Chapter 11

Toxicology in Emergency Medicine

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Additional information is available at the end of the chapter

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Abstract

Poisoning is a serious worldwide public health problem. Based on WHO data in 2012, almost 190,000 people died worldwide and the number of deaths due to poisoning in 2008 exceeded the number of deaths due to motor vehicular crashes; also, poisoning death rate nearly tripled worldwide. Number of patients presenting to the emergency departments with overdose, had been increased both intentionally and accidentally. All the previous facts make Toxicology an important field in emergency medicine. Management of intoxicated patients has a unique approach because of the challenge in diagnosis and treatment of overdose cases. This chapter is focusing on general approaches for intoxicated patients and initial management and on how the history and physical examinations could help physicians to have what drug have been abused as well as review the mechanism of action, physical finding and treatment of the most common drugs-causing toxicity in addition to the drugs with high mortality morbidity rates.

Keywords: approach, decontamination, toxidrome, acetaminophen, aspirin, cardiac drug toxicity, pesticides, toxic alcohol

1. Introduction

Poisoning is a serious worldwide public health problem. Based on World Health Organization (WHO) data in 2012, almost 190,000 people died worldwide and number of deaths due to poisoning in 2008 exceeded the number of deaths due to motor vehicular crashes; also, poisoning death rate nearly tripled worldwide. Number of patients presenting to the emergency departments with overdose, had been increased both intentionally and accidentally. All the previous facts make Toxicology an important field in emergency medicine [1, 2].

Management of intoxicated patients has a unique approach because of the challenge in diagnosis and treatment of overdose cases. This chapter is focusing on general approaches for intoxicated patients and initial management and on how the history and physical examinations could help physicians to have what drug have been abused as well as review the mechanism of action, physical finding and treatment of the most common drugs-causing toxicity in addition to the drugs with high mortality morbidity rates.

2. General approach to toxicological cases in emergency medicine

Approach for the poisoned patients in emergency includes: resuscitation, history, physical examination and management.

3. Resuscitation

The initial priorities for a poisoned patient presented emergency department are: securing the air-way and breathing and stabilizing the circulation. Inadequate ventilation may need intubation and mechanical ventilation. First-line treatment of hypotension is IV fluid bolus (10–20 mL/kg), if hypotension is not responding to fluid, it may be necessary to add specific antidote. If the patient presented with signs of opioid over dose (low Glasgow coma scale-GCS respiratory depression, meiosis), give him naloxone (0.1–2.0 mg I.V), check blood sugar and treat hypoglycaemia with 50% 50 mL dextrose [3].

4. History

History is very important and can be obtained from the patient, and in case the patient is comatose or cannot give his history, we may take collateral information from family, friends or medical records looking for past psychiatry illness, previous history of suicide or drugs abuse, chronic medication… 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…), missing tablets or any empty pill bottles or other material was found around him [4].

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), Skin (cyanosis, flashing, physical signs of intravenous drugs abuse (track marks), eyes: (pupil size reactivity lacrimation and nystagmus), odour (garlic, bitter almonds, glue, alcohol etc.…), Oropharynx hyper salivation or dryness, chest: breath sound, bronchorrhea, wheezing, heart rate, rhythm regularity), abdomen(bowel sound, tenderness, and rigidity), limbs(tremors and fasciculation), patient's clothing (looking for any medications, illegal drugs) [3].

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6. Toxidromes

The term toxidrome was coined in 1970 by Mofenson and Greensher. Toxidromes are group of abnormal physical examination and abnormal vital signs known to present with specific group of medications or substances. Most common toxidromes are Cholinergic, Anticholinergic, Sympathomimetic, opioids, and serotonin syndrome [4, 5].

6.1. Cholinergics

Patients with cholinergic toxidrome present with wet manifestation. SLUDGE+3 killer B's"or DUMBELLS are simple mnemonics for the common clinical symptoms.

"SLUDGE": Salivation, Lacrimation, Urination, Defecation, GI cramping, Emesis + "Killer B's": Bronchorrhea, Bradycardia, and Bronchospasm.

"DUMBELLS": Diarrhoea, Urination, Miosis (small pupils), Bradycardia, Emesis, Lacrimation, Lethargy, and Salivation.

Most common Causes: Organophosphate pesticides, Carbamates, Same type Mushrooms and Sarin (warfare agent) [4].

6.2. Anticholinergics

Patients with Anticholinergic toxidrome with dry manifestation, delirium, tachycardia, dry flushed skin, dilated pupils, clonus, elevated temperature, decreased bowl sounds, urinary retention. Simple mnemonics: "Hot as a Hare, Mad as a Hatter, Red as a Beet, Dry as a Bone, Blind as a Bat".

Most common Causes: Antihistamines, antiparkinsonians, atropine, scopolamine, amantadine, antipsychotics, antidepressants, muscle relaxants and plants (Jimson weed) [4].

6.3. Sympathomimetics

Patient present with CNS stimulation and psychomotor agitation, elevated blood pressure, tachycardia, dilated pupils, hyperthermia, diaphoresis and seizure in severe cases.

Most common causes: cocaine, amphetamine.

6.4. Opioids

Most common clinical presentation of opioids toxidrome are: coma, respiratory depression and meiosis, hypotension, hypothermia, bradycardia and seizure may occur in propoxyphene overdose, but small pupils not always present may present with normal size pupils such in meperidine and, propoxyphene toxicities [4].

6.5. Serotonin syndrome

Patient present with altered mental status, hypertensive, and tachycardia, Myoclonus hyperreflexia, hyperthermia and increase muscles rigidity. Most common causes: SSRI interaction or overdose [4].

7. Decontaminations

Decontamination of poisoned patient means remove the patient from the toxin and remove the toxin from patient, either outside patient's body by gross washing or inside the body by gastrointestinal decontamination or enhance elimination.

7.1. Gross decontamination

Patient must be fully undressed and washed thoroughly with copious amount of water; all the clothing must be removed, and decontamination must be in isolated specific area. Gross decontamination used in chemical, biological and radiation exposure.

7.2. Gastrointestinal decontamination

There are multiple methods used for gastrointestinal decontamination including:

Emesis and gastric Lavage.

Induced vomiting by ipecac syrup and gastric lavage: those methods were used in the past and now rarely indicated because there is no evidence supporting them. They can decrease absorption and they may also increase the risk of complications. Syrup ipecac and gastric Lavage may be considered in conscious, alert patients with ingestion of potentially number of toxic drugs and present in a very short time after ingestion (<1 h). Contradictions includes: unprotected airway, Corrosive/hydrocarbon ingestion and unstable patient status (hypotensive-seizure) [6].

7.3. Activated charcoal

Activated charcoal is super-heating carbonaceous material. Activated charcoal works by reducing the absorption of substance in the gastrointestinal lumen but it is not effective in metal, alcohols, corrosive, and lithium. Most effective action can be achieved when activated charcoal is given within the first hour of ingestion. Contraindications: absent gut motility or perforation, caustic ingestion and unprotected airway (can be given through nasogastric tube if patient intubated).Complications: aspiration of activated charcoal led to pneumonitis, ARDS and other complications such as small bowel obstruction [7].

7.4. 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. Indication includes: substance with a prolonged absorption phase like sustained released medication, potential toxin not absorbed by activated charcoal such—(metals, lithium) and Body packers or suffers. Adverse effects of whole bowel irrigation could be: vomiting, bloating and rectal irritation. Contradiction: absent bowel sound or perforation [8].

7.5. Enhanced elimination

Enhanced elimination is a method used to increase the rate of toxic removal from the body so reducing the severity and duration of clinical intoxication.

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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:

Multiple dose activated charcoal (MDAC): it can be used in cases of carbamazepine, Phenobarbital, Dispone sever toxicities,

Urinary alkalinisation:

Can be used in cases of Salicylates Phenobarbitone.

Extracorporeal elimination (e.g. haemodialysis, hemofiltration, and haemoperfusion, plasmapheresis and exchange transfusion:

Can be used in cases of lithium, carbamazepine, salicylates, theophylline, and toxic.

Alcohols: ethylene glycol and methanol metformin.

7.6. Antidotes

Antidote is a substance that can prevent further poisoning from specific substances. The table below showing most common antidote used in emergency department (see **Table 1**) [4].

8. Acetaminophen poisoning

First time acetaminophen had been clinically used was in 1950 and since that time acetaminophen become most common over-the-counter antipyretic and analgesic used in public. Acetaminophen is the most common cause of acute liver failure in the United States [9, 10].

8.1. Mechanism of action

Acetaminophen metabolized in the liver and converted to nontoxic metabolites via glucuronidation (40–67%) and sulfation (20–46%). In therapeutic doses of acetaminophen, the small amount of NAPQI formed which detoxified by conjugation with reduced glutathione (GSH). Glutathione is an important tripeptide which is reduced in a NADPH dependent reaction, and used to reduce oxidants (such as NAPQI).

In large overdoses of APAP, the usual pharmacokinetic pathways are overwhelmed and saturation of the nontoxic pathways occurs. Endogenous glutathione is depleted and NAPQI cannot be detoxified. Leaving excess NAPQI to bind to intracellular proteins, cause cell death [11].

8.2. Clinical features

Symptoms are frequently nonspecific or absent in early Acetaminophen toxicity.

Toxin	Antidote
Acetaminophen	N-acetylcysteine 150 mg/kg dextrose IV over 15–60 min then50 mg/kg NAC IV over 4 h. Then 100 mg/kg NAC IV over 16 h.
Cholinergic (organophosphates, carbamates)	Atropine 1–2 mg every 2–3 mins, until there is drying of secretions
	Pralidoxime (2-PAM) 70 mg/kg IV then infusion at 500 mg/h
Anticholinesterases	Physostigmine 0.5–1 mg IV as a slow push over 5 min and repeat every 10 min
Benzodiazepines	Flumazenil 0.2 Mg repeated max dose 2 mg
β-Blockers	Glucagon 3–10 mg
Calcium channel blockers	Calcium gluconate 10% 10–30 mL IV
Cyanide	Amyl nitrite
	Sodium thiosulfate
	Sodium nitrite (3% solution)
	Vitamin B12
Digoxin	Digoxin Fab 5–10 vials
Isoniazid	Pyridoxine (vitamin B6) 70 mg/kg IV (maximum 5 gm)
Methanol, ethylene glycol	Ethanol Loading 8 mL/kg of 10% ethanol then 1–2 mL/kg/h of 10% ethanol
	Fomepizole Loading: 15 mg/kg in 100 mL IV over 30 min
	Maintenance: 10 mg/kg IV over 30 min every 12 h for 48 h
Narcotics	Naloxone 0.1–0.4 mg, may repeated
Tricyclic antidepressants	Sodium bicarbonate
	1–2 mEq/kg IV bolus followed by 2 mEq/kg per h IV infusion
iron	Desferrioxamine IV infusion dose of 15 mg/kg/h
methaemoglobinaemia	Methylene Blue 1–2 mg/kg (0.1–0.2 mL/kg of 1% solution) IV slowly over 5 min
local anaesthetics	Intravenous lipid emulsion 1–1.5 mL/kg 20% IV bolus over 1 min Repeat bolus at 3–5 min
	Then Infuse 0.25 mL/kg/min

Table 1. Antidote.

Clinical presentation of Acetaminophen toxicity divided into four stages:

- Stage I (first 24 h): Patients may present nausea, vomiting, malaise, anorexia, or may be asymptomatic. Also hypokalaemia and metabolic acidosis can be found in blood test.
- -Stage II (Days 2–3): patients develop nausea, vomiting, right upper quadrant abdominal pain and laboratory evidence of hepatotoxicity. Aminotransferases (AST and ALT) elevate into thousands.
- -Stage III (3–4 days) defined by maximum hepatotoxicity, Patients exhibit coma, encephalopathy, coagulopathy, renal failure, Jaundice, acute respiratory distress syndrome (ARDS), sepsis and cerebral oedema.
- -Stage IV (7–8 d): recovery or deterioration to multi-organ failure and death [12, 13].

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8.3. Treatment

After initial support of airway, breathing and circulation, the clinician should consider gastrointestinal (GI) decontamination by activated charcoal. The cornerstone of acetaminophen overdose is N-acetylcysteine (NAC). NAC serves as a precursor to glutathione and may also directly reduce NAPQI. Clinical data suggest that if therapy is initiated within 8 h of ingestion, NAC is completely effective in preventing hepatotoxicity. Although NAC decreases in efficacy after 8 h, the drug has a benefit at all points in time, even for patients with fulminant hepatic failure.

N-acetylcysteine should only be given to patients with hepatotoxicity or risk of developing hepatotoxicity. The Rumack-Matthew nomogram is a tool for determining potential hepatotoxicity based on Acetaminophen level and time after ingestion. The nomogram is used to determine the risk for APAP hepatotoxicity for patients who present within 24 h of an acute ingestion. Risk determination of hepatotoxicity becomes more difficult

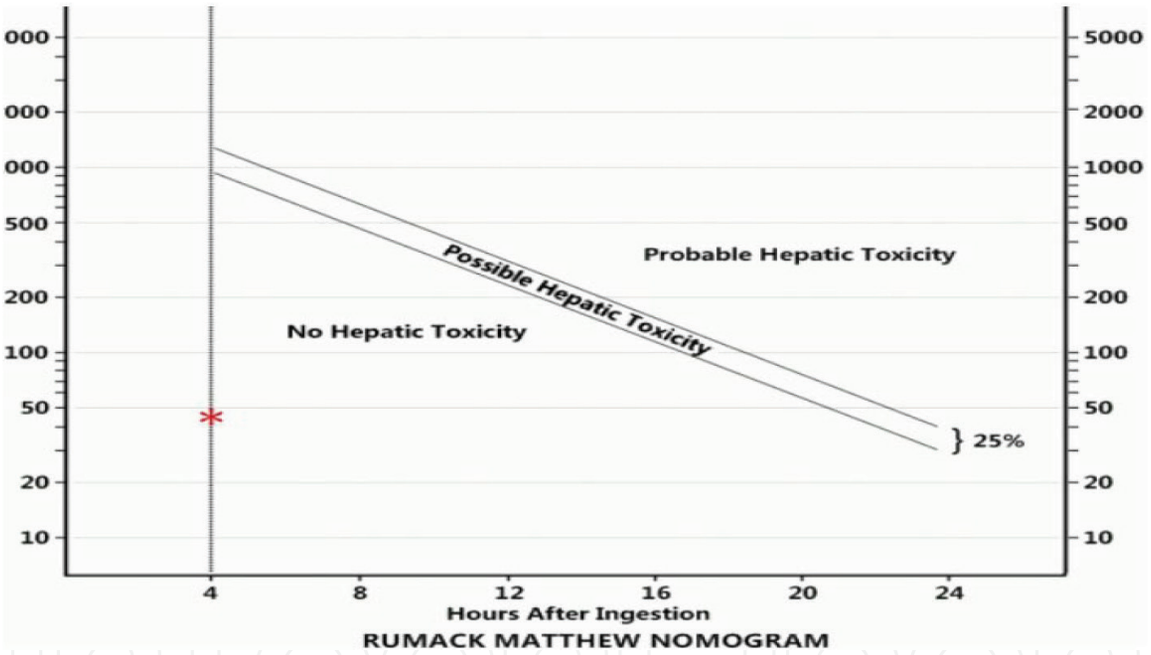

Figure 1. Rumack-Matthew nomogram.

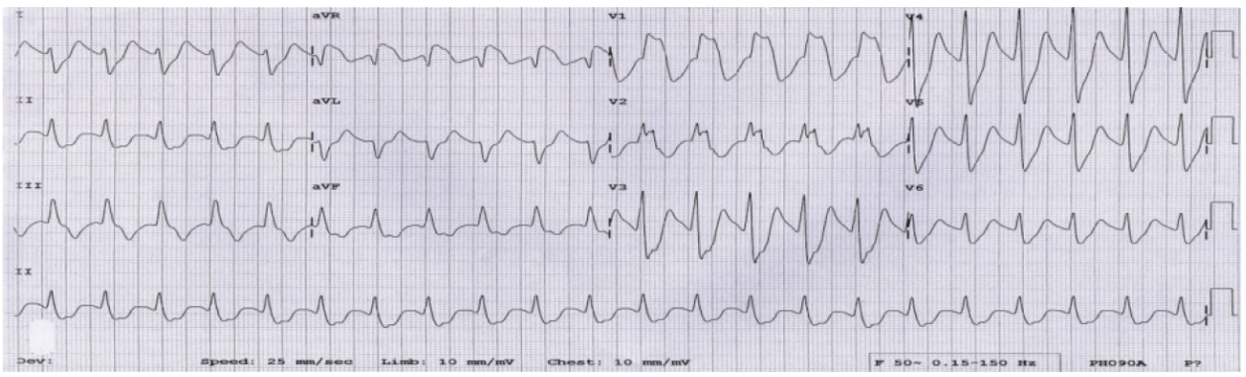

Figure 2. ECG changes in TCA toxicity.

when the nomogram is not applicable. Examples of such cases would be when the time of ingestion is unknown, when patients present more than 24 h after the ingestion and following ingestions that occur over many hours. In all of these cases NAC should be administered immediately. If aminotransferases (ALT, AST) are normal and APAP concentration is undetectable, the NAC may be discontinued. Otherwise, treatment with NAC should be continued.

N-acetylcysteine dose Oral 140 mg/kg loading dose 70 mg/kg q4 h × 17 doses or Intravenous 150 mg/kg loading dose 50 mg/kg over 4 h 100 mg/kg over 16 h [14–16] (**Figures 1** and **2**).

9. Cyclic antidepressants (CA) poisoning

Cyclic antidepressants were used to depression, but now their use has reduced greatly because of the presences of more safe agents. Cyclic antidepressants were most common antidepressants associated with overdose-related deaths in 2013 [17].

9.1. Mechanism of action

CA has multiple pharmacologic effects.

9.2. Antihistamine effects

Cyclic antidepressants are inhibiting postsynaptic histamine receptors, causing sedation, decrease level of conscious and coma.

9.3. Antimuscarinic effects

Antimuscarinic effects are divided to central and peripheral. Inhibition central acetylcholine receptors cause agitation, delirium, confusion, hallucinations, slurred speech, ataxia and coma. Inhibition Peripheral acetylcholine receptors inhibition cause dilated pupils, tachycardia, hyperthermia, hypertension, dry skin, ileus, urinary retention, increased muscle tone and tremor [18].

9.4. Inhibition of α-adrenergic receptors

This effects cause sedation, orthostatic hypotension, tachycardia and pupillary constriction, but because of the antimuscarinic effects, this action usually offsets pupillary dilatation [18].

9.5. Inhibition of amine reuptake

This effect produces mydriasis, diaphoresis, tachycardia, early hypertension, myoclonus and hyperreflexia.

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9.6. Inhibition sodium channel block

This effect produces decreased conduction velocity, increases the duration of repolarization and depressed myocardial contractility which lead to heart blocks, bradycardia and widening of the QRS complex [19].

9.7. Inhibition potassium channel block

This effect produces QT interval prolongation and rarely torsades de pointes can be seen [19].

9.8. Clinical features

Symptoms occur typically within 2 h of ingestion, which varies from mild antimuscarinic symptoms to severe cardio-toxicity. Patient may present with drowsiness, confusion, slurred speech, ataxia, sinus tachycardia, urinary retention, myoclonus and hyperreflexia. Serious toxicity is almost seen within 6 h of ingestion and patient present with: coma, cardiac conduction delays, supraventricular tachycardia, hypotension, respiratory depression, ventricular tachycardia and seizures [20, 21].

9.9. ECG changes in cyclic antidepressant poisoning

- Sinus tachycardia, most common
- Right axis deviation of the terminal 40 milliseconds positive terminal R wave in lead aVR and a negative S wave in lead I)
- Prolongation of QRS,(risk of seizures increases if the QRS complex is >100 milliseconds)
- Prolongation QT, PR
- Brugada pattern is seen 10–15%

9.10. Treatment

Treatment starts with supportive management securing airway, bolus i.v fluid in case of hypotension, GI decontamination with activated charcoal within 1 h of ingestion.

Add vasopressors if hypotensive refractory to IV normal saline. Cardiac conduction abnormalities, ventricular dysrhythmias, or hypotension refractory to IV fluid are indicated to start blood alkalization by Sodium bicarbonate Keep blood pH 7.50–7.55. Seizures, treat with Benzodiazepines if seizure refractory use Phenobarbital 10–15 mg/kg, The medication contraindication in CA toxicity are: Class I antiarrhythmic (lidocaine, phenytoin, and flecainide), Class III antiarrhythmic (amiodarone, sotalol), B-blockers, Ca channel blockers, Physostigmine and Flumazenil [22, 23].

10. Salicylate (aspirin) poisoning

Aspirin is the most common analgesic antiplatelet therapy used in cardiovascular and cerebrovascular disease. Aspirin is over-the-counter drugs and widespread used lead to accidental and intentional toxicity [24].

10.1. Mechanism of action

Salicylate Inhibit cyclooxygenase leads to decreased synthesis of prostaglandins; prostacyclin and thromboxane. It also leads to platelet dysfunction and gastric mucosal injury. Salicylate Stimulate the chemoreceptor trigger zone in the medulla which causes nausea and vomiting. Also activate respiratory centre of the medulla leading to hyperventilation and respiratory alkalosis. Uncoupling of oxidative and Inhibit the Krebs which lead to metabolic acidosis [25].

10.2. Clinical features

Salicylate toxicity divided to **acute** and **chronic** toxicities.

10.3. Acute toxicity

Acute salicylate toxicity manifests initially through GI, CNS effects and metabolic effects. Gastric irritation, vomiting and nausea may predominate early in the course and are more predominant in the acute poisoning. Rising CNS salicylate concentrations produce tinnitus, diminished auditory acuity, vertigo and hyperventilation. As the poisoning continues, the CNS effects may progress to agitation, hallucinations, delirium, seizure and lethargy. The metabolic effects of salicylate toxicity cause uncoupling of oxidative phosphorylation leading to temperature elevation (an indicator of severe toxicity) and a large anion gap metabolic acidosis. Subsequent squeal of salicylate toxicity include renal failure, acute lung injury and platelet dysfunction.

10.4. Chronic toxicity

In contrast, chronic poisoning occurs over a longer period of time, when patients ingest more drug than they can eliminate over a prolonged period. These patients tend to be older and the overdose is unintentional. The initial presenting signs and symptoms include those of acute toxicity although with slower onset and lesser severity. Chronic toxicity may easily be confused in the elderly for sepsis, ketoacidosis, delirium, dementia, CHF or respiratory failure. Diagnostic delay in the chronically poisoned patient has been shown to cause increased morbidity and mortality.

10.5. Treatment

Stabilization of the airway, breathing and circulation are the first steps in management. Intubation may increases the severity of the aspirin toxicity, so it is better to be avoided, but if intubation is necessary patients need appropriately high minute ventilation sitting. In case of volume depleted and acidosis, start treatment with I. V fluid. Gastrointestinal decontamination with Activated charcoal may help in early ingestion. Whole bowel irrigation

(WBI) is useful in case of massive ingestions or sustained preparation or enteric-coated. Sever Salicylate toxicity treated with serum Alkalinisation by sodium bicarbonate with a aim of a serum pH of ~7.5.Patients may need haemodialysis and the indications for haemodialysis are clinical deterioration, severe acid-base disturbance, altered mental status, and acute lung injury, failure of serum and urine alkalinisation and renal failure [26–28].

11. Opioids poisoning

Opioid abuse is a significant medical and social problem in the world. In the past 10 years, the number of abuses and deaths from opioid overdoses had been increased. Opioids are all substances related to opium. They have analgesic and sedative effects. Opiate is extracted from the poppy plants [29].

11.1. Mechanism of action

There are three main opioid receptors: μ (mu), κ (kappa), and δ (delta), and Opioids have agonists effect on this receptors. Stimulation of opioids receptors will cause miosis, respiratory depression, cough suppression, euphoria and decreased GI motility.

11.2. Clinical features

Classic signs of opioid intoxication toxidrome, depressed mental status, decreased respiratory rate miosis, (constricted) pupils. Other finding includes: decreased bowel sounds orthostatic hypotension, urinary retention and localized urticaria. Normal pupil examination can be seen, meperidine diphenoxylate, propoxyphene toxicity and co-ingestion of other toxin such as sympathomimetic or anticholinergic.

Same opioids have specific clinical feature (**Table 2**) [30, 32]:

Opioids agent	Specific clinical feature
Dextromethorphan	Serotonin toxicity; at high doses
Loperamide	QRS and QT prolongation; Wide-complex tachycardia
Meperidine	Seizure, normal pupils size
	Serotonin syndrome (in combination with other agents)
Methadone	long-acting;
	QT prolongation, Torsade de Pointes
Oxycodone	QT interval prolongation
Tramadol	Seizure
Heroin	Acute lung injury

Body packing: swallowing packets or containers of drug for the purposes of smuggling.
Body stuffing: swallowing of a smaller quantity of drug because of fear of arrest.

Table 2. Opioids with specific clinical feature.

11.3. Treatment

Secure Airway and maintain adequate oxygenation and ventilation by using bag-valve mask are the first important steps in treatment; serum glucose should be checked. After that administer naloxone 0.4 mg IV, in non-opioid-dependent with minimal respiratory depression abut if patient is opioid-dependent present with minimal respiratory depression, administer small dose of naloxone, 0.1 mg IV, because larger doses can induce opioid withdrawal symptoms. Patients presenting with apnea or near-apnea and cyanosis, start naloxone, 2 mg IV regardless of drug use history, can be repeated IV every 3 min [30–32].

12. Sympathomimetic (cocaine) poisoning

Cocaine is one of the most potent Sympathomimetic, extracted from the leaves of the coca by indigenous to South America; therapeutically, first time Cocaine was used in 1884 as a local anaesthetic for ophthalmologic procedures. In the United States Cocaine is one of the most common causes of acute drug-related emergency department visits.

12.1. Mechanism of action

Cocaine stimulates alpha and adrenergic receptors by increasing levels of norepinephrine, causing vasoconstriction in cardiovascular system, also inhibits neuronal serotonin reuptake which lead to euphoria. Cocaine blocks Sodium (Na+) channel causing QRS interval prolongation [33, 34].

12.2. Clinical features

Cocaine toxicity may cause sympathomimetic and vasoconstrictive effects on variety systems (cardiovascular, CNS …etc.).

Cardiovascular: patients with cocaine toxicity present with high blood pressure and dysrhythmias include tachycardia, such as sinus tachycardia, SVT, and AF. ECG changes include rightward shift of the terminal portion of the QRS complex and prolongation the QT interval. Patients may present with acute coronary syndromes (cocaine-associated acute coronary syndrome), aortic and coronary artery dissection, myocarditis and cardiomyopathy. CNS: patients with Cocaine present with a variety CNS clinical features including: agitation, seizures, and coma. Pulmonary: mainly seen in patients who smoke crack cocaine includes pulmonary haemorrhage, barotrauma, pneumonitis and asthma.

Gastrointestinal: Cocaine may cause intestinal ischemia, bowel necrosis and ischemic colitis, also increase risk for bleeding and ulcer perforation. Renal: acute kidney failure may occur because of rhabdomyolysis [35–37].

12.3. Treatment

Securing the airway and adequate breathing are initial steps in treatment. CNS manifestation (agitation, seizure) treated with sedation by Benzodiazepines, patient with Hyperthermia

should be cooled rapidly, severe hypertension not responding to sedation can be treated with a sodium nitroprusside infusion or phentolamine; (avoid B-ac blockers). Cocaine toxicity with acute coronary syndrome are treated with aspirin and nitroglycerin also may add calcium channel blockers, wide-complex tachycardia with cocaine toxicity treated with serum alkalinisation by sodium bicarbonate, make sure serum Ph do not exceed 7.55. Intravenous lipid emulsion can be used in severe cocaine toxicity, with refractory cardiovascular instability or refractory wide-complex tachycardia [37].

13. Digitalis glycosides poisoning

Cardiac glycosides were used in treatment of heart failure since long time. Since 1785 glycosides found in plants like lily of the valley foxglove and oleander. Digoxin is most common digitalis drug used today for treatment of atrial fibrillation and congestive heart failure [38].

13.1. Mechanism of action

Digoxin inhibits Na + -K + -ATPase during repolarization which leading to increase in intracellular sodium and a decrease in intracellular potassium leading to increase in the intracellular concentration of calcium causing Positive inotropic, also increase automaticity and shorten the repolarization intervals of the atria and ventricles [39].

13.2. Clinical features

Digoxin toxicity divided to acute and chronic toxicities.

13.3. Acute toxicity

The cause of acute toxicity is usually intentional or accidental ingestion, symptoms usually abrupt in onset, patients present with nausea, vomiting, non-specific abdominal pain, headache and dizziness. Sever toxicity may cause confusion and coma, Bradydysrhythmia and atrioventricular block or supraventricular tachydysrhythmia and hyperkalaemia. Xanthopsia is a classic eye future in digoxin toxicity (viewing yellow-green halos around objects), but the most common finding is nonspecific changes in their colour vision. Serum digoxin level usually marked elevated [40, 41].

13.4. Chronic toxicity

Chronic toxicity is commonly and mainly seen in elderly patients and common causes are interaction with other medications (calcium channel antagonists, amiodarone, β-receptor antagonists, and diuretics) or renal insufficiency which causes decree the clearance of digoxin.

In contract of acute toxicity, where Gastrointestinal symptoms are prominent in chronic toxicity CNS symptoms (weakness, fatigue, confusion, or delirium) are more prominent. Ventricular dysrhythmias are commonly seen in chronic toxicity. Serum potassium level can be normal or decreased, also serum digoxin level usually minimally elevated [40, 41].

13.5. Treatment

General supportive care is an Initial step in treatment of digoxin toxicity; it includes securing airway and adequate ventilation and boluses of fluid IV in case of hypotension. Activated charcoal helps in early acute ingestion [42], Atropine can be given in case of Symptomatic bradycardia). Digoxin-specific antibody fragments (digoxin-Fab) are antidotes for digoxin. The indication to use (digoxin- Fab) includes Life-threatening dysrhythmias unresponsive to standard therapy and hyperkalaemia excess 6 mEq/L. [43] Digoxin-Fab doses are based on the total-body load of digoxin, which can be calculated from either the estimated dose ingested or the serum digoxin level, each vial of Digoxin-Fab reverses approximately 0.5 mg of ingested digoxin. If the amount of ingested digitalis is unknown, digoxin Fab 10 vials for adults empirically can be given. Hyperkalaemia is treated with insulin, dextrose, sodium bicarbonate. The use of calcium salts in digoxin induced hyperkalaemia is controversial because old literature shows increase incidence of ventricular dysrhythmias and increase mortality [44].

14. Beta-blockers poisoning

Beta adrenergic antagonists (beta blockers) are groups of medications which have been used in treatment of different cardiovascular, neurological and ophthalmological diseases more than 30 years, Bête blockers toxicity has significant morbidity and mortality [17].

14.1. Mechanism of action

Beta receptors are divided by location and action to beta 1, beta 2, and beta 3 (see the **Table 3**).

There are two groups of beta-blockers: selective and non-selective.

Competitive antagonism of the beta receptor decreases cellular levels of cyclic adenosine monophosphate (cAMP). Beta-1 selective blocker causing in depressed myocardial contractility,

	Location	Action	Antagonism
B1	Myocardium	Increases inotropy	Decreases inotropy
	Kidney	Increases chronotropy	Decreases chronotropy
	Eye	Stimulates renin release	Inhibits renin release
B2	Bronchial smooth muscle	bronchodilation	Causes bronchospasm
	Skeletal muscle	Relaxes uterus	Inhibits glycogenolysis and gluconeogenesis
	Liver	Increases force of contraction	
	Vascular	Stimulates glycogenolysis and gluconeogenesis	Minimal vasoconstriction
		Vasodilation	
B3	Adipose tissue	Stimulates lipolysis	Inhibits lipolysis
	Skeletal muscle	Stimulates thermogenesis	Inhibits thermogenesis

Table 3. Beta receptor: Locations and actions.

decreased automaticity in pacemaker cells, and decreased conduction through the AV node. Non- selective beta blockade results in systemic effects including bronchoconstriction, impaired gluconeogenesis and decreased insulin release. Same Beta blockers (e.g., propranolol) have high lipid solubility leading to rapid cross of the blood brain barrier into the central nervous system, causing a neurological manifestation such as seizures and delirium [45, 47].

14.2. Clinical features

The major system affected by β-blocker toxicity is the cardiovascular system; patients present with bradycardia and hypotensive. The cause of bradycardia is sinus node suppression or conduction abnormalities but ingestion of β-blockers with partial agonist activity may cause hypertension and tachycardia as early presentation. The β-blockers with sodium channel block affect may cause a wide-complex bradycardia.

Sotalol causes potassium channels block leading to prolonging the QT interval.

B-Blockers also have effect on CNS and pulmonary system. Neurologic features include delirium, coma and seizures with more lipophilic. B-blockers (propranolol) have more neurological manifestations. Bronchospasm and hypoglycaemia can be in β-blockers toxicity [47, 48].

14.3. Treatment

GI decontamination can be done by giving Activated charcoal within 1 h of ingestion and air way is the main aim treatment in beta-blocker toxicity focusing on restore perfusion to critical organ systems by increasing cardiac output by: fluid resuscitation and glucagon (3–10 mg), vasopressor (e.g., epinephrine) and high dose Insulin- glucose (insulin 1 unit/kg IV bolus). Intravenous lipid emulsion therapy may be used in case of sever toxicity and refractory to treatment. In case of refractory to pharmacologic therapy, haemodialysis, haemoperfusion, cardiac pacing, placement of intra-aortic balloon pumps can be used. Wide QRS-interval dysrhythmias due to sodium channel blockade treated with sodium bicarbonate 2–3 mEq/kg over 1–2 min [49, 50].

15. Calcium channel blocker poisoning

Calcium channel blockers (CCBs) are mainly used in the treatment of cardiovascular diseases such as hypertension, coronary artery disseise- CAD and cardiac arrhythmias Calcium channel blockers one most prescribed cardiovascular drugs and can be immediate-release or extended-release [17].

15.1. Mechanism of action

The calcium channel blockers (CCBs) can be divided into two major groups based upon their major physiologic effects: the dihydropyridines, group which mainly block the L-type calcium channels in the vasculature and the non-dihydropyridines, which selectively block L-type calcium channels in the myocardium such as verapamil. Dihydropyridine group toxicity causes arterial vasodilation and reflex tachycardia, whereas non-dihydropyridines toxicity cause peripheral vasodilation decreased cardiac inotropy, and bradycardia [46].

15.2. Clinical features

Cardiovascular system is the most affected system in CCBs toxicity. Patient present with hypotension and bradycardia or reflex tachycardia. Verapamil or diltiazem toxicity usually patients present with sinus bradycardia, on the hand dihydropyridine overdoses cause peripheral vasodilatation causing reflex tachycardia [55]. CCBs have not primary effect on pulmonary and CNS System; CNS symptoms (seizures, delirium, and coma) occur secondary to decrease organ perfusion. Cardiogenic pulmonary oedema and acute lung injury (non-cardiogenic pulmonary oedema) have also been reported in severe toxicity [48].

15.3. Treatment

First step in management is secure airway, stabilize ventilation and circulation.

Decontamination can be done by oral activated charcoal if patient present within 1 h of ingestion also the whole-bowel irrigation is useful in case of extended-release CCBs. Hypotension treated with IV fluid, Calcium chloride or calcium gluconate, glucagon (3–10 mg), if not responding start Vasopressors (e.g., norepinephrine). If symptoms refractory to vasopressor therapy start, high dose Insulin -glucose. If patient still not responding, lipid emulsion can be started. Finally, circulatory support measures, such as the placement of intra-aortic balloon pumps may be used in case of sever toxicity not responding to standard therapy [49–51].

16. Carbon monoxide poisoning

Carbon monoxide (CO) is an odourless, tasteless, colourless and non-irritating gas.

Potential sources of Carbon monoxide (CO) are automotive exhaust, fuelled heaters, Wood- or coal-burning stoves, Structure fires and gasoline-powered generators other than fires.

The incidence of co -poisoning increases during winter time because the use of space heaters, wood-burning stoves and charcoal burning for heat.

16.1. Mechanism of action

Carbon monoxide (CO) diffuses fast in the pulmonary capillary membrane and because of his rapid binding affinity (more than oxygen by 200 times), carbon monoxide bind to haemoglobin, that cause impaired releasing oxygen to tissue leading to shift the oxyhaemoglobin dissociation curve to the left [51].

16.2. Clinical features

Carbon monoxide poisoning have variable clinical picture depend on severity of exposure ranging from non-specific symptoms like headache, nausea and dizziness in mild to moderate cases to confusion, seizure and coma in severe cases patients may present with mild fever, tachycardia, tachypnoea and hypertension. Acute myocardial injury and life-threatening dysrhythmias are the most cardiovascular complications in case of severe Carbon monoxide poisoning. Delayed neuropsychiatric syndrome is long term neurological complication in

severe cases characterized with different symptoms including cognitive deficiency, movement disorders and focal neurologic deficit. The standard pulse oximetry cannot differentiate carboxyhaemoglobin from oxyhaemoglobin, so it is unreliable in the diagnosis or screen carbon monoxide poisoning, so measuring carboxyhaemoglobin level in an arterial blood gas helps in diagnosis [52–55].

16.3. Treatment

After securing the airway, the most important step in treatment is oxygen 100% via non-rebreathing mask or intubation and mechanically ventilation with 100% oxygen if the patient is comatose and cannot secure his air way, half-life of carboxyhaemoglobin in room air 250–320 min while via non-rebreathing with 100% oxygen decreased to 90 min. Hyperbaric oxygen therapy could be considered in certain cases, the indication for Hyperbaric oxygen includes Pregnancy with carboxyhaemoglobin level > 15%, Carboxyhaemoglobin >25%, evidence of acute myocardial ischemia, and severe metabolic acidosis [56].

17. Iron toxicity

Iron tablets are usually available in homes with small children and young women especially pregnant women. Because of its colour, sugar taste and appearance like a candy make iron tablet more attractive for accidental ingestion for children [57].

17.1. Mechanism of action

Iron exerts a direct corrosive effect on the gastrointestinal tract at high plasma concentrations; it also possesses cytotoxic actions, particularly on the liver, leading to hepatocellular necrosis. Additionally, iron has a direct cardio- toxic effect acting as a negative inotrope and inhibits thrombin leading to a coagulopathy independent of hepatotoxicity. The direct corrosive effects and cellular toxicity contribute to metabolic acidosis [58].

17.2. Clinical features

Serious iron poisoning usually causes symptoms within 6 h of the overdose and if the ingested elemental iron more than 20 mg/kg body, the symptoms of iron poisoning typically occur in 5 stages:

Stage 1 (within 6 h after the overdose): Symptoms include vomiting, vomiting blood, diarrhoea, abdominal pain, irritability and drowsiness. If poisoning is very serious, rapid breathing, a rapid heart rate, coma, unconsciousness, seizures, and low blood pressure may develop.

Stage 2 (6–48 h after the overdose): condition can appear to improve (there is often a latent phase with minimal symptoms which may last up to 24 h and may be misinterpreted as an apparent recovery).

Stage 3 (12–48 h after the overdose): Very low blood pressure (shock), fever, bleeding, jaundice, liver failure, metabolic acidosis and seizures can develop.

Stage 4 (2–5 days after the overdose): The liver fails and people may die from shock, bleeding, and blood-clotting abnormalities. Sugar levels in the blood can decrease. Confusion and sluggishness (lethargy) or coma may develop.

Stage 5 (2–5 weeks after the overdose): The stomach or intestines can become blocked by scars [59, 60].

17.3. Treatment

First step stabilize the air way, breathing and circulation. An abdominal x-ray may be helpful to confirm the presence of iron tablets. Consider GI decontamination by whole bowel irrigation if the patient is stable and has no contraindications, especially for large ingestions of modified release products, providing the airway can be protected. Activated charcoal does not bind iron. Asymptomatic patients need observation for 6 h and serum iron levels less than 300–350 mcg/dL may be discharged.

Chelation therapy with deferoxamine is indicated for patients with serum iron levels >350 mcg/dL and have evidence of toxicity, or levels of >500 mcg/dL regardless of signs or symptoms. In patients with significant clinical manifestations of toxicity persistent emesis, metabolic acidosis, chelation therapy should not be delayed while one awaits serum iron levels. Haemodialysis does not remove iron effectively but should be considered on a supportive basis for acute renal failure as this will facilitate removal of the iron-deferoxamine complex [61, 62].

18. Toxic alcohol poisoning

The term toxic alcohol has generally referred to isopropanol, methanol, and ethylene glycol (EG). Poisoning involving toxic alcohols are relatively uncommon, but remain important causes of suicide or epidemic poisonings; Mortality and morbidity of toxic alcohols are high if prompt diagnosis and treatment are not initiated rapidly [63, 64].

18.1. .Mechanism of action and clinical features

Methanol also called methyl alcohol is found in paint removers or photocopying fluid, deicing products and windshield wiper fluid. Methanol metabolism in the liver by alcohol dehydrogenase to formaldehyde. Aldehyde dehydrogenase then rapidly converts formaldehyde to formic acid with no appreciable accumulation of formaldehyde in the blood.

The formic acid inhibits cytochrome c in the mitochondria, shifting the cell to anaerobic glycolysis, leading to lactic acid accumulation. The clinical features of methanol poisoning are the triad of severe anion gap metabolic acidosis, visual changes, and mental status depression. Other methanol intoxication symptoms include headache, light-headedness, nausea, vomiting, abdominal pain and dyspnoea. Methanol may produce pancreatitis by direct toxic effect on the pancreas.

Ethylene glycol is found in radiator antifreeze, metal cleaners, and degreasing agents. It has no smell or colour and tastes sweet. Ethylene glycol is metabolized in the liver to glycolaldehyde

by alcohol dehydrogenase. Glycolaldehyde is then converted to glycolic acid which is then converted to oxalic acid. Oxalic acid combines with serum calcium to form the classic calcium oxalate crystals found in the urine of patients who have consumed ethylene glycol.

Ethylene glycol causes an elevated anion gap metabolic acidosis. The neurologic effects of ethylene glycol are coma, seizures, meningism, muscle spasms, and paralysis of the extraocular muscles. It can also affect the heart and lungs, causing tachycardia, hyperventilation, ARDS, and heart failure. Hypocalcaemia and resulting QT prolongation are due to serum calcium combining with oxalic acid. Lastly, kidney failure is due to these calcium crystals depositing into renal tubules.

Isopropyl alcohol is found in solvents and disinfectants. It is also found in mouthwashes, lotions, as well as rubbing alcohol and hand sanitizers. It is also hepatically metabolized by alcohol dehydrogenase to acetone. Isopropanol produces an increased osmole gap; however, it normally does not produce a metabolic acidosis unless concomitant hypotension causes lactic acidosis. It can cause haemorrhagic gastritis and profound inebriation with cerebellar signs and coma [64–70].

18.2. Investigations

An osmolar gap more than 10 mOsm/kg is suggestive of ethylene glycol, methanol, isopropanol, ethylene oxide, or acetone toxicity. A high anion gap metabolic acidosis may be revealed at later stages of methanol and ethylene glycol poisoning. Hypoglycaemia may be detected with isopropanol, while hyperglycaemia and hypocalcaemia may be detected in methanol and ethylene glycol poisonings, respectively. Hyperkalaemia due to acidosis is observed in methanol and ethylene glycol poisoning, whereas hypokalaemia due to vomiting may occur in ethanol intoxication.

Urine calcium oxalate crystals can be seen in ethylene glycol intoxication. These findings should be evaluated together with the other manifestations and observations [71, 72].

18.3. Treatment

Any patient with serious poisoning may present in a critical condition. As with all poisoned patients, initial stabilization must be instituted before other possible treatments can be employed Initial evaluation should be focused on the improvement of vital signs: airway, respiration and circulation.

Consider toxic alcohol poisoning in a patient with an unexplained elevated anion gap metabolic acidosis and elevated osmolar gap.

Fomepizole competitively inhibits alcohol dehydrogenase, which is involved in the metabolism of all alcohols, including ethanol. It is given to prevent the build-up of toxic metabolites from ethylene glycol (glycolic acid, glyoxylic acid, and oxalic acid) and methanol (formic acid) whose deposition in tissues can cause irreparable damage.

Fomepizole is indicated for methanol or ethylene glycol ingestion resulting in a metabolic acidosis with an elevated osmolar gap and a serum Methanol or ethylene glycol level of at least 20 mg/dL.

Haemodialysis is indicated for toxic alcohol poisoning with an elevated osmolar gap and/or severe metabolic acidosis refractory to standard therapy, refractory hypotension, or end

organ damage (i.e. acute renal failure. Vitamin Supplementation: Give folic or folinic acid to patients with methanol toxicity to divert metabolism away from formic acid to carbon dioxide and water. Give folic acid, pyridoxine, and thiamine to patients with EG toxicity to divert metabolism to nontoxic metabolites [73–76].

19. Organophosphates poisoning

Organophosphates (OP) are used in insecticides for domestic and agricultural use. They are also the main toxins in nerve gases like Sarin. OP pesticide self-poisoning is a major clinical and public-health problem across much of rural Asia [77].

19.1. Mechanism of action

The most serious poisoning of OP occurs by ingestion; cutaneous absorption and inhalation of sprays rarely cause serious toxicity. OP is extremely toxic pesticides, which produce acetylcholine excess with muscarinic, nicotinic and CNS effects.

19.2. Clinical features

Patients present with degrees of cholinergic crisis, usually within 4 h of ingestion or exposure. Specific manifestations include: Muscarinic manifestations like bronchospasm, vomiting, pinpoint pupils, bradycardia and hypotension, excessive sweating, lacrimation, salivation, profuse diarrhoea and urination (**Table 4**).

Over-stimulation of nicotinic receptors causes tachycardia, hypertension and sweating. Accumulation of acetylcholine at the neuromuscular junction causes initial stimulation followed by depolarization and paralysis. This appears first as fasciculations, cramps and muscle weakness. Central nervous system (CNS) effects include delirium, coma and seizures. Most deaths are due to respiratory failure. Toxicity from gradual, cumulative exposure may be much more subtle. These patients commonly exhibit vague confusion or other central nervous system complaints; mild visual disturbances; or chronic abdominal cramping, nausea, and diarrhoea. A unique effect of organophosphorus insecticides results from "aging," the irreversible conformational change that occurs when the organophosphorus agent is bound to the

Diarrhoea
Urination
Miosis
Bronchospasm
Emesis
Lacrimation
Salivation

Table 4. DUMBELS mnemonic for signs of cholinergic excess.

cholinesterase enzyme for a prolonged time, causing clinical effects to persist for a prolonged time. On average, some aging for commercial organophosphorus agents will occur by 48 h but may take longer. The intermediate syndrome is distinct from OP in the following ways: start within 24–96 h after recovery from acute cholinergic crisis, cranial nerves INNERVATED muscle and proximal muscles weakness, and rapid clinical recovery over 4–18 days. Any patient with a clinically apparent cholinergic syndrome should be treated empirically without waiting for laboratory confirmation of decreased cholinesterase activity [78].

19.3. Treatment

Medical management of OP pesticide poisoning demands close observation, timely institution of antidote in adequate doses and duration and good supportive. The Treating staff should wear protective clothing. The patient's clothes should be removed and destroyed and the patient should be showered in a designated decontamination area.

Treatment includes: resuscitation of patients giving oxygen, a muscarinic antagonist (usually atropine), fluids and an acetylcholinesterase reactivator (an oxime that reactivates acetylcholinesterase by removal of the phosphate group).

Respiratory support is given as necessary. Patients must be carefully observed after stabilization for changes in atropine needs, worsening respiratory function because of intermediate syndrome, and recurrent cholinergic features occurring with fat-soluble OP [79].

20. Conclusion

Poisoned patient in emergency department have unique Approach because of difficulties in obtain history, poisoned patients need careful physical examination looking for toxidromes or sign of illegal drugs abuse. Intoxicated patient's management started with resuscitation and stabilization of air way, breathing and circulation. Consider decontamination in early time post ingestion. Most of the patient need laboratory test includes full cell count and electrolytes and kidney functions, specific drug level. Paracetamol level must be send for every present with history intestinal over dose. Symptomatic treatment is cornerstone treatment for post intoxicated patient also antidotes need for specific substances in specific conditions. Finally physicians in emergency department need to call the local poisoning centre to help them in management.

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