Introduction to Toxicology

History of Poisons

- 2700 – 800 BC
  Chinese, Egyptians and Hindus documented vast amounts of information related to the collection, preparation and administration of many plants and animals used as medicines and poisons.

History of Poisons

50-400 A.D.

- Greek physicians classified over 600 plant, animal, and mineral poisons.
- Romans used poisons for executions and assassinations.
- The philosopher Socrates was poisoned using hemlock for teaching radical ideas to youths.

History of Poisons

980-1200 AD

- In Islamic culture, Avicenna becomes the authority on poisons and antidotes.
- In Spain, Rabbi Maimonides wrote a first-aid book on poisonings.

History of Poisons

- 1493-1541 AD
  Swiss physician Paracelsus is credited with being “the father of modern toxicology”. He introduced the notion that too much of anything, even if it is good for you, can be a bad thing.

History of Poisons

1700's - 1800's

- Ramazzini, an Italian physician, first discussed environmental diseases such as those with asthma-like symptoms in laymen workers like bakers, farmers, glass-workers, tanners, millers, grain-sifters and stonecutters.
- In Spain, toxicology was established as a formal scientific discipline by Dr. Orfila.

History of Poisons

20th Century

- While trying to create different tissue stains and procedures, Dr. Paul Ehrlich found how toxicants affected biological tissues.
- Rachel Carson alarmed people about dangers of pesticides in the environment.
- Dr. Alan Scot accidentally invented Botox, a neurotoxin caused by the one of nature's deadliest bacteria.

- 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