EVE 491/591
Toxicology

Lecture #1
1. Introductory material
2. Chapter #1

What do you remember from EVE 486?

• **Toxicology**: the study of the adverse effects of chemical agents on living organisms; often lab animal testing 😊
• Important terms
  – Exposure pathways
  – Toxicity testing
    • Dose-response curves
    • acute (LD₅₀) vs. short term vs. long term
    • NOAEL, LOAEL, threshold
    • Endpoints (carcinogenesis, reproductive toxicity…)
    • Difficulties (extrapolations, artifacts…)

Keep this in mind…

• Public health (in broad terms) and toxicology (specifically) focus on **people**, but we must remember that the effects of chemical exposures are felt by plants and animals as well.
• Examples?
Chemicals are Everywhere

- Exposure to chemicals is unavoidable
- Adverse events can occur
  - Accidental exposure
    - Bhopal 1984
      - Methyl isocyanate discharge killed 4,000 and injured more than 100,000
  - Unanticipated result of deliberate use
    - Chronic low level exposures
    - Safety of new drugs and food additives often inferred from animal data
Chemical or Substance?

**Toxic chemical**
- any chemical which, through its chemical action on life processes, can cause death, temporary incapacitation, or permanent harm to humans or animals.

**Toxic substance**
- a generic term that does not differentiate between a particular chemical or a mixture of chemicals that collectively have toxic properties.

Poison

A **poison** is any substance that may, by its chemical action, cause death or injury.
- Toxic in *relatively small amounts*
- May be ingested, inhaled, absorbed, injected into, or developed within the body
- A poison therefore could be any of the numerous synthetic chemicals or a chemical produced by a living organism (toxin).

Toxin or Toxicant?

The terms toxicant and toxin are often used interchangeably but they are different:

**A Toxicant is:**
- Any chemical that can potentially produce harm
- May be specific or nonspecific
- Examples include:
  - heavy metal (e.g., lead)
  - a pesticide
  - organic solvent
  - toxin

**A Toxin is:**
- A chemical produced by living organisms
- Examples include:
  - Rattlesnake venom
  - Aflatoxin B (Aspergillus flavus)
  - Tetrodotoxin (Puffer fish, Amphibians)
Xenobiotics

literally foreign to the body

can refer to any chemical that is not a natural component of the body (e.g., a synthetic antibiotic).

Examples of Xenobiotics

<table>
<thead>
<tr>
<th>Toxicant and Source</th>
<th>Example of Tissue/System Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deltamethrin (insecticide)</td>
<td>Nervous System</td>
</tr>
<tr>
<td>Ethylene glycol monomethyl ether (solvent)</td>
<td>Toxic</td>
</tr>
<tr>
<td>n-Hexane (solvent)</td>
<td>Nervous System</td>
</tr>
<tr>
<td>Methyl isocyanate (used in tobacco manufacture)</td>
<td>Lung and Eye</td>
</tr>
<tr>
<td>1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPPP) (injury in dammal)</td>
<td>Nervous</td>
</tr>
<tr>
<td>Paraquat (herbicide)</td>
<td>Lung</td>
</tr>
<tr>
<td>Selenium (new gas)</td>
<td>Nervous System</td>
</tr>
</tbody>
</table>

The Roots of Toxicology

Early influences:

- Ebers papyrus (circa 1500 B.C.)
- Hippocrates (circa 400 B.C.)
- Theophrastus (371–287 B.C.)
- Dioscorides (40–90 A.D.)
- Maimonides (1135–1204 A.D.)
Ebers papyrus

- Contains the recipes of more than 800 "medicinal" and poisonous preparations:
  - hemlock ("Socrates’ nightcap")
  - Opium
- Also, explains the treatment for guinea worm disease we still use!

Hippocrates (circa 400 B.C.)

One of the first physicians to apply basic pharmacology and toxicology principles to the practice of medicine, including concepts of:
- bioavailability (the pharmacokinetic property)
- overdose

Early Treatises of Note
- *De Historia Plantarum* by Theophrastus
  - Described poisonous plants
- *De Material Medica* by Dioscorides
  - Greek pharmacist, physician and botanist serving Nero
  - Classified poison by origin
    - Animal
    - Vegetable
    - Mineral
  - Five-volume systematic description
    - 600 different plants
    - 1,000 different medications
  - Still relevant
Early Treatises of Note, cont.

- **Poisons and Their Antidotes** by Maimonides
  - Treatments for accidental or intentional poisonings and animal bites
  - Rejected numerous ‘remedies’ after testing their efficacy

Paracelsus (1493–1541)

- Father of Toxicology
- Wrote “On the Miners’ Sickness and Other Diseases of Miners”
  - First major work of occupational toxicology
- Developed concept of dose-response that is the basis of modern toxicology

“All things are poison and nothing is without poison, only the dose permits something not to be poisonous.”

Concept of Dose-Response

- Experimentation is essential in the examination of the response to chemicals.
- One should make the distinction between the therapeutic and toxic properties of a chemical.
- One can ascertain a degree of specificity of chemicals and their therapeutic or toxic effects.
- Therapeutic and toxic properties are sometimes only distinguishable by dose.
Unsavory Applications

Famous Suicides:
- ‘Execution’ of Socrates - hemlock
- Mithridates VI of Pontus - He had spent years successfully building tolerance to avoid assassination and resorted to his sword after suicide by poison failed.
  - ‘mithridate’ - antidote

Rogues Gallery:
- Giulia Toffana
  - ‘Google’ her 😊
- Heironyma Spara
  - Her, too
- Catherine Deshayes

Toxicology in the twentieth century

- Toxicology is multidisciplinary
- Explosive growth in past century
  - ‘patent’ medicines
  - Pollution
  - Occupational injuries and illnesses
- Public concerns led to
  - Legislative action
  - Regulatory agencies
  - Professional organizations