TOXICOLOGY



The traditional definition of **toxicology** is *"the science of poisons."*

- "the study of the adverse effects of chemicals or physical agents on living organisms".
- is the science dealing with properties, action, toxicity, fatal dose, detection, estimation of, interpretation of the result of toxicological analysis and management of Poisons
- Forensic Toxicology is a branch of Forensic Medicine dealing with Medical and Legal aspects of the harmful effects of chemicals on human beings.

Poison: A Poison is defined as any substance (solid, liquid or gaseous) which when administered in living body through any route (Inhalation, Ingestion, surface absorption etc) will produce ill-health or death by its action which is due to its physical, chemical or physiological properties. Eg: alphos, sulphuric acid, arsenic etc.

The definition of poison is vague and unsatisfactory for
1) A substance which is harmless in small quantities may act as poison, and cause death when taken in large amounts, and
2) bacterial toxins are not regarded as poisons in ordinary sense of terms

- **Drug (WHO 1996): "Drug is any substance or product that is** used or intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient." Eg: paracetamol, ciprofloxacin, salbutamol, oestrogen, insulin etc.
- Toxicant, toxin, and poison are often used interchangeably in the literature; however, there are subtle differences as indicated below:

TOXICANTS	Subs that produce adverse biological effects of any nature May be physical or chemical
TOXIN	Specific proteins produced by living organisms
POISON	

A toxic agent is anything that can produce an adverse biological effect. It may be chemical, physical, or biological in form. For example, toxic agents may be chemical (*such as cyanide*), physical (*such as radiation*) and biological (*such as snake venom*).

 If the invading organisms excrete chemicals which is the basis for toxicity, the excreted substances are known as biological toxins. The organisms in this case are referred to as toxic organisms. An example is tetanus toxin

- A **toxic substance** is simply a material which has toxic properties.
- It may be a discrete toxic chemical or a mixture of toxic chemicals. For example, lead chromate, asbestos, and gasoline are all toxic substances.
- Lead chromate is a discrete **toxic chemical**.
- Asbestos is a **toxic material** that does not consist of an exact chemical composition but a variety of fibers and minerals.
- Gasoline is also a toxic substance rather than a toxic chemical in that it contains a mixture of many chemicals.

Toxic substances may be systemic toxins or organ toxins.

- A **systemic toxin** is one that affects the entire body or many organs rather than a specific site. For example, potassium cyanide is a systemic toxicant in that it affects virtually every cell and organ in the body by interfering with the cell's ability to utilize oxygen.
- Toxicants may also affect only specific tissues or organs while not producing damage to the body as a whole. These specific sites are known as the **target organs** or **target tissues**.

Subdisciplines of toxicology

- Toxicogenomics involves applying molecular profiling approaches to the study of toxicology.
- Ecotoxicology: It is concerned with the toxic effects of chemical and physical agents on living organisms, especially in population and communities within defined population.
- Environment toxicology
- Forensic toxicology, and
- Medical toxicology.
- Aquatic toxicology
- Entomotoxicology: is the analysis of toxins in arthropods (mainly flies and beetles) that feed on carrion.

Chemical toxicology: study of structure and mechanism related to the toxic effects of chemical agents, and encompasses technological advances in research related to chemical aspects of toxicology.

- Clinical Toxicology: Deals with human diseases caused by, or associated with abnormal exposure to chemical substances.
- Toxinology: refers to toxins produced by living organism which are dangerous to man, eg: poisonous plants, snake venom, fungal and bacterial toxins etc.

Indian Shastras, Egyptian Papyri, Sumerian, Babylonian, Hebrew and Greek records.

• Atharv Veda (1500 B.C) describes many poisons

HISTORY

- Kalpasthana, Chikitsasthana, and Uttarasthana of the Shastras, symptoms and antidotes of poisons are given in detail.
- Sushruta (350 B. C)described poisons
- Kautilya in is Arthshastra (2nd century B.C)
- Theophrastus Phillipus Auroleus Bombastus von Hohenheim (1493–1541) (also referred to as Paracelsus included numerous references to plant poisons in De Historia Plantarum (is also considered "the father" of toxicology)
- Mathieu Orfila is considered to be the modern father of toxicology, having given the subject its first formal treatment in 1813 in his *Traité des poisons*, also called *Toxicologie générale*.



The Drugs and Cosmetics Act 1940.

Object of the Act : to regulate the import, manufacture, distribution and sale of all kind of drugs.

One of the main features is the control of quality, purity and strength of the drug.

Central Government appoints the Drugs Technical Advisory Board to advise the Central Government and the State Governments on technical matters arising out of the administration of this Act.

This act was amended in 1964

The Pharmacy Act was passed in 1948 and was amended in 1959, 1976 and 1984.

Aim:To regulate the profession of Pharmacy in India.

Central Government constitutes a Central Pharmacy Council.

The President and Vice-President of the Central Council of Pharmacy are elected by the members of the Council among themselves, hold office for five years and are eligible for re-election.

The conducting of courses of study for pharmacists, and the examinations in Pharmacy in the states are subject to the approval of the Central Council.

Besides the Council has the responsibility to supervise the Education of Pharmacy in the States. Where it is found that the course of study is not in conformity with the Education Regulations, the Council may withdraw approval accorded to the course or the examination. The Central Council can approve qualifications granted by an outside authority for qualifying for registration under this Act. **State Pharmacy Councils** The Act makes it incumbent upon the State Governments to constitute State Pharmacy Councils with the following members:

a) Six members elected from amongst themselves by registered Pharmacists of the state.

b) Five members of whom at least two shall be persons possessing a prescribed degree or diploma in Pharmacy or Pharmaceutical Chemistry or members of the Pharmaceutical profession nominated by the State Government.

c) One member elected by the State Medical Council.

d) The Chief Medical Officer of the State.

e) The State Drug Controller.

f) The Government Analyst.

Registration of Pharmacists

The State Government has under the provisions of the Pharmacy Act to get a register of the State Pharmacists prepared and it is the State Pharmacy Council which has to maintain the register. The register shall contain the name and residential address of Pharmacist, the date of his first admission to the register, qualifications for registration, his professional address, the name of his employer and prescribed particulars.

- THE DRUGS (CONTROL) ACT, 1950
- An Act to provide for the control of the sale, supply and distribution of drugs.
 - **1. Short title and extent. ?** (1) This Act may be called the Drugs(Control) Act, 1950.
- **2. Interpretation. ?** (1) In this Act, unless the context otherwise requires, ?
- (a) ?dealer? (b) ?drug (c) ?offer for sale? (d) ?producer?
- (2) A drug shall be deemed to be in the possession of a person ?
- **3. Drugs to which this Act applies. ?** The Central Government may by notification in official Gazette, declare any drug to be a drug to which this Act applies.
- 4. Fixing of maximum prices and maximum quantities which may be held or sold.
- 5. Restrictions on sale, etc., where maximum is fixed under Section. ?
- 6. General limitation on quantity which may be possessed at any one time.
- 7. Duty to declare possession of excess stocks.
 8. Refusal to sell.
 9. Cash memorandum to be given of certain sales.
 10. Marking of prices and exhibiting list of prices and stocks.
- 11. Obligation to state price separately on composite offer
- 12. Prohibition or regulation of the disposal of drugs.
- **13. Penalties. ?** (1) Whoever contravenes any of the provisions of this Act or fails to comply with any direction made under authority conferred by this Act shall be punishable with imprisonment for a term which may extend **to three years**, or with fine, or with both.
- 14. Offences by corporations..15. Procedure. ? 16. Powers of search and seizure. 17. Power to make rules. ?
- 18. Protection of action in good faith..19. Saving of other laws. ? 20.? [* * * Repealed].

4. The Drugs and Magic Remedies (Objectionable Advertisements) Act 1954

This Act is meant to control the Advertisements regarding drugs; it prohibits the advertising of remedies alleged to possess magic qualities and to provide for matters connected therewith.

The Drugs and Magic Remedies Act prohibits a person from taking part in publication of any advertisement referring to any drug which suggests use of the drug for: a) the procurement of miscarriage in women or prevention of conception in women; and

b) the maintenance or improvement of the capacity of the human being for sexual pleasure;

c) the correction of menstrual disorders in women;

d) the diagnosis, cure, mitigation, treatment or prevention of any venereal disease. No person shall import into or export from India any document containing advertisement of this nature.

Whoever contravenes the provisions of this Act shall, on conviction, be punishable with imprisonment which may extend to **six months**, **with or without fine**. In case of subsequent convictions the imprisonment can be extended to one year. The document, article or thing which contains the offending advertisement can be seized and confiscated.

If the person contravening any of the provisions of the Act is a company, every person who at the time the offence was committed was in charge of the business of the company shall be deemed guilty.

• 5) Narcotic Drugs and Psychotropic Substances Act, 1985 The cultivation, production, manufacture, possession, sale, purchase, transportation, warehousing, consumption, inter-State movement, trans shipment and import and export of narcotic drugs and psychotropic substances is prohibited, except for medical or scientific purposes and in accordance with the terms and conditions of any license, permit or authorization given by the Government.

- The Central Government is empowered to declare any substance, based on an assessment of its likely use in the manufacture of narcotics drugs and psychotropic substances as a controlled substance
- Assets derived from drugs trafficking are liable to forfeiture.

• The NDPS Act is in effect a comprehensive code not only for the control and regulation of Narcotics Drugs and Psychotropic Substances; but also for the control of selected chemicals - commonly known as precursors - which can be used in the illicit manufacture of narcotic drugs and psychotropic substances, as well as for the investigation and forfeiture of drug related assets.

ENFORCEMENT: Given India's size and the federal nature of our polity, a number of agencies both at the Centre and in the States have been empowered to enforce the provisions of the Act. These agencies include the Department of Customs and Central Excise, the Directorate of Revenue Intelligence, the Central Bureau of Narcotics and the Central Bureau of Investigation at the Central level and State Police and Excise Departments at the State level.
 INVESTIGATIVE PROCEDURES

Chapter V of the NDPS Act (Sections 41 to 68) sets out the powers as well as the procedures for the investigation of offences under the Act. This Chapter empowers officers duly authorized by the Central Government or a State Government to issue warrants, to enter and search premises, to stop and search conveyances, to seize narcotic drugs and psychotropic substances, to take statements and to arrest persons suspected of having committed an offence, punishable under the Act.

• The power to issue search and arrest warrants, is in terms of Section 41, been vested both in Magistrates as well as in specially designated (Gazetted) officers of the Central and State Governments.

LICIT OPIUM CULTIVATION

SPECIAL PROVISIONS RELATING TO FORFEITURE OF PROPERTY: This Chapter prohibits any person from holding any property derived from drug trafficking and authorizes officers empowered under the Act to investigate, identify and seize such property. The Chapter also sets out a quasijudicial procedure for the forfeiture of such property consequent to which it shall vest in the Central Government.

- **OFFENCES AND PENALTIES :** from imprisonment from 10 to 20 years for first offences to 15 to 30 years for any subsequent offences together with monetary fines.
- The Act, however, makes a distinction between possession for personal consumption and trafficking, the punishment for the former being limited to between six months and one year only.

THE PREVENTION OF ILLICIT TRAFFIC IN NARCOTIC DRUGS AND PSYCHOTROPIC SUBSTANCES ACT, 1988

(PIT NDPS Act)

• INTRODUCTION

- It was, therefore, felt that a preventive detention law should be enacted with a view to effectively immobilize persons engaged in any kind of illicit traffic in narcotic drugs and psychotropic substances. To achieve this objective the President promulgated the Prevention of Illicit Traffic in Narcotic Drugs and Psychotropic Substances Ordinance on 4 th July,1988. To replace this Ordinance the Narcotic Drugs and Psychotropic Substances Bill, 1988 was introduced in Parliament.
- The Act empowers Central Government and the State Governments have been empowered to make orders of detention with respect to any person (including a foreigner) if they are of opinion that it is necessary so to do with a view to preventing him from committing illcit traffic in narcotic drugs and psychotropic substances. The expression "illicit traffic" had been defined to include cultivation of any coca plant or gathering any portion of coca plants, cultivating the opium poppy or any cannabis plant, or engaging in the production, manufacture, possession, etc., of narcotic drugs or psychotropic substance.

• Laws in relation to poison and drugs:

Sec. 272 I.P.C. - Punishment for adulterating food or drink intended for sale, so as to make the same noxious, may extend upto 6 months imprisonment of either term and/or fine upto one thousand rupees.

- Sec. 273 I.P.C. Punishment for selling noxious food or drink may be imprisonment of either description for a period of 6. months and or fine upto one thousand rupees.
- Sec. 274 I.P.C. Punishment for adulteration of drugs in any form with any change in its effect knowing that it Will be sold and used as un-adulterated drug, may be imprisonment of either description for a period-of 6 months and or fine.
- Sec. 275 l.P.C. Punishment for knowingly selling adulterated drugs with less efficacy or altered action serving it for use as unadulterated may be imprisonment of either description for 6 months and or fine.

- **Sec. 276 I.P.C.** Punishment for selling a drug as a different drug or preparation, may be imprisonment of either description which may extend upto 6months and or fine. .
- Note In the State of West Bengal, the punishment for these offences described under sections 272 to 276 may be upto imprisonment for life with or without fine.
- Sec. 277 I.P.C. Punishment for fouling water of public spring or reservoir may be imprisonment of either description which may extend up to a period of 3 months and or fine.
- Sec. 278 I.P.C. Punishment for voluntarily making atmosphere noxious to health is fine which may extend upto five hundred rupees.

Sec. 284 I.P.C. Punishment for negligent conduct with

respect to poisonous substance may be imprisonment of either description which may extend upto 6 months and or fine which may extend upto one thousand rupees.

- Sec. 328 I.P.C. :Punishment' for causing hurt by means of poison or any stupefying, intoxicating or unwhlolesome drug or any other thing with the intent to commit an offence shall be imprisonment of either description for a term which may extend to ten years with or without fine.
- **Culpable Homicid**e: Sec 299 IPC; Causing death of a person by an act, with the intention of causing such bodily injury and is likely to cause death, or with the knowledge that he is likely, by such an act to cause death.

Sources of Poison:

- 1. Domestic or household sources In domestic environment poisoning may more commonly occur from detergents, disinfectants, cleaning agents, antiseptics, insecticides, rodenticides etc.
- 2. Agricultural and horticultural sources- different insecticides, pesticides, fungicides and weed killers.
- 3. **Industrial source**s- In factories, where poisons are manufactured or poisons are produced as by products.
- 4. **Commercial source**s- From store-houses, distribution centers and selling shops.

5. From uses as drugs and medicines – Due to wrong medication,

- overmedication and abuse of drugs.
- 6. Food and drink contamination in way of use of preservatives of food grains or other food material, additives like colouring and odouring agents or other ways of accidental contamination of food and drink.
- 7. **Miscellaneous source**s- snakes bite poisoning, city smoke, sewer gas poisoning etc.

Classification of poisons

- 1. According to the site and mode of action
- (A). local Action
- a) Corrosive :

Strong Acid: mineral acid: eg H2SO4, HCl : organic acid:Carbolic, oxalic,acetic,salicylic Strong alkali: Hydrates and carbonates of Na, K, & ammonia

Metallic salts: Mercuric Chloride, KCN,

b) Irritant

- 1) Agricultural
- 2) Inorganic

Nonmetallic: P, Iodine, Cl, bromine Metallic: Arsenic, Antimony, Pb, Cu, Zinc Mechanical: Glass, Diamond dust, Hair 3) Organic Animal: Snakes, insects Cantharides

Vegetable: Abrus, Castor, Croton, Calotropis

(B) Systemic Action

1) Cerebral

- i. Somniferous: opium and its alkaloids, Barbiturates.
- ii. Inebriant (Intoxicant): Alcohol, ether, Chloroform.
- iii. Psychotropic: AD: TCAD, Amphetamines, Caffeine, MAOI Neuroleptics: Phenothiazenes, thioxanthenes Hallucinogens: LSD, Phencyclidine, psilocybe
- iv. Deliriant: Dhatura, Belladona, Hyocyamus, cannabia Indica.
- vi. Hallucinogens
- 2) Spinal
- i . Strychnos Nux Vomica
- Ii. Gelsemium
- 3) **Peripheral Nerves**
 - i. Local Anaesthetics: Cocaine, Procaine.
 - ii. Relaxants (curare)

CNS DEPRESSANTS

- 1) Alcohols
- 2) General anaesthetics
- 3) Opioid analgesics
- 4) Sedative hypnotics
- Sedatives are those drugs that decrease activity, moderate excitement and exert a calming effect
- Hypnotics produce drowsiness and facilitate a state of sleep, resembling natural sleep.
- 1) Barbiturates

- 2) Benzodiazepines
- 3) Non barbiturates
- 5) Propanediols
- 4) Alcohols
- 6) Glutethimide
- 7) quinazolines: methaqualone

• 4) Cardiac Poisons

- KCN, NaCN, Digital is, Aconite, Nicotine, Quinine, Oleander
- 5) Asphyxiants: Carbon Dioxide, CO, hydrogen sulphide
- C) Miscellaneous: Food Poisons.

Classification of Poison according to motive or nature of use:

- 1. Homicidal: Arsenic, Aconite, Digitalis, Abrus Precatorius, Strychnos nux vomica.
- 2. **Suicidal:** Opium, Barbiturate, Organophosphorus, carbolic acid, copper sulphate.
- 3. Accidental: Aspirin, organophosphorus, copper sulphate, snakes bite, Ergot, CO, CO2, H2S.
- 4. Abortifacient: Ergot, Quinine, Calotropis, Plumbago.
- 5. **Stupefying agen**t: Dhatura, cannabis, chloral hybrate.

- 6. Agents used to cause bodily injury: Corrosive acids and alkalies.
- 7. **Cattle Poiso**n: Abrus precatorius, Calotropis, plumbago.
- 8. Used for malingering: semicarpus anacardium
- 9. Arrow Poison: Abrus precatorius, Calotropis, Aconite, Strychnos nux vomica.
- 10. Aphrodisiacs : Cantharides, Cannabis, Cocaine, arsenic, opium

- Ideal Suicidal poison: should be easily available, No bad taste, cause No pain, cheap, highly toxic, tasteless or pleasant taste, capable of being taken with food or drink.
- Ideal Homicidal poison: it should be cheap, easily available, colorless tasteless, odourless, highly toxic, No residual product left, S/S resembles natural diseases, No antidote, Shows no post-mortem changes, capable of being administered with food or drink.

• Route of Administration/absorption:

- Oral (commonest) eg: alphos, acids,
- Inhalation: gas poison
- Parenteral (IM, IV, Sub-Cutaneous, Intra-Dermal)
- Natural Orifices other than mouth (Nasal, Rectal, Vaginal, Urethral),
- Ulcers, wounds and intact skin.

Fate of poison in body:

Vomiting and purging, defecation.

- Before absorption the poison may exert its effects in the G.I. Tract.
- When absorbed, the poison reaches different parts of the body
- Cumulative poisons get accumulated in some organs or tissues.
- A part of poison is eliminated as such through different route of elimination. But major part is detoxified or metabolized in the body and than excreted
- Liver is the main organ to detoxify or metabolize most of the poisons.
- Certain poisons like Chloroform, Phosphorus, Nitrates and Acetic acid disappear by evaporation or oxidized or destroyed in the body and no trace of them can be detected in the body of post-mortem is delayed.

Excretion of poisons: Unabsorbed poisons are excreted through faeces and vomitus. Absorbed poisons are excreted mostly by urine. A part of volatile poison is exhaled out. Some portion of poison is excreted through bile, saliva, milk, sweat, tear, hair and nails.

Factors influencing the actions of a poison

in the body

- 1. Quantity:
- Quantity
 - large = more effect ?
 - idiosyncracy (individual susceptibility to a substance)
 - addiction (tolerance)
 - different actions of different doses
- A high dose of poison acts quickly and often resulting in fatal consequences. A moderate dose causes acute poisoning. A low dose may have sub-clinical effects and causes chronic poisoning on repeated exposure. Very large dose of Arsenic may produce death by shock without dose irritant symptoms, While smaller dose than lethal dose produces its therapeutic effects.

2. Physical form:

- Physical State: Gas > liquids > powders > solids
 Some poisonous vegetable seeds may pass through the intestinal canal ineffective when taken intact due to their impermeable pericarp. But when taken crushed, they may be rapidly fatal.
- Chemical Combination: Ag nitrate and HCL
- Mechanical Combination: relative density of the poison and the vehicle
- 3. Chemical form: Chemically pure arsenic and mercury are not poisonous because these are insoluble and are not absorbed.
- But white arsenic(arsenic oxide) and mercuric chloride are deadly poisonous. Barium sulphide is deadly toxic but barium sulphate is non-toxic.
- 4. **Concentration** (or dilution): concentrated form of poison are absorbed more rapidly and are also more fatal but there are some exceptions too.
- 5. **Condition of the stomach**: food content presence of foodstuff acts as diluent of the poison and hence protects the stomach wal l. Dilution also delays absorption of poison. Empty stomach absorbs poison most rapidly. In cases of achlorohydria, KCN and NaCN is ineffective due to lack of hydrochloric acid, which is required for the conversion of KCN and NaCN to HCN before absorption
- 6. **Route of administratio**n: absorption rate is different for different routes.

- 7. Age: some poisons are better tolerated in some age groups.
 Opium and its alkaloids are tolerated better by elderly subjects but badly by children and infants. Belladonna group of drugs are better tolerated by children than by adults.
- 8. **State of body health:** A well built person with good health can tolerate the action of poison better than a weak person.
- 9. **Presence of diseas**e: In certain diseased conditions some drugs are tolerated exceptionally well e.g.: sedatives and tranquilizers are tolerated in very high dose by manic and deliriant patients.
- 10. **Intoxication arid poisoning states** In certain poisoning cases some drugs are well tolerated, like, in case of strychnine poisoning, barbiturates and sedatives are better tolerated. Whereas in case of barbiturate poisoning any sedative or tranquilizer will accentuate the process of death.

- 11. **Sleep** Due to slow metabolic process and depression of other body functions during sleep, usual ly the absorption and action of the poison is also slow. But depressant drugs may cause, more harm during the state of sleep.
- 12. Exercise Action of alcohol on C.N.S. is slowed during exercise because more blood is drawn to the muscles during exercise.
- 13. Cumulative action of poisons: Preparations of cumulative poisons (poisons which are not readily excreted from the body and are retained in different organs of the body for a long time) like lead may not cause any toxic effect when enters the body in low dose. But when such poisons enter over a long period of time, may cause harm when their concentration in different tissue reaches high level due to their cumulative property.

- 14. **Tolerance** may develop by individuals on long term exposue to a particular poison.
- 15. **Idiosyncracy:** some persons may react adversely to a particular drug though the general population tolerates the drug well.

DEFINITIONS

Acute poisoning: is caused by an excessive single dose, or several dose of a poison taken over a short interval of time.

- **Chronic Poisoning:** is caused by smaller doses over a period of time, resulting in gradual worsening. eg: arsenic, Phosphorus, antimony and opium.
- **Subacute poisoning** shows features of both acute and chronic poisoning.
- Fulminant poisoning is produced by a massive dose. In this death occur rapidly, sometimes without preceding symptoms.
- **Parasuicide** (attempted suicide or pseudicide) is a conscious often impulsive, manipulative act, undertaken to get rid of an intolerable situation.
- Antidote: Antidotes are substances which counteract the effect of poison. They are divided into Mechanical, Chemical, Physiological and specific receptor antagonists.

Signs and symptoms:

- The signs and symptoms may be different for different poisons and is responsible on the nature and action of the poison.
- They can be local, remote or combined.

Diagnosis of poisoning

In the Living

- 1. History of the case
- 2. Signs and symptoms.
- 3. Details of examination.
- 4. Preservation and laboratory investigation

Diagnosis of poisoning (contd.)In the Dead:

- 1. History
- 2. Post-mortem Examination
- 3. Chemical Analysis
- 4. Preservation of viscera

PM Findings

External Examination

• 1. Postmortem staining:

Deep blue - In case of asphyxiant poisons and aniline.
Bright red - In case of CO poisoning
Cherry red - In case of HCN poisoning.
Dark brown or yellow - Phosphorus

- 2. Deep cyanosis With opium and cardiac poisons.
- 3. Early rigor mortis With strychnine.
- **4. Early appearance of the sign of decomposition** With H₂S gas.

External Examination (contd.)

- 5. Detectable smell In case of volatile poisons, opium and HCN, KCN or NaCN.
- 6. Haemorrhagic spots under the skin and mucus membrane: Phosphorus.
- 7. Ulceration on lips, angles of mouth Corrosive poisons.
- 8. Stain near mouth ,on hands HNO3 and CuSO4.
- 9. White froth from mouth and nose Opium and its alkaloids.

External Examination (contd.)

- 10. Blood tinged froth from mouth and nose Organophosphorus compounds.
- 11. Alopecia, hyper pigmentation and hyperkeratosis Ch. Arsenic poisoning.
- 12. Staining, erosion and ulceration near the female external genitalia - Use of abortifacient agents or torturing agents.
- 13. **Injection marks** Injection of poisons (snake bite or otherwise), sign of treatment.

Internal findings:

- Hyperemia, softening, ulceration and perforation.
- 1. Corrosion, ulceration and desquamation of inner aspects of lips, mucus membrane of mouth and tongue - Corrosive agents.
- 2. Soft, swollen, sodden, translucent, bleached tongue and mucus membrane of mouth- **Corrosive alkali**
- 3. Hardening of mucus membrane **Phenol**
- 4. Phenol Yellowish Nitric acid
- 5. Bluish Copper sulphate
- 6. Carbonization and charring- **Conc. Sulphuric acid**

- 7. Chalky appearance and consistency of teeth -:Sulphuric acid
- 8. Blue lining in the gum **Chronic lead poisoning**
- 9. Swollen gum, loose teeth, foetid smell Acute mercuric chloride poisoning; **Chronic phosphorus poisoning**
- 10. Corrosion, irritation, desquamation and hemorrhage in the inner wall of the esophagus - Corrosive and irritant poisons

- II. Hardening and whitish discolouration In case of Carbolic acid poisoning
- 12. Discoloration and staining of inner aspects of mouth With coloured poisons
- 13. Oesophageal stricture A complication of sulphuric acid ingestion

- 14. Stomach
- (a) Thickening and softening of the wall **-Corrosive and irritant poisons**
- (b) Hard wall- Carbolic acid
- (c) Hard and leathery wall- Formaldehyde
- (d) Hyperemia haemorrhage and desquamation of mucus membrane Irritant poison
- (e) Laceration and sloughing **Corrosive poison**
- (f) Perforation H2SO4 and HNO3
- (g) Yellowish discolouration of mucus membrane HNO3; Bluish - CuSO4; Slaty grey - HgCl3.

- (h) Stomach content Blood Corrosive and irritant;
 Yellowish HNO₃ Bluish CuSO₄
- Luminous in dark Phosphorus;
- Detectable tablet soneryl; Powder; oxalic acid, white arsenic;
- Detectable smell kerosene, alcohol, chloroform, organophosphorus compounds, chlorinated hydrocarbons, opium, cyanogen, formaldehyde, phosphorus;
- Detectable liquid kerosene.

- 15. **Small intestine** May show ulceration, perforation sometimes may show presence of poisonous remains.
- **16. Large intestine** May show ulcerations, as in case of HgCI3 similar in appearance of ulcers of bacillary dysentery. It particularly involves the ascending and transverse colons.

- 17. Liver Different degenerative changes.
- 18. Kidneys Swollen, reddish, soft, sometime greasy in touch with haemorrhage in calyces and other degenerative changes - mercury, oxalic acid carbolic acid, phosphorus, cantherides, viper snake venom etc. In case oxalic acid poisoning, white powder of oxalate crystals are present in the tubules and the calyces.
- **19. Urinary bladder** Haemorrhage in cases of abrus precatorius, viper snake bite, cantherides poisoning.

- 20. Larynx and trachea Hyperemic, inflamed -In cases of inhalation of irritating gases leaking of corrosive agents while ingestion vomiting; froth in the lumen of trachea and larynx in case of opium and organophosphorus poisoning.
- 21. Chest cavity -Smell of volatile poisons, cyanogens, opium etc. can be detected.
- 22. Lungs Voluminous, congested, presence of Tardieu's spots - In case of asphyxiants and inhaled poisons. Cut section gives blood stained frothy-fluid in case of opium and other asphyxiants.

- 23. Heart- Subendocardial haemorrhagic spots in cases of arsenic, phosphorus, mercuric chloride etc.
- 24. Brain and spinal cord Congestion and edema.
 Brain may be congested, oedematous with occasional haemorrhagic points at places - asphyxiant poisons.
- **25. Uterus and vagina** Staining, congestion haemorthage, ulceration in cases of attempted abortion by use of local abortifacient agents.

Preservation of viscera and other materials

- In all cases of poisoning
- 1. Stomach with its full contents.
- 2. A loop of small intestine with its contents.
- 3. Half of Liver or 500 gms whichever is more.
- 4. Half of each kidney.
- 5. Some portion of spleen
- 6. Blood 100ml

In some particular poisons

- 1. Blood 100ml : in cases of absorbed poisons.
- 2. Urine 100ml in all cases where blood is preserved.
- 3. Part of both lungs in cases of Volatile poisons.
- 4. Heart in case of cardiac poisons.
- 5. Brain in cerebral poisons.
- 6. Spinal in spinal poisons.

In some particular poisons (contd.)

- 7. Bones in arsenic and lead.
- 8. Hair in arsenic and copper.
- 9. Nails in arsenic.
- 10. Skin-scrap from areas stained with a suspected poison.
- 11. Stained areas of dress, suspected packet of poison, strips of tablets recovered from pocket.

Preservative used

- For Viscera: Saturated sol. Of common salt,
- absolute alcohol or rectified spirit. Exception: alcohol, chloroform, chloral hydrate, formaldehyde, ether, phosphorus (alcohol prevents the luminosity of phosphorus in dark) etc.
- Blood should be preserved in fluoride, oxalate, E.D.T.A., gold chloride or citrate
- Urine : 1 ml of conc. HCl, 10 mg of thymol, 100 mg of NaF for 10 ml urine
- clothes: without any preservative.

DUTIES OF A DOCTOR IN CASES OF POISONING

- Save life
- Protect from further exposure
- Collect samples for chemical analysis

 (vomit, urine, faeces, stomach wash fluid, remnants of food, medicine, suspect containers, clothes soiled with vomit, urine, faeces)
- Detailed History
- Admit preferably to a Government Hospital

DUTIES OF A DOCTOR IN CASES OF POISONING (contd.)

- Inform police
- Arrange for dying declaration
- Notify public health authorities
- Ask for autopsy in case of death (DO NOT ISSUE DEATH CERTIFICATE)
- Maintain detailed and proper records

PRINCIPLES OF MANAGEMENT OF A CASE OF POISONING

- Stabilization & Evaluation
- Decontamination
- Poison elimination
- Antidote administration
- Nursing and Psychiatric Care

1.Stabilization & Evaluation

- Assessment and correction of life-threatening problems

- 1. Hypoxia Assisted ventilation
- 2. Coma Coma cocktail (Dextrose + Thiamine + Naloxone)
- 3. Metabolic acidosis

1. Stabilization & Evaluation

- ABCD of resuscitation
- Complete, thorough and systematic examination of the patient (after stabilization)

Glasgow scoring

Category	Response	Points
E ye opening	Spontaneous, open with blinking at baseline	4
	Opens to verbal command, speech, or shout	3
	Opens to pain, not applied to face	2
	No response	1
V erbal response	Oriented conversation	5
	Disoriented, confused conversation, able to answer questions	4
	Inappropriate responses, words discernible	3
	Incomprehensible speech	2
	No response	1
	Intubated	1T
Motor response	Obeys commands for movement	6
	Purposeful movement to painful stimulus	5
	Withdraws from pain	4
	Abnormal (spastic) flexion, decorticate posture	3
	Extensor (rigid) response, decerebrate posture	2
	No response	1

2. Decontamination

- 1. Inhaled poisons
- 2. Injected poisons
- 3. Contact poisons
- 4. Ingested poisons
 - Emesis
 - Gastric lavage
 - Catharsis
 - Activated charcoal
 - Whole bowel irrigation

1 – Emesis

- Substances used- ipecacuanha
- Contraindications Relative
 - 1. Very young/very old
 - 2. Pregnancy

3. Heart disease/ingestion of cardiotoxic poison

4. Bleeding disorders

5. Time lapse of more than 6 – 8 hours

- 1 Emesis
- Contraindications Absolute
 - 1. Convulsions
 - 2. Corrosives
 - 3. Coma
 - 4. Petroleum distillates
 - 5. Foreign body ingestion
 - 6. Emetic poisons

1. Emesis

- Complications
- 1. Cardio toxicity bradycardia, AF, myocarditis
 - 2. Aspiration pneumonitis
 - 3. Mallory Weiss tears

2. Gastric lavage

- Indications

1. Ingestion of life-threatening dose of poison and presenting to the casualty with in 1 - 2 hours of ingestion

- 2. Presence of gastric concretions
- 3. Delayed gastric emptying
- 4. Sustained release preparations

2. Gastric lavage -Lavage fluids

- a) Warm water
- b) Saline
- c) Oxidizing solutions:
 - KMnO₄, tannic acid, Iodinated water
 - d)Na thiosulphate sol. For CN
 - e) Desferrioxamine- for iron
 - f) Castor oil in warm water- carbolic acid
- g) Ca gluconate- oxalic acid
2. Gastric lavage

Contraindications – Absolute

1. Corrosive substance ingestion (except Carbolic acid)

- 2. Marked hypothermiia
- 3. Prior significant vomiting
- 4. Petroleum distillate ingestion
- 5. Convulsions
- 6. Ingestion of sharp substances

- 2. Gastric lavage
 - Contraindications Relative
 - 1. Convulsions
 - 2. Hemorrhagic diathesis
 - 3. Coma
 - 4. Esophageal varices
 - 5. Recent surgery
 - 6. Advanced pregnancy

- 2. Gastric lavage
 - Complications
 - 1. Aspiration pneumonia
 - 2. Laryngospasm
 - 3. Sinus bradycardia and ST elevation on ECG
 - 4. Perforation of stomach or esophagus

3. Catharsis

Ionic or Saline cathartics:
1. Magnesium citrate – 4ml/kg
2. Magnesium sulfate – 30 g
3. Sodium sulfate – 30 g

Can lead to serious hypermagnesemia

3. Catharsis

Saccharides – Sorbitol
Cathartic of choice in adult
Dose – 50 ml of 70% solution
Efficacy – doubtful
Contraindicated in children due to risk of fluid and electrolyte imbalance

4.Activated Charcoal

- Universal adsorbent
- Produced by the controlled burning of various organic products at >600C, washed with inorganic acids and dried
- Small particle with highly developed internal pore system
- Surface area of 50 gm AC = 10 football fields

2

Dose – 1g/kg in 4-8 times the quantity of water

4. Activated Charcoal

- **Indications:** In Salicylates, paracetamol, barbiturates, TCA, theophylline and many other organic and inorganic substances, carbamezepine, Dapsone, Digoxin, Phenytoin Quinine Theophyline Barbiturates.

- **Disadvantages**: unpleasant taste, emesis, constipation/diarrhoea, pulmonary aspiration, intestinal obstruction, black stools

4.Activated Charcoal

Contraindications:

1. Absent bowel sounds/intestinal obstruction

2. Corrosives, heavy metals- lithium, iron, alcohol, ethylene glycol, petroleum distillates, etc.

Charcoal has no toxicity, may be given before inducing vomiting or gastric lavage

It is with a universal antidote (activated charcoal: magnesium oxide: tannic acid 2:1:1)

4. Activated Charcoal

Binds most compounds: easier to remember what it

5. Whole bowel irrigation

- NS instilled into the GI tract through a nasogastric tube at a rate of 1.2 to 1.8 l/hr till rectal effluent is clear or until 4 – 6 l have been used up.
- Complications: Vomiting, cramps, bloating and abdominal distension.

3.Antidote Administration

(Antidotes are substances that counteract the effects of poisons)

- Mode of action:

1. Inert complex formation metals

- 2. Accelerated detoxification
- 3. Reduced toxic conversion
- 4. Receptor site competition
- 5. Receptor site blockade atropine for OP compounds
- 6. Toxic effect bypass
- 7. Mechanical

chelating agents for

- thiosulfate for cyanide
- ethanol for methanol
- naloxone for opiates
- 100% O_2 in cyanide
- dilution in corrosives

Antidote (contd.)

- Antidotes are substances which counteract the effect of poison. They are divided into
- 1.Mechanical
- 2.Chemical
- 3.Physiological
- 4.Specific receptor antagonists.

Antidotes (contd.)

- **Physical or mechanical antidote** prevents the action of poison mechanically, without destroying or inactivating the damaging actions of the poisons. Eg: adsorbents like activated charcoal, Demulcents like egg albumin, starch or milk, Diluents like water or milk, bulky food like boiled rice or vegetables.
- **Chemical antidot**es are substances which disintegrate and inactivate poisons by undergoing chemical reaction with them. Eg: Weak acids and alkali, common salt, egg albumin, KMNO₄.

Antidotes (contd.)

- 3. Physiological antidote have their own action producing signs and symptoms opposite to that produced by the poison. Eg: Naloxone for morphine, Neostigmine for datura or hyoscin group, Barbiturate for strychnine.
- **4. Serological Antidot**e: Anti-snake venom serum for snake bites poisoning.

Antidotes (contd.)

Universal Antidote: It is a combination of physical and chemical antidotes. When the exact nature of poison is not known then universal antidote is used which acts against a wide range of poisons.

Constituents

- Activated charcoal 2 parts
- Magnesium oxide 1 part
- Tannic acid 1 part
- Dose 1TSF (15gms) in a glass water (can be repeated)
- Activated charcoal for its adsorbent action, Magnesium oxide neutralizes acids poisons, tannic acid precipitates alkaloids

Household antidotes:

- 1. Strong liquid **tea** (contains tannic acid) precipitate alkaloid and metallic poisons.
- 2. Starch for iodine.
- 3. Milk and raw egg for mercury, arsenic, heavy metal.
- 4. Flour suspension and mashed potatoes can be used in place of activated charcoal.
- 5. Milk of magnesia or soap solution for acid poisoning.
- 6. Orange, lemon juice or vinegar for alkali poisoning

4 Poison Elimination

- 1. Renal excretion
- 2. Purging
- 3. Whole bowel irrigation
- 4. Diaphoretics
- 5. Forced Diuresis
- 2. Extracorporeal Techniques
 - 1. Hemodialysis
 - 2. Hemoperfusion
 - 3. Peritoneal dialysis
 - 4. Plasmapheresis

What is a toxidrome?

- A collection of symptoms and signs that consistently occur after ingestion of a particular toxin or drug class or agent
- Often identified with a basic history & physical examination
- Rapid identification of the toxidrome saves time in evaluating and managing a poisoned patient

Anticholinergic

- Eg. TCA, antihistamines, atropine, benztropine
- Blind as a bat, hot as a hare, dry as a bone, red as a beet, mad as a hatter
 - Mydriasis
 - Blurred vision
 - Fever
 - Flushed dry skin
 - Psycosis, coma
 - Seizures

• Ileus

- Urinary retention
- Hypertension
- Tachycardia



AAnticholinergic Toxidrome –

ManagementBC, supportive care, consider GI decontamination Benzodiazepines

Physostigmine – specific antidote.

May be used if

Severe agitation or psychosis unresponsive to other therapy

Sever peripheral and central anticholinergic features

NO history of seizures

Normal ECG especially QRS duration

NO co-ingestion of drugs altering intraventricular conduction E.g. TCA's

Cardio-respiratory monitoring and resus facilities in place

Cholinergic

- Eg. organophosphates, nerve agents
- DUMBELS
 - D-diaphoresis, diarrhea, decreased BP
 - U-urination
 - M-miosis
 - B-bronchorrhea, bronchospasm, brady
 - E-emesis, excitiation of skeletal muscle
 - L-lacrimation
 - S-salivation, seizures

Sympathomimetic (adrenergic) toxidrome • Increased temp

- Tachycardia
- Hypertension
- Dilated pupils

- CNS excitiation
 - Seizures
- Nausea/vomiting
- Diaphoresis

Cocaine, MDMA ("ecstasy"), Amphetamines, Phencyclidine (PCP), Theophylline, Decongestants (Ephedrine Pseudoephedrine Phenylpropanolamine), Caffeine (very large doses)

Sympathomimetic (adrenergic) toxidrome • Increased temp

- Tachycardia
- Hypertension
- Dilated pupils

- CNS excitiation
 - Seizures
- Nausea/vomiting
- Diaphoresis

Adrenergic Toxidrome - Management

- ABC, supportive care, consider GI decontamination
- Investigations
 - Screen for other drugs & treatable toxins (eg, acetaminophen, salicylate)
 - Electrolytes (esp. sodium), urea, creatinine, blood sugar, anion gap.
 - CK levels to check for rhabdomyolysis
 - Consider cranial CT
 - EKG & Cardiac biomarkers (eg, CPK-MB, troponin)
- Sedation treats majority of effects
 - Benzodiazepines
- Temperature control
- Treat hypertension unresponsive to benzodiazepines
 - Nitroprusside
 - Nitroglycerine
 - Labetalol (avoid isolated β-blockade in mixed adrenergic agonist toxicity)

Narcotic

- Hypothermia
- Bradycardia
- Hypotension
- Respiratory depression
- Constricted pupils
- CNS depression

Opioid-Narcotic Toxidrome - Management

- ABC, supportive care
- GI decontamination for oral ingestion
- Naloxone
 - Specific antagonist
 - High doses may be needed for methadone & pentazocine
 - Short half-life compared to opioids
 - Infusion may be required
 - Pulmonary edema and seizures have been reported

Serotoninergic Toxidrome

Eg. SSRI's, MAOI's, ecstasy

Vital Signs	
Respiratory rate	Normal/increased
Heart rate	Increased
Temperature	Increased
Blood pressure	Normal/decreased
Physical examination	
Mental status	Agitated/irritable
Pupils	Normal/unreactive
Mucous membranes	Normal
Skin	Normal/flushed/sweating
Reflexes	Increased
Bowel sounds	Increased
Urination	Normal/decreased (SIADH possible)
Other	Diarrhoea, trismus, myoclonus, tremor, rhabdo

Serotoninergic Toxidrome - Features

Cardiovascular

- Sinus tachycardia (36%)
- Hypertension (35%)
- Hypotension (15%)

Motor Abnormalities

- Myoclonus (58%)
- Hyperreflexia (52%)
- Muscle rigidity (51%)
- Restlessness (48%)
- Tremor (43%)
- Ataxia/incoordination (40%)
- Shivering (26%)
- Nystagmus (15%)
- Seizures (12%)

Mental status changes

- Confusion (51%)
- Agitation (34%)
- Hypomania (21%)
- Anxiety (15%)
- Coma (29%)

Gastrointestinal

- Nausea (23%)
- Diarrhea (8%)
- Abdominal pain (4%)
- Salivation (2%)

Other

- Diaphoresis (45%)
- Unreactive pupils (20%)
- Tachypnea (26%)
- Hyperpyrexia (45%)

Serotoninergic Toxidrome - Management

- Stop intake of causative agent
- ABC, supportive care
- Absorption
 - Gastric lavage in early acute ingestion (1hr)
 - Activated charcoal
- Benzodiazepines
- Others
 - Chlorpromazine
 - Diphenhydramine
 - ? Serotonin antagonists e.g. cyproheptadine

Diagnosis - Investigation

- Essential labs
 - CBC, lytes, BUN, Cr, BS
 - Ptt, INR, LFTs
 - ABG (calculate AG)
 - Serum osmo (calculate osmo gap)
 - ASA
 - Acetaminophen
- Other
 - Drug levels
 - Urine

General Management

- ABC
- Consider thiamine, dextrose, naloxone if depressed GCS
- Prevent further absorption
 - Decontaminate eyes, clothes, skin, hair if appropriate
 - Activated charcoal + sorbitol (if < 1 hour from ingestion)
 - Gastric lavage (if < 1 hour from ingestion and life-threatening drug or dose)
 - In general not used
 - Whole bowel irrigation for "body packing" illicit drugs
 - In general not used
- Enhance elimination
 - Forced diuresis and urinary alkalinisation (salicylates and barbiturates)
 - Multiple dose activated charcoal 0.5 g/kg every 2-4 hours
 - binds toxin and interrupts enterohepatic recirculation
 - mainly life-threatening ingestion of carbamazepine, dapsone, phenobarbital, quinine or theophylline
 - Extracorporeal removal (for active metabolites, delayed toxicity or poor organ clearance)
 - *Haemodialysis* low MW (<500 d), soluble, low Vd (< 1L/kg) e.g. methanol, ethylene glycol, salicylates, lithium
 - Haemoperfusion e.g theophylline, phenobarbital, phenytoin, carbamazepine, paraquat
 - *Haemofiltration* for large Vd and extensive tissue bound toxins but removes virtually all drugs
- Antidotes

General Treatment

- Activated charcoal
 - Inert, non-toxic, non-specific adsorption
 - Risk of aspiration
 - Dose 1g/kg patients weight
 - Ineffective for alcohols or heavy metals
 - ? Multi-dose charcoal
 - may cause GI dialysis for some drugs
 - Check with poison control!!!

Activated Charcoal

Binds most compounds; easier to remember what it doesn't

Substances Not Absorbed by Activated Charcoal

Simple ions (e.g., iron, lithium, and cyanide)Strong acids or bases (e.g., hydrochloric acid and sodium hydroxide)Simple alcohols (e.g., ethanol and methanol)

Activated Charcoal

- Big question in the use of AC is when to use it
- Effectiveness is time dependent the longer the time from ingestion, the less effective AC is
 - Toxin already absorbed or past pyloris
- Effectiveness is lost between 1 and 2 hours

AC: problem

 Patients with toxin ingestions will present to the ED >3 hours after poisoning

• "should not be administered routinely"

Drugs and Extracorporeal Removal

Haemodialysis

- Methanol
- Ethylene glycol
- Salicylates
- Lithium

Haemofiltration

- Procainamide
- Methotrexate

Haemoperfusion (Charcoal)

- Theophylline
- Carbamazepine
- Amanita toxin (if early)
- Aminoglycosides
- Paraquat
- Phenobarbital
- Phenytoin
- Sotalol

Urinary Alkalinisation

- Fluoride
- Isoniazid
- Salicylic acid
- Barbiturates
- Methotrexate

Specific Ingestions

Acetaminophen

- Peak plasma <1hr post ingestion
- Metabolized in liver d/t glucuronidation
- Toxic metabolite NAPQ1
 - NAPQ1 binds to hepatocytes and causes necrosis
 - Detoxified by glutathione & eliminated by kidneys
- Toxic threshold adults 7.5-10g

Acetaminophen

- Phase I (<24 hrs):
 - Anorexia, malaise, N/V, diaphoresis
- Phase II (24-48 hr):
 - RUQ pain, [↑]LFTs, sx of phase I resolve

- Phase III (48-96 hr)
 - Severe liver failure
 - Encephalopathy, coagulopathy, \downarrow BS
 - Pancreatitis
 - ARF
- Phase IV (>4 days)
 - Death/full recovery/transplant

Acetaminophen

- Treatment
 - Activated charcoal
 - Given w/I 4-6 hr
 - Reduced absorption by 50-90%
- NAC
 - Replete glutathione
 - combines directly with NAPQ1
 - Antioxident properties
 - vasodilatory properties
 - Treat:
 - Based on nomogram
 - Level >5 w/o ingestion time known
 - Evidence of hepatotoxicity or level unknown

Alcohols

- Ethylene glycol, methanol, isopropanol
- Lab:
 - Anion gap MA, elevated osmolar gap
 - Exceptions:
 - Normal AG
 - Not yet formed metabolites
 - Isopropanol ingestion
- Sx may be delayed if co-ingested with ethanol