Toxicology

- Definitions
- Toxicological studies
- Dose-response correlations
- Threshold limit values
- Examples

Hazardous

- Denotes the probability of injury or illness from contact or use
- Industrial Hazards
  - Toxicity
  - Explosivity
  - Ignitability
  - Reactivity

Toxic Substance

- Capacity of a substance to produce injury or illness
- Acute Effects
  - Short term, appear shortly after exposure. Can be from single exposure
- Chronic Effects
  - There is a latency, long period of time before you see effect

Three Types of Toxic Hazardous Materials

- Chemical Agents (poisons)
- Physical Agents (dusts, fibers, heat, noise, corrosive)
- Biological Agents (pathogens)

Definitions

- Toxicology is the quantitative and qualitative study of the adverse effects of toxicants on biological organisms

- Toxicant is a chemical or physical agent that produces adverse effects on biological organisms.

So Toxicology is the study of:

- How toxicants enter the organism
- How toxicants effect the organism
- How toxicants are eliminated from (leave) the organism

All substances are toxic if taken in the wrong quantities

INTRODUCTION TO TOXICOLOGY

Definition of Toxicology

- the basic science of poisons (old)
- the study of the adverse effects of chemical agents on biological systems (new)

INTRODUCTION TO TOXICOLOGY

WHAT TOXICOLOGISTS DO

-involved in the recognition, identification, and quantitation of hazard

-develops standards and regulations to protect health and the environment

- involved in safety assessment and use of data as basis for regulatory control of hazards

- determines risk associated with use of chemicals

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RISK ASSESSMENT

- Hazard identification
- Dose Response Assessment
- Exposure Assessment
- Risk Characterization

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INTERRELATED COMPONENTS OF THE RISK ASSESSMENT

- chemical or physical agent
- biological system
- effect or response
- exposure situation

How toxicants enter organism

- Inhalation (mouth or nose to lungs) then into blood(+*)
- Ingestion (mouth to stomach) then into blood(+)
- Injection (cuts, punctures in skin) into blood
- Dermal absorption (through skin) into blood(+*)

+ Involve membrane transport

* Greatest threats in industry

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RISK AND SAFETY

-RISK; the probability that harm will occur under specified conditions

-SAFETY; the probability that harm will not occur under specified conditions

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MAJOR FACTORS THAT INFLUENCE TOXICITY

-route of administration

-duration and frequency of exposure

-dose or concentration

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RAPIDITY OF RESPONSE WITH RESPECT TO ROUTE OF EXPOSURE

-intravenous
-inhalation
-intraperitoneally
-subcutaneous
-intramuscular
-intradermal
-topical

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INTERACTION OF CHEMICALS

- Additive
- Synergistic
- Potentiation
- Antagonism (functional, chemical, dispositional, receptor)

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DOSE RESPONSE

-ASSUMPTIONS

-response is due to chemical administered

-the response is related to the dose

-there is a receptor site with which the chemical interacts

Effects of Toxicants

Irreversible Effects

- Carcinogen - causes cancer
- Mutagen - causes chromosome damage
- Reproductive hazard - damage to reproductive system
- Teratogen - causes birth defects

Effects of Toxicants

May or may not be reversible

- Dermatotoxic – affects skin
- Hemotoxic – affects blood
- Hepatotoxic – affects liver
- Nephrotoxic – affects kidneys
- Neurotoxic – affects nervous system
- Pulmonotoxic – affects lungs

Definitions

- Pharmacokinetics – the absorption, distribution, metabolism and excretion of chemicals through the (human) system.

- Bioaccumulation – things such as lead, mercury, PCBs, carbon tetrachloride that build up in organs and have low excretion rate. Low exposure over a long time leads to response

Elimination of toxins

- Excretion through kidneys, liver and lungs
- Detoxification is the biotransformation of chemicals into something less harmful
- Storage in fatty tissue

Toxicological Studies

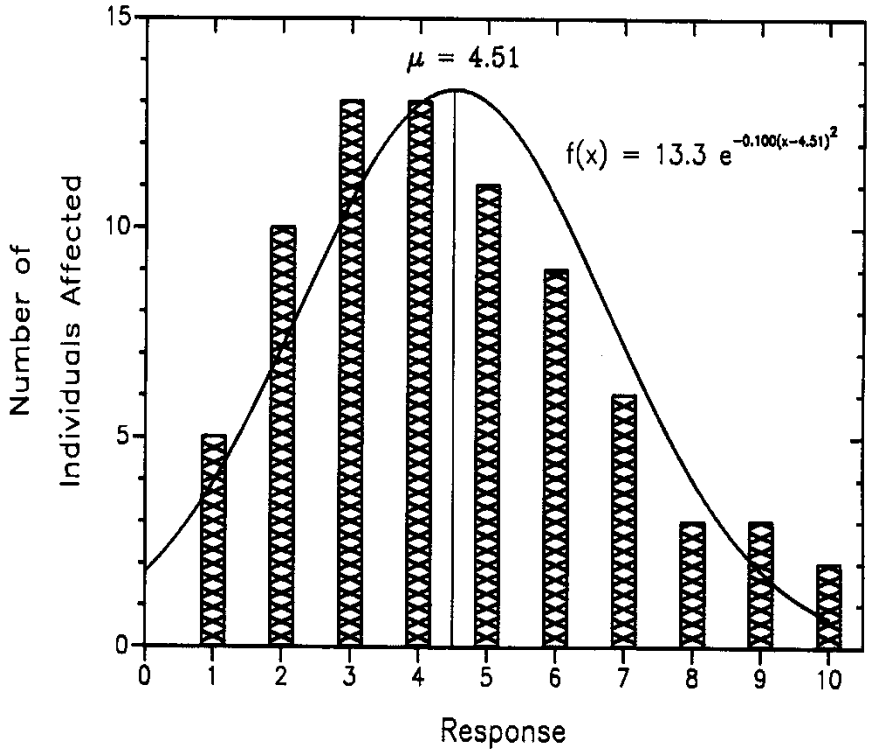
- Baseline study with no toxicant
- Toxicology study to quantify response to toxicants in specified physical state

Difficulties in Toxicological studies

- Baseline study required (control group)
- Response not necessarily numerical
- Specificity of individual response
  - Allergy or immunity
  - Statistical study required
  - Organism specific response, not applicable to humans
  - Dosage response
  - Response time, latency, acute versus chronic
  - Difficulty in measuring intended variable (lead in liver measured by lead in blood)

Dose versus Response

- Run test on “large” population
- Given same dose (usually in dose/body mass)
- Determine the number or fraction of individuals that have a response



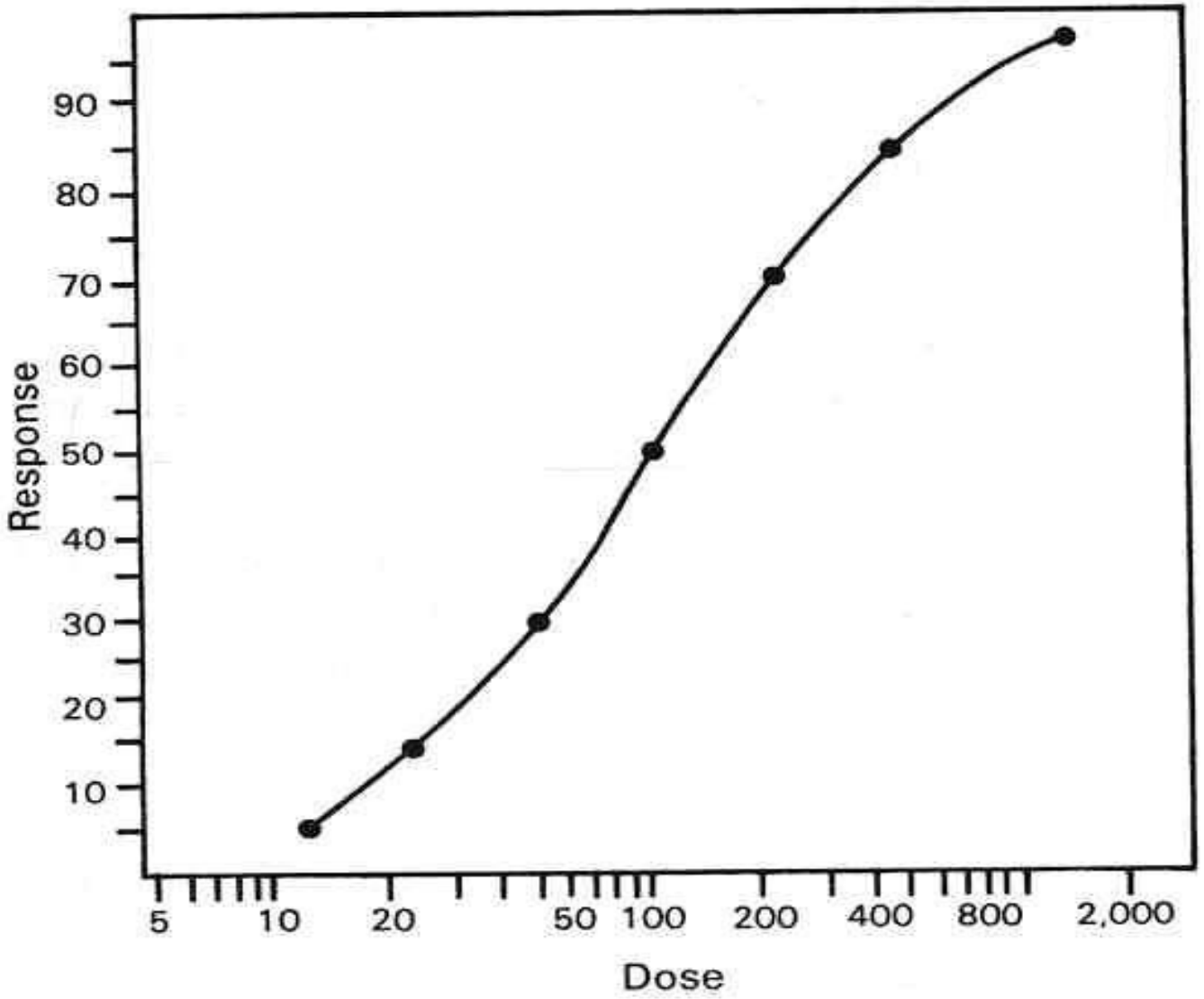


Figure 2–2. Diagram of dose-response relationship. Dosage is most often expressed as mg/kg and plotted on a log scale.

From Casarett & Doull's, Toxicology
3rd Edition, 1986

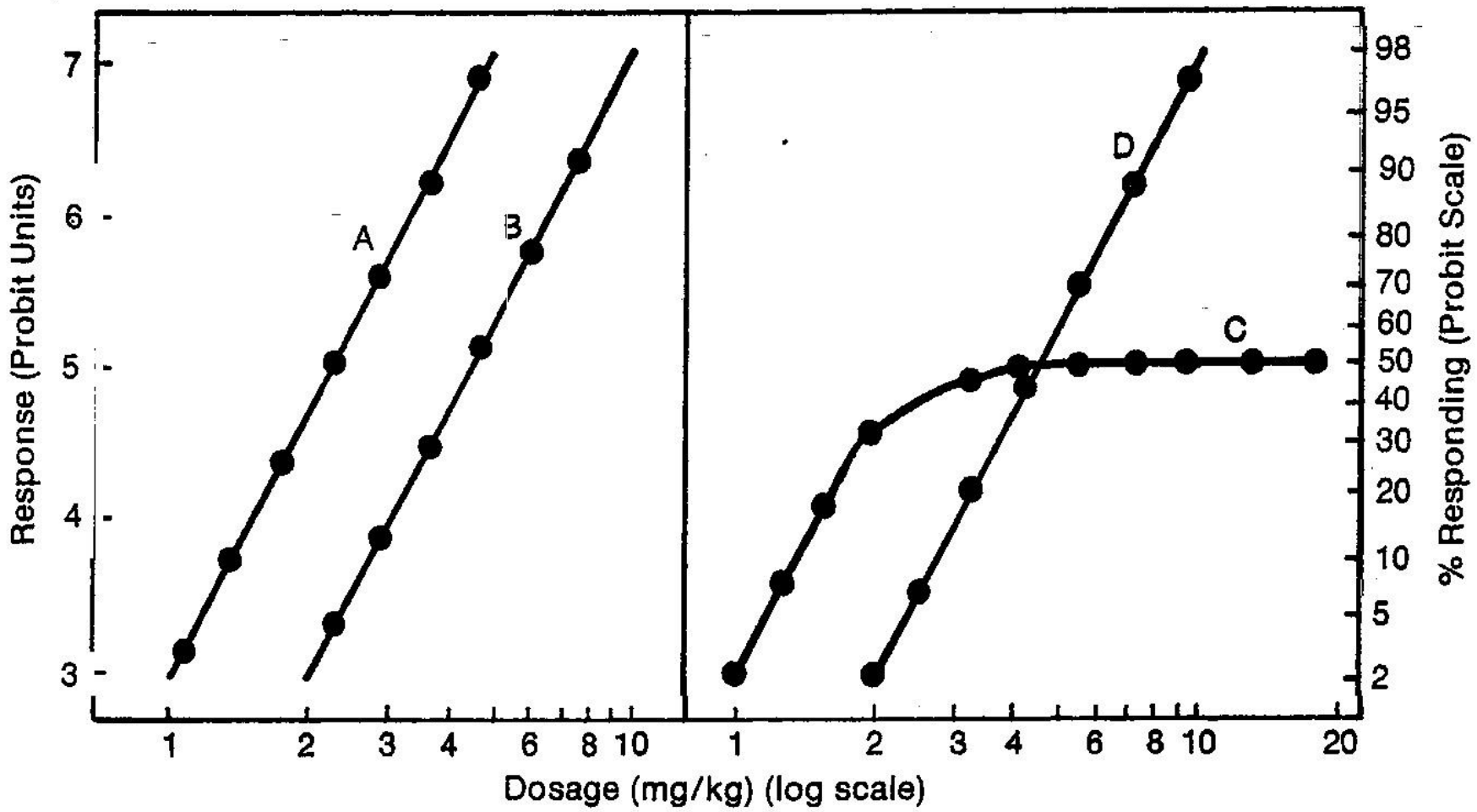


Figure 2–7. Schematic representation of the difference in the dose-response curves for four chemicals (*A–D*), to illustrate the difference between potency and efficacy (see text).

Table 2–1. APPROXIMATE ACUTE LD50'S OF SOME REPRESENTATIVE CHEMICAL AGENTS

AGENT	LD50 (mg/kg)*
Ethyl alcohol	10,000
Sodium chloride	4,000
Ferrous sulfate	1,500
Morphine sulfate	900
Phenobarbital sodium	150
Picrotoxin	5
Strychnine sulfate	2
Nicotine	1
d-Tubocurarine	0.5
Hemicholinium-3	0.2
Tetrodotoxin	0.10
Dioxin (TCDD)	0.001
Botulinum toxin	0.00001

* LD50 is the dosage (mg/kg body weight) causing death in 50 percent of the exposed animals.

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