INTRODUCTION TO TOXICOLOGY

Definition of Toxicology

- the basic science of poisons (old)

- the study of the adverse effects of chemical agents on biological systems (new)

WHAT TOXICOLOGISTS DO?

-Recognition, identification and quantitation of hazard

-Developing standards and regulations to protect health and the environment

- Safety assessment and use of data as basis for regulatory control of hazards

- Determines risk associated with use of chemicals

- **Orfila** is considered the **father of modern toxicology or founder of modern toxicology**

- **Paracelsus** is often referred to as the **father of toxicology**

TOXICOKINETICS & TOXICODYNAMICS

- **Toxicokinetics:** It is the study of how a chemical/drug/toxin gets into the body and what the body does to it. Involves 4 main processes:
    1. absorption
    2. distribution
    3. biotransformation
    4. elimination or excretion
- **Toxicodynamics:** Dynamic means a change or interaction so toxicodynamics is the study of the effects toxins may have on the body. It refers to the potential molecular, biochemical and physiological effects that toxins have on biological system. Deals with the binding, interaction and induction of toxic effects.

Common Toxicological Terminology

- ABSORPTION – The uptake of a chemical or water into or across a tissue, such as skin.
- ACCUMULATION – The build-up of chemical in the organism as a result of repeated, or long term exposure.
- ACUTE TOXICITY – adverse effects arising from a single exposure or short term exposure to a chemical.
- ALLERGEN – A substance which causes an allergic reaction.
- ALLERGY – An adverse reaction which is caused by an over-stimulation of the immune system in response to a specific allergen, which is otherwise harmless and would be normally tolerated by the majority of those who come in contact with it.

Common Toxicological Terminology

- BENIGN TUMOUR – A tumour that does not invade surrounding tissues or spread to other parts of the body.
- CARCINOGEN – A substance that is capable of causing cancer.
- CARCINOGENESIS – The process of the development of a cancer.
- CHRONIC TOXICITY – Adverse health effects arising from continuous or intermittent exposure to low concentrations of chemical over a lifetime.
- CORROSIVE – A chemical that causes irreversible alterations or destruction in living tissue at the site of contact.
- CUMULATIVE EXPOSURE – A summation of all the exposures that have been undergone by an organism during a specified period of time.

Common Toxicological Terminology

- DERMATITIS – Inflammation of the skin
- DEVELOPMENTAL TOXICOLOGY – Adverse toxic effects in the developing embryo or foetus
- DNEL – Derived No Effect Level. This is the dose above which exposure may give rise to adverse effects.
- DOSE – The amount of chemical administered. It is a measure of exposure.
- DOSE –RESPONSE – The relationship between the dose of a chemical and the degree/severity of the resulting effect.
- ELIMINATION/EXCRETION – The removal of a chemical from the body. This occurs mostly via exhalation of air, or in the urine or faeces.
- END POINT – A specific biological effect or response which is used as an indicator of the effect of the chemical on the organism.
- EPIDEMIOLOGY – The study of the incidence and distribution of disease in populations.
- EXPOSURE – Contact with a chemical. The most common routes are inhalation, skin contact and also by oral ingestion.

Common Toxicological Terminology

- GAVAGE – Oral feeding by a tube.
- GENOTOXIC – Chemicals that cause hereditary mutations as a result of directly interacting with the DNA.
- GENOTOXIC CARCINOGENS – Chemicals causing cancer as a result of directly interacting with DNA.
- HAZARD –The inherent ability of a chemical to cause an adverse effect
- HYPERSENSITIVITY – The state in which an individual reacts following exposure to a substance with allergic effects after having been exposed (sensitised).
- *IN VITRO* – Latin for "in glass". Studies which use tissue, cellular or subcellular extracts from a living organism.
- *IN VIVO* – Studies which are carried out in living organisms.
- IRRITANT – A chemical causing a localised inflammatory reaction to skin or mucous membranes at the site of contact.

Common Toxicological Terminology

- LC_{50} – Lethal Concentration 50%. This is the concentration which causes death in 50% of the test population.
- LIPOPHILIC – "fat loving." This term refers to the ability of a chemical to dissolve in lipids, fats, etc.
- LOAEL – Lowest Observable Adverse Effect Level. This is the lowest dose in the study which causes an observable adverse effect.
- MALIGNANT TUMOUR – A tumour which is cancerous and will metastasise into surrounding tissues.
- MUTATION – An alteration in the genetic material, which can be passed onto subsequent generations.
- NEOPLASM – Another word for tumour.
- NEUROTOXIN – A chemical that causes adverse effects in the nervous system.
- NOAEL – No Observed Adverse Effect Level. This is the largest dose in a given study that does not cause an adverse effect.

Common Toxicological Terminology

- NON GENOTOXIC CARCINOGEN – Chemical carcinogens that cause cancer by effects other than direct damage to the genetic material.
- PRIMARY IRRITANT – A chemical that causes an inflammatory reaction on first contact.
- SENSITISATION – The immune process by which individuals become hypersensitive to a substance to which they are exposed. Subsequent exposure can lead to the development of an allergic response.
- SYSTEMIC EFFECTS – Effects which occur somewhere within the body, for example in the liver or kidney, etc.
- TERATOGEN – A chemical agent causing adverse effects in the normal embryonic development without causing lethality in the foetus or maternal toxicity.
- XENOBIOTIC: chemical substance found within an organism that is not naturally produced or expected to be present within the organism

RISK AND SAFETY

-RISK; the probability that harm will occur under specified conditions

-SAFETY; the probability that harm will not occur under specified conditions

MAJOR FACTORS THAT INFLUENCE TOXICITY

-route of administration

-duration and frequency of exposure

-dose or concentration

SPECTRUM OF UNDERSIRED EFFECTS

-allergic reactions

    -chemical allergies

-idiosyncratic reactions

-immediate vs. delayed toxicity

-reversible vs. irreversible toxicity

-local vs. systemic toxicity

INTERACTION OF CHEMICALS

- Additive
- Synergistic
- Potentiation
- Antagonism (functional, chemical, dispositional, receptor)

BASIC SURVEY OF ENVIRONMENTAL TOXICANTS

Toxic materials are substances that may cause harm to an individual if it enters the body.

Toxic materials may enter the body in different ways. These ways are called the **routes of exposure**. The most common route of exposure is through inhalation (breathing it into the lungs)

CLASSIFICATION OF TOXICANTS

Toxic agents are classified in a number of ways depending on the interests and needs of the classifier.

Dioscorides classified substances using general char-acteristics i.e., whether they are toxic or therapeutic.

An early scheme by Orfila classified substances as being of animal, vegetable or mineral origin

No single classification is applicable for the entire spectrum of toxic agents and combina-tions of classification systems based on other factors may be needed to provide the best rating system. Nevertheless, classification systems that take into ac-count both the chemical and biological properties of the agent, and the exposure characteristics are most likely to be useful for toxicology in general. Many clas-sification schemes for toxic agents are available which are based on following points

1. Based on the source of toxicants:

a. **Plant toxicants**, e.g., morphine, curare, strychnine.

b. **Animal toxicants**, e.g. toxins (zootoxins), venoms.

c. **Mineral toxicants**, e.g. copper, lead, selenium, iron.

d. **Synthetic toxicants,** e.g. organophosphates, Organochlorines, carbamates, aluminium phosphide.

2.Based on the Physical state of toxicants:

a. **Gaseous toxicants**, e.g. hydrocyanic acid (HCN), sulphur dioxide, carbon monoxide, phosphine.

b. **Liquid toxicants**, e.g. sulphuric acid, carbon disulphide, nicotine.

c. **Solid toxicants**, e.g. strychnine, opium, atropine.

d. **Dust toxicants**, e.g. asbestos dust, silicon dust, metallic dusts.

3.Based on the physical characteristics:

Inflammable / Non-inflammable,
Explosive / Non-explosive

4.Based on the physical effects:

Irritant / Non-irritant
Corrosive / Non-corrosive3

5.Based on the Target organ/system: It is difficult to classify a toxicant on the basis of its target organ or system as it may affect other systems also. How-ever, action on the primary site has been taken as a basis of classification.

a. Hepatotoxins, e.g. carbon tetrachloride, aflatoxins, phenol.

b. Neurotoxins, e.g. organophosphorus insecticides, pyrethroids, anaesthetics, nicotine.

c. Nephrotoxins, e.g. heavy metals (lead, arsenic, cadmium), oxa-lates.

d. Pulmonotoxicants, e.g. alpha-naphthylthiourea (ANTU), hydrogen sulphide, ammonia gas.

e. Haematotoxins, e.g. warfarin, cyanide, phenothiazine, snake venom (pit viper venom).

f. Dermatotoxicants, e.g. coal tar compounds (petroleum oils), heavy metals (arsenic, mercury), p-tertiarybutyl phenol.

6.Based on the Chemical nature/structure of toxicants:

a. **Inorganic toxicants**: These include metals, metalloids, non-metals and their salts and derivatives, acids and alkalies.

i. Metals, e.g., lead, copper, mercury, antimony.

ii. Non-metals, e.g. phosphorus, sulphur, chlorine, nitrate/nitrite.

iii. Acids and alkalies, e.g. hydrochloric acid, sulphuric acid, potassium hydroxide.6

b. **Organic toxicants**: These include all carbon compounds other than the oxides of carbon, the carbonates, and the metallic car-bides and cyanides.

1. Hydrocarbons, e.g. cyclopropane, benzene, paraffin, naph-thalene.
2. Halogen derivatives of hydrocarbons, e.g. chloroform, BHC, DOT, carbon tetrachloride.
3. Alcohols and phenols, e.g. methyl alcohol, ethyl alcohol, phenol, cresol, pentachlorophenol.
4. Ethers, e.g. diethyl ether, divinyl ether.
5. Aldehydes and ketones, e.g. formaldehyde, paraldehyde.
6. Organic acids, e.g. formic acid, phenoxy acetic acid, salicylic acid.

7. Esters, e.g. organophosphorus insecticides, succinylcholine.
8. Amines, e.g. adrenaline, ephedrine, amphetamine.
9. Amides, e.g. phenacetin, sulphonamides.
10. Glycosides, e.g. digitoxin, cyanogenetic glycosides.
11. Alkaloids, e.g. nicotine, atropine, strychnine.
12. Proteins, e.g. ricin, crotin, abrin.

7.Based on the Analytical behaviour of toxicants: Toxicants can be classified into separate characteristic groups according to the analytical procedures involved. In the Stas-Otto scheme, toxicants have been divided into the following groups.

a. Volatile toxicants, e.g. hydrocyanic acid, alcohols, acetone, phenol, chloral hydrate.

b. Extractive toxicants

i. Toxicants extractable by ether from acid solution, e.g. organic acids, nitro compounds.

ii. Toxicants extractable by ether from alkaline solution e.g. alkaloids

iii. Metals and metalloids, e.g. Copper, mercury, zinc, silver, antimony.

8.Based on the Toxic effects: It is difficult to classify toxicants on the basis of toxic effects as a single compound may have number of effects.

a. Carcinogens, e.g. thiouracil, vinyl chloride, nickel.

b. Mutagens, e.g. ethyl methane sulphonate, UV light, nitrogen mus-tards, nitroso compounds.

c. Teratogens, e.g. phenylmercuric acetate, triazines, thalidomide.

d. Clastogens, e.g. UV light, caffeine.

9.Based on the principal uses of toxicants:

a.Insecticides, e.g. organophosphorus insecticides, carbamates, pyrethroids.

b.Fungicides, e.g. captan, folpet, pentachlorophenol.

c.Herbicides, e.g. triazine, paraquat, 2,4-D. Amine weed killer

d. Rodenticides, e.g. warfarin, fluoroacetate, red squill.

e. Food additives:

i. Preservatives, e.g. ascorbic acid, sodium bisulphite.

ii. Antioxidants, e.g. ascorbic acid.

iii. Emulsifying agents, e.g. cholic acid, desoxycholic acid.

iv. Colouring agents, e.g. amaranth, tartrazine.

v. Anticaking agents, e.g. aluminium-calcium silicate.

1O.Based on the Toxicity/Poisoning potential:

	Group	Lethal dose
a.	Extremely toxic	< 1 mg/kg
b.	Highly toxic	1-50 mg/kg
c.	Moderately toxic	50-500 mg/kg
d.	Slightly toxic	0.5-5 g/kg
e.	Practically non-toxic	5-15 g/kg
f	Relatively harmless	> 15 g/kg.

11.Based on the Mechanism of action:

a. **Anticholinesterase agents/cholinesterase inhibitors**, e.g. organophosphorus insecticides, carbamates.

b. **Sulphydryl** (-SH) **inhibitors**, e.g. mercury, arsenic.

c. **Protoplasmic toxicants**, e.g. heavy metals.

d. **Corrosive toxicants**, e.g. caustic alkalies, acids, heavy metals, ir-ritant gases.

e. **Methaemoglobin producers**, e.g. nitrite

f. **Inhibitors of mixed function oxidases** (MFO), e.g. pipronyl butoxide.

g. **Inhibitors of Kreb's cycle**, e.g. fluoroacetate.

h. **Uncoupler of oxidative phosphorylation,** e.g. dinitrophenols, chlorophenol fungicides.

12.Based on the environmental and human health consideration:

- Air pollutants,
- water pollutants,
- radiation hazards,
- occupational hazards, etc.

THANK YOU


WEED
KILLER
ANTIFREEZE
Bathroom
Cleaner
CLEANER
TURPENTINE