



Principles and  
Practice of  
**TOXICOLOGY**  
in Public Health

SECOND  
EDITION

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# Chapter 1

## Toxicology and Its Roots as a Science

# What is toxicology?

- Toxicology is the study of the adverse effects of chemicals in biological systems.
- Biological system can be:
  - Organism
  - Cell
- Public health focuses on people but we must remember that the effects of chemical exposures are felt by plants and animals as well.

# 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

# Toxic Chemicals

- Terms commonly used to refer to toxic chemicals are as follows:
  - Toxic chemical
  - Toxic substance
  - Toxic agent
  - Poison
  - Toxin
  - Toxicant
  - Xenobiotic

# 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

# Toxin

- Any chemical that can potentially produce harm
- May be specific or nonspecific
- Examples include:
  - heavy metal such as lead
  - a pesticide
  - organic solvent

# Toxicant

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

# Xenobiotics

- Literally mean “foreign to the body”
- Can refer to any chemical that is not a natural component of the body (e.g., a synthetic antibiotic).

# Table 1-2 Examples of Xenobiotics

Toxicant and Source	Example of Tissue/System Affected
Deltamethrin <i>(insecticide)</i>	Nervous
Ethylene glycol monomethylether <i>(solvent)</i>	Testis
n-Hexane <i>(solvent)</i>	Nervous
Methyl isocyanate <i>(used in insecticide manufacture)</i>	Lung and Eye
1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) <i>(impurity in demerol)</i>	Nervous
Paraquat <i>(herbicide)</i>	Lung
Soman <i>(nerve gas)</i>	Nervous

# Types of Epidemiologic Studies

- Cohort Studies
  - Prospective Cohort Study
  - Retrospective Cohort Study
- Case Control Studies
- Cross-Sectional Studies
- Ecological Studies

# Hill's Criteria of Causality

- Strength of Association
- Temporality
- Consistency Biological Plausibility
- Coherence
- Specificity
- Dose Response Relationship
- Experimental Evidence
- Analogy

# Weight of Evidence for Causality

- Causal
- Likely to be Causal
- Suggestive of Causality
- Evidence is Inadequate
- Not Likely to be Causal

# 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
  - aconite (a Chinese arrow poison)
  - heavy metals ( e.g. lead, copper, and antimony)

# 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
  - overdose

# Early Treatises of Note

- De Historia Plantarum by Theophrastus
  - Greek philosopher, successor to Aristotle
  - Described poisonous plants

# Early Treatises of Note

- 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
- “The dose makes the poison”
- 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

# 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.

# Emergence of Specialties: Occupational Toxicology

- Bernardino Ramazzini
  - De Morbis Artificum Diatriba (Diseases of Workers)
  - Outlined health hazards of irritating chemicals, metals, dusts encountered by workers
  - Standard in occupational medicine for the next 200 years
- Percival Pott
  - Studied scrotal cancer in chimney sweeps
  - Linked exposure to soot & poor personal hygiene

# Emergence of Specialties: Forensic Toxicology

- Mathieu Orfila
  - Spanish physician serving in the French court
  - Established forensic toxicology
  - Used chemical analysis and autopsy-related materials as proof of poisoning in legal proceedings
  - Developed a method for the analysis of arsenic that became the legal standard of the time
  - *Traité des Poisons* (1814) one of the most outstanding treatises in toxicology

# Unsavory Applications: Rogues Gallery

- Catherine de Medici –experimented on the poor
- Madame Giulia Toffana – ‘Agua Toffana’
- Heironyma Spara – ‘young widows club’
- Catherine Deshayes – ‘La Voisin’

# 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

# 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

# Society of Toxicology

- First professional organization for toxicologists
  - First meeting held April 15, 1962 in Atlantic City, New Jersey
  - Official journal is Toxicology and Applied Pharmacology
    - First dedicated publication for the dissemination of toxicology research