SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES
Sathy Main Road, SNS Kalvi Nagar,
Saravanampatti Post, Coimbatore - 641 035,
Tamil Nadu.

GENERAL PRINCIPLES OF POISONING

Poisoning is contact with a substance that results in toxicity. Symptoms vary, but certain common syndromes may suggest particular classes of poisons. Diagnosis is primarily clinical, but for some poisonings, blood and urine tests can help. Treatment is supportive for most poisonings; specific antidotes are necessary for a few. Prevention includes labeling drug containers clearly and keeping poisons out of the reach of children.

Most poisonings are dose-related. Dose is determined by concentration over time. Toxicity may result from exposure to excess amounts of normally nontoxic substances. Some poisonings result from exposure to substances that are poisonous at all doses. Poisoning is distinguished from hypersensitivity and idiosyncratic reactions, which are unpredictable and not dose-related, and from intolerance, which is a toxic reaction to a usually nontoxic dose of a substance.

Poisoning is commonly due to ingestion but can result from injection, inhalation, or exposure of body surfaces (eg, skin, eye, mucous membranes). Many commonly ingested nonfood substances are generally nontoxic (see Table: Substances Usually Not Dangerous When Ingested*); however, almost any substance can be toxic if ingested in excessive amounts.

Accidental poisoning is common among young children, who are curious and ingest items indiscriminately despite noxious tastes and odors; usually, only a single substance is involved. Poisoning is also common among older children, adolescents,

and adults attempting suicide; multiple drugs, including alcohol,acetaminophen, and other OTC drugs, may be involved. Accidental poisoning may occur in the elderly because of confusion, poor eyesight, mental impairment, or multiple prescriptions of the same drug by different physicians (see also

After exposure or ingestion and absorption, most poisons are metabolized, pass through the GI tract, or are excreted. Occasionally, tablets (eg, aspirin, iron,enteric-coated drugs) form large concretions (bezoars) in the GI tract, where they tend to remain, continuing to be absorbed and causing toxicity.

Symptoms and Signs

Symptoms and signs of poisoning vary depending on the substance (see Table: Symptoms and Treatment of Specific Poisons). Also, different patients poisoned with the same substance may present with very different symptoms. However, 6 clusters of symptoms (toxic syndromes, or toxidromes) occur commonly and may suggest particular classes of substances (see Table: Common Toxic Syndromes (Toxidromes)). Patients who ingest multiple substances are less likely to have symptoms characteristic of a single substance.

Symptoms typically begin soon after contact but, with certain poisons, are delayed. The delay may occur because only a metabolite is toxic rather than the parent substance (eg, methanol, ethylene glycol, hepatotoxins). Ingestion of hepatotoxins (eg, acetaminophen, iron, *Amanita phalloides* mushrooms) may cause acute liver failure that occurs one to a few days later. With metals or hydrocarbon solvents, symptoms typically occur only after chronic exposure tothe toxin.

Ingested and absorbed toxins generally cause systemic symptoms. Caustics and corrosive liquids damage mainly the mucous membranes of the GI tract, causing stomatitis, enteritis, or perforation. Some toxins (eg, alcohol, hydrocarbons) cause

characteristic breath odors. Skin contact with toxins can cause various acute cutaneous symptoms (eg, rashes, pain, blistering); chronic exposure may cause dermatitis.

Inhaled toxins are likely to cause symptoms of upper airway injury if they are water-soluble (eg, chlorine, ammonia) and symptoms of lower airway injury and noncardiogenic pulmonary edema if they are less water-soluble (eg, phosgene). Inhalation of carbon monoxide, cyanide, or hydrogen sulfide gas can cause organ ischemia or cardiac or respiratory arrest. Eye contact with toxins (solid, liquid, or vapor) may damage the cornea, sclera, and lens, causing eye pain, redness, and loss of vision.

Some substances (eg, cocaine, phencyclidine, amphetamine) can cause severe agitation, which can result in hyperthermia, acidosis, and rhabdomyolysis.

Diagnosis

- Consideration of poisoning in patients with altered consciousness or unexplained symptoms
- History from all available sources
- Selective, directed testing

The first step of diagnosis of poisoning is to assess the overall status of the patient. Severe poisoning may require rapid intervention to treat airway compromise or cardiopulmonary collapse.

Poisoning may be known at presentation. It should be suspected if patients have unexplained symptoms, especially altered consciousness (which can range from agitation to somnolence to coma). If purposeful self-poisoning occurs in adults, multiple substances should be suspected.

History is often the most valuable tool. Because many patients (eg, preverbal children, suicidal or psychotic adults, patients with altered consciousness) cannot provide reliable information, friends, relatives, and rescue personnel should be questioned. Even seemingly reliable patients may incorrectly report the amount or time of ingestion. When possible, the patient's living quarters should be inspected for clues (eg, partially empty pill containers, a suicide note, evidence of recreational drug use). Pharmacy and medical records may provide useful information. In potential workplace poisonings, coworkers and supervisors shouldbe questioned. All industrial chemicals must have a material safety data sheet

(MSDS) readily available at the workplace; the MSDS provides detailed information about toxicity and any specific treatment.

Testing

In most cases, laboratory testing provides limited help. Standard, readily available tests to identify common drugs of abuse (often called toxic screens) are qualitative, not quantitative. These tests may provide false-positive or false- negative results, and they check for only a limited number of substances. Also, thepresence of a drug of abuse does not necessarily indicate that the drug caused the patient's symptoms or signs. Urine drug screening is used most often but has limited value and usually detects classes of drugs or metabolites rather than specific drugs. For example, an opioid urine immunoassay test does not detect fentanyl or methadone but does react with very small amounts of morphine or codeine analogues. The test used to identify cocaine detects a metabolite rather than cocaine itself.

For most substances, blood levels cannot be easily determined or do not help guide treatment. For a few substances (eg, acetaminophen, aspirin, carbon monoxide, digoxin, ethylene glycol, iron, lithium, methanol, phenobarbital, phenytoin, theophylline), blood levels may help guide treatment. Many authorities

recommend measuring acetaminophen levels in all patients with mixed ingestions because acetaminophen ingestion is common, is often asymptomatic during the early stages, and can cause serious delayed toxicity that can be prevented by an antidote. For some substances, other blood tests (eg, PT for warfarin overdose, methemoglobin levels for certain substances) help guide treatment. For patients who have altered consciousness or abnormal vital signs or who have ingested certain substances, tests should include serum electrolytes, BUN, creatinine,

serum osmolality, glucose, coagulation studies, and ABGs. Other tests (eg, methemoglobin level, carbon monoxide level, brain CT) may be indicated for certain suspected poisons or in certain clinical situations.

For certain poisonings (eg, due to iron, lead, arsenic, other metals, or to packets of cocaine or other illicit drugs ingested by so-called body packers), plain abdominal x-rays may show the presence and location of ingested substances.

For poisonings with drugs that have cardiovascular effects or with an unknown substance, ECG and cardiac monitoring are indicated.

If blood levels of a substance or symptoms of toxicity increase after initially decreasing or persist for an unusually long time, a bezoar, a sustained-release preparation, or reexposure (ie, repeated covert exposure to a recreationally used drug) should be suspected.

Treatment

- Supportive care
- Activated charcoal for serious oral poisonings
- Occasional use of specific antidotes or dialysis
- Only rare use of gastric emptying

Seriously poisoned patients may require assisted ventilation or treatment of cardiovascular collapse. Patients with impaired consciousness may require continuous monitoring or restraints. The discussion of treatment for specific poisonings, below and in see Table: Common Specific Antidotes, see Table: Guidelines for Chelation Therapy, and see Table: Symptoms and Treatment of Specific Poisons , is general and does not include specific complexities and details. Consultation with a poison control center is recommended for any poisonings except the mildest and most routine.

Initial stabilization

- Maintain airway, breathing, and circulation
- IV naloxone
- IV dextrose and thiamine
- IV fluids, sometimes vasopressors

Airway, breathing, and circulation must be maintained in patients suspected ofa systemic poisoning. Patients without a pulse or BP require emergency cardiopulmonary resuscitation.

If patients have apnea or compromised airways (eg, foreign material in the oropharynx, decreased gag reflex), an endotracheal tube should be inserted (see Tracheal Intubation). If patients have respiratory depression or hypoxia, supplemental oxygen or mechanical ventilation should be provided as needed.

IV naloxone (2 mg in adults; 0.1 mg/kg in children; doses as high as 10 mg may be necessary in some cases) should be tried in patients with apnea or severe respiratory depression while maintaining airway support. In opioid addicts, naloxone may precipitate withdrawal, but withdrawal is preferable to severe respiratory depression. If respiratory depression persists despite use of naloxone, endotracheal

intubation and continuous mechanical ventilation are required. If naloxone relieves respiratory depression, patients are monitored; if respiratory depression recurs, patients should be treated with another bolus of IV naloxone or endotracheal intubation and mechanical ventilation. Using a low-dose continuous

naloxone infusion to maintain respiratory drive without precipitating withdrawal has been suggested but in reality can be very difficult to accomplish.

IV dextrose (50 mL of a 50% solution for adults; 2 to 4 mL/kg of a 25% solution for children) should be given to patients with altered consciousness or CNS depression, unless hypoglycemia has been ruled out by immediate bedside determination of blood glucose.

Thiamine (100 mg IV) is given with or before glucose to adults with suspected thiamine deficiency (eg, alcoholics, undernourished patients).

IV fluids are given for hypotension. If fluids are ineffective, invasivehemodynamic monitoring may be necessary to guide fluid and vasopressor therapy. The first-choice vasopressor for most poison-induced hypotension isnorepinephrine 0.5 to 1 mg/min IV infusion, but treatment should not be delayedif another vasopressor is more immediately available.

Topical decontamination

Any body surface (including the eyes) exposed to a toxin is flushed with large amounts of water or saline. Contaminated clothing, including shoes and socks, and jewelry should be removed. Topical patches and transdermal delivery systemsare removed.

Activated charcoal

Charcoal is usually given, particularly when multiple or unknown substances have been ingested. Use of charcoal adds little risk (unless patients are at risk of vomiting and aspiration) but has not been proved to reduce overall morbidity or mortality. When used, charcoal is given as soon as possible. Activated charcoal adsorbs most toxins because of its molecular configuration and large surface area. Multiple doses of activated charcoal may be effective for substances that undergo enterohepatic recirculation (eg, phenobarbital, theophylline) and for sustained-release preparations. Charcoal may be given at 4- to 6-h intervals for serious poisoning with such substances unless bowel sounds are hypoactive. Charcoal is ineffective for caustics, alcohols, and simple ions (eg, cyanide, iron, other metals, lithium).

The recommended dose is 5 to 10 times that of the suspected toxin ingested. However, because the amount of toxin ingested is usually unknown, the usual dose is 1 to 2 g/kg, which is about 10 to 25 g for children < 5 yr and 50 to 100 g for older children and adults. Charcoal is given as a slurry in water or soft drinks. It may be unpalatable and results in vomiting in 30% of patients. Administration via a gastric tube may be considered, but caution should be used to preventtrauma caused by tube insertion or aspiration of charcoal; potential benefits must outweigh risks. Activated charcoal should probably be used without sorbitol or other cathartics, which have no clear benefit and can cause dehydration andelectrolyte abnormalities.

Gastric emptying

Gastric emptying, which used to be well-accepted and seems intuitively beneficial, should not be routinely done. It does not clearly reduce overall morbidity or mortality and has risks. Gastric emptying is considered if it can be done within 1 h

of a life-threatening ingestion. However, many poisonings manifest too late, and whether a poisoning is life threatening is not always clear.

Thus, gastric emptying is seldom indicated and, if a caustic substance has been ingested, is contraindicated (see Caustic Ingestion).

If gastric emptying is used, gastric lavage is the preferred method. Gastric lavage may cause complications such as epistaxis, aspiration, or, rarely, oropharyngeal or esophageal injury. Syrup of ipecac has unpredictable effects, often causes prolonged vomiting, and may not remove substantial amounts of poison from the stomach. Syrup of ipecac may be warranted if the ingested agent is highly toxic and transport time to the emergency department is unusually long, but this is uncommon in the US.

For gastric lavage, tap water is instilled and withdrawn from the stomach via a tube. The largest tube possible (usually > 36 French for adults or 24 French for children) is used so that tablet fragments can be retrieved. If patients have altered consciousness or a weak gag reflex, endotracheal intubation should be donebefore lavage to prevent aspiration. Patients are placed in the left lateral decubitusposition to prevent aspiration, and the tube is inserted orally. Because lavage sometimes forces substances farther into the GI tract, stomach contents should be aspirated and a 25-g dose of charcoal should be instilled through the tube immediately after insertion. Then aliquots (about 3 mL/kg) of tap water areinstilled, and the gastric contents are withdrawn by gravity or syringe. Lavage continues until the withdrawn fluids appear free of the substance; usually, 500 to 3000 mL of fluid must be instilled. After lavage, a 2nd 25-g dose of charcoal is instilled.

Whole-bowel irrigation

This procedure flushes the GI tract and theoretically decreases GI transit time for pills and tablets. Irrigation has not been proved to reduce morbidity or mortality.

Irrigation is indicated for any of the following:

- Some serious poisonings due to sustained-release preparations or substances that are not adsorbed by charcoal (eg, heavy metals)
- Drug packets (eg, latex-coated packets of heroin or cocaine ingested by body packers)
- A suspected bezoar

A commercially prepared solution of polyethylene glycol (which isnonabsorbable) and electrolytes is given at a rate of 1 to 2 L/h for adults or at 25to 40 mL/kg/h for children until the rectal effluent is clear; this process may require many hours or even days. The solution is usually given via a gastric tube, although some motivated patients can drink these large volumes.

Alkaline diuresis

Alkaline diuresis enhances elimination of weak acids (eg, salicylates, phenobarbital). A solution made by combining 1 L of 5% D/W with 3 50-mEq ampules of $NaHCO_3$ and 20 to 40 mEq of K can be given at a rate of 250 mL/h in adults and 2 to 3 mL/kg/h in children. Urine pH is kept at > 8, and K must be repleted. Hypernatremia, alkalemia, and fluid overload may occur but are usually not serious. However, alkaline diuresis is contraindicated in patients with renal insufficiency.

Dialysis

Common toxins that may require dialysis or hemoperfusion include

- Ethylene glycol
- Lithium
- Methanol
- Salicylates
- Theophylline

These therapies are less useful if the poison is a large or charged (polar) molecule, has a large volume of distribution (ie, if it is stored in fatty tissue), or is extensively bound to tissue protein (as with digoxin, phencyclidine,phenothiazines, or tricyclic antidepressants). The need for dialysis is usually determined by both laboratory values and clinical status. Methods of dialysis include hemodialysis, peritoneal dialysis, and lipid dialysis (which removes lipid- soluble substances from the blood), as well as hemoperfusion (which more rapidly and efficiently clears specific poisons—see Overview of Renal Replacement Therapy).

Specific antidotes

For the most commonly used antidotes, see Table: Common Specific Antidotes. Chelating drugs are used for poisoning with heavy metals and occasionally with other drugs (see Table: Guidelines for Chelation Therapy). IV fat emulsions in 10% and 20% concentrations and high-dose insulin therapy have been used to successfully treat several different cardiac toxins (eg, bupivacaine, verapamil).

Antidote therapy N-acetylcysteine (NAC): gives maximum protection against hepatotoxicity when administered within 10 hours of paracetamol overdose, but can be given with (lesser) benefit upto 36 hours Indications 1. Paracetamol ingested is more than

100 mg/kg. 2. Likelihood exists of paracetamol-induced hepatic failure General Principles in Rx of Poisoning & common drug poisoning

Salicylates Acute Poisoning: a. Early : Nausea, vomiting, sweating,tinnitus, vertigo & hyperventilation due to respiratory alkalosis. disorientation,hyperactivity, slurred speech, ataxia, and restlessness may be early findings in patients with severe toxicity b. Late— Deafness, hyperactivity, agitation, delirium, convulsions, hallucinations, hyperpyrexia. Coma is unusual c. Complications—Metabolic acidosis, pulmonary oedema,rhabdomyolysis, cardiac depression, thrombocytopenic purpura General Principles in Rx of Poisoning & common drug poisoning

Chronic Poisoning (Salicylism): ¬ This is characterised by slow onset of confusion, agitation, lethargy, disorientation, slurred speech, hallucinations, convulsions, and coma

¬ Sometimes "salicylism" presents as pseudosepsis syndrome characterised by fever, leukocytosis, hypotension, and multi-organ system failure: ARDS, acute renal failure and coagulopathy (DIC) General Principles in Rx of Poisoning & common drug poisoning Salicylates must not be therapeutically administered to children under 15 years of age, especially if they are suffering from chicken pox or influenza. There is a serious risk of precipitating Reye's syndrome which can be fatal ¬ Main feature: onset of hepatic failure& encephalopathy General Principles in Rx of Poisoning & common drug poisoning

Treatment • Patients with major signs or symptoms (metabolic acidosis,dehydration, mental status changes, seizures, pulmonary oedema) should be admitted to the Intensive Care Unit regardless of serum salicylate level • Minor symptoms only (i.e. nausea, tinnitus) following acute overdose may be managed in the emergency department with decontamination and alkaline diuresis if the salicylate level is shown to be declining General

Principles in Rx of Poisoning & common drug poisoning

Stomach wash may be beneficial upto 12 hours after ingestion, since toxic doses of salicylates often cause pylorospasm and delayed gastric emptying. • Activated charcoal (AC): It is said to be very efficacious in the treatment of salicylate poisoning since each gram of AC can adsorb 550 mg of the drug. A 10:1 ratio of AC to salicylate ingested appears to result in maximumefficiency. The initial dose of AC can be combined with a cathartic to enhance elimination. General Principles in Rx of Poisoning & common drug poisoning

OP Poisoning 1. Acute Poisoning: a. Cholinergic Excess: • Muscarinic effects: bronchoconstriction with wheezing and dyspnoea,cough, pulmonary oedema, vomiting, diarrhoea,abdominal cramps, increased salivation, lacrimation, sweating, bradycardia,hypotension,miosis, & urinary incontinence • Nicotinic effects: Muscle weakness, fatiguability, and fasciculations are very common. General Principles in Rx of Poisoning & common drug poisoning

CNS Effects—Restlessness, headache, tremor, drowsiness, delirium, slurred speech, ataxia & convulsions.Coma supervenes in the later stages ⟩ Death usually results from respiratory failure due to weakness of respiratory muscles, as well as depression of central respiratory drive. θ Chronic Poisoning: Those who are engaged in pesticide spraying of crops. The following are the main features— a. Polyneuropathy: paraesthesias, muscle cramps, weakness, gait disorders. b. CNS Effects : drowsiness, confusion, irritability, anxiety General Principles in Rx of Poisoning & common drug poisoning

Acute Poisoning: a. Decontamination: ¬ If skin spillage has occurred, it is imperative that the patient should be undressed & washed thoroughly with soap & water ¬ If ocular exposure has occurred, copious eye irrigation should be done with normal saline or Ringer's solution. If these are not immediately available, tap water

can be used General Principles in Rx of Poisoning & common drug poisoning Treatment

Antidotes: ¬ Atropine—It is a competitive antagonist of acetylcholine at the muscarinic postsynaptic membrane & in the CNS & blocks the muscarinic manifestations of organophosphate poisoning ¬ Oximes—The commonest is pralidoxime, which is a nucleophilic

oxime that helps to regenerate acetylcholinesterase at muscarinic, nicotinic, & CNS sites GeneralPrinciples in Rx of Poisoning & common drug poisoning

Supportive Measures: ¬ Administer IV fluids to replace losses ¬ Maintain airway patency and oxygenation. Suction secretions. Endotracheal intubation and mechanical ventilation may be necessary. Monitor pulse oximetry or arterial blood gases to determine need for supplemental oxygen ¬ The following drugs are contraindicated: parasympathomimetics, phenothiazines, antihistamines General Principles in Rx of Poisoning & common drug poisoning

Barbiturates Poisoning is mostly suicidal,rarely accidental θ Characterized by respiratory failure,cardiovascular collapse,coma & renal failure θ Treatment : Gastric lavage,artificial respiration & forced alkaline diuresis with mannitol & sodium bicarbonate General Principles in Rx of Poisoning & common drug poisoning

Atropine • Belladonna poisoning may occur due to drug overdose or consumption of seeds & berries of belladonna/datura plant • Dry mouth, difficulty in swallowing & talking Dilated pupil, photophobia, blurring of near vision, palpitation, psychotic behaviour, ataxia, delirium, visual hallucinations,Hypotension, weak & rapid pulse, cardiovascular collapse with respiratory depression • Convulsions & coma occur only in severe poisoning General Principles in Rx of Poisoning & common drug

poisoning

Iron • Has a direct corrosive action on the stomach & proximal small bowel • Once absorbed, produces shock, metabolic acidosis, liver failure& death • Initially, GI symptoms prevail with persistent vomiting, abdominal pain& hemorrhage • A quiescent phase may be observed, followed by shock, coma, metabolic acidosis& liver failure General Principles in Rx of Poisoning & common drug poisoning

Treatment • Management of iron poisoning includes gastric lavage with normal saline • The treatment of choice is the antidote desferrioxamine, which chelates free serum iron in the plasma to form ferrioxamine • Indications : ¬ All critical patients who present with coma, shock, or hemorrhage ¬ All patients with a serum iron level higher than 500 mg/dL ¬ Patients who are

symptomatic with a serum iron > 300 mg/dL General Principles in Rx of Poisoning & common drug poisoning 53

Morphine • It may be accidental, suicidal or seen in drug abusers. The human lethal dose is estimated to be about 250 mg • Stupor or coma, flaccidity, shallow & occasional breathing, cyanosis, pinpoint pupil,fall in BP & shock; convulsions may be seen in few, pulmonary edema occurs at terminal stages, death is due to respiratory failure General Principles in Rx of Poisoning & common drug poisoning 54

Treatment • Consists of respiratory support & maintenance of BP (i.v.fluids, vasoconstrictors) • Gastric lavage should be done with pot. permanganate to remove unabsorbed drug • Specific antidote: Naloxone 0.4–0.8 mg i.v. repeated every 2–3 min till respiration picks up, is the specific antagonist of choice ⎫ Due to short duration of action, naloxone should be repeated every 1–4 hours, according to the response.