T O X I C O L O G Y / /

Study of poisons include …

1) Identification & characterisation
2) Physical & Chemical properties
3) Biological effects
4) Fate in the body

Terminology //
Toxin: cause adverse health effects when in contact / enters body
Toxic: describes the effects of poison on biological systems
Toxicosis: describe the syndrome of adverse health effects that result from exposure to toxin

*syndrome = combined effect of symptoms

Types //

- Metals
  - ❏ Lead from Batteries or Paint

- Mycotoxins/ Bacterial Toxins
  - ❏ Perennial Ryegrass Staggers - fungal infection of ryegrass, consumption leads to neurological syndrome
  - ❏ Blue Green Algae - cyanobacteria contaminated water

- Pharmaceutical Drugs
  - ❏ Paracetamol toxicity in cats

- Insecticides
  - ❏ Rodenticides

- Toxic Plants & Animals
  - ❏ Patterson's Curse - toxic to horses
  - ❏ Brown Snake's venom

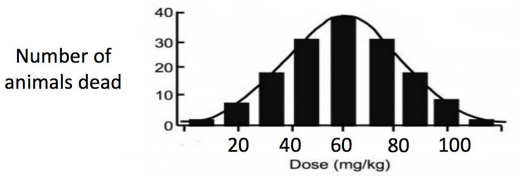
Challenges in Veterinary Toxicology //

1. Large no. of animals in herd
2. Numerous spp with different MoA & effects
3. Safe consumption of production animals in humans → Withdrawal Period
4. Malicious Poisoning

//

Dose-response relationship

Key Concept: Dose makes the Poison



No. of dead animals vs. dose.

Quantal //

→ either present or not present … dead or alive … liver failure or no liver failure

Continuous //

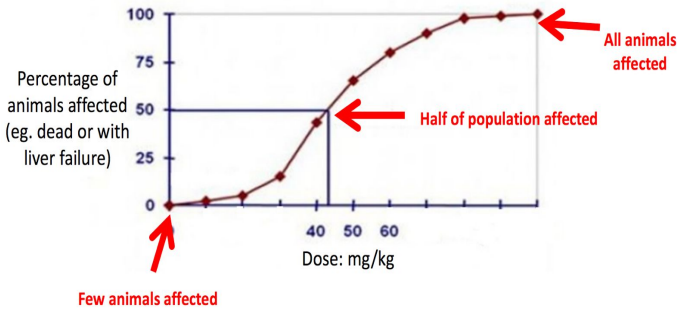
→ painkiller - mild to large to toxic relieve of pain

→ sedation - mild to strong to toxic sedation

→ <u>Normal distribution</u> *curve* above allows us to plot …

/ / DOSE-RESPONSE CURVE :

Graphical rep of distribution of responses in a **<u>POPULATION</u>** to different doses of a toxin



% of affected animals vs. dose

Dose-Response Curve measures …

- **Therapeutic Effect**

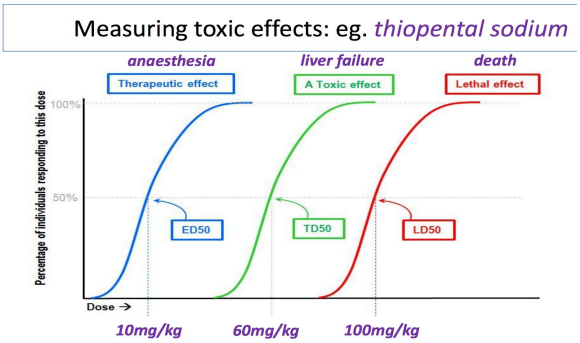
ED50 -- Effective Dose :
50% pop - therapeutic effect

- **Toxic Effect**

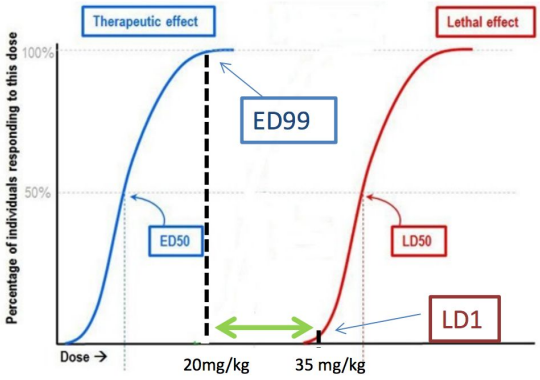
TD50 -- Toxic Dose : 50% pop - toxicity

- **Lethal Effect**

LD50 -- Lethal Dose : 50% pop - death



$$\text{Margin of safety} = \frac{LD1}{ED99}$$



Use dose-response curve to understand…
// **MARGIN OF SAFETY**
→ index of effectiveness & safety

NARROW Margin of Safety = **UNDESIRABLE!**

***LD1 = Lethal dose in 1% pop**
ED99 = Effective dose in 99% pop

//

Dose Calculation: TOTAL DOSE (mg) / WT OF ANIMAL (kg) = DOSE (mg/kg)
E.g. Cat ingests paracetamol …

1) Calculate total dose (mg) ingested
2) Divide total dose (mg) by weight of animal (kg)
3) Check value against TD50 of drug dose

T O X I C O K I N E T I C S / /

Movement and fate of toxins once they contact / enter the body.

A D M E

//

Absorption

Process where toxins gain entry to body from ext. envt by crossing cellular barrier via …

- GIT
- Respiratory
- Dermal
- (Injection) *when drug meant for therapy given at toxic dose
  - Subcutaneous
  - Intravenous
  - Intramuscular
  - Intrathecal (spinal cord)
  - Intravitreal (eye)

4 Mechanisms of Absorption …

1) Diffusion through lipid membrane
2) Diffusion through aqueous pores (formed by aquaporins)
3) Interact with solute carrier or other membrane transporter
4) Pinocytosis : CM invaginates the macromolecules into cytoplasm; not common to gain entry into cells

Routes of Absorption:

1. **Gastrointestinal Tract**
   - Mouth to Rectum
   - Factors affecting rate of absorption :
     a. pH
     b. GI motility
     c. GI Surface Area
     d. Lipid Solubility

   - Lipid soluble substances more readily absorbed than water soluble as it pass through lipid membrane

   - Barriers:
     a. Digestive enzymes in saliva, stomach, intestines
     b. Altered pH - acidity in stomach
     c. Motility of GIT - faster = reduced rate
     d. Interaction with food & other drugs in GI lumen

2. **Respiratory Tract**
    - Lungs
        - ➔ One-cell thin epithelium of alveoli → increased rate of diffusion
        - ➔ Close contact with blood capillaries → increased rate of diffusion

    - Toxic Agents
        - ➔ Gas, Vapours, Aerosols, Volatile Liquids

3. **Skin**
    - Impermeable unless there's breakage

    - Dermis layer: Blood capillaries
    - Stratum Corneum → outermost, keratinised cells … rate-limiting step for absorption

    - Passive Diffusion:
        - ➔ Through skin layers
        - ➔ Venous & Lymphatic Capillaries in Dermis
        - ➔ Systemic Circulation