Introduction to Toxicology

T**oxicology** is the study of the toxic effects of chemical, biological, and physical agents on biological systems.

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).

Classification of Toxic Agents:

Toxic agents are classified in number of ways depending on the interests and needs of the classifier. In toxicology, compounds are classified in various ways, by one or more of the following classes:

Classification based on sources of toxicants

1.Plant toxins
2.Animal toxicants
3.Mineral toxicants
4.Synthetic toxicants
5.Physical or mechanical agents.

Classification based on physical state of toxicants

1.Gaseous toxicants
2.Liquid toxicants

3.Solid toxicants

4.Dust toxicants.

Classification based on chemical nature/structure of toxicants

1.Metals

2.Nonmetals

3.Acids and alkalis

4.Organic toxicants (carbon compounds other than oxides of carbon, the carbonates, and metallic carbides and cyanides).

Classification based on their uses

1.Insecticides

2.Fungicides

3.Herbicides

4.Rodenticides

5.Food additives, etc.

Classification based on type of toxicity

1.Acute

2.Subacute

3.Chronic.

Acute toxicity occurs almost immediately (hours/days) after an exposure. An **acute exposure** is usually a single dose or a series of doses received within a 24 hour period. Death is a major concern in cases of acute exposures. Examples are:

- In 1989, 5,000 people died and 30,000 were permanently disabled due to exposure to methyl isocyanate from an industrial accident in India.
- Many people die each year from inhaling carbon monoxide from faulty heaters.

Non-lethal acute effects may also occur, e.g., convulsions and respiratory irritation.

Subacute toxicity results from repeated exposure for several weeks or months. This is a common human exposure pattern for some pharmaceuticals and environmental agents. Examples are:

- Ingestion of Coumadin tablets (blood thinners) for several weeks as a treatment for venous thrombosis can cause internal bleeding.
- Workplace exposure to lead over a period of several weeks can result in anemia.

Chronic toxicity represents cumulative damage to specific organ systems and takes many months or years to become a recognizable clinical disease. Examples of chronic toxic effects are:

- cirrhosis in alcoholics who have ingested ethanol for several years.
- chronic kidney disease in workmen with several years of exposure to lead.
- chronic bronchitis in long-term cigarette smokers.
- pulmonary fibrosis in coal miners *(*black lung disease*).*

Classification based on target organ or system

Toxic substances may be **systemic toxins** or **organ toxins**.

1. 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.

2. Organ toxin: is one that affects only specific tissues or organs known as the target organs or target tissues.
For examples: Benzene is a specific organ toxin in that it is primarily toxic to the blood-forming tissues.

Types of organ toxins:

- Blood and Cardiovascular Toxicity
- Dermal Toxicity
- Ocular Toxicity
- Hepatotoxicity
- Immunotoxicity
- Nephrotoxicity
- Neurotoxicity
- Reproductive Toxicity
- Respiratory Toxicity

Blood and Cardiovascular Toxicity results from xenobiotics acting directly on cells in circulating blood, bone marrow, and heart.
- leukemia due to benzene damage of bone marrow cells
- arteriosclerosis due to cholesterol accumulation in arteries and veins

Dermal Toxicity may result from direct contact or internal distribution to the skin. Effects range from mild irritation to severe changes, such as corrosivity, hypersensitivity, and skin cancer. Examples of dermal toxicity are:

- dermal irritation due to skin exposure to gasoline
- dermal corrosion due to skin exposure to sodium hydroxide
- dermal hypersensitivity due to skin exposure to poison ivy
- skin cancer due to ingestion of arsenic or skin exposure to UV light

Eye (Ocular) Toxicity results from direct contact or internal distribution to the eye. The cornea and conjunctiva are directly exposed to toxicants. Thus, conjunctivitis and corneal erosion may be observed following occupational exposure to chemicals. Many household items can cause conjunctivitis. Chemicals in the circulatory system can distribute to the eye and cause corneal opacity, cataracts, retinal and optic nerve damage.

- acids and strong alkalis may cause severe corneal corrosion
- corticosteroids may cause cataracts
- methanol may damage the optic nerve

Hepatotoxicity is toxicity to the liver, bile duct, and gall bladder. The liver is particularly susceptible to xenobiotics due to a large blood supply and its role in metabolism. Thus it is exposed to high doses of the toxicant or its toxic metabolites.

Immunotoxicity relates to the immune system. It can take several forms: hypersensitivity (allergy and autoimmunity), immunodeficiency, and

uncontrolled proliferation (leukemia and lymphoma). The normal function of the immune system is to recognize and defend against foreign invaders. This is accomplished by production of cells that engulf and destroy the invaders or by antibodies that inactivate foreign material. Examples:

- contact dermatitis due to exposure to poison ivy
- systemic lupus erythematosus in workers exposed to hydrazine
- immunosuppression by cocaine
- leukemia induced by benzene

Nephrotoxicity is toxicity to the kidneys. The kidney is highly susceptible to toxicants for two reasons. A high volume of blood flows through it and it filtrates large amounts of toxins which can concentrate in the kidney tubules. It can result in:

- decreased ability to excrete body wastes
- inability to maintain body fluid and electrolyte balance
- decreased synthesis of essential hormones (e.g., erythropoietin)

Neurotoxicity represents toxicant damage to cells of the central nervous system (brain and spinal cord) and the peripheral nervous system (nerves outside the CNS). The primary types of neurotoxicity are:

- neuronopathies (neuron injury)
- axonopathies (axon injury)
- demyelination (loss of axon insulation)
- interference with neurotransmission

Reproductive Toxicity involves toxicant damage to either the male or female reproductive system. Toxic effects may cause:

- infertility
- interrupted pregnancy (abortion, fetal death, or premature delivery)
- infant death or childhood morbidity
- altered sex ratio and multiple births
- chromosome abnormalities and birth defects
- childhood cancer

Respiratory Toxicity relates to effects on the upper respiratory system (nose, pharynx, larynx, and trachea) and the lower respiratory system (bronchi, bronchioles, and lung alveoli). The primary types of respiratory toxicity are:

- pulmonary irritation
- asthma/bronchitis
- reactive airway disease
- emphysema
- allergic alveolitis
- fibrotic lung disease
- pneumoconiosis

References

1. Gupta, PK. (2018). General toxicology. Illustrated Toxicology. Pp: 1-65. https://doi.org/10.1016/B978-0-12-813213-5.00001-8

2. Eaton D.L., & Gilbert S.G. (2013). Principles of toxicology. Klaassen C.D.(Ed.), Casarett and Doull's Toxicology: The Basic Science of Poisons, Eighth Edition. McGraw Hill. https://accesspharmacy.mhmedical.com/content.aspx?bookid=958&sectionid=53483721