Chapter

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# Common Poisonings in Medical Practice

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Poisoning is a major problem globally and its incidence is rising due to rapid industrialization and urbanization. The exact incidence of acute poisoning is not known in India because of lack of any central poison registry. The toxins involved in acute poisoning cases vary from place to place. In western countries, the commonest toxins are medicinal agents. In contrast, in India, insecticides and pesticides are the most commonly consumed agents in adults while kerosene oil is the most common toxin in children. Over the last decade or so, the number of cases with drug overdose has increased. Besides these agents, plant poisons constitute a significant proportion of patients reported from the southern part of India. Knowledge of commonly encountered poisons in a particular area is important for practicing physicians as it may help in early diagnosis and institution of life-saving treatment. Some of the important poisonings seen in medical practice will be discussed in this chapter.

## ORGANOPHOSPHATES AND CARBAMATES

Organophosphates (OPs) and carbamates are widely used as agricultural, industrial and domestic insecticides and are known as cholinesterase inhibitors. These compounds are rapidly absorbed by all routes—respiratory, gastrointestinal, eyes and skin. OPs include malathion, parathion, methylparathion, fenitrothion, diazinon, dichlorovas and trichlorophon, etc. Carbamates include carbaryl, propoxur and carbofuran.

### Mechanism of Toxicity

OPs and carbamates inhibit the enzyme, acetylcholinesterase (AChE) which hydrolyzes acetylcholine released at autonomic synaptic junctions. OPs cause irreversible inhibition of AChE while carbamates produce reversible inhibition. Inhibition of AChE leads to accumulation of acetylcholine at both sympathetic and parasympathetic synaptic junctions resulting in initial stimulation followed by paralysis of neurotransmission. The cholinergic synapses are present in CNS, somatic nerves, autonomic ganglion, parasympathetic nerve endings, neuromuscular junctions and some sympathetic nerve endings like in sweat glands[1].

### Clinical Features of Intoxication

Features of acute intoxication may be classified into 3 categories: muscarinic, nicotinic and central nervous system features[2].

***Muscarinic features:*** The muscarinic features of intoxication can be remembered by using the mnemonic DUMBELS - diarrhea, urination, miosis, bronchorrhea, bronchoconstriction, bradycardia (less common), emesis, lacrimation, salivation and sweating. Bronchorrhea and bronchoconstriction can lead to compromise of respiratory function.

***Nicotinic features:*** These features include mydriasis (rare), tachycardia, muscle weakness, hypertension, muscle cramps, fatigue, and muscle fasciculations.

***CNS features:*** These include severe headache, restlessness, generalized weakness, confusion, coma, convulsions, and finally depression of cardio-respiratory center.

***Other features:*** Acute garlic odour of exhaled breath is a characteristic feature of this poisoning. ECG changes in the form of ST-T changes and low voltage ECG are seen in about 50% cases. Uncommonly, arrhythmias like AV dissociation, multiform ventricular extrasystoles,

polymorphic ventricular tachycardia and torsade de pointes can occur.

### *Intermediate Syndrome*

A few patients with OP poisoning can develop muscular paralysis between 24 and 96 hours of poisoning, know as intermediate syndrome[3]. This syndrome is characterized by weakness of upper extremities and neck musculature, cranial nerve palsies (particularly ophthalmoplegia), and respiratory muscle paralysis producing respiratory failure.

### Management

Patients with respiratory paralysis, pulmonary edema, seizures and coma are considered to have severe poisoning and require management in an intensive care unit along with the use of antidotes. Patients without above-mentioned features but otherwise having muscarinic and nicotinic features will require antidotal therapy and if available, an intensive care monitoring. Various steps in management are as follows:

1. Establish airway, suctioning and oxygenation; if required, intubate the patient.
2. Decontaminate the gut and skin (if cutaneoeus exposure has occurred). For gut decontamination, a gastric lavage may be performed if the time between ingestion and presentation is below 4 hours unless the patient has serious toxicity when a delayed lavage may be justified. Activated charcoal (30-100 g in water or sorbitol) reduces the absorption of poison.
3. *Administration of specific antidote:*
   a. Atropine: Atropine is given intravenously in a dose of 2-5 mg IV in adults and 0.04-0.08 mg/kg in the children. The same dose is repeated every 5-10 minutes till signs of atropinization (clearing of crepitations, drying of pulmonary secretions, drying of mouth) appear. Tachycardia and pupillary dilatation are not good indicators of atropinization. After that, the dose of atropine and frequency of administration are gradually reduced while maintaining the signs of atropinization. The maintenance dose may also be given as a continuous infusion at the rate of 0.02-0.1 mg/kg/hour[4] and is continued for 2-5 days and then slowly withdrawn on 3rd to 7th day.
   b. Pralidoxime: Pralidoxime (PAM) is an oxime which regenerates cholinesterase enzyme at all sites. It is given in doses of 1-2 g (30 mg/kg in children) intravenously over 15-20 minutes.[4] Second dose may be given after 1 hour. Following this, PAM is administered by continuous infusion in a dose of 500 mg/hour in adults and 9 mg/kg/hour in children. PAM should not be used in patients with carbaryl poisoning. However, its role in the management of poisoning with other carbamates is not clear. PAM may be of use if the patient fails to respond to adequate atropine, or has severe poisoning by unidentified cholinesterase inhibitor.

## ALUMINIUM PHOSPHIDE

Aluminium phosphide (A1P) is a solid fumigant which is widely used as a pesticide to preserve grains. Since early 1980s, several series of poisoning due to ingestion of A1P have been reported from different northern states of India[5,7]. In 1990s, A1P was the leading cause of suicidal poisoning in north India. A1P is available as 3 g tablets or powder which liberates phosphine gas (PHa) on coming in contact with water.

### Clinical Features of Intoxication

The fatal dose of an unexposed pellet of aluminium phosphide is 150-500 mg. Clinical manifestations develop within 30 minutes of ingestion.

1. Initially, the patient complains of retrosternal burning, epigastric discomfort, and recurrent vomiting.[5,7] There is fishy smell from the breath.
2. Within next few hours, the patient develops features related to cardiovascular and respiratory systems. Hypotension and shock occur due to cardiotoxicity, recurrent vomiting and widespread vascular injury. Myocardial injury may produce ventricular arrhythmias, conduction blocks, ST depression and T wave inversion.
3. The respiratory features include cough, dyspnea, pulmonary edema and ARDS.
4. Severe metabolic acidosis is common.
5. Occasionally, elevation in levels of transaminases and bilirubin may occur. Rare manifestations include acute pericarditis, stroke and intravascular hemolysis[8].

### Diagnosis

The diagnosis of A1P poisoning is based on history of ingestion of A1P, clinical features, foul smell from breath and vomitus, and presence of cardiac arrhythmias and metabolic acidosis. Confirmation can be done by qualitative silver nitrate impregnated paper test on gastric aspirate or breath[9].

### Management

The main aim of management is to sustain life with appropriate resuscitation measures till phosphine is excreted from the body[10].

1. If the patient presents within few hours after ingesting A1P, absorption of phosphine can be reduced by performing a gastric lavage using potassium permanganate in 1:10000 dilution. Activated charcoal is useful as it adsorbs phosphine.
2. Phosphine is excreted through breath and urine; therefore, maintain adequate renal perfusion and ventilation. Diuretics do not have any role in enhancing its excretion.
3. No antidote is available to reduce the effects of phosphine on various organs. Magnesium sulphate has been tried in patients with A1P poisoning with variable results[10,11]. The dose is 1 g magnesium sulphate intravenously followed by 1 g for the next two hours and then 1.0-1.5 g after every 4-6 hours for 3-5 days.
4. Supportive measures are important in the management. Shock is managed initially by infusing 2-3 litres of saline during the first 3-6 hours, preferably under central venous pressure or pulmonary capillary wedge pressure monitoring. Low-dose dopamine (4-6 Hg/kg/min) and steroids may be useful in patients with continued hypotension. Metabolic acidosis should be corrected by infusing sodium bicarbonate.

## KEROSENE OIL

Ingestion of kerosene oil is the most common accidental poisoning in children[12].

### Clinical Features of Intoxication

1. Ingestion of kerosene oil generally produces an immediate burning sensation in the mouth along with nausea and vomiting.
2. In the absence of aspiration, kerosene can be tolerated without any systemic effects since it is poorly absorbed from the gut. However, aspiration is common and can occur within first 15 minutes of ingestion. Aspiration results in chemical pneumonitis producing cough, breathlessness, tachypnea, cyanosis and pulmonary edema.
3. CNS involvement occurs due to hypoxia and results in lethargy, dizziness, headache, drowsiness, convulsions, coma and death[1,12].
4. Radiographic findings consist of perihilar densities, pneumonitis, atelectasis and occasionally, areas of consolidation. Pleural effusion may develop in some cases. Rarely, cysts or pneumatoceles may form[13].

### Management

1. The most important step in the management is to evaluate and maintain the ventilatory status of the patient.
2. Do not induce vomiting or perform a gastric lavage so as to reduce the risk of aspiration. Activated charcoal is not effective.
3. Avoid epinephrine as it may precipitate ventricular arrhythmias.
4. Patients who remain asymptomatic after ingestion do not require hospital evaluation and should be observed at home. Patients who had some respiratory symptoms after ingestion, but are asymptomatic at the time of arrival should be observed in the hospital for development of respiratory compromise. A chest X-ray should be obtained after two hours of ingestion. If the patient is asymptomatic at that time and the chest X-ray is normal, he can be discharged for observation at home. However, if the chest X-ray is abnormal in such a patient, he should be observed for another 6-8 hours. Patients who have respiratory symptoms on arrival should be admitted.

## ORGANOCHLORINES

Organochlorines are used as insecticides and pesticides and include DDT, methoxychlor, lindane (benzene hexachloride), aldrin, dieldrin, endrin, heptachlor and endosulphan. These agents can be absorbed through any route though absorption is affected by the solvents in which they are contained.

### Clinical Features of Intoxication

1. Initial features are nausea, vomiting and epigastric distress.
2. The most serious feature of intoxication is seizures which can occur without any features of GIT toxicity[14,15].
3. Other features are dizziness, myoclonus, opsoclonus, weakness of legs, agitation and confusion. Death occurs due to respiratory failure.
4. Organic solvents present in many commercial insecticides decrease the convulsive effects of DDT but increase the CNS depression. They can also produce aspiration.

### Management

1. Monitor the ventilation of the patient as hypoxia can develop due to seizures, respiratory depression or aspiration.
2. Perform a gastric lavage if the toxin has been ingested within last 3-4 hours. Activated charcoal does not adsorb most organochlorins.
3. Administer cholestyramine (16 g / day in 4-6 divided doses) in all symptomatic patients as it interrupts the enterohepatic circulation of organochlorines.
4. Control seizures with diazepam and phenobarbital.
5. Avoid epinephrine; however, dopamine may be given in patients with resistant hypotension.
6. Dialysis is not effective in removing organochlorines.

## PHENOL

Phenol or carbolic acid is a corrosive agent which acts as a corrosive at the site of contact and also as a narcotic poison. The household phenol contains 5% of phenol in water.

### Clinical Features of Intoxication

1. Ingestion of phenol produces intense burning sensation in the mouth and the throat followed by abdominal pain and vomiting. The mucous membranes of lips and mouth become hard and white.
2. The patient develops giddiness and drowsiness which soon deepens into coma.
3. In severe cases, metabolic acidosis, cardiovascular depression and cardiac arrhythmias may occur.
4. Intravascular hemolysis, methemoglobinemia, and hepatic and renal failure can develop[1].

### Management

1. Institute measures to support the vital organs.
2. A cautious gastric lavage may be performed to remove the ingested phenol. As stomach hardens due to poison, there is very little danger of perforation.

## RODENTICIDES

Commonly used rodenticides include barium carbonate, zinc phosphide, and anticoagulants (superwarfarins).

### Barium Carbonate

Barium carbonate is marketed as white powder. Acute poisoning causes hypokalemia, neuromuscular blockade and respiratory failure[16]. Treatment involves decontamination and supportive care, including potassium replacement.

### Zinc Phosphide

Zinc phosphide is available as dark gray powder which releases phosphine gas in the stomach. The clinical features of intoxication are similar to those seen with aluminium phosphide though the onset may be a little slower[17]. Management is mainly supportive.

### Superwarfarins

Superwarfarins inhibit synthesis of factors II, VII, IX and X in the liver. These agents have a long duration of action and therefore act as "single-dose" rodenticides. These include bromadiolone, brodifacoum, difenacoum and diphacinone. Most patients who ingest superwarfarins do not get any significant abnormalities. A few may develop bleeding from various sites[18]. Prolongation of prothrombin time can be demonstrated after 36-48 hours and may persist for long periods. Most cases involve ingestion of small amounts of poison and do not require any treatment. In case of significant ingestion, patient may be admitted for 48-72 hours for observation and serial prothrombin time estimations. Vitamin $K_1$ or fresh frozen plasma is required if patient develops features of bleeding. Recombinant factor VII has been found to be useful[19].

## DATURA

*Datura stramonium* (Jimson seed, thorn apple) grows in India at high altitudes. All parts of this plant are poisonous but the seeds and fruit are the most poisonous and ingestion of 4-6 seeds may be fatal. The toxins are hyoscine, hyoscyamine, scopolamine and atropine.

### Clinical Features of Intoxication

Symptoms of toxicity usually appear within 30 minutes of ingestion and last for 24 to 48 hours[20,21].

1. The patient complains of a bitter taste, dry mouth and throat, burning pain in the epigastrium and vomiting.
2. Peripheral anticholinergic features are prominent and include tachycardia, dry and flushed skin, dry mucus membranes, dilated pupils, red conjunctiva,

hyperthermia, urinary retention, decreased bowel sounds, hypertension and later hypotension.

3. Central effects involve initial stimulation of the CNS with excitement and restlessness, followed by subsequent depression, delirium (muttering delirium, picking at bed clothes, trying to pull imaginary threads) and coma. Visual hallucinations, ataxia and extrapyramidal features are often seen. In fatal cases, stupor, coma and convulsions occur.

### Management

The mainstay of treatment is supportive. If the patient presents early after ingestion, a gastric lavage may be done. Activated charcoal is helpful. Catheterization is often required due to retention of urine. Hyperthermia should be controlled with external cooling. Benzodiazepines are effective in the treatment of agitation. Role of physostigmine, a cholinesterase inhibitor, is controversial.

## CANNABIS

Cannabis is derived from the leaves and flowers of the plant, *Cannabis sativa.* The main active ingredient is delta-9-tetrahydrocannabinol (THC). Marijuana, the most commonly abused form of cannabis, is dried plant material. It may be smoked or ingested[1].

### Clinical Features of Intoxication

Smoking cannabis produces its toxic effects within 5 minutes that may last for 2 hours or longer. In contrast, oral ingestion produces initial effects after 30 to 60 minutes which last for as long as 5 hours[1,22].

1. In early phase, the patient develops anxiety, fear of death and hyperactivity. Following early features, the patient develops calm euphoria, exhilarated behavior, vivid sense of happiness and feeling of lightness of limbs and body. After 2-4 hours, the patient becomes lethargic and drowsy.
2. The patient also develops sinus tachycardia and non-specific ST-T wave changes.
3. Hypothermia may occur particularly in children.

### Management

Specific treatment is usually not required since features of poisoning disappear within a few hours. Physical restraint may be required in some cases. If needed, diazepam may be used. For psychotic features, haloperidol 5-10 mg may be administered.

## OLEANDER

Poisoning by *pila kaner* or yellow oleander *(Cerebra thevetia)* and *Nerium oleander* (white oleander) is frequent in south India. The kernels of the seed are most toxic with the lethal dose being 8-10 seeds. These plants contain several glycosides, which resemble digitoxin.

### Clinical Features of Intoxication

Features of poisoning generally develop within 2-3 hours of ingestion[23].

1. The patient develops nausea, vomiting, diarrhea, abdominal pain, pupillary dilatation, tingling and numbness, restlessness, bradycardia, arrhythmias, hypotension and nervous system toxicity. Hyperkalemia is common.
2. ECG shows sinus bradycardia, AV blocks, ST-T changes, prolongation of PR interval, AV dissociation and ventricular ectopics. In severe cases, ventricular tachycardia and fibrillation can occur[23,24].

### Treatment

1. Correct fluid, electrolyte and acid-base disturbances, and institute cardiac monitoring.
2. Gastric emptying may be of some value in patients presenting early after ingestion.
3. Manage bradycardia with atropine and pacing. Ventricular tachyarrhythmias may be managed with lidocaine.
4. Digoxin-specific Fab antibody fragments are useful in life-threatening poisoning[25].

## OPIUM

Oral ingestion of crude opium from the plant, *Papaver somniferum,* is a common cause of poisoning, particularly in children.

### Clinical Features of Intoxication

1. The classical triad of opium poisoning is pinpoint pupils, respiratory depression and CNS depression[1,26].
2. Other features include tachycardia, cardiac conduction defects and occasionally, seizures. Hypothermia may develop due to muscular hypotonia and peripheral vasodilatation.

### Management

1. Establish adequate airway and ventilation.

2. Gastric lavage may be useful in cases presenting early after ingestion.
3. Control seizures with diazepam.
4. Naloxone is the antidote for opium poisoning and is administered in a dose of 0.4-2 mg intravenously. Observe the patient for 3 minutes with regard to change in pupil size, respiratory rate, and state of consciousness. If recovery is minimal or only partial, administer further doses of naloxone up to a maximum of 10 mg. The peak effects of naloxone last for about 10 minutes only. Therefore, repeated doses or infusion of naloxone may be required.

## BENZODIAZEPINES

Benzodiazepines (BZDs) have a wide therapeutic index and margin of safety. Fatalities with BZDs overdose are distinctly rare and are usually associated with concomitant ingestion of alcohol[27] or other toxins. However, in patients with underlying chronic obstructive lung disease, respiratory depression produced by BZDs may be of significance. Alprazolam overdose is probably more toxic than other benzodiazepines[28].

### Clinical Features of Intoxication

CNS depression is common in benzodiazepine poisoning. Patients will be drowsy, ataxic or may present with a low-grade coma. It is important to note that profound coma, significant hypotension, respiratory depression or hypothermia are extremely uncommon in pure overdose with benzodiazepines. Most overdose patients will become easily arousable within 12-24 hours. Complications may develop secondary to coma particularly in elderly or patients with chronic obstructive lung disease. The effect of an overdose is generally prolonged sleep (from which the patient can be aroused), without serious depression of cardiovascular and respiratory function.

### Treatment

1. Most patients require only supportive care.
2. Flumazenil is the specific antagonist of BZD. However, it is not required in most cases with BZDs poisoning. It may be indicated in patients who have respiratory depression or may develop complications due to prolonged coma. The dose is 0.1-0.2 mg IV over 30-60 seconds, which is repeated every 1-2 minutes to a total of 1-2 mg. Due to its short half-life, re-sedation can occur; in such cases, flumazenil may be given as an infusion at a rate of 0.3-1 mg / hour for 3-6 hours[29,30].

## METHANOL

Most cases of methanol or methyl alcohol poisoning occur due to consumption of adulterated ethyl alcohol. Ingestion of 15-30 mL of 40% methanol may be fatal. Methanol per se is not a toxic agent. However, its metabolites, formaldehyde and formic acid are responsible for its toxicity. The enzyme responsible for conversion of methanol to formaldehyde is alcohol dehydrogenase while aldehyde dehydrogenase converts formaldehyde to formic acid. Alcohol dehydrogenase has much greater affinity for ethyl alcohol than methyl alcohol and this is useful in managing patients with methanol poisoning.

### Clinical Features of Intoxication

The toxic features are usually delayed for 12-24 hours[1,31].

1. Initially, the patient may develop nausea and abdominal pain.
2. CNS features develop within the first few hours and include dizziness, weakness and headache. Later, the patient may develop coma and seizures.
3. Ocular toxicity is a delayed feature and the patient complains of visual difficulty. Examination may reveal pupillary dilatation, retinal edema and hyperemia of the optic discs.
4. Due to accumulation of formic acid, the patient develops Kussmaul's breathing. Typically, acidosis produced by methanol is of high anion gap type[32].

### Management

1. A gastric lavage is indicated if the patient is seen within 2 hours of ingestion.
2. Correct acidosis by administering sodium bicarbonate.
3. *Ethanol:* Conversion of methanol into active toxic substances can be prevented by saturating alcohol dehydrogenase enzyme with ethanol. The loading dose of ethanol is 0.75 g / kg and maintenance dose is 130 mg / kg / hour[1,31]. For a 60 kg patient, oral loading dose is 0.75 x 60 or 42 g of ethanol or 52 ml of 100% ethanol or 173 ml of 30% ethanol. For maintenance, give 0.130 x 60 or 7.8 g / hour or 9.8 ml / hour of 100% ethanol or 98 ml / hour of 10% ethanol.
4. Hemodialysis is indicated in following cases:
   - Serum methanol level > 50 mg / dl
   - CNS, visual or fundoscopy abnormalities
   - Consumption of > 30 ml of methanol

5. 4-methylpyrazole or fomepizole: It is a direct, potent inhibitor of alcohol dehydrogenase and therefore, may be more effective than ethanol which is a competitive antagonist. It has a longer half-life than ethanol and it does not produce CNS depression and inebriation[33].

## REFERENCES


1. Aggarwal P, Wali JP. Diagnosis and Management of Poisoning, Oxford University Press, Delhi, India 1997;297-304.
2. Namba T, Nolte CY, Jackirel J, Grob D. Poisoning due to organophosphorous insecticides: Acute and chronic manifestations. Am J Med 1971;50:475-8.
3. Singh S, Sharma N. Neurological syndromes following organophosphate poisoning. Neurol India 2000;48:308-13.
4. Singh S, Chaudhry D, Behera D, Gupta D, Jindal SK. Aggressive atropinisation and continuous pralidoxime (2-PAM) infusion in patients with severe organophosphate poisoning: experience of a northwest Indian hospital. Hum Exp Toxicol 2001;20:15-8.
5. Singh S, Dilawari JB, Vashist R, et al. Aluminium phosphides ingestion. Br Med J 1985;290:1110-11.
6. Chugh SN, Dushyant, Santram, Arora B, Malhotra KC. Incidence and outcome of patients of aluminium phosphide poisoning in a hospital study. Indian J Med Res 1991;94:232-5.
7. Chugh SN. Aluminium phosphide poisoning. Present status and management. J Assoc Phylnd 1992;40:401-5.
8. Aggarwal P, Handa R, Wig N, Biswas A, Saxena R, Wali JP. Intravascular hemolysis in aluminium phosphide poisoning. Am J Emerg Med 1999;17:488-9.
9. Chugh SN, Santram, Chugh K, et al. Spot diagnosis of AIP ingestion: An application of simple test. J Assoc Phys Ind 1989; 37:219-20.
10. Chugh SN. Aluminium phosphide poisoning with special emphasis on diagnosis and management. J Ind Assoc Clin Med 1995;1:20-22.
11. Chugh SN, Kumar P, Sharma A, et al. Magnesium status and magnesium sulfate therapy in acute aluminium phosphide poisoning. Magnesium Res 1994;7:289-344.
12. Gupta P, Singh RP, Murali MV, Bhargava SK, Sharma P. Kerosene oil poisoning—a childhood menace. Indian Pediatr 1992; 29:979-84.
13. Sharma A, Nain K, Nanda S. Pneumomediastinuni, pneumothorax and subcutaneous emphysema with kerosene oil. Indian J Chest Dis Allied Sci 1996;38:211-13.
14. Ozucelik DN, Karcioglu O, Topacoglu H, Fowler JR. Toxicity following unintentional DDT ingestion. J Toxicol Clin Toxicol 2004;42:299-303.
15. Roberts DM, Dissanayake W, Rezvi Sheriff MH, Eddleston M. Refractory status epilepticus following self-poisoning with the organochlorine pesticide endosulfan. J Clin Neurosci 2004;11: 760-2.
16. Koley TK, Goyal AK, Gupta MD. Barium carbonate poisoning mimicking Guillain-Barre syndrome. J Assoc Physicians India 2001;49:656-7.
17. Chugh SN, Aggarwal HK, Mahajan SK. Zinc phosphide intoxication symptoms: Analysis of 20 cases. Int J Clin Pharmacol Ther 1998;36:406-7.
18. Chua JD, Friedenberg WR. Superwarfarin poisoning. Arch Intern Med 1998;158:1929-32.
19. Zupancic-Salek S, Kovacevic-Metelko J, Radman I. Successful reversal of anticoagulant effect of superwarfarin poisoning with recombinant activated factor VII. Blood Coagul Fibrinolysis 2005;16:239-44.
20. Vanderhoff BT, Mosser KH. Jimson weed toxicity: Management of anticholinergic plant ingestion. Am Fam Physician 1992; 46:526-30.
21. Dyer S. Plant exposures: Wilderness medicine. Emerg Med Clin North Am 2004;22:299-313.
22. Grossman W. Adverse reactions associated with Cannabis products in India. Ann Intern Med 1969;70:529-33.
23. Bose TK, Basu RK, Biswas B, De JN, Majumdar BC, Datta S. Cardiovascular effects of yellow oleander ingestion. J Indian Med Assoc 1999;97:407-10.
24. Eddleston M, Ariaratnam CA, Sjostrom L, et al. Acute yellow oleander (Thevetia peruviana) poisoning: cardiac arrhythmias, electrolyte disturbances, and serum cardiac glycoside concentrations on presentation to hospital. Heart 2000;83:301-16.
25. Eddleston M, Persson H. Acute plant poisoning and antitoxin antibodies. J Toxicol Clin Toxicol 2003;41:309-15.
26. Sporer KA. Acute heroin overdose. Ann Intern Med 1999; 130:584-90.
27. Tanaka E. Toxicological interactions between alcohol and benzodiazepines. J Toxicol Clin Toxicol 2002;40:69-75.
28. Isbister GK, O'Regan L, Sibbritt D, Whyte IM. Alprazolam is relatively more toxic than other benzodiazepines in overdose. Br J Clin Pharmacol 2004;58:88-95.
29. Chern CH, Chern TL, Wang LM, Hu SC, Deng JF, Lee CH. Continuous flumazenil infusion in preventing complications arising from severe benzodiazepine intoxication. Am J Emerg Med 1998;16:238-41.
30. Mohan A, Mohan C, Aggarwal P, Handa R, Wali JP. Flumazenil in acute benzodiazepine overdose. J Assoc Physicians India 2002;50:1097-8.
31. Hovda KE, Hunderi OH, Tafjord AB, Dunlop O, Rudberg N, Jacobsen D. Methanol outbreak in Norway 2002-2004: Epidemiology, clinical features and prognostic signs. J Intern Med 2005;258:181-90.
32. Hovda KE, Hunderi OH, Rudberg N, Froyshov S, Jacobsen D. Anion and osmolal gaps in the diagnosis of methanol poisoning: Clinical study in 28 patients. Intensive Care Med 2004;30:1842-6.
33. Mycyk MB, Leikin JB. Antidote review: fomepizole for methanol poisoning. Am J Ther 2003;10:68-70.