

Toxic Substances

I. Introduction

A. Dose units

- mg/kg of body weight (for lethal dose)
- LD₅₀ - 50% of animals die with this dosage

B. Modes of action

- corrosive
- metabolic
- neurotoxic
- teratogenic
- mutagenic
- carcinogenic

II. Corrosive

A. Destroy tissues

B. Examples

- strong acids and bases cause hydrolysis of proteins
- ozone, hypochlorite, nitrogen dioxide , etc. are oxidizing agents

III. Metabolic

A. Interferes with a biochemical mechanism

B. Examples

1. CO - product of incomplete combustion
ties up hemoglobin with a compound much more stable than oxygen, thus causing asphyxiation

CN - found in seeds of many fruits including cherry, peach, apple; it interferes with oxidative enzymes such as cytochrome oxidase that help to metabolize glucose with oxygen; this causes asphyxiation

C. More examples - Heavy metals -

1. Tend to accumulate in the body
2. React and inhibit enzyme systems (with -SH) that are involved in production of cellular energy; symptoms also how in central nervous system
3. Common problems - Pb, Cd, As, Hg
 - Arsenic used in WWI. Chelating agent BAL useful as an antidote.
 - Mercury is volatile and is absorbed through the skin; tends to accumulate in the food chain

- Lead is present in soil and is found in foods and water supplies; it presents problems due to prior use of lead in paint and gasoline. Chelating agent EDTA useful as an antidote.

IV. Neurotoxins

A. Often act at the synapse where 2 nerve fibers come together. As an impulse is transmitted *acetylcholine* is often liberated and activates the adjoining nerve fiber. *Norepinephrine* is used by other nerves.

***Cholinesterase* breaks down acetylcholine and then *acetylase* reforms *acetylcholine*.**

B. Types

1. Anticholinesterase poisons deactivate cholinesterase. Excess acetylcholine overstimulates system leading to irregular heartbeat, convulsions and death.

Examples: organic phosphate insecticides, poisonous mushrooms, malathion, sevin

2. Some poisons block or mimic the receptors so they do not accept the acetylcholine.

Examples: curare, atropine, nicotine, caffeine, morphine, codeine, cocaine

3. A few poisons inhibit the synthesis of acetylcholine.

V. Teratogens - affect human reproduction

A. Types

1. Radiation
2. Viral agents
3. Chemical substances - heavy metals, caffeine, PCB's

B. Sensitive periods

1. Conception to implantation in uterine wall (1-17 days)
(abortion pill RU-486)
2. Organogenesis (18-55 days) Most sensitive period
3. Fetal period (56 days to term) Less sensitive

VI. Mutagens

- **Alter genes and chromosomes by altering structure of DNA**
- **Many substances have been shown to be mutagenic and cause abnormalities in offspring of lab animals but no conclusive evidence exists for humans**
- **Examples: nuclear radiation, benzopyrene, caffeine, chloroprene, LSD organic solvents, ozone, nitrous acid**

VII. Carcinogens - cause cancer

A. Cancer is an abnormal growth of cells

1. Rate of growth (fast or slow)
2. Spread to other tissues
3. Lose specialized function

B. Stages

1. Initiation - change in DNA
2. Promotion - time passes and some exposure or irritation causes a large destruction of cells. As these cells are replaced the abnormal growth starts.

C. Cells affected

1. Mainly epithelial cells (skin, glands, linings of lungs and intestines) -
- carcinomas are 85% of all cancers
2. Connective tissue -- sarcomas
3. Lymph system -- lymphomas
4. Blood -- leukemia
5. skin pigment - melanoma
6. sex cells - seminoma

D. Carcinogenic substances

1. Industrial
Metals (As, Cd, Cr, Ni, Asbestos)
Organic compounds (Benzene, benzopyrene, vinyl chloride)

2. Dietary

sodium nitrite, hydrazine, saffrole, ethanol

VIII. Chemical Warfare Agents

Mostly gases based on action of other types, used primarily in WWI and WWII

Choking gas	Phosgene	Corrosive
Blood gas	HCN	Metabolic
Nerve gas	Saran	Neurotoxins