

- **Toxicology**:- The study of the adverse effects of chemicals on living organisms.
- **Poison**:- Is any agent capable of producing a deleterious response in a biological system .
- **A mechanistic toxicologist**:- Identifies the Cellular, Biochemical, and Molecular mechanisms by which chemicals exert toxic effects on living organisms .
- **Toxin**:- Toxic substances that are produced by biological system such as plants, animals, fungi or bacteria .
- **Toxicant**:- substance that causes a harmful (or adverse) effect when in contact with a living organism at a sufficiently high concentration . Is used in speaking of toxic substances that are associated with human .
- **Exposure**: to cause an adverse effect , a toxicant must first come in contact with an organism . the means by which an organism comes in contact with the substance is the route of exposure (ex. In the air , water, soil, food , medication) for that chemical .
- **Dose**: the total amount of a toxicant administered to an organism at specific time intervals . the quantity can be further defined in terms of quantity per unit body weight or per body surface area .
- **LD₅₀** : The dosage of chemical needed to produce death in 50% of treated animals .

The characteristics of toxin or toxicant ;

1. The toxin or toxicant effect in Bio systems with low concentration.
2. It is accumulation in tissues.
3. The toxin low excretion.
4. The toxin is fast absorption.
5. The toxin able to reach the site of action.

6. Unionized.
7. Soluble in lipid.

General characteristics of Toxic response:

- ❖ One could define A poison as any agent capable of producing a deleterious response in a Biological system.
- ❖ Virtually every known chemical has the potential to produce injury or death if it is present in a sufficient amount.
- ❖ Table (1) shows the dosage of chemicals needed to produce death in (50 %) percent of treated animals (LD_{50}).
- ❖ It should be noted that measure of acute lethality such as (LD_{50}) may not accurately reflect the full spectrum of toxicity or hazard associated with exposure to chemical.
- ❖ For Example; some chemicals with low acute toxicity may have Carcinogenic or Teratogenic effects at doses that produce NO evidence of acute toxicity.

Spectrum of undesired effects:

The spectrum of undesired effects of chemicals is broad. For example, each drug produces a number of effects, but usually only one effect is associated with primary objective of the therapy, all the other, effects are referred to as side effects.

1. **Allergic Reaction:-** chemical allergy is an immunologically mediated adverse reaction to a chemical resulting from previous sensitization to that chemical or to structurally similar one. Once sensitization has occurred, allergic reaction may result from exposure to relatively very low doses of chemicals.

2. **Idiosyncratic Reaction:-** chemical idiosyncratic refers to a genetically determined abnormal reactivity to a chemical . For example individuals abnormally sensitive's readily oxidize the iron in hemoglobin to produce **Met hemoglobin** which is incapable of transporting oxygen to tissues .
3. **Immediate versus Delayed toxicity:-** Immediate toxic effects occurs or develop rapidly after a single administration of a substance, whereas, delayed toxic effects occur after the lapse of some time . Most substances produce immediate toxic effects, However, carcinogenic effects of chemicals usually have long latency periods of 10 - 20 - 30 years after the initial exposure , before tumors are observed in humans .
4. **Reversible versus irreversible Toxic effects:-** Some toxic effects of chemicals are reversible if a chemical produce pathological injury to a tissue, the ability of that tissue to regenerate largely determines whether the effects is reversible or irreversible for liver tissue with high regeneration ability, most injury are reversible. Carcinogenic effects of chemicals are considered irreversible toxic effects.
5. **Local versus systemic toxicity:-** Another distinction between types of effects is made on the basis the general site of action. Local effects occur at the site of first contact between the biological system and the toxicant. In contrast, systemic effects require absorption and distribution of toxicant from its entry point to a distant site, at which deleterious effects are produced. Most substances, except for highly reactive materials, produce systemic effects, for some material, both effects can be demonstrated. Most chemical that produce systemic

toxicity usually elicit their major toxicity in only one or two organs, which are referred to as the target organs of toxicity of particular chemical.

6. **Target organs** :- In order of frequency of involvement in systemic toxicity are the C N S; the circulatory system; the blood and hematopoietic system, liver, kidney, lung, skin, muscle and bone are seldom target tissues for systemic effects.

Interaction of chemicals;

Chemical interaction can occur via various mechanisms such as;

1. Alteration in absorption.
2. Protein binding.
3. The biotransformation.
4. Excretion of one or both of the interacting toxicants.
5. The response of the organism to combination of toxicants may be increased or decreased because of toxicology response at the site of action.

❖ **An additive effect**:-Most commonly observed when two chemicals are given together, occurs when the combined effect of two chemicals are equal to the sum of the effects of each agent given alone.

❖ **A synergistic effect**:- Occurs when the combined effects of two chemicals are much greater than the sum of the effects of each agent given alone for example (2+2=20).

❖ **Potentiation** : occurs when one substance does not have a toxic effect on a certain organ or system but when added to another chemical makes that chemical

much more toxic (ex. $0+2=10$) Isopropanol, for example, is not hepatotoxic but when it is administered in addition to carbon tetrachloride the hepatotoxicity of carbon tetrachloride is much greater than that when it is given alone

❖ **Antagonism**:- Occurs when two chemicals administered together with each other's actions or one interferes with action of the other.

There are four types of antagonism:

1. **Functional antagonism.** Occurs when two chemical counterbalance each other by producing opposite effects on the same physiologic function for example the marked fall in blood pressure during severe barbiturate intoxication can be effectively antagonized by the intravenous administration of a vasopressor agent such as norepinephrine or metaraminol.

2. **Chemical antagonism:** Chemical antagonism or inactivation is simply a chemical reaction between two compounds that produces a less toxic product , ex: chelators of metal ions decrease metal toxicity and antitoxins antagonize the action of various animal toxins .

3. **Dispositional antagonism :** occurs when the absorption , biotransformation , distribution , or excretion o a chemical is altered so that the concentration and / or duration of the chemical at the target organ are diminished

4. **Receptor antagonism.:** occurs when two chemical that bind to the same receptor produce less of an effect when given together than the addition of their separate effects ,(ex: $4+ 6 = 8$

) or when one chemical antagonizes the effect of the second chemical. Receptor antagonists are often termed blockers.

Tolerance

Tolerance :- Is a state of decreased responsiveness to a toxic effect of a chemical resulting from prior exposure to that chemical or to a structurally related chemical. Two major mechanisms are responsible for tolerance; once is due to a decreased amount of toxicant reaching the site where the toxic effect is produced and the others is due to a reduced responsive of a tissue to the chemical.

Characteristics of exposure

Toxic effect in a biological system are not produced by chemical agents unless that agent or its metabolic breakdown products reach appropriate sites in the body of a concentration and for a length of time sufficient to produce a toxic manifestation.

A toxic response occurs dependent on the chemical and physical properties of the agent, the exposure situation;

- a. **Rout and site of exposure**:- The major routs (pathways) by toxic agents gain access to the body are the gastrointestinal tract, lungs (inhalation) and skin.
- b. **Duration and frequency of exposure**:- Usually divided the exposure of experimental animals to chemicals into four categories;
 1. **Acute exposure**:- Is define as exposure to chemical for less than 24 hour, acute exposure usually refers to a single administration, repeated exposures may be given within a 24 hour period for some slightly toxic or partially non – toxic chemical. Acute

exposure by inhalation refers to continues exposure for less than 24 hour, most frequently for 4 hour.

2. **Sub acute exposure:-** *Refers to repeated exposure to chemical for ONE month or less.*
3. *Sub chronic for ONE to THREE months.*
4. *Chronic exposure for more than THREE months.*