
UNIT 15 POISONING

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15.1 INTRODUCTION

In the previous units you have learnt about the various hormones secreted from the body and their physiological and pharmacological actions. In this unit you shall study about the types of poisoning and their treatments with antidotes and chelating agents.

Objectives

After studying this unit, you should be able to:

- types and treatment of poisonings; and
- various antidotes and chelating agents.

15.2 TYPES AND TREATMENT OF POISONING

Poison is a substance which endangers life due to its toxic reaction/poisoning on certain vital functions in the body. The poisonous substances may be the toxins, very high doses of drug, industrial chemicals/gases, house-hold chemical like insecticides-DDT, BHC, etc.

15.2.1 General Treatment of Poisoning

The treatment of different drug poisoning is discussed in individual chapters. In this section, general treatment is discussed. The general principles of treatment are:

- i) Support ventilation.
- ii) Maintain cardiovascular function.
- iii) Reverse hypothermia if present.
- iv) Treat convulsions.
- v) Correct fluid, acid-base and electrolyte imbalance.
- vi) Relieve pain and good nursing care.

The treatment of poisoning is primarily based on following points:

a) Prevention of Poison Absorption

The most important aim is to reduce the further absorption of poison.

- i) Gastric lavage may be useful for six hours after ingestion of poison. The lavage should be done as early as possible but only if vital functions are adequate.
- ii) It is inappropriate to employ gastric lavage unless the lungs can be protected, either by virtue of patient having an adequate cough reflex or by means of a cuffed endotracheal tube.
- iii) Gastric lavage is **contraindicated** if corrosive or caustic substances have been taken, because oesophageal and gastric erosion and perforation may occur.
- iv) Activated charcoal is probably more effective than either emesis or lavage.

b) Accelerating Poison Elimination

Alkalinisation of urine (alkaline diuresis) is effective for salicylates and phenoxyacetate herbicides. Repeated dose of activated charcoal administered by oral route have been shown to enhance the non-renal elimination of carbamazepine, salicylates, phenobarbitone, phenytoin, digoxin, theophylline and meprobamate. In severe cases activated charcoal is to be administered via a nasogastric tube.

Haemoperfusion, using a cartridge containing charcoal or an uncharged resin is effective in enhancing drug excretion in few selected cases of poisoning e.g. theophylline, barbiturates, non-barbiturate hypnotics, etc.

Frequent administration of activated charcoal is effective for the following substances:

- i) *Substances which form masses:* Aspirin, iron, lithium, enteric-coated tablets, meprobamate.
- ii) *Substance which remain in the stomach for a long time:* Barbitol, aspirin, iron, alcohol, cholinergic blockers, narcotic drugs, phenytoin, antidepressants.
- iii) *Substances which have a long half-life when present in large amounts:* Theophylline, aspirin, alcohol, phenytoin, chloral hydrate, acetaminophen.
- iv) *Substances which have active metabolites:* Benzodiazepines, chloral hydrate, acetaminophen, antidepressants, procainamide.
- v) *Substances whose poisonous metabolites are eliminated slowly:* Ethylene glycol, methanol, primidone, isopropyl alcohol, carbon tetrachloride, levothyroxine.

- vi) *Substances which are reabsorbed from the urinary tubules in a pH dependent manner:* Phenobarbital, aspirin, amphetamine.
- vii) *Substances with persistent tissue accumulation:* Iron, lithium.
- viii) *Substances that undergo enterohepatic circulation:* digoxin, phenobarbital.

15.2.2 Common Types of Poisoning and Management

i) Organophosphorus Poisoning

These compounds are mainly used as agricultural and household insecticides. The poisoning may be occupational (for those who are involved professionally with these agents), accidental (accidental consumption) or suicidal due to intentional ingestion of these compounds.

- Local exposure produces miosis, spasm of accommodation, headache, irritation of eye, lacrimation and blurring of vision.
- On ingestion fall in blood pressure, tachycardia, cardiac arrhythmias, ataxia, convulsion, respiratory paralysis and vasomotor collapse occurs. The death is generally due to respiratory failure.

Treatment for Organophosphate poisoning

- Gastric lavage, fresh air for termination of further exposure to compound.
- Maintenance of a patent airway. Use oropharyngeal or nasopharyngeal airway or endotracheal intubation if airway obstruction persists.
- Washing of skin, mucous membrane and eye.
- Supportive therapy: Maintenance of blood pressure, artificial respiration, rehydration (fluid/electrolyte therapy) and control of convulsions.
- Antidote/Reactivators.
 - Atropine is the specific antidote and highly effective in counteracting the muscarinic symptoms. It is given in a dose of 2 mg IV every 10 min till muscarinic effects are controlled.
 - The cholinesterase reactivators are used to restore neuromuscular transmission. Pralidoxime (pyridine-2-aldoxime methiodide; 2-PAM) is an antidote and cholinesterase reactivator. It breaks the bond between the organophosphate poison and the molecular surface of acetylcholinesterase and the enzyme is freed and reactivated to hydrolyse the excess of acetylcholine at the receptor sites.

ii) Chronic Alcoholism

It is associated with development of psychic dependence, tolerance and physical dependence and sudden withdrawal of alcohol may lead to

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withdrawal syndrome. In addition, the alcohol addicts are liable to neuropsychiatric syndrome which is associated with hallucination, suicidal tendencies and encephalopathy. They may also suffer from hyperlipidemia, hyperuricemia, pancreatitis and hepatitis.

Alcoholism

The treatment is initiated with single dose which is gradually reduced to a maintenance dose daily and treatment may be continued up to one year. After a week's therapy, if a small quantity of alcohol is consumed by the patient, it produced unpleasant toxic reactions such as flushing, palpitation, nausea, vomiting throbbing head-ache, uneasiness, dizziness, visual disturbances, fall in blood pressure and even collapse. The patient thus realizes that during the treatment he can not tolerate even a small amount of alcohol and would abstain from alcohol drinking.

The drug disulfiram interferes with the oxidation of acetaldehyde formed during the metabolism of alcohol. This increases the blood level of acetaldehyde which acts directly on cardiovascular system and produce these toxic reactions.

iii) Methyl Alcohol (Methanol)

Methyl alcohol is only used to denature ethyl alcohol in 5% concentration. It is metabolized to formaldehyde and formic acid by alcohol and aldehyde dehydrogenases. Its absorption and distribution are similar to ethyl alcohol.

Ingestion of methyl alcohol produces the following signs and symptoms:

- Nausea and vomiting.
- Blurring of vision, hyperemia of optic disc and blindness.
- Pancreatitis.
- Albuminuria.
- Coma followed by death.

Treatment of Methanol Poisoning

- Gastric lavage, activated charcoal.
- Hospitalization: Correction of acidosis.
- IV/oral ethyl alcohol.
- Maintenance of nutrition.
- Administration of folinic acid together with folic acid to accelerate the metabolic degradation of formate.
- Administration of 4-methylpyrazole (inhibitor of alcohol dehydrogenase).
- In severe case: haemodialysis.

15.2.3 Antidotes

Antidotes are used in life threatening situations and are administered for a short treatment course.

The antidotes are classified into four main types.

- i) **Mechanical antidotes:** These substances interfere with the absorption of poison. They act by forming a coat over mucous membrane of the stomach. e.g. fats, oils, albumin, activated charcoal is specifically used in adsorbing alkaloid poisons.
- ii) **Chemical antidotes:** They react with poison to form harmless insoluble form e.g. acids are neutralized by alkalis, KMnO_4 used in opium poisoning.
- iii) **Systemic antidotes:** They produce the action which are opposite to that of poison e.g. caffeine for morphine and atropine for pilocarpine.
- iv) **Universal antidotes:** These antidotes can be given in all such conditions where nature of poison is not known or where more than one poison is suspected to be taken e.g. charcoal as adsorbent of toxins and alkaloids, tannic acid for precipitating alkaloids, glycoside and many metals.

The other antidotes are discussed below which are used in the treatment of different types of poisonings and addiction cases.

Disulfiram (Esperal)

It is relatively nontoxic, used as an adjunct in the treatment of chronic alcoholism.

a) Leucovorin

It is used as leucovorin calcium (calcium folinate). It is derivative of tetrahydrofolic acid and it acts as an antidote to folic acid antagonists like methotrexate or pyrimethamine which inhibit the enzyme dihydrofolate reductase.

b) Pralidoxime

It is indicated as antidote for organophosphorus poisoning like malathion, TEPP, parathion etc.

c) Nicotine

It is used in the treatment of nicotine dependence and as an aid to stop smoking.

d) Bupropion

It is also indicated in smoking cessation.

Antisnake Venom

Antivenom is the only specific antidote to snake venom. Antivenom is immunoglobulin purified from the serum or plasma of a horse or sheep that has been immunised with the venoms of one or more species of snake. Antivenom should be given by the intravenous route. Adrenaline should always be drawn

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up in readiness before antivenom is administered for any possible anaphylactic reactions.

The specific antidotes for various poisons are listed in Table 15.1.

Table 15.1: Common poisons and their antidotes

Poison	Antidote
1. Arsenic	Dimercaprol, BAL, D-penicillamine
2. Cyanide	Oxygen (100%), dicobalt edetate, Amyl nitrite, sod. nitrite
3. Ethylene glycol, methanol	Ethanol
4. Opioids	Naloxone
5. Organophosphorus insecticides	Atropine and pralidoxime mesylate
6. Iron	Desferrioxamine
7. Beta-blockers	Atropine for bradycardia, glucagon
8. Digoxin	Digoxin specific antibody fragments
9. Carbon monoxide	Oxygen (100%)
10. Oral anticoagulants	Vitamin K (phytomenadione)
11. Heparin	Protamine sulfate
12. Lead (inorganic)	Sodium calcium edetate, D-penicillamine
13. Mercury (inorganic)	Dimercaprol, D-penicillamine, BAL
14. Methanol	Ethanol
15. Paracetamol, gold	N-acetylcysteine
16. Benzodiazepines	Flumazenil
17. Atropine	Physostigmine
18. Isoniazid	Pyridoxine
19. Folic acid antagonists	Folinic acid
20. Acetaminophen (Paracetamol)	N-acetylcysteine
21. Copper	BAL, EDTA D-penicillamine
22. Methotrexate	Folic acid, Leucovorin
23. Snake bite	Antisnake venom polyvalent
24. Hydroxines	Pyridoxine
25. Theophylline	Esmolol
26. Curare compounds	Neostigmine
27. Insulin	Glucose

SAQ 1

- a) _____ is the drug used for de-addiction of chronic alcoholics.
- b) _____ is the only specific antidote to snake venom.
- c) _____ is the specific antidote and highly effective in counteracting the muscarinic symptoms in organophosphorous poisoning.
- d) _____ is the antidote for folic acid antagonists like methotrexate or pyrimethamine.

15.3 CHELATING AGENTS

Chelating agents are widely used as specific antidotes for heavy metals. They form stable, soluble, nontoxic complexes and in easily excreted form. They promote dissociation of bound metal from tissue enzymes and other functional macromolecules. These metal chelates are water soluble. e.g. EDTA, BAL, desferrioxamine etc.

a) Dimercaprol (British Anti Lewisite (BAL))

It acts by forming complexes between its sulphhydryl groups and metals. Its effectiveness is much more, if given immediately after exposure to the metal. It is indicated in metallic intoxication due to arsenic, mercury, gold, bismuth, lead, nickel, thallium and antimony; in conjunction with sodium calcium edetate for lead poisoning. It is also useful in Wilson's disease. It is contraindicated in iron and cadmium poisoning.

b) D-Penicillamine

It is used in poisoning due to copper, mercury and lead; Wilson's disease, cystinuria, scleroderma and rheumatoid arthritis.

c) Desferrioxamine

It is primarily a chelator used in acute iron poisoning and chronic iron overload as in thalassemia patients needing multiple transfusions.

d) Calcium Disodium Edetate

It is primarily indicated in lead poisoning. It is also useful in iron, zinc, copper, manganese and radioactive metal but not mercury poisoning.

e) Deferiprone

It is an orally active iron chelator. It is useful in acute iron poisoning, iron overload in cirrhosis, transfusion siderosis in thalassemia patients.

SAQ 2

- a) Dimercaprol is contraindicated in _____ and _____ poisoning.
- b) _____ is commonly used in the treatment of acute iron overload.
- c) _____ is an orally active iron chelator.

15.4 SUMMARY

- Poison is a substance which endangers life due to its toxic reaction/ poisoning on certain vital functions in the body.
- Alkalinisation of urine (alkaline diuresis) is effective for acidic substances and acidification of urine is effective for the rapid elimination of alkaline substances from the body.
- Antidotes are substances that are used for specific poisons in life threatening situations, and are administered for a short treatment course.
- Adrenaline should always be drawn up in readiness before antivenom is administered for any possible anaphylactic reactions.
- Chelating agents are widely used as specific antidotes for heavy metals. They form stable, soluble, nontoxic complexes and in easily excreted form.
- The commonly used chelating agents are dimercaprol, disodium edentate, d-penicillamine, deferrioxamine, etc.

15.5 TERMINAL QUESTIONS

1. What is a poison?
2. What are the general principles in the management of poisoning?
3. Define antidote. Write a brief note on the different types of antidotes.
4. Write a short note on the treatment of snake bite.
5. What are chelating agents? Write a brief note on the individual agents along with their therapeutic use.

15.6 ANSWERS

Self Assessment Questions

1. a) Disulfiram
b) Antivenom
c) Atropine
d) Leucovorin

2. a) Iron and cadmium
- b) Desferrioxamine
- c) Deferiprone

Terminal Questions

1. Poison is a substance which endangers life due to its toxic reaction on certain vital functions in the body. The poisonous substances may be a toxins, drug, industrial chemicals/gases, household chemical like insecticides-DDT, BHC, etc.
2. The general principles of treatment of poisoning can be enumerated as follows:
 - a) Support of ventilation.
 - b) Maintenance of cardiovascular function.
 - c) Reversal of hypothermia if present.
 - d) Treatment of convulsions.
 - e) Correction of fluid, acid-base and electrolyte imbalance.
 - f) Relief pain and good nursing care.
3. Antidotes are drugs or substances that are used in life threatening situations where a poison has been ingested. They are always administered for a short treatment course. The antidotes are classified into four main types.
 - i) **Mechanical antidotes:** These interfere with the absorption of poison. They act by forming a coat over mucous membrane of the stomach. e.g. fats, oils, albumin, activated charcoal is specifically used in adsorbing alkaloid poisons.
 - ii) **Chemical antidotes:** They react with poison to form harmless insoluble form e.g. acids are neutralized by alkalis, KMnO_4 used in opium poisoning.
 - iii) **Systemic antidotes:** They produce the action which are opposite to that of poison e.g. caffeine for morphine and atropine for pilocarpine poisoning.
 - iv) **Universal antidotes:** These antidotes can be given in all such conditions where nature of poison is not known or where more than one poison is suspected to be taken e.g. charcoal as adsorbent of toxins and alkaloids, tannic acid for precipitating alkaloids, glycoside and many metals.
4. Snakebite should be treated as early as possible and the patient should be continuously monitored. The only specific antidote available for snake envenomation is antivenom. Antivenom is immunoglobulin purified from the serum or plasma of a horse or sheep that has been immunised with the venoms of one or more species of snake. Antivenom should be given by the intravenous route. Adrenaline should always be drawn up in readiness before antivenom is administered for any possible anaphylactic reactions.

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Because of this, antivenom is never administered until the patient starts showing signs of envenomation. Apart from the specific antidote, supportive measures like administration of fluids, oxygen are maintained.

5. Chelating agents are drugs that are used as specific antidotes for heavy metals poisoning. They form stable, soluble, nontoxic complexes and in easily excreted form. They promote dissociation of bound metal from tissue enzymes and other functional macromolecules. Some important chelating agents are:

Dimercaprol (BAL): It acts by forming complexes between its sulphhydryl groups and metals. It is indicated in metallic intoxication due to arsenic, mercury, gold, bismuth, lead, nickel, thallium and antimony; in conjunction with sodium calcium edetate for lead poisoning.

D-penicillamine: It is used in poisoning due to copper, mercury and lead; Wilson's disease, cystinuria, scleroderma and rheumatoid arthritis.

Desferrioxamine and Deferriprone: These are primarily used in acute iron poisoning and chronic iron overload as in thalassemia patients needing multiple transfusions.

Calcium Disodium Edetate: It is primarily indicated in lead poisoning. It is also useful in iron, zinc, copper, manganese and radioactive metal but not mercury poisoning.