

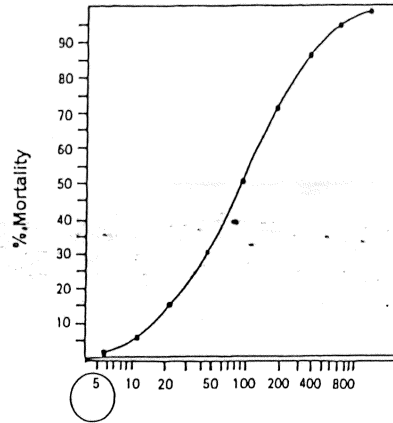


السنة الرابعة علم السموم

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نظري م 1+2+3

Dose-Response Relationship



The dose-response relationship

(from C.D. Klaassen, *Casarett and Doull's Toxicology*, 5th ed., New York: McGraw-Hill, 1996; reproduced with permission).

Gray Region Dose (mg/kg)

The Occupational Environment – *Its Evaluation and Control*

8.1

Exposure Limits Summary

Agent	OSHA PEL	NIOSH REL	AEC MLD

Categories of toxicity

- A substance with a median lethal dose of less than 1mg/ kg is considered to be extremely toxic
- Highly toxic substances less than 50mg/kg
- Moderately toxic substances less than 500mg/kg
- Slightly toxic substances greater than 500mg/kg and up to 5g/kg

DOSE - RESPONSE 3

D-R relationship determines relative toxicity rating

<i>LC50</i> 4-hr inhalation rat ppm	<i>LD50</i> single oral rat mg/kg	<i>Term</i>	<i>Rating</i>
< 10	5 or less	Super Toxic	1
10-100	5-50	Extremely Toxic	2
100-1,000	50-500	Highly Toxic	3
1,000-10,000	500-5,000	Moderately Toxic	4
10,000-100,000	5,000-15,000	Slightly Toxic	5
> 100,000	> 15,000	Nearly Non-Toxic	6

Mixtures

- -Mixtures of poisons can be more toxic or less toxic than predicted from the toxicity of the individual component of the mixture
- -Synergism : increased toxicity of a mixture
- -Antagonism : is the observation of less than predicted toxicity from a mixture

CHEMICAL INTERACTIONS

Combinations of chemicals can alter the usual effect of the individual chemicals

1 + 1 = 2 Additive ■

toxic chemicals affecting the same organ/system ■

1 + 1 > 2 Synergistic ■

toxic chemicals enhance each other's effects ■

1 + 0 > 1 Potentiation ■

non-toxic chemical increases the toxic effect of a toxic chemical ■

1 + 1 < 2 Antagonism ■

chemicals hinder the toxic effect(s) of one another or both (i.e., antidote) ■

Toxicity, hazard, and risk

- -The term hazard can be used to describe the actual risk of poisoning
- Its possible to reduce hazard of a toxic substance by reducing the practical risk of exposure

Toxicity vs. Hazard

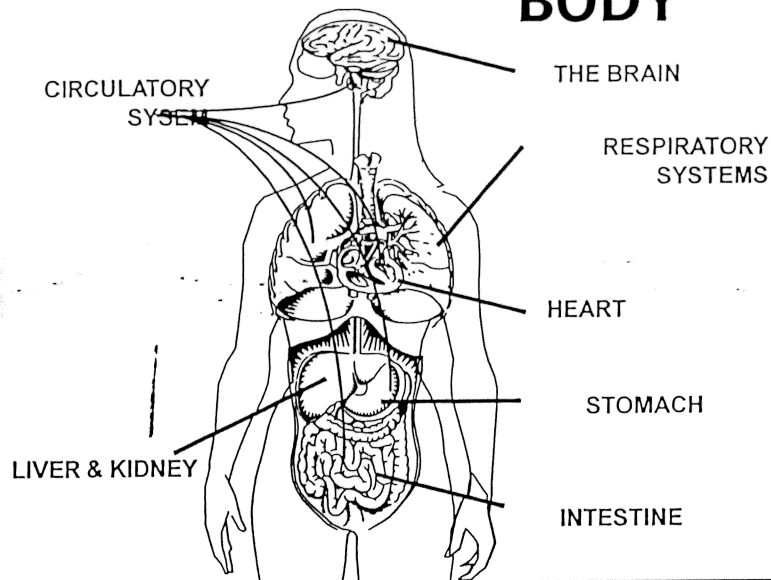
TOXICITY

- capacity of a substance to cause harm ■
 - inherent to the substance ■
- the effect a specific quantity or dosage of a specific toxin (Chemical) has on a living microorganism ■
 - not an absolute! ■

HAZARD

- probability of, potential for a substance or situation to cause harm (toxicity value + exposure factor) ■
 - determined by many factors; can be changed ■
 - eliminate hazards through control ■

TOXINS IN OUR BODY



Toxicokinetics

■ Pharmacokinetics and toxicokinetics

■ Absorption :

- oral route of absorption
- respiratory route of absorption
- Dermal route of absorption

■ Distribution

■ Elimination:

is the loss of the parent drug or toxicant from the body due to biotransformation of the parent drug to metabolites, and also from excretion of the parent drug in urine or feces .

The major routes of excretion are :

- ❖ kidney-urine
- ❖ Liver – blood-bile
- ❖ Gastro intestinal tract
- ❖ Respiratory system
- ❖ Dermal, hair
- ❖ Saliva
- ❖ Sweat
- ❖ Milk

Biotransformation

- Primary biotransformation (phase I)
 - -Hydrolysis
 - -oxidation
 - -reduction

■ **secondary metabolism (phase II reactions)**

- Products of phase I may enter a secondary phase of biotransformation in which they are rendered highly polar by conjugation to carbohydrates, amino acids, or small peptides.
- The products, or conjugates, are excreted from the body more efficiently than the parent or the phase I products .
 - Glucuronidation
 - Glutathione conjugation
 - Acetylation

Hydrolysis

- The enzyme that catalyze the hydrolysis are called hydrolases, hydrolases include amydases, peptidases, lipase and cholinester hydrolases
- **Methoprene** : an insecticide used for mosquito and fly control
 - Possesses chemistry similar to that of the fatty acid alkyl ester
 - is hydrolyzed to produce isopropanol and an aliphatic acid metabolite
- **Mirex** :
 - an insecticide, the unusual structure of this insecticide renders it practically impervious to biotransformation
 - Mirex has no ester present; therefore, there is no opportunity for ester hydrolysis

Oxidation