Introduction to Toxicology

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Overview

- Introduction to Toxicology
  - Definitions.
- Principles of Toxicology
  - Classification of Toxic Agents.
  - Spectrum of Undesired Effects.

Definition

- ***"the science of poisons."***

- ***"the study of the adverse effects of chemicals or physical agents on living organisms".***

Toxicology- Introduction

- All things are poison and nothing (is) without poison. Solely the **dose** determines that a thing is not a poison.

Paracelsus

(1493–1541)

Toxic Response

- P*oison:* 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 dose.

Classification of Toxic Agents

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

- Toxic agents may also be classified in terms of :

1- Physical state (gas, dust, liquid).

2- Chemical stability or reactivity (explosive, flammable, oxidizer).

3- General chemical structure (aromatic amine, halogenated hydrocarbon, etc.).

4- Poisoning potential (extremely toxic, very toxic, slightly toxic, etc.).

5- Biochemical mechanisms of action (alkylating agent, cholinesterase inhibitor, methemoglobin producer).

Toxic response

- Most toxic responses are usually are related to dose.
- Phenomenon that do not follow dose response
  - Allergy
  - Idiosyncratic reactions

Allergic Reactions

- An immunologically mediated adverse reaction to a chemical resulting from previous sensitization to that chemical or to a structurally similar one.
- Once sensitization has occurred, allergic reactions may result from exposure to relatively very low doses of chemicals.
- Reactions are sometimes very severe

Allergic Reactions

- Most chemicals and their metabolic products are not sufficiently large to be recognized by the immune system as a foreign substance and thus must first combine with an endogenous protein to form an antigen (hapten).

- The hapten–protein complex is then capable of formation of antibodies. Subsequent exposure to the chemical results in an antigen–antibody interaction, which provokes manifestations of allergy that range in severity from minor skin disturbance to fatal anaphylactic shock.

Idiosyncratic Reactions

- Refers to a genetically determined abnormal reactivity to a chemical.

- The response observed is usually qualitatively similar to that observed in all individuals but may take the form of extreme response to low doses or extreme irresponsive to high doses of the chemical.
- Examples: G6PD, Scoline apnea, Disulfiram reactions

Chemicals Interactions

- Toxicants administered or received simultaneously may act independently of each other.
- Presence of one chemical may drastically affect the response to another chemical.
- The toxicity of a combination of chemicals may be less or it may be more than would be predicted from the known effects of each individual chemical.

Types of Chemical Interactions

Types of interactions:

- Additive
- Synergistic
- Potentiation
- Antagonist:
  - Receptor
  - Functional
  - Chemical
  - Dispositional: Absorption, Metabolism, excretion

Additive

- The most common type of drug interaction.
- The effect occurs due to algebraic summation of the activity of individual substance

- Examples of chemical additive reactions:

  Two central nervous system (CNS) depressants taken at the same time, a tranquilizer and alcohol, often cause depression equal to the sum of that caused by each drug.

Potentiation

- Occurs when a chemical that does not have a specific toxic effect makes another chemical more toxic.
  - The hepatotoxicity of carbon tetrachloride is greatly enhanced by the presence of isopropanol.
  - Warfarin is bound to plasma albumin so that only 2% of the warfarin is active. Drugs which compete for binding sites on albumin increase the level of free warfarin to 4% causing increase hemorrhage.

Synergism

- Exposure to a chemical may drastically increase the effect of another chemical.
  - Exposure to both cigarette smoke and radon results in a significantly greater risk for lung cancer than the sum of the risks of each.
  - Combination of exposure to asbestos and cigarette smoke results in a significantly greater risk for lung cancer than the sum of the risks of each.
  - Hepatotoxicity of a combination of ethanol and carbon tetrachloride is much greater than the sum of the hepatotoxicity of each.

Antagonism

- Occurs when two chemicals are administered together interfere with each other's actions.
- Bases of Antidotes
- There are four major types:

    1- Functional Antagonism.

    2- Chemical Antagonism.

    3- Dispositional Antagonism.

    4- Receptor Antagonism.

Functional antagonism

- Occurs when two chemicals counterbalance each other by producing opposite effects on the same physiologic function (tachycardia, bradycardia, hypotension, hypertension, exc..)

Chemical antagonism

- Chemical reaction between two compounds that produces a less toxic product.
  - Chelators for heavy of metal toxicity
  - Protamine sulphate for Heparin

Dispositional antagonism

- Methods that interfere with **absorption, Metabolism and excretion** of a chemical that the concentration and/or duration of the chemical at the target organ are diminished to decease toxic response.

Receptor antagonism

- Occurs when two chemicals potentially bind to the same receptor, the one which occupy the receptor will dominate the action
  - Naloxone and Opiates
  - Flumazenil for Benzodiazepine
  - Atropine for toxins that increase acetylcholine
  - Physostigmine foe Atropine