

INTRODUCTION TO TOXICOLOGY & SCOPE

Toxicology:

Greek word Toxicon ----- Poisons

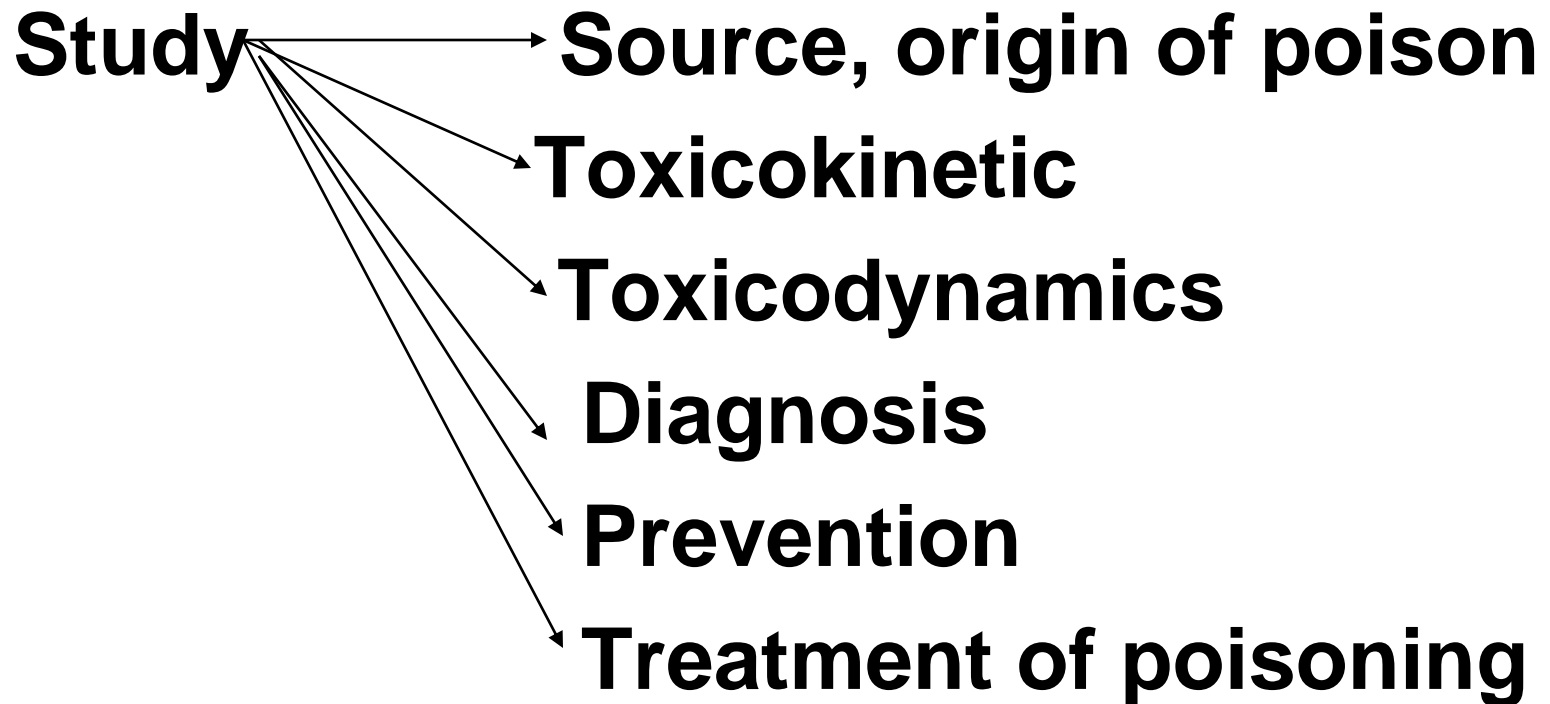
Logos ----- science

Def. Study of poisons & their harmful effects on living organism.

It refers to adverse effects of Biological, Chemical & physiological agents on living system

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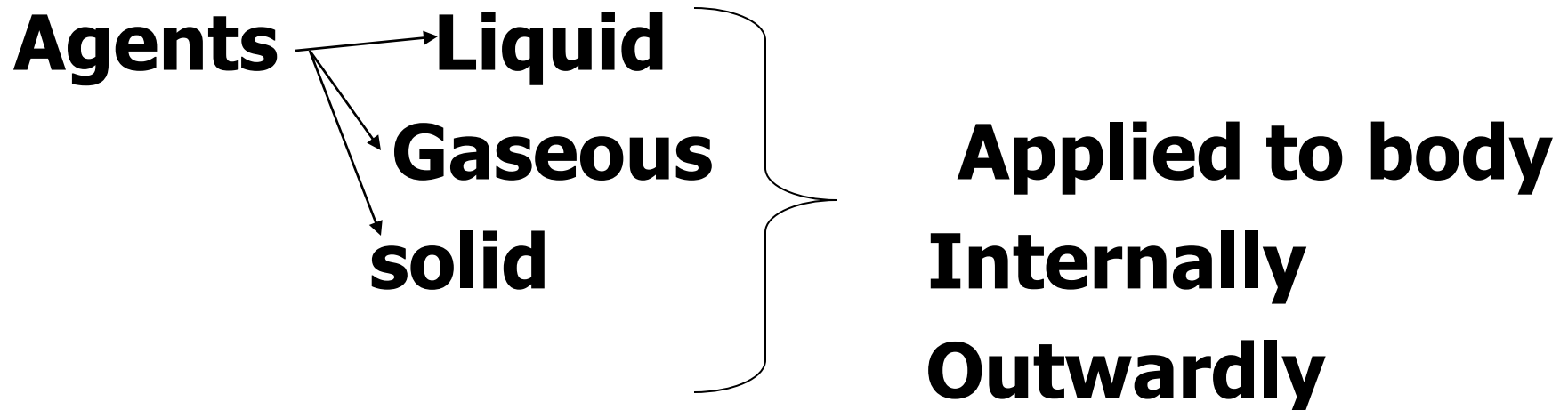
Toxicology



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Poisons/ Toxicants:

Agents capable of impairing normal physiological functions



Can destroy life without mechanically

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Xenobiotics: substances foreign to body & biologically active.

Toxicity: Inherent capacity of substance to cause adverse reaction & expressed as mg/kg

Hazard: Probability of appearance of an adverse effects due to agent depending upon its usage patterns.

Toxicity & Hazard are inversely related to each other.

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- **Justify this by taking example of DDT & Cyanide**

Oral median lethal dose in rats:

Extremely toxic

more than 1 mg/kg

High toxic

1 – 50mg/kg

Moderate toxic

50 – 500 mg/kg

slight toxic

5 – 15 mg/kg

non toxic

5 – 15 G/kg

harmless

More than 15 G/kg

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Toxicosis: It is state resulting from exposure to poisoning.

Toxins: poisonous substance liberated by living organism.

Toxins are of four types:

Phytotoxin: Plant toxins Abrin, Ricin

Mycotoxin: Fungal toxins Aflatoxin

Zootoxin: From lower animal Snake venom

Bacterial toxin: Tetanus, Botulinum

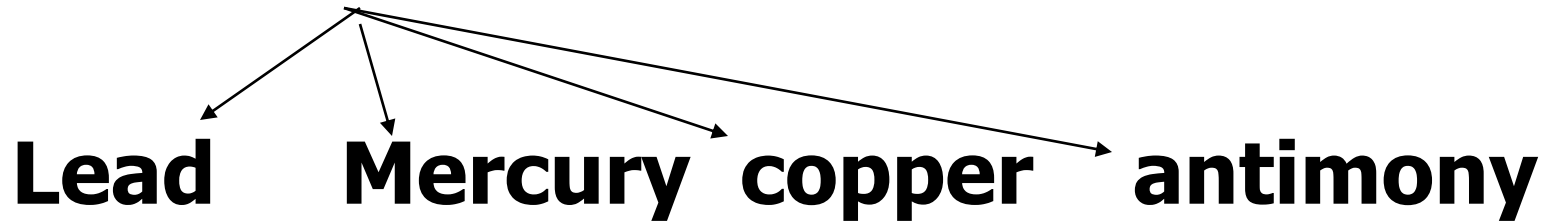
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Toxinology:

**Study of source ,nature & effects of
toxins on Man & Animal**

HISTORICAL DEVELOPEMENT

- **Earliest records of Egypt mentioned poisons of plants like Aconite & Opium**
- **Hippocratic schools of physicians recognized Metallic poisons**



& suggested emesis --- preventing absorption of oral poison

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- **Greek physician Discorides**

Classified poison into – plants, minerals & animal poisons

- **Middle age Toxic concentration, Onset of action, potency, specificity, site of action , clinical signs & symptoms of poisoning were recorded.**
- **Mosesben Maimon: poison& their antidotes**

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- **Paracelsus (1493-1541):**
Dose dependency of toxic effects
- **Geber Ibn Hajar (702-765):**
Differentiate Drug & Poison
& emphasized : drug can be become Poisons---
if given at high doses.
- **Spanish scientist– MJB Orfila(1787-1853)**
(**Mattie Josesph Benaventura Orfila**)
Develop method for detection of poisons
& Foundation of Forensic toxicology
Recognized as ***Father of Toxicology***

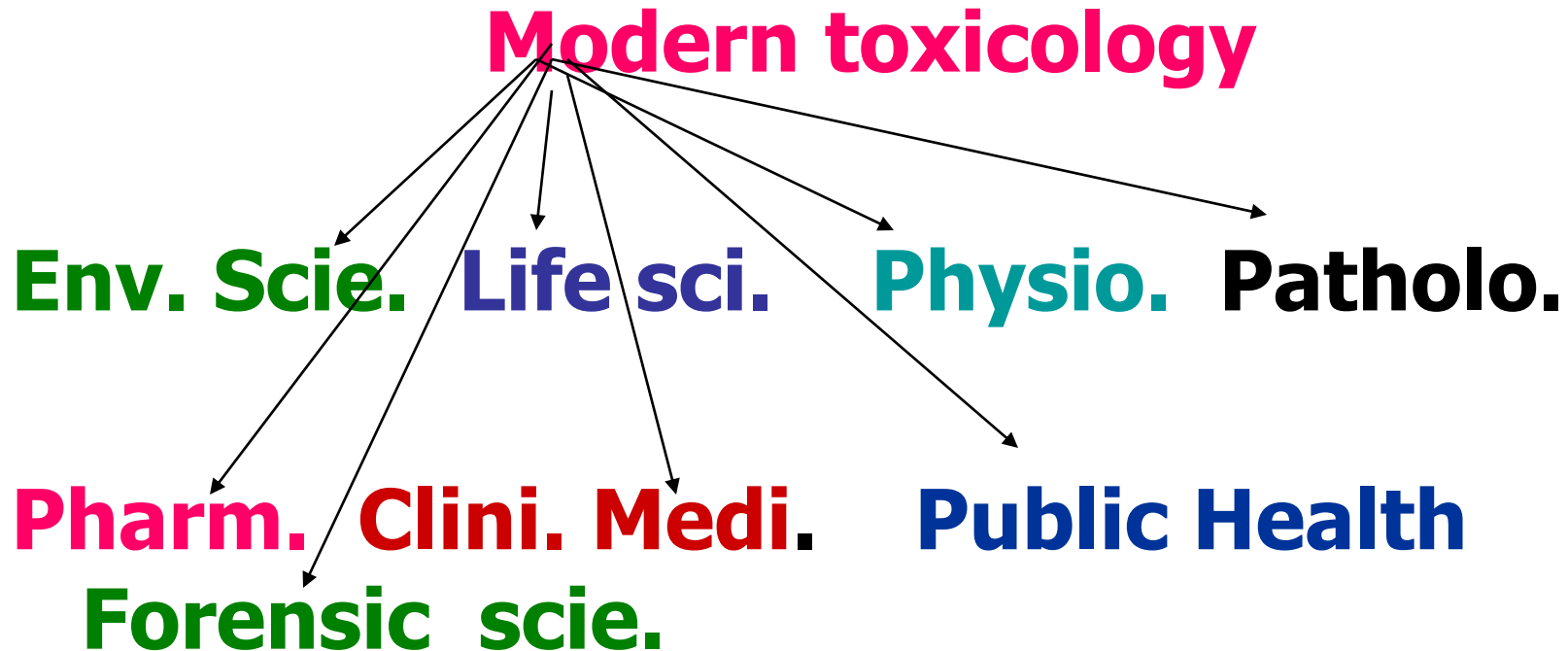
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- **Magendie discovers: Mechanism of action of emetic, strechine, arrow poisons**
- **Claude Bernard discovered: Curare & carbon monoxide**
- **Goal of study of toxicology:**
 - **Survival of humans , animal & ecosystem**
 - ***Application of discipline of toxicology in safety evaluation & risk assessment is of utmost importance in modern life***

SCOPE OF TOXICOLOGY

- Deals with study of toxicants on living organisms also deals with harmful effects of Chemicals, physical & biological agents on ecosystem.

Modern toxicology



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Role of Vety. Toxicologist:

- Direct Role: study of adverse effect of drug on different spp. of animal**
- Indirect role: Advancement of sciences mentioned above**
- He has to deal with different spp.**
- Animals are indiscriminate eaters of food & non food material**
- so scope of Vety. Toxicology is vast than human toxicology.**

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- **Indiscriminate industrialization**
- **Plant protection methods**
- **Risk of environmental pollution & toxicity in animals.**
- **Malicious poisoning**
- **Vety. Toxicologist has task in welfare of animals ,birds, through Prompt diagnosis, Rx & prevention of toxicities in animals.**

DEFINATIONS

- **Environmental toxicology:**
study of source & effect of pollutants
like
Food additives, preservatives &
pesticides residues

On living system in environment

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- **Occupational toxicology:**
Study of adverse effects of exposure to harmful chemicals due to occupation
e.g. industrial toxicology or exposure of farm animals to pesticides during agriculture operations.
- **Genetic toxicology: adverse effects of toxicants in alteration of genetic make up.**
- **Wild life toxicology: Effects of pollutants on wild animals & Birds.**

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- **Forensic toxicology: Deals with Medico-legal & Vetro -legal aspects of poisoning to arrive at accurate diagnosis & actual cause of death.**
- **Reproductive toxicology: Effects on male & female reproductive system.**
- **Developmental toxicology(Teratology) : Effects on developing fetus**
- **Toxicokinetic & Toxicodynamics**

SOURCE & CLASSIFICATION OF POISONING

SOURCES

Natural

Toxic plants

Toxic mineral

Toxic animals

Cosmic radiation

Man made

Mallacious poison

Accidental poison

**Environmental
pollutants**

Occupational

CLASSIFICATION OF POISONS

A. Based on Source & Origin:

1. **Natural occurring** : Toxic plants, minerals

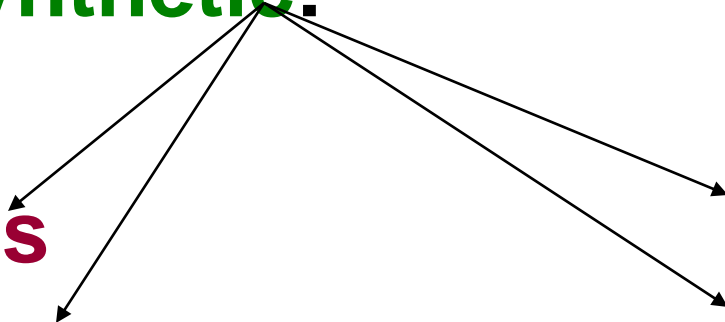
2. **Synthetic:**

Pesticides

Industrial waste

Dangerous drug

Food additives



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B. Based on effects on animal body:

a. Poisons causing respiratory insufficiency :

- 1. By inactivating haemoglobin: Nitrate**
- 2. By interfering with cellular utilization of oxygen : HCN**
- 3. By preventing erythropoiesis: Radioactive agents**

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4. By Causing lysis of erythrocytes:

Haemotoxic venoms

5. By causing Hemorrhages: Warfarin

Sweet clover

6. By interfering with oxygen exchange in pulmonary alveoli: ANTU

b. Poisons causing derangement of nervous system:

1. Depressant: Barbiturate & chloral hydrate

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2. Stimulants: Cocaine, Organochlorine insecticide

**3. By damaging brain & spinal cord:
Salt & organomercurials**

**4. By stimulants / depression:
Anti chE agents**

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c. Poisons causing visceral organs dysfunction:

1. Colic: Acids & Alkalis

2. Hepatic disease: aflatoxins

3. Renal dysfunction: Oxalates, Leads

4. Gastroenteritis: Mercury

5. Cardio toxicity: Digitalis, Oleander

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d. Poisons causing Lameness:

1. Abnormalities in long bones:

Fluorine, Copper, Selenium

**2. Painful tension on feet: Fluorine,
Ergot**

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C. Basing on Chemical nature:

1. Inorganic toxicants:

Metals : lead

Non metals: Nitrates

Acids: HCL, H2SO4

Alkalies: KOH

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2. Organic toxicants:

Hydrocarbons

e.g. **Benzene**

Alkaloids

e.g. **Strychnine**

Halogens

BHC, DDT

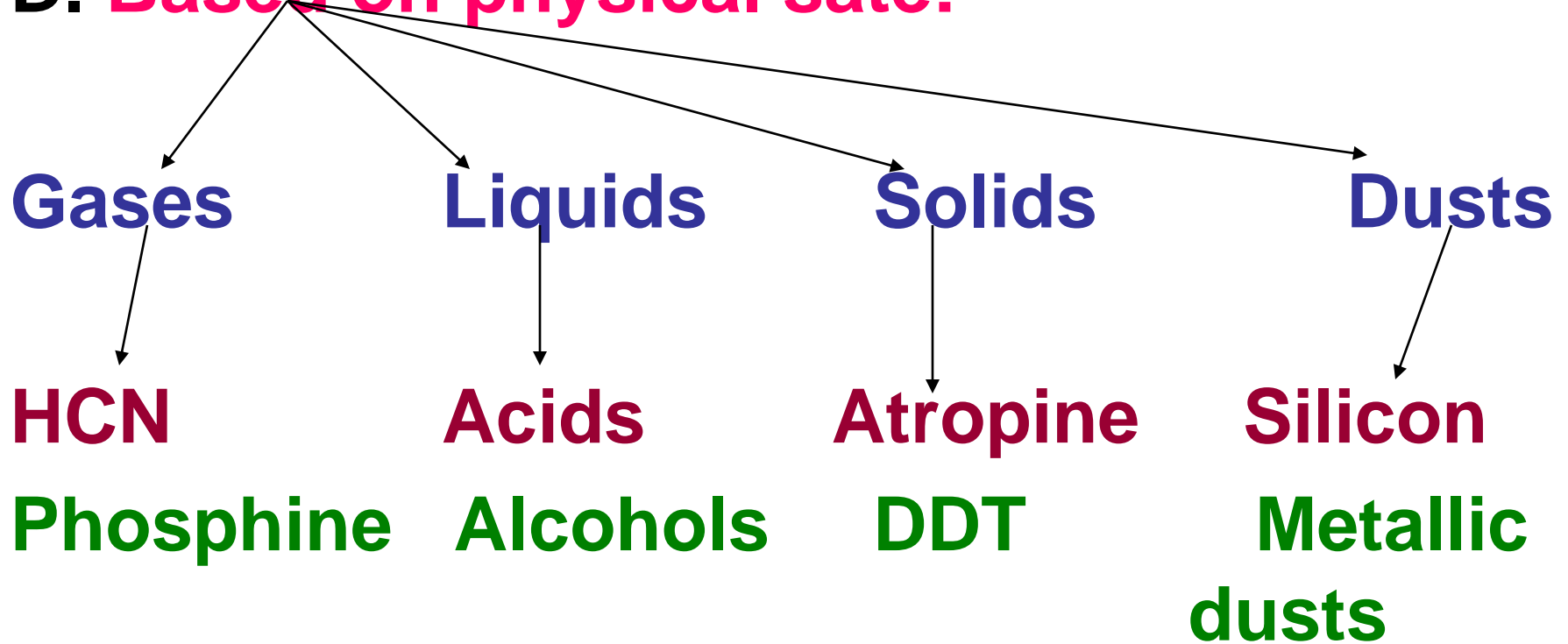
Proteins

Abrin

**Alcohols &
phenols**

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D. Based on physical state:



TOXICODYNAMIC

Two types

A. Specific action

B. Non specific

Receptor mediated

Enzyme related

Agonist

Antagonist

Carbamates,

Organophosphate

On neurotransmitter receptor

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NON SPECIFIC ACTION:

- 1. Physical toxicants:** Deposites in tissue /organs ---- Silicon, Asbestos, Lead
- 2. Direct chemical injury:** Corrosive & caustic --- Acids & Phenols, alcohols
- 3. Necrosis of epithelial cells :** Oxalates

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4. Interfering with metabolism:

i. **Inhibition of oxidative phosphorylation:**
Dinitrophenols, Chlorophenols

ii. **Inhibition of nucleic acid / protein synthesis:**
Aflatoxins

iii. **Interfering with Fat metabolism:**
Calcium Chloride

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5. Injury to blood & Vascular system:

Anti. Vit. K – warfarine, sweet clover

6. Interfering with function of ion channels: DDT, Pyrethroids

7. Formation of secondary toxic metabolites:

Ammonia from Urea

Fluroacetate from Flurocitrate

8. Immunodeficiency: Mycotoxins

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9. Teratogenicity: Quinine, Thalidomide

10. Carcinogenicity: DDT

11. Deficiency of nutrients:

Hypocalcaemia by oxalate poisoning

12. Deposition in tissues:

Fluoride: in teeth

Lead: Bones

Oxalates: Renal tubules

TOXICOKINETICS

- **It is similar to Pharmacokinetic of drug**
- **Absorption:**
 - **Simple diffusion**
 - **Filtration**
 - **Facilitated diffusion**
 - **Active transport**
 - **pinocytosis**

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- **Routes of entry of xenobiotics into body:**
 - **Percutaneous**
 - **Respiratory tract/ lung**
 - **Oral**
- **Distribution:**
 - **protein binding**
 - **BBB**
 - **Placental barrier**
 - **Redistribution**
- **Elimination:**

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- **Metabolism of Xenobiotics:**
 - **Detoxification:** Conversion toxic substance into inactive agents
eg. DDT ---- DDA
 - **Lethal synthesis:** Non toxic agent --- toxic agent eg. Malathion---- Malaxon
 - **Conversion of toxic compound into another toxic agent**
eg. Aflatoxin B1 ---- Aflatoxin M1
Hepatotoxic ---- Carcinogenic

TYPES OF TOXICITY

A. Acute Toxicity:

- **Single exposure to high dose**
- **Immediate toxic symptoms**
- **Sudden death. No hematological & biochemical or pathological changes**
- **To find out LD50 of drug**

B. Sub acute toxicity:

- **Repeated exposure to low dose upto 90 days**
- **Toxicity develops slowly**
- **Animal shows reduced feed intake, retarded growth & Hematobiochemical & pathological changes**

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- **C. Chronic toxicity:**
 - Long period exposure to very low dose up to 6 month
 - Shows symptoms like reduced growth , feed intake & specific hematological & biochemical changes
- **D. Cumulative:**
 - develops from agents which accumulate into body tissues /organs

Shows chronic /subacute toxicity

FACTORS AFFECTING TOXICITY

- **Similar to factors modifying drug response:**

A. Factors related to toxicants:

1. Nature of compound:

- **Lipid solubility: High---** highly toxic
- **Degree of ionization: Rapidly ionized -**
--- less toxic
- **polar: Non polar ---** highly toxic

- **Molecular wt.:** less mole. Wt.--- high toxic
- **Physical nature:** solid, liquid, fine powder, gases, dermal application
- **Chemical nature:** Trivalent arsenic-----
----- highly toxic ----- than polyvalent arsenicals.

2. **Dose of compound:** directly related to dose

3. **Source of compound:** widely grown—
highly toxic ---- cultivated, Seed & root
of toxic plants ---- more toxic than

B. Factors related to nature of exposure:

1. Frequency of exposure:

less toxic compound --- toxic on long exposure

2. Simultaneous exposure:

**exposure of more agents at a time ----
--- Potentiate, antagonist, each other**

Cu & Mb --- natural antagonist

3. Route of exposure: More toxic by inhalation than oral & dermal route

C. Factors related to the animal:

1. Species:

- **Atropine----- toxic to all spp except rabbit due to presences of atropinase enzyme**
- **Red squil : toxic to Rats but non toxic to dog & cat.**
- **Strychnine toxicity: Amphibian, poultry, Dog**
- **Monogastric are less susceptible to HCN**

2. Individual variation:

- **some are less susceptible**
- **some more susceptible due to biological variation**

3. Sex:

- **Male --- resistant than female ----
testosterone**

4. Age:

- **young & old ---- more susceptible**

5. Health status:

- **Hepatic / renal insufficiency----- more toxicity due to less detoxification**
- **Constipation----- increases toxicity**
- **Diarrhoea_ -- decreases toxicity**

6. Metabolism: generally detoxification

7. Size & weight:

- **Large size--- more dose of toxic agent**
- **Fatty animal----- tolerate fat soluble toxicity**
- **Ruminants --- more dose**

8. Nutritional status:

- **starved animal: more susceptible**
- **Malnourished animal :**

9. Genetic status:

- **through breed animals – resistant**
- **animal deficient to glucose 6 phosphate dehydrogenase --- more susceptible to hemolytic effect of Sulfonamide , Aspirin**


D. Factors related to Environment:

- **Temperature**
- **Relative humidity**
- **Light**
- **Environmental pollution**

Temperature:

- **Low Temp. Increase in metabolism of Xenobiotics**
- **Dermal toxicity of insecticides increase in hot weather because increase in blood supply to skin to keep body cool increases absorption of toxic agents.**

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- **Relative humidity: Dermal absorption of organophosphate insecticide is rapid in hot humid weather.**
- **Atmospheric pressure & Altitude: Toxicity of HCN, Barbiturate  in high altitude due to low oxygen tension**
- **Light: Photosensitization reaction is more in sun light.**
- **Eye toxicity of Atropine is more animals exposed to sun light**

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- **Environmental pollution:
alters metabolism of xenobiotics due to
inhibition of metabolic enzymes**

General Principles of Diagnosis & Treatment of Toxicity

- **Diagnosis of poisoning in animal three types**
 - A. Tentative :** Based on History & Clinical examination of affected animal
 - B. Presumptive:** Based on correct history, Specific clinical signs, pathological observations
 - C. Confirmative:** By qualitative & quantitative estimation of toxicants in feed, water & Ruminant contents

LINE OF TREATMENT OF TOXICITY

A. General Procedure:

- **Shifting of animals to fresh feed & water**
- **Removal of unabsorbed toxicant from body:**
 - Washing of skin**

By emesis

Purgation in oral poisoning

Rumenotomy in ruminants

Replacement of fresh ruminal contents

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- Relief from respiratory insufficiency
- Shifting of animal at quite place

B. General antidotal therapy:

- Nature of toxicant is unknown
- No specific antidote
- Use Universal antidote

2 Parts of activated Charcoal (absorb
poison)

1 Part Kaolin (Absorb poison)

1 part of tannic acid (Precipitate alkaloid)

1 part Magnesium oxide (Purgation)

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- **Dose: Small animals@ 5-50gm**
Large animals@ 250-500 gm
- **Neutralization of acid poisons by dilute alkalis**
- **Mild acids like 5% acetic acid & Vinegar neutralizes alkali poisons**

C. Specific antidotal therapy:

- **If cause of poisoning is known**
- **Atropine in OP & Carbamate insecticides**
- **ChE reactivators like 2-PAM in OP insecticide poisoning**
- **Sodium thiosulfate & Nitrite in HCN**
- **Vita. K in Warfarin poisoning**

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D. Symptomatic treatment:

- **Sedative in nervous excitability**
- **Analeptics in respiratory depressant**
- **Intestinal astringent in diarrhea**
- **Analgesic to relive pain**
- **Cardiac stimulants in heart failure**

E. Supportive Therapy:

- **Fluid & Electrolytes therapy**
- **Liver tonics & Corticosteroids**
- **Haematonics, Digestive stimulants**
- **Broad spectrum antibiotics**