Introduction to Toxicology

- Toxicology -- the study of poisons and their mechanism of action
- Toxicity -- the adverse effects that a chemical may produce
- Dose -- the actual amount of substance introduced into a body
- Exposure – contact providing the opportunity of obtaining a poisonous dose
- Hazard – the likelihood that the toxicity will be expressed

It's All in the Dose

- You have heard that too much of a good thing can be bad for you. A normally benign and harmless substance can become toxic at high doses.
- On the opposite end of the spectrum, highly toxic chemicals can be life-saving when given in small controlled doses.

Exposure Concepts

- Toxic responses may arise from different:
  - Routes of exposure
  - Frequencies of exposure
  - Duration of exposure (acute vs. chronic)

Routes of Exposure

- Ingestion
- Injection
- Inhalation
- Absorption

Duration & Frequency of Exposure

- Acute exposure -- less than 24 hours; usually entails a single exposure
- Subacute – repeat exposure up to a month
- Subchronic -- repeated exposure up to three months
- Chronic – repeated exposure for more than three months

Exposure Concepts

- Environmental
- Occupational
- Therapeutic
- Dietary
- Accidental
- Deliberate

Xenobiotics

- Defined as foreign chemicals which are synthesized within a living body (*Xeno-* meaning "strange")
- Many of these poisonous xenobiotics are defense mechanisms used for survival or are simply waste products in chemical form produced by plants, microorganisms, or animals, including humans.
  - Clostridium botulinum – waste product, not bacteria alone causes paralysis; use: Botox for relaxing muscles; still lethal
  - Clostridium tetani -- spores of bacteria found on rust cause paralysis; uses -- NONE

Xenobiotics

- Some chemicals are inactive until in the presence of another chemical to make their effects poisonous.
- Xenobiotics may also be produced by humans or bovine such as insulin converted into synthetic form for use
- Ancient plant Xenobiotics: digitalis for heart problems vs. hemlock for poisoning

Toxicokinetics -- Movement of Poisons

- Distribution -- the movement of poison through different routes
- Metabolism – the breakdown of chemicals from active to inactive forms starting with enzymes in the stomach and then in the liver
- Elimination -- removal of all by-products of poisons

Influencing factors affecting movement of poisons

- Different molecular weights
- Concentration of solutes versus solvent
- Victim's status of health

Mechanisms of Action for Xenobiotics

- Sometimes xenobiotics will work better once metabolized and the by-products become the harmful substances
- Substances work by disrupting normal cell function
  - Denature proteins
  - Cause a defect in DNA
  - Target lipids

Types of Toxic Effects

- Death – absence of cell function; causes -- cyanide and arsenic
- Organ Damage – loss of cellular function causing chronic diseases that have no cure; causes -- lead and ozone exposure
- Mutagenesis –a process by which the genetic information of an organism is changed, resulting in a mutation. May occur in nature, or as a result of exposure to mutagens; causes -- UV light
- Carcinogenesis -- process by which normal cells are transformed into cancer cells; causes -- benzene, asbestos
- Teratogenesis – process by which congenital malformations are produced in an embryo or fetus; cause – thalidomide

Challenges / Potential Dangers in Herbal Medicines

- Not enough / too much chemical isolated
- Plant variations leading to poor chemical production
- Variations in extraction techniques
- Not endorsed by Food and Drug Administration
  - Growth requirements not standardized as in pharmaceuticals
  - Variations in standards of growth and isolation can affect final prices

Occupational Versus Environmental Toxicology

- Environmental
  - Environmental toxicants -- agents hazardous to air, sea or land and potentially all humans
  - Agents can be naturally occurring and synthetic in nature and BOTH can be just as deadly

Occupational Versus Environmental Toxicology

- Occupational: many examples of diseases are associated with specific occupations
  - Miner's Disease came from inhaling metal vapors, and became foundation for chemotherapy
  - Linked chewing tobacco to cancer
  - Radium dial painters developed masses in mouth when they licked their brushes to make a fine point
  - Chimney sweepers were linked to scrotal cancer
  - Shoe salesmen who used fluoroscopes to take radiographs of client feet for fitting began to develop cancers

High cancer-risk occupations

- Health care workers
- Pharmaceutical
- Laboratory workers
- Refinery workers
- Rubber workers
- Furniture makers
- Pesticide workers

Methods of extracting poisons

- Gel-filtration chromatography -- separate particles by size
- Ion-Exchange chromatography -- separate particles by charge
- Electrophoresis -- separate particles by charge
- Affinity chromatography -- dependent on number of hydrogen bonds