examinations and abnormal vital signs known to be present with a specific group of medications or substances. The most common toxidromes are cholinergics, anticholinergics, sympathomimetics, opioids, and serotonin syndrome.

**6. Screening**

6.1 Electrocardiogram (ECG) ECG should be done on all patients who are symptomatic or who have been exposed to cardiotoxic agents looking for the rate and conduction; ECG abnormalities may help in diagnosis or may help as prognostic information. Specific attention should be paid to QRS interval and QT interval; in the case of prolongation of QT or QRS sodium bicarbonate infusion should be strongly considered.

6.2 Radiographic studies

Imaging examinations are not necessary in every poisoned patient but may be useful in some situations where the toxins are radiopaque. Chest x-ray is useful in the case of noncardiogenic pulmonary edema and the acute respiratory distress syndrome due to exposure to certain toxins.

6.3 Abdominal ultrasound

Ultrasound abdomen is not helpful in poisoned patient and the use of ultrasound is very limited and does not appear to be a reliable method of detecting ingested toxins .

6.4 Laboratory test

Blood test must be done with all intoxicated patients; especially in the case of intentional overdose, the laboratory test should include basic lab (full cell count and kidney function liver function and electrolytes). Acetaminophen screening is very important in every patient presenting with altered mental status or intentional overdose. For the patients with an acid-base abnormality, serum osmolarity needs to be checked, looking for increasing osmolar gap, which rolls out toxic alcohol ingestion. In the case of presence of anion gap, metabolic acidosis may help and give to physician a clue of ingestion of certain toxins like (salicylates, ethylene glycol, and methanol or other drugs which may cause high anion gap metabolic acidosis; also serum creatinine, glucose, ketones, and lactate should be tested to detect other causes of the anion gap acidosis.

6.5 Toxicology screening

Toxicology screening is not necessary in case of nonintentional ingestion are asymptomatic patient or have clinical findings that are match with the medical history. Drugs of abuse to opioids, benzodiazepines, cocaine metabolites, barbiturates, tricyclic antidepressants, tetrahydrocannabinol, and phencyclidine can be detected by using immunoassay screens in urine. Positive and negative screens for drugs do not necessarily confirm diagnosis of acute poisoning but require further investigations. 6.6 Limitations of toxicologic drug screening assays • Nonspecific—because most tests can detect only typical drugs within a class: opioids, amphetamines, benzodiazepines, cannabinoids, cocaine, barbiturates. For example, opioid screens do not detect meperidine and amphetamine screens do not detect methylenedioxymethamphetamine • Drugs may be detected days to weeks after exposure. A positive test may not mean acute poisoning • Cross reactivity in the case of carbamazepine, cyproheptadine, and chlorpromazine; the test can be positive for tricyclic antidepressants • Test can be negative if tested urine was diluted.

**7. General Management**

**Decontaminations**

Decontamination of poisoned patient means removing the patient from the toxin and removing the toxin from the patient, either outside the patient’s body by gross washing or inside the body by gastrointestinal decontamination or enhanced elimination.

**7.1 Gross Decontamination**

Patient must be fully undressed and washed thoroughly with copious amount of water twice regardless of how much time has elapsed since the exposure. All the clothing must be removed and placed in plastic bags, and then the bags must be sealed; no need to neutralize an acid with a base or a base with an acid because that may lead to more tissue damage because the heat could be generated by this reaction. Using any greases or creams must be avoided because they will only keep the xenobiotic in close contact with the skin and ultimately make its removal more difficult. Decontamination must be done in an isolated specific area. Gross decontamination is used in chemical, biological, and radiation exposure. Healthcare providers must wear universal precautions (gown, gloves, and eye protection) and sometimes may need personal protective equipment.

7.2 Ocular decontamination In the case of eye exposures to chemical substance, initially, application of a local anesthetic agent (e.g., 0.5% tetracaine) may be needed, then copious irrigation with crystalloid solution. Lid retraction facilitates the irrigation. Alkalis cause more injury than acids because of deep tissue penetration via liquefaction so may need prolonged irrigation (1 to 2 hours). pH of conjunctival sac should be tested and irrigation should be continued until pH is less than 7.4.

**7.3 Gastrointestinal decontamination**

There are multiple methods used for gastrointestinal decontamination including:

• Emesis

Induced vomiting by ipecac syrup can decrease absorption and was used in the past but now is rarely indicated because there is no evidence supporting its effectiveness in reducing toxin absorption. It may also increase the risk of complications. Syrup ipecac may be considered in conscious, alert patients with ingestion of a potential number of toxic drugs and present in a very short time after ingestion (60 mg/kg with opacities on abdominal radiograph • Life-threatening ingestion of diltiazem or verapamil • Body packers or stuffers • Slow-release potassium ingestion • Lead ingestion (including paint flakes containing lead) • Symptomatic arsenic trioxide ingestion • Life-threatening ingestions of lithium • Contraindications • Unprotected airway. Gastrointestinal obstruction absent bowel sound or perforation. Recurrent, unstoppable vomiting. Complications: • Nausea and vomiting • Pulmonary aspiration • Vomiting, bloating, and rectal irritation.

Emesis can be achieved by administration of syrup of ipecac. Syrup of ipecac is a plant-derived compound composed of two alkaloidal substances—emetine and cephaeline—that work both peripherally on the stomach and centrally on the chemotactic trigger zone to induce vomiting. Dosing of syrup of ipecac is 15 mL for children 1 to 12 years of age, and 30 mL for adults, usually followed by sips of water. The dose may repeated only once if vomiting does not occur within 30 min. Approximately 90 percent of patients vomit within 20 min after the first dose, and up to 97 percent vomit after a second dose. A typical patient vomits less than three to five times, and symptoms usually resolve within 2 h. The ingested toxin should be suspected as the etiology if protracted vomiting occurs.

Gastric lavage

Gastric lavage is an intervention widely used to remove the ingested toxin drugs from the stomach by an orogastric tube. Because of the absence of published evidence that shows that orogastric lavage may change the outcome, now orogastric lavage is rarely indicated. It may be considered in the case of recent (less than 1 hour) ingestion of life-threatening amount of a toxin for which there is no effective treatment once absorbed. This can be is performed with the patient lying in the left lateral decubitus position. A 36- to 40-French tube is used for adults and a 22- to 24-French tube for children. The tube is inserted after careful measurement of the length from the chin to the xiphoid process. Correct positioning must be assessed by insufflation of air to ensure accurate placement in the stomach. Lavage with room temperature water is commonly continued until the effluent becomes clear. Before the tube is removed, activated charcoal should be instilled in a dose of 1 g/kg, if indicated. The contraindications to lavage include pills that are known not to fit into the holes of the orogastric lavage hose, nontoxic ingestions, non-life-threatening ingestions, caustic ingestions, any patient whose airway integrity is not assured, or toxic ingestions that are more damaging to the lungs than to the GI tract.

Activated charcoal:

Activated charcoal is a super-heating carbonaceous material. Activated charcoal works by reducing the absorption of a substance in the gastrointestinal lumen but it is not effective in metal, alcohols, corrosives, and lithium. The most effective action can be achieved when activated charcoal is given within the first hour of ingestion. In the case of intubated patients, activated charcoal may be administered via an orogastric or nasogastric tube. Dose: • Children 1 to 12 years of age: 25 to 50 g or 0.5 to 1.0 g/kg (maximum dose 50 g) • Adults: 25 to 100 g (with 50 g representing the usual adult dose). Contraindications: Substances not adsorbed by activated charcoal. • Unprotected airway • Corrosive ingestion • Upper gastrointestinal perforation. Complications: • Vomiting • Aspiration of the activated charcoal • Reduce absorption of orally administered antidotes.

Whole-bowel irrigation:

Whole-bowel irrigation is a mechanical cleansing of the whole gastrointestinal track reducing toxin absorption. The whole-bowel irrigation can be done by Polyethylene glycol solution. Polyethylene glycol is an osmotically balanced electrolyte solution; polyethylene glycol can be given orally to cooperative, awake patients. Patient positioning (head up 30°) reduces the risk of pulmonary aspiration; during whole-bowel irrigation also bowel sounds must be present. Clear rectal effluent and imaging shows the absence of foreign bodies considered as endpoint of whole bowel irrigation treatment. Indication: • Iron ingestion >60 mg/kg with opacities on abdominal radiograph • Life-threatening ingestion of diltiazem or verapamil • Body packers or stuffers • Slow-release potassium ingestion • Lead ingestion (including paint flakes containing lead) • Symptomatic arsenic trioxide ingestion • Life-threatening ingestions of lithium • Contraindications • Unprotected airway. Gastrointestinal obstruction absent bowel sound or perforation. Recurrent, unstoppable vomiting.

**8. Enhanced elimination**

Enhanced elimination is a method used to increase the rate of toxic removal from the body so as to reduce the severity and duration of clinical intoxication. Enhanced elimination methods are not routinely used in poisoned patients. The indications for enhanced elimination include: [4]. • Severe toxicity • Poor outcome despite supportive care/antidote • Slow endogenous rate of elimination. There are different techniques to enhance elimination:

Cathartics, activated charcoal is administered with an osmotic cathartic, such as 70% sorbitol (1 g/kg), or a 10% solution of magnesium citrate (in a dose of 250 mL for adults and 4 mL/kg for children). Cathartics have been repeatedly shown to decrease the transit time for the passage of the activated charcoal (and presumably the adsorbed toxin) through the GI tract

Multiple dose activated charcoal (MDAC). MDAC is defined as at least two sequential doses of activated charcoal. Multidose activated charcoal can be given via orogastric or nasogastric tube to intubated patients. Mechanism of action: • Prevents ongoing absorption of toxin that persists in the GI tract (modifiedrelease preparation) • Enhances elimination in the post absorptive phase by delayed enterohepatic recirculation or enteroenteric recirculation (“gut dialysis”). Indications: Ingestion of a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine, salicylates, or theophylline. Ingestion of a life-threatening amount of another toxin that undergoes enterohepatic or enteroenteric recirculation and that is adsorbed to activated charcoal. Ingestion of a significant amount of any slowly released toxin. Contraindications: • Unprotected airway • Bowel obstruction. Complications: • Vomiting • Pulmonary aspiration • Constipation • Bowel obstruction or perforation. Dose: no optimal dose of MDAC has been established. But the acceptable regimen of 50 g is administered every 4 hours, or 25 g every 2 hours. Study on volunteer found no difference in effectiveness of larger doses spread out over time compared to smaller, more frequent dose.

Urinary Alkalinization

Urine alkalinization is a treatment regimen which enhances the elimination of toxins by administration of intravenous sodium bicarbonate to produce urine with pH > or = 7.5. Alkaline urine acts on ionization of acidotic toxins within renal tubules, stopping resorption of the ionized drug back across the renal tubular epithelium and enhancing elimination through the urine. Characteristics of drugs which respond to urinary alkalinization are • Eliminated predominantly unchanged by the kidney • Distributed primarily in the extracellular fluid compartment • Minimal protein-bound • Weak acids (3.0 to 7.5). Urinary alkalinization for poisoned patients can be done by the following steps: • Correct hypokalemia • Start with 1 to 2 mEq/kg IV sodium bicarbonate bolus • Infuse 100 mEq of sodium bicarbonate mixed with 1 L of D5W at 250 mL/h • Potassium chloride (20 mEq) can be added to maintain normokalemia • Monitoring serum potassium and bicarbonate level every 2 to 4 hours to prevent hypokalaemia • Urine pH should be checked regularly, keeping urine pH between 7.5 and 8.5.

Urinary acidification

U. Acidification, (urine pH below 5.5) with ammonium chloride or ascorbic acid was used in the past to treat toxicity of weak bases such as amphetamines, quinidine, or phencyclidine. However, this practice is not used now because of lack of evidence of efficacy and complications such as iatrogenic toxicity (from severe academia) and rhabdomyolysis may occur.

**9. Extracorporeal elimination**

It includes hemodialysis, hemoperfusion, and continuous renal replacement therapies, this method has limited indications in intoxicated patients, extracorporeal elimination need critical care setting also this procure are expensive and invasive, are not always available extracorporeal elimination were used in less than 0.1% of cases reported to U.S. poison control centers in 2010 . The toxins need to have a number of criteria to be effectively removed by extracorporeal elimination:

Hemodialysis/Hemoperfusion

Hemodialysis is generally reserved for specific toxins that must be both potentially life-threatening and amenable to removal by this method. The benefits include the ability to remove toxins that are already absorbed from the gut lumen, removal of substances that do not adhere to activated charcoal, and the ability to remove both the parent compound and the active toxic metabolites. Hemodialysis is much less effective when the toxin ingested has a large volume of distribution (>1 L/kg), has a large molecular weight (more than 500 Da), or is highly protein bound. Hemodialysis is rarely absolutely contraindicated, but relative contraindications include hemodynamic instability, very small children, and patients with poor vascular access or profound bleeding diatheses. Risks of hemodialysis are typically minimal in experienced centers, but they include large fluid shifts, electrolyte imbalances, infection and bleeding at the catheter site, and intracranial hemorrhage. Exchange transfusion should be considered in small children who cannot receive hemodialysis because of technical limitations.

Hemoperfusion, which is also used for decontamination of a patient's systemic circulation, involves placing a filter filled with activated charcoal into the circuit of the hemodialysis machine. This filtration alleviates the constraints of protein binding and molecular size, both of which limit the utility of hemodialysis. Toxins that can be removed by this method must adsorb well to activated charcoal and have a small volume of distribution. While potentially useful for phenobarbital, phenytoin, and ethchlorvynol, in practice, it is only commonly recommended for theophylline overdoses.

